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Conclusion should elucidate how the results communicate to the theory presented as the basis of the study and provide a concise explanation of the allegation of the findings.

ACKNOWLEDGEMENT

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Understanding Non-Hodgkin Lymphoma – A Growing Challenge in Cancer Care

OPEN ACCESS

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Non-Hodgkin lymphoma is a type of blood cancer that originates in the lymphatic system a system very crucial for immune function. Unlike Hodgkin's Lymphoma, NHL is a group of cancers progressing at different rates, ranging from slow to fast.

It originates in the lymphatic system making the diagnosis and treatment of this cancer particularly challenging, as each subtype requires a different approach. There rate of NHL has been increasing in recent years, and while the exact cause of this increasing number is still not clear there are factors that are contributing such as environmental influences, lifestyle changes, and an aging population. NHL affects people of all ages, but it is most commonly diagnosed in individuals ages 60 or older.

One of the major issues in managing NHL is the symptoms that seem subtle, and are often mistaken for less serious conditions. Swollen lymph nodes, fever, night sweats, and unexplained weight loss are common signs of NHL but they can be attributed to other illnesses. As a result NHL is often diagnosed late which delays treatment and reduces the chances of successful outcomes.

Recent advances in the treatment of NHL are promising. For fast-growing or the aggressive type chemotherapy remains the standard treatment, but some new therapies are making successful strides. Some therapies only focus on the cancerous cells and there is little damage done to the healthy tissues unlike chemotherapy which has proves to be more effective and less toxic Patients with refractory or relapsed NHL can be treated with immunotherapy which is the use of monoclonal antibodies and CAR T- cell therapy, strengthening the immune system to fight cancer more efficiently.

The progress in the treatment of NHL is encouraging however early detection of it could be beneficial. There is imperative need for increased awareness of NHL symptoms. Research into the molecular and genetic underpinnings of NHL is also crucial for developing more precise treatments tailored to individual patients.

A holistic approach is essential that addressing not just the physical needs but also the emotional needs of the patients. As healthcare providers, such as the oncologists, hematologists and pathologists collaborate their combined efforts can help improve survival rates as well as the quality of life.

In conclusion, while the challenges of Non-Hodgkin lymphoma remain, advances in treatment, early detection, and patient care bring renewed optimism for those battling the disease.

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Original Article

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Gender based Correlation between Hand measurement and Height in Medical Students of Shaheed Mohtarma Benazir Bhutto Medical University, Larkana, Sindh

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ABSTRACT

Anthropometry was an organized measurement procedure used in physical anthropology. Hand dimensions can represent an individual's identity. Stature, a complex of linear dimensions, correlates with various body parts. **Objective:** To explore the gender-wise correlation between hand measurement and stature across a diverse population for estimating the stature of MBBS Medical Students of Shaheed Mohtarma Benazir Bhutto Medical University, Larkana, Sindh. **Methods:** It was descriptive cross- sectional study and its sample size was calculated by using Open-epi online calculator. Non convenience sampling method adopted while collecting the data. Research invitations were extended to MBBS students of SMBBMU to participate in a research project and only 354 voluntarily agreed to participate out of which 169 (47.7%) males and 185 (52.3%) females fulfilled the inclusion criteria and written informed consent were taken before proceeding of data collection. **Results:** For both males and females, hand breadth measurements were strongly correlated with each other. The height of hands was also strongly correlated between left and right hands, particularly in males. Those who were involving age or overall height, were generally weaker and not always statistically significant. Males show more significant and stronger correlations between hand measurements and other variables compared to females, who have some significant but generally weaker correlations. **Conclusion:** The findings underscore that taller individuals generally possess larger hand dimensions, and marked differences exist in hand measurements between males and females.

INTRODUCTION

Allah subhanutaallah said in Quran in surat teen, we have indeed created man in the best of moulds" and in another surah (al-Sajdah 32:7). Man creation from clay commenced by Allah Subhanutallah and He Who created all the things perfect way. Beautiful creation of human beings and anthropometric measurements research is essential to focus on comprehensive biological variations according to human variations in different populations. Its essential knowledge about genetic makeup, nutritional habits, and growth trends can be achieved through information and measurement of the human body with the help of anthropometry [1]. Allah Subhanutaallah created every human as unique, and their identity is essential for recognizing the important task in forensic sciences; one of the common and authenticated tools in identification is the biometric and facial recognition techniques in which

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fingerprinting techniques are surest method of identification along with DNA techniques for their rapid and secure authenticated identification of a person. It further included prime importance at the crime scenes with their physiological parameters and auxiliary aids in palatal rugae pattern, lip printing, bite marks, and different dermatoglyphics patterns, which are also paramount for individualizing human identification [2-4]. Anthropometry, an organized measurement procedure used in physical anthropology, is a scientific approach for assessing the size of live bodies and skeletal remains. Stature, age, race, and sex are important anthropological factors in forensic medicine and contemporary science [5]. Stature estimation is vital in forensic examinations, particularly for unidentified remains that are decayed or fragmented or mutilated remains.it also plays a role in establishing personal and physical identity and could be affected by genetically makeup, puberty onset, nutritional factors along with its activity levels [6, 7]. In cases of natural calamity, terrorist activities, road or railway accidents and in war times role of identification have a paramount importance in this field of forensic medicine so pertinent to create various methods which can helps to estimate accurately identification. Forensic pathologists' experts must evaluate both identity and height of the subject which is also pertinent for examination of archeological skeletal remains. Furthermore, accurate weight and height measurements play a key role in assessing setting in educational settings along with patients' health and nutritional status [5-12]. Forensic science places great importance on estimating stature for personal identification [7, 10]. Every part of the human body is interconnected, foot and hand dimensions can represent an individual's identity [10]. Stature or height of the individual depended on various complex or variety of linear dimensions which helps to correlates with various different body parts. Previous research has highlighted relationships between stature and features like the face, head, feet, hands, lower limbs, and vertebral column. Mathematical and anatomical methods are used to establish stature standards. Height prediction can be identified with different methodical algorithms including topor LS, bayleyPinneau, roche-wainer –thissen and khamis roche methods [13, 14]. For Constructive personal identification forensic sciences prioritized the stature with age and sex. Considering the vertebral column, skull, pelvis, and lower extremities, it's evident that a significant relationship exists between stature and all body parts [11, 12]. Across a range of demographics, researchers have continuously discovered a relationship between height and hand measurements. It has been noted that there are global variations in the correlation between hand length and height among various ethnic groups [12, 15, 16]. Despite the fact that several research has been done, there is a dearth of them in the Larkana region.

This study aimed to determine the gender based anthropometric relationship between stature and hand measurement in medical students of MBBS.

METHODS

The study originated on 19 December 2022, when SMBBU granted the permission through institutional review board letter no. SMBBU/ORIC-33. Study data collected during the month of January-March, 2023. It was a descriptive cross-sectional study, and sample size was calculated by using a sample size online calculator. Data were collected through the non-convenience sampling method. This sample size ensures that the study results were reliable and that the true population value will lie within a 95% confidence interval with a margin of error of ±5%. By using the population proportion of 36% the calculated sample size ensures robust statistical power. If a proportion was unknown, using p value =0.5 would give the most conservative estimate, resulting in a larger sample size. However, since p-value > 0.05 was already specified, the sample size was smaller but still statistically valid. For quantitative parameters, normality of data was assessed through Shapiro Wilk test and based on the results parametric or non-parametric tests were applied. Research invitations were extended to MBBS students of SMBBMU to participate in a research project and only 354 voluntarily agreed to participate out of which 169 (47.7%) males and 185(52.3%) females fulfilled the inclusion criteria, and written informed consent was taken before proceeding with data collection. Inclusion criteria include male or female participants of any age who gave their permission, had no history of hand bone fractures, and no congenital hand malformations. And those participants who had a history of hand bone fractures with any congenital hand deformities or who did not consent to participate were excluded from the study. Participants were informed about the study protocols, and personal identifiers were removed before data collection. Data were entered in a pre-designed written proforma, which included the socio-demographic information along with the different anthropometric measurements of participants, including height, hand size in different dimensions, etc. For the measurement of stature, every participant was asked to stand in the anatomical position with bare feet while their height was measured using a stadiometer. Whereas, hand lengths were measured in centimeters(cm) from the transverse crease of the wrist to the distal end of the middle finger, representing the longest length of the hand. For measurement of hand length, Vernier calipers were used. The collected data was entered and analyzed using SPSS version 27.0. General descriptive test mean, standard deviation, and standard error mean

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were calculated, and an independent sample t test and correlation analysis were carried out.

RESULTS

A total of 354 MBBS students participated in this study, in which 169 (47.7%) males and 185 (52.3%) females participated. Table 1 demonstrated the larger mean values in males as compared to females. The mean values of right hand breadth in males highlighted the 9.254 ± 1.361 cm and left hand breadths 9.253 ±1.371 cm and in females mean values 8.525 ± 0.606 cm in right hand breadths and 8.502 ± 0.5859 cm observed in left hand breadths. Females exhibited smaller standard errors (right: 0.04; left: 0.04) as compared to males (right: 0.10; left: 0.11), indicating greater consistency. Height of right hand males was 19.575 ± 1.074 cm and Left hand height 19.651 ±1.084 cm, while females had a mean of right hand 17.76 ± 1.25 cm, and a mean of left hand 17.849 ± 1.02 cm. The mean values for female age 21.29 ± 2.691 and males showed 22.28 ± 6.503 years. The Standard error among the genders was lower in females 0.198 in comparison with male group 0.50, which demarcated the additional variability in males.

Table 1: Gender based Variation of Hand Measurements

Variables	Gender	N	Mean ± SD	Standard Error Mean	p-value
Right Hand Breadth	Male	169	9.254 ± 1.361	0.105	<0.0001
	Female	185	8.525 ± 0.606	0.045	< 0.0001
Left Hand Breadth	Male	169	9.253 ± 1.371	0.106	<0.0001
	Female	185	8.502 ± 0.586	0.043	< 0.0001
Height of Right Hand	Male	169	19.575 ± 1.074	0.083	<0.0001
	Female	185	17.765 ± 1.250	0.092	< 0.0001
Height of Left Hand	Male	169	19.651 ± 1.085	0.083	< 0.0001
	Female	185	17.849 ± 1.024	0.075	< 0.0001
Age	Male	169	22.28 ± 6.503	0.500	<0.068
	Female	185	21.29 ± 2.691	0.198	<0.068

Table 2 of independent t-test demarcated amongst groups of male and female for comparing of hand dimensions and age variation, independent sample t-test was applied with 95% confidence interval and p-Value $p < 0.001$ was considered as significant. It was demarcated that a significant difference in right hand breadth between the groups, $t(227.50) = 6.405$, $p < 0.001$, with a mean difference of 0.729 with 95% CI (0.505, 0.953) which suggested that one group had significantly wider right hands than the other left hand breadth, $t(223.07) = 6.598$, $p < 0.001$, with a mean difference of 0.751 with 95% CI (0.527, 0.976). This indicated a statistically significant greater breadth in one group's left hands compared to the other. The t-test showed a significant difference in the height of the right hand between the groups, $t(352) = 14.535$, $p < 0.001$, with a mean difference of 1.8097 units (95% CI: 1.565, 2.055). This demonstrated a significant variation in right hand height between the two groups height of left hand the t-test showed a significant difference in left hand height, $t(352) = 16.080$, $p < 0.001$, with a mean difference of 1.802 units, 95% CI (1.5819, 2.0227). This indicated a statistically significant difference in left hand height between the groups.

Table 2: Independent Samples Test

Variables		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Signifiant	T	df	Significant (2-tailed)	Mean Difference	Standard Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
Right Hand Breadth	Equal variances assumed	4.210	0.041	6.602	352	0.000	0.729	0.110	0.511	0.946
	Equal variances not assumed	-	-	6.405	227.499	0.000	0.729	0.114	0.505	0.953
Left Hand Breadth	Equal variances assumed	6.665	0.010	6.808	352	0.000	0.751	0.110	0.535	0.946
	Equal variances not assumed	-	-	6.598	223.065	0.000	0.751	0.114	0.527	0.976
Height of Right Hand	Equal variances assumed	0.043	0.836	14.535	352	0.000	1.809	0.125	1.5649	2.0546
	Equal variances not assumed	-	-	14.635	350.703	0.000	1.810	0.124	1.5665	2.0530
Height of Left Hand	Equal variances assumed	2.276	0.132	16.080	352	0.000	1.802	0.112	1.5819	2.0227
	Equal variances not assumed	-	-	16.038	344.445	0.000	1.802	0.112	1.5813	2.0233
Age	Equal variances assumed	1.076	0.300	1.893	352	0.059	0.986	0.521	-0.038	2.011
	Equal variances not assumed	-	-	1.833	219.758	0.068	0.986	0.538	-0.074	2.046

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Table 3 of correlation highlighted correlation among gender with hand dimensions and hand dimensions and with age. Male and female correlations with hand dimensions highlighted significant negative Pearson's correlation like in right hand breadth -0.332, -0.332, -0.332 and in left hand breadth -0.341 -0.341 -0.341, both were significant at p <0.001.strong positive correlations of right and left hand breadths (r = 0.956, r = 0.956, r= 0.956, p<0.001p < 0.001p<0.001) and between the correlation of heights of both hands (r=0.821r = 0.821r=0.821, p<0.001p < 0.001p<0.001) suggestive of there were closely related with each other. Weak correlations of age were observed with the hand dimensions and significant correlations with height of the hand (r=0.167r = 0.167r=0.167 and r=0.162r = 0.162r=0.162, both p=0.002p = 0.002p=0.002).

Table 3: Correlations of Gender with Hand Dimensions

Variables		Gender	Right Hand Breadth	Left Hand Breadth	Height of Right Hand	Height of Left Hand	Age
Gender	Pearson Correlation	1	-0.332**	-0.341**	-0.612**	-0.651**	-0. 100
	Significant (2-Tailed)	-	0.000	0.000	0.000	0.000	0. 059
	N	354	354	354	354	354	354
Right Hand Breadth	Pearson Correlation	-0.332**	1	0.956**	0.402**	0.454**	0. 043
	Significant (2-Tailed)	0.000	-	0.000	0.000	0.000	0.418
	N	354	354	354	354	354	354
Left Hand Breadth	Pearson Correlation	-0.341**	0.956**	1	0.390**	0.443**	0.0 46
	Significant (2-Tailed)	0.000	-	0.000	0.000	0.000	0.389
	N	354	354	354	354	354	354
Height of Right Hand	Pearson Correlation	-0.612**	0.402**	0.390**	1	0.821**	0.1 67**
	Significant (2-Tailed)	0.000	-	0.000	0.000	0.000	0.0 02
	N	354	354	354	354	354	354
Height of Left Hand	Pearson Correlation	-0.651**	0.454**	0.443**	0.821**	1	0.1 62**
	Significant (2-Tailed)	0.000	-	0.000	0.000	0.000	0.0 02
	N	354	354	354	354	354	354
Age	Pearson Correlation	-0.100	0.043	0.046	0.167**	0.162**	1
	Significant (2-Tailed)	0.059	0.418	0.389	0.002	0.002	-
	N	354	354	354	354	354	354
**Correlation is Significant at the 0.01 Level (2-Tailed)							

DISCUSSION

The pivotal role of identification in anthropometric studies highlighting the different body aspects for importantly crucial practical applications especially in normal physiological and forensic sciences. Revolutionary aspects of Identification through different gadgets in detecting identity and helping in identification from skeletal remains. Ergonomic and industrial designs may also benefit to relative size dimensions which helps to create various tools and gloves and multiple products to fit comfortably and with better functionality [11, 12, 14]. For improving patient care in medicine it can be useful for diagnosing certain conditions and ensuring custom fit prosthetic and apparel [15]. It also contributes in sports science, anthropological studies and various educational efforts enhancing the designs of personalized products [16]. This study demonstrated correlation of hand breadth with anthropometric measurements which revealed very realistic outcomes for males and female's participants. Strong positive correlation amongst the right hand breadth and left hand breadth in males (r=0.956, r = 0.956, r=0.956, p<0.001, p< 0.001, p<0.001) which suggested that both hands exhibited very similar dimensional characteristics, demonstrating that an increase in the breadth of one hand was likely to be mirrored by an increase in the other. P-value < 0.001 demonstrated in correlation significance seen in the right and left hand breadth with the height of right hand and left hands which highlighted broader hands which inclined to be interlaced with the taller hands. Height and heights of right and left hands also showed positive significant associations which demonstrated taller individuals inclined with proportionally larger extremities. Similar type of results was also seen in north and south Indian which was supportive for these results [17]. Another studies on Nigerian populations by which also highlighted relationships of height and hand length and supports [18]. Right and left hand breadth association with the age demonstrated weak correlation but height of the hand demonstrated a significant correlation. Gender and hand measurements of negatively significant association highlighting the proportions of male and female hands were different from each other. Such findings also dependable with another studies in Pakistan, India, Columbia, Nigeria supports the same results with men had bigger hand sizes as compared to females [19]. Age association with height also demonstrated any significance p-value >0.002. Such type of results also supported by Egyptians, Indian and Nigerian population studies [20]. The strong correlation between right and left hand breadths observed in this study highlighted the bilateral symmetry of hand measurements. Such symmetry was expected given the anatomical and functional similarities of the hands. Contrary to some expectations, age showed weak and non-significant correlations with hand dimensions. This indicated that within the age group of the samples, age does not significantly impact these anthropometric traits. This was in line with the study by Habib and Kamal (2010), which found minimal age-related changes in hand dimensions among Egyptian adults [20].

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CONCLUSIONS

It was concluded that normal anthropometric parameters significantly different among the gender, and no any significant difference was observed in age variation. Significant difference in hand breadth and height highlighted males had larger hand dimensions as compared to females. Such insights can be helpful for various fields like forensic science, ergonomic designs, and personalized health care, which insisted on further research for practical implications.

Authors Contribution

Conceptualization: HR, FAA
Methodology: HR, FAA, MGAT, NAQ
Formal analysis: HR, FAA, SAFK
Writing, review and editing: HR, MGAT, SAQ, SAFK, NAQ

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Sinha P, Chakraborty S, Balakrishnan MC, Das S, Banerjee I.Exploring craniofacial anthropometry in the ethnic adult population of Meghalaya, Northeast India: A Cross-Sectional Study. 2024 Oct; 76(5): 4200-4207. doi: 10.1007/s12070-024-04814-5.

[2] Taneja C and Jain LK. Stature Estimation from the Anthropometric Measurements of Hands in Tribal Population of Udaipur District by Regression Analysis. International Journal of Health Sciences and Research. 2014; 4(11): 117-22.

[3] Abeer Zubair Khan1 , Nusrat Jahan2,*, Mahboobul Haque1Estimation of stature based on hand length among students of Uttar Pradesh Khan, Jahan and Haque / Indian Journal of Clinical Anatomy and Physiology 2020; 7(3): 271-276 2. doi: 10.18231/j.ijcap.2020.054.

[4] Zafar U, Rahman SU, Hamid N, Zafar N, Ahsan J. Correlation between height and hand size, and predicting height on the basis of age, gender and hand size.Journal of Medical Sciences. 2017 Dec; 25(4): 425-8.

[5] Dikshit PC, Aggrawal A, Rani M. Estimation of stature from hand length. Journal of Indian Academy of Forensic Medicine. 2005; 27(4): 219-21.

[6] Asghar MJ, Butt M, Akbar A, Azam H, Zahra I. Stature prediction of Punjab population (Pakistan) from hand, forearm and foot measurements. Biological and Clinical Sciences Research Journal.2020;57.doi: 10.54112/bcsrj.v2021i1.57.

[7] Norton K, Olds T. Role of anthropometry in athlete performance and sports science. Journal of Sports Sciences. 2021; 39(1): 1–13. doi: 10.1080/02640414.2020.1853711.

[8] Topor LS, Feldman HA, Bauchner H, Cohen LE. Variation in methods of predicting adult height for children with idiopathic short stature. Pediatrics. 2010 Nov; 126(5): 938-44. doi: 10.1542/peds.2009-3649.

[9] Khamis HJ and Roche AF. Predicting adult stature without using skeletal age: the Khamis-Roche method. Pediatrics. 1994 Oct; 94(4): 504-7.

[10] Moreno JC. Advancements in anthropometry for prosthetic limb design. Prosthetics and Orthotics International. 2020; 44(5): 385–94. doi: 10.1177/0309364620933451.

[11] Krishan K, Kanchan T. Hand anthropometry and its application in forensic science: A review. Journal of Forensic and Legal Medicine. 2023; 95: 102506.

[12] Sharma S. Forensic Science, Age Estimation, Open Apex, Panoramic Radiographs [Doctoral Dissertation]. Rajiv Gandhi University of Health Sciences; 2023.

[13] Rani M, Gupta S. Hand breadth and height correlation in a North Indian population. International Journal of Anatomy and Research.2020; 8(3.2): 7635–9. doi: 10.18231/j.ijcap.2020.005.

[14] Gomez AM, Molero JE. Hand anthropometry and its relationship with stature and age in a Colombian population. Journal of Anthropological Sciences. 2019; 97: 61–70.

[15] Stojanovic E, Scanlan A. Influence of anthropometry on performance outcomes in elite athletes: A review. Sports Medicine. 2020; 50(3): 525–38. doi: 10.1007/s40279-019-01229-2.

[16] Ibeabuchi NM, Akpuaka FC, Okereke HC. Correlation between hand length and height in young Nigerian adults. International Journal of Medical Science and Health Research. 2018; 2(7): 24–9.

[17] Al-Asadi JN. Handgrip strength in medical students: Correlation with body mass index and hand dimensions. Asian Journal of Medical Sciences.2018 Jan; 9(1): 21-6. doi: 10.3126/ajms.v9i1.18577.

[18] Supare M, Pandit S, Bagul A. Estimation of stature from hand length and hand breadth in medical students of Maharashtra, India. International Journal of Health & Allied Sciences.2015 Jul; 4(3): 154. doi: 10.4103/2278-344X.160875.

[19] Aboul-Hagag KE, Mohamed SK, El-Shafy AM. Bilateral symmetry of hand dimensions and its relationship to

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body size in a sample of Egyptian population. Forensic Science International.2011; 206(1-3): 216.e1–8. doi: 10.1016/j.forsciint.2010.09.025.

[20] Habib SR and Kamal NN. Stature estimation from hand and phalanges lengths of Egyptians. Journal of forensic and legal medicine.2010 Apr; 17(3): 156-60. doi :10.1016/j.jflm.2009.12.004.

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Sensitivity Pattern of Uropathogens in Diabetic and Non-Diabetic Patients Presenting to a Tertiary Care Hospital

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ABSTRACT

Diabetes Mellitus (DM) is a prevalent global health issue, with Pakistan experiencing a high burden. Diabetic patients were more susceptible to Urinary Tract Infections (UTIs) and often exhibit greater antibiotic resistance. **Objective:** To determine the sensitivity/resistance patterns of DM and Non-DM UTI patients. **Methods:** A cross-sectional study was conducted on 208-UTI at Lady Reading Hospital, Peshawar, from January to July 2020. Patients were equally divided into DM (n=104) and non-DM (n=104) groups. **Results:** A total of 208 UTI cases were equally divided between diabetic and non-diabetic groups (104 in each). The mean age of patients was 42.49 ± 1.148 years with a male predominance 132 (63.4%). Dysuria was reported in 81 (38.9%), urinary frequency in 86 (41.3%), and fever in 41 (19.7%) patients. Significant differences were observed in antibiotic resistance patterns between diabetic and non-diabetic groups. Diabetic patients exhibited higher resistance to Meropenem 86 (78%) versus 24 (22%), p<0.001), Ciprofloxacin 95 (98%) versus 2 (2%), p<0.001), and Ceftazidime 93 (79.4%) versus 24(20.6%), p<0.001) compared to non-diabetics. Conversely, sensitivity were significantly lower in diabetic patients for Meropenem (18(18%) versus 80(82%), p<0.001), Ciprofloxacin (9(8%) versus 102(91.8%), p<0.001), and Ceftazidime (11(12.3%) versus 79(87.7%), p<0.001). No significant associations were found between age or gender and antibiotic sensitivity within either group. **Conclusion:** The study demonstrates that diabetic patients were at significantly higher risk for antibiotic-resistant UTIs, particularly against meropenem, ciprofloxacin, and ceftazidime. These findings highlight the importance of customized antibiotic therapies and better glycemic control in diabetic patients to reduce UTIs complications.

INTRODUCTION

Diabetes Mellitus (DM) is a chronic Non-Communicable Disease (NCD) marked by persistent hyperglycemia, arising from insulin-related problems. It is a leading cause of mortality and morbidity globally, impacting individuals across all age groups, genders, and regions [1]. With increasing prevalence in both developed and developing nations, including Pakistan, diabetes is now acknowledged as a major global health concern [2, 3]. Pakistan, a populous nation in South Asia, is experiencing a growing burden of (NCDs), with DM becoming a prominent public health challenge. The diabetic population in the country has escalated from 5.2 million in 2000 to nearly 33 million by 2021 [4]. In 2016, NCDs, including diabetes, accounted for 58% of all deaths in Pakistan. Diabetes directly caused 3% of these deaths and contributed to other NCDs, such as cardiovascular diseases and hypertension [5]. Addressing the diabetes epidemic is crucial for mitigating its widespread health and economic impacts. In Pakistan, the prevalence of diabetes mellitus is reported at 26.3%, with 19.2% of individuals having known DM and 7.1% being new diagnosis. In comparison to rural regions (25.3%), the prevalence of DM is greater in urban (28.3%). Additionally, the prevalence of prediabetes is recorded at 14.4%, with 15.5% in urban and 13.9% in rural regions. Major risk factors associated with diabetes include being 43 years or older, a positive family history, hypertension, obesity, and

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dyslipidemia [6]. In comparison to individuals without diabetes, those with the condition are at a higher risk for all types of infections, including infections of the mucous membranes, lower respiratory infections, Urinary Tract Infections (UTIs), sepsis, endocarditis, as well as skin, bone, and joint infections [7]. According to the available data, urinary tract infections (UTIs) are the most common bacterial infection in patients with diabetes [8], occurring in 15.35% of cases, compared to 12.28% in individuals without diabetes [9]. The clinical profiles of diabetic patients indicate various factors that contribute to the higher incidence of UTIs in this group, such as inadequate circulation, a compromised immune system due to reduced activity of white blood cells in combating infections, and impaired bladder contractions that cause bladder dysfunction [10]. Furthermore, physiological variables such as age, gender, length of diabetes, long-term anti-diabetic medication use, and other diabetic sequelae such glycosuria and neuropathy are thought to be predisposing factors for the higher incidence of UTI in diabetics. Patients with diabetes may experience asymptomatic or symptomatic UTI, which includes urethritis, cystitis, prostatitis, pyelonephritis, and asymptomatic bacteriuria (ABU) [11]. A study carried out across 12 clinical sites in Pakistan explored the prevalence of asymptomatic UTIs in Type II Diabetes Mellitus (T2DM) patients. The findings showed that 8.08% of the patients had positive urine cultures, with a significantly higher occurrence in females (77.27%, $p<0.001$). The age group 40–59 years was the most common among those with positive cultures (70.45%). *Escherichia coli* was the most frequently identified pathogen (52.3%), and all bacterial isolates were resistant to Ciprofloxacin [6]. A hospital-based study conducted in Peshawar found that the disease was more prevalent in females (63.9%) and among patients with suboptimal glycemic control (86.3%) compared to those with good glycemic control (13.7%). *Escherichia coli* was the most frequently identified pathogen (71%), followed by *Klebsiella pneumoniae* (17.1%), *Pseudomonas aeruginosa* (6.83%), *Enterococcus* (5.85%), and Candida species (0.98%). Imipenem, meropenem, fosfomycin, and nitrofurantoin were highly effective against both gram-positive and gram-negative bacteria [12]. The literature indicates that *Escherichia coli* is the most common organism responsible for UTIs in both DM and non-DM patients, accounting for 50% of infections in diabetics and 43.33% in non-diabetics [9, 13]. Following this, in diabetics, *Acinetobacter* accounted for 18.33% and *Klebsiella* for 15%, while in non-diabetics, *Acinetobacter* was present in 15% and *Pseudomonas* in 12% [9]. Imipenem showed the highest sensitivity (46.66% in diabetics, 43.33% in non-diabetics). Subsequently, nitrofurantoin and cotrimoxazole each displayed a sensitivity of 20% in diabetics and 13% in nondiabetics, norfloxacin (31.66%), amikacin (20%), and gentamicin (20%) exhibited sensitivity. High resistance was observed to ciprofloxacin (98.33% in diabetics, 78.33% in non-diabetics), followed by resistance to norfloxacin (91.66%) and ampicillin (66.66%) in diabetics, and 55% resistance to both nitrofurantoin and norfloxacin in non-diabetics. Diabetic patients showed a statistically significant reduction in susceptibility, particularly to norfloxacin, ciprofloxacin, gentamicin, cefotaxime, and ampicillin. Study revealed that 100% of DM patients and 81.66% of non-DM exhibited resistance to three or more antimicrobial agents [13]. Given the growing concern about antibiotic resistance, particularly in patients with diabetes who are prone to Urinary Tract Infections (UTIs), it is crucial to understand the microbial profile and resistance patterns in this population. Existing data suggest that diabetic individuals are more susceptible to infections due to factors like compromised immunity and glycemic control. By analyzing the resistance and sensitivity of common uropathogens.

This study seeks to contribute valuable insights into the emerging resistance trends and guide future research and clinical practices in managing UTIs.

METHODS

This comparative cross-sectional, study was carried out in the Department of Medicine, Lady Reading Hospital, Peshawar from 13th January 2020 to 13th July 2020, including both diabetic and non-diabetic patients. A sample of 208 patients was selected and calculated using the openepi sample size calculator, by keeping 5% level of significance, 80% power of test and anticipated frequency of sensitivity of E.coli to ceftazidime among non-diabetics patients 50% versus in diabetic UTI patients 31.1% [14]. The sample of 208 patients then equally divide in to two group (diabetic versus non diabetic UTI patients). Each group consists of 104 UTI patients. Non-probability consecutive sampling was employed for patient selection. The inclusion criteria comprised of adults of both genders, aged 18 to 60 years, including both diabetic and non-diabetic individuals presenting with a UTI. Diabetic patients were required to have a fasting glucose level >126 mg/dL and a postprandial (2-hour) glucose level >200 mg/dL, while non-diabetic patients were to have a fasting blood sugar level <110 mg/dL. All participants exhibited a fever exceeding 98.6°F. Exclusion criteria were patients with urinary tract calculi, those receiving immunosuppressive therapy, those with urinary tract abnormalities, and patients with a history of catheterization or instrumentation. These conditions were assessed via medical history, X-ray, ultrasound, and other diagnostic methods. Ethical clearance was obtained from the hospital's ethical committee under reference number 198/LRH, dated 12/09/2019, and informed consent was

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secured from all participants after explaining the benefits and risks involved. Data collection was carried out through a thorough medical history, physical examination, and the use of pre-structured questionnaires. Numerous laboratory tests were performed, including fasting and random blood glucose, urine culture and sensitivity tests, urine dipstick examinations, and total and differential leukocyte counts using an automated blood analyzer. Urine cultures were grown on MacConkey's agar and Cystine Lactose Electrolyte Deficient (CLED) medium, supervised by a pathologist at the hospital laboratory. Additional tests such as kidney, ureter, and bladder ultrasounds, blood culture, and sensitivity tests, as well as serum urea, creatinine, and electrolyte levels, were conducted where necessary. Data were analyzed using SPSS version 25.0, with numerical variables expressed as mean ± SD and categorical variables presented as frequencies and percentages. Antibiotic resistance and sensitivity of UTI patients were stratified based on diabetic status. Diabetic status of UTI patients were stratified among age, gender, and symptom presence to evaluate the influence of these factors on. A post-stratification chi-squared test was performed by considering p-value ≤0.05 statistically significant.

RESULTS

The study includes 208 individuals presenting with urinary tract infections (UTI) were analyzed, of which 104 (50%) patients were diabetic, and 104 (50%) patients were non-diabetic. The mean age of the patients was 42.49 ± 1.148 years, with a male predominance 132 (63.4%) patients compared to females 76 (36.5%). Regarding UTI symptoms, dysuria was reported in 81 (38.9%) patients, urinary frequency in 86 (41.3%), and fever in 41 (19.7%) patients. The table 1 highlights key differences in the baseline characteristics of Diabetic (DM) and Non-Diabetic (Non-DM) patients with Urinary Tract Infections (UTIs). A significant variation in age distribution was observed, with a higher proportion of DM patients in the 31-40 and 41-50 years age group 32 (30.77%) and 43 (41.35%) and Non-DM patients predominantly in the 41-50 and 51-60 age group 45 (43.27%) patients in each. The gender distribution reveals that most of DM patients were male 85 (81.73%), while the Non-DM group had a balanced gender distribution, with 47 (45.19%) males and 57 (54.81%) females, reflecting a statistically significant difference (P-value < 0.0001). Symptomatically, dysuria was more prevalent in Non-DM patients 46 (45.5%) patients compared to DM patients 35 (33.65%), while urinary frequency was more common in DM patients 47 (45.19%). Fever was relatively balanced between the two groups, with 22 (21.15%) patients in the DM group and 19 (18.27%) patients in the Non-DM group.

Table 1: Baseline Demographic Characteristics of DM and Non-DM UTI Patients (n=208)

Baseline Characteristics	Categories	DM N (%)	Non-DM N (%)	p-value
Age	18-30	9 (8.65%)	8 (7.69%)	<0.0001
	31-40	32 (30.77%)	6 (5.77%)	
	41-50	43 (41.35%)	45 (43.27%)	
	51-60	20 (19.23%)	45 (43.27%)	
	Total	104	104	
Gender	Male	85 (81.73%)	47 (45.19%)	<0.0001
	Female	19 (18.27%)	57 (54.81%)	
	Total	104	104	
Symptoms	Dysuria	35 (33.65%)	46 (44.23%)	0.2927
	Urinary Frequency	47 (45.19%)	39 (37.50%)	
	Fever	22 (21.15%)	19 (18.27%)	
	Total	104	104	

The table 2 showed a significant difference in the antibiotic sensitivity and resistance patterns between DM and Non-DM UTI patients for Meropenem, Ciprofloxacin, and Ceftazidime. In the DM group, 86 (78%) patients were resistant to Meropenem, compared to only 24 (22%) in the Non-DM group. Similarly, 95 (98%) of DM patients were resistant to Ciprofloxacin, while only 2 (2%) of Non-DM patients exhibited resistance. For Ceftazidime, 93 (79.4%) of DM patients were resistant, compared to 24 (20.5%) in the Non-DM group. In contrast, Non-DM patients showed significantly higher sensitivity to all three antibiotics. For Meropenem, just 18 (18%) of DM patients were sensitive, compared to 80 (82%) of Non-DM patients. Likewise, 9 (8%) of DM patients were sensitive to Ciprofloxacin, while 102 (91.8%) of Non-DM patients showed sensitivity. Finally, 11 (12.3%) of DM patients were sensitive to Ceftazidime, whereas 79 (87.7%) of Non-DM patients responded positively. The p-values for all comparisons were <0.001, indicating that these differences were statistically significant, with DM patients showing higher resistance and lower sensitivity to these antibiotics.

Table 2: Antibiotic Sensitivity and Resistance Pattern of DM and Non-DM UTI Patients (n=208)

Antibiotic Pattern		DM N (%)	Non-DM N (%)	p-value
Meropenem	Resistance	86 (78%)	24 (22%)	<0.001
	Sensitivity	18 (18%)	80 (82%)	<0.001
Ciprofloxacin	Resistance	95 (98%)	2 (2%)	<0.001
	Sensitivity	9 (8%)	102 (91.8%)	<0.001
Ceftazidime	Resistance	93 (79.4%)	24 (20.6%)	<0.001
	Sensitivity	11 (12.3%)	79 (87.7%)	<0.001

The table 3 examined the relationship between age, gender, and antibiotic sensitivity patterns for DM and Non-DM patients across three antibiotics: Meropenem, Ciprofloxacin, and Ceftazidime. For DM patients, the antibiotic sensitivity patterns by age and gender do not

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show significant differences. The p-value for age was 0.771, indicating no significant association between age groups (<40 and >40 years) and antibiotic sensitivity to Meropenem, Ciprofloxacin, or Ceftazidime. Similarly, the p-value for gender was 0.56, meaning there was no statistically significant difference in antibiotic sensitivity between males and females for any of the antibiotics tested. For Non-DM patients, the p-value for age was 0.115, suggesting that there was no strong evidence of an association between age groups (<40 and >40 years) and antibiotic sensitivity. However, while the p-value was higher than 0.05 (indicating non-significance), it was still relatively close, suggesting some potential for a difference in antibiotic sensitivity by age, particularly for Ciprofloxacin, where a higher percentage of patients >40 years were sensitive. The p-value for gender was 0.551, meaning there was no statistically significant difference in antibiotic sensitivity between males and females for Non-DM patients.

Table 3: Age and Gender versus Antibiotic Sensitivity Pattern of DM and Non-DM Patients

Antibiotic Sensitivity	DM		p-value	DM		p-value
	Age N (%)			Age N (%)		
	>40 Years	>40 Years		>40 Years	>40 Years	
Meropenem	11 (61.11%)	7(38. 89%)	0.771	14 (17.5%)	66 (82.5%)	0.115
Ciprofloxacin	5(55. 56%)	4(44. 44%)		9(8. 82%)	93(91. 18%)	
Ceftazidime	5(45. 45%)	6(54. 55%)		11(13. 92%)	68(86. 08%)	
Antibiotic Sensitivity	**Gender**		0.56	**Gender**		0.551
	Male	**Female**		**Male**	**Female**	
Meropenem	9(50. 0%)	9(50. 0%)		33(41. 25%)	47(58. 75%)	
Ciprofloxacin	6(66. 67%)	3(33. 33%)		47(46. 08%)	55(53. 92%)	
Ceftazidime	5(45. 45%)	6(54. 55%)		37(46. 84%)	42(53. 16%)	

Figure 1 presented multiple bar-chart for antibiotic sensitivity patterns for DM and Non-DM patients across symptoms (dysuria, urinary frequency, and fever). For DM patients, sensitivity was highest for dysuria across all antibiotics, with lower sensitivity for fever and the lowest for urinary frequency. In Non-DM patients, sensitivity was also highest for dysuria, with more balanced sensitivity across other symptoms. Non-DM patients consistently exhibit higher sensitivity to all antibiotics compared to DM patients, with the differences being most notable for urinary frequency and fever. The chart highlights that dysuria was associated with the highest sensitivity in both groups.

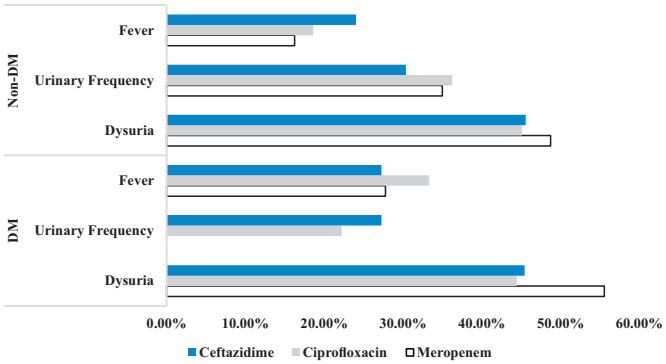

Figure 1: Multiple Bar-Chart for Antibiotic Sensitivity versus UTI Symptoms among DM and Non-DM Patients

DISCUSSION

Urinary Tract Infections (UTIs) pose a significant healthcare challenge, which was further exacerbated by the improper use of antibiotics. This study focuses on examining the sensitivity and resistance patterns of antibiotics in both Diabetic (DM) and Non-Diabetic (non-DM) patients. The results of this study showed that people with DM and those without DM have significantly different uropathogen sensitivity patterns, which has substantial therapeutic implications for the treatment of Urinary Tract Infections (UTIs) in these populations. Diabetic patients exhibited significantly higher rates of antibiotic resistance compared to non-diabetic patients, aligning with findings from Shill MC *et al.*, in 2023, which demonstrated that while Imipenem and meropenem showed 100% sensitivity against *Escherichia coli, Staphylococcus,* and *Klebsiella* in non-diabetic patients, their effectiveness was diminished in diabetic individuals [4, 15]. Additionally, antibiotics such as nitrofurantoin, ceftazidime, and ceftriaxone were markedly less effective in diabetic patients ($p \leq 0.0002$ to $p \leq 0.0168$). Overall, diabetic patients demonstrated lower antibiotic sensitivity, except for ciprofloxacin and levofloxacin, when compared to non-diabetic counterparts ($p < 0.05$ to 0.0001) [15]. This study revealed that significantly large amount (greater than 75%) of diabetic patients exhibited resistance to these three antibiotics, compared to much lower resistance rates in non-diabetic patients (22% for Meropenem, 20% for Ceftazidime, and 2% for Ciprofloxacin), highlighting the strong association between diabetes and antibiotic resistance. These results align with the study performed by Signing AT *et al.*, in 2020 [16]. Their study revealed a strong correlation between antibiotic resistance and diabetic status, showing significant resistance to ceftriaxone, cefixime, ceftazidime, cefotaxime, cefepime, and ciprofloxacin among diabetic patients (X^2 values ranging from 9.45 to 27.93, all with p-values < 0.01). Multidrug resistance was notably higher in diabetic patients, with 62.50% for *Escherichia coli,* 63.16% for *Klebsiella pneumoniae,* and

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78.57% for *Staphylococcus aureus*, compared to 37.50%, 36.84%, and 21.43%, respectively, in non-diabetic patients. This underscores the heightened antibiotic and multidrug resistance in diabetic UTI patients [16]. The literature suggests that inadequate glycemic control was a significant risk factor for increased antibiotic resistance [17-19]. This was supported by findings of the study, where all diabetic patients showed resistance to multiple antibiotics. Studies indicate that hyperglycemia fosters a more conducive environment for bacterial growth, leading to persistent or recurrent UTIs that require longer courses of antibiotics and result in increased resistance [18, 20, 21]. The age distribution in this study showed that diabetic patients were primarily between 31-50 years old, which was consistent with earlier findings linking older age with increased diabetes-related complications, including UTIs [22]. In contrast, non-diabetic patients were more evenly distributed between the 41-60 age groups. The observed male predominance in diabetic UTI patients diverges from the findings of other studies where females had a higher prevalence of UTIs [23, 24]. However, no significant association exist between age, gender, and antibiotic sensitivity among the study group. The study also demonstrated that diabetic patients more frequently presented with urinary frequency (45.19%) compared to dysuria (33.65%) and fever (21.15%), while non-diabetic patients were more likely to report dysuria (44.23%). Whereas literature reports high symptoms of dysuria among diabetic patients [25, 26]. The limitations of this study were single-center design, small sample size, and lack of longitudinal data, which may restrict the generalizability of the findings. The future study can conduct a randomized controlled trial to check the sensitivity pattern of diabetic patients to different antibiotic use among local population of Peshawar.

CONCLUSIONS

This study highlighted significant differences in antibiotic resistance patterns between DM and non-DM patients with UTIs. DM patients exhibited notably higher resistance, especially to meropenem, ciprofloxacin, and ceftazidime, compared to their non-diabetic counterparts. These findings, which were statistically significant, suggest that diabetic individuals face a greater challenge in effective UTI treatment due to increased resistance, potentially linked to poor glycemic control. Tailored antibiotic regimens and improved glycemic management were recommended to address these risks in diabetic patients.

Authors Contribution

Conceptualization: MN
Methodology: MN
Formal analysis: MN, AU
Writing, review and editing: MN, MWF

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Lancet T. Diabetes: a defining disease of the 21st century. Lancet (London, England). 2023 Jun; 401(10394): 2087. doi: 10.1016/S0140-6736(23)01296-5.

[2] Meroz P, Chevuri SP, Kumar V. An Observational Study of Bacteriological and Antibiotic Susceptibility Profile of Urinary Tract Infections in Diabetic and Non-Diabetic Patients in a Tertiary Health Centre. Journal of Advanced Medical and Dental Sciences Research. 2024 Mar; 12(3): 1-5.

[3] Shohid S, Ali MT, Saha S, Jahan M, Hossain MB, Roy PK. Current Antibiotic resistance pattern of prevalent uropathogens in urinary tract infection of diabetic patients in comparison with non-diabetics. Scholars Journal of Applied Medical Sciences. 2022 May; 5: 816-22. doi: 10.36347/sjams.2022.v10i05.024.

[4] Shill MC, Mohsin MN, Showdagor U, Hasan SN, Zahid MZ, Khan SI *et al*. Microbial sensitivity of the common pathogens for UTIs are declining in diabetic patients compared to non-diabetic patients in Bangladesh: An institution-based retrospective study.Heliyon.2023 Jan; 9(1). doi: 10.1016/j.heliyon.2023.e12897.

[5] Jankhwala S, Singh S, Nayak S. A comparative study of profile of infections in diabetic and non-diabetic patients. International Journal of Medical Science and Public Health. 2014 Aug; 3: 982-5. doi:10.5455/ijmsph .2014.050620142.

[6] Kumar R, Perswani P, Taimur M, Shah A, Shaukat F. Clinical and microbiological profile of urinary tract infections in diabetic versus non-diabetic individuals. Cureus. 2019 Aug;11(8). doi: 10.7759/cureus.5464.

[7] Chávez-Reyes J, Escárcega-González CE, Chavira-Suárez E, León-Buitimea A, Vázquez-León P, Morones-Ramírez JR *et al.* Susceptibility for some infectious diseases in patients with diabetes: the key role of glycemia. Frontiers in Public Health.2021 Feb; 9: 559595. doi: 10.3389/fpubh.2021.559595.

DOI:https://doi.org/10.54393/pjhs.v5i12.2243

[8] Nitzan O, Elias M, Chazan B, Saliba W. Urinary tract infections in patients with type 2 diabetes mellitus: review of prevalence, diagnosis, and management. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy. 2015 Feb: 129-36. doi: 10.2147/DMSO.S51792.

[9] Bamnote PT, Ovhal RS, Kulkarni DM, More SK. Prevalence of urinary tract infections and its antibiogram in diabetic and non-diabetic patients attending tertiary care hospital in Maharashtra. International Journal of Medical Microbiology and Tropical Diseases. 2018 Apr-Jun; 4(2): 76-9. doi:10.18231/2581-4761.2018.0017.

[10] Riaz S, Mohsin A, Shokat S, Shamim S. Molecular Level Microbiological and Clinical Profile of Urinary Tract Infection in Diabetes Mellitus. Journal of Microbiology. 2021 Apr. doi: 10.31080/ASMI.2021.04.0821.

[11] Lature LH, Lature ML, Pyadala N. Assessment of urinary tract infections among type 2 diabetic patients in a rural teaching hospital, Sangareddy. International Archives of Integrated Medicine. 2020 Jan; 7(1): 28-32.

[12] Ahmad S, Hussain A, Khan MS, Shakireen N, Ali I. Diabetes mellitus and urinary tract infection: Causative uropathogens, their antibiotic susceptibility pattern and the effects of glycemic status. Pakistan Journal of Medical Sciences.2020 Nov; 36(7): 1550. doi: 10.12669/pjms.36.7.2881.

[13] Patrad SG, Ahmed SM, Deepa S, Kishore MS. A comparative study of resistance to multiple antibiotics in urinary tract infection among diabetic versus non-diabetic patients in a tertiary care hospital. National Journal of Physiology, Pharmacy and Pharmacology. 2024 Jul; 14(7): 1351-. doi: 10.5455/njppp.2024.14.12582202326012024.

[14] Sain ZM, Rafeeq M, Murad HA, Hussain MB. Isolation and drug susceptibility pattern of uropathogens in Saudi diabetic and non-diabetic patients with urinary tract infection. Bioinformation.2022; 18(8): 710. doi:10.6026/97320630018710.

[15] Owusu E, Adjei H, Afutu E. Similarities in bacterial uropathogens and their antimicrobial susceptibility profile in diabetics and their non-diabetic caregivers at a National Diabetes Management and Research Centre, Accra-Ghana. Diseases.2022 Dec; 10(4): 124. doi:10.3390/diseases10040124.

[16] Signing AT, Marbou WJ, Beng VP, Kuete V. Antibiotic resistance profile of uropathogenic bacteria in diabetic patients at the Bafoussam Regional Hospital, West Cameroon Region. Cureus. 2020 Jul; 12(7). doi:10.7759/cureus.9345.

[17] Carrillo-Larco RM, Anza-Ramírez C, Saal-Zapata G, Villarreal-Zegarra D, Zafra-Tanaka JH, Ugarte-Gil C *et al*. Type 2 diabetes mellitus and antibiotic-resistant infections: a systematic review and meta-analysis. Journal Epidemiol Community Health. 2022 Jan; 76(1): 75-84. doi: 10.1136/jech-2020-216029.

[18] Nagendra L, Boro H, Mannar V. Bacterial infections in diabetes. Endotext [Internet]. 2022 Apr.

[19] Holt RI, Cockram CS, Ma RC, Luk AO. Diabetes and infection: review of the epidemiology, mechanisms and principles of treatment. Diabetologia.2024 Feb; 67: 1168–1180.

[20] Akash MS, Rehman K, Fiayyaz F, Sabir S, Khurshid M. Diabetes-associated infections: development of antimicrobial resistance and possible treatment strategies. Archives of Microbiology.2020 Jul; 202: 953-65. doi: 10.1007/s00203-020-01818-x.

[21] Darwitz BP, Genito CJ, Thurlow LR. Triple threat: how diabetes results in worsened bacterial infections. Infection and Immunity.2024 Mar: e00509-23. doi: 10.1128/iai.00509-23.

[22] Sewify M, Nair S, Warsame S, Murad M, Alhubail A, Behbehani K et al. Prevalence of urinary tract infection and antimicrobial susceptibility among diabetic patients with controlled and uncontrolled glycemia in Kuwait. Journal of Diabetes Research.2016 Dec; 2016(1): 6573215. doi: 10.1155/2016/6573215.

[23] Seifu WD and Gebissa AD. Prevalence and antibiotic susceptibility of Uropathogens from cases of urinary tract infections (UTI) in Shashemene referral hospital, Ethiopia. BioMed Central Infectious Diseases. 2018 Dec; 18: 1-9. doi: 10.1186/s12879-017-2911-x.

[24] Tan CW and Chlebicki MP. Urinary tract infections in adults. Singapore Medical Journal. 2016 Sep; 57(9): 485. doi: 10.11622/smedj.2016153.

[25] Ramrakhia S, Raja K, Dev K, Kumar A, Kumar V, Kumar B. Comparison of incidence of urinary tract infection in diabetic versus non-diabetic and associated pathogens. Cureus.2020 Sep; 12(9). doi: 10.7759/cureus.10500.

[26] Papaefstathiou E, Moysidis K, Sarafis P, Ioannidis E, Hatzimouratidis K. The impact of Diabetes Mellitus on Lower urinary tract symptoms (LUTS) in both male and female patients. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2019 Jan; 13(1): 454-7. doi: 10.1016/j.dsx.2018.11.009.

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Original Article

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Assessing Risk Factors, Patterns, and Knowledge of Preventive Measures in Traumatic Dental Injuries among School Children

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ABSTRACT

Traumatic Dental Injuries (TDIs) were among the most prevalent conditions affecting children. Data on dental trauma primarily stem from studies conducted across various regions of the world. These injuries can have significant functional, aesthetic, and psychological implications for affected children. Effective prevention and timely treatment were essential, as untreated dental trauma can lead to long-term complications, including infection, malocclusion, and impaired oral development. **Objective:** To evaluate risk factors, patterns, and knowledge of preventive measures in traumatic dental injuries among school children. Methods: A study was conducted to evaluate dental trauma in children. The data were collected from 312 children aged 8 to 15 using a convenience sampling technique. The inclusion criteria encompassed children with erupted permanent anterior teeth. The relationships were analyzed using the Chi-Square test in SPSS version 26. **Results:** The data showed that 63.5% of the children were male, with 57.7% having experienced traumatic dental injuries. Falls (21.8%), sports injuries (15.7%), and biting (5.8%) were the most frequent causes present in the study. and maxillary central incisors had the highest tooth loss at 57.95%, while 57.7% of participants were aware of using mouth guards to prevent dental trauma. **Conclusions:** It identified several predisposing factors, particularly affecting the anterior teeth. Based on these results, strategic preventive measures should be implemented, specifically targeting the identified risk groups.

INTRODUCTION

The International Association of Dental Traumatology (IADT) defines dental trauma as an external force impacting dental tissue, which can manifest clinically as injuries to hard tissues (such as enamel fractures, enamel and dentin fractures with or without pulp exposure, root fractures, and alveolar fractures) or supportive tissues (including concussion, subluxation, intrusive, extrusive, or lateral dislocation, and avulsion) [1]. Traumatic Dental Injuries (TDIs) significantly affect children's chewing abilities and quality of life, also impacting parents emotionally and financially [2]. The prevalence of TDIs is from 6% to 34.8% in children and adolescents, with annual incidence rates of 1% to 3.3% in those aged 7 to 15, influenced by environmental and cultural factors [3]. Boys experienced more injuries which occurred primarily at home due to falls. Tooth loss most frequently occurs in the maxillary central and lateral incisors, as well as the lower anterior teeth [4]. Traumatic Dental Injuries (TDIs) arise from various causes, including sports injuries, road traffic accidents, falls, and violence, commonly occurring at home, school, playgrounds, streets, parks, and in school buses. Identified risk factors include dental profile, molar relationship,

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overjet, lip coverage, socio-economic status, and weight/BMI. These injuries can lead to complications like crown fractures, tooth discoloration, pulp necrosis, and root resorption. Additionally, research shows that children with front tooth trauma are often less likely to smile or participate in social activities than other children [5]. Numerous systematic reviews have indicated that various anatomical and biological factors contribute to a higher prevalence of TDIs, including obesity, pronounced overjet, anterior open bite, and poor lip seal [6]. The use of protective gear, like mouth guards, is deemed essential for preventing dentofacial injuries due to their capability to absorb and disperse impact energy [7]. The loss of permanent front teeth can be highly distressing for the children and parents, impacting facial appearance and potentially lowering a child's self-esteem. Furthermore, TDIs can adversely disturb the children's quality of life [8]. TDIs are affecting children and adolescents globally and they can lead to serious consequences, including tooth discoloration, pulp necrosis, reduced quality of life, and financial burdens [9]. It's essential to improve and upgrade school facilities, infrastructure, and playgrounds to create a safer environment for children. Educating teachers, parents, and students about preventive measures for dental injuries in both schools and at home is crucial. Additionally, using proper safety gear should be mandatory for children and adolescents during outdoor sports and recreational activities to minimize the risk of injuries [10]. Other epidemiological studies indicate that 50% of children have experienced Traumatic Dental Injuries (TDIs). Previous research has reported the prevalence of dental trauma in developed countries to be between 4% and 30%. This significant prevalence highlights the necessity for dental care programs that include public and parental education. Numerous studies have assessed parental knowledge regarding TDIs, with most findings showing a lack of awareness, particularly among fathers, underscoring the need for improved educational efforts for parents [11]. Identifying and addressing the risk factors associated with TDIs is essential for implementing effective preventive strategies and educational programs. This understanding allows public health initiatives to reduce the incidence of TDIs and enhance oral health among children.

Therefore, this study aimed to investigate the risk factors, patterns, and knowledge of preventive measures in TDI in school children.

METHODS

A cross-sectional study was performed to evaluate dental trauma in children. Ethical approval was obtained from the Gandhara University (No. GU/Ethical Committee/2023/205) and the data collection was started from 20th November 2023 to 10th June 2024, and data were collected using a convenience sampling technique. The sample size was calculated using OpenEpi version 3.01, with a 5% precision, a 95% confidence interval, and a prevalence of dental trauma estimated at 28.3% [12]. The total sample included 312 children. A pilot study was executed on 10 members to assess the feasibility and validity of the questionnaire. The inclusion criteria for the study focused on children, aged 8 to 15 years who attended school and had erupted permanent anterior teeth, with at least 75% of their crowns emerging into the oral cavity and those with signed consent forms from their parents were included. Conversely, the exclusion criteria eliminated children with filled or missing central and lateral incisors, peg laterals, large diastemas, excessive crowding, open bites, severely rotated teeth, or orthodontic appliances. Additionally, students who lost teeth due to dental caries, fractured roots, severe dental fluorosis, or those with physical, mental, or medical disabilities were excluded. The students were asked about the age, gender, presence or absence of dental trauma, risk factors and tooth loss and knowledge of the use of mouth guards and face guards as preventive measures. The children were examined with the help of a tongue depressor in day light. The examination proceeded systematically from the maxillary right quadrant to the mandible in a clockwise manner, relying on visual assessment without evaluating tooth vitality or using radiographs. The data were analyzed by using SPSS version 26.0. The frequency and percentages were calculated for the demographic profile of the children, risk factors, various preventive measures, and a chi-square test was used for the association between child's gender and risk factors. A P-value of ≤0.05 was established as significant.

RESULTS

The data showed that the majority of the children were male, with 63.5% being male, 36.5% being female and 68.3% being aged 12 to 15. Additionally, 57.7% of the children had experienced a traumatic dental injury, whereas 42.3% had not.

Table 1: Demographic Profile of the School Children (n=312)

Variables	Frequency (%)
Gender of Child	
Male	198 (63.5%)
Female	114 (36.5%)
Age of Child	
8-11	99 (31.7%)
12-15	213 (68.3%)
Presence or Absence of Dental Trauma	
Yes	180 (57.7%)
No	132 (42.3%)
Place of Trauma	
School	74 (23.7%)

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Home	78 (25.0%)
Street	27 (8.7%)

The data showed that falls (21.8%) were the most common risk, followed by sports injuries (15.7%). Road traffic accidents (5.1%), biting (5.8%), overjet (5.1%), and physical fights (4.2%) were less frequent contributors.

Table 2: Showing the Risk Factors for Dental Trauma (n=312)

Risk Factors for Dental Trauma	
Risk factors	**Frequency (%)**
Fall	68 (21.8%)
Sports	49 (15.7%)
RTA	16 (5.1%)
Biting Hard Objects	18 (5.8%)
Overjet	16 (5.1%)
Physical Fight	13 (4.2%)

The data revealed significant gender differences in dental trauma risk factors (p = 0.007). Males had higher rates of falls (23.2%) and sports injuries (20.7%), while females had more falls (19.3%) but fewer sports injuries (7.0%).

Table 3: Association of Children's Gender and Risk Factors (n=312)

Gender	Fall Frequency (%)	Sports Frequency (%)	RTA Frequency (%)	Biting Frequency (%)	Overjet Frequency (%)	Physical Fight Frequency (%)	p-Value
Male	46 (23.2%)	41 (20.7%)	9 (4.5%)	13 (6.6%)	11 (5.6%)	9 (4.5%)	0.007
Female	22 (19.3%)	8 (7.0%)	7 (6.1%)	5 (4.4%)	5 (4.4%)	4 (3.5%)	

The findings indicated that the upper front teeth experienced tooth loss at 57.95%, followed by upper lateral incisors at 39.74%, and 57.7% were aware of the use of mouth guard.

Table 4: Pattern of Permanent Teeth Loss and Knowledge about Preventive Measures (n=312)

Pattern of Teeth Loss	
Tooth Loss	**Frequency (%)**
Maxillary Central Incisor	175 (57.95%)
Maxillary Lateral Incisor	120 (39.74%)
Mandibular Central Incisor	5 (1.65%)
Knowledge about Preventive Measure	
Mouth Guard	180 (57.7%)
Face Guard	132 (42.3%)

DISCUSSION

The study involved 312 children, with 63.5% being male and 68.3% aged 12-15 years. Among the participants, 57.7% reported experiencing traumatic dental injuries, predominantly occurring at home. According to the previous study involving 1,100 participants, age and gender were found to influence dental injuries. The results indicated that boys had a dental injury rate of 11.5%, whereas girls had a lower rate of 10.2%. Furthermore, among 12-year-olds, the prevalence was recorded at 10.6%, while 15-year-olds showed a slightly higher prevalence of 11.3% [13]. This study identified various risk factors for dental trauma with which the most common risk factor was falling in both males (23.2%) and females (19.3%). Males had more sports-related injuries. A previously conducted study indicated that falls (61%) were the frequent reason of dental injuries, followed by biting hard objects (11%) and sports-related incidents (9%) [14]. Similar findings were also found by Nagarajappa R *et al.*, in which boys accounted for 67.4% of dental trauma more than girls 32.6%. The major cause was falls in the play area (46.0%), with pushing being the core reason for the injuries at 65.2% [15]. Another study was conducted on dental trauma in which the affected age bracket was 13 to 20 years (46%). The majority of trauma incidents resulted from falls while playing (36.6%), followed by bicycle accidents at 19.5% [16]. A study reported the findings that falls were identified as the leading cause of dental injuries (43.8%), road traffic accidents were 42.1%, and sports-related injuries accounted for 9.1% of the incidents [17]. However, Violence was the leading cause of dental trauma (42.5%), followed by roadway accidents (24.1%), impacts with people or objects (16.0%), and falls (9.1%) as reported in a study [18]. This study revealed that tooth loss occurred most frequently in the maxillary central incisors (57.95%), with the maxillary lateral incisors following at 39.74%. In comparison, the mandibular central and lateral incisors experienced much lower loss rates. Similar results were found by the previous literature suggesting that traumatic injuries were more commonly associated with maxillary teeth than mandibular teeth [18]. The increased susceptibility of maxillary teeth was attributed to their prominent position and protruded alignment, while the flexible lower jaw absorbed impacts, reducing trauma to the lower anterior teeth [19]. A study revealed the findings that boys (62.4%) had significantly more instances of multiple teeth being affected than girls (37.6%). The most commonly affected teeth were the maxillary central incisors (81.6%), followed by maxillary lateral incisors (12.7%) and mandibular central incisors (5.7%) [20]. Another study involving 443 teachers showed that children's safety improved with safe playgrounds (75.8%), 10.6% acknowledged that having a nurse on-site could effectively reduce and manage dental trauma and the remaining suggested the use of face guards and mouth guards were essential for child' safety [21]. Numerous studies indicated that mouth guard users reduced sports-related orofacial injury risk by 1.6 to 1.9 times, while education regarding the use of mouth guards by dental

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practitioners further reduced the TDIs[22].

CONCLUSIONS

The data highlights that males were more prone to dental trauma, particularly from falls and sports injuries. To reduce these risks, schools should implement safety programs, sports injury prevention measures, and oral health education. Policymakers must enforce stricter safety standards, and parents should supervise children during high-risk activities.

Authors Contribution

Conceptualization: SZSS,
Methodology: SLSS, AH, SGSS, FJS
Formal analysis: SLSS
Writing, review and editing: SZSS, SLSS, AH, SGSS, FJS

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] de Andrade Vieira W, Pecorari VG, Figueiredo-de-Almeida R, Junior NC, Vargas-Neto J, Santos EC *et al*. Prevalence of dental trauma in Brazilian children and adolescents: a systematic review and meta-analysis. Cadernos de Saúde Pública.2021 Dec; 37(12). doi: 10.1590/0102-311x00015920.

[2] Patnana AK, Chugh A, Chugh VK, Kumar P, Vanga NR, Singh S. The prevalence of traumatic dental injuries in primary teeth: a systematic review and meta-analysis. Dental Traumatology. 2021 Jun; 37(3): 383-99. doi: 10.1111/edt.12640.

[3] Bani-Hani TG, Olegário IC, O'Connell AC.The cost of dental trauma management: a one-year prospective study in children. Dental Traumatology. 2020 Oct; 36(5): 526-32. doi: 10.1111/edt.12561.

[4] Vyas D, Garg K, Ramasamy R, Malik K, Suraj U, Asmin PK. A Cross Sectional Study to Determine Anterior Tooth Trauma Prevalence among Children Aged 9-13 Years. International Journal of Health Sciences. 2022; 6(S3): 11150-7. doi: 10.53730/ijhs.v6nS3.8513.

[5] Lima J, Caldarelli PG, Rocha JS, Tomazinho FS, Fariniuk LF, Baratto-Filho F, Gabardo MC. Educational approaches for assessing knowledge about and actions of educators in response to dental avulsion. Journal of Indian Society of Pedodontics and Preventive Dentistry.2021 Apr; 39(2): 138-46. doi: 10.4103/JISPPD.JISPPD_186_20.

[6] Magno MB, Nadelman P, Leite KL, Ferreira DM, Pithon MM, Maia LC. Associations and risk factors for dental trauma: a systematic review of systematic reviews. Community Dentistry and Oral Epidemiology.2020 Dec; 48(6): 447-63. doi: 10.1111/cdoe.12574.

[7] Oliveira Werlich M, Honnef LR, Silva Bett JV, Domingos FL, Pauletto P, Dulcineia Mendes de Souza B *et al*. Prevalence of dentofacial injuries in contact sports players: a systematic review and meta-analysis. Dental Traumatology.2020 Oct; 36(5): 477-88. doi: 10.1111/edt.12556.

[8] Olatosi OO, Mgbemere OJ, Oyapero A, Omotuyole AS, Okolo CC. Awareness and preferred mode of getting information on first aid management of avulsed permanent teeth: Survey of Nigerian mothers. Pesquisa Brasileira em Odontopediatria e Clínica Integrada. 2020 Dec; 21: e0124. doi: 10.1590/pboci.2021.008.

[9] Guerra C, Braido A, Ferraz DC, Paranhos LR, de-Jesus-Soares A, Vieira WA. Family structure and social vulnerability as risk factors for traumatic dental injuries in children and adolescents: a systematic review and meta-analysis. Clinical Oral Investigations. 2024 Jul; 28(8): 451. doi: 10.1007/s00784-024-05841-w.

[10] Khan MK and Jindal MK. Assessment of the environmental risk factors associated with traumatic dental injuries among WHO index-aged children and adolescents. Journal of Education and Health Promotion. 2023 Nov; 12(1): 396. doi: 10.4103/jehp.jehp_1572_22.

[11] Kebriaei F, Ms DD, Attarzadeh H, Ms DD, Sadri L, Ms DD *et al*. Knowledge of Iranian parents of elementary school children about traumatic dental injuries and its management. Journal of Dentistry. 2020 Sep; 21(3): 202.

[12] Kundu P, Tandon S, Chand S, Jaggi A. Assessing the Prevalence of Traumatic Dental Injuries and its Impact on Self-esteem among Schoolchildren in a Village in Gurugram. Journal of Indian Association of Public Health Dentistry. 2023 Oct; 21(4): 294-9. doi: 10.4103/jiaphd.jiaphd_58_21.

[13] Alshammary F, Alhur T, Alshammari KN, Siddiqui AA, Abideen MZ, Alghaythi KS *et al*. Prevalence and Risk Factors of Dental Trauma in Ha\'il, Saudi Arabia. The Journal of Contemporary Dental Practice.2022 Sep; 23: 628-33. doi: 10.5005/jp-journals-10024-3354.

[14] Gupta R, Kaur N, Sharma V, Bhalla M, Srivastava M, Sisodia S. Prevalence and risk factors associated with traumatic dental injuries among 12-15 year old school

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going children, Mathura city.Journal of Indian Association of Public Health Dentistry. 2021 Jan; 19(1): 76-80. doi: 10.4103/jiaphd.jiaphd_87_19.

[15] Nagarajappa R, Ramesh G, Uthappa R, Kannan SP, Shaikh S. Risk factors and patterns of traumatic dental injuries among Indian adolescents. Journal of Dental Sciences. 2020 Mar; 15(1): 96-103. doi: 10.1016/j.jds.2019.07.003.

[16] Memon M, Al Absi MA, Siya ZH, Memon A, Shaikh AG. Analysis of Types and Causes of Traumatic Dental Injuries to Permanent Dentition among Patients Attending Tertiary Care Hospital of Pakistan.Open Journal of Stomatology.2020 Jul; 10(8): 211-7. doi: 10.4236/ojst.2020.108020.

[17] Shrestha D and Upadhyay S. Pattern of traumatic dental injuries and associated risk factors: a hospital-based study. Orthodontic Journal of Nepal. 2018 Oct; 8(1): 40-4. doi: 10.3126/ojn.v8i1.21347.

[18] Marcenes W, Beiruti NA, Tayfour D, Issa SJ. Epidemiology of traumatic injuries to the permanent incisors of 9-12-year-old school children in Damascus, Syria. Dental Traumatology. 1999 Jun; 15(3): 117-23. doi : 10.1111/j.1600-9657.1999.tb00767.x.

[19] Okolo CC, Oredugba FA, Denloye OO, Adeyemo YI. The risk factors and pattern of traumatic dental injuries in 10-12-year olds in Kano, Nigeria. Nigerian Postgraduate Medical Journal.2022 Jul; 29(3): 272-7. doi: 10.4103/npmj.npmj_145_22.

[20] Abdel Malak C, Chakar C, Romanos A, Rachidi S. Prevalence and etiological factors of dental trauma among 12-and 15-year-old schoolchildren of Lebanon: a national study. The Scientific World Journal.2021 Mar; 2021(1): 5587431. doi: 10.1155/2021/5587431.

[21] Gaffar B, AlHumaid J, Ashraf Nazir M, Alonaizan F. Traumatic dental injuries in the Eastern Region of Saudi Arabia: Factors influencing teachers' management practices. Dental Traumatology.2021 Feb; 37(1): 65-72. doi: 10.1111/edt.12598.

[22] Bawazir OA, Alqoair AI, Alayed YN. Sport-related dental trauma and mouthguard use among athletes in Riyadh, Saudi Arabia: A cross-sectional survey. World. 2022 Jan; 13(1): 21-5. doi: 10.5005/jp-journals-10015-1897.

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Original Article

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Assessment of Various Tooth Brushing Techniques and its Association with Dental Plaque

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ABSTRACT

Dental plaque and poor oral hygiene are well-known risk factors for gingivitis, periodontitis, and other dental diseases. Using a manual toothbrush to remove plaque mechanically is essential for maintaining good oral hygiene every day and avoiding dental problems. Consequently, different toothbrushes are assessed to evaluate their effectiveness in plaque removal. **Objective:** To find the association between types of tooth brushing techniques and dental plaque in school children. **Methods:** A cross-sectional study was conducted in schoolchildren aged 15-18 years and convenience sampling was used to get data from the sample size of 211. Utilizing SPSS version 26.0, the data were examined to determine frequencies and percentages. The chi-square test was utilized to investigate potential associations of plaque with brushing techniques. **Results:** It showed that 58.3% of the children were male, while 41.7% were female. A majority (76.8%) used toothpaste, 59.2% brushed once daily, a smaller group brushed thrice a day (10%) and 45% have never visited a dentist. The Modified Bass technique proved the most effective, with 42.2% showing no plaque. The vertical and combined techniques showed moderate plaque levels, highlighting the significant impact of the brushing technique on plaque accumulation, as shown by the p-value of <0.001. **Conclusion:** The study revealed that the Modified Bass technique had the highest rate of reducing plaque, while horizontal brushing showed the greatest plaque buildup.

INTRODUCTION

Dental plaque is a soft, non-mineralized bacterial deposit that adheres to tooth surfaces and cannot be removed by water alone. Mechanical methods like brushing and flossing are required, with brushing being the most effective approach [1]. High dental disease rates in children result from host factors, microorganisms, parental behavior, and poor hygiene [2]. Tooth brushing is a widely recommended contemporary practice and serves as the main method for maintaining oral hygiene [3]. Dental plaque, a microbial biofilm on tooth surfaces, is a key cause of periodontal diseases like gingivitis and periodontitis. Plaque buildup near the gingival margin triggers inflammation, which worsens as the biofilm matures but resolves completely when the biofilm is removed [4]. The effective plaque removal relies on both the type and technique of toothbrushing. Over the past 20 to 30 years, various brushing techniques have been recommended, including the Bass, Stillman, Charters, horizontal, Fones, and roll methods [5].Brushing techniques vary in brush movements (horizontal, vertical, circular) and bristle alignment with the gingiva and tooth surfaces, affecting removal of plaque [6]. There is no agreement among dental professionals and companies on manual toothbrushing techniques. Brushing twice daily with fluoride toothpaste for two minutes is essential, yet manual brushing often leaves plaque, particularly on lingual surfaces. Bristle splaying and wear from prolonged use reduce plaque removal efficiency, increase gingivitis risk, and may

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damage teeth and gums, making timely toothbrush replacement crucial for effective oral hygiene. Studies examine plaque removal effectiveness by toothbrush type, technique, and frequency [7]. Studies have explored how plaque removal differs by toothbrush type, technique, and brushing frequency. While dental professionals recommend brushing for at least two minutes twice daily, guidelines from associations are limited, and actual brushing times often range from 30 to 60 seconds [8]. Modern dentifrices, available as pastes or gels, support tooth brushing and deliver agents that help prevent calculus, reduce plaque, protect against cavities, whiten teeth, and relieve sensitivity in exposed roots. Mild abrasives and detergents assist in plaque removal, though the abrasives may cause damage to exposed root surfaces [9]. Effective plaque control depends on proper hygiene tools, training, and motivation, highlighting the importance of tooth brushing in children's oral health.

The study aimed to find the relationship between various brushing methods and plaque buildup in school children.

METHODS

A cross-sectional study was conducted involving school children, carried out during the 10/1/24 to 10/7/24. The Lahore Medical and Dental College's Ethical Review Board granted ethical approval (LMDC/FD/65/24). The Open Epi calculator version 3.01 was calculated to be 200, using a 5% margin of error, a confidence interval of 95%, and a prevalence of 15.3% on Open Epi [10]. However, the 211 sample size was calculated due to missing data and dropouts. The data were collected by using convenience sampling technique. The consent form outlined the objectives, procedures, assurances of confidentiality, and dedication to scientific integrity. Participants were invited to inquire or seek clarification regarding any section of the consent form. They were also made aware of their rights to refuse or withdraw from the study at any time. A pilot survey was conducted on 10 students to validate the questionnaire before the beginning of the study. The study included healthy, cooperative school children aged 15-18 in both sexes, without mental and physical disabilities. Children with orthodontic or prosthodontic appliances, caries, periodontal issues, or any chemical agents for preventing plaque or oral infections were excluded. Information was gathered on age, gender, school type, tooth cleaning material, dentist visits, toothbrush types, and brushing techniques. Written consent was obtained from parents. The oral examinations were performed in natural daylight using a mouth mirror and a dental explorer to assess the Plaque visually. Plaque levels were assessed using the Silness and Loe plaque index (1964), with scores ranging from 0 to 3: Excellent (0), Good (0.1–0.9), Moderate (1–1.9), and Poor (2–3). The distobuccal, buccal, mesiobuccal, and lingual surfaces of six selected teeth (16, 12, 24, 36, 32, 44) were examined to calculate plaque scores. The plaque index (PI) was determined as the average of the area scores. Plaque was measured on four surfaces (distal, facial, mesial, and lingual) of the cervical portion of the teeth using an explorer. Scoring criteria were as follows: 0 indicated no plaque, 1 denoted plaque detectable by a probe but not visible, 2 represented moderate plaque visible to the naked eye, and 3 indicated an abundance of soft plaque [11]. Data analysis was conducted with SPSS version 26.0, where descriptive statistics, including percentages and frequencies, were calculated. A chi-square test assessed the relationship between tooth-brushing techniques and plaque index. A significance level (p-value) of ≤ 0.05 was deemed statistically significant.

RESULTS

It showed that the majority of the children were male (58.3%) and aged 17-18 (72.5%). Toothpaste was the most used as a cleaning material (76.8%). Over half (54.5%) had visited a dentist (Table 1).

Table 1: Showing the Demographic Information of the School Children (n:211)

Variables		Frequency (%)
Gender of Children	Male	123 (58.3)
	Female	88 (41.7)
Age	15-16	58 (27.5)
	17-18	153 (72.5)
Tooth Cleaning Material Used	Toothpaste	162 (76.8)
	Powder	37 (17.5)
	Nothing	12 (5.7)
Frequency of Brushing	Once a Day	125 (59.2)
	Twice a Day	57 (27)
	Thrice a Day	21 (10)
	None	8 (3.8)
Dental Visit	Yes	115 (54.5)
	No	96 (45.5)
Frequency of Dental Visit	Every 3 Months	26 (12.3)
	Whenever Needed	90 (42.7)
	Never	95 (45)

The Modified Bass technique shows the highest percentage (54.5%) of "No plaque" cases, while horizontal brushing has the most cases with abundant plaque (56.7%). P-value (<0.001) indicates a significant difference in plaque outcomes among the techniques, favoring modified bass (Table 2).

Table 2: Association between Types of Tooth Brushing and Plaque Index

Plaque Index	Brushing technique				P-Value
	Modified Bass	Horizontal	Vertical	Combined	
0= No Plaque	18	5	8	2	>0.001
	54.5%	15.2%	24.2%	6.1%	

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1= Plaque on Free Gingival Margin	11	18	12	15	
	19.6%	32.2%	21.4%	26.8%	
2= Moderate Plaque	7	24	11	12	
	13.0%	44.4%	20.4%	22.2 %	
3= Abundance of Soft Matter	6	34	11	9	
	10%	56.7%	18.3%	15.0%	

DISCUSSION

According to present study, 58.3% of the children were male. Most participants (76.8%) used toothpaste for cleaning, while 59.2% brushed once a day. Additionally, 54.5% reported visiting the dentist, and 45% had never visited one. Regarding dental visits, 12.3% went every three months, 42.7% visited when needed, and 45% never visited. In research on tooth brushing habits, Davidovich *et al.*, found that most kids (63.5%) used manual toothbrushes, 36.3% used electric toothbrushes that could be recharged, and 72% of kids brushed their teeth twice a day [12]. According to the study, over 60% of participants visited the dentist less frequently than every two years, with 22.7% never going, and only 9% attending regular checkups. Regarding dental hygiene behaviors, 53% brushed twice daily, while the use of mouth rinse (11%) and interdental cleaning was infrequent, occurring in only 3% of the participants [13]. Current study's findings showed that the Modified Bass approach was the most successful in lowering plaque, with 42.2% of participants showing no plaque. In contrast, the horizontal brushing technique resulted in 44% of children having abundant plaque. An earlier study reported that the forty-six orthodontic patients compared modified Bass and Charter's techniques, showing similar plaque removal effectiveness across all tooth surfaces as present results [14]. On the contrary, the study showed that the most commonly used brushing technique among children was the combined method (42.9%), followed by the horizontal technique (32.6%), the circular method (15.2%), and the least used was the vertical technique (9.3%) [10]. In a study with participants aged 12.161±0.493 years, both Group A and B showed good plaque scores, with the Bass method being significantly more effective in plaque reduction compared to other techniques ($p<0.001$) [15]. Previous studies revealed significant differences in brushing techniques recommended for adults and youngsters. The Bass and its modified version were typically advised for adults, while the Scrub and Fones techniques were more common for youngsters. The Modified Bass procedure proved superior in removing plaque, especially on lingual and buccal sites [16]. The American Academy of Pediatric Dentistry guidelines clearly explained that plaque buildup was strongly linked to the caries in young children and was important for assessing risk, particularly in preschoolers [12]. Another study demonstrated that the effectively optimized tooth brushing technique reduced dental diseases. It also found that toothbrush type significantly facilitated plaque removal, while brushing frequency was key in preventing oral diseases.[17]. Moreover, it was observed that 15- to 16-year-olds had lower plaque levels, indicating improvements in oral hygiene compared to the 11- to 12-year-old group [18]. Therefore, manual toothbrushes effectively remove dental plaque, although, mastering effective tooth brushing requires practice and professional training. Previous research on disseminating training through mass media showed unsatisfactory outcomes due to a lack of repetition and reinforcement [19]. Parents and teachers can promote behavior change by delivering dental health education through methods and media tailored to the child's developmental stage, ensuring effective and age-appropriate learning [20].

CONCLUSIONS

The majority of children were using toothpaste for oral hygiene and it was revealed that the Modified Bass approach was the most successful in keeping teeth free of plaque and 54.5% of children showed no plaque (P-value < 0.001 while the horizontal technique had the poorest outcomes (56.7% with abundant plaque). These findings highlight the need for school-based oral health education, parental guidance on effective techniques like the Modified Bass method, and improved access to dental care.

Authors Contribution

Conceptualization: SLSS
Methodology: SLSS
Formal Analysis: SLSS, AH, ZK
Writing Review and Editing: AH, RS

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Weng L, Wen J, Cui G, Liang J, Pang L, Lin H. Comparison of Modified Bass, Rolling, and Current Toothbrushing Techniques for the Efficacy of Plaque Control–A Randomized Trial. Journal of Dentistry. 20 23 Aug; 135: 104571.

[2] Ngatemi PT, Kasihani NN. Independence of Brushing Teeth to Free-Plaque Score in Preschool Children: A Cross Sectional Study. Indian J Forensic Med Toxicol. 2021 Jul;15(3):3722-7.

DOI:https://doi.org/10.54393/pjhs.v5i12.2376

[3] Adamu VE, Eneojo NI, Eze CJ. Tooth Brushing Techniques among Pupils Attending a Nigerian Unity Basic School. Orapuh Journal. 2020 Jun; 1(1): 703.

[4] Deinzer R, Weik U, Eidenhardt Z, Leufkens D, Sälzer S. Manual toothbrushing techniques for plaque removal and the prevention of gingivitis—A systematic review with network meta-analysis. Plos one. 2024 Jul 5;19(7):e0306302.https://doi.org/10.1371/journal.pone.0306302.

[5] Rajwani AR, Hawes SN, To A, Quaranta A, JC RA. Effectiveness of Manual Toothbrushing Techniques on Plaque and Gingivitis: A Systematic Review. Oral health & preventive dentistry. 2020 Oct; 18(1): 843-854.

[6] Kaneyasu Y, Shigeishi H, Niitani Y, Takemoto T, Sugiyama M, Ohta K. Manual toothbrushes, self-toothbrushing, and replacement duration to remove dental plaque and improve gingival health: A scoping review from recent research. Journal of Dentistry. 2024 Jul 20:105240.https://doi.org/10.1016/j.jdent.2024.105240

[7] Silva FH, Montagner AF, Silveira MC, Muniz FW. Antiplaque and antigingivitis efficacy of new and worn manual toothbrushes: A systematic review and meta-analysis. International Journal of Dental Hygiene. 2023 Feb;21(1):95-105.https://doi.org/10.1111/idh.1264.

[8] Pavani B, Anu V, Cinthiya GS, Deepika V, Ayesha MS, Reddy AA. The Effect of Toothbrushing Duration on Plaque Removal: A Randomized Crossover Trial. Journal of Datta Meghe Institute of Medical Sciences University. 2023 Jul; 18(3): 369-371. doi:10.4103/jdmimsu.jdmimsu_16_22.

[9] Pullishery F, Abuzenada BM, Alrushnudi NM, Alsafri MM, Alkhaibari WM, Alharbi MF, *et al.* Comparison of Efficacy of Different Supervision Methods of Toothbrushing on Dental Plaque Scores in 7–9-year-old Children. International Journal of Clinical Pediatric Dentistry.2021 Mar; 14(2): 263. doi: 10.5005/jp-journals-10005-1927.

[10] Ibrahim RE, Helaly MO, Ahmed EM. Assessment of Brushing Techniques in School Children and its Association with Dental Caries. International Journal of Dentistry. 2021; 2021(1). doi: 10.1155/2021/4383418.

[11] Naureen H, Firdous SN, Ali S, Shafeeq S, Haider I. Effect of Proper Tooth Brushing Technique on Dental Plaque Among School Going Children. Pakistan Journal of Medicine and Dentistry.2024 Oct 24;13(4):49-https://doi.org/10.36283/ziun-pjmd13-4/007.

[12] Davidovich E, Grender J, Zini A. Factors Associated with Dental Plaque, Gingivitis, and Caries in a Pediatric Population: A Records-Based Cross-Sectional Study. International Journal of Environmental Research and Public Health. 2020 Nov; 17(22): 8595. doi: 10.3390/ijerph17228595

[13] Khalifa N, Allen PF, Abu-bakr NH, Abdel-Rahman ME, Abdelghafar KO. A Survey of Oral Health in a Sudanese Population. BMC Oral Health. 2012 Dec; 12: 1-9.

[14] Shabbir A, Syed K, Khan AS, Shah SL. Comparison of Plaque Removal Efficacy of Modified Bass Technique and Charter's Technique in Orthodontic Patients. Pakistan Journal of Medical & Health Sciences.2023 Mar; 17(03): 130. doi: 10.53350/pjmhs2023173130.

[15] Naureen H, Firdous SN, Ali S, Shafeeq S, Haider I. Effect of Proper Tooth Brushing Technique on Dental Plaque Among School Going Children. Pakistan Journal of Medicine and Dentistry.2024 Oct; 13(4): 49-57. doi: 10.36283/ziun-pjmd13-4/007.

[16] Kushali R, Ravindran V. Dentists's Preference of Brushing Technique Taught to Children with Permanent Dentition. International Journal of Dentistry Oral Science.2021 Sep; 8(9): 4500-4504. doi: 10.19070/2377-8075-21000915.

[17] Skorfu H, Kurt S, Atalar F, Olamat A, Ersoy A. Analysis of a New Toothbrushing Technique through Plaque Removal Success. Open Journal of Stomatology. 2024;14(03).https://doi.org/10.4236/ojst.2024.143012

[18] Eidenhardt Z, Ritsert A, Shankar-Subramanian S, Ebel S, Margraf-Stiksrud J, Deinzer R. Tooth Brushing Performance in Adolescents as Compared to the Best-Practice Demonstrated in Group Prophylaxis Programs: An Observational Study. BMC Oral Health. 2021 Dec; 21: 1-6. doi: 10.1186/s12903-021-01692-z.

[19] Jeong JS, Kim KS, Lee JW, Kim KD, Park W. Efficacy of Tooth Brushing via a Three-Dimensional Motion Tracking System for Dental Plaque Control in School Children: A Randomized Controlled Clinical Trial. BMC Oral Health.2022 Dec; 22(1): 626. doi: 10.1186/s12903022-02665-6.

[20]Purnama T, Rasipin R, Ngatemi N. Tedi's behavior change model to improving brushing teeth behavior parents. Journal of Applied Health Management and Technology. 2020 Feb 1;2(1):1-2.DOI: https://doi.org/10.31983/jahmt.v2i1.5475.

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Micronutrient Profiles in Severe Acute Malnutrition: Analyzing Vitamin B12, Zinc, Copper, Selenium, Manganese, Molybdenum, and Cobalt Levels

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ABSTRACT

Severe Acute Malnutrition (SAM) is a critical public health issue affecting millions of people globally. **Objective:** To evaluate the status of micronutrients and their relationship with malnutrition severity. **Methods:** A cross-sectional study was conducted over six months from November 2023 to April 2024 at Pead's Department Of Khairpur Medical College, KhairpurMirs. The study included 384 participants diagnosed with SAM. Micronutrient levels were assessed using quantitative colorimetry. Statistical analyses were descriptive, independent t-tests, Pearson and Spearman correlation analyses to evaluate micronutrient deficiencies. **Results:** The mean age of the children was 24.5 months, with a male predominance of 54.7%. Micronutrient levels showed significant variation between children with mild and severe malnutrition: p = 0.03), zinc (62.7 vs. 55.8 µg/dl, p = 0.01), vitamin B12 (312.4 vs. 278.6 pg/ml, p = 0.02), copper (97.3 vs. 89.2 µg/dl, p = 0.03), and selenium (45.7 vs. 40.2 µg/l, p < 0.05). Positive correlations between micronutrient levels and anthropometric variables were found by correlation analysis. Logistic regression indicated that deficiencies in Vitamin B12 (OR: 1.45, p = 0.02), Zinc (OR: 1.62, p = 0.01), and Copper (OR: 1.35, p = 0.03) were significant predictors of severe malnutrition. **Conclusions:** The findings emphasized that the need for targeted nutritional interventions addressing Vitamin B12, Zinc, and Copper deficiencies to improve health outcomes in malnourished children. Further research was essential to evaluate the impact of supplementation strategies on growth and recovery.

INTRODUCTION

Severe acute malnutrition (SAM) is a leading cause of childhood mortality, mostly due to Gram-negative infections. It has been found that micronutrient deficiencies, including Vitamin B12, Zinc, Copper, Selenium, Manganese, Molybdenum and Cobalt are important in the etiology and treatment of SAM. Nutrients play an essential role in various metabolic functions, quality of immunological response and also for the growth in children [1]. In fact, Stand's report found that more than 40% of all the children under five worldwide went anemia. The most common type of anemia is due to micronutrient deficiencies, such as iron, folate and vitamin B12-based deficiencies. In SAM, anemia is rife with iron deficiency as the most prevalent stimulant [2]. Childhood is a critical stage for growth and development, which in turn are influenced by numerous factors including dietary intake. Among these parameters, micronutrients are one of the critical requirements that are necessary for various biological functions Vitamins and Minerals: These are micronutrients needed for the enzyme and protein productions that assist metabolic process, as well as immunological function, health proliferation [3, 4].

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Sufficient intake of all essential micronutrients in the diets of children is crucial for normal growth, cognitive development and avoidance of deficiency related diseases. Micronutrients are not just required for growth also function as regulators of numerous biochemical pathways that operate in physiological and developmental reactions [5]. Vitamin B12 deficiencies, as well as low levels of Zinc, Copper and Selenium have been associated with growth retardation, developmental delay and an increased susceptibility to infections [6]. Micronutrients are important indicators of nutritional status in children, especially those affected by Severe Acute Malnutrition (SAM)[7]. SAM is associated with dramatic weight loss and nutritional deficiencies that can cause significant health consequences. Assessment of micronutrient status among this vulnerable group could shed light on their nutritional requirements and mitigate specific therapeutic strategies which are conducive to achieve better health outcome [8]. Vitamin B12 deficiency is a long-known problem, especially in exclusively breast-fed newborn infants of mother's low in this vital mineral. Babies need adequate amount of vitamin B12 for healthy growth and development, particularly in the initial phase of life from feeding is their only source of nutrients. Babies born to vitamin B12-deficient mothers are also at risk for a deficiency, as the breast milk of these women may not provide enough of this crucial nutrient [9]. This situation is so common in deprived communities of mother nourishing or with very strict food restrictions, e.g. strict vegetarians and vegans. In infants, deficiency can lead to a wide range of impairments such as sensory neuropathy, myelopathy, motor disturbances or paraplegia failure to thrive and developmental delays which may be irreversible thus making routine monitoring for Vitamin B12 in maternal postpartum Prescription in critically ill children an everyday emergency. Given the importance of vitamin B12 for normal growth and development, the nutritional status of mums and babies should be monitored and intervened on as appropriate, particularly in high-risk groups. Early recognition and treatment of vitamin B12 inadequacy will be beneficial for breastfeeding infants [10].

To evaluate the status of micronutrients and their relationship with malnutrition severity.

METHODS

A cross-sectional study was carried out from November 2023 to April 2024 at Pead's department of Khairpur medical college, Khairpur Mirs after getting approval with IRB reference number KMC/RERC/84. The formula for estimating a proportion in a population was n=Z2·P·(1–P) / d2, where Z=1.96Z = 1.96Z=1.96 (for a 95% confidence interval), prevalence (P=50%) and d=0.05 (5% margin of error), n=0.9604/ 0.0025=384.16. The sample size was N=384 participants. Children who meet the inclusion criteria for Severe Acute Malnutrition (SAM), including bilateral nutritional edema or a Mid-Upper Arm Circumference (MUAC) of less than 115 mm, aged between six months and five years. Signed consent in writing from parents or legal guardians was obtained. Children with chronic infections, congenital disorders, metabolic conditions, kidney diseases, or liver diseases were excluded from this study. A digital scale was used to measure weight, recording it to the nearest 100 grams. A stadiometer was used to measure height (for children over two years), and an infant meter was used to measure the length of the child. A non-stretchable tape was used to measure the Mid-Arm Circumference (MAC) of the left arm, midway between the olecranon and acromion processes. Using WHO tables, the weight for height and length was determined. Head Circumference (HC), Chest Circumference (CC), Mid-Arm Circumference (MAC), and length/height measurements were recorded to the nearest 0.5 cm, mm, and cm, respectively. 3 ml of venous blood were drawn. Hemagglutinin-treated blood was used for the hemogram, and serum from plain tubes was used to assess micronutrients and Vitamin B12. WHO criteria were used to define anemia, vitamin B12 level below 203 pg/ml was taken as deficient and that above 911 pg/ml were taken as high range. Zinc and copper were considered deficient, if levels were < 65 µg/dl and < 63.5 µg/dl. Other micronutrients were considered deficient if, selenium (< 60 µg/dl and manganese < 7.10 µg/dl, molybdenum < 0.70 µg/dl and cobalt<1.0 µg/dl. Samples were sent in a cold chain to the testing facility (Arogyam Centre, Navi Mumbai) after being kept at -80°C. A chemiluminescent immunoassay was used to assess Vitamin B12 (Advia Centaur XP, Siemens). Colorimetric techniques (Elico, Hyderabad) were utilized to assess serum copper and zinc, while Thermo Fisher's ICP-MS was employed to analyze other micronutrients [11]. With SPSS version 26.0, data analysis was done. Descriptive statistics were used to collect clinical and demographic information. For continuous variables, means and standard deviations were computed. The micronutrient levels in children with mild and severe forms of malnutrition were compared using independent t-tests. A Pearson or Spearman correlation analysis was used to look at the relationships between anthropometric markers and micronutrient levels. The predictive value of micronutrient deficiencies for the severity of malnutrition was ascertained by the application of logistic regression analysis.

RESULTS

Severe Acute Malnutrition (SAM) was identified in 384 of the study's participants. Given that the children's mean age was 24.5 ± 6.3 months, it was clear that the majority of the sample's participants were young children the majority

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being two years old. Out of the total number of children, 210 (54.7%) were male and 174 (45.3%) were female. As the gender differences were not particularly noticeable, this suggests a slight male predominance in the research population. The children's mean weight was 6.8 ± 2.1 kg, which was considerably less than what was normal for youngsters of this age, indicating that the participants were malnourished. The average Mid-Upper Arm Circumference (MUAC) was 113.5 ± 12.7 mm, while the average height was 65.4 ± 5.2 cm (Table 1).

Table 1: Descriptive Statistics of Demographic and Clinical Features (n = 384)

Variables	Mean ± SD/N (%)
Age (Months)	24.5 ± 6.3
Age (Months)	24.5 ± 6.3
Gender	
Male	210 (54.7%)
Female	174 (45.3%)
Weight (Kg)	6.8 ± 2.1
Height (cm)	65.4 ± 5.2
MUAC (mm)	113.5 ± 12.7
Degree of Malnutrition	
Mild	160 (41.7%)
Severe	224 (58.3%)

The children who suffered from severe malnutrition had considerably lower levels of vitamin B12 (278.6 ± 52.3 pg/ml) than the children who suffered from moderate malnutrition (312.4 ± 56.7 pg/ml). A p-value of 0.02 indicated a serious deficit in the severe cases. With a p-value of 0.01 zinc levels were similarly substantially lower in the severe malnutrition group (55.8 ± 10.1 µg/dl) than in the mild malnutrition group (62.7 ± 11.3 µg/dl). A p-value of 0.03 indicated a significant decrease in copper levels between severely malnourished children (89.2 ± 15.5 µg/dl) and mildly malnourished children (97.3 ± 14.9 µg/dl). The severe malnutrition group had considerably lower selenium levels (40.2 ± 7.6 µg/l) than the moderate group (45.7 ± 8.5 µg/l) (p-value = 0.04). Manganese levels were similar in both groups (p = 0.15), with mean values of 9.8 ± 2.3 µg/l for severe malnutrition and 10.4 ± 2.7 µg/l for mild malnutrition. Molybdenum levels were not significantly different (p = 0.09), with mean values of 4.2 ± 1.2 µg/l for severe and 4.7 ± 1.1 µg/l for mild deficiency. Children with severe malnutrition had significantly lower cobalt levels (0.54 ± 0.3 µg/l) than those with mild malnutrition (0.65 ± 0.2 µg/l) (p-value = 0.04), see Table 2.

Table 2: Comparison of Micronutrient Levels between Mild and Severe Malnutrition (Independent t-test)

Micronutrient	Standard Values	Mild Malnutrition (Mean ± SD)	Severe Malnutrition (Mean ± SD)	p-value
Vitamin B12 (pg/mL)	< 200-900 pg/mL	312.4 ± 56.7	278.6 ± 52.3	0.02*
Zinc (µg/dL)	< 70-120 µg/dL	62.7 ± 11.3	55.8 ± 10.1	0.01*
Copper (µg/dL)	< 70-140 µg/dL	97.3 ± 14.9	89.2 ± 15.5	0.03*
Selenium (µg/L)	<70-150 µg/L	45.7 ± 8.5	40.2 ± 7.6	0.04*
Manganese (µg/L)	< 4-15 µg/L	10.4 ± 2.7	9.8 ± 2.3	0.15
Molybdenum (µg/L)	0.2-1.5 µg/L	4.7 ± 1.1	4.2 ± 1.2	0.09
Cobalt (µg/L)	0.2-1.0 µg/L	0.65 ± 0.2	0.54 ± 0.3	0.04*

*Significant at p < 0.05

The statistical analysis revealed significant positive relationships between micronutrient levels and anthropometric indicators, with vitamin B12, zinc, and copper having the highest associations. Zinc showed the strongest correlation values with weight (r = 0.35, p < 0.05), height (r = 0.32, p < 0.05), and MUAC (r = 0.33, p < 0.05), demonstrating a substantial link with growth indices. Vitamin B12 had a significant connection with weight (r = 0.31, p < 0.05), height (r = 0.27, p < 0.05), and MUAC (r = 0.29, p < 0.05). Copper had moderate but statistically significant relationships with weight (r = 0.28, p < 0.05), height (r = 0.25, p < 0.05), and MUAC (r = 0.21, p < 0.05). Selenium, Manganese, Molybdenum, and Cobalt had lesser correlations that did not achieve statistical significance, with R-values ranging from 0.09 to 0.22 and p > 0.05, showing a less meaningful relationship with the anthropometric markers. Thus, zinc, vitamin B12, and copper were more important in determining the growth and nutritional condition of children with severe acute malnutrition see Table 3.

Table 3: Correlation between Micronutrient Levels and Anthropometric Markers (Pearson or Spearman Correlation)

Micronutrient	Weight (Kg) (R-Value)	Height (cm) (R-Value)	MUAC (mm) (R-Value)
Vitamin B12 (pg/mL)	0.31*	0.27*	0.29*
Zinc (µg/dL)	0.35*	0.32*	0.33*
Copper (µg/dL)	0.28*	0.25*	0.21*
Selenium (µg/L)	0.22	0.20	0.18
Manganese (µg/L)	0.15	0.14	0.12
Molybdenum (µg/L)	0.10	0.12	0.09
Cobalt (µg/L)	0.20	0.17	0.15

*Significant at p < 0.05

Significant predictors included Vitamin B12 deficiency (OR: 1.45 [95% CI: 1.12 - 1.89], P = 0.02), with children who were deficient in vitamin B12 having 45% increased odds of malnutrition. Zinc deficiency was also strongly associated with severe malnutrition, OR 1.62, 95% (CI): 1.23 -2.14 p =0.01, suggesting a relative risk of +62%. The deficiency of copper also showed highly significant association with (OR = 1.35, 95% CI: 1.05 - 1.74, p = 0.03) where risk of severe malnutrition was increased for a person consuming diet

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deficient in Copper by appxiciently factor of 35%. Positive association was also seen with selenium deficiency, but it did not reach statistical significance (OR = 1.28; 95% CI: 0.98–1.67; p = 0.08). No significant association was observed for Severe Malnutrition with Manganese deficiency (OR = 1.10; 95% CI: 0.85 -1.42; p = 0.27) and Molybdenum deficiency (OR = 1.20; 95% CI: 0.94-1.54, p = 0.15). Cobalt deficiency had a borderline significant association, with an OR of 1.32 (95% CI: 1.00-1.74; p = 0.05), suggesting the potential for increased likelihood of implant revision due to aseptic loosening see Table 4.

Table 4: Logistic Regression for Predictive Value of Micronutrient Deficiencies for Severe Malnutrition

Variables	Odds Ratio (OR)	95% Confidence Interval (CI)	p-Value
Vitamin B12 Deficiency	1.45	1.12-1.89	0.02*
Zinc Deficiency	1.62	1.23-2.14	0.01*
Copper Deficiency	1.35	1.05-1.74	0.03*
Selenium Deficiency	1.28	0.98-1.67	0.08
Manganese Deficiency	1.10	0.85-1.42	0.27
Molybdenum Deficiency	1.20	0.94-1.54	0.15
Cobalt Deficiency	1.32	1.00-1.74	0.05*

*Significant at $p < 0.05$

DISCUSSION

Developmental delays were linked to deficiency in vital micronutrients in children with Severe Acute Malnutrition (SAM), namely in zinc, copper, selenium, manganese, molybdenum, and cobalt. These data indicate clear biologically plausible associations between a subset of the vitamins and severity of malnutrition, as has been supported by previous research [12]. There were slightly more males (54.7%) and the average age was 24.5 months according to patient demographics. The present outcomes associate with other previous literature on childhood undernutrition among children of similar age groups as rapid growth and development pose particular risks to the young ones. The proportion of medical data linked with children with severe malnutrition (58.3%) was in accordance with available information from other countries, further emphasizing the ongoing public health challenge posed by SAM in kids from this age group [13]. According to these results to showed significant differences between mild and severe malnourished children in mean values of Vitamin B12, Zinc, Copper and Selenium [14]. Previous research demonstrates that malnourished children consistently show low levels of the micronutrients, suggesting that deficiencies in these nutrients exacerbate malnutrition and associated morbidities. Previous research by Arfi *et al.*, in 2022 stressed the importance of zinc in immune function and growth, with zinc deficiency associated with morbidities including malnutrition in children [15]. In the present study to reveals that of correlations between vitamin B12, Zinc and Copper levels with anthropometric parameters (Weight, Height and MUAC) means being positively associated [16]. In the current study to found that, the study variables; vitamin B12, zinc and copper deficiencies were significant predictors for cases of severe malnutrition [17, 18]. Vitamin B12 deficiency indicate a meaningful risk that was why even more nursing research was needed in Pakistan to investigate this phenomenon as has been identified and found a significant association of Vitamin B12 deficiency with severe malnutrition among young children [19]. Zinc deficiency, with an OR of 1.62 highlights the critical role plays in normal immune function and overall childhood growth. Kurmi *et al.*, 2023 have previously shown that zinc supplementation could protect from malnutrition and reduced disease manifestation in immunocompromised, destitute populations [20].

CONCLUSIONS

The objective was to ascertain the frequency of nutritional deficiencies and their correlation with the demographics, socioeconomic status, and severity of childhood malnutrition. The marked unadjusted relationships noted for Vitamin B12, Zinc, Copper illustrate specific candidates for targeted nutrition interventions to correct these deficiencies among children with SAM.

Authors Contribution

Conceptualization: UB
Methodology: MAB, BAB, KA
Formal analysis: MAB, FKA
Writing, review and editing: AAK, FKA

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Yaikhomba T, Poswal L, Goyal S. Assessment of iron, folate and vitamin B12 status in severe acute malnutrition.The Indian Journal of Pediatrics.2015 Jun;82: 511-4. doi: 10.1007/s12098-014-1600-7.

[2] Verma GK, Chand R, Khan IA, Kumar A, Yadav RK. Association of developmental milestones with vitamin B12 and folate status among hospitalized severe acute malnutrition children at a tertiary care center in North India. MGM Journal of Medical Sciences.2023 Apr;10(2) : 235-40. doi: 10.4103/mgmj.MGMJ_34_23.

[3] Dos Santos ME, da Silva KG, da Silva Souza AP, da Silva

DOI:https://doi.org/10.54393/pjhs.v5i12.2423

AB, da Silva RF, da Silva EH *et al*. Relationship between vitamin B12 levels and motor development: a systematic review. Clinical Nutrition ESPEN.2024 Jun.doi: 10.1016/j.clnesp.2024.06.026.

[4] Chen Y, Liu X, Li B, Li J, Meng L, Ye C et al. Explorative case control study on the associations of serum vitamin D3, folic acid and vitamin B12 levels on Kawasaki disease and coronary artery lesions. Frontiers in Nutrition. 2024 Jun;11: 1402316. doi: 10.3389/fnut.2024.1402316.

[5] Godswill AG, Somtochukwu IV, Ikechukwu AO, Kate EC. Health benefits of micronutrients (vitamins and minerals) and their associated deficiency diseases: A systematic review. International Journal of Food Sciences. 2020 Jan 7;3(1):1-32. DOI:10.47604/ijf.1024.

[6] Peroni DG, Hufnagl K, Comberiati P, Roth-Walter F. Lack of iron, zinc, and vitamins as a contributor to the etiology of atopic diseases. Frontiers in Nutrition. 2023 Jan 9;9:1032481. doi: 10.3389/fnut.2022.1032481

[7] Alflah YM, Alrashidi MA. Severe acute malnutrition and its consequences among malnourished children. Journal of Clinical Pediatrics Research. 2023;2(1):1-5. doi: 10.2147/JMDH.S428873

[8] Kumar M, Kumar D, Sharma A, Bhadauria S, Thakur A, Bhatia A. Micronutrients throughout the Life Cycle: Needs and Functions in Health and Disease. Current Nutrition & Food Science. 2024 Jan; 20(1): 62-84. doi: 10.2174/1573401319666230420094603.

[9] Collins S, Dent N, Binns P, Bahwere P, Sadler K, Hallam A. Management of severe acute malnutrition in children. The Lancet. 2006 Dec;368(9551): 1992-2000. doi: 10.1016/S0140-6736(06)69443-9.

[10] Vishwakarma B and David A. Underlying risk determinants of acute and moderate malnutrition in children and its preventive management. Pharmaceutical and Biosciences Journal.2021 Aug: 01-11. doi: 10.20510/10.20510/pbj/9/i4/1640.

[11] Kamath L, Ratageri VH, Kanthi AS, Fattepur SR, Desai RH. Status of vitamin B12, zinc, copper, selenium, manganese, molybdenum and cobalt in severe acute Malnutrition.Indian Journal of Pediatrics. 2023 Oct;90(10):988-93.

[12] Saleem J, Zakar R, Bukhari GM, Fatima A, Fischer F. Developmental delay and its predictors among children under five years of age with uncomplicated severe acute malnutrition: a cross-sectional study in rural Pakistan. BioMed Central Public Health.2021 Dec;21: 1-0. doi: 10.1186/s12889-021-11445-w.

[13] Gavhi F, Kuonza L, Musekiwa A, Motaze NV. Factors associated with mortality in children under five years old hospitalized for Severe Acute Malnutrition in Limpopo province, South Africa, 2014-2018: A cross-sectional analytic study. PLOS One.2020 May;15(5): e0232838. doi: 10.1371/journal.pone.0232838.

[14] Atiq A, Shah D, Sharma S, Meena RK, Kapoor S, Gupta P. Prevalence and Predictors of Vitamin B12 Deficiency in Children with Severe Acute Malnutrition, and its Association with Development. Indian Journal of Pediatrics.2023 Nov: 1-7. doi: 10.1007/s12098-023-04909-x.

[15] Arfi N, Khatoon K, Alim F. Zinc malnutrition in children and its consequences on health. Microbial biofertilizers and micronutrient availability: the role of zinc in agriculture and human health.2022:35-67. DOI: 10.1007/978-3-030-76609-2_2

[16] Bahati YL, Delanghe J, Balaluka GB, Philippé J. Exploration of the relationship between anemia and iron and zinc deficiencies in children under 5 years of age living in the malaria endemic area of South Kivu/Democratic Republic of Congo. Annals of Hematology. 2022 Jun;101(6):1181-9. doi: 10.1007/s00277-022-04816-9.

[17] Berger MM, Pantet O, Schneider A, Ben-Hamouda N. Micronutrient deficiencies in medical and surgical inpatients. Journal of clinical medicine. 2019 Jun; 8(7): 931. doi: 10.3390/jcm8070931.

[18] Joshi S, Tabassum N, Mobeen A, Bora J. Micronutrients. In: Food Fortification. Boca Raton: CRC Press; 2024. 33-54. doi: 10.1201/97810031606633.

[19] Adhaulia A, Maurya M, Tiwari AD. Developmental delay in children with severe acute malnutrition and its association with vitamin B12 deficiency. Indian Journal of Child Health. 2019; 6(10): 548-51. doi:1.10.18203/2349-3291.ijcp20194721.

[20]Kurmi A, Jayswal DK, Saikia D, Lal N. Current Perspective on Malnutrition and Human Health. InNano-Biofortification for Human and Environmental Health 2023 Aug 11 (pp. 155-177). Cham: Springer International Publishing. DOI:10.1007/978-3-031-35147-1_9.

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Comparison of Suprachoroidal Triamcinolone Injection and Modified Grid Laser in Treatment of Refractory Diabetic Macular Edema

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ABSTRACT

Diabetic macular edema is the leading cause of blindness in diabetic eye disease. The most important cause of visual impairment is diabetes-induced macular edema also called DME which involves central part of the macula lutea. **Objective:** To compare the outcome of suprachoroidal triamcinolone injection and modified grid laser in the treatment of refractory diabetic macular edema. **Methods:** This prospective cohort study was done for 12 months (January 2021 to December 2021) on 56 patients having refractory diabetic macular edema. The technique of non-probability consecutive sampling was used. Patients in Group A received a suprachoroidal injection of 4 mg triamcinolone. Patients in Group B underwent modified grid photocoagulation. After 4 months of treatment, the patients' visual acuity and central macular thickness were assessed again using Snellen's chart and Optical Coherence Tomography (OCT) respectively. **Results:** After 4 months, the mean BCVA in Group-A was 0.57 + 0.127 and in Group-B was 0.83 + 0.150 (P=0.000) while the mean improvement (change line) was 1.6 + 0.318 and 0.89 + 0.229 (P=0.001), respectively In Group-A, improvement in Central Macular Thickness (CMT) was observed in 24 (85.7%) patients, while in Group-B, improvement in Central Macular Thickness was seen in 17 (60.7%) patients. After 4 months, the mean CMT in Group-A was 302.68 + 14.427 um and in Group-B was 339.71 + 54.821 um (P=0.009) while the mean improvement (change) was 153.89 + 30.902 um and 95.57 + 41.111 um (P=0.024), respectively. **Conclusion:** Suprachoroidal triamcinolone injection was found to be more effective than modified grid laser in treatment of DME.

INTRODUCTION

Diabetes is major health issue of the 21st century [1]. Worldwide 425 million patients are diabetic presently and it is projected that this figure can approach 629 million in 2045 [2]. A microvascular consequence of diabetes called diabetic retinopathy affects around 34.6% of diabetic people. Diabetic macular edema (DME) is a complication of diabetic retinopathy that affects 6.8% of diabetic patients. It is a major cause of blindness [3]. Diabetic macular edema can be present at any stage of diabetic retinopathy (DR), however, as the disease advances there are more chances of developing Diabetic macular edema [4]. High blood sugar level, hypertension, low blood protein levels, and smoking are major risk factors of DME [5]. Macular edoema is defined as an abnormal accumulation of fluid within the macula's retinal layers [6] A delicate balance between fluid entering and leaving the retinal layers usually exists. To maintain tissue transparency, this balance is necessary for retinal homeostasis [7]. Macular edoema is characterized by fluid deposition between the retinal layers, resulting in progressive vision deterioration that can lead to chronic vision loss [8]. Due to metabolic changes and inflammatory responses, diabetic individuals may also experience loss of

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endothelial tight junctions and subsequent blood-retinal barrier (BRB) disruption [9]. DME Treatment has achieved major change over the years. Previously photocoagulation by Argon laser was a treatment option for DME and it was discovered by the Early Treatment of Diabetic Retinopathy Study (ETDRS) group. More than 50% decreased incidences of moderate visual loss with reduction in central macular thickness (CMT) were observed in treated eyes after 03 years of macular laser [10]. However, many complications occurred like subretinal fibrosis, choroidal neovascularization (CNV), visual field scotomas and progressive photoreceptor atrophy, due to grid and focal macular laser [11]. Anti-VEGF injections have been demonstrated by Diabetic Retinopathy Clinical Research Network (DRCR.net) to be a more effective and safe form of treatment for DME, with better visual results [12]. Numerous researches have looked into the pharmacologic properties of the suprachoroidal region for administering medications, particularly triamcinolone acetonide, to the eye [13]. For the treatment of DME, advanced methods are being used i.e. Injection Suprachoroidal Triamcinolone Acetonide so an alternative treatment option could be tried for refractory DME [14].

The study aimed to compare the outcome of suprachoroidal triamcinolone injection and modified grid laser in treatment of refractory diabetic macular edema.

METHODS

This prospective cohort study was done in 12 months (January 2021 to December 2021) with 56 patients, 28 in each group, with refractory diabetic macular edema in the Ophthalmology Department of Services Hospital Lahore. Prior informed consent was taken from the study participants. The duration of the study was 12 months, after approval of synopsis. Participants with age 40-80 years, both genders were included in the study. Patients already taken treatment of intravitreal corticosteroids, peribulbar steroid injection in last 6 months, photocoagulation 15 weeks before, panretinal scatter photocoagulation four months before, or PPV (on medical record), patients who had open-angle glaucoma or steroid-induced rise of intraocular pressure and needed treatment to decrease intraocular pressure and patients with intraocular pressure ≥25 mm Hg were excluded from the study. Diabetic macular edema with central macular thickness more than 300 micrometers. A sample size of 56 cases; 28 in each group, was calculated with 80% power of the study, 5% level of significance, and confidence level of 95%, and taking an expected percentage of improvement in central macular thickness i.e. 63% with Suprachoroidal triamcinolone [15] and 37% with Modified Grid Laser [16] by using the following formula:

$$n = (Z\alpha/2+Z\beta)2 * (p1(1-p1) + p2(1-p2)) / (p1-p2)2$$

The non-probability consecutive sampling technique was used. Subjects were divided into two groups using the lottery method. Patients in Group A received a suprachoroidal injection of 4 mg triamcinolone. Patients in Group B underwent modified grid photocoagulation. After 4 months of treatment, the patient's visual acuity and central macular thickness were assessed again using Snellen's chart and OCT respectively. The hospital ethical committee of SIMS approved the study (Ref No. IRB/2020/735/SIMS), which involved 56 patients. The researcher performed every procedure, explained it to the patients, and obtained their informed consent. Every patient's profile was noted, including their gender, age, diabetes duration, HbA1c, lateral side, and duration of ocular symptoms. Subjects were then split into two groups at random using the lottery method. Subjects in group A received a suprachoroidal injection of triamcinolone at a dose of 4 mg/0.1ml. Subjects in group B received modified grid photocoagulation. Visual acuity and central macular thickness were measured at the beginning point. Then, patients were checked on at the OPD at 7 days, 1- and 4-month intervals. After four months of intervention, the patients underwent a second evaluation of their visual acuity using the Snellen chart and an OCT scan to measure the central macular thickness. On the Snellen chart, improvements in visual acuity of one or more lines were detected. On optical coherence tomography, it was observed that the central macular thickness had decreased by more than 50% from the starting point. On the proforma, all the information was accurately recorded. Data analysis was done using the SPSS software, version 20,0. After stratification, the outcomes of the two groups were compared using the chi-square test and t-test for each stratum, with a p-value of 0.05 was considered significant.

RESULTS

Table indicates that in Group-A, improvement in visual acuity was observed in 25 (89.3%) patients while in Group B, improvement was observed in 21 (75.0%) patients (P=0.016) showing there is a significant association present. For non-improvement also significant association was found between the groups with a p-value of 0.001.

Table 1: Comparison of Improvement in Visual Acuity between Groups

Visual Acuity	Group – A (Suprachoroidal Triamcinolone Injection)	Group – B (Modified Grid Laser)	Chi-Square = 1.913
	Frequency (%)	Frequency (%)	P-Value
Improved	25 (89.3%)	21 (75.0%)	0.016
Not Improved	3 (10.7%)	7 (25.0%)	0.001
Total	28 (100%)	28 (100%)	–

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Table 2 shows that among both groups of patients, improvement after 4 months of treatment was observed regarding BCVA (best-corrected visual acuity) with a statistically significant difference. Pretreatment mean BCVA in Group-A was 0.920.104, while 1.070.411 in Group-B. After 4 months, the mean BCVA in Group-A was 0.570.127 and in Group-B was 0.860.150 (P=0.000) and the p-value suggest significance statistically as p-value is less than 0.05, while the mean lines improvement was 1.60.318 and 0.890.229 (P=0.001) and this p-value shows there is significant association between the two groups, respectively.

Table 2: Comparison of Mean BCVA between Groups

Mean BCVA (logMAR)	Group – A (Suprachoroidal Triamcinolone Injection)	Group – B (Modified Grid Laser)	T-Test P-value
Baseline	0.92 0.104	1.07 0.411	0.011
After 4 Months	0.57 0.127	0.86 0.150	0.000
Change	1.71 0.713	0.65 0.629	0.001
Lines Improvement	1.6 0.318	0.89 0.229	0.001

Table 3 asserts that 24 (85.7%) patients were observed having improvement in central macular thickness in Group-A while 17 (60.7%) patients showed improvement in Group-B (P=0.010) and shows statistical significance between groups and for non-improvement the p-value is 0.016 which also shows significant statistically.

Table 3: Comparison of Improvement in Central Macular Thickness Between Groups

CMT	Group – A (Suprachoroidal Triamcinolone Injection)	Group – B (Modified Grid Laser)	P-value
Improved	24 (85.7%)	17 (60.7%)	0.010
Not Improved	4 (14.3%)	11 (39.3%)	0.016
Total	28 (100.0%)	28 (100.0%)	-

Table 4 depicts that among both groups' patients' improvement after 4 months of treatment was observed regarding CMT (central macular thickness) with statistically significant difference. After 4 months, the mean CMT in Group-A was 302.68+14.427 um and in Group-B was 339.71+54.821 um (P=0.009). A p-value of 0.009 revealed statistically significant difference, indicating Group A had a greater reduction in CMT, while the mean improvement (change) was 153.89+30.902 um and 95.57+41.111 um (P=0.024), respectively. There was no statistically significant difference in baseline CMT between the groups with a p-value of 0.051.

Table 4: Comparison of Mean Central Macular Thickness between Groups

Mean CMT (um)	Group – A (Suprachoroidal Triamcinolone Injection)	Group – B (Modified Grid Laser)	T-Test P-value
Baseline	456.57 + 40.428	435.50 + 57.953	0.051
After 4 Months	302.68 + 14.427	339.71 + 54.821	0.009
Change	153.89 + 30.902	95.57 + 41.111	0.024

Table 5 elucidates that among Group A and B, patients who were <50 years old, the mean BCVA was 0.560.114 and 0.80142 (P=0.107) respectively, while among patients who were >50 years old, the mean BCVA was 0.58151 and 0.900.149 (P=0.149) respectively. However, Group-A and B, patients who were <50 years old, the mean CMT was 304.24+17.587 um and 323.1148.306 um (P=0.000) respectively, while among patients who were >50 years old, the mean CMT was 300.277.525 um and 374.78+53.427 um (P=0.000), respectively.Group-A and B patients, who had duration of diabetes <5 years, the mean BCVA was 0.530.176 and 0.880.114 (P=0.003) respectively. While patients who had duration of diabetes >5 years, the mean BCVA was 0.590.096 and 0.790.169 (P=0.005) respectively. However, Group-A and B patients, who had a duration of diabetes <5 years, the mean CMT was 302.11+13.214 and 354.3158.774 (P=0.000), respectively. Among patients who had da duration of diabetes >5 years, the mean CMT was 302.9515.310 um and 327.07+49.658 um (P=0.036), respectively.

Table 5: Comparison of Age and Duration of Diabetes with Mean BCVA (logMAR) and Mean CMT (µm) after Treatment between Groups

Category	Group A Mean BCVA (logMAR)	Group B Mean BCVA (logMAR)	T-Test P-value (BCVA)	Group A Mean CMT (µm)	Group B Mean CMT (µm)	T-Test P-value (CMT)
Age <50 yrs	0.56 ± 0.114	0.80 ± 0.142	0.107	304.42 ± 17.587	323.11 ± 48.306	0.000
Age <50 yrs	0.58 ± 0.151	0.90 ± 0.149	0.149	300.27 ± 7.525	374.78 ± 53.427	0.000
Duration <5 years	0.53 ± 0.176	0.88 ± 0.114	0.003	302.11 ± 13.214	354.31 ± 58.774	0.000
Duration <5 years	0.59 ± 0.096	0.79 ± 0.169	0.005	302.95 ± 15.310	327.07 ± 49.658	0.036

DISCUSSION

Diabetes mellitus is thought to be the leading global health problem of the twenty-first century, and diabetic macular edema is a major cause of blindness in diabetic eye disease. The DME involving the Macular Centre is a major cause of vision loss. Argon grid laser and intravitreal triamcinolone acetonide have been used to treat patients who have not responded to anti-VEGF endothelial growth factor agents. Currently, triamcinolone injected through the suprachoroidal pathway has demonstrated comparable efficacy with less risk of increased intraocular pressure. As

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a result, the current study compared the efficacy of modified grid laser and suprachoroidal triamcinolone injection in the treatment of refractory diabetic macular edoema. To acquire adequate results, 56 patients were included in the study and divided into two equal groups (28 patients in each group) namely Group A and -B. In Group-A, patients were treated with Suprachoroidal Triamcinolone Injection (STI) while in Group-B, patients were treated with Modified Grid Laser (MGL). Age is a leading factor as increasing age boosts the severity of diseases. It is believed that elderly patients are more affected by diabetic macular edema due to the long duration of diabetes. The findings of our study showed that in both groups (Suprachoroidal Triamcinolone Injection [STI] and Modified Grid Laser [MGL]) more than half of the patients were up to 50 years old (60.7% vs. 67.9%) while the remaining proportion was above 50 years old. (39.3% vs. 32.1%). The mean age of the patients in the STI group was 49.46+5.022 years while in the MGL group was 49.82+5.004 years. However, the findings of a study undertaken by Abdelshafy Tabl *et al* [17] showed that the mean age of the patients treated with STI was 55+3 years while a study done by Khanzada and colleagues [15] reported the mean age of the patients treated with MGL was 59.45+8.23 years. It was found during the study that most of the patients in both groups were female (STI: 53.6% vs. MGL: 60.7%). The results of our study are comparable with a study undertaken by Munir and associates who also confirmed that the disease was more prevalent among female patients (64.0%) treated with STI [18]. However, the results of a study conducted by Khanzada and colleagues highlighted that male patients (53.2%) treated with MGL were in the majority [16]. For DME, elevated HbA1c is also a major risk factor like several other risk factors namely diabetes duration, history of cardiovascular disease, and use of diuretics. The study demonstrated that patients in the STI group had a mean HbA1c of 9.036+0.5933% while in MGL group had 9.457+0.8561%. The results of a similar study carried out by Khanzada and colleagues [16] are better than our study results which reported that the mean HbA1c among patients with DME was 7.85+0.78%. The STI group was found much better than MGL groups regarding visual acuity as improvement was observed among 89.3% of patients in the STI group while 75.0% in the MGL group (P=0.016). When a comparison was made among patients of both groups regarding BCVA, the study showed better improvement among patients treated with suprachoroidal triamcinolone injection than with modified grid lasers. In the STI group, the mean BCVA (best-corrected visual acuity) was 0.920.104 at baseline and after 4 months of treatment was 0.570.127 while in the MGL group, the mean BCVA was 1.070.411 and after treatment was 0.860.150. The mean line improvement (change) after treatment in the STI group was observed better (1.60.318) than in the MGL group (0.890.229) with statistically significant results (P=0.001). When a mean comparison of BCVA was performed in both groups after treatment. Insignificant results (P>0.05) were found regarding age in both groups. For gender, significant results were in the STI group but insignificant results (P>0.05) in the MGL group. Insignificant results for the lateral side in both groups while significant results for the duration of diabetes and HbA1c in both groups. However, significant results for the duration of symptoms in the STI group while insignificant results for the MGL group. A study conducted by Tufan *et al* [19], revealed statistically not significant, best correct visual acuity (BCVA) improvement was observed in the third and sixth months following IVTA injection. A statistically significant decrease in central macular thickness (CMT) occurred in the third month, and this effect persisted after six months. Previous research has shown that intra-vitreal triamcinolone acetonide improves visual acuity (VA) and reduces diffuse macular edema. [20, 21]. Likewise, when the mean comparison of CMT was performed in both groups after treatment, significant results were found regarding age while insignificant results regarding gender. Insignificant results were found regarding the lateral side, while significant results regarding the duration of diabetes, HbA1c, and symptoms were found in both groups. A study conducted by Aslam *et al* [22] revealed that there was not any significant association between the two groups at baseline CMT with a p-value of 0.29, although a significant association was found at 3-month CMT with a p-value less than 0.001. There were not many complications found in either group.

CONCLUSIONS

This study concluded that suprachoroidal triamcinolone injection is superior to modified grid laser therapy for treating diabetic macular edema that is resistant to Anti-VEGF treatment.

Authors Contribution

Conceptualization: NA, MAA
Methodology: TR, NA
Formal analysis: NUA, HMUA
Writing, review and editing: NA, FR

All authors have read and agreed to the published version of the manuscript

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REFERENCES

[1] Hsia NY, Lin CJ, Chen HS, Chang CH, Bair H, Lai CT, *et al*. Short-Term Outcomes of Refractory Diabetic Macular Edema Switch from Ranibizumab to Dexamethasone Implant and the Influential Factors: A Retrospective Real-World Experience. Frontiers in Medicine.2021 Apr; 8: 649979. doi: 10.3389/fmed.2021.649979.

[2] Federation ID. IDF Diabetes Atlas 8th Edition. International Diabetes Federation. 2017; (1): 905-911.

[3] Yau JW, Rogers SL, Kawasaki R, Lamoureux EL, Kowalski JW, Bek T, *et al*. Global Prevalence and Major Risk Factors of Diabetic Retinopathy. Diabetes Care. 2012 Mar; 35(3): 556-64. doi: 10.2337/dc11-1909.

[4] He Y, Ren XJ, Hu BJ, Lam WC, Li XR. A Meta-Analysis of the Effect of a Dexamethasone Intravitreal Implant Versus Intravitreal Anti-Vascular Endothelial Growth Factor Treatment for Diabetic Macular Edema. BMC ophthalmology. 2018 Dec; 18: 1-1. doi: 10.1186/s12886-018-0779-1.

[5] Cosgrove, Benedict. 2020."8 Risk Factors for Diabetic Macular Edema." https://www.healthcentral.com/slideshow/dme-riskfactors(December 20, 2024).

[6] Daruich A, Matet A, Moulin A, Kowalczuk L, Nicolas M, Sellam A, *et al*. Mechanisms of Macular Edema: Beyond the Surface. Progress in Retinal and Eye Research. 2018 Mar; 63: 20-68. doi: 10.1016/j.preteyeres.2017.10.006.

[7] Sacconi R, Giuffrè C, Corbelli E, Borrelli E, Querques G, Bandello F. Emerging Therapies in the Management of Macular Edema: A Review. F1000 Research.2019; 8. doi: 10.12688/f1000research.19198.1.

[8] Vidal PL, de Moura J, Díaz M, Novo J, Ortega M. Diabetic Macular Edema Characterization and Visualization Using Optical Coherence Tomography Images. Applied Sciences. 2020 Oct; 10(21): 7718. doi: 10.3390/app10217718.

[9] Torabi H. Management of Refractory Diabetic Macular Edema: A Review Article. International Journal of Medical Reviews.2018 Mar; 5(1): 27-34. doi: 10.29252/IJMR-050105.

[10] Zakaria YG, Salman AG, Said AM, Abdelatif MK. Suprachoroidal Versus Intravitreal Triamcinolone Acetonide for the Treatment of Diabetic Macular Edema. Clinical Ophthalmology.2022 Mar: 733-46. doi: 10.2147/OPTH.S351853.

[11] Park YG, Kim EY, Roh YJ. Laser-Based Strategies to Treat Diabetic Macular Edema: History and New Promising Therapies. Journal of Ophthalmology. 2014; 2014(1): 769213. doi: 10.1155/2014/769213.

[12] Kuroiwa DA, Malerbi FK, Regatieri CV. New Insights in Resistant Diabetic Macular Edema. Ophthalmologica. 2021 Dec; 244(6): 485-494. doi: 10.1159/000516614.

[13] Fazel F, Malekahmadi M, Feizi A, Oliya B, Tavakoli M, Fazel M. Suprachoroidal Injection of Triamcinolone Acetonide Plus Intravitreal Bevacizumab in Diabetic Macular Edema: A Randomized Pilot Trial.BMC Ophthalmology. 2023 Jan; 23(1): 40. doi: 10.1186/s12886-023-02790-y.

[14] Yousef MS, Abd Elhafez YA, Farag MH. Assessment of Suprachoroidal Injection of Triamcinolone Acetonide in Cases of Diabetic Macular Edema. International Journal of Medical Arts.2021 Apr; 3(2): 1384-1389. doi: 10.21608/ijma.2021.55079.1230.

[15] Tayyab H, Ahmed CN, Sadiq MA. Efficacy and Safety of Suprachoroidal Triamcinolone Acetonide in Cases of Resistant Diabetic Macular Edema. Pakistan Journal of Medical Sciences.2020 Jan; 36(2): 42. doi: 10.12669/pjms.36.2.1194.

[16] Khanzada MA, Ahmed M, Mirza AA, Mari GK, Mahmood MA. Results of Intravitreal Bevacizumab as an Adjunct to mETDRS Grid Laser in Diabetic Macular Edema. Pakistan Journal of Ophthalmology. 2021; 37(1). doi:10.36351/pjo.v37i1.1135.

[17] Abdelshafy Tabl A, Tawfik Soliman T, Anany Elsayed M, Abdelshafy Tabl M. A Randomized Trial Comparing Suprachoroidal and Intravitreal Injection of Triamcinolone Acetonide in Refractory Diabetic Macular Edema Due to Epiretinal Membrane. Journal of Ophthalmology.2022; 2022(1): 7947710. doi: 10.1155/2022/7947710.

[18] Munir MS, Rehman R, Nazir S, Sharif N, Chaudhari MZ, Saleem S. Visual Outcome After Suprachoroidal Injection of Triamcinolone Acetate in Cystoid Macular Edema of Different Pathology. Pakistan Journal of Medical & Health Sciences.2022 May; 16(05):164-164. doi: 10.53350/pjmhs22165164.

[19] Tufan HA, Özdek Ş, Hasanreisoğlu B. Comparison of Intravitreal Triamcinolone Treatment and Intravitreal Triamcinolone with Grid Laser Treatment in Patients with Diffuse Diabetic Macular Edema. Balkan Medical Journal.2012 Jun; 2012(2): 166-169. doi: 10.5152/balkanmedj.2012.008.

[20] Jonas JB, Söfker A. Intraocular Injection of Crystalline Cortisone as Adjunctive Treatment of Diabetic Macular Edema. American Journal of Ophthalmology. 2001 Sep; 132(3): 425-427. doi: 10.1016/S0002-9394(01)01010-8.

[21] Martidis A, Duker JS, Greenberg PB, Rogers AH, Puliafito CA, Reichel E, et al. Intravitreal Iriamcinolone for Refractory Diabetic Macular Edema. Ophthalmology.2002 May; 109(5): 920-927. doi: 10.1016/S0161-6420(02)00975-2.

[22] Aslam M, Nazir T, Haq RI, Asghar A, Nadeem S, Obaid N. Efficacy of Suprachoroidal Versus Intravitreal

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Triamcinolone Acetonide in Refractory Macular Edema; A Quasi-experimental study. Pakistan Armed Forces Medical Journal.2024 Oct; 74(5): 1365. doi:10.51253/pafmj.v74i5.10818.

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Frequency and Clinical Correlates of Hypoalbuminemia in Colorectal Cancer Patients at A Tertiary Care Hospital

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ABSTRACT

Colorectal cancer is often associated with hypoalbuminemia, a marker of poor nutritional status and systemic inflammation. Low albumin levels in colorectal cancer patients are linked to worse outcomes, including higher morbidity and mortality. **Objectives:** To assess the frequency of hypoalbuminemia and its association with clinical and biochemical variables among colorectal cancer patients at Liaquat University Hospital, Hyderabad. **Methods:** This cross-sectional study was conducted from January 14, 2022, to July 13, 2022, at the Department of Surgery, Liaquat University Hospital, Hyderabad. 124 patients who were diagnosed with colorectal cancer aged between 20 to 60 years and of either gender were included in the study. Colorectal cancer was confirmed histopathologically. Patients with other gastrointestinal malignancies, chronic liver diseases, nephrotic syndrome, and those on corticosteroid or immune-suppressive therapy were excluded from the study. **Results:** The study identified the presence of hypoalbuminemia in n=73 (58.9%) of the patients. Among them, 38 (52.1%) were classified as obese (≥30.0), with a p-value of 0.001. The mean duration of the disease was found to be 49.2 ± 7.10 weeks, which also showed a significant correlation (p=0.01). Additionally, elevated C-reactive protein levels and erythrocyte sedimentation rates showed a strong association with hypoalbuminemia (p=0.001). Hypocalcaemia (34.2%) and hypomagnesemia (27.4%), were significantly associated with hypoalbuminemia. **Conclusions:** It was concluded that hypoalbuminemia is a prevalent and clinically significant condition among colorectal cancer patients. The high prevalence of hypoalbuminemia is strongly associated with obesity, longer disease duration, rural residency, elevated inflammatory markers,and electrolyte imbalances (hypocalcaemia, hypomagnesemia).

INTRODUCTION

Colorectal cancer (CRC) is one of the leading causes of cancer-related morbidity and mortality worldwide [1]. Accounting for a significant disease burden, CRC ranks among the most common cancers globally, affecting millions of individuals each year [2]. In recent decades, the global incidence of CRC has increased, particularly in developed countries, largely due to ageing populations and lifestyle changes such as diet, smoking, and decreased physical activity. Sedentary behaviours, high consumption of red and processed meats, low fiber intake, and obesity have been well-documented as risk factors contributing to this rise. Concurrently, improved diagnostic tools and awareness campaigns in developed nations have also led to earlier detection and an apparent rise in incidence rates [3]. In Pakistan, CRC has become increasingly prevalent, with cases primarily affecting individuals over 50 years of age, despite the country being historically considered a low-risk region for this malignancy [4]. The shift may be attributed to urbanization, dietary transitions, and inadequate screening practices. Unlike developed countries, where screening programs have been systematically implemented, the lack of such initiatives in Pakistan contributes to delayed diagnoses and a higher proportion of advanced-stage presentations. Additionally, sociocultural factors and limited healthcare access further exacerbate the burden of CRC in the region [5]. CRC is

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frequently associated with systemic complications, among which hypoalbuminemia stands out as an important prognostic marker. Albumin, a protein produced in the liver, is a major contributor to maintaining plasma oncotic pressure and transporting molecules such as hormones, fatty acids, and drugs [6]. Traditionally, serum albumin levels have been used to assess nutritional status, but in cancer patients, hypoalbuminemia is often linked to more complex factors, such as systemic inflammation and tumor burden [7]. Systemic inflammation in cancer, driven by cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), disrupts albumin synthesis and contributes to increased protein catabolism. Tumor-related cachexia, another hallmark of advanced cancer, also plays a key role in hypoalbuminemia [8]. Hypoalbuminemia has profound clinical implications for CRC patients. Some studies have reported that hypoalbuminemia occurs in up to 60% of patients with CRC [9], and is associated with poor prognosis, including increased postoperative complications, prolonged hospitalization, and mortality [10]. Furthermore, hypoalbuminemia often reflects a combination of malnutrition, disease progression, and inflammatory responses, making it a valuable marker for assessing overall patient health and predicting outcomes. In surgical CRC patients, low preoperative albumin levels are linked to delayed wound healing, infections, and an elevated risk of morbidity and mortality, highlighting the need for early identification and intervention [11]. In low- and middle-income countries like Pakistan, the management of hypoalbuminemia in CRC is particularly challenging due to limited access to nutritional support and palliative care. Despite its clinical importance, hypoalbuminemia remains an under-recognized issue in resource-constrained settings, further emphasizing the need for comprehensive care strategies.

The study aims to assess the frequency of hypo-albuminemia in patients with CRC at the University Hospital and to investigate the association of hypo-albuminemia with various demographic and clinical factors such as disease stage, comorbidities and inflammatory markers between different types

METHODS

This cross-sectional study was conducted over from January 14, 2022, to July 13, 2022, at the Department of Surgery, Liaquat University Hospital, Hyderabad. 124 patients who were diagnosed with colorectal cancer aged 20-60 years and of either gender were included in the study. Colorectal cancer was confirmed histopathologically. The inclusion criteria focused on adult patients within this age range to minimize the impact of extreme age-related variables on hypoalbuminemia and to align with the typical age range for CRC onset in Pakistan. Patients with other gastrointestinal malignancies, chronic liver diseases, nephrotic syndrome, and those on corticosteroid or immune-suppressive therapy were excluded to eliminate confounding factors that independently contribute to hypoalbuminemia and systemic inflammation. The sample size was calculated via WHO Open Epi software by taking the prevalence of hypoalbuminemia in Colorectal Cancer Patients as 8.85% with a 5% margin of error and 95% confidence interval [12]. Informed consent was taken. The study was approved by the Ethical Review Committee of Liaquat University of Medical & Health Sciences, Jamshoro vide letter No. LUMHS/REC/-110; dated. CRC diagnosis was confirmed histopathologically through biopsies obtained during colonoscopy or surgical procedures. The staging of CRC was conducted using the tumor/node/metastasis (TNM) classification system, developed by the American Joint Committee on Cancer (AJCC) [13]. This TNM classification system evaluates tumor size (T), regional lymph node involvement (N), and distant metastasis (M), providing a comprehensive assessment of disease progression. Demographic data, clinical history, and laboratory results were recorded for each patient. Serum albumin levels were measured using venous blood samples collected under standardized fasting conditions. CRP levels were quantified using a high-sensitivity immune-turbid-metric assay. Hypoalbuminemia was defined as serum albumin levels <3.5 g/dL, based on standard clinical thresholds for malnutrition and inflammation. Additional parameters included body mass index (BMI), C-reactive protein (CRP) levels, serum creatinine, serum calcium, magnesium and serum bilirubin, erythrocyte sedimentation rate (ESR), and comorbidities such as hypertension, diabetes mellitus, and smoking status. Quality controls and standard calibration protocols for all laboratory parameters were implemented to ensure the reliability and reproducibility of results. Duration of disease was also noted, and the relationship between these variables and hypoalbuminemia was analyzed. Data analysis was performed using SPSS version 22.0. Frequencies and percentages were calculated for categorical variables, while means and standard deviations were calculated for continuous variables. The chi-square test was used to assess the significance of the association between hypoalbuminemia and the other variables of interest. A p-value≤0.05 was considered statistically significant.

RESULTS

Among 124 patients, the mean age was 57.83 ± 8.65 years, with a slightly higher proportion of male (54%) than female (46%). The majority (61.3%) were from rural areas, and nearly half (46%) were classified as obese (BMI≥30.0).

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Notably, 52.4% had diabetes mellitus, 37.9% had hypertension, and 36.3% were smokers. Biochemically, inflammatory markers were elevated in a significant portion of patients, with 54% showing elevated CRP and 58.1% elevated ESR. Hypoalbuminemia was also linked with low calcium levels (25%) and low magnesium levels (20.2%). Elevated bilirubin and creatinine levels were observed in 34.7% and 13.7% of patients, respectively (Table 1).

Table 1: Demographics and Clinical Characteristics of Colorectal Cancer Patients (n=124)

Characteristics	Value
Mean Age (years)	57.83 ± 8.65
Gender	
Male	67 (54%)
Female	57 (46%)
Residential Area	
Rural	76 (61.3%)
Urban	48 (38.7%)
BMI Category	
Underweight (<18.5)	8 (6.5%)
Normal weight (18.5–24.9)	32 (25.8%)
Overweight (25.0–29.9)	27 (21.0%)
Obesity (≥30.0)	57 (46.0%)
Mean Duration of Disease (weeks)	48.62 ± 7.93
Comorbidities	
Hypertension	47 (37.9%)
Smoking	45 (36.3%)
Diabetes Mellitus	65 (52.4%)
Biochemical Profile	
Elevated CRP	67 (54.0%)
Elevated ESR	72 (58.1%)
Raised Creatinine	17 (13.7%)
Raised Bilirubin	43 (34.7%)
Hypocalcemia	31 (25.0%)
Hypomagnesemia	25 (20.2%)

The frequency of hypoalbuminemia in colorectal cancer patients was found to be 58.9% (n=73). A comparison of the patients with and without hypoalbuminemia revealed that patients with hypoalbuminemia had a slightly higher mean age (58.2 years) compared to those without (56.1 years). A larger proportion of rural residents (67.1%) exhibited hypoalbuminemia compared to urban patients (32.9%). Obesity (BMI ≥30.0) was significantly more common in hypoalbuminemia patients (52.1%) versus those without (15.7%), and they also had a longer mean disease duration (49.2 vs. 37.2 weeks). In terms of clinical markers, hypoalbuminemia was strongly associated with elevated CRP (76.7% vs. 21.6%) and ESR (83.6% vs. 21.6%). Biochemical disturbances, such as hypocalcaemia and hypomagnesemia, were also more prevalent in hypoalbuminemia patients (Table 2).

Table 2: Hypoalbuminemia Distribution in Associated Factors

Characteristics	Hypoalbuminemia Present (n=73)	Hypoalbuminemia Absent (n=51)
Mean Age (years)	58.2 ± 8.45	56.1 ± 8.80
Gender		
Male	39 (53.4%)	28 (54.9%)
Female	34 (46.6%)	23 (45.1%)
Residential Area		
Rural	49 (67.1%)	27 (52.9%)
Urban	24 (32.9%)	24 (47.1%)
BMI Category		
Underweight (<18.5)	4 (5.5%)	4 (5.5%)
Normal Weight (18.5–24.9)	15 (20.5%)	17 (33.3%)
Overweight (25.0–29.9)	16 (21.9%)	11 (21.6%)
Obesity (≥30.0)	38 (52.1%)	8 (15.7%)
Mean Duration of Disease (Weeks)	49.2 ± 7.10	37.2 ± 8.80
(Comorbidities) Hypertension		
Present	30 (41.1%)	17 (33.3%)
Absent	43 (58.9%)	34 (66.7%)
Smoking		
Present	28 (38.4%)	17 (33.3%)
Absent	45 (61.6%)	34 (66.7%)
Diabetes Mellitus		
Present	38 (52.4%)	27 (52.9%)
Absent	35 (47.6%)	24 (47.1%)
Biochemical Markers		
Elevated CRP	56 (76.7%)	11 (21.6%)
Elevated ESR	61 (83.6%)	11 (21.6%)
Raised Creatinine	12 (16.4%)	5 (9.8%)
Raised Bilirubin	30 (41.1%)	13 (25.5%)
Hypocalcemia	25 (34.2%)	6 (11.8%)
Hypomagnesemia	20 (27.4%)	5 (9.8%)

Among the 73 patients with hypoalbuminemia, 38 (52.1%) were classified as obese (≥30.0), with a p-value of 0.001. The mean duration of the disease (measured from the onset of symptoms) was found to be 49.2 ± 7.10 weeks, which also showed a significant correlation (p=0.01). Hypoalbuminemia in colorectal cancer patients was strongly associated with obesity (52.1%, p=0.001) and elevated inflammatory markers, including CRP (76.7%, p=0.001) and ESR (83.6%, p=0.001). A moderate association was observed with longer disease duration (49.2 weeks, p=0.01), hypocalcaemia (34.2%, p=0.01), and hypomagnesemia (27.4%, p=0.02), highlighting the roles of systemic inflammation, chronic illness, and nutritional imbalances in its development (Table 3).

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Table 3: Prevalence of Hypoalbuminemia and Clinical Correlations(n=73)

Characteristics	Hypoalbuminemia (n=73)	p-value
Obesity (≥30.0)	38 (52.1%)	0.001
Mean Duration of Disease (Weeks)	49.2 ± 7.10	0.01
Elevated CRP	56 (76.7%)	0.001
Elevated ESR	61 (83.6%)	0.001
Hypocalcemia	25 (34.2%)	0.01
Hypomagnesemia	61 (83.6%)	0.02

DISCUSSION

The prevalence of hypoalbuminemia in this study was 58.9%, a figure consistent with global reports on CRC patients. The study identified key associations of hypoalbuminemia with factors such as obesity, prolonged disease duration, elevated inflammatory markers (CRP and ESR), and biochemical disturbances, notably hypocalcaemia and hypomagnesemia. In terms of prevalence, the rate of hypoalbuminemia observed in this study (58.9%) closely matches that reported in similar populations globally. A study from South Korea found that 55% of CRC patients undergoing surgery had hypoalbuminemia, a figure nearly identical to this study [14]. The high prevalence can be attributed to a combination of chronic inflammation, cancer-related cachexia, and malnutrition common factors in CRC patients worldwide. The association between obesity (BMI ≥30.0) and hypoalbuminemia observed in the current study contributes to the expanding research on the obesity paradox in cancer patients. Despite being categorized as obese, patients in the cohort displayed hypoalbuminemia, a phenomenon that has been similarly reported in other studies. For instance, one review done by a Cancer Research Group in Spain found that obesity and malnutrition coexist in cancer patients due to metabolic dysregulation and systemic inflammation [15]. This contrasts with findings from a multicentre study conducted in China, where underweight patients are often at a higher risk of hypoalbuminemia [16]. In the current study, inflammation—indicated by elevated C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) was strongly linked to hypoalbuminemia. Specifically, 76.7% of patients with hypoalbuminemia had elevated CRP levels, and 83.6% showed elevated ESR levels. These results are consistent with international research that emphasizes the significant role of systemic inflammation in the onset of hypoalbuminemia in cancer patients. For example, a meta-analysis by Sofic et al., in 2021 confirmed that elevated CRP and ESR are key predictors of hypoalbuminemia in colorectal cancer (CRC) patients, suggesting that chronic inflammation caused by the tumour or cancer-related cachexia contributes to lower albumin levels [17]. The inflammatory response, often persistent in CRC patients, triggers the release of cytokines such as IL-6 and TNF-α, which inhibit albumin production and increase protein breakdown, worsening malnutrition and hypoalbuminemia [18]. A study in Saudi Arabia by Almasaudi et al., has also observed significant associations between hypoalbuminemia and low calcium and magnesium levels in cancer patients, suggesting a multifaceted origin of these imbalances involving poor nutrition, inflammation, and the direct metabolic impact of cancer [11]. Interestingly, no significant relationship was found between hypoalbuminemia and age or residential background, implying that demographic factors may play a lesser role in its development among CRC patients. Instead, clinical factors such as disease duration, comorbidities, and inflammation seem to have a greater influence on serum albumin levels [19]. These findings underscore the importance of a holistic approach to managing hypoalbuminemia in CRC patients, focusing not only on nutritional interventions but also on controlling systemic inflammation and addressing comorbidities [20]. Clinically, these associations underscore the need for early nutritional and inflammatory management strategies to improve patient outcomes and mitigate complications associated with hypoalbuminemia. However, the relatively small sample size and single-centre design may limit the generalizability of the results to broader populations.

CONCLUSIONS

It was concluded that hypoalbuminemia is frequently observed in colorectal cancer patients and is significantly associated with obesity, longer disease duration, rural residency, elevated inflammatory markers (CRP and ESR), and electrolyte imbalances (hypocalcemia and hypomagnesemia). These findings highlight the important roles of systemic inflammation and metabolic dysfunction in the development of hypoalbuminemia within this population. Clinically, these associations underscore the need for early nutritional and inflammatory management strategies to improve patient outcomes and mitigate complications associated with hypoalbuminemia.

Authors Contribution

Conceptualization: TN
Methodology: TN, SN, AMB, AIM
Formal analysis: MM, FM
Writing review and editing: SN, AMB

All authors have read and agreed to the published version of the manuscript

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REFERENCES

[1] Xi Y and Xu P. Global Colorectal Cancer Burden in 2020 and Projections to 2040. Translational Oncology.2021 Oct; 14(10): 101174. doi: 10.1016/j.tranon.2021.101174.

[2] Hossain MS, Karuniawati H, Jairoun AA, Urbi Z, Ooi DJ, John A *et al*. Colorectal Cancer: A Review of Carcinogenesis, Global Epidemiology, Current Challenges, Risk Factors, Preventive and Treatment Strategies. Cancers.2022 Mar; 14(7): 1732. doi: 10.3390 /cancers14071732.

[3] Roshandel G, Ghasemi-Kebria F, Malekzadeh R. Colorectal Cancer: Epidemiology, Risk Factors, and Prevention.Cancers.2024 Apr; 16(8): 1530. doi: 10.3390 cancers16081530.

[4] Khan S, Masood Ai, Tahir M. Association Analysis Between Age and Colorectal Cancer. Age(Years). 202 0;40(54): 77-15.

[5] Khan SZ and Lengyel CG. Challenges in the Management of Colorectal Cancer in Low-and Middle-Income Countries. Cancer Treatment and Research Communications.2023 Jan; 35: 100705. doi: 10.1016/j. ctarc.2023.100705.

[6] Soeters PB, Wolfe RR, Shenkin A. Hypoalbuminemia: Pathogenesis and Clinical Significance. Journal of Parenteral and Enteral Nutrition.2019 Feb; 43(2): 181-9 3.doi: 10.1002/jpen.1451.

[7] Rawla P, Sunkara T, Barsouk A. Epidemiology of Colorectal Cancer: Incidence, Mortality, Survival, and Risk Factors. Gastroenterology Review/Przegląd Gastroenterologiczny.2019 Jan; 14(2): 89-103. doi: 10.5 114/pg.2018.81072.

[8] Das A and Chaudhuri S. Prevalence of Anaemia and Hypoalbuminemia in Newly Diagnosed Carcinoma Cases: A Real World Experience. Journal of Cardiovascular Disease Research. 2023; 14(10): 679-638. doi: 10.48047/jcdr.2023.14.10.80.

[9] Christina NM, Tjahyanto T, Lie JG, Santoso TA, Albertus H, Octavianus D *et al*. Hypoalbuminemia and Colorectal Cancer Patients: Any Correlation? A Systematic Review and Meta-Analysis. Medicine. 2023 Feb; 102(8): E32938. doi: 10.1097/MD.000000000 0032938.

[10] Do Woong Choi J, Kwik C, Vivekanandamoorthy N, Shanmugalingam A, Allan L, Gavegan F *et al*.Is Preoperative Hypoalbuminemia or Hypoproteinemia a Reliable Marker for Anastomotic Leakage Risk in Patients Undergoing Elective Colorectal Surgery in an Enhanced Recovery After Surgery (Eras) Program? International Journal of Colorectal Disease. 2023 May; 38(1): 152. doi: 10.1007/s00384-023-04450-5.

[11] Almasaudi AS, Dolan RD, Edwards CA, Mcmillan DC. Hypoalbuminemia Reflects Nutritional Risk, Body Composition and Systemic Inflammation and Is Independently Associated with Survival in Patients with Colorectal Cancer. Cancers.2020 Jul; 12(7): 1986. doi: 10.3390/cancers12071986.

[12] Hu WH, Eisenstein S, Parry L, Ramamoorthy S. Preoperative Malnutrition with Mild Hypoalbuminemia Associated with Postoperative Mortality and Morbidity of Colorectal Cancer: A Propensity Score Matching Study. Nutrition Journal. 2019 Dec; 18: 1-7. doi: 10.1186/ s12937-019-0458-y.

[13] Amin MB, Greene FL, Edge SB, Compton CC, Gershenwald JE, Brookland RK *et al*. The Eighth Edition Ajcc Cancer Staging Manual: Continuing to Build a Bridge from A Population-Based to A More "Personalized" Approach to Cancer Staging. Ca: A Cancer Journal for Clinicians.2017 Mar; 67(2): 93-9. doi : 10.3322/caac.21388.

[14] Chen WS, Huang YS, Xu LB, Shi MM, Chen XD, Ye GQ *et al*. Effects of Sarcopenia, Hypoalbuminemia, and Laparoscopic Surgery On Postoperative Complications in Elderly Patients with Colorectal Cancer: A Prospective Study. Neoplasma.2020 Jul; 67 (4). doi: 10.4149/neo_2020_190908N882.

[15] Kang B, Zhao ZQ, Liu XY, Cheng YX, Tao W, Wei ZQ et al. Effect of Hypoalbuminemia On Short-Term Outcomes After Colorectal Cancer Surgery: A Propensity Score Matching Analysis. Frontiers in Nutrition.2022 Aug; 9: 925086. doi: 10.3389/fnut.2022.925086.

[16] Constantin GB, Mihailov R, Serban C, Firescu D, Voicu D, Rebegea L *et al*. The Impact of Hypoalbuminemia On Patients with Complicated Colon Cancers, Operated in Emergency. Romanian Journal of Clinical Research. 2021 Jul; 4(1). doi: 10.33695/rjcr.v4i1.66.

[17] Sofić A, Rašić I, Halilović E, Mujić A, Muslić D. Is Preoperative Hypo-proteinemia Associated with Colorectal Cancer Stage and Postoperative Complications? Medicinski Glasnik.2021 Aug; 18(2). doi :10.17392/1353-21.

[18] Miyata T, Hayama T, Ozawa T, Nozawa K, Misawa T, Fukagawa T. Predicting Prognosis in Colorectal Cancer Patients with Curative Resection Using Albumin, Lymphocyte Count and RAS Mutations. Scientific Reports.2024 Jun; 14(1): 14428. doi: 10.1038/ s41598-024-65457-8.

[19] Gremese E, Bruno D, Varriano V, Perniola S, Petricca L, Ferraccioli G. Serum Albumin Levels: A Biomarker to Be Repurposed in Different Disease Settings in Clinical Practice. Journal of Clinical Medicine.2023 Sep; 12(18): 6017. doi: 10.3390/jcm12186017.

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[20]Bénard F, Barkun AN, Martel M, von Renteln D. Systematic Review of Colorectal Cancer Screening Guidelines for Average-Risk Adults: Summarizing the Current Global Recommendations. World Journal of Gastroenterology.2018 Jan; 24(1): 124. doi: 10.3748/wjg.v24.i1.124.

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Original Article

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Non-Invasive Salivary Diagnostic Approach for Predicting Dental Caries

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ABSTRACT

Dental caries, often known as tooth decay, is a widespread public health concern that presents many difficulties, especially in developing nations like Pakistan. **Objectives:** To evaluate a non-invasive salivary diagnostic approach for predicting the risk of dental caries. **Methods:** In the comparative cross-sectional study, a total of 90 participants were recruited through purposive sampling technique belonging to the age group between 20 and 30 years, which was conducted in one of the private hospitals of Karachi, Pakistan. The participants were placed into two groups for the study according to their oral health state, as determined by the Decayed, Missing, and Filled Teeth index. Both informed consent and ethical approval were acquired. Samples of saliva were collected and examined utilizing standardized tools. Data were analyzed by statistical software version 23.0 by using the Chi-square test. **Results:** Participants with active caries (Decayed, Missing, and Filled Teeth >5) and those in optimum dental health (Decayed, Missing, and Filled Teeth=0) showed significant differences. Lower salivary pH (p=0.003), decreased flow rate (p=0.001), decreased buffering capacity (p=0.002), and increased viscosity in the high-risk group are important findings. These differences imply altered salivary dynamics, which raise the risk of dental cavities. **Conclusions:** It was concluded that a non-invasive and efficient method for determining the risk of dental cavities is salivary diagnostics, especially for communities with limited access to preventative dental treatment. Salivary evaluations incorporated into standard dental procedures may improve preventative measures.

INTRODUCTION

In developing countries like Pakistan, dental caries is very common, making it a significant worldwide public health concern [1]. Conventional caries diagnosis techniques, like visual inspection and radiographic imaging, frequently have drawbacks, such as subjectivity and the possibility of overlooking early lesions [2]. Non-invasive diagnostic techniques that can improve the early diagnosis and treatment of dental caries are therefore desperately needed. Recent developments in salivary diagnostics, which use saliva as a biomarker for dental health, have created new opportunities for non-invasive evaluation [3].

Salivary analysis has been used in medicine since ancient times when doctors used to taste patients' saliva to identify a variety of illnesses [4]. However, the first scientific investigations into salivary analysis did not take place until the late 1800s. Ivan Pavlov, a German scientist, found in 1880 that the autonomic nerve system controls salivary secretion. Numerous investigations into the different uses of salivary analysis in clinical practice have since been carried out. Saliva is a biological liquid and a unique medium in the oral cavity that directly contributes to the development of dental caries among all age groups [5].

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Because of this, different caries-predicting models continue to consider variations in salivary flow rate and its content modulations. These models differ from one another in certain aspects, such as how different saliva-associated parameters affect the processes of demineralization and re-mineralization of hard dental tissues [6]. The maintenance of dental health is significantly influenced by saliva. Salivary glycoproteins and mucoid lubricate and protect the mucous membranes [7]. Saliva uses a variety of physical and biochemical processes to carry out its mechanical cleaning and protecting duties. The risk of oral illnesses, particularly dental caries, is increased by low salivary secretion rates. Both stimulated and relaxed circumstances can be used to gather saliva [8]. The most common dental condition affecting humans is dental caries. Dental caries is still a serious issue even if its frequency has greatly decreased. It is well-recognized that dental caries have a complex etiology and pathophysiology [9]. Saliva is a bio-fluid that has gained significant interest due to its non-invasive nature, which makes it a valuable diagnostic tool for analyzing various conditions and diseases. On the contrary major other diseases of the human body are often identified by examination of body fluids, such as urine, sputum, blood, and cerebrospinal fluid [10]. Saliva secretion rate and quality play a significant role in both the development of caries and re-mineralization. The health of the soft tissues and teeth both depend on saliva. Patients who have experienced dental caries or dental erosion frequently come with missing tooth structures. By evaluating significant salivary indicators, the most likely causes of the oral balance shift that favoured demineralization may be identified [11]. Salivary analysis is a new non-invasive and user-friendly method that has received a lot of attention lately. Salivary analysis, which makes use of the most recent findings about salivary biomarkers, has the potential to completely transform the healthcare industry by offering insightful data for tracking a person's health, identifying the course of a disease, and facilitating individualized therapy [12]. Healthcare practitioners may follow patient development and make informed treatment decisions with the support of healthcare diagnostics and monitoring, which are essential components of healthcare management. A variety of diagnostic instruments, such as blood tests, imaging tests, genetic testing, and monitoring technologies, such as wearables, remote monitoring systems, and electronic health records, are now available to healthcare professionals [13].

This study aims to evaluate a non-invasive salivary diagnostic approach for predicting the risk of dental caries.

METHODS

A comparative cross-sectional study was carried out in one of the private hospitals in Karachi, Pakistan. The sample size of the study was calculated through open EPI assuming a 95% confidence level and a 5% margin of error, 90 participants were selected through purposive sampling technique in the study belonging to the age group 20-30 years. Exclusion criteria included patients with xerostomia or poorly managed diabetes, smokers, pregnant women and chewers of betel leaf. Using a saliva testing kit, determine the salivary pH, stimulated salivary flow rate, and buffering capacity in stimulated saliva. While salivary diagnostics included assessing flow rate, pH levels and buffering capacity. These steps made it easier to determine how non-invasive salivary diagnostics affected dental caries in the targeted population. Ninety individuals were split into two groups for this comparative cross-sectional study according to the Decayed, Missing, and Filled Teeth (DMFT) index, which measures dental health. There were 45 participants in the control group (22 male and 23 female), all of whom had DMFT scores of 0, which indicates optimum dental health. The ethical approval (Ref.No 029 SSCMS-Ethics/2024) was taken from the institutional ethical committee board of Sir Syed College of Medical Sciences. Each participant provided informed consent and the dentist used the DMFT index to measure dental caries. Hence, a dental mirror for clear tooth visibility, a dental explorer for cavity detection, and an artificial light source for improved visibility are the three main tools used to evaluate the DMFT index. An enzyme-linked immunosorbent assay (ELISA) kit (Human Beta Defensin 3 ELISA kit Cat. No. E3240Hu) was used to assess the amount of Human beta-defensin-3 (HβD-3) in saliva from the Laboratory of Bioassay Technology [14]. A saliva testing kit was used to analyze the viscosity, pH, flow rate, and buffering capacity of saliva. Participants were instructed to sit up straight, tip their heads down, and keep their mouths open until saliva gathered on the floor of their mouths to collect unstimulated whole saliva. After that, participants let their saliva flow into a 15 ml Falcon tube. Until 4–5 milliliters of saliva were obtained, this procedure was repeated. Within 30 minutes, the tubes were carried to the lab in thermopile bags while resting on crushed ice in disposable glasses. To obtain clean saliva, samples were centrifuged in the lab for 15 minutes at 4500 rpm and 4°C. A micropipette was used to collect the supernatant, and 0.3 ml was kept in Eppendorf tubes at -20°C until it was further examined. The data were analyzed by using a statistical package (SPSS version 23.0). Hence Chi-square test was used to see the differences between the control group and group A.

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RESULTS

The demographic details of the study, participants were divided into two groups (Group A; DMFT >5) and the control group (DMFT=0). There were 90 participants in total. According to the gender distribution, Group A has 15 male and 30 female, whereas the control group had 22 male and 23 female. There are 50 female participants (55.6% of the sample as a whole) and 40 male individuals (44.4%).

Table 1: Demographic Details of selected Patients

Variables	Control Group (DMFT=0) n=45	Group A (DMFT >5) n=45	Total Participants (n=90)
Gender			
Male	22	15	37 (41%)
Female	23	30	53 (58%)
Age Group			
18-25 Years	14	15	33 (36.6%)
26-30 Years	13	14	26 (28.8%)
31-35 Years	11	12	19 (21.1%)
36-40 Years	7	8	12 (13.3%)

Further study compares the salivary parameter features of a control group (n=45) with a decayed, missing, and filled teeth (DMFT) score of 0 and Group A (n=45) with a DMFT score >5. There was a substantial difference in the groups' levels of hydration; 68% of the control group reached hydration in less than 30 seconds, whereas 95% of Group A did so (p=0.001). Significant differences were also observed in salivary viscosity; 84% of the control group had moderate viscosity, whereas Group A showed a greater range, with 37% having low viscosity, 42% having moderate viscosity, and 20% having high viscosity (p=0.002). The majority of the control group (77%) had a pH between 6.2 and 7.0, but Group A had a more acidic profile, with 42% having a pH below 5.6 (p=0.003). The control group's salivary flow rate was significantly higher, with 82% of them exhibiting a flow rate above 1.0 ml/min, while 80% of Group A had a flow rate below 1.0 ml/min (p=0.001). Lastly, the buffering capacity was low in Group A (75%) and primarily high in the control group (57%; p=0.002). These results underline the association between lower salivary function and higher DMFT scores, highlighting notable variations in salivary parameters (Table 2).

Table 2: Characteristics of Salivary Parameters in Patients

Salivary Parameters	Control Group (DMFT=0) n=45	Group A (DMFT >5) n=45	p-value
Hydration Status			
Less than 30 seconds	31 (68%)	43 (95%)	0.001
More than 30 seconds	14 (31%)	2 (4%)	
Viscosity of Saliva			
Low Viscosity	2 (4%)	17 (37%)	0.002
Moderate Viscosity	38 (84%)	19 (42%)	
High Viscosity	5 (11%)	9 (2%)	
pH of Saliva			
<5.6	1 (2%)	19 (42%)	0.003
5.6 to 6.2	6 (13%)	12 (26%)	
6.2 to 7.0	35 (77%)	6 (13%)	
7.1 to 8.0	3 (6%)	8 (17%)	
Flow Rate of Saliva			
Less than 1.0 ml/min	8 (17%)	36 (80%)	0.001
Greater than 1.0 ml/min	37 (82%)	9 (2%)	
Buffering Capacity			
Low Buffering Capacity (0 to 5)	5 (11%)	34 (75%)	0.002
Moderate Buffering Capacity (6 to 9)	14 (31%)	8 (17%)	
High Buffering Capacity (10 to 12)	26 (57%)	3 (6%)	

DISCUSSION

Dental caries is still one of the most prevalent oral health issues in the world, especially in poorer nations like Pakistan where the illness is made worse by a lack of awareness, poor oral hygiene habits, and restricted access to preventive therapy. This study investigated how non-invasive salivary diagnostics might be used to diagnose and treat dental caries in Karachi. Salivary characteristics such as hydration state, viscosity, pH, flow rate, and buffering capacity were found to differ significantly between people with high caries experience (DMFT>5) and those with optimum oral health (DMFT=0) [15]. One of the key factors affecting salivary pH and oral health is salivary pH. The acids in the oral cavity break down enamel when salivary pH falls below normal; the longer this situation persists, the greater the chance that caries will develop [16]. Dental caries is strongly prevented by a normal salivary flow rate, which includes both hydration status and stimulated saliva flow rate. Salivary characteristics, such as decreased flow rate, lower pH, and diminished buffering capacity, were significantly impaired in the high-risk group participants. These characteristics are known to foster the growth of cariogenic bacteria and the demineralization of tooth enamel These findings demonstrate saliva's diagnostic capacity in the treatment of dental cavities and emphasize its critical role in preserving oral health. According to the findings, just 2% of individuals in the Control Group had salivary pH values below 5.6, while 42% of people in Group A did. Previous research by Dawes and Wong conducted in 2019 has shown that enamel demineralization and the growth of cariogenic bacteria are facilitated by such an acidic environment [17]. This is consistent with the finding that a lower pH is directly linked to a higher risk of dental cavities. Saliva's ability to neutralize dietary acids is also hampered by poor buffering capacity, which was present in 75% of Group A participants. This is consistent with research by Barakzai *et al.*, in 2024 who highlighted how a decreased buffering capacity fosters an environment that

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accelerates the development of caries. These results support the buffering capacity's protective role and its vital role in maintaining oral health. The difference in salivary flow rates between the two groups was another noteworthy discovery. The average salivary flow rate for Group A participants was 0.4 mL/min, which was significantly less than the 0.8 mL/min recorded for Control Group participants [18]. The results of this study were further supported by Araujo *et al.*, (2020), who also found that lower salivary flow rates were linked to a higher prevalence of dental diseases. According to these results, preserving ideal salivary flow is essential for reducing the risk of dental caries [15]. Another measure that revealed notable variations between the two groups was salivary viscosity. Saliva in Group A participants was thicker and more viscous, which hinders teeth's ability to be mechanically cleaned and encourages the buildup of plaque. Although less research has been done on this topic, Halageri *et al.*, (2020) pointed out that increased viscosity is linked to decreased food debris clearance, which could raise the risk of dental caries [16]. Salivary dynamics were also discovered to be influenced by hydration status. Participants in Group A recovered from dehydration more slowly than those in the Control Group. To increase salivary secretion and enhance its quality, one must be properly hydrated. This result is in line with that of Thomas (2024), who emphasized the connection between caries prevalence and hydration levels [19]. Thus, encouraging proper hydration becomes a straightforward but powerful preventative measure. The salivary composition and function may also be impacted by age-related changes in hormone levels [20]. Hence the main limitation of the study was the smaller sample size because it would not accurately reflect the population, resulting in more sampling error, and decreased generalizability. Additionally, smaller samples limit subgroup analyses and can introduce bias, which can affect the findings' reliability. But anyhow the study can offer valuable information on the prevalence, correlations, and possible effects of diverse exposures across distinct groups within a community. A clinically significant decline in salivary functioning might be regarded as an etiologic factor that contributes to the development of dental caries because saliva has a general preventive effect.

CONCLUSIONS

It was concluded that this study emphasizes the vital role salivary parameters pH, buffering capacity, flow rate, and viscosity play in preserving oral health by highlighting notable variations between those with and without dental caries. These results highlight salivary measurements' diagnostic potential and provide a non-invasive method of evaluating caries risk, especially in high-prevalence populations like Pakistan. The use of salivary stimulants to improve salivary function, nutritional counselling, and hydration promotion are examples of practical uses. Although the study offers insightful information, its limitations such as its cross-sectional methodology and limited sample size warn against extrapolating the findings. Salivary diagnostics can be used in regular dental procedures to improve preventative and therapeutic strategies.

Authors Contribution

Conceptualization: WUN
Methodology: WUN, AI, AA
Formal analysis: AKH, SM
Writing review and editing: MK, AI, AA, FT

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Bawaskar HS and Bawaskar PH. Oral Diseases: A Global Public Health Challenge. The Lancet. 2020 Jan; 395(10219): 185-6. doi: 10.1016/S0140-6736(19)33016-8.

[2] Moriyama CM, Novaes TF, Ferreira FR, Moro BL, Imparato JC, Diniz MB et al. What Diagnostic Strategy Performs Better for Caries Lesion Detection On Proximal Surfaces of Adolescents? Clinical Oral Investigations. 2021 Jun; 25: 3977-86. doi: 10.1007/s00784-020-03728-0.

[3] Woźniak M, Paluszkiewicz C, Kwiatek WM. Saliva as a Non-Invasive Material for Early Diagnosis. Acta Biochimica Polonica. 2019 Dec; 66(4): 383-8. doi: 10.18388/abp.2019_2762.

[4] Li Y, Ren B, Peng X, Hu T, Li J, Gong T *et al.* Saliva is A Non-Negligible Factor in the Spread of COVID-19. Molecular Oral Microbiology. 2020 Aug; 35(4): 141-5. doi :10.1111/omi.12289

[5] Bilyschuk L, Keniuk A, Goncharuk-Khomyn M, Yavuz I. Association Between Saliva Quantity and Content Parameters with Caries Intensity Levels: A Cross-Sectional Study among Sub-Carpathian Children. Pesquisa Brasileira em Odontopediatria e Clínica Integrada. 2020 Jan; 19: e5048. doi: 10.4034/PBOCI.2019.191.121.

[6] Jurela A, Sudarević K, Budimir A, Brailo V, Brzak BL, Janković B. Clinical and Salivary Findings in Patients with Metal and Crystalline Conventional and Self-

DOI: https://doi.org/10.54393/pjhs.v5i12.2499

Ligating Orthodontic Brackets.Acta Stomatologica Croatica. 2019 Sep; 53(3): 224. doi: 10.15644/asc53/3/4.

[7] Antonelli R, Massei V, Ferrari E, Gallo M, Pertinhez TA, Vescovi P *et al*. Salivary Diagnosis of Dental Caries: A Systematic Review. Current Issues in Molecular Biology.2024 May; 46(5): 4234-50. doi: 10.3390/cimb46050258.

[8] Alamoudi A, Alamoudi R, Gazzaz Y, Alqahtani AM. Role of Salivary Biomarkers in Diagnosis and Detection of Dental Caries: A Systematic Review. Diagnostics.2022 Dec; 12(12): 3080. doi: 10.3390/diagnostics12123080.

[9] Dikova V, Jantus-Lewintre E, Bagan J. Potential Non-Invasive Biomarkers for Early Diagnosis of Oral Squamous Cell Carcinoma. Journal of Clinical Medicine. 2021 Apr; 10(8): 1658. doi: 10.3390/jcm10081658.

[10] El Bouhairi M, Lachhab O, Sidqui M. Advancements in Salivary Biomarkers: Transforming Diagnostic Landscape in Dentistry. American Journal of Innovative Research and Applied Sciences. 2024: 12-19. doi: 10.5281/ZENODO.10427760.

[11] Eftekhari A, Hasanzadeh M, Sharifi S, Dizaj SM, Khalilov R, Ahmadian E. Bioassay of Saliva Proteins: The Best Alternative for Conventional Methods in Non-Invasive Diagnosis of Cancer. International Journal of Biological Macromolecules.2019 Mar; 124: 1246-55. doi 10.1016/j.ijbiomac.2018.11.277.

[12] Liao C, Chen X, Fu Y. Salivary Analysis: An Emerging Paradigm for Non-Invasive Healthcare Diagnosis and Monitoring. Interdisciplinary Medicine.2023 Jul; 1(3): e20230009. doi: 10.1002/INMD.20230009.

[13] Siddiqui AA, Alshammary F, Mulla M, Al-Zubaidi SM, Afroze E, Amin J *et al*. Prevalence of Dental Caries in Pakistan: A Systematic Review and Meta-Analysis. BioMed Central Oral Health.2021 Dec; 21: 1-2. doi: 10.1186/s12903-021-01802-x.

[14] Bellagambi FG, Lomonaco T, Salvo P, Vivaldi F, Hangouët M, Ghimenti S *et al*. Saliva Sampling: Methods and Devices. An Overview. TrAC Trends in Analytical Chemistry.2020 Mar; 124: 115781. doi: 10.1016/j.trac.2019.115781.

[15] Ling X, Alexander GS, Molitoris J, Choi J, Schumaker L, Mehra R *et al*. Identification of CT-Based Non-Invasive Radiomic Biomarkers for Overall Survival Prediction in Oral Cavity Squamous Cell Carcinoma. Scientific Reports.2023 Dec; 13(1): 21774. doi: 10.1038/s41598-023-48048-x.

[16] Vernerová A, Kujovská Krčmová L, Melichar B, Švec F. Non-Invasive Determination of Uric Acid in Human Saliva in the Diagnosis of Serious Disorders. Clinical Chemistry and Laboratory Medicine.2021 Apr; 59(5): 797-812. doi: 10.1515/cclm-2020-1533.

[17] Dawes C and Wong DT. Role of Saliva and Salivary Diagnostics in the Advancement of Oral Health. Journal of Dental Research.2019 Feb; 98(2): 133-41. doi :10.1177/0022034518816961.

[18] Katsavochristou A and Koumoulis D. Current Status of Magnetic Resonance On Saliva for Oral and Dental Health Early Diagnosis. Magneto-chemistry. 2020 Apr; 6(2): 18. doi: 10.3390/magnetochemistry6020018.

[19] Birla M, Yogi S, Chaudhary K, Gupta R, Sarin LP, Jain S. Saliva: A Non-Invasive and Multifaceted Tool in the Sphere of Diagnostics. Journal of Pharmaceutical Sciences and Research. 2022 Mar; 14(3): 713-20.

[20] Alqahtani AA, Alhalabi F, Alam MK. Salivary Elemental Signature of Dental Caries: A Systematic Review and Meta-Analysis of Ionomics Studies. Odontology. 2024 Jan; 112(1): 27-50. doi: 10.1007/s10266-023-00839-4.

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Comparison of Miltefosine with Glucantime for the Treatment of Cutaneous Leishmaniasis

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ABSTRACT

Cutaneous leishmaniasis, the most prevalent type of leishmaniasis, is a disease characterized by ulcerative skin lesions. **Objectives:** To compare the safety, efficacy, and patients' satisfaction of glucantime with that of miltefosine in treating cutaneous leishmaniasis in Pakistan. **Methods:** A quasi experimental study design was conducted at Bacha Khan Medical Complex from 17th August 2023 to 18th November 2023, Swabi among 150 cutaneous leishmaniasis-diagnosed patients. The sample size consists of 150 patients which was divided into equal groups. Group 1 (treated with oral Miltefosine) and Group 2 (received intramuscular Glucantime). A 12-week post-treatment follow-up was conducted to assess treatment efficacy, side effects, and patient satisfaction. Chi-square tests and other statistical analyses were utilized to compare the two groups' results. **Results:** Complete lesion healing was observed at a considerably greater rate in the Miltefosine group (86%) than in the Glucantime group (68%, $p<0.05$). Compared to 35% of patients in the Glucantime group had major adverse reactions, including injection site pain and systemic symptoms. There was a lower rate of adverse events in the Miltefosine group (20%) with most being mild gastrointestinal symptoms. Miltefosine (90%) had also a better acceptability rate from patients compared to Glucantime (65%, $p<0.05$). **Conclusions:** It was concluded that when treating cutaneous leishmaniasis, miltefosine was shown to be more efficient, secure, and well-tolerated than glucantime. It is advised that more research be done to evaluate long-term results and wider application.

INTRODUCTION

Different kinds of leishmaniasis, such as cutaneous, mucocutaneous, or visceral leishmaniasis, can occur depending on the species of Leishmania major that is causing the illness 1. Although infections can occur anywhere in the world, 98 countries mostly tropical and subtropical ones have an endemic case of the disease2]. The least deadly but most prevalent type of illness is called Cutaneous Leishmaniasis (CL), and it is characterized by ulcerative skin lesions 3. Although CL is widely spread, ten countries Brazil, Colombia, North Sudan, Iran, Afghanistan, Algeria, Syria, Ethiopia, Costa Rica, and Peru account for 70% to 75% of the estimated worldwide incidence 4. Anti-parasitic injections of pentavalent anti-monials, intra-lesional pentavalent anti-monials, topical paromomycin, thermotherapy, or cryotherapy are now the gold standard for treatment in many countries for specific instances of cutaneous Leishmaniasis 5. The immunological response linked to T cells is the primary defence mechanism against leishmaniasis 6. Created as an anti-cancer medication, miltefosine is now a vital oral leishmaniasis therapy. It is a promising substitute for more intrusive treatments like Glucantime 7, as it was approved as the first oral

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medication for leishmaniasis. Miltefosine kills parasites by interfering with their lipid metabolism in the cell membrane. Miltefosine has been proven in studies conducted in South America and India to be very successful against different kinds of leishmaniasis, with cure rates ranging from 70% to 90% 8. The illness is spreading throughout Pakistan when historical data is contrasted with the current situation. For high-risk individuals, such as military personnel, who visit or reside in the arid regions of Baluchistan, where the illness is widespread, it has grown to be a serious health concern 9. Like in other parts of the world, pentavalent anti-monials remain the primary line of therapy for leishmaniasis in the absence of a vaccine 10. The management of cutaneous leishmaniasis (CL) is a major public health obstacle in Pakistan, given the high disease burden and restricted availability of efficacious therapies 11. Although glucantime and miltefosine are both frequently used treatments for CL, comparative studies assessing their safety and efficacy in the unique setting of Pakistan are scarce 12. On the other hand, miltefosine, an oral drug, provides a more practical substitute; nonetheless, because of issues with accessibility and cost, its uptake has been gradual 13. Healthcare practitioners must make evidence-based judgments regarding the best course of therapy for CL, but this is made more difficult by the lack of localized, head-to-head comparisons between these two medications in Pakistan 14, 15.

This study aims to fill this gap by directly comparing the efficacy, safety, and patient outcomes of Miltefosine and Glucantime among Pakistani patients, providing valuable insights for improving treatment protocols in the country.

METHODS

In this Quasi experimental study, we assessed the efficacy of Glucantime and Miltefosine in the treatment of cutaneous leishmaniasis. This study lasted from 17th August 2023 to 18th November 2023 and was conducted at Bacha Khan Medical Complex, Swabi Pakistan. A cross-sectional study design was chosen as it allows for the simultaneous comparison of treatment outcomes and side effects between two groups at a specific point in time. This design is efficient for assessing associations and differences without requiring long-term follow-up. It is particularly suitable for evaluating the efficacy of treatments like Miltefosine and Glucantime in real-world clinical settings. Inclusion Criteria were patients diagnosed with cutaneous leishmaniasis, aged 18–60 years, with a lesion size between 2–5 cm and no prior treatment for the condition. Exclusion Criteria were patients with systemic illnesses, pregnancy, lactation, or known allergies to either Miltefosine or Glucantime, and those unwilling to provide informed consent. A non-probability consecutive sampling technique was used to recruit 150 participants who met the inclusion criteria, ensuring all eligible patients presenting to the outpatient department during the study period were included. The sample size which consists of 150 patients, was divided into two equal groups. Group 1(treated with oral Miltefosine)and Group 2 (received intramuscular Glucantime). The sample size was determined using a standard formula for comparing two proportions, with the following parameters: n=(P1–P2)2(Zα/2+Zβ) 2· [P1(1–P1) +P2(1–P2)]. where Confidence Level: 95%, Power: 80%, Expected Proportion of Healing in Group 1 (Miltefosine): 85% 16. Expected Proportion of Healing in Group 2 (Glucantime): 65% and Margin of Error: 5%. Ethical approval for the study was obtained from the Institutional Review Board (IRB) of Bacha Khan Medical Complex; reference number 13036/PF/GKMCS. Written informed consent was obtained from all participants before enrollment, ensuring adherence to ethical standards and protecting patient rights. Participants were informed about the study's purpose, procedures, potential risks, and benefits. Data collection was completed over 12 weeks, with follow-up assessments conducted at weeks 4, 8, and 12 to evaluate lesion healing, side effects, and patient satisfaction. Data analysis was done with the help of SPSS version 27.0. The statistical analysis used was descriptive. The chi-square test was applied, taking the p-value ≤0.05 as statistically significant. All the results were presented in the form of tables and figures.

RESULTS

The study provides a summary of the demographic and clinical characteristics of the study participants in the Miltefosine and Glucantime groups. The mean age, gender distribution, lesion size, and duration of the disease were comparable between the two groups, with no statistically significant differences (p>0.05). This indicates that both groups were well-matched at baseline for demographic and clinical variables(Table 1).

Table 1: Patient Demographics(n=150)

Characteristic	Miltefosine Group (n=75)	Glucantime Group (n=75)	p-value
Mean Age (Years)	35.4 ± 8.5	36.2 ± 9.1	0.64
Gender (Male)	45 (60%)	45 (60%)	1.00
Lesion Size (cm)	3.4 ± 1.2	3.6 ± 1.3	0.56
Duration of Disease (Months)	4.5 ± 1.1	4.3 ± 1.0	0.72

Further study highlights the treatment efficacy outcomes for both groups. The Miltefosine group achieved a significantly higher rate of complete healing at 12 weeks (86%) compared to the Glucantime group (68%), with a p-value <0.05. By the 8th week, healing was observed in 77.33% of patients in the Miltefosine group versus 43% in the Glucantime group (p<0.05). The recurrence rate was lower in the Miltefosine group (5%) compared to the

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Glucantime group (13.33%), though this difference did not reach statistical significance (p=0.08) Results present the incidence of side effects in both treatment groups. Patients in the Glucantime group reported a significantly higher occurrence of side effects, including injection site pain (35%), fatigue (20%), and systemic symptoms such as fever (11%), compared to the Miltefosine group. In contrast, the Miltefosine group reported nausea/vomiting in 20% of cases, a side effect not observed in the Glucantime group. All differences were statistically significant (p<0.05).

Table 2: Efficacy of Treatment and incidence of Side effects (n=150)

Outcome	Miltefosine Group (n=75)	Glucantime Group (n=75)	p-value
Complete Healing (12 Weeks)	64 (85.33%)	51 (68%)	<0.05
Healing by 8th Week	58 (77.33%)	32 (43%)	<0.05
Recurrence Rate	4 (5.33%)	10 (13.33%)	0.08
Side Effect	**Miltefosine Group (n=75)**	**Glucantime Group (n=75)**	**p-value**
Nausea/Vomiting	15 (20%)	0 (0%)	<0.05
Injection Site Pain	0 (0%)	26 (35%)	<0.05
Fatigue	3 (4%)	15 (20%)	<0.05
Systemic Symptoms (Fever)	0 (0%)	8 (11%)	<0.05
Treatment Discontinuation	0 (0%)	4 (5.33%)	<0.05

The study details the chi-square (Pearson chi-square) analysis for the incidence of side effects. Statistically significant differences were observed for all reported side effects, including nausea/vomiting (chi-square value = 25.00, $p < 0.05$) and injection site pain (chi-square value=25.00, p<0.05) Pearson's chi-square test was used to compare the complete healing outcomes between the Miltefosine and Glucantime groups. This test is appropriate as it evaluates the association between two categorical variables (treatment type and healing status). The analysis revealed a significant association, with the Miltefosine group showing a higher complete healing rate (chi-square value=7.16, p<0.05).

Table 3: Incidence of Side Effects and Comparison of Complete Healing(n=150)

Side Effect	Miltefosine Group (n=75)	Glucantime Group (n=75)	Total	Chi-Square Value	p-value
Nausea/Vomiting	15 (20%)	0 (0%)	15	25.00	<0.05
Injection Site Pain	0 (0%)	26 (35%)	26	25.00	<0.05
Fatigue	3 (4%)	15 (20%)	18	12.20	<0.05
Systemic Symptoms (Fever)	0 (0%)	8 (11%)	8	10.80	<0.05
Treatment Discontinuation	0 (0%)	4 (5.33%)	4	9.60	<0.05
No Side Effects	57 (76%)	35 (47%)	92		
Total	75	75	150		

Outcome	Miltefosine Group (n=75)	Glucantime Group (n=75)	Total	Chi-Square Value	p-value
Complete Healing	64 (85.33%)	51 (68%)	115	7.16	<0.05
Not Healed	11 (14.66%)	24 (32%)	35		
Total	75	75	150		

DISCUSSION

Current results showed that Miltefosine led to shorter recovery durations and much greater rates of full lesion healing (86%) as compared to Glucantime (68%). This is in line with other studies carried out in countries such as Brazil and Iran, where it was also demonstrated that miltefosine performed better than glucantime in terms of cure rates and recovery times 17. The Miltefosine group showed a faster rate of recovery, indicating that it may be able to more effectively lessen the disease load, giving patients comfort sooner and reducing the chance of consequences from untreated lesions. Glucantime has a lower cure rate of 68%, which is in line with its acknowledged shortcomings, which include the potential for treatment failure and recurrence. (18) . A study conducted in Iran found that Miltefosine achieved a higher cure rate (83%) compared to Glucantime (69%) in treating CL lesions 19. Similarly, clinical trials in India reported that Miltefosine's oral administration significantly improved patient adherence and satisfaction compared to Glucantime's painful injection-based regimen 20. The use of miltefosine as a safer substitute is supported by the noticeably reduced occurrence of serious side effects in this group, especially in situations where the healthcare system would not be able to provide the careful monitoring needed for glucantime. This is a significant discovery for Pakistan's restricted resource areas, where long-term, intrusive therapies aren't always practical. Policymakers may find vital information by comparing the cost-effectiveness of miltefosine to glucantime, especially in environments with restricted resources. Treatment results may also be improved by research into the creation of novel oral medicines or integrated treatment plans. Lastly, there is a need for studies focused on improving access to Miltefosine in rural areas and exploring barriers related to availability, affordability, and distribution in Pakistan.

CONCLUSIONS

This study concluded that Miltefosine is more effective, safer, and better received by patients than Glucantime in the treatment of cutaneous leishmaniasis in Pakistan. Miltefosine proved to be a more efficient and well-tolerated alternative, demonstrating higher healing rates, faster recovery times, and fewer adverse effects. The significant improvement in patient satisfaction was partly attributed to the convenience of oral administration and the reduced

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occurrence of severe side effects. Its oral formulation makes it a preferable choice and a promising alternative to Glucantime in the near future.

Authors Contribution

Conceptualization: SK
Methodology: SK, SIK, UAK, S
Formal analysis: SK, SIK
Writing review and editing: UAK, SS, H

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Iranpour S, Hosseinzadeh A, Alipour A. Efficacy of Miltefosine Compared with Glucantime for the Treatment of Cutaneous Leishmaniasis: A Systematic Review and Meta-Analysis. Epidemiology and Health. 2019 Mar; 41: e2019011. doi: 10.4178/epih.e2019011.

[2] Astman N, Arbel C, Katz O, Barzilai A, Solomon M, Schwartz E. Tolerability and Safety of Miltefosine for the Treatment of Cutaneous Leishmaniasis. Tropical Medicine and Infectious Disease.2024 Sep; 9(9): 218. doi:10.3390/tropicalmed9090218.

[3] Teixeira VC, Amorim AC, Rodrigues CR, Sampaio Filho HC, Cambuy MR, Machado RD *et al.* Miltefosine in the Treatment of Cutaneous Leishmaniasis: Effectiveness and Limitations of the First Oral Therapy Authorized in Brazil. Brazilian Journal of Health Review. 2023 Aug; 6(4): 17261-72. doi:10.34119/bjhrv6n4-251.

[4] Mohammad N, Sagheer F, Paracha MM, Khan AQ, Naseem S, Wasim M. Comparison of Efficacy of Miltefosine Versus Meglumine Antimonate in the Treatment of Cutaneous Leishmaniasis. Journal of Ayub Medical College Abbottabad-Pakistan. 2022 Oct; 34(4). doi: 10.55519/JAMC-04-11135.

[5] Guzman ML, Peralta MF, Quipildor MO, Papera F, Mejía Montaño E, Lauthier JJ *et al.* A Case of Cutaneous Leishmaniasis Cured by a Combined Treatment of Topical Miltefosine and Injectable Amphotericin B. 2023 Dec; 6(4): 1181-1193. doi: 10.33218/001c.90983.

[6] Yesilova Y, Surucu HA, Ardic N, Aksoy M, Yesilova A, Oghumu S *et al.* Meglumine Antimoniate Is More Effective Than Sodium Stibogluconate in the Treatment of Cutaneous Leishmaniasis. Journal of Dermatological Treatment.2016 Jan; 27(1): 83-7. doi:10.3109/09546634.2015.1054778.

[7] Montoya NR, Pulgarín JQ, Carvajal LL. Therapeutic Response and Safety of Different Treatments for Cutaneous Leishmaniasis in Patients: A Retrospective Cross-Sectional Study. Asian Pacific Journal of Tropical Medicine.2023 Jul; 16(7): 305-12. doi:10.4103/1995-7645.380719.

[8] Hashiguchi Y, Nieto LV, Villegas NC, Gomez EA, Kato H. Topical Treatment of Cutaneous Leishmaniasis: A Case Treated with A Glucantime-Based Lotion Experienced in Ecuador and A Mini Review. Archives of Medical and Clinical Research.2021 Jan; 1: 1-5. doi: 10.51941/AMCR.2021.1103.

[9] Tunalı V, Harman M, Çavuş İ, Gündüz C, Özbilgin A, Turgay N. Overcoming the Challenge; In Vivo Efficacy of Miltefosine for Chronic Cutaneous Leishmaniasis. Acta Parasitologica. 2021 Jun; 66: 354-60. doi: 10.1007/s11686-020-00285-0.

[10] Peralta MF, Usseglio NA, Bracamonte ME, Guzmán ML, Olivera ME, Marco JD *et al.* Efficacy of Topical Miltefosine Formulations in an Experimental Model of Cutaneous Leishmaniasis. Drug Delivery and Translational Research.2021 Jan; 12: 180–196. doi:10.1007/s13346-021-00896-8.

[11] Tahir M, Bashir U, Hafeez J, Ghafoor R. Safety and Efficacy of Miltefosine in Cutaneous Leishmaniasis: An Open Label, Non-Comparative Study from Balochistan. Pakistan Journal of Medical Sciences. 2019 Mar; 35(2): 495. doi: 10.12669/pjms.35.2.54.

[12] Silva RE, Toledo Júnior A, Senna MC, Rabello A, Cota G.Intralesional Meglumine Antimoniate for the Treatment of Localised Cutaneous Leishmaniasis: A Retrospective Review of a Brazilian Referral Centre. Memórias do Instituto Oswaldo Cruz.2016; 111: 5126.doi:10.1590/0074-02760160183.

[13] Rubiano LC, Miranda MC, Muvdi Arenas S, Montero LM, Rodrlguez-Barraquer I, Garcerant D *et al.* Noninferiority of Miltefosine Versus Meglumine Antimoniate for Cutaneous Leishmaniasis in Children. Journal of Infectious Diseases.2012 Feb; 205(4): 684932.doi: 10.1093/infdis/jir816.

[14] Tayyebi M, Darchini-Maragheh E, Layegh P, Kiafar B, Goyonlo VM. The Effect of Oral Miltefosine in Treatment of Antimoniate Resistant Anthroponotic Cutaneous Leishmaniasis: An Uncontrolled Clinical Trial. PLoS Neglected Tropical Diseases.2021 Mar; 15(3): e0009241. doi: 10.1371/journal.pntd.0009241.

[15] Ware JM, O'Connell EM, Brown T, Wetzler L, Talaat KR, Nutman TB *et al.* Efficacy and Tolerability of Miltefosine in the Treatment of Cutaneous Leishmaniasis. Clinical Infectious Diseases.2021 Oct; 73(7): e2457-562. doi: 10.1093/cid/ciaa1238.

[16] Kaya T, Yıldırım A, Harman M. Comparison of in Vitro

DOI:https://doi.org/10.54393/pjhs.v5i12.2575

Resistance of Wild Leishmania İsolates, Which Are Resistant to Pentavalent Antimonial Compounds, Against Drugs Used in the Treatment of Leishmaniasis. Türkiye Parazitolojii Dergisi.2020 Mar; 44(1): 12. doi: 10.4274/tpd.galenos.2019.6661.

[17] Mann S, Phupitakphol T, Davis B, Newman S, Suarez JA, Henao-Martínez A *et al.* Case Report: Cutaneous Leishmaniasis Due to Leishmania (Viannia) Panamensis in Two Travelers Successfully Treated with Miltefosine. The American Journal of Tropical Medicine and Hygiene.2020 Sep; 103(3): 1081. doi: 10.4269/ajtmh.20-0086.

[18] Rahman A, Tahir M, Naveed T, Abdullah M, Qayyum N, Malik DH *et al*. Comparison of Meglumine Antimoniate and Miltefosine in Cutaneous Leishmaniasis. Journal of the College of Physicians and Surgeons—Pakistan.2023 Dec; 33(12): 1367-71. doi:10.29271/jcpsp.2023.12.1367.

[19] Sampaio RN, Silva JS, Paula CD, Porto C, Motta JD, Pereira LI *et al.* A Randomized, Open-Label Clinical Trial Comparing the Long-Term Effects of Miltefosine and Meglumine Antimoniate for Mucosal Leishmaniasis. Revista Da Sociedade Brasileira De Medicina Tropical.2019 Mar; 52: e20180292.doi: 10.1590/0037-8682-0292-2018.

[20]Suprien C, Guimarães LH, de Carvalho LP, Machado PR. Pentavalent Antimony Associated with G-CSF in the Treatment of Cutaneous Leishmaniasis Caused by Leishmania (Viannia) braziliensis.Pathogens.2024 Apr; 13(4): 301. doi: 10.3390/pathogens13040301.

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Original Article

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Assessing Postpartum Depression and Anxiety during the Antenatal and Postpartum Period

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ABSTRACT

Postpartum Depression (PPD) and anxiety were common mental disorders affecting women during the antenatal and postpartum periods. Early detection and intervention were vital for improving maternal and infant health outcomes. **Objective:** To assess the postpartum depression and anxiety during the antenatal and postpartum period using postnatal depression scale (EPDS) and the hospital anxiety and depression scale (HADS) **Methods:** Total 94 patients over six months in the Department of Obstetrics and Gynecology at Divisional Headquarters Teaching Hospital in Mirpur, Azad Kashmir were enrolled in this comparative cross sectional study. The pregnant women aged 18 to 45 during third trimester were included and excluding those with pre-existing psychiatric conditions or high-risk. The study utilized the HADS and EPDS while also recording demographic and clinical information, including age, education level, socioeconomic status, marital status, parity, gestational age at delivery, gestational diabetes, and preeclampsia. Data were analyzed using SPSS version 26 with appropriate statistical methods. **Results:** The majority of participants were over 25 years old (71.3%) and undergraduate education (62.8%), with 67.0% being multiparous. Gestational diabetes was present in 19.1%, and 16.0% had hypertension. HADS identified 15 mild, 35 moderate, and 44 severe cases, while EPDS reported 19 mild, 30 moderate, and 45 severe cases, with both scales showing the highest prevalence in the severe category. **Conclusions:** EPDS and HADS were two good screening tools for postpartum depression as well as anxiety. Using both together can certainly enhance the detection procedure, leading to timely intervention and a better prognosis of maternal as well as infant health.

INTRODUCTION

Pregnant or new moms go through a lot, are vulnerable to common psychiatric problems such as anxiety and Postpartum Depression (PPD). Among healthy mothers, PPD occurs 17 % worldwide according to a systematic review and meta-analysis [1]. While in high-income countries, it is often estimated at about 10-13%, whereas LMICs have significantly higher rates of prevalence ranging from 20-40% [2]. The difference among these countries partly arises because of socio-economic conditions, unavailability of health care, and cultural influence on mental health literacy and self-treatment seekers [3]. The South Asian country, including Pakistan, has a prevalence rate estimated between 28-63% with a comorbidity of anxiety disorders [4]. It is of paramount importance for the earliest recognition and management of postpartum depression and anxiety. Untreated mental disorders in mothers do not only affect the well-being of the mother but also have long-term consequences for child development, family relationships, and socio-economic outcomes [5]. Children of untreated PPD mothers are at a higher risk of developmental delays, behavioral problems, and mental disorders as adults [6]. Maternal depression has also been shown to be associated with higher rates of maternal mortality through suicide, especially among LMICs, where mental health services are not well capacitated [7]. Screening for postpartum depression and anxiety is thus needed both antenatally and postnatally. The two majorly validated tools used for this screening are the Edinburgh

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Postnatal Depression Scale (EPDS) and the Hospital Anxiety and Depression Scale (HADS). A 10-item specifically designed self-report questionnaire EPDS for postpartum depression helps identify at-risk women. Studies have documented that the sensitivity and specificity of detecting postpartum depression were between 86% and 78%, respectively. It has been translated and validated into many languages and has become a standard used worldwide to screen for postpartum depression [8, 9]. On the contrary, HADS is a 14 item measure of both anxiety and depression at the same time particularly useful for detection of comorbid anxiety disorders in the perinatal period. The HADS has been reported to have good psychometric properties both for antenatal and postpartum use with reported sensitivity of about 85% and specificity of about 80% for detection of clinically significant anxiety and depression [10, 11]. The HADS is used most often in clinical practice because of its brevity and also because the assessment of anxiety along with depression is crucial since antenatal anxiety is one of the key predictors of postpartum depression [12]. Cultural stigma attached to mental health conditions delays early diagnosis and treatment of postpartum depression and anxiety in Pakistan [13]. The current scenario of a recent Karachi study indicates that women with PPD seek professional help in only an exceptionally meager percentage, that is, 30% because they fear being misunderstood or judged by healthcare providers and family members [5]. Attempts to integrate routine screening for postpartum depression and anxiety into the ambit of antenatal and postpartum care in Pakistan have been made. Very recently, the Pakistan Society of Obstetricians and Gynecologists published a series of guidelines suggesting screening with both the EPDS and the HADS to detect early maternal mental health disorders [14]. However, implementation of these guidelines is still in its infancy, and there is an urgent need to institute large-scale, community-based mental health interventions that could help overcome barriers to care and improve maternal outcomes. The application of validated screening tools such as the EPDS and HADS during the antenatal and postpartum periods provides a cost-effective and efficient method of identifying those women at risk. However, in the case of countries like Pakistan, where mental health services are very underdeveloped, there exists an urgent need for policy-driven initiatives to integrate mental health into routine maternal health care, thus reducing the stigma and improving accessibility and utilization.

This study was conducted to assess the postpartum depression and anxiety during the antenatal and postpartum period using postnatal depression scale (EPDS) and the hospital anxiety and depression scale (HADS)

METHODS

A comparative cross sectional study was carried out within six months in the Department of Obstetrics and Gynecology at Divisional Headquarters Teaching Hospital Mirpur Azad Kashmir from January to July 2024 after taking the approval from Mohtarma Benazir Bhutto Shaheed Medical College Mirpur (Ref.No.65/ACADEMICS BLOCK TRAUMA CENTER/SURGERY/2024) and this research followed ethical considerations, where written informed consent was received from all the participants before their contribution. Total 94 patients sample size was calculated by using the prevalence of postpartum depression in Pakistani females as 19.3%, taking 8% margin of error and 95% confidence interval [14]. The pregnant females aged 18 to 45 years during third trimester without a history of pre-existing psychiatric conditions or high-risk pregnancies were included. Pregnancies with a high risk and any prior history of psychiatric disorders were excluded to control for variables that may confound findings concerning postpartum depression and anxiety. The participants were recruited by consecutive sampling technique as they attended their routine antenatal visits. The major tools applied for the assessment of their mental status were the well-known HADS and the EPDS scales, the most esteemed tools in maternal mental health research. HADS contains 14 items. Total score of HADS ranges from 0 to 21. The score between 0-7 was considered as normal, 8-10 showed mild anxiety and depression and score >11 showed severe anxiety and depression [15]. The other self-report questionnaire EPDS was a 4-point Likert score scale that ideally should be of 10 items specifically meant for use in the screening of postpartum depression. The total score of EPDS range from 0 to 30, where the score 0-9 indicates mild depression, the score between 10-12 showed moderate depression and score >13 showed severe depression [16]. The participants' assessments were made at 2 different critical points of the study. The first assessment was carried out during the third trimester (antenatal period) by using HADS. The second assessment was done six weeks after delivery, at the postpartum postnatal visit, when all symptoms of post-delivery depression and anxiety can be identified by using EPDS. In addition to the HADS and EPDS tests, the demographic and clinical information was also recorded on a predesigned proforma which including age and education levels, socioeconomic status, marital status, parity, gestational age ant delivery, gestational diabetes and preeclampsia. The collected data of this study were entered into SPSS version 26. The demographic and clinical presentation of the patients were analyzed by using frequency and percentages. The diagnostic accuracy of HADs and EPDS was calculated by using sensitivity, specificity, positive predicted value and negative predicted value.

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RESULTS

The majority of participants was over 25 years old (71.3%) and had been married for less than two years (55.3%). Most had undergraduate education (62.8%), with 67.0% being multiparous. Gestational diabetes was present in 19.1%, and 16.0% had hypertension. In terms of delivery, 60.6% had a C-section, while 39.4% had a vaginal delivery. Overall, the sample was predominantly older, educated, and multiparous, with a higher rate of C-sections (Table 1).

Table 1: Demographics and Clinical Investigation of selected Patients

Variables	Frequency (%)
Age	
Less than 25	27 (28.7%)
More than 25	67 (71.3%)
Marriage Duration	
< 2 Years	52 (55.3%)
> 2 Years	42 (44.7%)
Education	
Illiterate	8 (8.5%)
FA	25 (26.6%)
Undergraduate	59 (62.8%)
Postgraduate	2 (2.1%)
Parity	
Primiparity	31 (33.0%)
Multiparity	63 (67.0%)
Gestational Diabetes Mellitus	
Yes	18 (19.1%)
No	76 (80.9%)
Hypertension	
Yes	15 (16.0%)
No	79 (84.0%)
Mode of Delivery	
Vaginal Delivery	37 (39.4%)
C-Section	57 (60.6%)

HADS identified 15 mild, 35 moderate, and 44 severe cases, while EPDS reported 19 mild, 30 moderate, and 45 severe cases. Both scales demonstrate a higher number of participants in the severe category, with HADS recording 44 severe cases and EPDS identifying 45 severe cases. The distribution across mild and moderate categories was also similar, with EPDS detecting slightly more mild cases and HADS identifying more moderate cases (Figure 1).

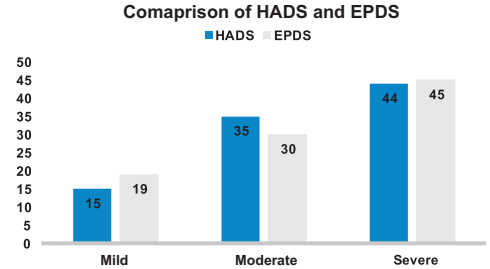

Figure 1: Comparison of HADS Scores Assessed During the Antenatal Period and EPDS Scores n The Postpartum Period Among Pregnant Women

A total of 68 participants tested positive on the EPDS, while 26 tested negative. Of those testing positive on EPDS, 45 also tested positive on HADS, yielding a sensitivity of 72.58%, indicating that HADS correctly identified about 73% of participants who had depression or anxiety according to EPDS. However, the specificity was relatively low at 28.12%, meaning that HADS only correctly identified about 28% of those who did not have depression or anxiety according to EPDS. The positive predictive value was 66.18%, suggesting that 66% of those who tested positive on HADS truly had depression or anxiety based on EPDS results. The negative predictive value was 34.62%, indicating that only about 35% of those who tested negative on HADS were truly free from depression or anxiety. Overall, the diagnostic accuracy of HADS in this study was 57.45%, meaning that HADS correctly classified participants according to EPDS just over half of the time. These findings suggest that while HADS has good sensitivity, its specificity and overall diagnostic accuracy was limited in this population (Table 2).

Table 2: Diagnostic Accuracy of HADS and EPDQ for Evaluating Depression and Anxiety among Postpartum Female

HADS	EPDS (%)		Total
	EPDS (%)	Negative	
Positive	45	23	68
Negative	17	9	26
Total	62	32	94
Sensitivity	72.58%		
Specificity	28.12%		
Positive Predicted Value	66.18%		
Negative Predicted Value	34.62%		
Diagnostic Accuracy	57.45%		

DISCUSSION

The findings of this study underscore the critical importance of early and reliable detection of Postpartum Depression (PPD) and anxiety through the use of validated screening tools. In this study, HADS identified 15 mild, 35 moderate, and 44 severe cases, while EPDS reported 19 mild, 30 moderate, and 45 severe cases. Both scales demonstrate a higher number of participants in the severe category, with HADS recording 44 severe cases and EPDS identifying 45 severe cases. This was consistent with existing research, as EPDS, being specifically designed to screen for postpartum depression, may better capture emotional and cognitive symptoms, such as anhedonia and guilt, which were prevalent in this population [17]. Additionally, the dual functionality of HADS in screening for both anxiety and depression was particularly beneficial, as anxiety was a common comorbidity with PPD, and HADS identified moderate to severe anxiety in 20% of

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participants. The ability to assess anxiety alongside depression was valuable, as untreated anxiety can exacerbate depressive symptoms and negatively affect maternal-infant bonding, which highlights the complementary roles of HADS and EPDS in clinical practice [18]. A study reported that 33.3% of women experienced Postpartum Depression (PPD). A significant correlation indicated that women with higher EPDS scores shortly after delivery were more likely to continue experiencing depressive symptoms weeks later, underscoring the importance of early screening to monitor those at risk [19]. Another study conducted on the Chinese population found that the prevalence of antenatal major and minor depression was 9.6% and 30.5%, respectively. This elevated rate of both major and minor depressive disorders underscores the substantial mental health challenges encountered by this group, especially in relation to obstetric complications [20]. Another study was conducted on the diagnostic accuracy of EPDQ, it was reported that the EPDQ showed excellent diagnostic accuracy for depression in postpartum women [21]. In currents study it was demonstrated that amongst the two scales, EPDS has shown promising results to diagnose postpartum depression compared to HADS in differentiating these two conditions. These findings were consistent with cross-sectional study assessing the psychometric properties of depression and anxiety scales, found both scales exhibited good internal consistency and fair correlation. The highest Cohen's kappa was 0.46, showing fair agreement between the two. Both scales were reliable tools for assessing antepartum depression, with focusing on EPDS detecting depressive symptoms accompanied by anxiety. The study suggests that using both scales together could improve the identification of antepartum depressive disorders in clinical practice [22]. In a community-based cross-sectional study conducted among 270 postpartum women at public health facilities, 92 women (34.6%) screened positive for depression using the EPDS, 89 women (33.3%) were scored with HADS-A and were anxious. A total of 69 women experienced both anxiety and depression. It was widely believed that EPDS was a better measure of depression due to being focused toward postpartum populations while the HADS-A was better for measuring anxiety [23]. This study emphasizes the importance of repeated mental health assessments during pregnancy and the postpartum period, as symptoms can change over time. The study recommends the combined use of the HADS and EPDS in routine clinical practice to achieve a more comprehensive understanding of maternal mental health. Utilizing both tools may enhance the detection of anxiety disorders, which were often underdiagnosed, ensuring that a wider array of mental health challenges in postpartum women was addressed.

The study has few limitations in particular the small sample size, which could invite selection bias and perhaps limit the external validity of the study findings. If the sample size was relatively small in proportion to the population that was being tested, it was plausible that these findings would be wrong and would have lower relevance in other populations or contexts.

CONCLUSIONS

Amongst the two scales, EPDS has shown promising results to diagnose postpartum depression compared to HADS in differentiating these two conditions. Hence, using both of these scales would complement the value toward clinical practice. Important for this was early detection, and timely interventions, as efforts to enhance maternal mental health outcomes have always highlighted the need for integrating routine antenatal and postpartum care with mental health screening in preventing the possible long-term consequences on mothers and their children.

Authors Contribution

Conceptualization: SR
Methodology: SR, FS, SA
Formal analysis: SR
Writing, review and editing: SR, SS, NH, FS, SA, MH

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Venkatachari R. Maternal mental health and child outcomes: a human-centered design perspective on preventive mental health care.[Doctoral Dissertation]. Massachusetts Institute of Technology; 2020.

[2] Liu X, Wang S, Wang G. Prevalence and risk factors of postpartum depression in women: A systematic review and meta-analysis. Journal of Clinical Nursing. 2022 Oct; 31(19-20): 2665-77. doi: 10.1111/jocn.16121.

[3] Rahman A, Patel V, Maselko J, Kirkwood B. The neglected 'm'in MCH programmes-why mental health of mothers is important for child nutrition. Tropical Medicine & International Health. 2008 Apr; 13(4): 579-83. doi: 10.1111/j.1365-3156.2008.02036.x.

[4] van der Zee-van Al, Boere-Boonekamp MM, Groothuis-Oudshoorn CG, Reijneveld SA. Postpartum depression and anxiety: a community-based study on risk factors before, during and after pregnancy.

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Journal of Affective Disorders. 2021 May; 286: 158-65. doi: 10.1016/j.jad.2021.02.062.

[5] Layton H, Owais S, Savoy CD, Van Lieshout RJ. Depression, anxiety, and mother-infant bonding in women seeking treatment for postpartum depression before and during the COVID-19 pandemic. The Journal of Clinical Psychiatry. 2021 Jul; 82(4): 35146. doi: 10.4088/JCP.21m13874.

[6] Cheng CY, Chou YH, Chang CH, Liou SR. Trends of perinatal stress, anxiety, and depression and their prediction on postpartum depression. International journal of environmental research and public health. 2021 Sep; 18(17): 9307. doi: 10.3390/ijerph18179307.

[7] Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression: development of the 10-item Edinburgh Postnatal Depression Scale. The British Journal of Psychiatry.1987 Jun; 150(6): 782-6. doi: 10.1192/bjp.150.6.782.

[8] Matthey, S., Henshaw, C., Elliot, S., & Barnett, B. (2006). The Edinburgh Postnatal Depression Scale: A review of the literature.Journal of Affective Disorders, 91(1), 3-15. https://doi.org/10.1016/j.jad.2005.11.035. \

[9] Zigmond AS and Snaith RP.The hospital anxiety and depression scale.Acta Psychiatrica Scandinavica.1983 Jun; 67(6): 361-70. doi: 10.1111/j.1600-0447.1983.tb09716.x.

[10] Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale: an updated literature review.Journal of Psychosomatic Research. 2002 Feb; 52(2): 69-77. doi: 10.1016/S0022-3999(01)00296-3.

[11] Matthey S, Barnett B, Howie P, Kavanagh DJ. Diagnosing postpartum depression in mothers and fathers: whatever happened to anxiety?. Journal of Affective Disorders. 2003 Apr; 74(2): 139-47. doi: 10.1016/S0165-0327(02)00012-5.

[12] Sakina R, Khan SE, Chaudhry AG. Stigma of postpartum depression: The role of lady health workers in health care-A qualitative study. Health Care for Women International.2022 Jul; 43(9): 1095-104. doi: 10.1080/07399332.2021.1973009.

[13] Safi-Keykaleh M, Aliakbari F, Safarpour H, Safari M, Tahernejad A, Sheikhbardsiri H *et al.* Prevalence of postpartum depression in women amid the COVID-19 pandemic: a systematic review and meta-analysis. International Journal of Gynecology & Obstetrics. 2022 May; 157(2): 240-7. doi: 10.1002/ijgo.14129.

[14] Lodhi FS, Elsous AM, Irum S, Khan AA, Rabbani U. Psychometric properties of the Urdu version of the Hospital Anxiety and Depression Scale (HADS) among pregnant women in Abbottabad, Pakistan. General Psychiatry. 2020 Aug; 33(5). doi: 10.1136/gpsych-2020-100276.

[15] Levis B, Negeri Z, Sun Y, Benedetti A, Thombs BD. Accuracy of the Edinburgh Postnatal Depression Scale (EPDS) for screening to detect major depression among pregnant and postpartum women: systematic review and meta-analysis of individual participant data. British Medical Journal.2020 Nov; 371. doi: 10.1136/bmj.m4022.

[16] Saeed A, Raana T, Saeed AM, Humayun A. Effect of antenatal depression on maternal dietary intake and neonatal outcome: a prospective cohort. Nutrition Journal.2015 Dec; 15: 1-9. doi: 10.1186/s12937-016-0184-7.

[17] Edinburgh Postnatal Depression Scale (EPDS) – A Review. (2016). Journal of Affective Disorders, 202, 917. https://doi.org/10.1016/j.jad.2016.04.037.

[18] El-Hachem C, Rohayem J, Bou Khalil R, Richa S, Kesrouani A, Gemayel R et al. Early identification of women at risk of postpartum depression using the Edinburgh Postnatal Depression Scale (EPDS) in a sample of Lebanese women. BioMed Central Psychiatry. 2014 Dec; 14: 1-9. doi: 10.1186/s12888-014-0242-7.

[19] Gavin NI, Gaynes BN, Lohr KN, Meltzer-Brody S, Gartlehner G, Swinson T. Perinatal depression: A systematic review of prevalence and incidence. Obstet Gynecol.2005;106(5):1071-1083. doi: 10.1097/01.AOG.0000183597.31630.d2.

[20] Park SH and Kim JI. Predictive validity of the Edinburgh postnatal depression scale and other tools for screening depression in pregnant and postpartum women: a systematic review and meta-analysis. Archives of Gynecology and Obstetrics.2023 May; 307(5): 1331-45. doi: 10.1007/s00404-022-06525-0.

[21] Schoretsanitis G, Gastaldon C, Ochsenbein-Koelble N, Olbrich S, Barbui C, Seifritz E. Postpartum hemorrhage and postpartum depression: a systematic review and meta-analysis of observational studies.Acta Psychiatrica Scandinavica.2024 Nov; 150(5): 274-83. doi: 10.1111/acps.13583.

[22] Agbaje OS, Anyanwu JI, Umoke PI, Iwuagwu TE, Iweama CN, Ozoemena EL *et al.* Depressive and anxiety symptoms and associated factors among postnatal women in Enugu-North Senatorial District, South-East Nigeria: a cross-sectional study. Archives of Public Health. 2019 Dec; 77: 1-6. doi: 10.1186/s13690-018-0329-6.

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A Comprehensive Analysis of Risk Factors Associated with Type 1 Diabetes Mellitus in Children and Adolescents at a Tertiary Healthcare Facility

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ABSTRACT

Type 1 Diabetes is an autoimmune condition affecting the pancreas. **Objectives:** To assess the associations between genetic and environmental risk factors and the development of Type 1 Diabetes Mellitus in children and adolescents. **Methods:** It was a case-control study conducted over 6 months at the Department of Pediatric Endocrinology and Diabetes, the Children's Hospital Lahore. The study population consisted of two groups. Cases consisted of children with Type 1 Diabetes while controls were without Type 1 Diabetes. Data were collected using a pre-designed questionnaire by interview method from parents of children participating in the study. The incidence of various environmental and genetic factors reported to be associated with Type 1 Diabetes was compared between the groups. **Results:** 300 children participated in the study (n=150 cases and n=150 control group). The mean age of the participants was 7.90 + 4.553 years. Pearson chi-square test revealed a significant association between Type 1 Diabetes and various factors like cow's milk in infancy, early weaning, and vitamin D supplementation. Amongst the genetic factors, the association was significant for history of autoimmunity, family history of autoimmunity and family history of Type 1 Diabetes (p-value=<0.05). **Conclusions:** It was concluded that children with a history of autoimmunity or Type 1 Diabetes in self or family, early introduction to cow's milk and supplementary foods are at higher risk for Type 1 Diabetes. Meanwhile, no relationship was established between Type 1 Diabetes and prior COVID-19 infection or recurrent infections. Further studies are needed to establish cause and effect relationship.

INTRODUCTION

Type 1 diabetes (T1D) is a chronic autoimmune disease with a significant impact on children and adolescents worldwide. It is a disease of the islet cells of the pancreas. Autoimmunity results in the destruction of islet cells and consequent insulinemia. About 17 –70 % of cases with T1D present with a life-threatening complication called diabetic ketoacidosis (DKA), due to delay in the diagnosis. Furthermore, mortality from DKA is <1 % in developed countries and 3-13% in developing countries [1]. Pathophysiology of T1D is complex and is a consequence of a combination of genetic predisposition along with largely unknown environmental factors. The increasing incidence of Type 1 Diabetes Mellitus (T1D) coupled with a reduction in the proportion of individuals with the highest risk of Human Leukocyte Antigen haplotypes, highlights the significant contribution of environmental exposures in the pathogenesis of T1D [2]. Other than genetic risk factors, several environmental risk factors were proposed to be linked with the pathogenesis of T1D. Age is considered an important risk factor, as studies have shown that T1DM commonly manifests during childhood and adolescence [3]. Research has now expanded from merely treatment to preventive strategies focusing on the risk factors and etiologies of the development of autoimmunity, aiming to identify individuals at risk before diabetes has set in and be able to modify the natural course of illness [4, 5].

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International research has shown that both genetic and environmental factors have a relationship with the onset of T1D [6, 7]. Amongst the genetic factors, the most strongly associated with T1D are the Major Histocompatibility Complex Human Leukocyte Antigen (MHC/HLA) and non-MHC/HLA genes [8].

This study aims to determine the association of various genetic and environmental risk factors with T1DM. It will provide a better understanding of the pathogenesis of T1DM in children and adolescents of our local population as such extensive data is missing in previously published literature. Identifying these potential risk factors will provide valuable insights for the development of targeted preventive strategies and risk factor modification. It will also help us in making guidelines for screening T1DM in our local population which helps in early diagnosis and prevention of Diabetic ketoacidosis (DKA).

METHODS

A case-control study was conducted at the University of Child Health Sciences, the Children's Hospital, Lahore. The study was carried out in the Department of Pediatric Endocrinology and Diabetes over 6 months from November 2023 to May 2024 after prior approval from the Ethical Review Board from the respected hospital vide letter no. 694. Open-Epi online calculator was used to calculate the sample size. Sample size was calculated with a 2-sided confidence interval of 95% and power of 80% taking the equal ratio of controls and cases. The hypothetical incidence of T1D amongst those who were breastfed was taken as 11% while the incidence of T1D amongst those who were not was taken as 55% [9]. Convenience sampling was used to include 150 children diagnosed with T1D from the outpatient department and wards of Children's Hospital, Lahore. Similarly, 150 children were enrolled in the control group of the study who did not have T1D. This method was employed because of its simplicity, efficiency and its cost-effectiveness. The inclusion criteria for the case group were all children between the ages of one year and 18 years and diagnosed with Type 1 Diabetes Mellitus. Both male and female were included in the study. Controls were children of both genders between the ages of one year and 18 years who were not diagnosed with T1D and did not have any symptoms of polyuria, polydipsia, or unexplained weight loss. Exclusion criteria were formulated extensively to ensure the removal of any confounders in the study. Any child who was found to have Maturity Onset Diabetes of the Young, Type 2 Diabetes Mellitus, neonatal diabetes, or diabetes secondary to other illnesses like cystic fibrosis, thalassemia, chronic pancreatitis, or drug-induced. Also, children with any history of chemotherapy or radiotherapy or history of intake of a drug that might contribute to diabetes were excluded. Any child with syndromic features, developmental delay, or disorders of sexual development was also excluded from the study. Chronic infections like hepatitis B, Hepatitis C, tuberculosis and human immunodeficiency virus (HIV) were also part of the exclusion criteria. Non-probability consecutive sampling technique was used to gather the samples. All patients and controls participating in the study gave informed consent for enrollment in the study. Data were collected on a predesigned questionnaire by one-to-one interview. The questionnaire consisted of three parts. The first part had questions about age, gender, demographic data and questions regarding any of the above-mentioned conditions to rule out any of the exclusion criteria. The second part was regarding genetic factors that may or may not have any association with T1D. The third part concerned the environmental factors investigated for a possible association with T1D. It was validated by experts in the field of pediatric endocrinology and by researchers constituting the Research Ethics Board (ERB) of our hospital. Avoidance of breastfeeding was defined as the deliberate decision or practice of not breastfeeding (either from a biological mother or donor) either partially or entirely to a child below one year of age. Early introduction of cow's milk was defined as the addition of cow's milk to an infant's diet before the completion of 12 months. Similarly, early weaning was defined as the introduction of supplementary foods before the completion of six months. Vitamin D supplementation was taken as any oral supplements given to children in the form of syrups, tablets, drops or mega dose ampoules. Recurrent infections were defined as two or more severe infections in any one year or three or more infections in one year. Family history of Autoimmune illnesses like celiac disease, Hashimoto's thyroiditis, Grave's disease, Addison's disease, juvenile idiopathic arthritis, autoimmune hepatitis, autoimmune hepatitis, autoimmune thrombocytopenia purpura, and systemic lupus erythematosus were also excluded by interview to remove any confounding factors. Data were analyzed using a statistical package for social sciences version 23.0. Descriptive statistics were employed to describe the data. Mean and standard deviation were calculated for age in years. Discrete data regarding the frequency of genetic and environmental factors was expressed as percentages. Both groups were analyzed for any differences in the relationship of various genetic and environmental factors between the two groups. Pearson chi-square test was employed to determine if the difference between the two groups was statistically significant. The difference was considered statistically significant if the p-value was less than or equal to 0.05.

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RESULTS

A total of 300 subjects were enrolled in this study. 150 were allotted to the control group and 150 to the cases group. 172 subjects were male and 128 were female. The mean age of all participants was 7.90 ± 4.55 years. In the total study population, 125 children were a product of consanguineous marriages. 68 had a history of avoidance of breastfeeding. 93 children were introduced to cow's milk before the age of one year while 73 children were weaned with supplemental foods before the age of six months (Table 1).

Table 1: Demographic Features of Children Participating in the Study (n=300)

Variables	Frequency (%)
Age (Years)	
Mean ± SD	7.90 ± 4.553 Years
Gender	
Male	172 (57.3%)
Female	128 (42.7%)
Consanguinity	
Yes	125 (41.7%)
No	175 (58.3%)
Avoidance of Breastfeeding	
Yes	68 (22.7%)
No	232 (77.3%)
Cow's Milk Introduction in Infancy	
Yes	93 (31%)
No	207 (69%)
Early Weaning	
Yes	73 (24.3%)
No	227 (75.7%)

When the two groups were compared it was found that there were 83 males amongst the cases and 89 amongst controls. The p-value was 0.484 and hence the difference was not significant. Similarly, there were 66 products of consanguineous marriages amongst cases and 59 of the controls were products of consanguinity. The difference was not statistically significant as the p-value was 0.412. 15 patients amongst cases had a history of other co-existing autoimmune illnesses besides type 1 diabetes mellitus. At the same time, only three of the controls had such diseases. The p-value was 0.004. History of autoimmune illness besides type 1 diabetes mellitus in the family was found in 10 of the cases while only five of the controls had such history. The p-value was 0.003. Family history of type 1 diabetes mellitus was found in 46 of the cases and 10 of controls. The p-value was <0.001. Hence, amongst the genetic factors, the difference between the two groups was statistically significant for autoimmunity in self, and family history of autoimmunity or T1D while being most striking for family history of T1D (Table 2).

Table 2: Association between Genetic Factors and Type 2 Diabetes (*= Pearson Chi-square)

Genetic Factor	Cases	Controls	p-Value
Gender			
Male	83 (55.3%)	89 (59.3%)	0.484*
Female	67 (44.7%)	61 (40.7%)	
Consanguinity			
Yes	66 (44%)	59 (39.3%)	0.412*
No	84 (56%)	91 (60.7%)	
History of Autoimmune Illness in Self			
Yes	15 (10%)	3 (2%)	0.004*
No	135 (90%)	147 (98%)	
Family History of Autoimmunity			
Yes	19 (12.7%)	5 (3.3%)	0.003*
No	131 (87.3%)	145 (96.7%)	
Family History of T1D			
Yes	46 (30.7%)	10 (6.7%)	<0.001*
No	104 (69.3%)	140 (93.3%)	

Similar tests were employed to establish whether there was a statistically significant relationship between environmental factors and T1D. 60 children from amongst cases and 33 children from amongst controls had a history of early cow's milk introduction. The p-value was 0.001. Statistical analysis of early weaning trends yielded similar results. 49 cases and 24 individuals from the control group had a history of weaning before six months. The p-value was calculated to be 0.001. Avoidance of breastfeeding was observed in 39 cases and 29 controls. The p-value was 0.168. Vitamin D supplementation revealed the most striking difference among the environmental factors. 61 of those with type 1 diabetes mellitus had been supplemented with some form of vitamin D while only 18 of those without type 1 diabetes mellitus had received any supplements of vitamin D. Thus the p-value was less than 0.001. The incidence of recurrent infections amongst diabetics was 34 while amongst the non-diabetics it was 41. Covid-19 infections were low in both groups with 5 individuals from cases and 4 individuals from the control group being infected. The p-value was statistically non-significant for both at 0.351 and 0.735, respectively (Table 3).

Table 3: Pearson Chi-Square Test for the Relationship of Various Environmental Factors with T1D. (*= Pearson Chi-square)

Environmental Factor	Cases	Controls	p-Value
Avoidance of Breastfeeding			
Yes	39 (26.0%)	29 (19.3%)	0.168*
No	111 (74.0%)	121 (80.7%)	
Cow's Milk Introduction in Infancy			
Yes	60 (40%)	33 (22%)	0.001*
No	90 (60%)	117 (78%)	
Early Weaning			
Yes	49 (32.7%)	24 (16%)	0.001*
No	101 (67.3%)	126 (84.0%)	

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Vitamin D Supplementation			
Yes	61 (40.7%)	18 (12%)	<0.001*
No	89 (59.3%)	132 (88%)	
Recurrent Infections in 1st Year of Life			
Yes	34 (22.7%)	41 (27.3%)	0.351*
No	116 (77.3%)	109 (72.7%)	
Prior Covid-19 Infection			
Yes	5 (3.3%)	4 (2.7%)	0.735*
No	145 (96.7%)	146 (97.3%)	

DISCUSSION

Pakistan is a population of over 200 million individuals with almost two-thirds of the population being under 18 years [10]. While the incidence of T1D is estimated to be less than five per 100,000, it still amounts to a staggering figure of more than 6500 patients per year [11]. Previously, the environmental factors mostly included infections and dietary supplements. However, recently it has expanded to the relationship between the timing of food introduction and the role of gut microbiome with T1D, as was shown by our results. Though cause and effect have not been established as yet there is evidence that they may alter the course of illness [8]. While recent advances are changing the management landscape of T1D, they are still widely unavailable for the developing world. Considering their cost and technological requirements the hope for resource-limited countries relies mostly on insulin therapy. However, that is not to say technology cannot be employed to improve patient outcomes in third-world countries. Studies have shown how telemedicine has widened the scope of treatment and how mobile phones can play a role in the management of T1D. A recently published study from Pakistan proved how health education regarding various aspects of T1D was imparted via a short messaging service and results have been promising for HbA1c and most of the secondary outcomes [12]. Infections play a two-way role in association with T1D. While poorly controlled diabetes increases the risk of susceptibility to infections, infection itself may be a contributing factor to poor glycemic control and resultant decompensation leading to a diagnosis of T1D. Though, in our study, we did not find a significant relationship between infections and diabetes, Piccolo et al postulated otherwise [13]. Other studies also reveal that repeated infections could potentially disrupt immune regulation and increase the risk of developing T1D [14]. Our findings were similar to that of Rahmati *et al.* Their meta-analysis comprising seven studies involving more than 11 million participants revealed that the risk of T1D in patients with a history of COVID-19 infection was not found in any studies except those from the United States. This further extrapolates to their being a geographic link that has remained unexplored by researchers [15]. The association of the Covid pandemic with a new surge of T1D is still undergoing investigation and some studies reported a fair rise in T1D cases after the Covid pandemic [16]. Similarly, another systematic review and meta-analysis by Lampoussi *et al.*, from the world over concluded that the risk of T1D was lower in individuals who were exclusively breastfed and those introduced to cow's milk and supplemental foods at a later age. Our result was similar except for breastfeeding which did not establish a significant difference. One explanation could be that Lampoussi *et al.*, focused on exclusive breastfeeding while our study included both exclusive and partially breastfed children in the cohort [17]. Various studies have proposed a link between autoimmunity among diabetics and their relatives [18, 19]. Lorini *et al.*, while studying 55 children found that 58% of these children had one or more autoantibodies [18]. Family history was investigated by Gilliam *et al.* Their results were supportive of our findings during the study. They further found that age at diagnosis was directly related to the age of a family member at the time of diagnosis. Hence, the sooner the history of presentation in the family, the more likely the child to be diagnosed at a younger age [20].

CONCLUSIONS

It was concluded that current study has conclusively established a relationship between T1D and autoimmunity in self and family history of both and also for early introduction of cow's milk and supplementary foods being risk factors. It is pertinent that further research is carried out to establish a more strong relationship between these factors and T1D. These factors could be used later on to predict and prevent T1D. A multi-center study may reflect more reproducible results.

Authors Contribution

Conceptualization: AN
Methodology: SHU, NUAM, KFM, SA
Formal analysis: AN
Writing review and editing: AN, SA, KA

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Curtis JR, To T, Muirhead S, Cummings E, Daneman D. Recent Trends in Hospitalization for Diabetic Ketoacidosis in Ontario Children. Diabetes Care. 2002 Sep; 25(9): 1591-6. doi: 10.2337/diacare.25.9.15

DOI: https://doi.org/10.54393/pjhs.v5i12.2403

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[2] Fourlanos S, Varney MD, Tai BD, Morahan G, Honeyman MC, Colman PG *et al.* The Rising Incidence of Type 1 Diabetes Is Accounted for by Cases with Lower-Risk Human Leukocyte Antigen Genotypes. Diabetes Care. 2008 Aug; 31(8): 1546-9. doi: 10.2337/dc08-0239.

[3] American Diabetes Association. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes—2021. Diabetes Care. 2021 Jan; 44(Supplement_1): S15-33. doi: 10.2337/dc21-S002.

[4] Sherr JL, Laffel LM, Liu J, Wolf W, Bispham J, Chapman KS *et al.* Severe Hypoglycemia and Impaired Awareness of Hypoglycemia Persist in People with Type 1 Diabetes Despite Use of Diabetes Technology: Results from A Cross-Sectional Survey. Diabetes Care. 2024 Jun; 47(6): 941-7. doi: 10.2337/dc23-1765.

[5] Gregory GA, Robinson TI, Linklater SE, Wang F, Colagiuri S, de Beaufort C *et al.* Global Incidence, Prevalence, and Mortality of Type 1 Diabetes in 2021 with Projection to 2040: A Modelling Study. The Lancet Diabetes and Endocrinology. 2022 Oct; 10(10): 741-60. doi: 10.1016/S2213-8587(22)00218-2.

[6] Vurallı D, Jalilova L, Alikaşifoğlu A, Özön ZA, Gönç EN, Kandemir N. Cardiovascular Risk Factors in Adolescents with Type 1 Diabetes: Prevalence and Gender Differences. Journal of Clinical Research in Pediatric Endocrinology. 2024 Mar; 16(1): 11. doi: 10.4274/jcrpe.galenos.2023.2023-12-12.

[7] Ramos EL, Dayan CM, Chatenoud L, Sumnik Z, Simmons KM, Szypowska A *et al.* Teplizumab and β-cell Function in Newly Diagnosed Type 1 Diabetes. New England Journal of Medicine. 2023 Dec; 389 (23): 2151-61. doi: 10.1056/NEJMoa2308743.

[8] Ramaphane T, Gezmu AM, Tefera E, Gabaitiri L, Nchingane S, Matsheng-Samuel M *et al.* Prevalence and Factors Associated with Microalbuminuria in Pediatric Patients with Type 1 Diabetes Mellitus at a Large Tertiary-Level Hospital in Botswana. Diabetes, Metabolic Syndrome and Obesity. 2021 Nov; 14: 4415-22. doi: 10.2147/DMSO.S322847.

[9] Oza C, Khadilkar V, Karguppikar M, Ladkat D, Gondhalekar K, Shah N *et al.* Prevalence of Metabolic Syndrome and Predictors of Metabolic Risk in Indian Children, Adolescents and Youth with Type 1 Diabetes Mellitus. Endocrine. 2022 Mar; 75(3): 794-803. doi: 10.1007/s12020-021-02924-6.

[10] Abrahim AM, Tilahun T, Gelana B. Glycemic Control and Associated Factors Among Children and Adolescents with Type 1 Diabetes Mellitus, Southwest Ethiopia. Diabetes, Metabolic Syndrome and Obesity. 2023 Dec; 16: 2025-37. doi: 10.2147/DMSO.S412529.

[11] Patterson CC, Karuranga S, Salpea P, Saeedi P, Dahlquist G, Soltesz G *et al.* Worldwide Estimates of Incidence, Prevalence and Mortality of Type 1 Diabetes in Children and Adolescents: Results from the International Diabetes Federation Diabetes Atlas. Diabetes Research and Clinical Practice. 2019 Nov; 157: 107842. doi: 10.1016/j.diabres.2019.107842.

[12] Rahman A, Razzaq A, Khan MS, Nawaz S, Akhtar S. Short Message Service as a Tool for Health Education in Families of Children with Type 1 Diabetes in Pakistan: A Randomized Control Trial. Pakistan Armed Forces Medical Journal. 2024 Apr; 74(2): 506-511. doi: 10.51253/pafmj.v74i2.10215

[13] Piccolo G, De Rose EL, Bassi M, Napoli F, Minuto N, Maghnie M *et al.* Infectious Diseases Associated with Pediatric Type 1 Diabetes Mellitus: A Narrative Review. Frontiers in Endocrinology. 2022 Aug; 13: 966344. doi: 10.3389/fendo.2022.966344.

[14] Calliari LE, Almeida FJ, Noronha RM. Infections in Children with Diabetes. Journal of Pediatric. 2020 Apr; 96(Suppl-1): 39-46. doi: 10.1016/j.jped.2019.09.004.

[15] Rahmati M, Yon DK, Lee SW, Udeh R, McEvoy M, Kim MS *et al.* New-Onset Type 1 Diabetes in Children and Adolescents as Postacute Sequelae of SARS-Cov-2 Infection: A Systematic Review and Meta-Analysis of Cohort Studies. Journal of Medical Virology. 2023 Jun; 95(6): e28833. doi: 10.1002/jmv.28833.

[16] D'Souza D, Empringham J, Pechlivanoglou P, Uleryk EM, Cohen E, Shulman R. Incidence of Diabetes in Children and Adolescents During the COVID-19 Pandemic: A Systematic Review and Meta-analysis. Journal of the American Medical Association. Network Open. 2023 Jun; 6(6): e2321281-. doi: 10.1001/jamanetworkopen.2023.21281.

[17] Lampousi AM, Carlsson S, Löfvenborg JE. Dietary Factors and Risk of Islet Autoimmunity and Type 1 Diabetes: A Systematic Review and Meta-Analysis. E Bio Medicine. 2021 Oct; 72: 103633. doi: 10.1016/j.ebiom.2021.103633.

[18] Lorini R, Larizza D, Livieri C, Cammareri V, Martini A, Plebani A *et al.* Auto-Immunity in Children with Diabetes Mellitus and Their Relatives. European Journal of Pediatrics. 1986 Aug; 145: 182-4. doi: 10.1007/BF00446060.

[19] Frazzei G, van Vollenhoven RF, de Jong BA, Siegelaar SE, van Schaardenburg D. Preclinical Autoimmune Disease: A Comparison of Rheumatoid Arthritis, Systemic Lupus Erythematosus, Multiple Sclerosis and Type 1 Diabetes. Frontiers in Immunology. 2022

DOI: https://doi.org/10.54393/pjhs.v5i12.2403

Jun; 13: 899372. doi: 10.3389/fimmu.2022.899372.

[20] Gilliam LK, Liese AD, Bloch CA, Davis C, Snively BM, Curb D *et al* SEARCH for Diabetes in Youth Study Group. Family History of Diabetes, Autoimmunity, and Risk Factors for Cardiovascular Disease among Children with Diabetes in the SEARCH for Diabetes in Youth Study. Pediatric Diabetes. 2007 Dec; 8(6): 354-61. doi: 10.1111/j.1399-5448.2007.00241.x.

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Effectiveness of Gemcitabine with or without Radiotherapy in Gallbladder Carcinoma

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ABSTRACT

Gallbladder carcinoma is the most common malignancy of the hepatobiliary tract and the 5th most common cancer of the gastrointestinal tract. **Objective:** To compare the efficacy of gemcitabine as a single agent or in combination with radiation in terms of response rate and relief of symptoms in gallbladder carcinoma. **Methods:** This retrospective study was accomplished at the department of oncology, Nishter Hospital Multan, Pakistan, from January 2021 to December 2022. Inclusion criteria were patients with a histopathologically proven diagnosis of gallbladder carcinoma, and they were advised gemcitabine with or without radiation therapy as per the treating physician's discretion. The treatment response rate and alleviation of symptoms were noted. **Results:** Among a total of 50 patients, 40 (80.0%) were female. The mean age was 56.58 ± 6.14 years. At baseline, 33 (66.0%) patients had stable disease, while the remaining 17 (34.0%) had progressive disease. Gemcitabine alone revealed stable disease, and progressive disease in 14 (56.0%), and 11 (44.0%) patients, respectively, whereas among patients receiving gemcitabine plus radiotherapy, partial response, stable disease, and progressive disease were observed in 7 (28.0%), 14 (50.0%), and 4 (16.0%) patients, respectively (p=0.006). Regarding symptom relief, 8 (32.0%) patients in the gemcitabine alone group had pain relief versus 20 (80.0%) in the gemcitabine plus radiotherapy group (p=0.001). **Conclusion:** Gemcitabine plus concomitant radiotherapy was more effective in achieving higher response rates and alleviation of symptoms when compared to gemcitabine alone in gallbladder carcinoma patients.

INTRODUCTION

Gallbladder carcinoma is known to be the commonest hepatobiliary tract malignancy, and the 5th most frequent gastrointestinal tract related carcinoma [1]. The incidence of gall bladder cancer shows regional variation; it is more common in whites than in black women and more common in Native Americans and Mexican Americans. In Asian countries, there is a much higher incidence in Japan, Thailand, Korea, and the subcontinent [2]. Gallbladder carcinoma usually has a silent course and a dismal prognosis [3]. Initial symptoms of gall bladder carcinoma include pain in the abdomen, more often confined to the right hypochondrium, vomiting, loss of appetite, early satiety, and jaundice [4]. Initially, the disease does not create an alarming state, and thus, patients usually present late when the disease is advanced or often unresectable [5]. Various risk factors associated with this gall bladder disease include obesity, the presence of gall stones, choledochal cysts, estrogen excess, typhoid carriers, porcelain gallbladder, and multiparity [6, 7]. As gallbladder carcinoma is not very common, not much is stated about the standard regimen for managing these cases, but surgery, radiation therapy, and chemotherapy have their roles in the palliation and control of disease [8]. Surgical resection is the only curative option in gallbladder carcinoma. With localized disease, surgery, either simple cholecystectomy or extended radical cholecystectomy, plays an important role and offers better disease control for gallbladder carcinoma [9]. As gallbladder carcinoma usually presents in advanced stages, adjuvant therapy is usually required in most of the patients [10]. Depending on the stage of the disease, chemotherapy and radiotherapy are used in addition to surgery. Various chemotherapeutic

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agents have been used in different settings. Various trials have shown that gemcitabine is effective in gallbladder cancer, especially when used in combination with cisplatin [11, 12]. Initial phase 1 and 2 trials have produced encouraging results, but it is still not considered a standard drug as the available data are of short duration and the number of patients accrued in these trials is small [13, 14]. Radiation therapy has a palliative role, and it has been used in advanced stages for relief of pain and pressure effects. Radiation therapy has also been used in addition to surgery, and it has proved to be beneficial for longer disease control [15]. To improve the response rate in gallbladder cases with radiation alone, the dose of radiation has to be increased, which can lead to high hepatic toxicity [16]. A better reaction and a lower radiation dosage are obtained by using a radiosensitizer. Although gemcitabine has been characterized as a strong radiosensitizer, the ideal dose for radiosensitization is still up for debate. Doses ranging from 200 mg to 600 mg have been used concurrently with radiation [13, 14]. It was hypothesized that gemcitabine combined with radiation may be better in terms of relief of symptoms when compared to gemcitabien alone.

The aim of this study was to compare the efficacy of gemcitabine as a single agent or in combination with radiation in terms of response rate and relief of symptoms in gallbladder carcinoma.

METHODS

This retrospective study was carried out at the department of oncology, Nishter Hospital Multan, Pakistan, from January 2021 to December 2022. Ethical approval was obtained from the Institutional Ethical Review Board of Nishtar Medical University, Multan, under Reference Number 428.The inclusion criteria were record of patients of either gender, irrespective of age, with a histopathologically proven diagnosis of gallbladder carcinoma, adequate marrow reserve (Hb ≥ 9 g/dl, WBC ≥ 4000/mm3, ANC > 2000/mm3, platelet count > 100,000/mm3), renal parameters within the normal range, liver function tests not deranged, Karnofsky performance score of 60 or above, life expectancy of 3 months or greater, a normal x-ray chest, and were admitted to the oncology department during the study period. A record of patients was included if they were advised to take gemcitabine with or without radiation therapy as per the treating physician's discretion. The exclusion criteria were patients who had prior chemotherapy or radiotherapy. The sample selection was done using a non-probability convenience sampling technique. During the study period from January 2021 to December 2022, data of total 75 patients with gallbladder carcinoma were reviewed. Out of these, 50 patients met the inclusion acriteria and were reviewed in the study. The remaining 25 patients were excluded due to factors such as prior chemotherapy or radiotherapy, inadequate marrow reserve, deranged liver function tests, or a Karnofsky performance score below 60. Demographic data like gender, age, residential status, presenting symptoms, and their duration were noted. WHO performance status was graded as 0 (fully active, able to carry on all pre-disease activities without restriction), 1 (restricted in physically strenuous activity but ambulatory and able to carry out light work), 2 (ambulatory and capable of all self-care but unable to work; up and about more than 50% of waking hours), 3 (capable of only limited self-care; confined to bed or chair for more than 50% of waking hours), or 4 (completely disabled; cannot carry out any self-care; totally confined to bed or chair). Patients who received chemotherapy were given gemcitabine 1000 mg/m2 (on days 1, 8, and 22 for a total of three cycles), while gemcitabine 200 mg was given in addition to radiation therapy (commencing with the first scheduled radiation treatment day and continuing every week until the radiation is accomplished) to the remaining patients. The intended radiation dosage involved employing the shrinking field approach to administer a 4500 cGy midway tumor dose to the right hypochondrium. Radiation therapy was administered for five weeks at a dose of 180 cGy each day, five days a week. The first port, which included the gallbladder bed and local lymph nodes, was marked. For the first 14 days, a radiation dose of 180 cGy was administered. After 14 days, by ultrasound evaluation, the portal was reduced to the tumor site. The liver's tolerance limit was taken into consideration when choosing this approach. The tumor area was radiated for the remainder of the treatment once a smaller portal was created. At follow-ups, patients underwent a thorough physical examination and a history taking. The primary endpoint was the determination of the response rate (effectiveness). The effectiveness was assessed based on how the tumor responded to the treatment. The categories for response included Complete Response (CR) as complete disappearance of all clinically detectable disease, Partial Response (PR) as at least a 50% reduction in measurable disease, Stable Disease (SD) as Neither sufficient shrinkage to qualify as PR nor sufficient increase to qualify as PD, or Progressive Disease (PD) as growth in measurable disease or the appearance of new lesions. The secondary endpoint was the alleviation of symptoms and it was labeled as reduction in reported and relevant complaint when compared to the baseline severity. All the concerned statistics were gathered using a specifically predesigned proforma. The analysis of the data was conducted through "IBM-SPSS statistics" version 26.0. The quantitative variables like age, height, and weight were shown in the form of a mean and a Standard Deviation (SD). For the qualitative variables like gender, the level of response, and elevated symptoms, frequencies and

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percentages were calculated. Applying the chi-square test, different variables were assessed for any relationship between them. A p-value ≤ 0.05 was taken as standard to mark significance.

RESULTS

The records of 50 patients, matched as per inclusion and exclusion criteria, were analyzed for this study. Among a total of 50 patients, 40 (80.0%) were female, representing a female-to-male ratio of 4:1. The mean age was 56.58 ± 6.14 years, ranging between 42 and 75 years. The residential status of 34 (68.0%) patients was rural. The socio-economic status of 28 (56.0%) patients was low. The presence of gallstones, and jaundice were noted in 41 (82.0%) and 23 (46.0%) patients, respectively. At baseline, 33 (66.0%) patients had stable disease, while the remaining 17 (34.0%) had progressive disease. Table 1 showed characteristics of patients (Table 1).

Table 1: Baseline Characteristics of Patients (N=50)

Variables	Categories	Gemcitabine Alone N (%)	Gemcitabine and Radiotherapy N (%)	p-value
Socioeconomic Status	Male	4 (16.0%)	6 (24.0%)	0.480
	Female	21 (84.0%)	19 (76.0%)	
Age Groups (Years)	40-50	4 (16.0%)	2 (8.0%)	0.596
	51-60	10 (40.0%)	9 (36.0%)	
	61-70	11 (44.0%)	13 (52.0%0	
	71-80	-	1 (4.0%)	
Residence	Urban	6 (24.0%)	10 (40.0%)	0.225
	Rural	19 (76.0%)	15 (60.0%)	
Socioeconomic Status	Low	13 (52.0%)	15 (60.0%)	0.838
	Middle	8 (32.0%)	7 (28.0%)	
	High	4 (16.0%)	3 (12.0%)	
WHO Performance Status	1	1 (4.0%)	3 (12.0%)	0.181
	2	11 (44.0%)	15 (60.0%)	
	3	13 (52.0%)	7 (28.0%)	
TNM Stage	T_3 $N_{0/1}$ M_0	6 (24.0%)	9 (36.0%)	0.507
	$T_{3/4}$ $N_{1/2}$ M_0	14 (56.0%)	10 (40.0%)	
	$T_{3/4}$ $N_{1/2}$ M_1	5 (20.0%)	6 (24.0%)	
Presence of Gallstones		18 (72.0%)	23 (92.0%)	0.066
Presence of Jaundice		11 (44.0%)	12 (48.0%)	0.777
Loss of Appetite		21 (94.0%)	23 (92.0%)	0.384
Abdominal Pain		24 (96.0%)	24 (96.0%)	1
State of Disease	Stable Disease	18 (72.0%)	15 (60.0%)	0.370
	Progressive Disease	7 (28.0%)	10 (40.0%)	

Overall, a partial response rate was seen in 7 (14.0%) patients, stable disease was seen in 28 (56.0%), and the remaining 15 (30.0%) had a progressive disease. None of the patients reported a complete response. When both groups were compared, Gemcitabine alone revealed a stable disease, and progressive disease in 14 (56.0%) and 11 (44.0%) patients, respectively, whereas among patients receiving gemcitabine plus radiotherapy, partial response, stable disease, and progressive disease were observed in 7 (28.0%), 14 (50.0%), and 4 (16.0%) patients, respectively. The overall comparison of response rates among patents of both study groups revealed statistically significant differences favoring gemcitabine plus radiotherapy (p=0.006), and the details are shown in Figure 1.

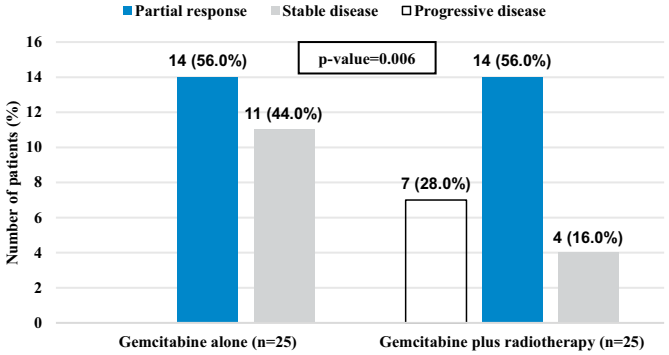

Figure 1: Comparison of Response Rate between Study Groups (N=50)

Regarding symptom relief, 8 (32.0%) patients in gemcitabine alone group had pain relief versus 20 (80%) in gemcitabine plus radiotherapy group (p=0.001), as shown in Table 2.

Table 2: Treatment Outcomes in Patients Receiving Chemo Alone and Chemo Plus RT (N=50)

Symptoms Relief	Chemo Alone N (%)	Chemo Plus RT N (%)	p-Value
Yes	8 (32.0%)	20 (80.0%)	0.007
No	17 (68.0%)	5 (20.0%)	

Nausea/vomiting, anorexia, and abdominal pain were the most frequent treatment related side-effects, noted in 25 (50.0%), 15 (30.0%), and 7 (14.0%) patients, respectively. None of the side effects were serious and no treatment breaks required in both groups. Symptomatic medication relieved the side effects. Mucositis was significantly associated with chemo alone group (p=0.018). Abdominal pain was significantly more prevalent in chemo plus RT group (24.0% versus 4.0%, p=0.042). Anorexia was significantly associated with chemo plus RT group (44.0% versus 16.0%, p=0.031). Table 3 is showing comparison of treatment related side-effects in both treatment groups (Table 3).

Table 3: Comparison of Treatment Related Side-Effects in both Study Groups (N=50)

Side-Effects	Category	Chemo Alone N (%)	Chemo Plus RT N (%)	p-Value
Neutropenia	Yes	3 (12.0%)	0	0.074
	No	22 (88.0%)	25 (100%)	
Nausea/ Vomiting	Yes	11 (44.0%)	14 (56.0%)	0.396
	No	14 (56.0%)	11 (44.0%)	
Diarrhea	Yes	3 (12.0%)	0	0.074
	No	22 (88.0%)	25 (100%)	

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Mucositis	Yes	5 (20.0%)	0	0.018
	No	20 (80.0%)	25 (100%)	
Abdominal Pain	Yes	1 (4.0%)	6 (24.0%)	0.042
	No	24 (96.0%)	19 (76.0%)	
Anorexia	Yes	4 (16.0%)	11 (44.0%)	0.031
	No	21 (84.0%)	14 (56.0%)	

DISCUSSION

In this study, 80.0% of patients with gallbladder carcinoma were female. The literature describes a high predominance of female gender among patients with gallbladder carcinoma, so these findings are pretty consistent with what has already been described earlier [17]. It was noted that the mean age mean of patients with gallbladder carcinoma was 56.58 ± 6.14 years. A local study from Karachi showed the mean age of patients with gallbladder carcinoma to be 52.8 ± 8.4 years [18, 19]. The age group involved, the 5th and 6th decade of life, seems to be the most probable age groups for gallbladder carcinoma. For advanced gallbladder carcinoma disease, adjuvant therapy is commonly utilized all over the globe, including radiation therapy and chemotherapy [15]. While 5FU has long been the standard chemotherapy medicine, more recent studies have looked into different medications. Of all the novel drugs, gemcitabine, a purine analogue, has shown promising results [10]. The study's findings showed that chemo-radiation or combination treatment offered improved palliation, disease management, and symptom relief for issues like pain and anorexia. One study conducted at the University of Chile Clinical Hospital showed gemcitabine as an effective drug with a 37% response rate. Treatment related to toxicity was mild. Researchers have shown that response rates with gemcitabine range between 8 and 30%, while it seems to be a well-tolerated and clinically active drug in unresectable gallbladder carcinoma [17-21]. It has been discovered that using radiation treatment in combination to chemotherapy or the medication used as a radiosensitizer, such as gemcitabine, cisplatin, and 5FU, is beneficial in managing pain and lessening the effects of pressure [22]. According to published data, radiation therapy has been used in a variety of settings, including intra-operative and conformal radiotherapy. The results have demonstrated that adding radiation therapy to chemotherapy or surgery has significantly improved disease control without having a noticeable negative impact on side effects [23, 24]. Some others have also revealed that postoperative gemcitabine significantly delays the recurrence of disease following a complete resection of pancreatic cancer compared to observation alone. These findings endorse the use of gemcitabine as an adjuvant chemotherapy [24]. A systematic review conducted by Dingle and colleagues exhibited that surgery offered the best chance of survival for people with gallbladder cancer or cholangiocarcinoma and should continue to be the main course of treatment. However, gemcitabine, either by itself or in conjunction with a fluoropyrimidine (such as 5-fluorouracil or capecitabine), proved to be a reasonable substitute for the finest supportive treatment for patients who were not candidates for surgery but were able and willing to take chemotherapy [24]. Possible limitations of this study could include a retrospective design, a small sample size, which may limit the generalizability of the results, potential variability in patient response due to individual differences in tumor biology, and the challenge of accurately measuring symptom relief. The study might face difficulties isolating the effects of gemcitabine from those of radiation when used in combination. Future studies should include prospective data collection to ensure comprehensive reporting of adverse events, which is crucial for evaluating the overall safety and tolerability of these treatment modalities.

CONCLUSIONS

Gemcitabine plus concomitant radiotherapy was revealed to be more effective in achieving higher response rates and alleviation of symptoms when compared to gemcitabine alone in gallbladder carcinoma patients. Further randomized controlled trials evaluating the longer duration of follow-ups are required to ascertain the impact of various management approaches among patients with gallbladder carcinoma.

Authors Contribution

Conceptualization: AL
Methodology: AL
Formal analysis: AL
Writing, review and editing: AL

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Okumura K, Gogna S, Gachabayov M, Felsenreich DM, McGuirk M, Rojas A *et al.* Gallbladder cancer: Historical treatment and new management options. World Journal of Gastrointestinal Oncology. 2021 Oct; 13(10): 1317. doi: 10.4251/wjgo.v13.i10.1317.

[2] Li ZZ, Guan LJ, Ouyang R, Chen ZX, Ouyang GQ, Jiang HX. Global, regional, and national burden of gallbladder and biliary diseases from 1990 to 2019. World Journal

DOI: https://doi.org/10.54393/pjhs.v5i12.1989

of Gastrointestinal Surgery.2023 Nov; 15(11): 2564. doi: 10.4240/wjgs.v15.i11.2564.

[3] Bojan A, Foia LG, Vladeanu MC, Bararu Bojan I, Plesoianu C, Plesoianu A *et al*. Understanding the mechanisms of gallbladder lesions: A systematic review. Experimental and Therapeutic Medicine. 2022 Jul; 24(3): 604. doi: 10.3892/etm.2022.11541.

[4] Teng TZ, Chua BQ, Shelat VG. Carcinosarcoma of gallbladder: a world review. World Journal of Clinical Oncology.2021 Dec; 12(12): 1244. doi: 10.5306/ wjco. v1 2.I12.1244.

[5] Al Jaber F, Almaher E, Al-Ibrahim R, AlQahtani M. Curative surgical resection for initially unresectable metastatic gallbladder cancer following neoadjuvant chemotherapy: Case report and review of literature. International Journal of Surgery Case Reports.2022 Nov; 100: 107694. doi: 10.1016/j.ijscr.2022.107694.

[6] Stinton LM and Shaffer EA. Epidemiology of gallbladder disease: cholelithiasis and cancer. Gut and liver. 2012 Apr; 6(2): 172. doi: 10.5009/gnl.2012.6.2.172.

[7] Pérez-Moreno P, Riquelme I, García P, Brebi P, Roa JC. Environmental and lifestyle risk factors in the carcinogenesis of gallbladder cancer. Journal of Personalized Medicine.2022 Feb; 12(2): 234. doi: 10.33 90/jpm12020234.

[8] Hu ZI and Lim KH. Evolving paradigms in the systemic treatment of advanced gallbladder cancer: updates in year 2022.Cancers.2022 Feb; 14(5): 1249. doi: 10.33 90 /cancers14051249.

[9] Shao J, Lu HC, Wu LQ, Lei J, Yuan RF, Shao JH. Simple cholecystectomy is an adequate treatment for grade I T1bN0M0 gallbladder carcinoma: Evidence from 528 patients. World Journal of Gastroenterology.2022 Aug; 28(31): 4431. doi: 10.3748/wjg.v28.i31.4431.

[10] Pahlajani NH, Ruth KJ, Freedman GM, Meropol NJ, Cohen SJ, Watson JC *et al*. Radiation therapy in gallbladder cancer treatment: the Fox Chase Cancer Center experience. International Journal of Radiation Oncology, Biology, Physics. 2007 Nov; 69(3): S301. doi: 10.1016/j.ijrobp.2007.07.1351.

[11] Vergara-Gómez L, Bizama C, Zhong J, Buchegger K, Suárez F, Rosa L *et al*. A novel gemcitabine-resistant gallbladder cancer model provides insights into molecular changes occurring during acquired resistance. International Journal of Molecular Sciences. 2023 Apr; 24(8): 7238. doi: 10.33 90 /ij ms 2 4 087238.

[12] Ioka T, Kanai M, Kobayashi S, Sakai D, Eguchi H, Baba H *et al*. Randomized phase III study of gemcitabine, cisplatin plus S-1 versus gemcitabine, cisplatin for advanced biliary tract cancer (KHBO1401- MITSUBA). Journal of Hepato-Biliary-Pancreatic Sciences.2023 Jan; 30(1): 102-110. doi: 10.1002/jhbp.1219.

[13] Boxberger F, Jüngert B, Brueckl V, Brueckl WM, Hautmann M, Hohenberger W *et al*. Palliative chemotherapy with gemcitabine and weekly high-dose 5-fluorouracil as 24-h infusion in metastatic biliary tract and gall bladder adenocarcinomas. Anti-Cancer Drugs.2003 Jan; 14(1): 87-90. doi: 10.10 97/ 000 01813-200301000-00012.

[14] Penz M, Kornek GV, Raderer M, Ulrich-Pur H, Fiebiger W, Lenauer A *et al*. Phase II trial of two-weekly gemcitabine in patients with advanced biliary tract cancer. Annals of Oncology.2001 Feb; 12(2): 183-6. doi: 10.1023/A:1008352123009.

[15] Kumar D, Kiran NM, Khosla D. Reviewing the potential role of radiation therapy in gallbladder cancer: an update. Radiation Oncology Journal. 2022 Mar; 40(1): 1. doi: 10.3857/roj.2021.00717.

[16] Agrawal S, Gupta A, Kapoor V, Rahul R, Singh A, Mishra P *et al.* Predictors of Toxicity in a Randomized Study of Consolidation Chemoradiation Versus Observation After First Line Chemotherapy in Advanced Gall Bladder Cancers. Advances in Radiation Oncology. 2024 May; 9(5): 101468. doi: 10.1016/j .adro .2024 .1014 68.

[17] Rawla P, Sunkara T, Thandra KC, Barsouk A. Epidemiology of gallbladder cancer. Clinical and Experimental Hepatology.2019 May; 5(2): 93-102. doi: 1 0.5114/ceh.2019.85166.

[18] Sturm N, Schuhbaur JS, Hüttner F, Perkhofer L, Ettrich TJ. Gallbladder cancer: current multimodality treatment concepts and future directions. Cancers. 2022 Nov;14(22): 5580.doi:10.3390/cancer s14225580.

[19] Tsavaris N, Kosmas C, Gouveris P, Gennatas K, Polyzos A, Mouratidou D *et al.* Weekly gemcitabine for the treatment of biliary tract and gallbladder cancer. Investigational New Drugs.2004 Apr; 22: 193-8. doi: 10. 1023/B:DRUG.0000011797.09549.53.

[20] Gong L, Zhang Y, Liu C, Zhang M, Han S. Application of radiosensitizers in cancer radiotherapy. International Journal of Nanomedicine.2021 Feb:1083-102. doi: 10. 2147/IJN.S290438.

[21] Yuan Z, Shui Y, Liu L, Guo Y, Wei Q. Postoperative recurrent patterns of gallbladder cancer: possible implications for adjuvant therapy. Radiation Oncology. 2022 Jul; 17(1): 118. doi: 10.1186/s13014-022-02091-6.

[22] Kang S, Yoo C, Lee SH, Oh D, Song TJ, Lee SS et al. Real-world outcomes of adjuvant gemcitabine versus gemcitabine plus capecitabine for resected pancreatic ductal adenocarcinoma.Therapeutic Advances in Medical Oncology.2022 May; 14:1758 83 59221097190. doi: 10.1177/17588359221097190.

DOI: https://doi.org/10.54393/pjhs.v5i12.1989

[23] Oettle H, Post S, Neuhaus P, Gellert K, Langrehr J, Ridwelski K *et al*. Adjuvant chemotherapy with gemcitabine vs observation in patients undergoing curative-intent resection of pancreatic cancer: a randomized controlled trial. Journal of the American Medical Association. 2007 Jan; 297(3): 267-77. doi: 10.1001/jama.297.3.267.

[24] Sasaki T, Takeda T, Okamoto T, Ozaka M, Sasahira N. Chemotherapy for biliary tract cancer in 2021. Journal of Clinical Medicine.2021 Jul; 10(14): 3108. doi: 10.3390/jcm10143108.

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Relationship between Self-Directed Learning and Self-Regulated Learning in Problem-Based Learning

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ABSTRACT

Self-Directed Learning (SDL) was crucial for developing Self-Regulated Learning (SRL) skills, essential for success in Problem-Based Learning (PBL) settings. **Objective:** To explore the association between SDL and SRL, focusing on motivation, self-efficacy, and cognitive strategies. **Methods:** A longitudinal study design was conducted with 250 medical students in the PBL curriculum at Rawal Institute of Health Sciences Islamabad. Stratified random sampling ensured representation across academic performance levels. A structured survey assessed SDL (goal-setting, time management, and self-assessment) and SRL (motivation, self-efficacy, cognitive strategies, and behavioural regulation) using a 5-point Likert scale. Data were analysed using Chi-Square Goodness-of-Fit tests to explore distribution patterns, Bivariate Pearson correlation for relationships between SDL and SRL, and One-Way ANOVA to identify SRL differences across performance levels, with a significance threshold set at $p < 0.05$. **Results:** Significant engagement in SDL components, goal-setting and intrinsic motivation ($p = 0.001$), with moderate correlations between specific SDL skills and SRL outcomes. Time management showed a weak but significant correlation with cognitive strategies ($p = 0.03$), suggesting an impact on SRL behaviours. No significant differences were observed in SRL skills across academic performance levels ($p > 0.05$), indicating a uniform development of self-regulation skills regardless of prior achievement. High engagement in PBL discussions and peer collaboration further underlines these activities as central to fostering SDL and SRL. **Conclusion:** SDL in PBL shows a positive, however modest, impact on SRL outcome, management and self-assessment, which could further enhance SRL in medical education settings.

INTRODUCTION

In modern education, SDL has developed as an essential component for raising independence and resilience in students [1]. In medical education, SDL is highlighted as it aligns with the demands of continuous, lifelong learning in the healthcare profession [2, 3]. Within PBL environments, SDL encourages students to take responsibility for their education by actively identifying learning objectives, seeking resources, and evaluating their understanding [4]. This autonomy has been related to improved academic performance and increased adaptability, essential skills for future healthcare providers. PBL is structured as a real-world clinical problem and provides students with a dynamic and interactive framework for relating theoretical knowledge to practical situations [5]. Contrasting traditional didactic teaching, PBL compels students to collaborate, communicate effectively, and think critically [6, 7]. SDL engagement allows students to set personal goals and take possession of their learning journey [8]. This autonomy improves comprehension and strengthens SRL skills as students develop methods to monitor and control their learning behaviour. SRL refers to students' ability to deliberately manage their learning through goal-setting,

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self-monitoring, and self-reflection [9]. Vital components of SRL include motivation, self-efficacy, cognitive strategies, and behavioural regulation. These skills allow students to challenge complex and rigorous academic content with an organised approach [10]. In medical education, where vast amounts of knowledge must be retained and applied across diverse clinical scenarios, SRL provides a framework for students to process information and develop effective professional learning habits. Despite the theoretical alignment of SDL and SRL within PBL, observed evidence on the extent of their relationship remains limited. Previous studies have highlighted SDL as a foundational skill that can improve SRL [11-13]. Yet, the specific influence of SDL component goal-setting, time management, and self-assessment on SRL outcomes, motivation and self-efficacy were not well-documented. Additionally, there is interest in understanding how these skills may vary based on academic performance, as students with different achievement levels may exhibit varying degrees of SRL in response to SDL practices. This study aims to bridge this gap by examining the relationship between SDL skills and SRL outcomes within a PBL environment. By assessing SDL components alongside SRL variables like motivation, cognitive strategy used, and self-efficacy, the study seeks to determine how students' self-directed efforts translate into self-regulated behaviours. Furthermore, it explores whether SRL outcomes differ across academic performance levels, providing insight into how students of varying capabilities engage in SDL within PBL frameworks. The objective was to investigate the impact of SDL skills on SRL outcomes among medical students participating in PBL.

The study inspected components of SDL, goal-setting and time management in relation to SRL variables, including intrinsic motivation and cognitive strategies.

METHODS

This longitudinal study design, 6 months, 18th March 2024 – 18 September 2024 study investigated the relationship between SDL and SRL among students engaged in PBL. The study was conducted at the Rawal Institute of Health Sciences, Islamabad, involving medical students enrolled in the PBL curriculum during the academic year under study. The design allowed for a snapshot analysis of SDL and SRL characteristics within a defined population, focusing on their interplay across diverse academic performance levels. The sample size calculation was based on statistical power analysis to ensure reliable detection of moderate effect sizes. Using Cohen's guidelines for effect size determination (d=0.5), a significance level (α) of 0.05, and a desired statistical power of 0.80, the minimum required sample size was estimated to be 64 participants per group. For three groups (high, average, and low academic performers), this yields a total sample size of 191 participants. To account for potential non-responses and strengthen the study findings' robustness, the sample size was increased to 250 participants. This exceeds the calculated minimum requirement and enhances the sample's representativeness. The study included students actively participating in a PBL course during the academic year were included in the study. Students who missed more than two sessions were excluded to ensure that participants had sufficient exposure to PBL activities. This criterion was applied to maintain data quality and ensure that reported SDL and SRL behaviors reflected consistent engagement with the PBL curriculum. Attendance data was carefully reviewed to minimise the potential for selection bias and ensure the exclusion criteria were applied uniformly across all performance groups. This step helped to ensure that the excluded students did not systematically differ in ways that would skew the analysis. By addressing attendance variability, the study maintained a balance between ensuring data reliability and reducing bias. Stratified random sampling was applied to ensure proportional representation across academic performance groups, thereby reducing bias and improving the generalizability of the results. Stratified random sampling was employed to ensure representation across academic performance groups (high, average, low), categorised based on students' grades. This approach facilitated meaningful comparisons of SRL outcomes across performance levels, contributing to a comprehensive analysis of how SDL impacts students differently depending on their academic standing. To minimise the impact of variability in PBL implementation across tutors and groups, several measures were taken to ensure consistency. All tutors received standardised guidelines detailing the objectives and processes for PBL sessions, ensuring alignment with the curriculum. Training sessions were conducted periodically to standardise facilitation techniques and reduce discrepancies in implementation. Students were randomly allocated to PBL groups to prevent systematic differences in group composition that could influence SDL and SRL outcomes. Despite these efforts, minor differences in facilitation styles and group dynamics may persist, and future studies could consider incorporating tutor or group as a random effect in statistical models to better account for such variability. Before data collection, the Institutional Review Board (IRB) of Rawal Institute of Health Sciences Islamabad Ref.no reviewed and approved the study. RIHS/IRB/18/2024 All participants provided informed consent. Measures were taken to handle data securely and ethically with institutional and research standards. The structured survey to assess SDL and SRL was adapted from validated instruments to ensure relevance to the student population.

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SDL items focused on goal-setting, time management, and self-assessment, while SRL items addressed motivation, cognitive strategies, and behavioural regulation. The survey was grounded in established theoretical frameworks, including Zimmerman's self-regulated learning model and Knowles' principles of self-directed learning, ensuring alignment with established constructs. To validate the constructs of SDL and SRL, medical education specialists conducted expert reviews to ensure the survey items were clear, contextually relevant, and aligned with theoretical frameworks. Pilot testing with a representative sample of the target population further validated reliability, achieving Cronbach's alpha values exceeding 0.7 for all constructs, which indicates good internal consistency. While exploratory factor analysis (EFA) was not performed to confirm the statistical distinction between SDL and SRL constructs, the conceptual alignment and expert validation provide confidence in the survey's ability to measure these domains. Future studies could employ EFA to statistically confirm the theoretical distinction between SDL and SRL, further strengthening the survey's construct validity. Composite scores for SDL and SRL were calculated to reflect an aggregate measure of students' engagement and skills in these domains. Each SDL component (goal-setting, time management, and self-assessment) and SRL variable (motivation, cognitive strategies, and behavioural regulation) was assessed using multiple survey items rated on a 5-point Likert scale ranging from "Strongly Disagree" (1) to "Strongly Agree" (5). Each item contributed equally to its respective component score. The goal-setting component included several items, and the responses for these items were summed and then averaged to calculate the composite score for goal-setting. All items within a component were weighted equally, ensuring a proportional representation of all aspects of that component in the composite score. Differential weighting was not applied as no evidence suggested variable importance among items. An overall SDL score was calculated by averaging the composite scores of its three components: goal-setting, time management, and self-assessment. Similarly, an overall SRL score was calculated by averaging the composite scores of its variables: motivation, cognitive strategies, and behavioural regulation. High scores in individual components or overall scores indicated more substantial proficiency and engagement in the respective SDL or SRL skill areas. These scores provided a quantitative basis for analysing the relationships between SDL and SRL and comparing outcomes across different academic performance levels. The survey was administered at the end of the academic term to ensure students' complete exposure to PBL activities. The inclusion criteria were: (1) students actively participate in a PBL course within the academic year of the study, and (2) students with complete attendance for the sessions under investigation. The exclusion criteria included (1) students who had missed more than two PBL sessions, as their engagement levels might not accurately reflect SDL practices, and (2) students who were not participating in PBL as part of their curriculum. This careful selection ensured the data's consistency and relevance, enhancing the findings' reliability. The data were collected through a structured survey administered at the end of the academic term. The survey was planned to assess SDL skills (goal-setting, time management, self-assessment) and SRL outcomes (motivation, cognitive strategies, and behavioural regulation). For apprehension SDL skills, students responded to items related to their engagement in goal-setting, time management, and self-assessment during PBL sessions. The survey assessed intrinsic motivation, self-efficacy, cognitive strategies, and behavioural regulation for SRL. Answers were collected on a '5-point Likert scale', ranging from "Strongly Disagree" (1) to "Strongly Agree" (5), allowing for a quantitative measure of both SDL and SRL skills. Data were analysed using SPSS version 25.0. The data were analysed using SPSS version 25.0. To appropriately handle the ordinal nature of Likert-scale responses, ordinal logistic regression was applied to assess the relationship between SDL and SRL components. This method is particularly suited for Likert-scale data as it accounts for the ordinal structure while providing insights into the probability of specific response categories. Additionally, Bivariate Pearson Correlation and One-Way ANOVA were employed to explore relationships and group differences where appropriate. Results were interpreted using p-values and effect sizes to ensure practical and statistical significance. The analysis began with the Chi-Square Goodness-of-Fit test, which assessed whether the observed SDL and SRL skill responses significantly deviated from the expected distribution. This test was particularly suitable for categorical and ordinal data, responses collected on a Likert scale, to determine whether certain SDL or SRL skills were more prevalent among participants. Then, to examine relationships between SDL and SRL skills, a Bivariate Pearson Correlation was conducted. Alongside the correlation coefficients (r) and their associated p-values, effect sizes were calculated to determine the practical significance of the observed relationships. Effect sizes were interpreted based on Cohen's benchmarks (r=0.1: small, r=0.3: medium, r=0.5: large). This analysis identified significant associations between SDL practices and SRL outcomes, with statistically significant correlations at p-values below 0.05. a significant correlation between goal-setting and intrinsic motivation would suggest that students who set clear goals also experience higher motivation in their PBL

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work. Finally, a One-Way Analysis of Variance (ANOVA) was used to explore differences in SRL scores across academic performance groups (High, Average, Low). Alongside p-values, partial eta squared (η^2) was calculated as an effect size measure for ANOVA, with thresholds of 0.01 (small), 0.06 (medium), and 0.14 (large). This test compared mean scores of SRL skills among the three groups, with significant differences highlighted by p-values below 0.05. Post hoc analyses were performed where significant differences were found to determine which specific performance groups differed. Still, there was no significant association of ANOVA, so no post hoc was performed.

RESULTS

Frequency distribution of SDL and SRL skills, goal-setting and intrinsic motivation showed significant engagement among students (p = 0.001), indicating strong adoption in PBL settings. Time management received high disagreement (p = 0.001), suggesting it was challenging for students. Self-assessment showed mixed engagement (p = 0.023), indicating room for improvement. Non-significant results in learning strategy selection and behavioural regulation suggest variability in these areas, with inconsistent adoption.

Table 1: Frequency Distribution of SDL and SRL Skills

Variables	Strongly Disagree (1)	Disagree (2)	Neutral (3)	Agree (4)	Strongly Agree (5)	p-value
Goal-Setting	-	-	-	76	174	0.001
Time Management	41	209	-	-	-	0.001
Self-Assessment	-	-	107	-	143	0.023
Learning Strategy Selection	-	-	-	132	118	0.37
Motivation (Intrinsic)	72	-	-	-	178	0.001
Motivation (Extrinsic)	-	-	121	129	-	0.613
Self-Efficacy	-	-	-	160	90	0.001
Cognitive Strategies	110	-	-	-	140	0.05
Behavioural Regulation	-	-	122	-	128	0.7

Table 2 showed that engagement in PBL sessions, discussions, and collaboration with peers were highly rated (p = 0.001), indicating active student involvement in these core PBL activities. Application of critical thinking showed a non-significant result (p = 0.3), reflecting varied engagement. Seeking clarification was significantly engaged (p = 0.004), highlighting students' tendency to seek understanding.

Table 2: Engagement in PBL Sessions

PBL Component	Strongly Disagree (1)	Disagree (2)	Neutral (3)	Agree (4)	Strongly Agree (5)	p-value
Participation in Discussions	-	-	-	103	147	0.001
Collaboration with Peers	66	-	-	-	184	0.001
Application of Critical Thinking	-	-	133	117	-	0.3
Seeking Clarification	-	-	-	148	102	0.004

Table 3 showed a weak but significant positive correlation between time management and cognitive strategies (r=0.134, p=0.03, small effect size). No significant correlations were observed for goal-setting, motivation, or self-efficacy (r <0.1, negligible effect sizes).

Table 3: Correlation between SDL and SRL Skills

SRL Variables	SDL Variable Goal-Setting	Time Management	Self-Assessment	Learning Strategy
Motivation	r = 0.02, p = 10.73	r = 0.052, p = 0.41	r = 0.075, p = 0.23	r = -0.086, p = 0.173
Self-Efficacy	r = 0.025, p = 0.69	r = -0.050, p = 0.42	r = -0.025, p = 0.69	r = -0.37, p = 0.55
Cognitive Strategies	r = 0.065, p = 0.30	r = 0.134, p = 0.03	r = 0.114, p = 0.07	r = 0.037, p = 0.55
Behavioural Regulation	r = 0.058, p = 0.36-	r = -0.069, p = 0.27	r = -0.060, p = 0.34	r = -0.028, p = 0.664

In table 4 differences in self-regulated learning by academic performance: No significant differences in SRL scores were observed across academic performance groups (p>0.05), but the effect size (η^2 =0.03) suggests a small practical difference in behavioral regulation."

Table 4: Difference in Self-Regulated Learning by Academic Performance

Academic Performance Group	Motivation (Mean)	Self-Efficacy (Mean)	Cognitive Strategies (Mean)	Behavioral Regulation (Mean)	N	p-value
High Performers	3.75	4.36	4.65	3.88	96	0.635
Average Performers	4.01	4.29	4.53	4.01	73	0.234
Low Performers	3.81	4.42	4.57	3.96	81	0.314
Total	-				250	-

DISCUSSION

The findings from this study reveal the relationship between SDL and SRL skills, with specific SDL components of time management showing weak yet significant correlations with specific SRL outcomes. This supports previous research that underscores time management as a vital skill in enhancing learning efficiency and promoting self-regulation [14]. Although SDL and SRL were conceptually aligned, the modest strength of correlations indicates that SDL skills alone may not fully account for SRL outcomes, suggesting that other factors, personal motivation and external influences, could play a role in shaping SRL within PBL contexts [15, 16]. Several

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moderating or mediating factors may influence the weak correlations observed between SDL and SRL components. Intrinsic motivation, for instance, could serve as a mediator, enhancing the impact of SDL practices like goal-setting and self-assessment on SRL outcomes, cognitive strategies and behavioural regulation. Students with higher intrinsic motivation may be more likely to effectively translate SDL efforts into self-regulated learning behaviours, suggesting that motivation could amplify this relationship. External support from peers, tutors, and the structured PBL environment could also act as a moderator, either strengthening or dampening the connection between SDL and SRL. Students receiving consistent feedback and encouragement in collaborative settings may exhibit better integration of SDL practices into SRL outcomes. Conversely, such support's absence might limit SDL practices' effectiveness, leading to weaker correlations. These findings highlight the complexity of the SDL-SRL relationship and suggest that the interplay of personal and external factors may significantly shape these dynamics. Future studies could explore these moderating and mediating factors in greater depth, using advanced statistical techniques like mediation or moderation analysis to better understand their roles in shaping SDL and SRL relationships. The significance of intrinsic motivation and self-efficacy among students engaged in PBL highlights the role of internal drivers in self-regulation. Intrinsic motivation, as indicated by high engagement levels, aligns with prior studies showing that intrinsically motivated students tend to exhibit stronger SRL behaviours [17, 18]. The findings support that PBL naturally fosters intrinsic motivation by providing a collaborative, real-world context that engages students beyond grades or external rewards. While several SDL and SRL components showed significant correlations, some variables, such as learning strategy selection and behavioural regulation, did not yield statistically significant results. This lack of significance may be attributed to several factors. One potential explanation is the inherent variability in how students interpret and engage with these constructs. Behavioural regulation, for instance, may depend heavily on external factors like tutor guidance or group dynamics, which were not explicitly controlled or measured in this study. Similarly, learning strategy selection might be less apparent in a PBL setting, where collaborative and problem-solving tasks take precedence over individually selected strategies. Measurement limitations may also have contributed to these findings. The survey items for learning strategy selection and behavioural regulation, while adapted from validated instruments, may not have fully captured the nuances of these constructs in a PBL context. Additionally, the reliance on self-reported data could have introduced response biases, particularly for variables that require introspective assessments and behavioural regulation. Analytical limitations, including using longitudinal study design correlations for these variables, may have also constrained the ability to detect subtle relationships. Future research should consider employing longitudinal designs, refining measurement tools, and incorporating complementary data sources, such as tutor observations or peer evaluations, to capture the complexity of these constructs better. This study's weak correlations and insignificant results may partly be attributed to methodological limitations. One potential issue is the survey design, which relied on self-reported responses. While validated instruments were used, self-report surveys are prone to biases such as social desirability and recall errors, which may have affected the accuracy of responses for constructs like time management and behavioural regulation. Another limitation could be the limited scope of the survey items in capturing the full complexity of SDL and SRL behaviours within the PBL context. For example, learning strategy selection may require more nuanced or context-specific items to fully reflect students' experiences and practices in a collaborative environment. From an analytical perspective, using longitudinal study design methods, Pearson Correlation and ANOVA may have restricted the ability to detect dynamic or complex relationships between SDL and SRL components. Advanced statistical techniques, such as structural equation modelling (SEM), could better capture the interplay between these constructs, while longitudinal designs could reveal causal relationships over time.Addressing these methodological challenges in future research could enhance the robustness and validity of findings, providing deeper insights into the dynamics of SDL and SRL in PBL settings. This environment allows for cultivating curiosity and persistence, crucial for maintaining SRL behaviours over time. Self-efficacy, another key component of SRL, was also positively perceived among participants, aligning with the notion that confidence in one's ability enhances learning effectiveness. Despite high levels of engagement in collaborative activities during PBL sessions, students reported weaker time management skills. This apparent contradiction can be interpreted using established theoretical frameworks. According to Zimmerman's self-regulated learning model, collaboration in PBL fosters external regulation through peer feedback and shared goals, which can overshadow individual time management responsibilities. Similarly, Knowles' principles of self-directed learning suggest that while PBL encourages autonomy, its collaborative structure may lead to a

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diffusion of personal responsibility for managing time effectively. This imbalance could reflect the challenge of balancing shared group tasks with individual responsibilities within a structured PBL environment. Students may prioritise immediate group-based demands, such as collaboration and discussion, over self-regulation activities like time management. These findings highlight a potential area for intervention, such as incorporating explicit time management training into PBL sessions to complement the collaborative focus. Future research could further explore this dynamic to better integrate individual and group regulatory processes in PBL settings. Prior studies have linked self-efficacy to academic resilience, suggesting that students who believe in their capabilities are likelier to persist through challenges and employ effective cognitive strategies [19, 20]. In this study, the high levels of self-efficacy observed underscore the role of PBL in building student confidence, as it encourages active problem-solving and provides immediate feedback through peer and tutor interactions. No significant differences in SRL skills across academic performance levels provide comprehension into the consistency of SRL behaviours among 'high, average, and low performers in PBL settings'. This finding suggests that PBL may serve as an aligning environment where all students, regardless of prior performance, have the opportunity to develop SRL skills. The lack of significant differences may also be attributed to the relative homogeneity of SRL development across academic performance groups. All students were exposed to the same PBL curriculum, which likely provided a consistent framework for fostering SRL skills, reducing observable group-level variations. Additionally, while the longitudinal design captured changes over time, the six-month duration might not have been sufficient to reveal more pronounced differences. Small effect sizes ($\eta 2=0.03$) indicated that minor variations in behavioural regulation exist but did not reach statistical significance due to the subtle nature of these changes. Future studies with longer durations or larger group-specific sample sizes could better uncover these differences. Studies have shown that PBL can reduce performance differences by providing structured yet flexible opportunities for students to engage in SDL and SRL practices '. This study highlighted the potential of PBL as an outline for integrating SDL and SRL. PBL fosters vital SRL skills for academic and professional success by providing an environment that inspires goal-setting, active learning, and collaboration. It suggests that SDL contributes to SRL, and there was scope for educational strategies that directly support students in managing time and self-assessing effectively. These insights may help future curriculum development in medical education, highlighting SDL and SRL necessary for developing independent, competent healthcare practitioners. A key limitation of this study is its reliance on self-reported data to measure SDL and SRL. While validated instruments were used, self-reported responses are inherently subjective and may be influenced by social desirability bias. Incorporating multiple data sources is recommended to strengthen the validity of results in future research. Peer evaluations could provide an external perspective on students' collaborative behaviours and self-regulation in group settings, complementing self-reported data. Similarly, tutor feedback would offer valuable insights into students' engagement, time management, and goal-setting behaviours observed during PBL sessions. Academic performance metrics, grades, task completion rates, or attendance could serve as objective indicators of SDL and SRL outcomes. These additional data sources would allow for triangulation, reducing bias and enhancing the robustness of findings. Implementing such approaches in future studies could offer a more comprehensive understanding of SDL and SRL dynamics within PBL contexts. To address this limitation, future studies could incorporate complementary data collection methods. Observational assessments during PBL sessions can provide direct insights into students' behaviours related to goal-setting, time management, and collaboration. Additionally, performance-based metrics, such as academic grades or task completion efficiency, could be objective measures of SDL and SRL outcomes. Furthermore, peer and tutor feedback could offer a third perspective, strengthening the validity of the findings through data triangulation. Implementing these approaches in future research will reduce reliance on self-reported measures and enhance the robustness of conclusions drawn.

CONCLUSIONS

This study highlighted the association of SDL and SRL within problem-based learning PBL environments. While SDL skills, goal-setting and time management correlate modestly with SRL outcomes, motivation and cognitive strategies, these skills alone were insufficient predictors of self-regulation. High engagement in PBL activities, discussions, and peer collaboration develops intrinsic motivation and self-efficacy, supporting SRL across varied academic performance levels. PBL thus emerges as a promising approach for developing autonomous and self-regulated learners necessary for the medical profession.

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Authors Contribution

Conceptualisation: WUN
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All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Buch AC, Rathod H, Naik MD. Scope and challenges of self-directed learning in undergraduate medical education: A systematic review. Journal of Medical Education. 2021; 20(1). doi: 10.5812/jme.114077.

[2] Ricotta DN, Richards JB, Atkins KM, Hayes MM, McOwen K, Soffler MI *et al*. Self-directed learning in medical education: training for a lifetime of discovery. Teaching and Learning in Medicine. 2022 Oct; 34(5): 530-40. doi: 10.1080/10401334.2021.1938074.

[3] Charokar K and Dulloo P. Self-directed learning theory to practice: a footstep towards the path of being a life-long learne. Journal of Advances in Medical Education & Professionalism. 2022 Jul; 10(3): 135. doi: 10.30476/JAMP.2022.94833.

[4] Kiran M and Hema NG. Perspectives of medical undergraduate students toward self-directed learning. Indian Journal of Physiology and Pharmacology. 2024 Jul; 68(2): 176-80. doi: 10.25259/IJPP_30_2023.

[5] Deep S, Ahmed A, Suleman N, Abbas MZ, Nazar U, Razzaq HS. The problem-based learning approach towards developing soft skills: A systematic review. The Qualitative Report. 2020 Nov; 25(11): 4029-54. doi: 10.46743/2160-3715/2020.4114.

[6] Trullàs JC, Blay C, Sarri E, Pujol R. Effectiveness of problem-based learning methodology in undergraduate medical education: a scoping review. BioMed Central Medical Education.2022 Feb; 22(1): 104 .doi: 10.1186/s12909-022-03154-8.

[7] Gonzalez-Argote J and Castillo-González W. Problem-Based Learning (PBL), review of the topic in the context of health education. InSeminars in Medical Writing and Education 2024 Jan; 3: 57-57. doi: 10.56294/mw202457.

[8] Salih KM, Al-Faifi J, Alamri MM, Mohamed OA, Khan SM, Marakala V *et al*. Comparing students' performance in self-directed and directed self-learning in College of Medicine, University of Bisha. Journal of Taibah University Medical Sciences. 2024 Jun; 19(3): 696-704. doi: 10.1016/j.jtumed.2024.05.003.

[9] Zheng B and Sun T. Self-Regulated Learning and Learning Outcomes in Undergraduate and Graduate Medical Education: A Meta-Analysis. Evaluation & the Health Professions.2024Oct:01632787241288849. doi: 10.1177/01632787241288849.

[10] Ali K, Daud A, Ba Hattab R, Philip N, Matoug-Elwerfelli M, Anweigi L *et al*. Development of self-regulation amongst dental students in problem-based learning curricula: A qualitative study. European Journal of Dental Education.2023 May; 27(2): 388-95. doi: 10.1111/eje.12820.

[11] Bibi W, Akbar H, Bashir H, Ahmad SS. Navigating The Path To Success: A Comprehensive Examination Of Self-Regulated LEARNING Strategies And Their Influence On University-Level Students Academic Achievement. Kurdish Studies.2024 Feb; 12(2): 6817-924. doi: 10.53555/ks.v12i2.3129.

[12] Onah DF, Pang EL, Sinclair JE. Cognitive optimism of distinctive initiatives to foster self-directed and self-regulated learning skills: A comparative analysis of conventional and blended-learning in undergraduate studies. Education and Information Technologies. 2020 Sep; 25(5): 4365-80. doi: 10.1007/s10639-020-10172-w.

[13] Tempelaar D, Bátori A, Giesbers B. Understanding self-regulation strategies in problem-based learning through dispositional learning analytics. InFrontiers in Education. Frontiers Media SA. 2024 Jun; 9: 1382771. doi: 10.3389/feduc.2024.1382771.

[14] Nosair EA, Omar M, AlWawi G. Evaluation of Self-Directed Learning Readiness among Medical Students in Sharjah, the United Arab Emirates. Cureus.2024 Sep; 16(9): e70096. doi: 10.7759/cureus.70096.

[15] Bana KF, Shamim MS, Shahid Z. Self-assessment of active learning and critical thinking during problem-based learning: An exploratory study. Journal of the Pakistan Medical Association. 2022 Sep; 72(9): 1771-4. doi: 10.47391/JPMA.4473.

[16] Shitarukmi S, Claramita M, Rahayu GR. How self-regulated learning influences undergraduate medical students to conduct student-centred learning: a scoping review protocol. British Medical Journal Open. 2023 Oct; 13(10): e072675. doi: 10.1136/bmjopen-2023-072675.

[17] Akdogan HD, Velipasaoglu S, Musal B. Perceptions of medical faculty students: The effect of problem-based learning on self-regulated learning skills: The Effect of Problem-Based Learning on Self-Regulated

DOI: https://doi.org/10.54393/pjhs.v5i12.2501

Learning Skills. Medical Science and Discovery. 2021 Oct; 8(10): 594-600. doi: 10.36472/msd.v8i10.614.

[18] Foong CC, Ghouse NLB, Lye AJ, Holder NAKA, Pallath V, Hong WH *et al*. A qualitative study on self-regulated learning among high performing medical students. BioMed Central Medical Education. 2021 Jun; 21(1): 320 . doi: 10.1186/s12909-021-02712-w.

[19] Farrukh K and Usmani A. Self-regulated learning attributes of high-performing medical and dental students in teacher-centered culture. The Professional Medical Journal. 2022 Oct; 29(11): 1726-3 2.doi: 10.29309/TPMJ/2022.29.11.7064.

[20] Nomura O, Soma Y, Kijima H, Matsuyama Y. Adapting the Motivated Strategies for Learning Questionnaire to the Japanese problem-based learning context: a validation study. Children. 2023 Jan; 10(1): 154. doi: 10. 3390/children10010154.

[21] Bains M, Kaliski DZ, Goei KA. Effect of self-regulated learning and technology-enhanced activities on anatomy learning, engagement, and course outcomes in a problem-based learning program. Advances in Physiology Education. 2022 Jun; 46(2): 219-27. doi: 10.1 152/advan.00039.2021.

[22] Rovers SF. Growing knowledge: supporting students' self-regulation in problem-based learning. 2020 Jan. doi: 10.26481/dis.20200916sr.

DOI: https://doi.org/10.54393/pjhs.v5i12.2157

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Original Article

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Diagnostic Accuracy of MRI and CT Scan in Non-Invasive Evaluation of Liver Cirrhosis

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ABSTRACT

Liver cirrhosis is a chronic, non-reversible disease which results from fibrosis of the healthy liver tissue and compromise of its functioning. Adequate diagnostic procedures that do not involve invasive procedures are necessary for early diagnosis of cirrhosis to minimize the risk of complications. Even though liver biopsy is considered the gold standard, this procedure is invasive and thus, non-invasive imaging studies, including Megnatic Resonance Imaging and Computed Tomography scan must be further emphasized. **Objective:** To determine the diagnostic accuracy of combination imaging techniques MRI and CT scan in the non-invasive assessment of liver cirrhosis taking histopathology as gold standard. **Methods:** This cross-sectional study was conducted at the department of Gastroenterology, Hayatabad Medical Complex, Peshawar, during the period 1st July 2023 till 30th June 2024. Male and female patients aging 18 to 80 years with suspected liver cirrhosis on ultrasound were enrolled. MRI and CT scan of the liver were carried out and the findings were compared with histopathology to draw the diagnostic accuracy. **Results:** The study comprised of 75 (58.6%) male and 53 (41.4%) female. The mean age was 55.4 ± 7.2 years. Liver morphology in patients with cirrhosis had sensitivity of 96.8% and specificity of 100%, with the PPV of 100% and NPV of 33.3%. For vascular features the sensitivity was 88.9% and a specificity of 30.0% respectively, with the PPV of 93.7% and an NPV of 18.7%. As an imaging finding, ascites had a sensitivity of 46.0% and a specificity of 59.6%, with a PPV of 62.5% and an NPV of 43.0%. **Conclusion:** Combining non-invasive imaging modalities like MRI and CT scan enhances the diagnostic accuracy in detecting liver cirrhosis and the degree of fibrosis.

INTRODUCTION

Liver cirrhosis is a chronic and progressive disease of the liver in which healthy liver cells are replaced by fibrotic tissue and is therefore a non-reversible disease [1]. This disease has become a global threat to human life and affects mortality and socio-economic costs in the delivery of health care services. Early diagnosis of liver cirrhosis is important since it enables the practitioner to take actions that will help to control the development of complications like portal hypertension, ascites, and hepatocellular carcinoma [2-4]. Traditionally, liver biopsy has been considered as the reference method in the diagnosis and staging of liver cirrhosis. However, because of invasiveness, it has certain risks and limitations, and therefore, there has been a transition to non-invasive imaging [5, 6]. The new techniques in imaging, especially the MRI and CT have shown promises in offering structural and functional information from anatomical perspective, but without the necessity of invasive procedures [7-9]. As these imaging modalities seem very promising, there is still a lack of published data comparing the efficacy of these imaging techniques in diagnosing liver cirrhosis without biopsy. Several studies have pointed out that MRI and CT are useful in detecting various diseases. Still, insufficient evidence shows which modality is more accurate, and no significant difference is observed between modalities [10, 11]. It is critical to have accurate and timely diagnosis of

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liver cirrhosis through non-invasive techniques as it is a major burden to healthcare systems in the world, [12]. This research will therefore seek to establish the specificity and sensitivity of MRI and CT in the diagnosis of liver cirrhosis using histopathology as the gold standard.

This study aimed to address the gaps found in the local literature arising from scarcity of studied on this topic and inconsistencies in studies carried out on western population.

METHODS

This cross-sectional study was carried out at Gastroenterology Unit of Hayatabad Medical Complex during the period 1st July 2023 till 30th June 2024. Ethical approval for the study was obtained from the Research Review Board of Hayatabad Medical Complex (Approval No: 1529). Consent to participate in the study was sought before they were recruited to the study. Male and female patients in the age range 18 to 80 years with clinical suspicion of liver cirrhosis (patients having jaundice, ascites or variceal bleed) and laboratory findings (platelet count <150,00cells/mm3, albumin <3.5gm/dl or INR >1.2) and ultrasound features of liver cirrhosis (coarse shrunken liver with irregular margins) were included. Patients with hepatic encephalopathy, active upper or lower gastrointestinal bleed, severe cardiopulmonary compromised patients, patients with platelets count less than 50,000 cells/mm3, patients unable to undergo liver biopsy or MRI or CT scan were excluded. Total sample size was 128 which was calculated taking the anticipated prevalence of liver cirrhosis as 26.0% with 7.6% margin of error and 95% confidence level. Patients were enrolled using non-probability consecutive sampling technique. Relevant clinic data were recorded including patient characteristics and medical history. Tests like liver function tests, blood tests for pertinent viral serological markers. All enrolled patients underwent both MRI and CT scanning with hepatobiliary protocol. Contrast-enhanced sequences for each modality (CT and MRI) were utilized in evaluating the liver parenchyma. The imaging results were examined by qualified radiologists who were blinded to clinical information. The severity of liver cirrhosis was classified based on recognized criteria, namely using the Child-Pugh classification. Imaging findings were compared with liver biopsy findings which was considered as gold standard. Image guided liver biopsy was performed by consultant interventional radiologist and sent to hospital laboratory for assessment of fibrosis by consultant histopathologist blinded to clinical data. Imaging findings for liver cirrhosis were compared with biopsy findings to draw the diagnostic accuracy. The efficacy of these approaches was evaluated in terms of their capacity to provide quantitative assessments of liver stiffness and fibrosis. Diagnostic accuracy was recorded as sensitivity, specificity, positive predictive value, and negative predictive value. Descriptive statistics were used to present demographic and clinical data. Continuous data were presented as means and standard deviation while categorical data were presented as frequency and percentages. 2x2 table was used to draw the diagnostic accuracy of combined CT and MRI recorded as sensitivity, specificity, positive predictive value and negative predictive value. p-value≤0.05 was considered statistically significant. Data were analyzed using SPSS (version 25). The participants were also explained about the study and the procedures that will be followed, the risks that may be encountered and the participant's right to withdraw from the study at any time without any reason being given. All data collected were kept confidential and used solely for research purposes.

RESULTS

The study included 128 patients, with demographic characteristics indicating that 58.6% were male and 41.4% were female, with a mean age of 55.4 ± 7.2 years. The age distribution showed that the largest group (35.16%) was aged 50-59 years, followed by those aged 60-69 years (29.67%)(Table 1).

Table 1: Frequency and Percentages of Patients According to Demographic Parameters,(n=128)

Demographic Characteristic		N(%)
Gender	Male	75(58.6%)
	Female	53(41.4%)
Age (years) Mean ± SD		55.4 ± 7.2
40-49 Years		25(19.53%)
50-59 Years		45(35.16%)
60-69 Years		38(29.67%)
70 and above		20(15.64%)

In terms of clinical signs, 71.9% of patients exhibited symptoms suggestive of cirrhosis, including jaundice, ascites, variceal bleed, and spider nevi. Serological markers for both HBV and HCV were positive in 81.3% of patients(Table 2).

Table 2: Frequency and Percentages of Patients According to Presenting Features (Clinical, Laboratory and Ultrasound Parameters)

Presenting Characteristics	N(%)
Symptoms Related to Cirrhosis (Like Jaundice, Ascites, Variceal Bleed, Spider Nevi)	92(71.9%)
Deranged Liver function Tests (Albumin <3.5gm/dl and INR>1.2)	116(90.6%)
Serological Markers (HBV and HCV Markers)	104(81.3%)
Ultrasound Findings (Coarse Shrunken Liver with Irregular Margins)	43(33.6%)

Out of all patients, MRI imaging revealed that 93.8% of the patients in terms of liver morphology, shrunken liver,

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coarse parenchyma and irregular margins. Also, changes in the vascular architecture were noted in 82.0% cases as shown in table 3.

Table 3: Imaging Findings – Magnetic Resonance Imaging (MRI)

MRI Findings	N (%)
Liver Morphology (Shrunken Liver, Coarse Parenchyma, Irregular Margins)	120 (93.8%)
Vascular Architecture (Portal Vein Diameter >15mm, Collaterals Formation, Cavernous Transformation)	105 (82.0%)
Ascites	32 (25.0%)

The examination of CT scans revealed the same with MRI in terms of liver morphology changes with 95.3% of the patients, vascular abnormities in 80.5% of the patients, whereas the presence of ascites was noted in 27.3% as reported in table 4.

Table 4: Imaging Findings - Computerized Tomography (CT) Scan

CT findings	N (%)
Liver, Morphology (Shrunken Liver, Coarse Parenchyma,Irregular Margins)	122 (95.3%)
Vascular Architecture (Portal Vein Diameter >15mm, Collaterals Formation, Cavernous Transformation)	103 (80.5%)
Ascites	35 (27.3%)

Table 5 summarizes the diagnostic accuracy of various imaging features (CT + MRI) in relation to liver biopsy. Liver morphology had a sensitivity of 96.8% and specificity of 100%, with a PPV of 100% and an NPV of 33.3%. For vascular features, sensitivity was 88.9%, specificity was 30.0%, with a PPV of 93.7% and an NPV of 18.7%. Ascites demonstrated a sensitivity of 46.0% and specificity of 59.6%, with a PPV of 62.5% and an NPV of 43.0%.

Table 5: 2x2 Table for Diagnostic Accuracy According to Various Features (CT + MRI)

Imaging findings (CT + MRI)	Imaging findings (CT + MRI)			Diagnostic Accuracy
	Yes	No	Total	
Liver Morphology Consistent with Cirrhosis	122 (99.1%)	03 (18.8%)	128 (100.0%)	Sensitivity = 96.8% Specificity = 100.0% PPV = 100%, NPV = 33.3%
	04 (66.7%)	02 (33.3%)	06 (100.0%)	
	126 (98.4%)	02 (1.6%)	128 (100.0%)	
Vascular Features Consistent with Cirrhosis	105 (93.7%)	07 (6.3%)	112 (100.0%)	Sensitivity = 88.9% Specificity = 30.0%PPV = 93.7%, NPV = 18.7%
	13 (81.2%)	03 (18.8%)	16 (100.0%)	
	118 (92.1%)	10 (7.9%)	128 (100.0%)	
Ascites	35 (62.5%)	21 (37.5%)	56 (100.0%)	Sensitivity = 46.0% Specificity = 59.6% PPV = 62.5%, NPV = 43.0%
	41 (56.9%)	31 (43.1%)	72 (100.0%)	
	76 (59.3%)	52(40.7%)	128 (100.0%)	

DISCUSSION

The results of the study provide an insight about diagnostic performance of various imaging features in relation to histopathology. On the demographic level, majority of patients were male (n = 75, 58.6%) with mean age of 55.4 years, which is in concordance with Basha *et al.*, who noted that patients with cirrhosis was more frequent in male patients (n = 134, 55.8%). The mean age of participants in the later study was 61.5 years which was slightly higher compared to our study [13]. The variation in mean age may be because of overall difference in life expectancy of patients belonging to different ethnicities. Majority of our patients were in sixth decade of life. Basha *et al* didn't report age related sub-group analysis hence comparison cannot be drawn in this regard. In a retrospective analysis of 300 patients by Wang G *et al*, the mean age of patients was 43.46 years which was considerably lower than our cohort of patients. [14]. The difference may be due to selection of patients with hepatocellular carcinoma on background of liver cirrhosis as compared to our patients where patients with cirrhosis and cirrhosis related complications were included. Thought the overall proportion of male patients were slightly higher in study by Wang G and colleagues, the higher prevalence of cirrhosis in male patients compared to female was like our findings [14]. In this study, the sensitivity, specificity, positive predictive value and negative predictive value of CT scan and MRI for the detection of cirrhosis, in relation to liver biopsy were 96.8%, 100%, 100% and 33.3% respectively for morphological presentation of cirrhosis, 88.9%, 30.0%, PPV, 93.7%, 18.7% respectively for cirrhosis related vascular changes and 46.0%, 59.6%, 62.5% and 43.0% for portal hypertension leading to ascites on the background of chronic liver disease. Imaging results showed that MRI and CT scans were highly sensitive in showing features of cirrhosis and MRI identified liver changes in 93.8% of patients and CT in 95.3%. Kim et al, concluded that MRI was superior to ultrasound in radiological assessment of cirrhosis and complications of cirrhosis. The diagnostic accuracy for various findings could be increased by combining the two modalities. Moreover, accuracy of MRI was further enhanced using contrast techniques, at the cost of expenses [15]. Basha and colleagues showed that, taking histopathology as gold standard, the sensitivity, specificity and overall accuracy for MRI and CT scan alone were 85.3%, 86.3%, 83.6% and 67.6%, 54.1% and 91.3% respectively. Combining the two modalities, the values obtained were 91.2%, 90.7% and 92.1% which were better than either technique alone similar to our observations [13]. Higaki *et al*, segregated patients based on Child Pugh Score and assessed morphological changes using radiological techniques. MRI was found more sensitive for soft tissue changes including nodular changes in liver parenchyma, focal lesion and vascular alternations and thrombosis compared to CT or ultrasound, however, additional measures were required for better visualization of vascular changes like contrast enhancement.The

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accuracy for complications such as ascites was like CT scan [16]. Wang and colleagues retrospectively analyzed CT and MRI based vascular models for assessment of cirrhosis related hepatic vascular changes. It was concluded that venous pressure gradients are better evaluated using CT and MRI with both modalities carrying similar diagnostic accuracy [17]. Among the morphological changes in liver parenchyma in cirrhosis, regenerative nodules are the hallmark of persistent fibrosis. It is important to establish the benign and malignant nature of nodules radiologically. Triphasic techniques differentiate the two with better accuracy. The reported sensitivity of triphasic CT in the regard is 50% to 96% and specificity of 75% to 96%. Diagnostic accuracy was shown to decrease as nodule size decreases below 2 cm. No such discrepancy was reported with MRI [18]. Accuracy of CT is also compromised with fat containing lesions exhibiting mass like appearance yielding diagnostic dilemma [19]. Such effect is not observed with protein deposition while cirrhosis resulting from fibrosis of liver is governed by proteins deposition [20].

CONCLUSIONS

Imaging studies, particularly the MRI and CT scans have been identified to play a crucial role in diagnosis of liver cirrhosis in the present study. Liver morphology in patients with cirrhosis had sensitivity of 96.8% and specificity of 100%, with the PPV of 100% and NPV of 33.3%. For vascular features the sensitivity was 88.9% and a specificity of 30.0% respectively, with the PPV of 93.7% and an NPV of 18.7%. As an imaging finding, ascites had a sensitivity of 46.0% and a specificity of 59.6%, with a PPV of 62.5% and an NPV of 43.0%. Although ascites may be a complication of liver cirrhosis, it cannot be used as a single marker for diagnosing liver cirrhosis.

Authors Contribution

Conceptualization: SHH, SA, AK, R
Methodology: SHH, MS
Formal analysis: SHH, FMK, MY, MS
Writing, review and editing: SA, MI, R

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Soresi M, Giannitrapani L, Cervello M, Licata A, Montalto G. Non-Invasive Tools for the Diagnosis of Liver Cirrhosis. World Journal of Gastroenterology. 2014 Dec; 20(48): 18131-50. doi: 10.374 8/wjg .v20.I 48.1 8131.

[2] Singh S, Hoque S, Zekry A, Sowmya A. Radiological Diagnosis of Chronic Liver Disease and Hepatocellular Carcinoma: A Review. Journal of Medical Systems. 2023 Jul; 47(1): 73. doi: 10.1007/s10916-023-01968-7.

[3] D'Amico G, Garcia-Tsao G, Pagliaro L. Natural History and Prognostic Indicators of Survival in Cirrhosis: A Systematic Review of 118 Studies. Journal of Hepatology.2006 Jan; 44(1): 217-231. doi:10. 1002/h ep .30635.

[4] Nayak A, Baidya Kayal E, Arya M, Culli J, Krishan S, Agarwal S, *et al.* Computer-Aided Diagnosis of Cirrhosis and Hepatocellular Carcinoma using Multi-Phase Abdomen CT. International Journal of Computer Assisted Radiology and Surgery.2019 Aug; 14(8): 1341-1352. doi: 10.1007/s11548-019-01991-5.

[5] Aubé C, Bazeries P, Lebigot J, Cartier V, Boursier J. Liver Fibrosis, Cirrhosis, and Cirrhosis-Related Nodules: Imaging Diagnosis and Surveillance. Diagnostic and Interventional Imaging.2017 Jun; 98(6): 455-468. doi: 10.1016/j.diii.2017.03.003.

[6] Okada M, Aoki R, Nakazawa Y, Tago K, Numata K. CT and MR Imaging of Hepatocellular Carcinoma and Liver Cirrhosis. Gastroenterology Insights.2024; 15(4): 976-997. doi: 10.3390/gastroent15040068.

[7] Yeom SK, Lee CH, Cha SH, Park CM. Prediction of Liver Cirrhosis, using Diagnostic Imaging Tools. World Journal of Hepatology.2015 Aug; 7(17): 2069-2079. doi: 10.4254/wjh.v7.i17.2069.

[8] Kudo M, Zheng RQ, Kim SR, Okabe Y, Osaki Y, Iijima H, *et al.* Diagnostic Accuracy of Imaging for Liver Cirrhosis Compared to Histologically Proven Liver Cirrhosis. A Multicenter Collaborative Study. Intervirology.2008; 51 (1): 17-26. doi: 10.1159/000122595.

[9] Loomba R and Adams LA. Advances in Non-Invasive Assessment of Hepatic Fibrosis. Gut.2020 Jul; 69(7): 1343-1352. doi: 10.1136/gutjnl-2018-317593.

[10] Singh D and Kaushik C. Comparative Analysis of CT and MRI in Emergency Assessment of Stroke: A Review. Journal of Multidisciplinary Research in Healthcare. 2019 Apr; 5(2): 57-63. doi: 10.15415/jmrh.2019.52007.

[11] Liu W, Liu J, Xiao W, Luo G. A Diagnostic Accuracy Meta-Analysis of CT and MRI for the Evaluation of Small Bowel Crohn Disease. Academic Radiology.2017 Oct; 24(10): 1216-1225. doi: 10.1016/j.acra.2017.04.013.

[12] Lu K, Sui J, Yu W, Chen Y, Hou Z, Li P, *et al.* An Analysis of the Burden of Liver Cirrhosis: Differences between

DOI: https://doi.org/10.54393/pjhs.v5i12.2157

the Global, China, the United States and India. Liver International.2024 Dec; 44(12): 3183-203. doi: 10.11 11/ liv.16087.

[13] Basha MAA, AlAzzazy MZ, Ahmed AF, Yousef HY, Shehata SM, El Sammak DAEA, *et al.* Does A Combined CT and MRI Protocol Enhance the Diagnostic Efficacy of LI-RADS in the Categorization of Hepatic Observations? A Prospective Comparative Study. European Radiology.2018 Jun; 28(6): 2592-2603. doi: 10.1007/s00330-017-5232-y.

[14] Wang G, Zhu S, Li X. Comparison of Values of CT and MRI Imaging in the Diagnosis of Hepatocellular Carcinoma and Analysis of Prognostic Factors. Oncology Letters.2019 Jan; 17(1): 1184-1188. doi: 10.389 2/ol.2018.9690.

[15] Kim HA, Kim KA, Choi JI, Lee JM, Lee CH, Kang TW, *et al*. Comparison of Biannual Ultrasonography and Annual Non-Contrast Liver Magnetic Resonance Imaging as Surveillance Tools for Hepatocellular Carcinoma in Patients with Liver Cirrhosis: A Study Protocol. BMC Cancer.2017 Dec; 17(1): 877. doi: 10.118 6/ s12885-017-3819-y.

[16] Higaki A, Kanki A, Yamamoto A, Ueda Y, Moriya K, Sanai H, *et al*. Liver Cirrhosis: Relationship Between Fibrosis-Associated Hepatic Morphological Changes and Portal Hemodynamics using Four-Dimensional Flow Magnetic Resonance Imaging. Japanese Journal of Radiology.2023 Jun; 41(6): 625-636. doi: 10.100 7/s1 1604-023-01388-0.

[17] Wang C, Huang Y, Liu C, Liu F, Hu X, Kuang X, *et al.* Diagnosis of Clinically Significant Portal Hypertension Using CT- and MRI-based Vascular Model. Radiology. 2023 Apr; 307(2): 221648. doi: 10.1148/radiol.221648.

[18] Sangster GP, Previgliano CH, Nader M, Chwoschtschinsky E, Heldmann MG. MDCT Imaging Findings of Liver Cirrhosis: Spectrum of Hepatic and Extrahepatic Abdominal Complications. HPB Surgery. 2013; 2013(1). doi: 10.1155/2013/129396.

[19] Hochhegger B, Zanon M, Patel PP, Verma N, Eifer DA, Torres PP, *et al.* The Diagnostic Value of Magnetic Resonance Imaging Compared to Computed Tomography in the Evaluation of Fat-Containing Thoracic Lesions. The British Journal of Radiology. 2022 Dec; 95(1140). doi: 10.1259/bjr.20220235.

[20] Im WH, Song JS, Jang W. Noninvasive Staging of Liver Fibrosis: Review of Current Quantitative CT and MRI-Based Techniques. Abdominal Radiology. 2022 Sep; 47(9): 3051-3067. doi: 10.1007/s00261-021-03181-x.

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Original Article

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Prevention and Control of Cervical Cancer by WHO-Endorsed Guidelines for Visual Inspection with Acetic Acid (Via) As a Simple Screening Method

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ABSTRACT

Despite the availability of primary prevention through Human Papillomavirus (HPV) vaccination, cervical cancer remains one of the leading causes of cancer-related deaths among women worldwide. And imposes an enormous global public health burden most notably for those living in low- or middle-income countries. **Objective:** To determine the diagnostic accuracy of VIA in diagnosing cervical cancer as compared to conventional methods. **Methods:** This retrospective study analyzed a cohort of women who underwent VIA screening for cervical cancer at Divisional Headquarters Teaching Hospital. The sample included 1,200 women aged 25-65 who had not been screened for cervical cancer in the previous three years. VIA screening followed WHO-recommended procedures, with presumptive diagnoses made through naked eye examination based on WHO guidelines for low-resource settings. Data was entered and analyzed by SPSS 25.0. **Results:** Among 1,200 women screened for cervical abnormalities using VIA, 280 tested positive (23.3%). The highest VIA-positive rates were in the 45-54 age group (112 positives), followed by the 35-44 group (70 positives). The diagnostic accuracy of VIA for cervical abnormalities shows high sensitivity (89.34%) and specificity (96.23%). VIA's positive predictive value was 85.83%, while the negative predictive value was 97.25%, indicating reliable detection of true positives and negatives. **Conclusions:** VIA was an accurate, affordable screening tool with a high level of sensitivity and specificity in detecting cervical precancerous lesions, particularly for low-resource settings. These results highlight the effectiveness of VIA screening across age groups, with higher detection rates in women over 35.

INTRODUCTION

The primary prevention with Human Papillomavirus (HPV) vaccination, cervical cancer is still one of the leading causes of death from any type in women worldwide and imposes an enormous global public health burden most notably for those living in low- or middle-income countries [1]. In fact, the incidence and mortality rates due to cervical cancer are grossly higher in Low- and Middle-Income Countries (LMICs). Because of poor access to cost-effective preventive measures viz. screening services supplemented with effective treatment options [2]. Cervical cancer is the second most frequent type in this region that has been affecting 5,008 women confirmed annually with cervical cancer and causing 3,197 deaths each year as per reported data. The high prevalence of cervical cancer in Pakistan leads to a large burden, thus necessitating improved prevention and early detection strategies [3, 4]. Cervical cancer represents as a major public health issue in India, with 134420 cases per annum and responsible for 72825 deaths [5]. The World Health Organization WHO recognizes the urgent requirement of simple inexpensive methods for screening and these can be utilized in resource-poor countries to decrease cervical cancer burden globally [6]. There are several methods and one of them is Visual Inspection with Acetic Acid (VIA) which has been recognized as a cost-effective method in low-resources settings [7-9]. This exam consists in the application of acetic acid onto the cervix, temporarily highlighting regions which a priori seem to indicate

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abnormal areas suggestive for precancerous or cancerous alterations what can actually be visually accessed [10, 11]. The VIA testing involves the application of 3–5% acetic acid to the cervix, which makes premalignant or malignant lesions appear white — these can be seen with a doctor's naked eye [12]. VIA is referred as a primary screen for cervical cancer by the WHO in LMIC and plays an important role to be used with "screen-and-treat" that encourages same day treatment after positive VIA screening, thereby increasing likelihood patient are not lost on follow-up [13]. These assays are especially useful when recognized advanced screening technologies like the Pap smears or HPV DNA testing might not be possible due to financial and logistical issues [14]. Literature have shown that VIA is a cost-effective and very sensitive screening method for cervical lesions to be used as the basis of large-scale monitoring programs in low-resource settings [15]. The challenges facing the proper implementation of this successfully working VIA-based screening program include proper training of healthcare providers, ensuring quality control, and overcoming cultural and other logistical barriers to take up screening [16]. Nevertheless, VIA remains one of the cornerstones of cervical cancer prevention strategies in LMICs, where many countries worldwide integrate it into their national public health programs.

The study was conducted to determine the diagnostic accuracy of VIA in diagnosing cervical cancer as compared to conventional methods.

METHODS

It was a retrospective study on the prevention and control of cervical cancer, with a particular emphasis on the sensitivity of VIA as a screening modality. The study was carried out at the Divisional Headquarters Teaching Hospital, Mirpur, Azad Kashmir, Pakistan after taking ethical approval from Mohtarma Benazir Bhutto Shaheed Medical College Mirpur (Ref.No.66/Academic Block Trauma Center/Surgery). Presumptive diagnosis of cervical cancer by naked eye examination according to guidelines set by the WHO, particularly in low-resource settings where facilities for higher-level screening tests such as Pap smear and testing for HPV were unavailable, was the basis on which the study was performed. The study collected follow up data of females from January 1, 2012, to December 31, 2022, uninterruptedly for a period of ten continuous years. The population included women aged 25-65 years presenting to the hospital for routine cervical cancer screening. These were selected using a non-probability consecutive sampling technique. Cochran formula was used to calculate sample size by taking margin of error (e) 0.05, an estimated proportion of population (p) 0.5, population of 20,000, and Z(a/2) score from the Z table at 95% confidence interval which was 1.96 and 20% drop out rate. The total sample included 1200 women. The inclusion criteria had been the specification of the age stated above and those who had never undergone cervical cancer screening in the last three years. Women with a known history of cervical cancer, previous hysterectomy, or active vaginal infection were excluded from the study. VIA screening was done using the procedure recommended by WHO [17]. During the performance of the procedure, the cervix was swabbed with 3-5% acetic acid, and after one minute, it was observed visually for appearance of the acetowhite lesions that indicate possible precancerous changes or cervical cancer. The screening was performed by trained health professionals who had undergone previous training in VIA. All data were thoroughly screened and cleaned prior to analysis to ensure accuracy. This process included identifying missing data and addressing participants lost to follow-up. To account for potential attrition, a 20% dropout rate was incorporated, ensuring the study sample remained representative of the target population. It was a retrospective collection of data regarding the demographic information (like age, marital status, socio-economic status) VIA screening results, and follow-up diagnostic procedures such as colposcopy and biopsy from the hospital records. These diagnostic procedures, namely colposcopy and biopsy, were also conducted on all cases to further confirm the presence of either CIN or cervical cancer. The main outcome measures were diagnostic precision of VIA, expressed through its sensitivity, specificity, PPV, and NPV regarding precancerous lesions and cervical cancer. Sensitivity was the proportion of true positives-women with histologically confirmed CIN or cancer-out of all women who tested positive on VIA. Specificity was calculated as the proportion of true negatives-women without CIN or cancer-among all women who tested negative on VIA. The PPV was the proportion of true positives among all women testing positive, whereas NPV was the proportion of true negatives among all women testing negative. Data were cleaned, entered, and analyzed using SPSS version 24.0. The chi-square test was conducted to determine the difference in cervical cancer incidence among VIA-positive and VIA-negative groups. Sensitivity, specificity, PPV, and NPV of VIA were computed. The p-values ≤ 0.05 were considered significant. After taking the ethical approval from Institutional Review Board of Divisional Headquarters Teaching Hospital, Mirpur. No patient consent to review the patients' data was required since this study followed a retrospective analysis. However, in order to keep the patient confidentiality, all of the data were anonymized.

RESULTS

Mean age of the women screened was 43.7 ± 8.6 years. The sample consists of 1,200 participants, with 889 (74.2%)

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being married and 311 (25.8%) not married. Regarding socioeconomic status, the majority of participants were classified as poor, with 665 (55.4%) falling into this category. A smaller proportion of participants had a middle socioeconomic status 348 (29.0%), while 187 (15.5%) participants were classified as having a high socioeconomic status (Table 1).

Table 1: Demographic and Screening Characteristics of VIA Study Sample

Variables	Outcomes Mean ± SD/ N (%)
Age (Years)	43.7 ± 8.6
Marital Status	
Yes	899 (74.1%)
No	311 (25.9%)
Socioeconomic Status*	
Poor	665 (55.4%)
Middle	348 (29.0%)
High	187 (15.5%)

*Socioeconomic status was calculated by individual's monthly household income

The figure 1, compared the diagnostic outcomes of cervical cancer screening using Visual Inspection with Acetic Acid (VIA) and colposcopy. Of the 1,200 women screened by VIA, 280 (23.3%) turned out to be positive for precancerous or cancerous lesions. All patients who tested positive on VIA were subsequently followed up and underwent colposcopy and biopsy for confirmation. VIA detected 23.3% of cases as positive and 76.6 % as negative, while colposcopy identified only 18.10% of cases as positive and 81.90% as negative. This suggests a significant discrepancy between the two methods, with VIA identifying a higher proportion of positive cases, potentially indicating its higher sensitivity compared to colposcopy (Figure1).

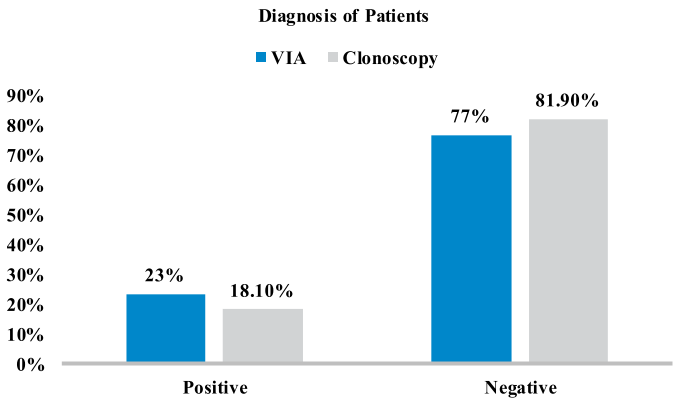

Figure 1: Diagnostic Outcomes of Cervical Cancer Screening using Visual Inspection with Acetic Acid (VIA) and Colposcopy

Among 1,200 women screened for cervical abnormalities using VIA, 280 tested positive (23.3%). The proportion of VIA-positive cases increased with age, with the highest number of positives (112) in the 45-54 age group, followed by 70 in the 35-44 age group. Notably, despite screening fewer women in the 55-65 age group, 50 VIA positives were identified, suggesting a higher prevalence of abnormalities in older women. The number of biopsies conducted closely followed the VIA-positive results. The 35-44 and 45-54 age groups had a high rate of follow-up biopsies (68 and 77, respectively), with nearly all VIA-positive women in these groups undergoing further evaluation. In contrast, the 25-34 and 55-65 age groups had lower biopsy rates (38 and 35, respectively), though still proportionally significant. These findings indicate that the VIA screening method identified a substantial number of potential abnormalities across all age groups, with follow-up biopsies further confirming the need for medical evaluation, particularly among women aged 35-54 (Table 2).

Table 2: Comparison of Age Group with VIA Positivity, and Colposcopy-Guided Biopsy Results

Age Group (Years)	Women Screened	VIA Positives N (%)	Colposcopy-Guided Biopsies N (%)	p-Value
25-34	300	48 (17.1%)	38 (17.4%)	0.000
35-44	400	70 (25.0%)	68 (31.1%)	
45-54	350	112 (40.0%)	77 (35.3%)	
55-65	150	50 (17.8%)	35 (16.0%)	
Total	1200	280	218	

From 2012 to 2022, there was general trend showing fluctuation in both screening and confirmed cases. Notably, the year 2017 recorded the highest number of both VIA positive (45) and colonoscopy positive (37) results. Similarly, 2016, 2018, and 2020 had relatively higher numbers of both metrics, indicating increased detection or participation in those years. Conversely, the lowest figures were observed in 2022, where VIA positive cases dropped to 12, with colonoscopy-confirmed positives at just 7. This decreasing trend in the last two years (2021 and 2022) may indicate reduced screening or fewer confirmed cases. (Figure 2).

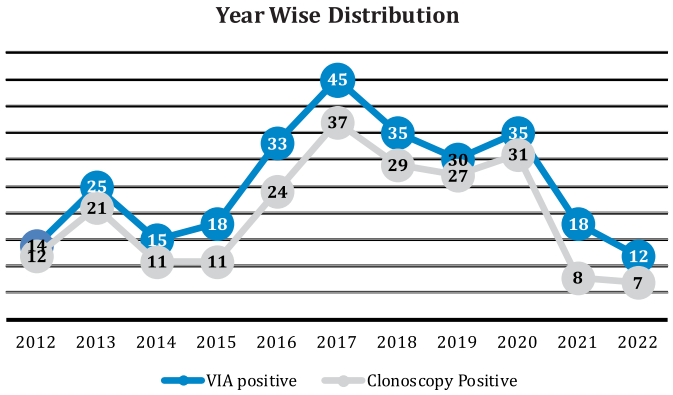

Figure 2: Year-wise distribution of positive cases

Out of the 1200 women screened, 280had a positive result on VIA, with 218 of those confirmed as true positives by

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biopsy, and 62 classified as false positives. In contrast, 920 women had a negative result on VIA, of which 844 were true negatives confirmed by biopsy, and 36 were false negatives. The diagnostic accuracy of VIA for cervical abnormalities shows high sensitivity (85.8%) and specificity (93.4%). VIA's positive predictive value was 77.8%, while the negative predictive value was 96.1%, indicating reliable detection of true positives and negatives (Table 3).

Table 3: Diagnostic Accuracy of VIA and Colonoscopy Guided Biopsy

Variables	Result
Total Women Screened	1,200
VIA Positive Cases	280
True Positives (confirmed by biopsy)	218
False Positives	62
VIA Negative Cases	920
True Negatives (confirmed by biopsy)	844
False Negatives	36
Diagnostic Accuracy Metrics	
Sensitivity	85.8%
Specificity	93.4%
Positive Predictive Value (PPV)	77.8%
Negative Predictive Value (NPV)	96.1%

DISCUSSION

The present study has furnished useful information regarding the performance of VIA as a screening modality for cervical cancer, especially in resource-poor environments. It was observed that VIA may be a good detection method for precancerous and cancerous lesions as it showed sensitivity (89.34%) and specificity (96.23%). These findings suggest that VIA represents a good initial screening method when facilities for Pap smears or HPV testing were not available due to resource constraints. Recent studies confirm the utility of VIA in screening, demonstrating its high accuracy and cost-effectiveness, with added value coming from new techniques like artificial intelligence enhancing detection [18]. The results of current study were supported by the literature available on cervical cancer screening in developing countries. One study reported the usefulness of VIA as a low-cost and easily implementable approach for early detection of cervical lesions, especially in areas where cytological screening approaches were not available [19]. In current study it was demonstrated that however VIA detected 23.3% of cases as positive and 76.6 % as negative. However, these findings were comparable with a cohort study which reported that the true positive rate by VIA was 21% and false positive as 5%. These trends show that the VIA was reliable and cost-effective tool for the detection of cervical cancer in low resource settings [20]. Moreover, positive predictive value was 85.83%, while the negative predictive value was 97.25%. Showed further assurance that VIA was reliable in correctly identifying those women who need further diagnostic evaluation, such as colposcopy and biopsy. These findings agree with other studies also reporting similarly high diagnostic validity for VIA in ruling out, as well as in detecting, precancerous lesions. Another study that was conducted found that positive predictive value, negative predictive value and diagnostic accuracy of Pap smear in diagnosis of cervical carcinoma were 84.15%, 81.94% and 83.12% respectively. The study finally concluded that VIA has a greater sensitivity and accuracy than that of Pap smear [21]. The age distribution of the confirmed lesions in the study showed that from the age group 45-65 years, the incidence of cervical lesions was higher compared to the age group 25-44 years. This agrees with other studies reporting increased risk of cervical cancer in older women probably due to accumulation of exposure to risk factors over time [22]. The strong association of age with the diagnosis of lesions, represented by a p-value of less than 0.05, points out that targeted screening strategies should be prioritized for older women because the risk of cervical cancer increases with age. A systematic review of VIA found a sensitivity of 71.8%, specificity of 79.4%, positive predictive value of 16.7%, and negative predictive value of 99.0%. According to a study, VIA was more sensitive than Pap smear and was also easy, safe, cheap and needs little training making it possible for primary health care workers to perform. Owing to its high sensitivity and NPV, VIA was suggested as an effective substitute for screening women with precancerous cervical lesions. As compared to conventional cytology, VIA has the superior sensitivity and NPV, qualities that will make it a reliable and appropriate cervical cancer screening method especially in resource-poor countries [23]. However, this study has limitations also, the main limitation the type of study design, which was retrospective in nature which leads selection bias in the samples if data from hospital records were solely depended on, and a nonrandomized form of sampling may weaken the generalization of results. The study did not take into consideration the variation that may occur due to differences in skill levels among health providers performing VIA. Another limitation of the study was to comparing the results of VIA and colposcopy guided biopsy. However, we consider it necessary to mention that other screening methods, including HPV testing and Pap smear, must be addressed in future studies for more in-depth evaluation of screening techniques. The study had these limitations, yet it offers extensive evidence for the application of VIA as a screening tool in resource-constrained settings.

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CONCLUSIONS

This investigation demonstrated that VIA was a valid method of detection of precancerous and cancerous lesions with considerable diagnostic accuracy, especially in resource-poor settings. There was a higher incidence of cervical lesions in women aged between 45 to 65 years, indicating the necessity of targeted screening in older women. The study thus supports VIA to continue being used in cervical cancer prevention strategies, despite its limitations, to supplement the lack of advanced screening technologies in these areas.

Authors Contribution

Conceptualization: SR, SS, NH
Methodology: MSK, AF, SA, SS
Formal analysis: SS
Writing, review and editing: MSK, AF, NH

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Hull R, Mbele M, Makhafola T, Hicks C, Wang SM, Reis RM, Mehrotra R, Mkhize-Kwitshana Z, Kibiki G, Bates DO, Dlamini Z.Cervical cancer in low and middle-income countries. Oncology letters. 2020 Sep 1;20(3):2058-74.

[2] Parham GP, Mwanahamuntu MH, Kapambwe S, Muwonge R, Bateman AC, Blevins M *et al*. Population-level scale-up of cervical cancer prevention services in a low-resource setting: development, implementation, and evaluation of the cervical cancer prevention program in Zambia. PLOS One.2015 Apr; 10(4): e0122169. doi: 10.1371/journal.pone.0122169.

[3] Awan UA and Khattak AA. Has Pakistan failed to roll back HPV?.The Lancet Oncology.2022 May; 23(5): e204. doi: 10.1016/S1470-2045(22)00141-3.

[4] Chughtai N, Perveen K, Gillani SR, Abbas A, Chunara R, Manji AA, Karani S, Noorali AA, Zakaria M, Shamsi U, Chishti U. National cervical cancer burden estimation through systematic review and analysis of publicly available data in Pakistan. BMC public health. 2023 May 5;23(1):834.

[5] Wright Jr TC and Kuhn L. Alternative approaches to cervical cancer screening for developing countries. Best Practice & Research Clinical Obstetrics & Gynaecology. 2012 Apr; 26(2): 197-208. doi: 10.1016/j.bpobgyn.2011.11.004.

[6] World Health Organization. Strategic framework for the comprehensive prevention and control of cervical cancer in the Western Pacific Region 2023-2030.

[7] Denny L, Saidu R, Boa R, Mbatani N, Castor D, Moodley J *et al*. Point-of-care testing with Xpert HPV for single-visit, screen-and-treat for cervical cancer prevention: a demonstration study in South Africa. Scientific Reports.2023 Sep; 13(1): 16182. doi: 10.1038/s41598-023-43467-2.

[8] Poli UR, Bidinger PD, Gowrishankar S. Visual inspection with acetic acid (via) screening program: 7 years experience in early detection of cervical cancer and pre-cancers in rural South India. Indian Journal of Community Medicine. 2015 Jul; 40(3): 203-7. doi: 10.4103/0970-0218.158873.

[9] Mustafa MS, Jindal AK, Singh PM. Visual inspection using acetic acid for cervical cancer in low resource settings. Medical Journal Armed Forces India. 2010 Oct 1;66(4):382-4.

[10] Laxmi M, Reddy SS. Cervical Cancer Screening by Simple Visual Inspection After Acetic Acid. International journal of health sciences.;6(S4):9371-8.

[11] Rajpar SA, Memon FA, Munawar RA. Visual Inspection of the Cervix with Acetic Acid for Screening of Cervical Cancers. Pak J Med Health Sci. 2021;15(1):516-9.

[12] Sankaranarayanan R, Wesley RS, World Health Organization. A practical manual on visual screening for cervical neoplasia. 2003.

[13] Chamot E, Kristensen S, Stringer JS, Mwanahamuntu MH. Are treatments for cervical precancerous lesions in less-developed countries safe enough to promote scaling-up of cervical screening programs? A Systematic Review. BioMed Central Women's Health. 2010 Dec; 10: 1-1. doi: 10.1186/1472-6874-10-11.

[14] Rajaram S and Gupta B. Screening for cervical cancer: Choices & dilemmas. Indian Journal of Medical Research. 2021 Aug; 154(2): 210-20. doi: 10.4103/ijmr.IJMR_857_20.

[15] Taha T, Yousuf S, Rehmani D. Direct Visual Inspection with Acetic Acid: A Cost-Effective Test for Cervical Cancer Screening. Pakistan Journal of Medicine and Dentistry. 2021 Apr-Jun; 10(2): 36-42. doi: 10.36283/PJMD10-2/007.

[16] Cubie HA, Campbell C. Cervical cancer screening–the challenges of complete pathways of care in low-income countries: focus on Malawi. Women's Health. 2020 May;16:1745506520914804.

[17] World Health Organization. New recommendations for screening and treatment to prevent cervical cancer.(2021)[Internet]. 2023

[18] Vinals R, Jonnalagedda M, Petignat P, Thiran JP,

DOI: https://doi.org/10.54393/pjhs.v5i12.2494

Vassilakos P. Artificial intelligence-based cervical cancer screening on images taken during visual inspection with acetic acid:A systematic review. Diagnostics. 2023 Feb; 13(5): 836. doi: 10.3390/diagnostics13050836.

[19] Malabadi RB, Sadiya MR, Prathima TC, Kolkar KP, Mammadova SS, Chalannavar RK.Cannabis sativa: Cervical cancer treatment-Role of phytocannabinoids-A story of concern. World Journal of Biology Pharmacy and Health Sciences. 2024 Feb; 17(2): 253-96. doi: 10.30574/wjbphs.2024.17.2.0076.

[20]Shastri SS, Mittra I, Mishra G, Gupta S, Dikshit R, Badwe RA. Effect of visual inspection with acetic acid (VIA) screening by primary health workers on cervical cancer mortality: A cluster randomized controlled trial in Mumbai, India. 2014 Feb; 106(3): dju009. doi: 10.1093/jnci/dju009.

[21] Adnan Z, Khan AA, Nayyar S, Nayyar A, Anwar Z, Ahsan S. Diagnostic Accuracy of Visual Inspection with Acetic Acid (VIA) and PAP Smear in Diagnosing Cervical Cancer, Taking Histopathology as Gold Standard. Journal of the Society of Obstetricians and Gynaecologists of Pakistan. 2021 Apr; 11(1): 36-40.

[22]Huy NV, Tram NV, Thuan DC, Vinh TQ, Thanh CN, Chuang L. The value of visual inspection with acetic acid and Pap smear in cervical cancer screening program in low resource settings-A population-based study. Gynecologic Oncology Reports. 2018 May; 24: 18-20. doi: 10.1016/j.gore.2018.02.004.

[23]Ameena L. Comparative Study of Pap Smear Verses Visual Inspection with Acetic Acid in Screening for Cervical Cancer. Indian Journal of Public Health Research & Development. 2021 May; 12(3): 106-14. doi: 10.37506/ijphrd.v12i3.16050.

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Root Canal Configuration Using Cone Beam Computed Tomography in Mandibular Incisors of Pakistani Individuals

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ABSTRACT

A thorough understanding of root canal morphology is crucial for successful endodontic therapy. Variations in root canal anatomy, including differences in configuration and disposition, can significantly affect treatment outcomes, emphasizing the importance of population-specific investigations. **Objectives:** To assess and identify anatomical variations in the root canal morphology of mandibular incisors among Pakistani individuals using cone beam computed tomography imaging. **Methods:** In this retrospective cross-sectional study, 440 cone beam computed tomography scans of mandibular incisors from 115 patients were analyzed. Data on patient demographics (age and gender), tooth characteristics (central or lateral incisors), root count, and root canal morphology were recorded. Statistical analysis using Chi-squared and Kruskal-Wallis tests was performed to explore associations between demographic variables and root canal configurations. **Results:** Out of 115 patients, 110 cone beam computed tomography scans were included, while five were excluded due to missing teeth. The mean age of participants was 36.49 years, with a gender distribution of 43.6% female and 56.4% male. Type I and Type III configurations were the most prevalent. Statistically significant gender differences were found in lateral incisors ($p<0.01$), with male more frequently exhibiting Type III configurations in central incisors, while female displayed Type I configurations in lateral incisors. No significant age-related differences were observed. **Conclusions:** It was concluded that mandibular incisors in Pakistani individuals exhibit notable anatomical variations, primarily Type I and Type III configurations. These findings underscore the importance of using advanced imaging tools like bone beam computed tomography for population-specific studies, enabling more tailored and effective endodontic treatments.

INTRODUCTION

The root canal is the space within the root of a tooth that houses the pulp and extends from the pulp chamber to the root apex. Root canal systems are integral to maintaining tooth vitality, and their complexity requires a detailed understanding of effective endodontic treatment. Endodontic therapy can present a challenge for dental practitioners if the structure of the root canal is not fully comprehended. The root canal morphology is complex, as it varies among teeth, and the shape alters from simple, straight to complex, and tortuous canals. Additionally, discrepancies in the location, shape, and number of accessory canals and apical foramina add to this complexity, necessitating a thorough understanding of each tooth's unique anatomy to ensure successful treatment outcomes [1]. Maxillary incisors, which are typically single-rooted with one canal, are among the most commonly treated teeth in endodontics. However, their morphology often deviates from the typical structure,

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making treatment more complex. Mandibular incisors, while typically exhibiting a single root canal, demonstrate a higher frequency of anatomical variations when compared to their maxillary counterparts [2]. Mandibular incisors typically exhibit a straighter and shorter root canal morphology, with an average length of around 15-17 mm. However, studies indicate that approximately 40% of mandibular incisors and 25% of maxillary incisors exhibit alterations in their root canal anatomy [3]. These variations include additional canals, lateral canals, and apical deltas, which significantly complicate treatment [1, 4]. This highlights the inherent complexity of root canal systems, which can vary not only in shape but also in the number and location of accessory canals. Understanding these morphological variations is crucial, as it can directly impact the debridement process and the overall success of endodontic treatment. Research conducted on populations such as those in Saudi Arabia has further emphasized unique morphological patterns in permanent maxillary and mandibular incisors, which can influence the outcomes of root canal therapy within specific demographic groups [5, 6]. Thus, knowledge of these anatomical differences is essential for tailoring treatment strategies to meet the unique needs of each population, ultimately optimizing patient care and treatment outcomes. To ascertain the anatomy of root canals, various methods have been employed. Most notable among them were cross-sections, clearing techniques and radiographic evaluations. Recently, Cone-beam computed tomography (CBCT) has appeared as a valuable noninvasive tool for visualizing the morphology of root canals in three dimensions [7]. CBCT provided an accurate and comprehensive understanding of root canal morphology by presenting precise imaging with reduced radiation exposure [8]. The advent of CBCT has significantly improved the field of endodontics, allowing clinicians to tailor their treatment strategies to the precise anatomical configuration of each tooth, thereby improving treatment outcomes and patient care [9]. The ability to visualize the full complexity of the root canal system enables endodontists to better plan and execute treatments, reducing the risk of complications and improving overall success rates. Despite the advancements in imaging technology and the growing body of literature on root canal morphology, there remains a gap in understanding the specific variations in certain populations [10]. Root canal treatment strategies must be tailored to address these population-specific variations to optimize patient outcomes.

This study aims to investigate the root canal anatomy of permanent mandibular incisors in Pakistani individuals using CBCT imaging. By analyzing canal morphology, variations, and configurations, this study will provide valuable insights into the specific anatomical characteristics of the local population. This knowledge will, in turn, allow for the development of more precise, population-specific endodontic treatment strategies, optimizing care and ensuring better outcomes for patients.

METHODS

A retrospective cross-sectional study was conducted from April 2024 to June 2024 to review CBCT images of mandibular incisors in patients presenting with orthodontic and maxillofacial concerns. Ethical approval was obtained from the Institutional Ethical Committee (Ref: UCD/ERCA/24/182), with patient consent obtained for the use of CBCT data, and all images were anonymized to ensure patient confidentiality. The sample size for this study was calculated using the formula for cross-sectional studies based on a finite population [11]. The expected prevalence of root canal variations in mandibular incisors was estimated at 30%, based on previous studies [12]. The sample size was calculated using the following formula: n=Z2.P(1-P)/E2. Where: n is the sample size, Z is the Z-score corresponding to a 95% confidence level (1.1), P is the expected prevalence of root canal variations (0.3) and E is the margin of error (0.05). Using this formula, the calculated sample size was 110, rounded up to 115 to account for potential dropouts or incomplete data. This sample size provides a confidence level of 95% with a margin of error of 5%, ensuring that the study has sufficient power to detect significant differences in root canal morphology. Images were obtained from patients aged 18-50 years, including both genders from four different dental hospitals, namely, University College of Dentistry Lahore, Pakistan Institute of Medical Sciences Islamabad, Multan Medical and Dental College, and Peshawar Dental Hospital. CBCT images were acquired using a Planmeca Pro Max 3D Max (Planmeca OY Asentajankatu 6, 00880 Helsinki, Finland) unit with a voxel size of 0.4mm, and a field of view of 5 x 5.5 cm or 10 x 9 cm for high-resolution imaging. CBCT images were analyzed using Planmeca Romexis software. The coronal, axial, and sagittal sections of each mandibular incisor were carefully examined to determine the root canal configuration according to the Vertucci classification system. To ensure consistent image analysis, a calibration session was conducted for the three trained assessors (two general dental practitioners and one endodontist) to familiarize them with the Vertucci classification system. Each assessor independently reviewed the images, and discrepancies between the assessors were resolved through consensus. Images with poor image quality, incomplete root formation, or evidence of previous endodontic treatment were excluded. The classification of root canal morphology was determined according to the Vertucci classification system, which categorizes root

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canals into eight distinct types based on their anatomical configuration [13]. Type I: Single canal with a single foramen, Type II: Two separate canals merging into a single foramen, Type III: One canal dividing and reuniting into a single foramen, Type IV: Two separate canals each having one foramina, Type V: One canal bifurcating into two separate foramina, Type VI: Two separate canals first merge and then split into two foramina, Type VII: One canal first divides then reunites and finally terminates in two foramina and Type VIII: Three separate canals with three foramina. Classification of the root canal system is shown (Figure 1).

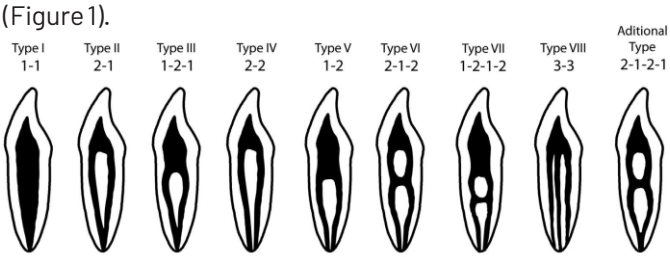

Figure 1: Classification of Root Canal Systems: Vertucci's 8 Types

Data were entered and analysed using SPSS version 29.0. Quantitative data were interpreted by Mean + SD and qualitative data were represented in the form of frequencies and percentages. The chi-square test was used to analyse the association between qualitative variables (gender, types of root configuration). The Kruskal-Wallis test was carried out to find the association between age and root configuration. $p<0.05$ was considered statistically significant, with two-tailed tests used for all analyses.

RESULTS

The study consisted of 115 CBCT images, procured from dental hospitals across Pakistan. Out of these, five cases were excluded owing to the absence of teeth, calcified canals, and external resorption. Therefore, 110 CBCT images were included in the analysis. The mean age of the sample population was 36.49 ± 14.04. Most of them were male 62 (56.4%) whereas females were 48 (43.6%). The predominant root anatomy of mandibular incisors was predicted. Among the samples, two left permanent central incisors, one left permanent lateral incisor, two right permanent central and one right permanent lateral incisor were missing (Table 1).

Table 1: Root Canal Configurations by Tooth Type

Root Configuration	Left Permanent Lateral Incisor n (%)	Left Permanent Central Incisor n (%)	Right Permanent Central Incisor n (%)	Right Permanent Lateral Incisor n (%)
Type I	67 (60.9%)	69 (62.7%)	71 (64.5%)	69 (62.7%)
Type II	2 (1.8%)	2 (1.8%)	1 (0.9%)	2 (1.8%)
Type III	33 (30%)	33 (30%)	32 (29.1%)	34 (30.9%)
Type IV	5 (4.5%)	-	-	-
Type V	1 (0.9%)	4 (3.6%)	3 (2.7%)	4 (3.6%)
Type VI	1 (0.9%)	-	-	-
Additional Type	-	-	1 (0.9%)	-

An additional root type was observed in the central incisor. As compared to female, more male was observed with type III canal configuration in left central (72.7% vs 27.3%) and right central incisors (71.9% vs 28.1%). On the contrary, when compared to male, more female patients had type I in the left lateral incisor (43.3% vs 56.7%) and right lateral incisor (44.9% vs 55.1%). The bivariate analysis revealed statistically significant associations between differences in root configurations between male and female for left lateral incisors (χ^2=16.19, $p<0.01$) and right lateral incisors (χ^2=12.41, $p<0.01$). However, no significant gender-based differences were observed in central incisors (Table 2).

Table 2: Gender-Wise Association of Root Configuration

Root Configuration	Left Lateral n (%)		Left Central n (%)		Right Central n (%)		Right Lateral n (%)	
	Male	Female	Male	Female	Male	Female	Male	Female
Type I	29 (46.8%)	38 (80.9%)	33 (55%)	36 (75%)	35 (58.3%)	36 (75%)	31 (50%)	38 (80.9%)
Type II	2 (3.2%)	0 (0%)	1 (1.7%)	1 (2.1%)	0 (0%)	1 (2.1%)	1 (1.6%)	1 (2.1%)
Type III	26 (41.9%)	7 (14.9%)	24 (40%)	9 (18.8%)	23 (38.3%)	9 (18.8%)	26 (41.9%)	8 (17%)
Type IV	4 (6.5%)	1 (2.1%)	-	-	-	-	-	-
Type V	1 (1.6%)	0 (0%)	2 (3.3%)	2 (4.2%)	2 (3.3%)	1 (2.1%)	4 (6.5%)	0 (0%)
Type VI	0 (0%)	1 (2.1%)	0 (0%)	0 (0%)	0 (0%)	1 (2.1%)	0 (0%)	0 (0%)
Additional type								
p-value	0.006*		0.128		0.124		0.006*	

Note: * denotes p-value is significant

Upon investigating the association between patient age and the different root configuration types, non-significant results were obtained (Table 3).

Table 3: Association of Age with Root Configuration among Different Types of Teeth

Type of Tooth	p-value
Right Central Incisor	0.26
Right Lateral Incisor	0.06
Left Central Incisor	0.08
Left Lateral Incisor	0.32

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Type I was the predominant canal configuration observed in both central and lateral incisors, followed by Type III (Figure 2).

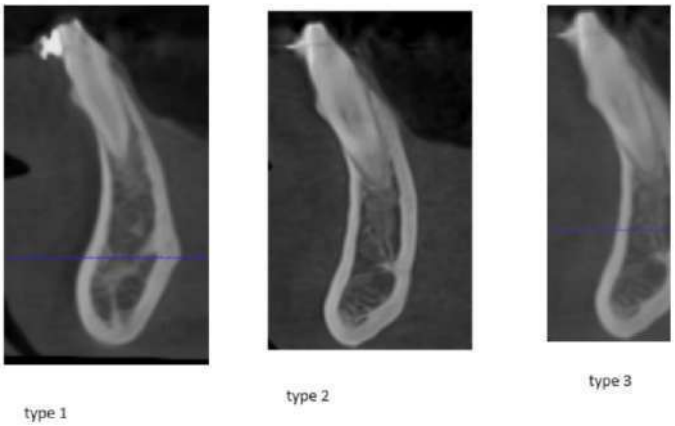

Figure 2: Root Canal Morphology Visible on CBCT

DISCUSSION

Traditionally, root morphology has been examined through invasive staining and clearing techniques. However, CBCT offers a revolutionary and non-invasive method for exploring and understanding root canal anatomy, providing a more comfortable and efficient experience for patients [14]. The integration of CBCT technology in this study permitted a precise and non-invasive examination of variation in root canal anatomy, which will help in tailoring effective treatments for better patient outcomes [15]. Previous studies have exhibited a significant range of anatomical variations, mandibular incisors exhibit complex root canal morphology, with diverse configurations, shapes, and sizes, posing challenges for endodontic treatment [16]. In this study, the Type I root canal was the predominant anatomical configuration in both central and lateral mandibular incisors, followed by Type III. These findings are comparable with with studies that have been conducted in three geographically diverse locations Saudi Arabia, China, and Turkey. Hence, it is a suggestion of a homogeneous pattern across different populations [17-19]. A rare anatomical variation in the current study was observed a noteworthy finding of the central incisor presenting with an additional root type. This finding is of great importance, as it spotlights the impact of comprehensive review and accurate diagnosis in root canal treatment. Similar findings were manifested by Alqahtani et al., reporting the incidence of additional root canals in central incisors and supporting our results [20]. From our study, it was observed that gender significantly influenced the occurrence of root canal configurations in mandibular incisors, with notable differences between males and females. Peculiarly, males displayed a greater percentage of Type III root canals in mandibular central incisors, while females showed a greater frequency of Type I canal morphology in mandibular lateral incisors. Interestingly, a recent study conducted on the Chinese population by Zhu et al., 2022 showed indistinguishable results, with males exhibiting a greater proportion of Type III root canal patterns in central incisors, mirroring our results [21]. However, this study did not depict a notable gender-based difference in lateral incisors, contrary to our results. Differences in sample size and demographics may explain the divergent findings between the two studies. Both studies highlighted the significance of believing gender is an important factor in understanding root canal morphology, which can lead to the perception of more diversities and tailoring more effective endodontic treatment strategies accordingly. Contrary to our apprehension, the difference in the root configuration of incisors between different gender groups was insignificant in the present study. Additionally, no significant relationship was observed between the patient's age and different types of root configurations. Nearly similar results were reported by Zhu et al., [21]. The present research emphasized that age may not play a significant role in shaping root canal anatomy. Similarly, a recent study analyzing the interrelation between age and root canal anatomy in mandibular incisors found no significant association between them. However, a greater frequency of alterations in root canal morphology in older individuals was observed which was not evident in our study. The observed dissimilarity between the two studies may be attributed to discrepancies in sample size and demographic characteristics. Despite these dissimilarities, both studies focused on the importance of considering individual alterations in root canal morphology, rather than only depending on age or gender as predictors, to ensure accurate diagnosis and treatment [20].

CONCLUSIONS

It was concluded that this research provided considerable insight into the pulp canal anatomy of mandibular incisors in a Pakistani population, exhibiting a greater prevalence of Type I and Type III root canal patterns. These inventions concentrated on improving the existing knowledge, highlighting the need for continued research for morphological variations and personalized treatment approaches to enhance patient care and improve treatment outcomes.

Authors Contribution

Conceptualization: SS
Methodology: AF, AA, IH, IR
Formal analysis: KT, AA, SS, IH
Writing review and editing: AF, SS, KT, AC

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All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Karobari MI, Parveen A, Mirza MB, Makandar SD, Nik Abdul Ghani NR, Noorani TY *et al.* Root and Root Canal Morphology Classification Systems. International Journal of Dentistry.2021; 2021(1): 6682189. doi: 10.1155/2021/6682189.

[2] Herrero-Hernández S, De Pablo ÓV, Bravo M, Conde A, Estevez R, Haddad Y *et al.* Cone-beam Computed Tomography Analysis of the Root Canal Morphology of Mandibular Incisors Using Two Classification Systems in a Spanish Subpopulation: A Cross-Sectional Study. European Endodontic Journal. 2024 Feb; 9(2): 106-13. doi:10.14744/eej.2023.10327.

[3] Dhuldhoya DN, Singh S, Podar RS, Ramachandran N, Jain R, Bhanushali N. Root Canal Anatomy of Human Permanent Mandibular Incisors and Mandibular Canines: A Systematic Review.Journal of Conservative Dentistry and Endodontics.2022 May; 25 (3): 226-40. doi: 10.4103/jcd.jcd_40_22.

[4] Ahmed HM. A Critical Analysis of Laboratory and Clinical Research Methods To Study Root and Canal Anatomy. International Endodontic Journal. 2022 Apr; 55: 229-80. doi: 10.1111/iej.13702.

[5] Iqbal A, Karobari MI, Alam MK, Khattak O, Alshammari SM, Adil AH *et al.* Evaluation of Root Canal Morphology in Permanent Maxillary and Mandibular Anterior Teeth in Saudi Subpopulation Using Two Classification Systems: A CBCT Study. BioMed Central Oral Health. 2022 May; 22(1): 171. doi: 10.1186/s12903-022-02187-1.

[6] Mustafa M, Batul R, Karobari MI, Alamri HM, Abdulwahed A, Almokhatieb AA *et al.* Assessment of the Root and Canal Morphology in the Permanent Dentition of Saudi Arabian Population Using Cone Beam Computed and Micro-Computed Tomography–A Systematic Review. BioMed Central Oral Health.2024 Mar; 24(1): 343. doi: 10.1186/s12903-024-04101-3.

[7] Yan Y, Li J, Zhu H, Liu J, Ren J, Zou L. CBCT Evaluation of Root Canal Morphology and Anatomical Relationship of Root of Maxillary Second Premolar to Maxillary Sinus in A Western Chinese Population. BioMed Central Oral Health.2021 Dec; 21: 1-9. doi: 10.1186/s12903-021-01714-w.

[8] Thanaruengrong P, Kulvitit S, Navachinda M, Charoenlarp P. Prevalence of Complex Root Canal Morphology in the Mandibular First and Second Premolars in Thai Population: CBCT Analysis. BioMed Central Oral Health.2021 Dec; 21: 1-2. doi: 10.1186/s12903-021-01822-7.

[9] Karobari MI, Noorani TY, Halim MS, Ahmed HM. Root and Canal Morphology of the Anterior Permanent Dentition in Malaysian Population Using Two Classification Systems: A CBCT Clinical Study. Australian Endodontic Journal.2021 Aug; 47(2): 202-16. doi: 10.1111/aej.12454.

[10] De-Deus G, Souza EM, Silva EJ, Belladonna FG, Simões-Carvalho M, Cavalcante DM *et al.* A Critical Analysis of Research Methods and Experimental Models to Study Root Canal Fillings. International Endodontic Journal.2022 Apr; 55: 384-445. doi: 10.1111/iej.13713.

[11] Martins JN, Ensinas P, Chan F, Babayeva N, von Zuben M, Berti L *et al.* Worldwide Prevalence of the Lingual Canal in Mandibular Incisors: a Multicenter Cross-Sectional Study with Meta-analysis. Journal of Endodontics.2023 Jul; 49(7): 819-35. doi: 10.1016 /j.joen.2023.05.012.

[12] Herrero-Hernández S, López-Valverde N, Bravo M, Valencia de Pablo O, Peix-Sánchez M, Flores-Fraile J *et al*. Root Canal Morphology of the Permanent Mandibular Incisors By Cone Beam Computed Tomography: A Systematic Review. Applied Sciences. 2020 Jul; 10(14): 4914. doi: 10.3390/app10144914.

[13] Vertucci FJ. Root Canal Morphology and Its Relationship to Endodontic Procedures. Endodontic Topics.2005 Mar; 10(1): 3-29. doi: 10.1111/j.1601-1546. 2005.00129.x.

[14] Pires M, Martins JN, Pereira MR, Vasconcelos I, Costa RP, Duarte I *et al.* Diagnostic Value of Cone Beam Computed Tomography for Root Canal Morphology Assessment–A Micro-CT Based Comparison. Clinical Oral Investigations.2024 Mar; 28(3): 201. doi: 10.1007/s00784-024-05580-y.

[15] Kaur K, Saini RS, Vaddamanu SK, Bavabeedu SS, Gurumurthy V, Sainudeen S *et al*. Exploring Technological Progress in Three-Dimensional Imaging for Root Canal Treatments: A Systematic Review. International Dental Journal.2024 Jul. doi: 10.1016/j.identj.2024.05.014.

[16] Usha G, Muddappa SC, Venkitachalam R, VP PS, Rajan RR, Ravi AB. Variations in Root Canal Morphology of Permanent Incisors and Canines among Asian Population: A Systematic Review and Meta-Analysis. Journal of Oral Biosciences.2021 Dec; 63(4): 337-50. doi: 10.1016/j.job.2021.09.004.

DOI: https://doi.org/10.54393/pjhs.v5i12.2115

[17] Mashyakhy M, AlTuwaijri N, Alessa R, Alazzam N, Alotaibi B, Almutairi R *et al.* Anatomical Evaluation of Root and Root Canal Morphology of Permanent Mandibular Dentition among the Saudi Arabian Population: A Systematic Review. Biomed Research International.2022; 2022(1): 2400314. doi: 10.1155/2022/2400314.

[18] Qiao X, Zhu H, Yan Y, Li J, Ren J, Gao Y *et al*. Prevalence of Middle Mesial Canal and Radix Entomolaris of Mandibular First Permanent Molars in A Western Chinese Population: An in Vivo Cone-Beam Computed Tomographic Study. BioMed Central Oral Health.2020 Dec; 20: 1-8. doi: 10.1186/s12903-020-01218-z.

[19] Aydin H. Analysis of Root and Canal Morphology of Fused and Separate Rooted Maxillary Molar Teeth in Turkish Population. Nigerian Journal of Clinical Practice.2021 Mar; 24(3): 435-42. doi: 10.4103/ njcp.njcp_316_20.

[20] Almohaimede A, Alqahtani A, Alhatlani N, Alsaloom N, Alqahtani S.Analysis of Root Canal Anatomy of Mandibular Permanent Incisors in Saudi Subpopulation: A Cone-Beam Computed Tomography (CBCT) Study. Scientifica.2022; 2022(1): 3278943. doi: 10.1155/2022/3278943.

[21] Qian Y, Li Y, Song J, Zhang P, Chen Z. Evaluation of C-Shaped Canals in Maxillary Molars in A Chinese Population Using CBCT. BioMed Central Medical Imaging.2022 May; 22(1): 104. doi: 10.1186/s12880-022-00831-4.

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Original Article

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Dermatoglyphics and Their Association with Gender and Blood Group in Medical Students at Islam Medical and Dental College

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ABSTRACT

Dermatoglyphics is defined as the study of the patterns present on fingers, toes, palms and soles which develop by the 24th week of gestation and remain permanent throughout life. A significant association has been confirmed between the different ABO blood groups, gender and dermatoglyphic patterns. **Objectives:** To investigate the fingerprint patterns among male and female students at Islam Medical and Dental College, Sialkot, and their relationship with blood groups. **Methods:** This cross-sectional study was conducted at Islam Medical and Dental College, Sialkot, in the year 2023 from mid-November to mid-December. 300 healthy students, aged 20 to 22 years, including 108 male and 192 female, participated. Fingerprints were collected using an ink pad, while blood grouping was performed using the slide method. Using SPSS version 26.0, the data were analyzed. The chi-square test ($p<0.05$) was used to evaluate relationships, and continuous variables were given as mean ± SD and categorical variables as frequencies. **Results:** The most prevalent blood type among all students was O+, and the most common fingerprint pattern was the loop pattern. Blood group and fingerprint pattern were shown to be significantly correlated in female medical students; those with loop patterns indicated a higher frequency of the B+ blood group, while those with whorl patterns indicated a higher frequency of the O+ blood type. **Conclusions:** It was concluded that a significant association of blood groups with dermatoglyphic patterns in female medical students was seen whereas in male, there was no link between blood groups and fingerprint patterns.

INTRODUCTION

Every individual possesses distinctive characteristics, which differentiate him from other individuals. These specific features can be categorized as structural, physiological, pathological and psychological which are important for an individual as personal, social or legal purposes in forensic anatomy [1]. Dermatoglyphics, the study of epidermal ridge patterns on fingers, toes, and palms begins in the 10th week of gestation and is fully developed by the 24th week [2]. These patterns are determined by dermal papillae during fetal development and remain permanent and consistent throughout life [3]. Both environmental factors and genetic factors influence the dermatoglyphic patterns which make them relevant in identifying variations in the genotype and phenotype among populations [4]. Numerous studies have explored the relationship between gender, blood group and dermatoglyphic patterns as loop patterns are frequently observed in individuals with blood group B, while whorl patterns are prevalent in those with blood group O, indicating potential genetic links between ABO blood groups and fingerprint types. This association suggests a strong potential genetic correlation between the ABO blood group system and dermatoglyphic patterns in distinct genders [5, 6]. Gender differences in fingerprint patterns are also notable with male often exhibiting more loops and whorls, and females displaying more arches [7].

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Research has been done on the association between medical students' blood groups and dermatoglyphic patterns, but not much on the relationship between gender and blood groups in Punjab's tertiary medical institutions (Pakistan).

This study aims to examine fingerprint patterns and how they differed across genders to evaluate how the students at Islam Medical and Dental College in Sialkot related to their blood types. Because this study is multilayered and covers both the genetic foundation of dermatoglyphics and the significance of gender variations in fingerprint patterns related to blood groups, the results may be useful as a prediction tool for health consequences.

METHODS

The cross-sectional study was conducted at Islam Medical and Dental College, Sialkot in the Anatomy Department, Sialkot. After the approval of the synopsis by the Ethical Review Board, Islam Medical College, Sialkot, the study was done from mid-November 2023 to mid-December 2023 (reference letter no 900/IMC/ERC/000103). An open epi sample size calculator was used to calculate the sample size [8]. At a 95% confidence level, the population proportion of students was 50%, the error margin was 5%, and the total population was 1000.10, with a computed sample size of 278. Three hundred healthy students, ages twenty to twenty-two, participated in the study. Of them, 192 (64%) were female and 108 (36%) were male first, second-year MBBS and first-year BDS medical students. The study population consisted of all the willing and healthy students who showed up on the day of blood grouping and fingerprinting. Students with blood-related illnesses, hand injuries, bandages on their hands, and hand deformities were not allowed to participate in the study. A straightforward, practical sampling method was applied. Before taking the prints, informed written consent was obtained. The fingerprinting process was carried out under strict scrutiny. The participants' hands were cleaned with soap and water and allowed to air dry. After that, each participant's right thumb was placed on an ink pad. Along with their age and gender, the prints were taken from the questionnaire page. Code numbers were assigned to each student. After that, the fingerprints were examined under a magnifying glass to determine if they were loop, whorl, or arch, and the results were noted on a data sheet. For blood grouping, a clean glass slide was taken, and three circles were drawn on it. Anti-A was added to the first circle followed by Anti-B to the second circle and Anti-D in the third circle with a dropper. The ring finger was then carefully rubbed and cleaned with an alcohol swab in the vicinity of the fingertip, where a blood sample was to be taken. Using the lancet, pricked the ring fingertip and removed the first drop of blood. Once the blood began to flow, it was allowed to land on the three glass slide circles by gently pressing with the fingertip. A toothpick was then used to mix the blood sample gently, and the results were recorded on the questionnaire after a minute of waiting. The SPSS version 26.0 software was used to do statistical analysis. The mean ± SD is used to represent continuous data, whereas frequency and percentages were used to represent categorical ones. To verify the relationship, the chi-square test was employed. p-values less than 0.05 were regarded as statistically significant.

RESULTS

Three hundred healthy students, aged 21 ± 0.85, took part in the research of which 108 (36%) were male and 192 (64%) were female. The most observed blood group was O+ (31%) followed by B+ (28.3%) and A+ blood group (22.3%) whereas the blood types with the lowest observation rates were AB− (1%) and B− (3.7%). The fingerprint pattern with the highest frequency of observation was the loop (50.6%) and whorl (40.7%) whereas the least was the arch (8.7%) (Table 1).

Table 1: Percentage and Frequency of Gender, Blood Group and Fingerprint Patterns (n=300)

Frequency of Gender	Frequency of Blood Groups									Frequency of Fingerprint Patterns		
Male	Female	A+	A-	B+	B-	AB+	AB−	O+	O−	Loop	Whorl	Arch
108 (36%)	192 (64%)	67 (22.3%)	11 (3.7%)	85 (28.3%)	11 (3.7%)	19 (6.3%)	3 (1%)	94 (31.3%)	10 (3.3%)	152 (50.6%)	122 (40.7%)	26 (8.7%)

In female, the commonest blood group was O+ (n=58) and B+ (n=57) and the least observed was AB− (n=2) and A− (n=5) (Figure 1).

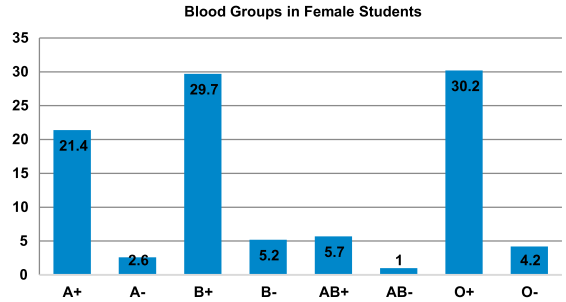

Figure 1: Percentage of Blood Groups in Female Students (n=192)

Whereas the loop pattern was the most frequent (n=99), and the arch pattern was the least frequent (n=11) in females, (Figure 2).

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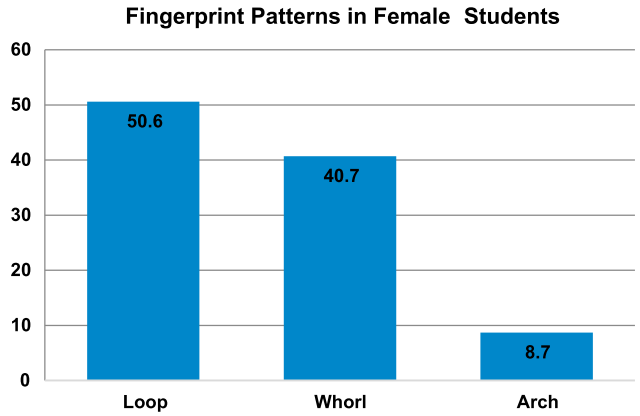

Figure 2: Percentage of Fingerprint Patterns in Female Students (n=192)

Comparing the blood groups with the fingerprint patterns, we found that female students with loop had higher frequency of B+ blood group (38.4%) and those having whorl patterns had increased frequency of O+ blood group (41.5%). This demonstrated a strong significance between female medical students' blood types and fingerprint patterns (p=0.033) (Table 2).

Table 2: Association of Fingerprint Patterns and Blood Groups with Corresponding Percentages in Female Students

Fingerprint Pattern	Blood Group Percentage within Fingerprint Patterns								p-value (Chi-Square)
	A+	A-	B+	B-	AB+	AB-	O+	O-	
Loop	23.2%	4.0%	38.4%	2.0%	4.0%	1.0%	22.2%	5.1%	0.033
Whorl	19.5%	1.2%	17.1%	7.3%	8.5%	1.2%	41.5%	3.7%	
Arch	18.2%	0.0%	45.5%	18.2%	0.0%	0.0%	18.2%	0.0%	

In male, O+ (n=36) and B+ (n=28) were the most frequent blood group, subsequently the least observed was B− and AB−(n=1)(Figure 3).

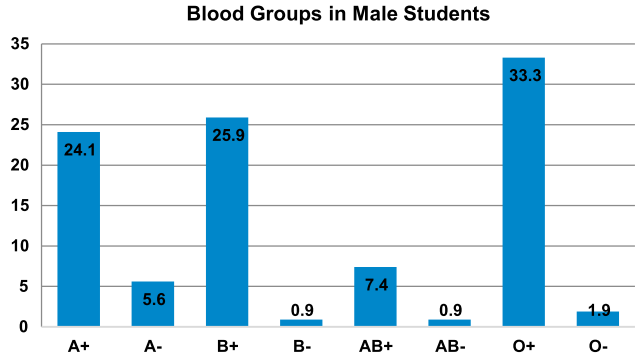

Figure 3: Percentage of Blood Groups in Male Students (n=108)

Whereas the loop pattern was most frequent (n=53), and the arch pattern was the least frequent in male gender (n=15)(Figure 4).

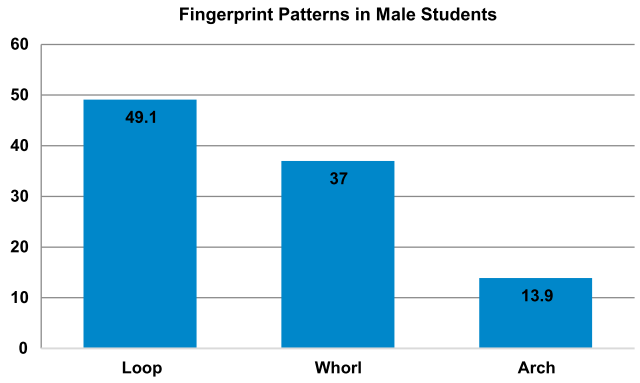

Figure 4: Percentage of Fingerprint Patterns in Male Students (n=102)

Comparing the blood groups with the fingerprint patterns, we found that male students with loop had almost equal frequency of A+ (24.5%) and O+ (28.3%) blood group and those having whorl patterns had equal amounts of B+ and O+ blood group (35%). These results also reflected an association between the blood group and fingerprint patterns in male medical students as it was not significant (p=0.250).

DISCUSSION

Our main objective was to prove a relationship between fingerprint patterns and blood groups with the gender of medical students at Islam Medical College, Sialkot in this study. The percentage of blood group O+ and loop pattern was most prevalent among the medical students. In both genders, the common blood group and fingerprint pattern were O+ and B+ and loop. B+ was the most prevalent blood group in females with loop patterns, while O+ was more common in those with whorls. In male students, findings were mixed as loop patterns had both A+ and O+ blood groups and those having whorl patterns had equal amounts of B+ and O+ blood groups. In female medical students, the relationship between blood type and fingerprint was statistically significant whereas in male medical students, the blood group frequencies were almost equally distributed among different fingerprint patterns and showed no association. The most common blood group in our analysis was O+, which is consistent with another study that found that O is the most common blood group in Pakistan. [9]. Loop pattern was the most common fingerprint pattern among the students which is in line with multiple previous studies conducted in Pakistan have consistently found that loop patterns are the most common fingerprint type among medical students in KPK and Punjab. As Iqbal *et al.*, reported loops as the predominant pattern in Peshawar [10], while Khan *et al.*, found 58% of students in Abbottabad had loop patterns [11]. Similarly, Abbasi *et al.*, observed in medical students of Lahore that a 50% loop pattern was common [12]. Female students having loop pattern fingerprints had the majority

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of the B+ blood group which is supported by one significant study by Manikandan *et al.*, which indicated that the B+ blood group was more likely to have the loop pattern. [13]. However, in another research, it was assessed that in female loops were the most common fingerprint, but it did not specifically link this prevalence to the B+ blood group as loops are the major pattern among the populations [14]. Similarly, in another study loop patterns had a higher prevalence of blood group O+ [15]. These conflicting results indicate that although loop patterns are prevalent, the distribution of various blood groups is balanced across different populations which implies that the association between B+ and loop patterns may not be as strong as suggested [16]. The female having whorl pattern had the majority of the O+ blood group which is backed by a study conducted by Aamir *et al.*, which indicated that blood group O was prevalent among individuals with whorl patterns [17], but a different study on the Omani population discovered that the A–, B+, and O– blood groups had the highest frequency of the arch pattern. This suggests that there can be substantial population-to-population variations in the correlation between blood types and fingerprint patterns [18]. The patterns of fingerprints and blood types were significantly correlated in female medical students which is in line with a previous study done by Koura *et al.*, in which they examined the correlation between ABO/Rh blood groups and fingerprint patterns in an Egyptian population. The results showed that there was a statistically significant correlation between blood groups and certain fingerprint patterns, especially in females. This links the genetic factors influencing blood group determination with the factors responsible for the development of fingerprint patterns. [16]. A research study by Alam *et al.*, in Karachi, Pakistan, assessed the linkage between fingerprints, lip prints, and blood groups. They found that certain fingerprint patterns were significantly associated with specific blood groups among females, indicating that blood groups may influence the distribution of fingerprint patterns in this demographic [19]. Furthermore, findings from the Pratinidhi *et al.*, study lend credence to this idea by showing that Rh-positive people especially women had a significantly higher frequency of loops and whorls. This discovery suggests that fingerprint creation may be influenced by the same genetic factors that underlie blood group inheritance [20]. More research work needs to be done with a large demographic sample size across multiple institutions to find out the association between gender, blood group and dermatoglyphics.

CONCLUSIONS

It was concluded that the most prevalent fingerprint pattern was the loop pattern, while the most common blood group throughout the sample size was O+. Blood group and fingerprint pattern were shown to be significantly correlated in female medical students; those with loop patterns indicated a higher frequency of the B+ blood group, while those with whorl patterns indicated a higher frequency of the O+ blood type. In comparison to female, no significant association was found between blood group and fingerprint patterns in male medical students. These findings suggest that while some associations may exist between blood group and fingerprint patterns in female, further investigation is needed to clarify these relationships, particularly in male students where no significant associations were observed. Since this study was conducted in a single medical institution, the results may not be generalizable.

Authors Contribution

Conceptualization: RMZ, RA
Methodology: RA, MJ, AR
Formal analysis: AA
Writing review and editing: AA, MZ

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Patil A, Kruthi R, Gornale S. Analysis of Multi-Modal Biometrics System for Gender Classification Using Face, Iris and Fingerprint Images. International Journal of Image, Graphics and Signal Processing. 2019 May; 12(5): 34. doi: 10.5815/ijigsp.2019.05.04.

[2] Sharma A, Sood V, Singh P, Sharma A. Dermatoglyphics: A Review On Fingerprints and Their Changing Trends of Use. Chrismed Journal of Health and Research.2018 Jul; 5(3): 167-72. doi: 10.4103/cjhr.cjhr_112_17.

[3] Rastogi A, Bashar MA, Sheikh NA. Relation of Primary Fingerprint Patterns with Gender and Blood Group: A Dermatoglyphic Study from a Tertiary Care Institute in Eastern India. Cureus.2023 May; 15(5). doi: 10.7759/cureus.38459.

[4] Bhuvaneshwari S, Chand S, Chaudhari D, Manohar B, Buyan L, Srinivasan S. Dactoscopy in Human Identification: A Retrospective Study in Bhubaneswar City. Journal of Pharmacy and Bioallied Sciences. 2023 Jul; 15(Suppl 1): S326-9. doi: 10.4103/jpbs.jpbs_526_22.

[5] Kumar P, Singh P, Sharma M, Kumari K, Ajmal M, Ahmed A. Study of Fingerprint Patterns about Gender and ABO Blood Groups. Indian Journal of

DOI: https://doi.org/10.54393/pjhs.v5i12.2400

Forensic Medicine and Toxicology.2023 Oct; 17(4). doi: 10.37506/ijfmt.v17i4.19953.

[6] Sah SK, Mahat S, Jha M, Bhagat P, Pokharel S, Jayshwal R. Evaluation of Blood Group in Co-relation with the Dermatoglyphics Patterns among Medical Students: A Cross-Sectional Study. MedS Alliance Journal of Medicine and Medical Sciences.2023 Jun; 3(5): 16-9. doi: 10.3126/mjmms.v3i5.59940.

[7] Ekanem AU, Abubakar H, Dibal NI. A Study of Fingerprints about Gender and Blood Group among Residents of Maiduguri, Nigeria. Arches.2014; 200(5.00): 328.

[8] Charan J and Biswas T. How to Calculate Sample Size for Different Study Designs in Medical Research? Indian Journal of Psychological Medicine.2013 Apr; 35(2): 121-6. doi: 10.4103/0253-7176.116232.

[9] Ansari H, Ansari MF, Das M. Relationship Between Dermato-glyphics And Blood Group of Male And Female First-Year Medical Students at Rama Medical College, Kanpur. Asian Journal of Medical Sciences. 2023 Dec; 14(12): 82-5.

[10] Iqbal F, Alam N, Yasmin RS, Khattak MA, Farid N, Aziz I. Pattern of Fingerprints and Its Association with Gender among Medical Students of Peshawar Medical College: Fingerprint patterns and gender association. Pakistan Journal of Health Sciences. 2024 Jun; 5(6): 114-7. doi: 10.54393/pjhs.v5i06.1667.

[11] Khan O, Haroon MZ, Rashid MA, Khan MN, Khan D. Left Hand Thumb Imprint Patterns Among Medical Students. Journal of Ayub Medical College Abbottabad. 2017 Jun; 29(3): 466-7.

[12] Abbasi MH, Mengal MA, Khan RM. Comparative Study of Dactylography among the Students of Avicenna Medical College, Lahore. Pakistan Journal of Medical and Health Sciences. 2012; 6(2): 362-5.

[13] Manikandan S, Devishamani L, Vijayakumar S, Palanisamy GS, Ponnusamy P, Jayakar SL. Dermatoglyphics and Their Relationship with Blood Group: An Exploration. Journal of Pharmacy and Bioallied Sciences. 2019 May; 11(Suppl 2): S285-8. doi: 10.4103/JPBS.JPBS_13_19.

[14] Deshpande SM, Choudhari S, Kavle P, Patil A, Kale P. Gender Identification by Fingerprint Pattern and Salivary Blood Group Antigen Expression: A Forensic Approach. Cureus.2024 Mar; 16(3). doi: 10.7759/ cure us.56324.

[15] Devi J, Das B, Das J. Study on Inheritance of Fingerprint Pattern and its Association with ABO Blood Groups at Nagaon, Assam. Indian Journal of Science and Technology.2023 Sep; 16(23): 1694-701. doi: 10.17485/IJST/v16i23.1941.

[16] Koura SM, Abdel-Rahman RH, Emam NM. Role of Fingerprints Patterns and ABO/Rh Blood Groups in Sex Dimorphism among Egyptian Population. Mansoura Journal of Forensic Medicine and Clinical Toxicology. 2022 Jul; 30(2): 1-7. doi: 10.21608/mjfmct .2022.133891.1044.

[17] Aamir Y, Masood R, Irshad N, Malik R, Farid N, Shahab MA. Relationship Between Pattern of Fingerprints and Blood Groups. Pakistan Journal of Medical and Health Sciences. 2022 Nov; 16(09): 698-. doi: 10.5335 0/pjmhs22169698.

[18] Al Habsi T, Al Khabori H, Al Qasmi S, Al Habsi T, Al Mushaiqri M, Das S *et al.* The Association Between Fingerprint Patterns and Blood Groups in the Omani Population. Arab Gulf Journal of Scientific Research. 2023 Jul; 41(3): 283-92. doi: 10.1108/AGJSR-10-2022-0223.

[19] Alam BF, Anwar MA, Syed KA, Ahsan TA, Bajwa SJ, Hussain TA *et al.* Assessing Relationship Between Lip Prints, Finger Prints and Different Blood Groups Within the Population of Karachi. Pakistan Journal of Medical Health Science. 2021; 15(10): 2262-66. doi: 10.53350/pjmhs2115102663.

[20] Pratinidhi SA, Lunawat V, Tilokchandani M, Bhujbal C, Shejul R, Sahoo M. Study of Fingerprint Patterns about Gender and Blood Groups. International Journal of Clinical Biochemistry and Research. 2023 Jul; 10(2): 149-53. doi: 10.18231/j.ijcbr.2023.025.

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Analysis of Achievement, Motivation and Self-Efficacy among Undergraduate Nursing Students

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ABSTRACT

Strong self-efficacy enhances motivation and performance, while strong achievement motivation boosts self-efficacy. **Objective:** To determine achievement motivation and self-efficacy levels among undergraduate nursing students. **Methods:** A cross-sectional study was conducted from September 2023 to July 2024 at three nursing institutes. A total of 222 undergraduate nursing students participated using convenience sampling. Data were collected through a self-efficacy questionnaire developed by Ralf Schwarzer. Achievement motivation was measured using McInerney's tool. Data analysis was performed using SPSS version 21.0. **Results:** Most participants were females, with 90.1% aged 20–25. The study was conducted at the College of Nursing Rawalpindi and PIMS Islamabad. Findings indicated that participants with confidence in their skills, improvement in work, and good academic performance had the highest motivation levels. External factors, such as praise or awards, were less influential. The average achievement-oriented behavior score was 4.12. Self-efficacy data revealed varied confidence levels, with most participants believing they could learn challenging content, overcome obstacles, influence personal growth, maintain relationships, and solve problems innovatively. The average self-efficacy score was also 4.12, indicating high confidence. **Conclusions:** The research highlights that highly motivated individuals achieve better outcomes, demonstrate faith in their skills, and perform well academically. Motivation is primarily driven by intrinsic factors like self-efficacy and personal growth, rather than external recognition. Enhancing self-efficacy and intrinsic motivation is crucial to improving overall performance, emphasizing persistence, diligence, and innovation as key drivers of success.

INTRODUCTION

Achievement motivation is the internal drive that encourages individuals to enhance their abilities and successfully pursue their goals in daily life and various activities. Individuals' conduct and motivation are strongly correlated, specifically, high motivation can encourage good behavior, while negative motivation can inhibit it [1]. It also means the ability to initiate, sustain, and guide goal-oriented action. Academic achievement and the learning process both depend on motivation. Motivation is not the same as motive. The incentive is characterized as a force that propels, guides, and sustains goal-oriented behavior, whereas the motivation is thought of as a common element encompassing requests, demands, interests, and urges. In educational activities that aim to mold human behavior, motivation is a crucial component. It is also necessary for people to learn along their procedures. Numerous explanations, ideas, and hypotheses regarding motivation have been put presented. The term "intrinsic motivation" describes motivation that comes from inside the person, such as interest, curiosity, knowledge, understanding, need, sufficiency, etc. The sources of extrinsic motivation are external to the person, such the workplace. It is often administered to the motivated subject by a different person, the motivator, who uses a variety of instruments

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(reward, punishment, compulsion, demands, etc.). When people are unable to make a link between their acts and the results of their actions, they lack motivation, which is known as negative motivation [2]. The majority of individuals describe motivation as desire to achieve goals and the means that maintain that desire. Motivation is the capacity to persuade oneself and others to engage in a certain action or set of behaviors, it also permits people to perform remarkable feats [3]. Individual's acts are sometimes assessed by contrasting with those of others or with benchmark. Motivation has been linked to cognitive, biological, and social factors, influencing human behavior in various ways. This multifaceted phenomenon has diverse explanations. Motivation acts like energy, directing one's behavior toward a specific goal. In essence, motivation, as described by is an internal drive that gives activities focused on reaching a goal direction, stimulus, and support [4, 2]. Human goal-directed conduct is known as motivated behavior, and it is characterized by three key elements: it is persistent, goal-directed, and it results from a perceived need [5]. Self-efficacy is the foundation for motivation, well-being, and personal achievement in all spheres of life, it is crucial for the individual [6]. Self-efficacy reflects confidence in the ability to exert control over one's own motivation, behavior and social environment. One of the main tenets of bandura's social and cognitive theory is self-efficacy, which is predicated on the notion that one can visualize things in order to reach their intended state of appropriate conduct [7]. Stated differently, self-efficacy is associated with one's attitudes and convictions on achieving one's objectives [8]. Stress brought on by a lack of drive lowers self-efficacy, and instead of obtaining adequate motivation and social support, the feeling of self-efficacy rises in individuals [9]. A high level of self-efficacy among the group's leader can disseminate to its members and effect the intended the group's performance. Members of the group's high self-esteem and self-efficacy impact and strengthen the drive. Self-efficacy is influence by encouragement and discouragement pertaining to an individual's performance or ability to perform [10]. Nursing students who had positive beliefs about their capabilities would have best academic performance in contras of those students who had less motivation and ability in academic activities [11, 12]. Limited research on achievement motivation and self-efficacy among Pakistani undergraduate nursing students is crucial for understanding their performance, professional growth, and clinical readiness, enabling educators and policymakers to design effective interventions. [13].

Therefore, the objective of this study was to investigate the level of achievement motivation and self-efficacy among under graduate nursing students."

METHODS

A Quantitative cross-sectional analysis was conducted in three institute Pakistan Institute of Medical Sciences (PIMS) School and College in Islamabad and the Rawalpindi AFPGMI College of Nursing. Third year and fourth-year undergraduate nursing students made up the target group. Written consent forms were signed before the data collection. The study's aims, pertinent data, and accepted medical literature and procedures served as a basis for choosing the target population and any subgroups that could exist. The study involved 500 students from the College of Nursing Rawalpindi and PIMS Islamabad as population. Convenience sampling method was used. This method was quick and cost-effective, but may lead to biased results as the sample may not represent the larger population. Yamane formula was used to calculate sample size [14]:

Yamane formula n = n / 1+n(e)2

Where n= sample size, n= total population=500, e= margin of error=0.05

N=500/1+500(0.05)2 =222

The calculated sample size was 222 of undergraduate nursing students. All enrolled undergraduate nursing students who have agreed to take part in the research were included and all those nursing students who were on leave on medical ground and any other purpose at that particular time were excluded. Participants may be disqualified if their data answers were insufficient. Two questionnaires had been employed in this research. One tool in order to scale self-efficacy that was created by Ralf Schwarzer (2008) and second used to assess achievement motivation, by McInerney (2006), Permission from the author was obtained before the data was collected [3, 6]. Five questions were related to demographic data 15 questions were about achievement motivation and 10 questions were to assess self-efficacy. 5-point Likert scale was used, Scoring Key: 1) NT= Never True 2) RT= Rarely True, 3) ST= Sometimes True, 4) OT= Often True, 5) AT= Always True. The study duration was, from March 2024 to July 2024. The ethical committee approval (Re: 464-AAA-ERC-AFPGMI) was obtained. Permission from the Dean of the institutes was gained. Thirty minutes' conversation was carried out with participants, clear description provided regarding questionnaire. The statistical package for the social sciences (SPSS), version 21.0 for data entry and analysis were used. Descriptive statistical test was employed. Frequency and percentage were calculated for demographic data. Level of achievement motivation and self-efficacy was assessed by mean and standard deviation.

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RESULTS

The study sample was 222 in which included 70.7% females and 29.3% males, with 90.1% aged 20-25. The age range was mostly 20-25, with a low frequency of 26-30 and above 40. The distribution of respondents by gender shown in the table 1. There were two genders indicated in this table. Female 157 out of the total respondents who make up 70.7% of all respondents. Male count 65 out of all respondents they make up 29.3% of the entire sample, also shown in figure 1.

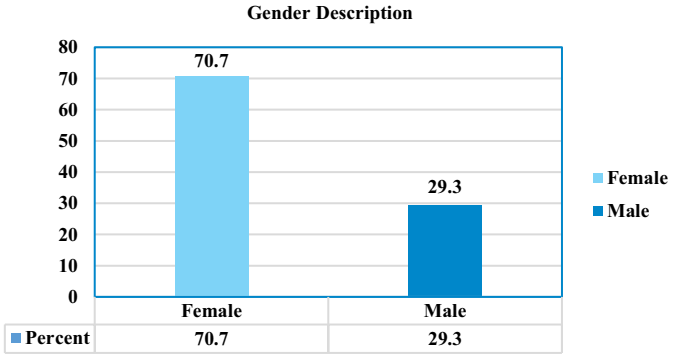

Figure 1: Gender Distribution of Study Participants

The percentages of participants' answers were listed in the table 2. The participants who see an improvement in their work (50.5% "Always True"), feel confidence in their skills (45.5% "Always True"), and obtain good marks (67.1% "Always True") exhibit the highest levels of motivation. Though at a slightly lower degree, motivations linked to external acknowledgment, like praise or awards, also exhibit high levels of agreement. Overall, the evidence points to the superiority of internal factors, such as problem-solving and personal development, over external ones, such as authority or recognition. The average score for achievement-oriented behavior was 4.12 overall, which suggests that individuals were typically highly motivated percentage responses of participant about achievement motivation (Table 1).

Table 1: Percentages of Participants about Achievement Motivation

S. No.	Items	NT	RT	ST	OT	AT	Mean ± SD
1	I am motivated when I work with others	5.4	5.9	13.1	41.0	34.7	3.93 ± 1.09
2	I am motivated when I work in group	3.2	5.4	18.5	31.1	41.9	4.03 ± 0.05
3	I am motivated when I am helping others	1.4	2.7	9.5	31.5	54.5	4.44 ± 1.52
4	I am motivated when I am showing concern for others	3.2	5.4	20.3	34.2	36.9	3.96 ± 1.03
5	I am motivated when I am notice by others	12.2	10.8	28.8	25.7	21.6	3.34 ± 1.27
6	I am motivated when I see my work improve	2.3	4.1	10.8	32.4	50.5	4.24 ± 0.95
7	I am motivated when I am good at something	1.8	3.6	7.2	23.9	63.1	4.44 ± 0.91
8	I am motivated when I solve a problem	1.4	2.7	9.5	31.5	55.0	4.36 ± 0.86
9	I am motivated when I am becoming better at my work	1.8	4.5	6.8	20.7	66.2	4.4 ± 0.93
10	I am motivated when I am confident that I can do my college work	1.8	5.0	9.5	38.3	45.5	4.20 ± 0.93
11	I am motivated when I get a reward	3.6	5.0	10.8	19.4	61.3	4.29 ± 1.07
12	I am motivated when I get good marks	1.8	5.0	9.0	16.7	67.1	4.50 ± 1.52
13	I am motivated when I am in-charge of a group	4.5	9.9	27.5	23.9	34.2	3.73 ± 1.16
14	I am motivated when I am praised	2.3	6.3	16.2	34.2	41.0	4.05 ± 1.01
15	I am motivated when I am doing better than others	3.2	8.6	21.2	22.5	44.1	3.96 ± 1.13
Achievement Oriented Behavior							M=4.12

*NT= Never True, RT= Rarely True, ST= Sometimes True, OT= Often True, AT= Always True

The participant's self-efficacy data reveals differing levels of confidence in various scenarios in table 2. Most people think they can learn difficult course content (55.4% ranked 4 or 5). There was a significant belief that obstacles may be overcome with effort; 77% strongly agree (mean: 4.10). With sufficient effort, participants believe they can influence both their academic and personal improvement (83.3% scored 4 or 5, mean: 4.24). Maintaining relationships and believing in innovative problem-solving techniques received excellent marks as well. The average self-efficacy score of 4.12 indicates that individuals generally have a high level of confidence (Table 2).

Table 2: Percentages of Participants about Self-Efficacy

S. No.	Items	NT	RT	ST	OT	AT	Mean ± SD
1	I firmly believe that I can master the necessary material for even the most challenging courses	4.5	12.2	27.5	27.9	27.5	3.61 ± 1.14
2	I can do even the hardest things when I put in a lot of effort subjects	0.9	5.9	15.8	36.5	40.5	4.10 ± 0.93
3	I believe I can still help myself well, even if I'm not feeling great on a particular day when I was preparing a test	2.7	11.3	30.2	33.8	21.6	3.60 ± 1.03
4	If I put in enough effort, I believe I can positively impact both my personal and academic growth	0.5	3.6	12.2	37.8	45.5	4.24 ± 0.84
5	I'm confident I can come up with creative solutions to tackle problems like budget cuts and administrative issues, all while continuing to grow	2.7	5.4	27.0	30.6	33.8	3.87 ± 1.03
6	I'm certain that I can keep a good connection with my parents. Even in the face of conflict	1.8	6.3	12.2	36.0	43.2	4.13 ± 0.97
7	I have no doubt that as time passes, my capacity to assist in meeting the requirements of my classmates will only grow	0.5	7.7	21.6	33.3	36.5	3.98 ± 0.96

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8	I'm aware that I can take part in innovative projects	3.2	6.3	25.2	35.6	29.3	3.81 ± 1.02
9	Even if interruptions occur during my learning process, I'm confident I can remain composed and carry on. to learn effectively	2.3	8.1	24.3	39.2	25.2	4.00 ± 3.58
10	I believe I can successfully do creative projects even if some people doubt or disagree with me	0.9	7.2	20.7	37.8	32.9	3.95 ± 0.95
Self-Efficacy of Respondent							4.12

*NT= Never True, RT= Rarely True, ST= Sometimes True, OT= Often True, AT= Always True

DISCUSSION

The study reveals that nursing students' motivation was influenced by job prospects, recognition, and rewards, but often undervalued in educational institutions. Low motivation can hinder academic performance, clinical competence, and long-term commitment to the profession. The results also indicate that a variety of internal and external factors might impact undergraduate nursing students' desire for achievement. This study confirmed that internal variables like self-improvement and personal interest were important motivators by showing a strong correlation between improved academic performance and the preparation of nursing students for licensing examinations and their intrinsic motivation [15]. Further supporting the premise that internal motivators have a more significant effect than external acknowledgment [16]. According to research in educational psychology, students who have a strong desire to learn and self-assurance in their abilities, qualities that were frequently fostered through problem-solving exercises accomplish better academically and exhibit higher levels of motivation. For instance, studies on math problem-posing show that children who complete these mentally taxing activities have higher levels of self-efficacy, which increases intrinsic drive [17]. Higher levels of self-efficacy were correlated with better resilience and academic success, according to [18]. Investigation of the ways in which undergraduate students' self-efficacy affects their capacity to manage academic pressure, uphold relationships, and solve issues creatively. Several studies that support this result that self-efficacy significantly aids individuals in overcoming challenges, as it helps manage stress and maintain motivation. High self-efficacy students exhibit greater resilience, enabling them to tackle academic challenges confidently [19]. Self-efficacy significantly influences academic performance and persistence, with students who believe in effort-based improvement achieving higher success rates and exhibiting achievement-oriented behavior. The same findings were also found by Abdolrezapour *et al.*, as mentioned above [20].

CONCLUSIONS

The study concluded that motivation is primarily driven by internal factors like self-efficacy and personal growth. Individuals who observe progress, have confidence in their abilities, and achieve good grades exhibit higher motivation and success. While external rewards play a role, their impact is less significant. A high self-efficacy score of 4.12 highlights perseverance, hard work, and creativity as key contributors to achievement, emphasizing the importance of intrinsic motivation and self-assurance in driving success.

Authors Contribution

Conceptualization: TK
Methodology: AN, SY, SN, RT, FAS
Formal analysis: FF
Writing, review and editing: TK, AN, SY, SN, RT, FAS, FF

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Li X, Pu R, Phakdeephirot N. The influence of achievement motivation on college students' employability: a chain mediation analysis of self-efficacy and academic performance. Frontiers in Psychology. 2022 Oct; 13: 972910. doi: 10.3389/fpsyg.2022.972910.

[2] Zhang ZJ, Zhang CL, Zhang XG, Liu XM, Zhang H, Wang J *et al.* Relationship between self-efficacy beliefs and achievement motivation in student nurses. Chinese Nursing Research. 2015 Jun; 2(2-3): 67-70. doi: 10.1016/j.cnre.2015.06.001.

[3] McInerney DM, Ali J. Multidimensional and hierarchical assessment of school motivation: Cross-cultural validation. Educational Psychology. 2006 Dec; 26(6): 717-34. doi: 10.1080/01443410500342559.

[4] Ryan RM and Deci EL. Self-determination theory and the facilitation of intrinsic motivation, social development, and well-being. American Psychologist. 2000 Jan; 55(1): 68. doi: 10.1037//0003-066X.55.1.68.

[5] Uko JO, Ihebom B. Content approach to motivation of employees in tertiary institutions. International Journal of Institutional Leadership, Policy and Management. 2020; 2(3): 567-83.

DOI: https://doi.org/10.54393/pjhs.v5i12.2447

[6] Schwarzer R, Hallum S. Perceived teacher self-efficacy as a predictor of job stress and burnout: Mediation analyses. Applied psychology. 2008 Jul; 57: 152-71. doi: 0.1111/j.1464-0597.2008.00359.x.

[7] Bandura A. Perceived self-efficacy in cognitive development and functioning. Educational psychologist. 1993 Mar; 28(2): 117-48. doi: 10.1207/s15326985ep2802_3.

[8] Conner M and Norman P. Health behaviour: Current issues and challenges. Psychology & health. 2017 Aug; 32(8): 895-906. doi: 10.1080/08870446.2017.1336240.

[9] Xin DA, Huang Y, Jian-Hua RE, Ya-Lin TI, Ya-Lin HE. Professional nursing practice environment and work engagement: the mediating roles of self-efficacy and achievement motivation. Journal of Nursing Research. 2023 Aug; 31(4): e285. doi: 10.1097/jnr.0000000000000563.

[10] Redmond ML and Lewis RK. Are there gender differences in perceived sexual self-efficacy among African-American adolescents?. Journal of Health Disparities Research and Practice. 2014; 7(5): 1.

[11] Reid C, Jones L, Hurst C, Anderson D. Examining relationships between socio-demographics and self-efficacy among registered nurses in Australia. Collegian. 2018 Feb; 25(1): 57-63. doi: 10.1016/j.colegn.2017.03.007.

[12] Damari H. Effectiveness of resilience on achievement motivation and self-efficacy in students of nursing. Revista Turismo Estudos e Práticas-RTEP/UERN. 2020 Jun; 1(3): 1-8.

[13] Majzub RM and Yusuf M. Investigating relationship between self-efficacy, achievement motivation, and learning strategies of UKM undergraduate students. Advanced Educational Technologies. 2010 Dec; 1: 187-90. doi: 10.1016/j.sbspro.2011.04.156.

[14] Quora. What are the advantages of the Yamane formula? [Last cited 29th Dec 2024]. Available at: https://www.quora.com/what-are-the-advantages-of-the-yamane-formula.

[15] El-Sayed MM, Mousa MA, Abd-Elhamid EA. Academic Motivation, Academic Voica C, Singer FM, Stan E. How are motivation and self-efficacy interacting in problem-solving and problem-posing?. Educational Studies in Mathematics. 2020 Nov; 105(3): 487-517. doi: 10.1007/s10649-020-10005-0.

[16] Yim KH, Lee I. The effect of achievement motivation on learning agility of nursing students: The mediating effect of self-leadership. The Journal of Korean academic society of nursing education. 2021 Feb; 27(1): 80-90. doi: 10.5977/jkasne.2021.27.1.80.

[17] Al-Osaimi DN, Fawaz M. Nursing students' perceptions on motivation strategies to enhance academic achievement through blended learning: a qualitative study. Heliyon. 2022 Jul; 8(7). doi: 10.1016/j.heliyon.2022.e09818.

[18] Cassidy S. Resilience building in students: The role of academic self-efficacy. Frontiers in Psychology. 2015 Nov; 6: 1781. doi: 10.3389/fpsyg.2015.01781.

[19] Bulfone G, Badolamenti S, Biagioli V, Maurici M, Macale L, Sili A et al. Nursing students' academic self-efficacy: A longitudinal analysis of academic self-efficacy changes and predictive variables over time. Journal of advanced nursing. 2021 May; 77(5): 2353-62. doi: 10.1111/jan.14771.

[20] Abdolrezapour P, Jahanbakhsh Ganjeh S, Ghanbari N. Self-efficacy and resilience as predictors of students' academic motivation in online education. PLOS One. 2023 May; 18(5): e0285984. doi: 10.1371/journal.pone.0285984.

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Original Article

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E-Portfolios in Medical Education: A Reflective Exploration of Learning Experiences from Faculty Perspective

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ABSTRACT

E-portfolios are electronic collections of evidence that the students gather over some time during their educational journey. The learner has the flexibility of incorporating not only written notes but also videos, audio and pictures in an e-portfolio. **Objectives:** To explore the perception of the mentors regarding the benefits and challenges of implementing an e-portfolio. **Methods:** It was a qualitative cross-sectional study. The mentors involved in mentoring the student's e-portfolio development process were invited for semi-structured interviews. Thematic analysis was performed to analyze the data and provide an understanding of the perception of the mentors regarding e-portfolios. **Results:** The -e-portfolio not only enhances digital literacy among the students but also promotes reflective practices through which they reflect on their learning experience and self-assess their areas of improvement while at the same time promoting lifelong learning. Implementation of e-portfolios is also associated with challenges which include technological hurdles, lack of digital infrastructure, internet connectivity, effective time management and content selection. **Conclusions:** It was concluded that despite the challenges, the ability to enhance skills through e-portfolios remains evident. The provision of digital structure and training can help the institutes achieve the full benefits of an e-portfolio.

INTRODUCTION

Portfolios are systematic collections of varied data sources that showcase evidence of activities and achievements throughout an educational experience. They enhance learning, encourage critical thinking, and support a lifelong commitment to learning. By allowing individuals to document their accomplishments, portfolios act as an invaluable assessment tool, providing insights into performance over time [1]. Besides their role in assessment, portfolios also facilitate self-reflection and self-evaluation, affirming ongoing professional development. These attributes render portfolios vital instruments in both academic and professional growth [2].

Paper-based portfolios first became important instruments in the mid-1980s. However, technological advancements resulted in the creation of e-portfolios, which overcome traditional forms' limitations, such as accessibility, bulkiness, and management [3]. E-portfolios provide a digital platform for students and professionals to collect, organize, and present material relevant to their long-term development. These digital resources offer a structured and flexible approach to documenting learning events, making them highly adaptable to a variety of disciplines and educational settings [4]. E-portfolios offer various advantages over traditional portfolios. One

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significant advantage is the ease of administration and reduced danger of data loss. Unlike conventional portfolios, which are susceptible to damage or loss, e-portfolios allow users to safely save their work in digital formats [5]. Furthermore, e-portfolios enable remote engagement between instructors and students, allowing educators to provide comments, track progress, and direct learning from a distance. This feature is consistent with the increasing reliance on technology in education, establishing e-portfolios as a practical answer for modern learning contexts [6]. E-portfolios are vital in competency-based medical education because they allow students to demonstrate both theoretical knowledge and practical skills over time. They encourage reflective activities, which are essential for developing critical thinking skills, ethical reasoning, and lifelong learning habits [7]. For example, medical students can use e-portfolios to track their progress in acquiring essential qualities like clinical communication and decision-making while receiving continuous feedback from their supervisors [8]. Furthermore, e-portfolios are very adaptable to a variety of educational methodologies, such as problem-based and case-study learning. They can record students' interactions with real-world settings, problem-solving tactics, and reflections on significant learnings [6]. This versatility makes e-portfolios useful not only for personal development but also for institutional assessment and accreditation, providing insights into program efficacy and student outcomes [9]. E-portfolios can contribute significantly to lifetime learning by encouraging continuous documentation and reflection. For professionals, they serve as a repository for credentials, research, and clinical accomplishments, facilitating career growth and accreditation processes [4]. They also improve reflective behaviours, which are well-suited to the demands of medical and allied students and professionals looking for tools for competency-based learning and career development [10].

This study aims to investigate the mentors' opinions on the benefits and obstacles of deploying e-portfolios.

METHODS

This was a cross-sectional qualitative study that explored the perspectives of mentors involved in mentoring the development of e-portfolios in an undergraduate medical program. The study was conducted in Fatima Memorial Medical College from 1st February to 1st March 2024. An integrated curriculum is being implemented in the institute that spans over five years. E-portfolios were recently introduced in the 1st year of MBBS. Competencies for each year to be recorded in the portfolio were identified. Before formal implementation, students were trained to create e-portfolios using Google Sites. The entire class was divided into six groups, and each group was allocated a mentor, who supervised the e-portfolio development of their respective mentees' group. Only the mentors of the 1st year MBBS integrated curriculum were included in the study; the mentors of the traditional MBBS curriculum were not included in the study. The study was submitted to the Institutional Review Board for approval. Mentors were encouraged to participate voluntarily after gaining IRB approval (FMH-13/12/2023-IRB-1350). All participants provided written informed consent before the interviews began. Data were gathered using semi-structured interviews. Two main frameworks helped shape the guide's development. First, Kallio et al., suggested a framework that focuses on methodical activities such as setting objectives, examining relevant literature, and piloting questions to refine content. Second, the guide benefited from Jordan et al., and has practical advice, such as framing open-ended questions to promote meaningful debates in medical education. The handbook completed a pilot test with a group of medical educationists, and adjustments were made based on their comments [11, 12]. Purposive sampling was used to choose mentors, focusing on those who were directly involved in e-portfolio-building mentoring within the integrated curriculum. Six mentors in all were interviewed. The duration of each interview was 45 to 50 minutes. After the interviews were recorded, they were transcribed. The transcribed data were cross-checked with the field notes for consistency, and member checking was done to confirm the accuracy of the transcriptions. To determine the advantages and difficulties of e-portfolio implementation, a thematic analysis was carried out. Throughout the study, ethical standards were upheld, including participant confidentiality and anonymity. Transcripts were coded, and all data were safely stored. To guarantee this, participants were made aware of their freedom to leave the study at any time without facing any repercussions.

RESULTS

Four major themes emerged from the thematic analysis of faculty opinions on the use of e-portfolios in student learning, each supported by more specific participant insights and minor sub-themes. These findings paint a clear picture of the advantages, difficulties, and requirements that educational institutions must meet for e-portfolios to be successful. Teachers reported that by integrating several aspects of their student's academic and personal development, e-portfolios allowed them to see the larger picture of how students learn (Figure 1).

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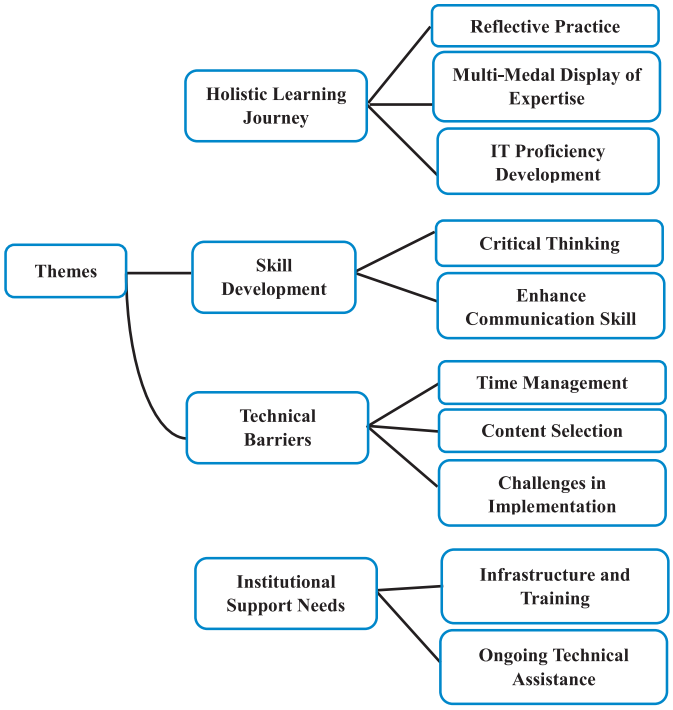

Figure 1: Themes and Subthemes

Teachers reported that e-portfolios helped students become more self-aware of their academic strengths and areas for improvement by encouraging them to participate in reflective practices. As one faculty member mentioned reflection on their assignments helped students identify where they excelled and where improvement was needed. Another faculty member observed that students gained a clearer understanding of their academic journey and long-term goals. Faculty saw e-portfolios as a useful addition to exams because they gave students a chance to demonstrate their abilities and achievements outside of the confines of traditional assessments. In support of this, one faculty member stated that E-portfolios allowed students to highlight achievements in areas like design and creativity that exams often overlook. Another participant remarked this platform revealed talents that may not have surfaced in standard assessments. The process of creating and maintaining e-portfolios enhanced students' digital literacy, a benefit faculty recognized as essential in today's technological landscape. As one faculty member explained Students' engagement with digital tools through e-portfolios improved their IT skills, which is critical for their future careers. Another faculty member added many students gained confidence in navigating online platforms and tools, a skill that will serve them well beyond the classroom. Faculty found that the process of developing e-portfolios improved students' critical thinking and communication skills significantly. Structured reflection and curation of e-portfolios required students to think critically about their work, which was constantly highlighted by professors. One faculty member noted the reflective nature of e-portfolios encouraged students to delve deeper into the significance of their work. Another pointed out that students were learning to connect their academic efforts with broader learning objectives. Faculty found that creating e-portfolios increased students' capacity to explain their ideas and show their work in an organized manner. One faculty member shared that the e-portfolio process significantly enhanced students' ability to communicate their ideas effectively. Another commented that this platform helped students develop structured and clear ways of expressing their academic and personal achievements. While faculty recognized the benefits of e-portfolios, they also identified significant problems for both students and instructors. The challenges were divided into three sub-themes. Faculty frequently encountered technological concerns, such as system navigation problems and unstable internet connectivity, which hampered the e-portfolio process. One faculty member expressed that Both students and faculty faced frustrations with system usability and internet connectivity. Another reported that there were instances where students lost progress due to system crashes or poor connectivity. Balancing the time required for e-portfolio construction with other academic duties presented substantial hurdles for students and instructors. One faculty member remarked that students struggled to manage their coursework alongside creating e-portfolios. Another added that Providing detailed and timely feedback on e-portfolios was more time-consuming than anticipated. Faculty reported that students often needed extensive guidance in deciding which elements to include in their e-portfolios, adding to the workload for educators. As one faculty member explained students frequently sought help to determine what content was relevant and meaningful for their portfolios. Another noted that Guiding students through content curation required considerable time and effort from faculty. Faculty stressed the importance of institutional support in overcoming the hurdles connected with e-portfolio deployment. Reliable technological infrastructure and comprehensive training for both students and instructors were regarded as necessary for successful e-portfolio utilization. One faculty member stressed that seamless internet connectivity is crucial; its absence created significant hurdles in the e-portfolio process. Another faculty member noted that Training sessions on efficient use of the platform would have alleviated many of the initial challenges. Faculty underscored the necessity of continuous technical support to address issues promptly, minimizing disruptions to the e-portfolio process. As one faculty member pointed out technical assistance should be readily available to ensure smooth progress for students and faculty. Another faculty member suggested that Having immediate troubleshooting support would save time and

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reduce frustration. In summary, the teachers saw e-portfolios as an effective approach to promoting well-rounded learning and skill development activities in students. However, getting them up and running was not easy. Big challenges were technical difficulties, time management issues, and the need to lead students through the process of developing valuable content. Faculty stressed the importance of strong institutional support, such as solid infrastructure, rigorous training, and continuing technical assistance, in making e-portfolios successful in education.

DISCUSSION

The findings of this comprehensive study are strikingly consistent with the vast body of existing literature, which emphasizes the importance of e-portfolios as innovative tools that significantly improve students' learning experiences by expertly integrating reflective practices while simultaneously showcasing a diverse array of skills that students possess. Faculty observations about the critical role that reflection plays in developing self-awareness in students are strikingly similar to the findings that emphasize how e-portfolios facilitate productive learning through the mechanism of self-assessment and organized reflection [13]. This intricate reflective process allows students to gain a profoundly deeper understanding of their individual strengths, weaknesses, and long-term goals, which is entirely consistent with observations about the enormous value of critical self-reflection in higher education [14]. E-portfolios have the astonishing ability to empower students by allowing them to highlight their successes in creative domains such as creativity and design, which goes far beyond the restrictions of traditional assessment methods that are frequently used. This noteworthy discovery is consistent with research that has identified e-portfolios as dynamic platforms for educational innovation, supporting students in demonstrating a wide range of talents that traditional testing techniques may inevitably fail to effectively capture [15]. Similarly, the development of digital literacy a benefit that faculty members have notably recognized is inextricably linked to ongoing discussions about how active engagement with e-portfolios significantly improves the technical skills that are critical for student's future career prospects [16]. The observed improvements in students' critical thinking and communication skills reflect a multitude of insights on how e-portfolios, particularly those reinforced with advanced analytics, stimulate much deeper engagement with specific learning objectives [17]. While these various benefits are certainly substantial, the limitations found in this study ranging from technological difficulties and time restrictions to the critical need for extensive guidance are not uncommon in the deployment of e-portfolios. Similar issues have been documented in various evaluations of postgraduate medical training, highlighting the importance of the usability of the systems used and the reliability of internet connectivity in determining the overall success of these educational initiatives [18]. Technical challenges, such as unexpected system crashes and limited connectivity, were specifically noted in the study's findings, implying that a smooth technological infrastructure is vitally necessary for the effective operation of e-portfolio operations [19]. Furthermore, time management appeared as a major worry for both students and staff members. Faculty members reported that they frequently struggled to strike a balance between the demanding requirements of coursework and the intricate process of e-portfolio development, a concern echoed in extensive research emphasizing the time-intensive nature of e-portfolios in assessing student achievement [20]. Furthermore, the need to provide detailed and constructive feedback on e-portfolios increased the overall workload, which is consistent with the findings that highlight the resource-intensive nature of guiding students in the curation of meaningful and relevant portfolio content [21]. Institutional support was widely acknowledged as a critical factor in overcoming the identified challenges, with faculty members advocating for the establishment of dependable technological infrastructures, comprehensive training programs, and ongoing technical assistance. These sensible recommendations are consistent with the findings, which emphasize the critical importance of ensuring that e-portfolio deployment is effectively linked with institutional capabilities to ensure a smooth adoption process [22]. Similarly, the necessity for timely troubleshooting support to ease irritation and maintain continuous progress is consistent with research highlighting the importance of proactive technical support in efficiently minimizing possible disruptions [15].

CONCLUSIONS

It was concluded that regardless of the limitations, the benefits of using an e-portfolio to improve students' skill sets are clear. It is critical that institutes address these problems and provide ongoing support to staff and students in order to facilitate the successful adoption of e-portfolios and improve the overall student learning experience.

Authors Contribution

Conceptualization: HT
Methodology: HT, AZ, HS, SNM, MMHN, TA
Formal analysis: AZ
Writing review and editing: HS, MMHN

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Siddiqui ZS, Fisher MB, Slade C, Downer T, Kirby MM, McAllister L *et al.* Twelve Tips for Introducing E-Portfolios in Health Professions Education. Medical Teacher. 2023 Feb; 45(2): 139-44. doi: 10.1080/0142159X.2022.2053085.

[2] Van der Schaaf MF, Slof B. Feedback in the Workplace: The Potential of E-Portfolios with Learning Analytics. Journal of Higher Education. 2023 Apr; 41(1). doi: 10.59532/tvho.v41i1.13951.

[3] Rachbauer T and Rachbauer M. Das E-The E-Portfolio as a Competence-Oriented Instrument for Individual Examination Assessment. Schule Verantworten. 2023 Sep; 3(3): 42–47. doi: 10.53349/schuleverantworten.2023.i2.a291.

[4] Nasser Dahmash J. Female English Majors' Perceptions of E-portfolios at Some Saudi Universities. Arab World English Journal (April 2023) Theses ID. 2023 Apr; 293. doi: 10.2139/ssrn.4431195.

[5] Yadav S. Designing Effective E-Portfolios for Authentic Assessment: Encouraging Reflection and Promoting Student Ownership. In Cases on Authentic Assessment in Higher Education. 2024: 235-258. doi: 10.4018/979-8-3693-1001-4.ch011.

[6] Walland E and Shaw S. E-portfolios in Teaching, Learning and Assessment: Tensions in Theory and Praxis. Technology, Pedagogy and Education. 2022 May; 31(3): 363-79. doi: 10.1080/1475939X.2022.2074087.

[7] Bramley AL, Thomas CJ, Mc Kenna L, Itsiopoulos C. E-portfolios and Entrustable Professional Activities to Support Competency-Based Education in Dietetics. Nursing and Health Sciences. 2021 Mar; 23(1): 148-56. doi: 10.1111/nhs.12774.

[8] Younghusband CH. E-Portfolios and Practicum in Teacher Education. The Open/Technology in Education, Society, and Scholarship Association Conference. 2021 Dec; 1(1): 1-5. doi: 10.18357/otessac.2021.1.1.59.

[9] Rathnayake A. The Impact of Post-E-Learning On Psychological Conditions in University Students. International Journal of Scientific and Research Publications. 2021; 11(5): 445-9. doi: 10.29322/IJSRP.11.05.2021.p11355.

[10] Li S. Key Stakeholders' Perceptions of Using E-Portfolio in Preschool Teacher Education. Advances in Education, Humanities and Social Science Research. 2022 May; 1(1): 207-. doi: 10.56028/aehssr.1.1.207.

[11] Kallio H, Pietilä AM, Johnson M, Kangasniemi M. Systematic Methodological Review: Developing A Framework for a Qualitative Semi-Structured Interview Guide. Journal of Advanced Nursing. 2016 Dec; 72(12): 2954-65. doi: 10.1111/jan.13031.

[12] Jordan J, Clarke SO, Coates WC. A Practical Guide for Conducting Qualitative Research in Medical Education: Part 1—How to Interview. Academic Emergency Medicine Education and Training. 2021 Jul; 5(3). doi: 10.1002/aet2.10646.

[13] Yang M, Tai M, Lim CP. The Role of E-Portfolios in Supporting Productive Learning. British Journal of Educational Technology. 2016 Nov; 47(6): 1276-86. doi: 10.1111/bjet.12316.

[14] Lu H. Electronic Portfolios in Higher Education: A Review of the Literature. European Journal of Education and Pedagogy. 2021 Jul; 2(3): 96-101. doi: 10.24018/ejedu.2021.2.3.119.

[15] Lozada XE, Sánchez SE, Galimberti JV. Pedagogical Innovation Through Use of Electronic Portfolios in Higher Education. ESPOCH Congresses: The Ecuadorian Journal of Science, Technology, Engineering, Arts, and Mathematics. 2021 Aug: 1053-60. doi: 10.18502/espoch.v1i2.9531.

[16] Arifin MH. Development of Electronic Portfolios and Self-Assessment Based on Order Thinking Skills in Pancasila and Citizenship Learning at Students of Al-Islam Bandung Polytechnic. In Journal of Physics: Conference Series. 2021 Feb; 1764(1): 012144. doi: 10.1088/1742-6596/1764/1/012144.

[17] Van der Schaaf M, Donkers J, Slof B, Moonen-van Loon J, van Tartwijk J *et al.* Improving Workplace-Based Assessment and Feedback by an E-Portfolio Enhanced with Learning Analytics. Educational Technology Research and Development. 2017 Apr; 65: 359-80. doi: 10.1007/s11423-016-9496-8.

[18] De Swardt M, Jenkins LS, Von Pressentin KB, Mash R. Implementing and Evaluating an E-Portfolio for Postgraduate Family Medicine Training in the Western Cape, South Africa. BioMed Central Medical Education. 2019 Dec; 19: 1-3. doi: 10.1186/s12909-019-1692-x.

[19] Nkonki V, Tsipa-Booi N, Mqukuse B. Student Perspectives on WhatsApp Support for Developing School Experience e-Portfolios on Google Sites. In 22nd European Conference on e-Learning 2023. 2023 Oct. doi: 10.34190/ecel.22.1.1866.

[20] Sata M and Karakaya I. Investigation of the Use of Electronic Portfolios in the Determination of Student Achievement in Higher Education Using the Many-Facet Rasch Measurement Model. Educational Policy Analysis and Strategic Research. 2020 Mar; 15(1): 7-

DOI: https://doi.org/10.54393/pjhs.v5i12.2574

21. doi: 10.29329/epasr.2020.236.1.

[21] Shami AA. The Effectiveness of Using Electronic Portfolios as a Learning Tool in Enhancing the Writing Performance of Saudi Female Intermediate Students at Taif University: Teachers' Perspectives Abrar Adel Mohammed Shami. English Journal (ID Number: 306). 2024 Jun; 1: 40. doi: 10.24093/awej/th.306.

[22] Fabunmi Olaiya K and Olaiya OO. Developing Electronic Portfolios to Align with Diverse National Standards to Showcase Students' and Teachers' Performance: A Design Approach. Innovare Journal of Education. 2023 Nov. doi: 10.22159/ijoe.2023v11i6.49207.

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Original Article

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Comparing Dyslipidemia Patterns in Newly Diagnosed and Long-Term Type 2 Diabetics in a Tertiary Care Hospital at Mirpur Khas, Sindh

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ABSTRACT

Dyslipidemia is a common metabolic condition linked with type 2 diabetes mellitus and is a substantial risk factor for cardiovascular disease. The pathogenicity and pattern of dyslipidemia may vary with the duration of diabetes, requiring investigation of these changes to improve treatment approaches. **Objectives:** To compare the prevalence and patterns of dyslipidemia in newly diagnosed compared with long-term type 2 diabetes mellitus patients in a tertiary care hospital in Pakistan. **Methods:** A comparative cross-sectional study was conducted with 300 type 2 diabetes mellitus patients, divided into two groups: 150 newly diagnosed and 150 long-term diabetics. HbA1c and Lipid profiles (total cholesterol, low-density lipoprotein, high-density lipoprotein, and triglycerides) were assessed. Dyslipidemia was defined per American Diabetes Association guidelines. Statistical analysis was performed using SPSS version 25.0, with a p-value of <0.05 considered significant. **Results:** The results show that the patients with long-term type 2 diabetes mellitus are associated with significantly increased (92%, p<0.05) levels of lipid profile parameters as compared with the newly diagnosed type 2 diabetes mellitus patients (78%). Moreover, the mean HbA1c levels in blood are positively associated with the severity of dyslipidemia. **Conclusion:** It was concluded that dyslipidemia progressively increases with the advancement of type 2 diabetes mellitus.

INTRODUCTION

Hyperglycaemia, a metabolic disease caused by deficiencies in either insulin release, its action, or both, is the hallmark of type 2 diabetes mellitus (DM) [1]. Diabetes's high morbidity and mortality rate, up to 80% of deaths from cardiovascular disease (CVD), are a result of the disease's long-term macrovascular consequences [2]. Patients with diabetes frequently experience both aberrant lipoprotein metabolism and hormone therapy (HT). Among the main risk factors for CVD in Type 2 Diabetes Mellitus (T2DM) is dyslipidaemia. Hypertriglyceridemia decreased high-density lipoprotein (HDL) cholesterol, and an increase in the proportion of tiny, dense low-density lipoprotein (LDL) particles are the most prevalent patterns of dyslipidaemia. Although the exact etiology of diabetic dyslipidaemia is unknown, a substantial amount of data points to insulin resistance as a key factor in the illness's progression. Increased free fatty acid flow due to insulin resistance is thought to be the primary source of the lipid alterations linked to diabetes mellitus [3]. In light of this, the goal of the physician should be to lower the patient's risk of CVD by

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managing hyperglycaemia, hyperglycaemia, and dyslipidaemia through lifestyle changes and/or medication. Blood pressure and lipid objectives are lowered for diabetes patients, a high-risk population because macrovascular disease is the primary cause of death in this population [4]. Extended periods of hyperglycaemia in type 2 diabetes (T2DM) alter the glycosylation of proteins, particularly the connective tissue proteins (collagen crosslinking) and matrix proteins found in artery walls [5]. Atherosclerosis is the main outcome of this harmful process, which is the growth of endothelial function. The metabolism of proteins, fats, and carbohydrates is altered due to a lack of insulin activity [6]. In type 2 diabetes, hypertriglyceridemia, a drop in serum HDL cholesterol, and sporadic elevated serum LDL cholesterol are all correlated with relative insulin shortage, insulin resistance, and obesity. Dyslipidaemia, which elevated LDL-C characterizes, decreased HDL-C, or elevated triglycerides TG levels, is linked to type 2 diabetes [7]. An individual factor for coronary artery disease (CAD) is raised triglyceride (TG) levels. Due to its highest risk of developing macrovascular problems, which impact 10-73% of diabetic patients, dyslipidaemia in T2DM is a major concern [8, 9]. Additionally, diabetes mellitus is ranked in the highest risk group due to expert reports from the Adult Treatment Panel III (ATP III) panel on detecting, evaluating, and treating high blood cholesterol in adults, which compares it to CAD [10]. Duration of diabetes is a significant factor in the progression of dyslipidaemia. As the disease advances, dyslipidaemia patterns also get worse, resulting in an increased risk of cardiovascular complications. Research has shown that long-term T2DM patients are more associated with severe lipid abnormalities compared to newly diagnosed patients. This chronological aspect of dyslipidaemia progression highlights the need for continuous lipid monitoring and management in the case of diabetes.

This study aims to provide a valuable understanding of the progression of dyslipidemia in T2DM patients, thereby updating clinical practice and more treatment strategies to improve patient outcomes.

METHODS

The current cross-sectional analytical study was conducted at Bhitai Dental and Medical College, Mirpur Khas, Sindh, Pakistan, for two years, from February 2022 to January 2024.The sample size was calculated by the following formula: $n=Z^2 x(p^1 x q^1+p^2 xq^2) / d^2$.In this equation: Z is the chosen level of confidence that is considered as 1.96 for 90% confidence, p^1 and p^2 are the expected prevalence of dyslipidemia in newly diagnosed and long-term diabetics, respectively while, q1 indicates 1-p1 and q2 as 1-p2. d is the required margin of error. Based on findings from previous studies, the prevalence of dyslipidemia in newly diagnosed diabetics (p1) was estimated to be 89% [11], and in long-term diabetics (p2) it was 92% [12], d^2 as 5.57=6%. Using these values, a sample size of 300 (150 patients per group) patients was calculated as sufficient to detect a statistically significant difference in dyslipidemia patterns. The patients diagnosed with T2DM within the last 6 months with no previous history of lipid-lowering treatment were included as newly diagnosed diabetic patients while the long-term diabetic group included the patients with at least five years of T2DM. The age for both groups was 30 to 70 years. The patients with a history of type 1 and gestational diabetes, chronic renal disease, and liver disorders, were excluded from both study groups. The patients with a history of bariatric surgery, medication (lipid-lowering, antihypertensive or hormone replacement therapy), chronic alcohol addiction and cigarette smoking were also excluded from the research. All the respondents were informed about the objective, methods, possible risks, and usefulness of the research. Informed consent from the participants was taken in written form. They were allowed to quit the study at any point without any pressure. Data were collected through a non-probability consecutive sampling technique, from the selected participants by relevant medical history, clinical examination, and laboratory reports. A blood sample was taken from all participants in fasting condition to measure lipid profile biomarkers, such as Total cholesterol (TC), LDL, HDL, and TG. Glycemic control was evaluated by measuring fasting blood glucose and HbA1c levels. The lipid profiles of newly diagnosed and long-term diabetic patients were then compared to find significant differences in dyslipidemia patterns. For male, the reference cut-off values for lipid profiles were as follows: TC levels below 200 mg/dL, LDL below 100 mg/dL, HDL above 40 mg/dL, and TG below 150 mg/dL. For female TC levels below 200 mg/dL, LDL below 100 mg/dL, HDL above 50 mg/dL, and TG below 150 mg/dL were considered within the normal range. Statistical analysis of the obtained data was carried out using SPSS version 25.0. Descriptive statistics were used to represent the values related to the demographic features and clinical presentations. Continuous study variables were described as mean ± standard deviation (SD), and the categorical variables were shown in the form of frequencies and percentages. The data normality was tested using the Shapiro-Wilk test, and the data were found to be normally distributed. An Independent t-test was used for the comparison of the means of lipid profiles between newly diagnosed and long-term diabetic patients and the Pearson correlation test was applied to find a correlation between glycaemic control and various lipid parameters. p-values less than 0.05 were regarded as statistically

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significant. Ethical approval for the research was obtained from the relevant institutional review board before the start of the study(BDMC/R&D/ERC/2022-01).

RESULTS

The demographic characters and clinical findings of all the participants are displayed. The mean age of the newly diagnosed group was 48.6 ± 10.3 years, while the long-term diabetic group showed a mean age of 55.2 ± 8.7 years. The gender distribution was comparable between the two groups, with a slightly higher proportion of male. Poor glycemic control, as indicated by higher HbA1c levels, was more pronounced in the long-term diabetic group (mean HbA1c: 8.9% ± 1.6%) compared to the newly diagnosed group(mean HbA1c: 7.6% ± 1.3%, p≤0.05). HbA1c levels were seen positively (p≤0.05) correlated with the severity of dyslipidemia, particularly with elevated LDL cholesterol and triglycerides, in both groups. Body mass index (BMI) was significantly higher in the long-term diabetic group (mean BMI: 29.3 ± 4.8 kg/m^2) compared to the newly diagnosed group (mean BMI: 27.8 ± 5.2 kg/m^2, p<0.05). Higher BMI was positively correlated with elevated LDL cholesterol and triglycerides (p<0.05) in both groups, indicating that increased body weight exacerbates lipid abnormalities, particularly in long-term diabetics. Gender differences in lipid abnormalities were also analyzed, with male showing a higher prevalence of elevated LDL cholesterol and triglycerides, while female had a higher prevalence of low HDL cholesterol. This gender-specific dyslipidemia pattern was consistent across both groups (Table 1).

Table 1: Clinical, Demographic, and Baseline Investigations of the Study Population

Characteristic	Newly Diagnosed Diabetics (n=150)	Long-Term Diabetics (n=150)
Mean Age (Years)	48.6 ± 10.3	55.2 ± 8.7
Male Gender n (%)	80 (53.3)	84 (56)
Mean HbA1c (%)	7.6 ± 1.3	8.9 ± 1.6
Mean BMI (kg/m^2)	27.8 ± 5.2	29.3 ± 4.8
Fasting Blood Glucose (mg/dL)	152.4 ± 28.7	178.6 ± 34.2
Postprandial Blood Glucose (mg/dL)	192.3 ± 45.1	212.5 ± 48.7
Total Cholesterol (mg/dL)	192.3 ± 45.1	212.5 ± 48.7
LDL Cholesterol (mg/dL)	112.3 ± 27.4	130.8 ± 31.2
HDL Cholesterol (mg/dL)	41.6 ± 8.9	38.4 ± 9.5
Triglycerides (mg/dL)	170.5 ± 38.2	192.7 ± 45.6

The study participants' lipid profiles were examined to compare the two groups' dyslipidemia prevalence and trends. The American Diabetes Association (ADA) defines dyslipidemia as having high LDL cholesterol (≥100 mg/dL), low HDL cholesterol (<40 mg/dL in men and <50 mg/dL in women), elevated total cholesterol (≥200 mg/dL), and elevated triglycerides (≥150 mg/dL). The cut-off values for male and female are provided in brackets where applicable. Table 3 shows the prevalence of each dyslipidaemia type. 78% of patients in the newly diagnosed diabetic group had dyslipidemia in some form, with hypertriglyceridemia (42%), low HDL cholesterol (45%), and increased LDL cholesterol (55%), being the most dominant abnormalities. In contrast, the long-term diabetic group had a much greater prevalence of dyslipidemia (92% of patients affected). Of the patients in this group, 72% had increased LDL cholesterol, 58% had low HDL cholesterol, and 66% had hypertriglyceridemia. Females in the long-term diabetic group showed significantly lower HDL cholesterol levels (36.4 ± 8.9 mg/dL) compared to males in the same group (39.7 ± 9.2 mg/dL, p<0.05). The significantly different values among both study groups were seen, in the overall incidence of dyslipidemia(p≤0.05)(Table 2).

Table 2: Comparison of Dyslipidemia Patterns Between Newly Diagnosed and Long-Term Type 2 Diabetics

Dyslipidemia Parameter	Newly Diagnosed Diabetics (n=150)	Long-Term Diabetics (n=150)	p-value
Any Dyslipidemia, n (%)	117 (78%)	138 (92%)	<0.001*
Raised Total Cholesterol (>200 mg/dL), n (%)	42 (28%)	66 (44%)	0.002*
Raised LDL Cholesterol (>100 mg/dL), n (%)	83 (55%)	108 (72%)	0.001*
Low HDL Cholesterol (<40 mg/dL for men, <50 mg/dL for women), n (%)	45 (30%)	87 (58%)	<0.001*
Elevated Triglycerides (>150 mg/dL), n (%)	63 (42%)	99 (66%)	<0.001*
Mean LDL Cholesterol (mg/dL)	112.3 ± 27.4	130.8 ± 31.2	<0.001**
Mean HDL Cholesterol (mg/dL)	39.8 ± 9.0	37.8 ± 9.4	0.045**
Mean Triglycerides (mg/dL)	170.5 ± 38.2	192.7 ± 45.6	<0.001**

*Chi-square test was applied for categorical variables. **Independent sample t-test was applied for continuous variables. p<0.05 indicates statistically significant differences.

The group with diabetes for a longer duration had considerably greater mean levels of LDL cholesterol (138.2 ± 32.6 mg/dL vs. 124.4 ± 30.2 mg/dL, p<0.05), triglycerides (189.7 ± 58.3 mg/dL vs. 159.6 ± 49.2 mg/dL, p<0.05), total cholesterol (212.3 ± 40.7 mg/dL vs. 196.5 ± 35.4 mg/dL, p<0.05), and LDL cholesterol (188.2 ± 32.6 mg/dL vs. 159.6 ± 49.2 mg/dL, p<0.05) in comparison to the newly diagnosed group. On the other hand, the group with a history of diabetes had lower HDL cholesterol levels (38.1 ± 9.6 mg/dL) than the group with a recent diagnosis (44.3 ± 10.2 mg/dL, p≤0.05)(Table 3).

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Table 3: Lipid Profile Parameters and Cutoff Values for Male and Female Patients

Lipid Parameter (mg/dL)	Newly Diagnosed		p-value	Long-Term		p-value*
	Male (n=A)	Female (n=B)		Male (n=C)	Female (n=D)	
Total Cholesterol (Male/Female: >200)	196.5 ± 35.4	198.0 ± 32.5	0.021*	212.3 ± 40.7	215.5 ± 38.2	0.031*
LDL Cholesterol (cut-off >100)	124.4 ± 30.2	126.0 ± 28.3	0.001*	138.2 ± 32.6	140.0 ± 30.5	0.034*
HDL Cholesterol (cut-off <40 for men,<50 for women)	44.3 ± 10.2	48.1 ± 9.4	0.017*	38.1 ± 9.6	42.0 ± 8.8	0.019*
Triglycerides (cut-off >150)	159.6 ± 49.2	165.0 ± 50.1	0.021*	189.7 ± 58.3	192.5 ± 55.4	0.014*

*p-value refers to statistical significance between newly diagnosed and long-term diabetics, based on the independent t-test. Cut-off values: Total Cholesterol >200 mg/dL, LDL >100 mg/dL, HDL <40 mg/dL for men and <50 mg/dL for women, Triglycerides >150 mg/dL.

The study findings suggest that the length of T2DM has a significant impact on the severity and pattern of dyslipidemia. Long-term diabetics not only exhibited higher rates of dyslipidemia but also had more pronounced lipid abnormalities, which may subsidize their higher risk for cardiovascular complications. These results underscore the need for more aggressive lipid management strategies in long-term diabetic patients. Positive correlation coefficients (r) indicate that as HbA1c increases, lipid levels also tend to increase. Negative correlation coefficients of HDL levels indicate that as HbA1c increases, it tends to decrease. The correlations are stronger in long-term diabetics compared to newly diagnosed diabetics, particularly for total cholesterol, LDL cholesterol, and triglycerides (Table 4).

Table 4: Correlation Between Glycaemic Control (Measured by Hba1c) and Various Lipid Parameters for Both Newly Diagnosed and Long-Term Diabetics

Lipid Parameter (mg/dL)	Newly Diagnosed (r)	p-value	Long-Term (r)	p-value*
Total Cholesterol	0.25	0.02	0.30	0.01
LDL-Cholesterol	0.22	0.03	0.28	0.02
HDL-Cholesterol	-0.19	0.04	-0.24	0.04
Triglycerides	0.31	0.01	0.35	0.01

DISCUSSION

In the current research study, the incidence of dyslipidemia was observed in 78% of newly diagnosed T2DM patients, compared to 92% in the long-term diabetic group. The difference was significant at p≤0.05, indicating that the severity of dyslipidemia is significantly associated with the progression of T2DM. These findings align with previous studies that reported variable prevalence rates of dyslipidemia in known T2DM cases. For example, a study by Habib reported a prevalence rate of 85.33% in T2DM patients [13], which is similar to the 89% prevalence observed by Rizwan *et al.*, [14]. The findings of our study also display a positive correlation of TC, TG and LDL with HbA1c levels and a negative correlation of HDL with HbA1c levels in both the study groups. It indicates that dyslipidemia is present in patients with increased HbA1c and increases with the increase in HbA1c levels. This finding of our study is well supported by Sharahili *et al.*, who also reported a positive association of HbA1c with all biomarkers of lipid profile other than HDL-C, which showed a negative correlation [15]. Samimagham *et al.*, in their research, showed a significant positive association of HbA1c with lipid profile parameters [16]. These studies suggest that HbA1c is important biomarkers to check long-term glycemic index and it also predicts the level of dyslipidemia [17, 18]. The results of our study are other findings that highlight the risk of controlling dyslipidemia in diabetic patients. For example, studies from South Africa and Nigeria reported dyslipidemia prevalence rates of 90.3% and 90.7%, respectively, in T2DM patients [19-21]. Some of the limitations of our study are acknowledged, including a small cohort size, conducted at a single tertiary care hospital, and not including the duration of disease and treatment for diabetes. The study also did not include some confounding variables like diet and physical activity. However, our study delivers valuable information about the incidence and progression of dyslipidemia in T2DM patients. Healthcare providers should prioritize early screening for dyslipidaemia. Routine lipid profile assessments should be part of diabetes management to detect and address dyslipidaemia early.

CONCLUSIONS

It was concluded that the study shows a clear variation in dyslipidemia patterns between newly diagnosed and long-term type 2 diabetic patients. Long-term diabetics show a significantly higher prevalence and severity of lipid abnormalities. Early and regular screening for lipid abnormalities should be part of routine laboratory diagnosis. Strict glycemic control is essential, as it correlates with better lipid outcomes, and therefore optimizing HbA1c should be a priority.

Authors Contribution

Conceptualization: NA
Methodology: NA, MA, RS, WUK, FN
Formal analysis: WUK
Writing review and editing: RS, SA, FN

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Bonilha I, Zimetti F, Zanotti I, Papotti B, Sposito AC. Dysfunctional High-Density Lipoproteins in Type 2 Diabetes Mellitus: Molecular Mechanisms and Therapeutic Implications. Journal of Clinical Medicine.2021 May; 10(11): 2233. doi: 10.3390/ jcm1 011 2233.

[2] Zhong X, Xiao C, Wang R, Deng Y, Du T, Li W *et al.* Lipidomics Based on UHPLC/Q-TOF-MS to Characterize Lipid Metabolic Profiling in Patients with Newly Diagnosed Type 2 Diabetes Mellitus with Dyslipidemia. Heliyon.2024 Feb; 10(4). doi: 10.10 16/j.h eliyon.2024.e26326.

[3] Martagon AJ, Zubirán R, González-Arellanes R, Praget-Bracamontes S, Rivera-Alcántara JA et al. HDL Abnormalities in Type 2 Diabetes: Clinical Implications. Atherosclerosis.2024 Jul; 394: 117213. doi: 10.1016/j.atherosclerosis.2023.117213.

[4] Peng J, Zhao F, Yang X, Pan X, Xin J, Wu M *et al.* Association Between Dyslipidemia and Risk of Type 2 Diabetes Mellitus in Middle-Aged and Older Chinese Adults: A Secondary Analysis of a Nationwide Cohort. BioMed Journal Open. 2021 May; 11(5): e042821. doi: 10.1136/bmjopen-2020-042821.

[5] Mehta RK, Koirala P, Mallick RL, Parajuli S, Jha R. Dyslipidemia in Patients with Type 2 Diabetes Mellitus in a Tertiary Care Centre: A Descriptive Cross-Sectional Study. Journal of the Nepal Medical Association.2021 Apr; 59(236): 305. doi: 10.31729/ jnma.6278.

[6] Shekhawat VS, Behera V, Nayak AK, Kamal KD, Ramamoorthy A, Kumar RR *et al*. Evaluation of the Prevalence and Pattern of Dyslipidemia in Newly Detected Type 2 Diabetes Mellitus Patients and Nondiabetic Controls. Journal of Marine Medical Society.2024 Sep; 26(3): 392-7. doi: 10.4103 /jmms. jmms_160_23.

[7] Kaze AD, Santhanam P, Musani SK, Ahima R, Echouffo-Tcheugui JB. Metabolic Dyslipidemia and Cardiovascular Outcomes in Type 2 Diabetes Mellitus: Findings from the Look AHEAD Study. Journal of the American Heart Association. 2021 Apr; 10(7): e016947. doi: 10.1161/JAHA.120.016947.

[8] Haile K and Timerga A. Dyslipidemia and Its Associated Risk Factors among Adult Type-2 Diabetic Patients at Jimma University Medical Center, Jimma, Southwest Ethiopia. Diabetes, Metabolic Syndrome and Obesity. 2020 Nov: 4589-97. doi: 10.2147/DMSO.S283171.

[9] Tomlinson B, Patil NG, Fok M, Lam CW. Managing Dyslipidaemia in Patients with Type 2 Diabetes. Expert Opinion on Pharmacotherapy.2021 Nov; 22(16): 2221-34. doi: 10.1080/14656566.2021.1912734.

[10] Aslam R, Suhail S, Sajid R, bin Younis B. Type 2 Diabetes Mellitus (T2DM) in Pakistan: Prevalence, Trends and Management Strategies. Annals of King Edward Medical University.2022 Aug; 28(2): 247-54. doi: 10.216 49/akemu.v28i2.5117.

[11] Khan AR, Muhammad T, Razaq A. Prevalence of Dyslipidemia in Newly Diagnosed Type 2 Diabetes Patients at Diagnosed at KGNTH Bannu.Gomal Journal of Medical Sciences. 2017; 15(4): 178-82.

[12] Haq AU, Usman K, Ullah N, Hassan T, Akhtar J, Ullah I. A Cross-Sectional Study on Prevalence and Pattern of Dyslipidaemia and Its Associated Factors among Patients with Type 2 Diabetes Mellitus. Pakistan Journal of Medical & Health Sciences. 2023 Mar; 17(01): 836-. doi: 10.53350/pjmhs2023171836.

[13] Habib SS. Frequency Distribution of Atherogenic Dyslipidemia in Saudi Type 2 Diabetic Patients. Pakistan Journal of Physiology.2006 Dec; 2(2): 31-4.

[14] Rizwan A, Attaullah S, Jawad M, Ullah F, Zahid M, Saeed F *et al.* Prevalence and Association of Dyslipidemia with Diabetic and Hypertension in Population of Takht-e-Nasrati, Khyber Pakhtunkhwa, Pakistan. Pure and Applied Biology.2022 Sep; 11(3): 696-703. doi: 10.190 45 /bspab.2022.110070.

[15] Sharahili AY, Mir SA, ALDosari S, Manzar MD, Alshehri B, Al Othaim A et al. Correlation of HbA1c Level with Lipid Profile in Type 2 Diabetes Mellitus Patients Visiting A Primary Healthcare Center in Jeddah City, Saudi Arabia: A Retrospective Cross-Sectional Study. Diseases.2023 Oct; 11(4): 154. doi: 10.3390/ disease s11 040154.

[16] Samimagham H, Bargak M, Ghasemzadeh M, Jahromi MK. The Association of Glycated Hemoglobin with Lipid Profile Indices in Type 2 Diabetic Patients. Acta Medica Iranica.2020 Nov: 376-82. doi: 10.18502/ acta.v 58i8.4587.

[17] Omar GM, Mehdi MA, AL-Arabi FY, Fawade MM. Correlation between Glycated Hemoglobin Values and the Lipid Profile in Type 2 Diabetic Patients. International Journal of Pharmaceutical Research. 2021 Jan; 13(1). doi: 10.31838/ijpr/2021.13.01.470.

[18] Luo B, Xu W, Ye D, Bai X, Wu M, Zhang C *et al.* Association Between Glycated Hemoglobin and the Lipid Profile at the Central Yunnan Plateau: A Retrospective Study. Diabetes, Metabolic Syndrome and Obesity.2024 Dec: 2975-81. doi: 10.2147/ DMSO. S4 69368.

DOI:https://doi.org/10.54393/pjhs.v5i12.2225

[19] Aliyu FO, Orimogunje T, Bello SI, Abdulbaki M, Jamiu MO, Ogaji IJ. Prevalence of Dyslipidemia, Drug Therapy Problems, and Medication Adherence in Type 2 Diabetes Mellitus Patients in North Central Nigeria. Libyan International Medical University Journal.2024 Feb; 9(1): 021-027. doi: 10.1055/s-0044-1779340.

[20]Ekpor E, Addo-Mensah D, Akyirem S. Prevalence of Dyslipidemia Among Persons with Type 2 Diabetes in Africa: A Systematic Review and Meta-Analysis. Annals of Medicine and Surgery.2024 Jun; 86(6): 3468-77. doi: 10.1097/MS9.0000000000002122.

[21] Omodanisi EI, Tomose Y, Okeleye BI, Ntwampe SK, Aboua YG. Prevalence of Dyslipidaemia Among Type 2 Diabetes Mellitus Patients in the Western Cape, South Africa. International Journal of Environmental Research and Public Health.2020 Nov; 17(23): 8735. doi: 10.3390/ijerph17238735.

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Knowledge, Attitude and Practice (KAP) of Laboratory Safety among Laboratory Workers

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ABSTRACT

Clinical laboratories have an essential part in the diagnosis of disease. However, they also pose several hazards, including exposure to infectious agents, chemicals and radiation, as well as physical hazards such as ergonomic injuries. Adequate safety measures must be designed and practiced to minimize the risk of hazards and make sure the safety of laboratory workers. **Objectives:** To assess Knowledge, Attitude and Practice of Laboratory Safety among laboratory workers. **Methods:** It was an observational cross-sectional study conducted over two months in all the affiliated laboratories of Mayo Hospital, Lahore. The questionnaire regarding Knowledge, Attitude and Practice regarding Laboratory Safety was filled by 75 participants. All the collected data were analyzed using SPSS 23. The qualitative variables were mentioned as frequency and percentage and the quantitative variables as mean ± SD. **Results:** Out of 75 participants, 59% were male and 41% were female. The Knowledge, Attitude and Practice scores were 23.15 2.88, 11.0 1.26 and 11.73 1.97 respectively. The job title was associated with knowledge significantly (p= 0.03) and practice level (p=0.01). The participants' knowledge was significantly correlated with attitude (r=0.341, p=0.003) and practice (r=0.379, p=0.001). **Conclusions:** It was concluded that the laboratory workers had overall excellent knowledge, good attitude and practice level. The job title had a significant association with knowledge and practice level. The correlation of knowledge with attitude and practice was significant

INTRODUCTION

The clinical laboratory is an integral part of every hospital and plays a vital role in making a diagnosis. Due to various potential hazards, laboratory workers encounter a large number of health hazards during their routine work [1-3]. Laboratory personnel should be aware of these potential hazards to prevent them by adopting safety measures [4]. Unsafe behaviour accounts for 80-90% of occupational incidents [5, 6]. Laboratory safety is an approach to prevent injuries in the laboratory [7, 8]. Safety begins with identifying potential hazards and adopting a safety-oriented personal behaviour, attitude and good housekeeping and practicing good laboratory techniques consistently [9-11]. Occupational Safety and Health Act (OSHA) ensures the health of employees and provides safety standards as well as guidance for the effective control of laboratory hazards [12, 13]. Both employers and employees must show optimal compliance with OSHA initiatives by collaborating and getting actively involved in the implementation of OSHA programs to avoid hazards [14]. Generally, there are seven types of laboratory hazards:

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1) Chemical hazards 2) Biological hazards 3) Fire hazards 4) Electrical hazards 5) Mechanical hazards 6) Radiation hazards 7) Ergonomic hazards. The most commonly encountered hazard to laboratory personnel is biological hazard which can be transmitted via direct contact with blood and body fluids, needle stick injuries and inhalation of airborne droplets [13-15]. Chemical hazards in the laboratory are mainly due to chemicals such as acids, alkalis, carcinogens, corrosives and irritants [10, 11]. In addition to this, flammable liquids can also cause fire hazards. Another cause of fire hazard is the short-circuiting of electrical equipment. Electrical hazards can also result from naked electricity wires, overloaded circuits and touching the electrical equipment with wet hands [16, 17]. The mechanical hazards in the laboratory are associated with equipment such as centrifuges, homogenizers and autoclaves and improper use or disposal of glassware [11,18]. The radiation hazards are due to radioactive material and non-ionizing radiations from microwaves, heating lamps and safety cabinets used. In addition to these hazards, the ergonomic hazards are due to repetitive manual tasks, continuous microscopy and manual pipetting resulting in ganglion cysts, bursitis, tenosynovitis and musculoskeletal disorders [9, 14]. Laboratory hazards have drastic effects on laboratory personnel and the environment. Most of the time hazards remain unrecognized due to inadequate awareness of safety measures, apathetic attitude and improper practice of safety protocols.

This study aims to assess the knowledge, attitude and practices of laboratory personnel of Mayo Hospital/ King Edward Medical University Lahore towards laboratory safety.

METHODS

This observational cross-sectional study was conducted from November 2022 to December 2022 at all affiliated laboratories of King Edward Medical University/Mayo Hospital, Lahore after approval from IRB (Letter No. 918/RC/KEMU) of King Edward Medical University (KEMU). The sample size was calculated by taking the confidence level of 95%, absolute precision as 5% and the expected percentage of good knowledge of laboratory safety as 96.5% among laboratory workers [12]. Non-probability, convenient sampling technique was used. The data were collected after getting consent from 75 laboratory workers both male and female using a questionnaire designed by keeping in view the formats designs [12, 17]. All technicians and doctors working at the affiliate laboratories and who gave consent to participate were included. While, workers from other laboratories were excluded. The questionnaire was validated by two medical educationists. It was comprised of four sections. Demographic data on age, gender and job title was included in the first section. The second section consisted of questions related to knowledge (n=28), the third section focused on questions related to attitude (n=12) and the last section included questions related to participant's practice regarding Laboratory Safety (n=15). The scoring of knowledge, attitude and practice was based on Bloom's cutoff. The knowledge score was divided into three levels based on correct answers out of 28 questions; Excellent Knowledge [19-21], Good Knowledge [14], and Bad Knowledge (0-13). The score for attitude was characterized by two levels based on correct answers out of 12 questions; Good Attitude (8-12) and Bad Attitude (0-7). Practice score was also labelled by two levels based on correct answers out of 15 questions; Good Practice (10-15) and Bad Practice (0-9). Statistical Package for Social Science (SPSS), version 23 was used to analyze the collected data. The quantitative data were presented as mean ± SD, while the qualitative data was presented as frequency and percentage. The chi-square test was used to determine the association of job title with knowledge, attitude and practice level. Pearson's correlation (r) was applied to measure the correlation of knowledge with practice and attitude score. Results were considered statistically significant with p-value<0.05.

RESULTS

The age of participants showed a mean ± SD 31 ± 8.5 years. There were 44 (59%) male and 31 (41%) female. Out of 75 participants, there were 30 (40%) laboratory technicians, 17 (23%) doctors and 28 (37 %) other laboratory workers including laboratory supervisors, and undergraduate and internship students. The mean ± SD score for knowledge, attitude and practice is given in Table 1

Table 1: Mean ± SD Scores for Knowledge, Attitude and Practice

Variables	n (%)
Age	
Mean ± SD	31 ± 8.5
Gender	
Male	44 (59%)
Female	31 (41%)
Profession	
Laboratory Technicians	30 (40%)
Doctors	17 (23%)
Other Laboratory Workers	28 (37 %)

The mean ± SD score for knowledge, attitude and practice is given in Table 2.

Table 2: Mean ± SD Scores for Knowledge, Attitude and Practice

Variables	Mean ± SD
Knowledge	23.15 ± 2.88
Attitude	11.0 ± 1.26
Practice	11.73 ± 1.97

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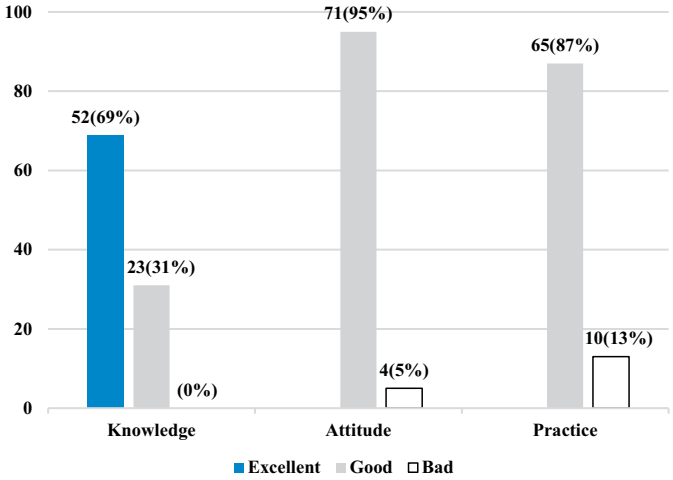

Figure 1: Frequency Distribution of Participants Based On Knowledge, Attitude and Practice Score

The association of job title with Knowledge, Attitude and practice level was determined by using the Chi-square test. p-value<0.05 was considered significant. Job title was found to be significantly associated with knowledge level (p=0.03) and practice level (p=0.01) while no significant association was found between job title and attitude level (p=0.37)as shown in Table 3.

Table 3: Association of Job Title with Knowledge, Attitude and Practice Levels

Variables	Job Title			p-value
	Technicians	Doctors	Others	
Knowledge Level				
Excellent	20	16	16	0.03
Good	10	1	12	
Bad	0	0	0	
Attitude Level				
Good	28	17	25	0.03
Bad	2	0	3	
Practice level				
Good	29	16	20	0.01
Bad	1	1	8	

Knowledge score correlation with Attitude and Practice score was established by applying Pearson's correlation(r). p-value<0.05 was considered statistically significant. Knowledge score was found to be significantly correlated with Attitude score (r=0.341, p=0.003, CI=95%) and Practice score (r=0.379, p=0.001, CI=95%) as shown in Table 4.

Table 4: Knowledge Score Correlation with Attitude Score and Practice Score

Variables	p-value	
	r value	p-value
Attitude Score	0.341	0.003
Practice Score	0.379	0.001

DISCUSSION

Clinical laboratories have potential risk hazards that can lead to life-threatening injuries. The risk of these injuries can be minimized by proper hazard identification and adopting appropriate safety measures. The rational model of health promotion by WHO (2012) assumed that increased knowledge would ultimately be transmitted into a positive, good attitude as well as improved behaviour [7]. So, the study was conducted to assess the Knowledge, Attitude and Practice among laboratory workers regarding laboratory safety measures. The overall mean ± SD knowledge score was 23.15 ± 2.88 with 69% excellent and 31% good knowledge level. These results are comparable with the study of Paul *et al.*, [19]. These results are not in agreement with those of Izegbu *et al.*, which showed a low level of awareness among laboratory workers [20]. The reason behind this low knowledge level may be that the majority of the workers had never attended any informative program on safety measures. The overall mean ± SD attitude score was 11.0 ± 1.26 with 95% of participants having good and 5% having bad attitude levels. The results are in agreement with the study of Goswami *et al.*, [12]. However, the study results of Zaveri *et al.*, and Al-Zyoud *et al.*, stated that most of the respondents had poor attitudes regarding the laboratory [6, 17]. The overall mean practice score was 11.73 ± 1.97 with 65 (87%) of the respondents having good and 10 (13%) having bad practice levels regarding waste management, following spillage protocols, reporting needle stick injuries and use of emergency safety equipment. Likewise, Aluko *et al.*, and Goswami *et al.*, showed good practice levels among healthcare workers [7, 12]. However, our results are contrary to the study by Ahmad *et al.*, [21]. Our study demonstrated a statistically significant association of job title with knowledge (p=0.03) and practice level (p=0.01). While no significant association of job title was shown with attitude level (p=0.37). These results are comparable with the study of Aluko *et al.*, as well as with Ramli *et al.*, [7, 22]. Ndu *et al.*, stated that doctors had a high knowledge of standard precautions as compared to other laboratory staff [23].The Knowledge score was found to be significantly correlated with the Attitude score (r=0.341, p =0.003)as well as with the practice score (r=0.379, p=0.001) and this shows agreement with the results of Mahmoud *et al.*, [11]. According to a study by Rahmat *et al.*, safety perception has a significant impact on safety behaviour. The knowledge positively affects attitude and practice [1]. Compliance with safety standards, use of PPE and proper vaccination of laboratory workers can reduce the risk of occupational hazards. Training programs for laboratory personnel regarding safety procedures can improve their knowledge and therefore attitude and practice in clinical laboratories[9].

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CONCLUSIONS

It was concluded that based on the findings of our study, the laboratory workers had overall excellent knowledge, good attitude and practice levels. The job title showed significant association with knowledge and practice level and knowledge showed significant correlation with attitude and practice. Therefore, our study emphasizes the fact that laboratory workers must be provided with safety equipment and training programs to improve knowledge, attitude and practice to minimize the hazard probability. The study was conducted on a small scale so its results cannot be generalized over other setups.

Authors Contribution

Conceptualization: RD
Methodology: SI, RD, MA[2], SA
Formal analysis: RD, MS
Writing review and editing: RA, Ma[1]

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Rahmat N, Muhammad D, Muhammad H. Correlation of Safety Perceptions and Safety Behavior in University Teaching Laboratory. Malaysian Journal of Public Health Medicine.2020 Aug;20(Special1):1-5. doi: 10.3 7 268/mjphm/vol.20/no.Special1/art.673.

[2] Yang Y, Reniers G, Chen G, Goerlandt F. A Bibliometric Review of Laboratory Safety in Universities. Safety Science.2019 Dec; 120: 14-24. doi: 10.1016/ j.ssci. 201 9. 06.022.

[3] Islam MN, Kabir MH, Yusuf MA, Salam MB, Perveen I, Shirin S. Knowledge of Biosafety Measures among Laboratory Personnel at Tertiary Level Public Hospitals in Dhaka City. Bangladesh Journal of Infectious Diseases.2020; 7(2): 49. doi: 10.332 9/bji d.v 7i2.51509.

[4] El-Gilany AH, El-shaer S, Khashaba E, El-Dakroory SA, Omar N. Knowledge, Attitude, And Practice (KAP) of 'Teaching Laboratory'technicians Towards Laboratory Safety and Waste Management: A Pilot Interventional Study. Journal of Hospital Infection. 2017 Jun; 96(2): 192-4. doi: 10.1016/j.jhin.2017.02.007.

[5] Wader JV, Kumar V, Mutalik AV. Knowledge, Attitude, Practice of Biosafety Precautions Amongst Laboratory Technicians in a Teaching Hospital. International Journal of Health Science and Research. 2013; 3(6): 28-33.

[6] Zaveri J and Karia J. Knowledge, Attitudes and Practice of Laboratory Technicians Regarding Universal Work Precaution. National Journal of Medical Research. 2012 Mar; 2(01): 113-5.

[7] Aluko OO, Adebayo AE, Adebisi TF, Ewegbemi MK, Abidoye AT, Popoola BF. Knowledge, Attitudes and Perceptions of Occupational Hazards and Safety Practices in Nigerian Healthcare Workers. BioMed Central Research Notes.2016 Dec; 9: 1-4. doi: 10.118 6/ s13104-016-1880-2.

[8] Dalyan O, Özkaya N, Pişkin M, Öztürk ÖF. Investigation and Comparison of Some Laboratories in Terms of Occupational Health and Safety by ELMERI Observation Method. Journal of Advanced Research in Natural and Applied Sciences.2021; 7(2): 282-94. doi: 10.28979/jarnas.903664.

[9] Hussein BA and Shifera G. Knowledge, Attitude, And Practice of Teachers and Laboratory Technicians Toward Chemistry Laboratory Safety in Secondary Schools. Journal of Chemical Education.2022 Aug; 99(9): 3096-103. doi: 10.1021/acs.jchemed.2c00043.

[10] Elbayoumi M. Professional Laboratory Safety Practice of Basic Science Teachers in Gaza Strip. ISRAA University Journal of Applied Science.2020; 4(1): 52-67. doi: 10.52865/PNKH3781

[11] Mahmoud AA and Sabry SS. Safety Training Program for Clinical Laboratory Workers Regarding Prevention of Occupational Hazards. American Journal of Nursing. 2019; 7(2): 116-27. doi: 10.12691/ajnr-7-2-3.

[12] Goswami HM, Soni ST, Patel SM, Patel MK. A Study On Knowledge, Attitude and Practice of Laboratory Safety Measures among Paramedical Staff of Laboratory Services. National Journal of Community Medicine. 2011 Dec; 2(3): 470-3.

[13] Yavuz Ş, Özbek HE, Tatar D. Examination of Occupational Health and Safety Perception Levels of Employees in the Health Sector. International Journal of Social and Humanities Sciences Research.2022 Jun; 9(84): 1256-65. doi: 10.26450/jshsr.3148.

[14] Almutairi NS, Tamrin SB, Guan NY, How V. Review of Knowledge, Attitude, and Practice Among Laboratory Workers Towards Occupational Safety and Health. Malaysian Journal of Medicine and Health Sciences. 2020 Jan; 16(1).

[15] Mossburg S, Agore A, Nkimbeng M, Commodore-Mensah Y. Occupational Hazards among Healthcare Workers in Africa: A Systematic Review. Annals of Global Health. 2019; 85(1). doi: 10.5334/aogh.2434.

[16] Soltanzadeh A, Heidari H, Javadi Hoseini ZS, Sorooshnia M, Rahimifard H. Safety Risk Assessment

DOI: https://doi.org/10.54393/pjhs.v5i12.2390

in Medical and Paramedical Education Laboratories. Archives of Occupational Health.2021 Apr; 5(2): 971-9. doi: 10.18502/aoh.v5i2.6192.

[17] Al-Zyoud W, Qunies AM, Walters AU, Jalsa NK. Perceptions of Chemical Safety in Laboratories. Safety. 2019 Apr; 5(2): 21. doi: 10.3390/safety5020021.

[18] Asiry S and Ang LC. Laboratory Safety: Chemical and Physical Hazards. Bio-banking: Methods and Protocols.2019: 243-52. doi: 10.1007/978-1-4939-8935-5_21.

[19] Paul E, Abidin EZ, Mahmmud NA, Ismail NH. Assessment of Knowledge and Practice on Occupational Safety and Health Among Laboratory Workers in OSHMS Certified and Non-Certified Public Universities in Malaysia. Malaysian Journal of Medicine and Health Sciences.2022 Sep; 18(5): 3-12. doi: 10.47836/mjmhs.18.5.2.

[20] Izegbu MC, Amole OO, Ajayi GO. Attitudes, Perception and Practice of Workers in Laboratories in the Two Colleges of Medicine and Their Teaching Hospitals in Lagos State, Nigeria as Regards Universal Precaution Measures. Biomedical Research. 2006; 17(1): 49-54.

[21] Ahmad S, Ali B, Khan S, Fatima A, Saeed M, Asghar A *et al.* A Survey on Biosafety Practices in Lab Personnel in 12 Selected Areas of Karachi, Pakistan. Journal of Biosafety and Biosecurity.2019 Mar; 1(1): 68-72. doi: 10.1016/j.jobb.2018.12.001.

[22] Ramli FB, Mokhtar SN, Jamaluddin MH, Harun MN, Salim MA, Lokman MN *et al.* Awareness among students and staff on occupational safety and health (OSH) in Universiti Teknologi Malaysia. International Conference on Student and Disable Student Development 2019.2020 Sep: 13-18). doi: 10.2991/assehr.k.200921.003.

[23] Ndu AC and Arinze-Onyia SU. Standard Precaution Knowledge and Adherence: Do Doctors Differ from Medical Laboratory Scientists? Malawi Medical Journal.2017; 29(4): 294-300. doi: 10.4314/mmj.v29i4.3.

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Determinants of Rural-Urban Disparities in Surgical Treatment Accessibility for Carpal Tunnel Syndrome

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ABSTRACT

Carpal Tunnel Syndrome is a common neuropathic condition that causes pain, numbness, and weakness in the affected hand. **Objective:** To investigate the determinants of surgical treatment accessibility for Carpal Tunnel Syndrome. **Methods:** For this purpose, a prospective cohort study study was carried out at a tertiary care hospital in Pakistan. The research included 284 patients diagnosed with Carpal Tunnel Syndrome who were suggested for surgery. Data were collected using a structured questionnaire, focusing on demographic factors, socioeconomic status, and healthcare system-related questions. Descriptive statistics was performed using SPSS version 26.0 to calculate means ± standard deviations for all the continuous variables, and chi-square tests for categorical variables. **Results:** Results show that most of the patients (57.75%) in the study belong to rural areas, and 42.25% of patients belong to urban areas. A multivariable logistic regression shows that living in a rural area was significantly linked with older age and body mass index. **Conclusions:** It was concluded that people living in rural areas of Pakistan are deprived of surgical treatment for Carpal Tunnel Syndrome. Other associated factors that contribute to the poor accessibility of surgical treatment of the disease are older age and body mass index.

INTRODUCTION

Carpal tunnel syndrome (CTS) is associated with compression of the median nerve, resulting in pain, numbness, tingling, and weakness near the base of the hand. It affects the index, thumb, radial, and middle sides of the ring finger, and can lead to decreased grip strength and compromised hand function over time. The condition often causes gradual weakening of the muscles at the base of the thumb [1]. Medical history and physical inspection, with or without additional confirmatory testing, are used to establish the diagnosis of CTS [2-4]. Genetic predisposition, diabetes mellitus, thyroid conditions, obesity, rheumatoid arthritis, and pregnancy are a few risk factors for CTS [5, 6]. However, idiopathic carpal tunnel syndrome accounts for the majority of cases [7]. People of working age are frequently affected by CTS, which can result in missed work and a noticeable drop in productivity. The condition is 15% prevalent in the general population, regardless of risk factors [8, 9]. To diagnose CTS, electro-diagnostic (EDS) testing is essential, especially if surgery is being considered. Electromyography (EMG) and nerve conduction studies (NCS) are typical EDS examinations. By identifying compromised median nerve conduction across the carpal tunnel while maintaining normal conduction elsewhere, NCSs verify CTS. The abductor policies brevis

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muscle, which is usually innervated by the median nerve, is one of the muscles whose pathologic alterations are evaluated by EMG [10]. An EMG sample of the abductor policies brevis muscle will show indications of denervation in cases of severe and prolonged compression [11]. Reducing health disparities between urban and rural areas has received attention lately [8, 9]. Individuals residing in urban locations tend to self-report worse health and are more prone to medical comorbidities such as obesity, high blood pressure, and diabetes mellitus, as well as behavioural risk factors like smoking [12, 13]. Patients in rural areas of Pakistan are more likely to be poor and have little health literacy. However, patients living in urban areas frequently have to pay more and spend more time travelling to obtain healthcare resources due to the lack of a workforce and inadequate infrastructure in remote areas. Urban-rural health disparities are exacerbated by these socioeconomic factors [12]. Hand surgery differences between rural and urban areas have never been investigated before. Since CTS is a popular, elective, ambulatory operation that doesn't require a lot of resources, we decided to use it as a model to investigate the differences in hand surgery between rural and urban areas. It's unclear if patients with CTR who present from rural and urban areas have comparable demographics or are at similar stages of the illness. To close this knowledge gap, we set out to compare rural and urban patient populations receiving CTR in terms of (1) patient demographic characteristics, (2) the use of confirmatory electro-diagnostic (EDS) testing, and (3) preoperative EDS severity.

This study aimed to investigate the determinants of surgical treatment accessibility for carpal tunnel syndrome.

METHODS

This prospective cohort study study was conducted over one year, from April 2022 to March 2023, at Pakistan International Medical College, Hayatabad, Peshawar, Pakistan. The study received approval from the Department of Medical Research at Pakistan International Medical College, with the approval number PIMC/DMR/4. The primary focus of the study was to assess the accessibility and outcomes of Carpal Tunnel Release (CTR) surgery among patients diagnosed with CTS who underwent surgery during this period. Eligible participants were those diagnosed with CTS and had undergone open CTR surgery performed by certified surgeons. A sample size of 284 participants was calculated using a formula for diagnostic studies, based on 80% statistical power and a significance level of ≤0.05. The following formula for sample size calculation in diagnostic studies was used: $n=Z2\times P\times(1-P)/d2$. where Z is the Z-value (1.96 for 95% confidence), P is the expected prevalence (assumed to be 0.5 for maximum sample size), and d is the desired precision (0.1), the sample size was determined to be 284 participants. The patients were informed about the study, and written consent was taken for their data to be used for research purposes. The participants who experienced acute injury or infections within two weeks following CTR, revision surgery for the CTR in request, inadequate or missing medical history, or tumor excision surgery were excluded from the research. The study collected data on several pre-surgery variables, including patient demographic factors such as age, gender, BMI, and electro-diagnostic studies (EDS) used to confirm the severity of CTS before surgery, with disease severity categorized as normal, mild to moderate, or severe. Medical comorbidities were identified through electronic medical records and included factors such as tobacco use, diabetes mellitus, hypothyroidism, hypertension, chronic kidney disease, and cervical radiculopathy. Post-surgery outcomes were assessed through follow-ups conducted at three and six months after the CTR procedure. These intervals were chosen to capture both short-term recovery (three months) and medium-term outcomes (six months), as these are critical milestones for evaluating post-surgical recovery and functional improvements in CTS patients. Symptom relief was evaluated using the Boston Carpal Tunnel Questionnaire (BCTQ), which assessed improvements in pain, numbness, and functional capacity. Grip strength was measured using a dynamometer, while the time taken to resume normal daily activities or return to work post-surgery was also recorded. To assess the quality of care after surgery, patient satisfaction was measured through structured surveys, which evaluated communication with healthcare providers, hospital facilities, and overall satisfaction with surgical outcomes. Post-surgical complications, such as wound infections, nerve damage, or symptom recurrence, were documented, and follow-up compliance was recorded as the percentage of patients who adhered to scheduled post-operative visits. Accessibility to surgical treatment was evaluated by examining the time between diagnosis and surgery, the distance patients traveled for treatment, and any delays in receiving care. Data analysis was conducted using SPSS version 26.0. Descriptive statistics were applied to all variables, with means and standard deviations calculated for continuous variables, and frequencies and percentages for categorical variables. Relationships between patient demographics, clinical presentation, and accessibility to surgical therapy were evaluated using t-tests for continuous variables and Chi-square tests for categorical variables, with a significance threshold set at less than 0.05.

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RESULTS

The final group of 284 patients had a median BMI of 30.5, a mean age of 58.1 years, and 72.2% of them were female. Of the cohort, 9% had cervical radiculopathy, 16% had hypothyroidism, 19% had diabetes mellitus, and 11% used tobacco. Electro-diagnostic study (EDS) testing was obtained in 246 patients (86.6%). Of the 232 individuals for whom preoperative EDS severity grading was available, 3% had normal, 18% had mild, 47% had moderate, and 32% had severe CTS. Post-surgery follow-up at 3 months revealed that 85% of patients reported significant improvement in pain and numbness based on the Boston Carpal Tunnel Questionnaire (BCTQ). Urban participants showed slightly better improvement (90%) compared to rural participants (83%) ($p<0.05$). Mean grip strength increased by 25% from baseline in urban patients and 20% in rural patients, with the difference being statistically significant ($p<0.05$). Urban patients returned to work or resumed daily activities within a mean of 8 weeks' post-surgery, while rural patients took 10 weeks on average ($p<0.05$). Patient Satisfaction: 82% of urban patients and 75% of rural patients reported being "very satisfied" with their overall care ($p=0.06$). Satisfaction was linked to communication with healthcare providers and the perceived quality of surgical outcomes. Post-surgical complications were noted in 10% of patients overall, with a lower rate in urban patients (8%) compared to rural patients (12%), though this was not statistically significant ($p=0.14$). Follow-up compliance was higher in urban participants (92%) compared to rural participants (85%) ($p<0.05$). Patients from rural areas experienced a longer time to surgery and travelled farther distances to receive care, compared to urban patients. There were no significant delays in receiving care once patients were scheduled for surgery (Table 1).

Table 1: Various Features of the Selected Patients (n=284)

Variables	Urban Participants (n=120)	Rural Participants (n=164)	Total Participants (n=284)	p-Value
Age (Years)	58.1	63.2	55.8	<0.05
Median (IQR)				
BMI (kg/m^2)	30.5 (25.9-35.2)	28.4 (23.8-32.2)	31.4 (26.2-36.1)	<0.05
n (%)				
Female Sex	205 (72.2)	78 (65)	127 (77.4)	0.18
Male Sex	79 (27.8)	42 (35)	37 (22.6)	
Urdu Speaking Participants	258 (90.8)	112 (93.3)	146 (89.0)	0.12
Non-Urdu Speaking	26 (9.2)	8 (6.7)	18 (11.0)	
Confirmatory EDS Testing	246 (86.6)	106 (88.3)	140 (85.4)	0.43
EDS Grade Normal	7 (3.0)	6 (5.0)	1 (0.6)	<0.05
EDS Grade Mild	42 (18.1)	8 (6.7)	34 (20.7)	<0.05
EDS Grade Moderate	109 (46.8)	46 (38.3)	63 (48.7)	0.72
EDS Grade Severe	74 (32.1)	38 (31.7)	36 (30.0)	0.61
Diabetes Mellitus	54 (19.0)	16 (13.3)	38 (23.2)	0.09
Hypertension	129 (45.4)	60 (50.0)	69 (42.1)	0.35
Hypothyroidism	45 (15.8)	15 (12.5)	30 (18.3)	0.54
Chronic Kidney Disease	12 (4.2)	5 (4.2)	7 (4.3)	0.96
Cervical Radiculopathy	26 (9.2)	5 (4.2)	21 (12.8)	0.11
Tobacco Use	31 (10.9)	10 (8.3)	21 (12.8)	0.33
Post-Surgery Symptom Relief	241 (85.0)	108 (90.0)	133 (83.3)	<0.05
Grip Strength (kg, Mean ± SD)*	26.5 ± 5.3	28.7 ± 4.8	24.9 ± 5.7	<0.05
Grip Strength Improvement**	243 (85.6)	108 (90.0)	135 (82.3)	<0.05
Return to Work/ Activities	230 (81.0)	108 (90.0)	122 (74.4)	<0.05
Patient Satisfaction	217 (76.4)	98 (81.7)	119 (72.6)	0.06
Follow-Up Compliance	248 (87.3)	110 (91.7)	138 (84.1)	<0.05

Grip strength improvement was assessed using a dynamometer. *Actual grip strength values were recorded; they are reported in kilograms (kg) as mean ± standard deviation. **Results are presented as the percentage of patients reporting improvement.

The results of the multivariable logistic regression analysis indicated that living in an urban area was independently associated with older age, lower BMI, and normal EDS severity, similar to the findings in the bivariate analysis (Table 2).

Table 2: Multivariable Logistic Regression Analysis for Variables Associated with Urban Residence in Patients Undergoing Carpal Tunnel Release

Variable	OR	95% CI	p-Value
Age	1.042	1.012–1.072	≤0.05
BMI	0.937	0.890–0.988	≤0.05
EDS Severity (Normal)	5.241	1.621–16.932	≤0.05
EDS Severity (Mild)	0.482	0.134–1.730	0.22

DISCUSSION

There is an increasing recognition of the need to address Urban-Rural disparities in healthcare outcomes. Previous studies have highlighted poorer accessibility of various medical facilities and higher mortality rates in rural patients with conditions such as cardiac disease and stroke [9, 10]. However, no prior research has specifically examined Urban-Rural differences in patients undergoing hand surgery, particularly Carpal Tunnel Release (CTR). This study aimed to assess the demographic similarity between Urban and Rural CTR patients, the rate at which they undergo confirmatory electro-diagnostic study (EDS) testing, and the degree of illness severity at presentation as determined by EDS grading. According to present research, compared to rural patients, urban patients having CTR are likely to be older, have a lower body mass index (BMI), and have normal EDS scores. However, it is essential to acknowledge that these observed trends do not imply causality and are likely multifactorial in nature.

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For instance, socioeconomic factors, healthcare literacy, transportation challenges, and occupational differences may all contribute to these disparities. The usage of confirmatory EDS testing for CTR patients did not change significantly among the urban and rural groups, according to the current study. Considering that EDS evaluation is the main preoperative cost burden and is frequently a cause of delay before surgical therapy, this outcome is encouraging [14, 15]. The most recent Urban-Rural classification codes are based on national census data for 2011. Therefore, even though current data collection was done almost ten years ago, it is still applicable [16]. Nevertheless, evolving diagnostic criteria for Carpal Tunnel Syndrome (CTS) and advances in alternative confirmatory tests may influence future research in this area [17, 18]. EDS has drawbacks, including false-positive and false-negative results, even though it was once regarded as a reference standard [17]. Alternative diagnostic instruments, such as the CTS-6 or ultrasonography, are increasingly gaining popularity [2–4]. The lower BMI observed among urban patients in the present study appears counterintuitive, given that a higher BMI is a well-established risk factor for CTS. This finding could reflect broader societal trends or demographic differences, such as occupation type or activity levels, which warrant further investigation. Additionally, the older age of urban patients may suggest delayed presentation, possibly influenced by systemic healthcare barriers such as limited hospital availability or a shortage of healthcare providers in certain urban areas [19]. These factors should be explored in future studies to fully understand their impact on healthcare accessibility. To guarantee fair access to care, future research should keep examining how confirmatory tests and surgical time differ across urban and rural areas. The study's observed demographic differences, specifically the lower BMI and older age of urban patients, could be indicative of wider societal changes. These disparities in demography may also be related to changes in occupation between populations in urban and rural areas, which may have an impact on the prevalence of CTS [20]. Notably, urban patients did not exhibit a higher probability of presenting with advanced EDS of disease. This finding implies that urban patients, despite potential barriers, have reasonable access to CTS therapy. However, systemic factors such as healthcare policies, travel burden, and scheduling delays may still disproportionately affect rural populations, depriving them of timely surgical treatment. Addressing these healthcare system barriers is crucial to achieving equity in surgical outcomes [9]. The usefulness of EDS as a confirmation test in these people is called into question, nevertheless, given the greater frequency of EDS scores in normal illness in urban patients receiving CTR. One hypothesis is that urban patients frequently have long commutes, which may exacerbate the symptoms of CTS and increase the number of EDS-negative CTS diagnoses in this population. Alternatively, urban patients may be more likely to pursue surgical interventions due to higher healthcare awareness or better access to medical advice [19]. Alternative confirmatory tests, such as CTS-6 or ultrasound, may be more appropriate for this group of people given the increased false-negative frequency of EDS to detect CTS in urban areas [2–4]. Adopting telemedicine for preoperative assessments could mitigate accessibility challenges in underserved areas. Current research has various limitations which should be acknowledged. First, the study did not include other potential determinants of healthcare accessibility, such as healthcare policies, the quality of postoperative care, and the availability of skilled professionals, which could further explain the disparities in surgical outcomes between rural and urban patients. Additionally, the study was conducted at a single institution, which may limit the generalizability of the findings to other regions or healthcare settings.

CONCLUSIONS

It was concluded that this study was designed to identify the determinants of rural-urban disparities in accessing surgical treatment for CTS by comparing patient demographics, the use of EDS, and preoperative disease severity between rural and urban populations. The findings revealed significant disparities in access to confirmatory EDS testing, with rural patients being less likely to receive timely diagnostic evaluations, contributing to delays in diagnosis and prolonged suffering from CTS before receiving surgical intervention. Rural patients also presented with more advanced disease severity at the time of surgery, which shows that delayed access to testing and treatment may aggravate their condition. The availability of diagnostic facilities and timely treatment contributes to the observed differences in treatment accessibility between rural and urban populations.

Authors Contribution

Conceptualization: FQ
Methodology: FQ, MA
Formal analysis: AC, ZIB
Writing review and editing: NA, HM

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Conflicts of Interest

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REFERENCES

[1] Hayder A, Fatimah A, Asghar HM, Maqbool S, Shad M, Zaheer B et al. Prevalence of Carpal Tunnel Syndrome among Butchers in Pakistan: Carpel Tunnel Syndrome among Butchers. Pakistan BioMedical Journal. 2022 Jul; 5(7): 183-7. doi: 10.54393/pbmj.v5i7.676.

[2] Wang WL, Hanson T, Fowler JR. A Comparison of 6 Diagnostic Tests for Carpal Tunnel Syndrome Using Latent Class Analysis. Hand. 2020 Nov; 15(6): 776-9. doi: 10.1177/1558944719833709.

[3] Hudson Jr HT, Moore R, Elver AA, Herrera FA. Are Patient Demographics and Payor Status Associated with Practice Patterns in the Surgical Management of Carpal Tunnel Syndrome? Sage Journals. 2024 Jan; 19(1): 128-35. doi: 10.1177/15589447221107693.

[4] Holle AM, Gill VS, Lin E, Cancio-Bello AM, Iturregui JM, Haglin JM *et al.* Differences in Volume, Reimbursement, Practice Styles, and Patient Characteristics Between Male and Female Surgeons for Open and Endoscopic Carpal Tunnel Release. Orthopedics. 2024 Nov: 1-7. doi: 10.3928/01477447-20241127-03.

[5] Kastilong MP, Winifred K, Sekeon SA. Quality of Life of Carpal Tunnel Syndrome with Non-Operative Treatment: Cohort Study. International Journal of Research in Medical Sciences. 2020 Jul; 8(7): 2502. doi: 10.18203/2320-6012.ijrms20202886.

[6] Semehkin OM, Izmalkov CH, Bractiichuk AH, Solopikhina EB, Balakleets CB, Bogdanova MA *et al.* Results of Surgical Treatment of Patients with Carplastic Tunnel Syndrome Depending on the Severity of the Disease. Orthopedics. 2021; 27(1): 24-31.doi: 10.18019/1028-4427-2021-27-1-24-31.

[7] Kerluku J, Walker P, Amen T, Almeida BA, McColgan R, Urruela A *et al.* Evaluation of Racial, Ethnic, and Socioeconomic Disparities in Indication for Carpal Tunnel Release. The Journal of Bone and Joint Surgery. 2023 Sep; 105(18): 1442-9. doi: 10.2106/JBJS.22.01045.

[8] Snyder JE, Jensen M, Nguyen NX, Filice CE, Joynt KE. Defining rurality in Medicare administrative data. Medical care. 2017 Dec 1;55(12):e164-9. 10.1097/MLR.0000000000000607.

[9] Earp B, Blazar P, Zhang D. Rural-Urban Disparities in the Surgical Treatment of Carpal Tunnel Syndrome in the United States. Cureus. 2024 Jul; 16(7). 10.7759/cureus.65687

[10] Coombs NC, Campbell DG, Caringi J. A Qualitative Study of Rural Healthcare Providers' Views of Social, Cultural, and Programmatic Barriers to Healthcare Access. BioMed Center Health Services Research. 2022 Apr; 22(1): 438. doi: 10.1186/s12913-022-07829-2.

[11] Pomerance J, Zurakowski D, Fine I. The Cost-Effectiveness of Nonsurgical Versus Surgical Treatment for Carpal Tunnel Syndrome. The Journal of Hand Surgery. 2009 Sep; 34(7): 1193-200. doi: 10.10 16/j.jhsa.2009.04.034.

[12] Bűhler M, Atmore C, Perry M, Crengle S, Norris P, Baxter GD. Patient experiences and perspectives of health service access for carpal tunnel syndrome in Aotearoa New Zealand: a normalisation process theory-informed qualitative study. BMC health services research. 2024 Apr 13;24(1):465. 10.1097/BRS.0000000000003811

[13] Wright MA, Beleckas CM, Calfee RP. Mental and Physical Health Disparities in Patients with Carpal Tunnel Syndrome Living with High Levels of Social Deprivation. The Journal of Hand Surgery. 2019 Apr; 44(4): 335-e1. doi: 10.1016/j.jhsa.2018.05.019.

[14] Osiak K, Mazurek A, Pękala P, Koziej M, Walocha JA, Pasternak A. Electrodiagnostic studies in the surgical treatment of carpal tunnel syndrome—a systematic review. Journal of Clinical Medicine. 2021 Jun 18;10(12):2691. 10.3390/jcm10122691

[15] Billig JI, Lu YT, Hayward RA, Sears ED. Surgical Timing for Carpal Tunnel Syndrome: A Comparison of Health Care Delivery in the Veterans Administration and Private Sector. The Journal of Hand Surgery. 2021 Jul; 46(7): 544-51. 10.1016/j.jhsa.2021.02.022.

[16] Stock LA, Brennan JC, Johnson AH, Gelfand J, Turcotte JJ, Jones C. Disparities in Hand Surgery Exist in Unexpected Populations. Cureus. 2023 May; 15(5). 10.7759/cureus.39736.

[17] Gabriel DC, Demetri L, Zhang D. The Role of Confirmatory Testing in Carpal Tunnel Syndrome: Electrodiagnostic Study, Ultrasound and CTS-6. The Journal of Hand Surgery (Asian-Pacific Volume). 2024 Oct 8. 10.1142/S2424835525400016

[18] Chen K, Duan GY, Wolf JM, Stepan JG. Health Disparities in Hand and Upper Extremity Surgery: A Scoping Review. The Journal of Hand Surgery. 2023 Sep, 48(11): 1128-1138. 10.1016/j.jhsa.2023.08.005

[19] Boddu SP, Lin E, Gill VS, Hinckley NB, Lai CH, Renfree KJ. Low Income, Poor Physical Health, Poor Mental Health, and Other Social Risk Factors Are Associated with Decreased Access to Care in Patients with Carpal Tunnel Syndrome. Journal of Primary Care & Community Health. 2024 Mar; 15. doi: 10.1177/21501319241240348.

[20] Azadvari M, Haghshomar M, Feijani FA, Abdolrazagh H, Razavi SZ, Tayebi O. Demographical, Anatomical, Disease-Related, and Occupational Risk Factors for Carpal Tunnel Syndrome. Archives of Neuroscience. 2021 Nov; 8(4). 10.5812/ans.117607.

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Original Article

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Evaluation of Post Obturation Pain Associated with Tricalcium Silicate and Resin-Bond Root Canal Sealer in Single Visit Root Canal Treatment-Quasi-Experimental Study

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ABSTRACT

Despite advancements in root canal sealers, post-obturation pain remains a concern for both patients and clinicians. **Objectives:** To compare the post-obturation pain associated with tricalcium silicate and resin-bond root canal sealer. **Methods:** This quasi-experimental study was conducted at Liaquat University of Medical and Health Sciences, Jamshoro, Hyderabad, using non-probability consecutive sampling on 254 patients. Participants, aged 18 to 45, needed root canal therapy on a permanent single-rooted tooth with a single canal with irreversible pulpitis without apical periodontitis. Group A received AH Plus resin-based sealer, while Group B was treated with BioRoot RCS calcium silicate-based sealer. Root canal procedures followed endodontic guidelines, including pulp testing, anesthesia, canal shaping with nickel-titanium rotary files, obturation with gutta-percha and sealers, and composite resin restoration. The visual analogue scale assessed Pain and treatment efficacy at 24 hours and 7 days post-obturation. **Results:** Group A had 46 male (36.2%) and 81 female (63.8%) with a mean age of 30.2 years (11.2), while Group B had 59 male (46.5%) and 68 female (53.5%) with a mean age of 34.5 years (12.4). At 24 hours, postoperative pain was significantly lower in Group B (3.13 ± 1.23) than in group A (3.59 ± 1.38, p=0.008), while pain differences were not significant preoperatively (p=0.78) or after seven days (p=0.08). **Conclusions:** It was concluded that in single-visit root canal treatment, both BioRoot root canal sealers (Septodont) tricalcium silicate-based sealer and AH Plus (Dentsply) resin-based sealer demonstrated similar efficacy in post-obturation pain.

INTRODUCTION

Single-visit root canal treatment is increasingly common because it requires less time, has a lower risk of infection, and leads to higher patient satisfaction [1]. Although endodontic treatment can relieve the pain of pulpitis, postoperative discomfort may still occur in some cases [2]. There are several potential causes of postoperative discomfort in endodontic therapy, including chemical, mechanical, or bacterial damage to the periodontal tissues [3]. To ensure the success of root canal therapy and prevent microbial invasion from the oral environment into the periradicular tissue, it is essential to thoroughly debride the root canal system using chemomechanical methods and seal the canal space. An inadequate seal during obturation might cause oral fluids to seep into

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spaces in the obturated root canal and trigger an inflammatory response in the periapical region, which can cause discomfort after surgery [4]. Post-obturation pain can occur in 3% to 58% of cases, with discomfort most commonly reported in the first two days after treatment [4, 5]. Gutta-percha points in the root canal require sealers as luting agents to ensure a secure fit and reduce leakage, contributing to long-term success. Sealers can also fill lateral or accessory canals that obturation material may not adequately infiltrate [6, 7]. AH Plus (Dentsply) is an epoxy resin-based sealer broadly consumedly because of its favorable physical properties, strong adhesion to root dentin, low solubility, effective apical sealing, and sufficient antibacterial properties. However, AH Plus has been shown to have varying levels of cytotoxicity and lacks mineralization potential [8]. BioRoot RCS, a tricalcium silicate-based sealer, provides a robust three-dimensional seal along the root canal, enhancing the integrity and longevity of fillings for successful endodontic outcomes. It releases growth factors, reducing cytotoxicity in the periodontal ligament and increasing antibacterial activity [9]. It has excellent penetration capacity into the dentinal tubules and outstanding radiopacity [10]. Moreover, residual calcium hydroxide did not influence the penetrative extent of BioRoot RCS when it was used as an intracanal medicine [11]. Post-obturation pain is a common concern following root canal treatment, impacting patient comfort and satisfaction. This study compares two widely used root canal sealers tricalcium silicate-based sealer (BioRoot RCS) and resin-based sealer (AH Plus)—to evaluate their effectiveness in minimizing post-treatment pain in a single-visit setting. Currently, no local studies have explored this comparison, making this research essential for informing clinical decisions within the region. By assessing the pain outcomes associated with these materials, this study aims to guide sealer selection for effective treatment and improved patient comfort.

This study aims to compare the post-obturation pain associated with tricalcium silicate and resin-bond root canal sealer.

METHODS

This quasi-experimental study was conducted from January 2022 to December 2022 at the Department of Operative Dentistry, Liaquat University of Medical and Health Sciences, Jamshoro, Hyderabad, using non-probability sequential sampling. The minimum required sample size was calculated using OpenEpi software to be 96, based on a 72.3% pain incidence on day 3 after obturation with a resin-based sealer and 27.7% with a calcium-based sealer, at 90% power and a 95% confidence level. However, 254 patients (127 per group) were included in the study. Written informed consent was obtained from all participants. Ethical approval was obtained before the start of the study (LUMHS/REC/.186). Patients were divided into two groups: Group B received resin bond sealer treatment (127 patients), and Group A received tricalcium silicate sealer treatment (127 patients). Patients aged 18 to 45 years requiring root canal therapy for a permanent single-rooted tooth with a single non-calcified canal diagnosed with irreversible pulpitis were included in the study, while patients having active periodontal disease or apical periodontitis were excluded from the study. Additionally, these patients needed to present with moderate to severe pain, scoring between 4 and 10 on a visual analogue scale. Before treatment, pulpal sensibility was evaluated using the Waldent electric pulp tester and the cold test (ethyl chloride). Percussion and palpation tests were also performed. Patients with irreversible pulpitis received treatment according to the dental endodontic guidelines. The tooth was anaesthetized with 2% lignocaine containing 1:100,000 epinephrine (Septodont) and isolated using a rubber dam. An access cavity was created with a No.2 round carbide bur after carious lesions and flawed restorations were eliminated and enlarged with an Endo Z bur using a sterile high-speed handpiece (Easy) with water irrigation. A periapical radiograph was used to validate the working length, which was established utilizing an electronic apex finder (E-PEX PRO Eighteeth, Changzhou Sifary Medical Tech) and a No. 10 K-file (Mani) following coronal flaring of the cervical third of the root canal. Using the crown-down technique, nickel-titanium rotary files (M3-Pro Gold) and 3% sodium hypochlorite (Canasol) were used to clean and shape the canals. Stainless steel K-files were used to complete the process in larger canals. Following shaping and cleaning, the canals were allowed to dry before being obturated with Gutta Percha cones (Gapadent) and either AH Plus or Bioroot RCS sealers. The subjects were allocated into two groups without randomization as per the type of sealer used. In group A, AH Plus (Dentsply) was employed as the root canal sealer: Radiographs were used to validate the apical range of the master cone. The sealer was prepared as per the manufacturer's suggestions. The root canal was sealed utilizing lentulospirals and a slow-speed handpiece. The obturation was carried out with the lateral compaction technique and gutta-percha cones (Gapadent). Group B: BioRoot RCS, a calcium silicate-based sealant was used. The sealer was prepared following the instructions provided by the manufacturer. The obturation procedure followed the same protocol as Group A. Enduring restoration was performed with composite resin (Biodinamica-Master fill), and the occlusion was relieved. A visual analogue scale (VAS) was employed to quantify postoperative pain after obturation. The patient was contacted 24 hours and 7 days later to measure pain and

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efficacy using the VAS. When there was little or no pain (0–3) on the VAS, the clinical effect was classified as positive, and when there was pain (4–10) on the VAS, it was classified as negative. The data were analyzed using version 22.0 of SPSS. Frequencies and percentages were calculated for qualitative factors, including background, tooth type (anterior and posterior), sex, and distribution according to effectiveness. Mean and standard deviation were calculated for age and pain. Pain scores and the presence of pain were compared between the two groups using independent samples t-tests and chi-square tests, respectively. A threshold of p≤0.05 was considered the level of significance.

RESULTS

There were 46 male (36.2%) and 81 female (63.8%) in Group A, while Group B had 59 male (46.5%) and 68 female (53.5%). The difference was not significant (p=0.09). The AH plus sealer group (n=127) had a mean age of 30.2 years (SD 11.2) and an age range of 18 to 55 years, while the BioRoot RCS sealer group (n=127) had a mean age of 34.5 years (SD 12.4) with an age range of 18 to 70 years. The difference was statistical significance (p=0.004). Patients had the anterior tooth type (65.4%); however, 83 subjects in AH plus sealer and 86 subjects in BioRoot RCS were found, whereas posterior tooth types were seen less frequently (34.6%) with 44 subjects in AH plus sealer and 41 participants in BioRoot RCS. There was no significant difference (p=0.69) (Table 1).

Table 1: Tooth Type Distribution in Both Groups (n=254)

Tooth Type	AH Plus Sealer (n=127)	BioRoot RCS Sealer (n=127)	p-value*
Anterior	83 (65.4%)	86 (67.7%)	0.690
Posterior	44 (34.6%)	41 (32.3%)	

*Chi-Square Test

Pre-operative pain scores were similar for both groups, with mean scores of 7.54 ± 1.13 for the AH plus sealer and 7.56 ± 1.20 for the BioRoot RCS sealer (p=0.78). However, significant differences were observed in postoperative pain after 24 hours, with the AH plus sealer group reporting a mean pain score of 3.59 ± 1.38 compared to 3.13 ± 1.23 in the BioRoot RCS sealer group (p=0.008). After 7 days, the pain scores were minimal, with the AH plus sealer group reporting 0.02 ± 0.15 and the BioRoot RCS group reporting 0.00, showing no significant difference (p=0.08) (Table 2).

Table 2: Comparison of Pain at Various Time Points Between Both Groups (n=254)

Time of Pain Measures	AH Plus Sealer (n=127)	BioRoot RCS Sealer (n=127)	p-value*
Pre-operative Pain	7.54 ± 1.13	7.56 ± 1.20	0.78
Postoperative Pain After 24 Hours	3.59 ± 1.38	3.13 ± 1.23	0.008
Postoperative Pain After 7 Days	0.02 ± 0.15	0.00	0.08

*Independent Samples T-Test

After 24 hours, the pain was reported by 126 participants (99.2%) in the AH plus sealer group and by 125 participants (98.4%) in the BioRoot RCS sealer group and the results were not statistically significant (p=0.56). After 7 days, all participants in both groups reported pain relief (p=1.0) (Table 3).

Table 3: Comparison of Pain at Various Time Points Between Both Groups (n=254)

Variables		AH Plus Sealer (n=127)	BioRoot RCS Sealer (n=127)	p-value
Pain After 24 Hours	Yes	126 (99.2%)	125 (98.4%)	0.561
	No	1 (0.8%)	2 (1.6%)	
Pain After 7 Days	Yes	127 (100.0%)	127 (100.0%)	1.000
	No	0 (0.0%)	0 (0.0%)	

DISCUSSION

The adoption of clinical treatments in endodontic therapy is contingent upon the reduction of patient suffering, in addition to their effectiveness and biological implications. Studies have concentrated on problems associated with therapies or methods meant to provide proof to bolster medical judgements. In this study, pre-operative assessment of pain shows a non-significant difference (p-value=0.788) in both groups i.e., 7.54 ± 1.13 and 7.56 ± 1.20 in group A and group B respectively. Postoperative assessment of pain showed a significant difference (p-value=0.008) in both groups (3.59 ± 1.38 and 3.13 ± 1.23, respectively) after 24 hours and a non-significant difference (p-value=0.082) in both groups i.e., 0.02 ± 0.15 and 0.0 ± 0.0 after 7 days in group and group B respectively. According to a study by Tan *et al.*, there was no discernible difference in pain experienced 1, 3, and 7 days after obturation between teeth filled with AH Plus or Total Fill BC Sealer and those filled with resin-based sealers [12]. This study evaluated post-obturation discomfort associated with these sealer procedures. In a study published in 2013, the effectiveness of poxy-based sealer (AH plus) and calcium silicate sealer (BioRootTM RCS) was examined by Zavattini *et al.*, [13]. Comparing BioRoot RCS (Septodont) with a single cone to warm vertical condensation and AH Plus (Dentsply DeTrey, Konstanz), they discovered that the success rate for patients was comparable. A meta-analysis and systematic review of clinical trials comparing the outcomes of nonsurgical endodontic therapy using calcium silicate-based vs. resin-based sealers was conducted by Chopra *et al.*, [14]. According to research, sealers based on calcium silicate functioned as well as resin-based sealers, exhibiting comparable outcomes regarding mean post-obturation discomfort level, onset threat, and pain threshold at 24 and 48 hours. In a different research, Song *et al.*, [15]. examined the use of epoxy-resin-based and calcium-silicate-based sealers for root canal obturation. They found no discernible differences between the sealers, and postoperative discomfort was

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not strongly influenced by either form. To evaluate the effects of one epoxy resin-based sealer and two calcium silicate-based sealers on postoperative pain, Aslan *et al.*, [16]. performed a study. The findings revealed no discernible variation in the degree of postoperative discomfort after a single-visit root canal procedure between AH Plus, Endoseal Mineral Trioxide Aggregate (MTA), and Endosequence BC Sealer. Ferreira *et al.*, investigated post-procedure pain after root canal filling with several endodontic sealers and found that EndoFill, MTA Fillapex, and AH Plus caused the same amount, frequency, and need for analgesic use [17]. Based on Thakur *et al.*, [18]. MTA may be utilized as a root canal sealer, as well as sealers based on epoxy resin or zinc oxide eugenol when comparing pain, periapical status, and area measurement after root canal filling with various endodontic sealers. A possible reason for postoperative pain can be preoperative discomfort [19, 20]. Current research is significant because it showed that the AH Plus resin-based sealer is more effective than the BioRoot RCS tricalcium silicate-based sealer in managing post-obturation pain during single-visit root canal treatments at 24 hours but the effect becomes similar after one week.

CONCLUSIONS

It was concluded that in single-visit root canal treatment, both BioRoot RCS (Septodont) tricalcium silicate-based sealer and AH Plus (Dentsply) resin-based sealer demonstrated similar efficacy in terms of post-obturation pain.

Authors Contribution

Conceptualization: TE
Methodology: TE, MAAA, AGS
Formal analysis: SS[2]
Writing review and editing: KM, BB, SS[1]

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

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REFERENCES

[1] Mergoni G, Ganim M, Lodi G, Figini L, Gagliani M, Manfredi M. Single Versus Multiple Visits For Endodontic Treatment Of Permanent Teeth. Cochrane Database of Systematic Reviews. 2022 Dec. doi: 10.1002/14651858.CD005296.pub4.

[2] Azizi H, Hadad A, Levy DH, Ben Itzhak J, Kim HC, Solomonov M. Epoxy vs. Calcium Silicate-Based Root Canal Sealers for Different Clinical Scenarios: A Narrative Review. Dentistry Journal. 2024 Mar; 12(4): 85. doi: 10.3390/dj12040085.

[3] Pandey NK, Goud KM, Bhalla V, Kumari P, Jose S. Comparative Evaluation of A Resin-Based and Calcium Silicate-Based Root Canal Sealer On Postoperative Pain: A Split-Mouth Randomized Controlled Trial. International Journal of Dental Science and Innovative Research. 2020; 240(2): 245.

[4] Rana MJ, Rana MA, Alam M, Bangash AY, Bhangar F, Munir A. A Comparison Between AH 26 and Sealapex for Post-Obturation Pain. Pakistan Armed Forces Medical Journal. 2022 Dec; 72(6): 1925-28. doi: 10.51253/pafmj.v72i6.5460.

[5] Sadaf D and Ahmad MZ. Factors Associated With Postoperative Pain In Endodontic Therapy. International Journal of Biomedical Science: 2014 Dec; 10(4): 243. doi: 10.59566/IJBS.2014.10243.

[6] Komabayashi T, Colmenar D, Cvach N, Bhat A, Primus C, Imai Y. Comprehensive Review of Current Endodontic Sealers. Dental Materials Journal. 2020 Sep; 39(5): 703-20. doi: 10.4012/dmj.2019-288.

[7] Zhang W and Peng B. Tissue Reactions After Subcutaneous and Intraosseous Implantation of iRoot SP, MTA and AH Plus. Dental Materials Journal. 2015 Nov; 34(6): 774-80. doi: 10.4012/dmj.2014-271.

[8] Alsubait S, Albader S, Alajlan N, Alkhunaini N, Niazy A, Almahdy A. Comparison of the Antibacterial Activity of Calcium Silicate-and Epoxy Resin-Based Endodontic Sealers Against Enterococcus Faecalis Biofilms: A Confocal Laser-Scanning Microscopy Analysis. Odontology. 2019 Oct; 107: 513-20. doi: 10.1007/s10266-019-00425-7.

[9] Siboni F, Taddei P, Zamparini F, Prati C, Gandolfi MG. Properties of BioRoot RCS, a Tricalcium Silicate Endodontic Sealer Modified with Povidone and Polycarboxylate. International Endodontic Journal. 2017 Dec; 50: e120-36. doi: 10.1111/iej.12856.

[10] Viapiana R, Moinzadeh AT, Camilleri L, Wesselink PR, Tanomaru Filho M, Camilleri J. Porosity and Sealing Ability of Root Fillings with Gutta-Percha and Bioroot RCS Or AH Plus Sealers. Evaluation By Three Ex Vivo Methods. International Endodontic Journal. 2016 Aug; 49(8): 774-82. doi: 10.1111/iej.12513.

[11] Uzunoglu-Özyürek E, Erdoğan Ö, Türker SA. Effect of Calcium Hydroxide Dressing on the Dentinal Tubule Penetration of 2 Different Root Canal Sealers: A Confocal Laser Scanning Microscopic Study. Journal of Endodontics. 2018 Jun; 44(6): 1018-23. doi: 10.1016/j.joen.2018.02.016.

[12] Tan HS, Lim KC, Lui JN, Lai WM, Yu VS. Postobturation Pain Associated with Tricalcium Silicate and Resin-Based Sealer Techniques: A Randomized Clinical Trial. Journal of Endodontics.

DOI: https://doi.org/10.54393/pjhs.v5i12.2226

2021 Feb; 47(2): 169-77. doi: 10.1016/j.joen.2020.10.013.

[13] Zavattini A, Knight A, Foschi F, Mannocci F. Outcome of Root Canal Treatments Using A New Calcium Silicate Root Canal Sealer: A Non-Randomized Clinical Trial. Journal of Clinical Medicine. 2020 Mar; 9(3): 782. doi: 10.3390/jcm9030782.

[14] Chopra V, Davis G, Baysan A. Clinical and Radiographic Outcome of Non-Surgical Endodontic Treatment Using Calcium Silicate-Based Versus Resin-Based Sealers—A Systematic Review and Meta-Analysis of Clinical Studies. Journal of Functional Biomaterials. 2022 Apr; 13(2): 38. doi: 10.3390/jfb13020038.

[15] Song M, Park MG, Kwak SW, Kim RH, Ha JH, Kim HC. Pilot Evaluation of Sealer-Based Root Canal Obturation Using Epoxy-Resin-Based and Calcium-Silicate-Based Sealers: A Randomized Clinical Trial. Materials. 2022 Jul; 15(15): 5146. doi: 10.3390/ma15155146.

[16] Aslan TU and Dönmez Özkan H. The Effect of Two Calcium Silicate-Based and One Epoxy Resin-Based Root Canal Sealer On Postoperative Pain: A Randomized Controlled Trial. International Endodontic Journal. 2021 Feb; 54(2): 190-7. doi: 10.1111/iej.13411.

[17] Ferreira ND, Gollo EK, Boscato N, Arias A, Silva EJ. Postoperative Pain After Root Canal Filling with Different Endodontic Sealers: A Randomized Clinical Trial. Brazilian Oral Research. 2020 Jul; 34: e069. doi: 10.1590/1807-3107bor-2020.vol34.0069.

[18] Thakur S, Emil J, Paulaian B. Evaluation of Mineral Trioxide Aggregate As Root Canal Sealer: A Clinical Study. Journal of Conservative Dentistry and Endodontics. 2013 Nov; 6(6): 494-8. doi: 10.4103/0972-0707.120944.

[19] Yu YH, Kushnir L, Kohli M, Karabucak B. Comparing the Incidence of Postoperative Pain After Root Canal Filling with Warm Vertical Obturation with Resin-Based Sealer and Sealer-Based Obturation with Calcium Silicate-Based Sealer: A Prospective Clinical Trial. Clinical Oral Investigations. 2021 Aug; 25: 5033-42. doi: 10.1007/s00784-021-03814-x.

[20] Alí A, Olivieri JG, Duran-Sindreu F, Abella F, Roig M, García-Font M. Influence of Preoperative Pain Intensity On Postoperative Pain After Root Canal Treatment: A Prospective Clinical Study. Journal of Dentistry. 2016 Feb; 45: 39-42. doi: 10.1016/j.jdent.2015.12.002.

DOI:https://doi.org/10.54393/pjhs.v5i12.2348

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Original Article

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Assessment of Diagnostic Accuracy of Interleukins and Procalcitonin in Patients with Severe Illness and Suspected Sepsis

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ABSTRACT

The immune system's dysregulated response to infection, known as sepsis, is a severe potentially fatal illness that results in organ failure, tissue destruction, and systemic inflammation. **Objectives:** To explore the correlation between levels of interleukins and pro-calcitonin and the severity of sepsis and clinical outcomes. **Methods:** This cross-sectional study was conducted at Khairpur Medical College Civil Hospital Khairpur. The participants were n=200 including both male and female. The age range was 18-45 years. Procalcitonin levels were measured using enzyme-linked fluorescent assay and flow cytometry to elevate levels of different cytokines. Serum cytokine concentrations were compared between sepsis patients and healthy controls using the Mann-Whitney U-test for two-group comparisons. The diagnostic accuracy of cytokine levels at study entry was assessed through the area under the receiver operating characteristic curve derived from logistic regression analysis. **Results:** A positive culture report of microbial infectious disease was found in 100/200 (50%) of the patients after microbiological investigation. The male-to-female ratio in the investigated demographic was 3:2. Interleukin-6 levels were significantly higher, p<0.001 in the infectious diseases group than non-infectious Diseases Group. The area under the receiver operating characteristic value of interleukin-6 was found to be excellent and significantly higher (0.95(0.75-0.97)). **Conclusions:** Cytokines including Interleukin-6 and Interleukin-8 are strong biomarkers for diagnosing microbial infections in suspected sepsis cases, with interleukin-6 showing the highest diagnostic accuracy (AUC=0.912). Procalcitonin also demonstrated good discriminative power (AUC=0.895). While cytokines like Interleukin-2, tumor necrosis factor, and Interleukin-17A showed moderate value, interleukin-4 and interferon-gamma were less useful.

INTRODUCTION

Severe sepsis and septic shock, with a mortality rate of 40-50%, are major contributors to deaths in critically ill patients. Blood culture, the standard method for identifying infections in sepsis, is labor-intensive and can take days or weeks for results. Total leukocyte count (TLC) has also proven inconsistent for sepsis detection, highlighting the need for more sensitive and specific biomarkers [1, 2]. Scientists are increasingly exploring alternative markers that better differentiate between infectious and non-infectious states. Receptors like the lipopolysaccharide (LPS) receptor aid the immune system in distinguishing pathogens from non-harmful molecules, leading to the production of various cytokines, such as Interleukins (IL)-1, IL-6, IL-8, IL-12, IL-15, IL-18, IL-23, and tumor necrosis factor (TNF) [3]. For instance, TNF, the primary mediator in toxic shock and sepsis, triggers inflammation and vascular permeability, contributing to symptoms such as fever, anorexia, and hypotension in septic shock [4, 5]. Several cytokines, including pro-calcitonin (PCT), C-reactive protein (CRP), IL-6, and IL-8, have shown promise as biomarkers for sepsis. Procalcitonin, in particular, has demonstrated a strong

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correlation with infection severity, often outperforming traditional markers like TLC and CRP [6]. IL-6, a pro-inflammatory cytokine, plays a key role in the early response to infections and has potential as a guide for antibiotic therapy, as its levels correlate with infection severity [7]. Monitoring IL-6 may help differentiate bacterial infections from other inflammatory conditions and track disease progression or remission, making it a valuable tool for infection management [8]. IL-10, an anti-inflammatory cytokine, helps regulate immune responses by limiting tissue damage. Although it typically acts to moderate inflammation, high IL-10 levels in sepsis may indicate an excessive inflammatory reaction, often seen in worsening sepsis cases. Elevated IL-10 has been associated with severe sepsis and septic shock, reflecting the immune system's struggle to contain widespread inflammation [9]. Additionally, interferon-gamma (IFN-γ), primarily produced by T cells and Natural killer (NK) cells, plays a role in the immune response against infections and inflammation [10]. Technological advances now allow for the rapid detection of multiple interleukins through methods like the flow cytometric cytokine bead array (CBA) assay, which provides results within hours using a small sample volume [11]. Such advances could lead to more efficient and accurate sepsis diagnosis and monitoring, offering the potential for improved outcomes in critically ill patients.

Although the role of interleukins and procalcitonin in assessing sepsis is well-established, the sensitivity and specificity of these biomarkers when used in combination for early diagnosis, especially in critically ill patients with ambiguous clinical symptoms, remains underexplored. Current studies often rely on one marker or lack a comprehensive comparison with clinical presentation. This study aims to fill the gap by evaluating the diagnostic accuracy of both biomarkers together, potentially leading to improved early detection and management strategies for sepsis.

This study aims to evaluate the diagnostic accuracy of procalcitonin (PCT) with interleukins in patients and to determine, and compare the most useful biomarkers for sepsis diagnosis.

METHODS

This cross-sectional study was conducted at Khairpur Medical College Civil Hospital, Khairpur Mirs, for six months (December 2023–May 2024). The study included 200 participants, both male and female, aged 20–45 years, admitted to the Intensive Care Unit (ICU) with suspected infection. Inclusion criteria encompassed clinical signs of infection, such as fever and tachycardia, while exclusion criteria included pregnancy, lactation, chronic autoimmune diseases, immunosuppressant use, and refusal to consent. Participants were divided into three groups: Infectious (microbiologically confirmed infections, Microbial-Infectious diseases (MDI)-positive), Non-Infectious (symptoms of infection but MDI-negative), and Healthy Controls (no signs of infection). A convenience sampling method was employed, with a sample size determined using the formula n= Z2×p×(1–p) /E2: Z-value (Z): assuming a 95% confidence level (Z=1.96), an estimated proportion (p) of 0.5, and a margin of error (E) of 0.0693. Microbiological testing, including cultures from various sources, was conducted. Plasma samples, collected before antibiotic administration, were stored at -80°C for cytokine analysis. Cytokines (IL-2, IL-4, IL-6, IL-10, TNFα, IFN-γ, and IL-17A) were measured using a BDTM Cytometry bead array (CBA) Cytokine Kit and flow cytometry, and procalcitonin (PCT) was measured using ELFA stands for Enzyme-Linked Fluorescent Assay. Data were analyzed using SPSS version 24.0, with cytokine concentrations compared between groups via the Mann-Whitney U test and diagnostic accuracy assessed by the area under the Receiver operating characteristic (ROC) curve from logistic regression analysis. A p-value of <0.005 was considered significant. Institutional Review Board approval was obtained (KMC/RERC/76) from Khairpur Medical College Civil Hospital, Khairpur Mirs and informed consent was secured from all participants.

RESULTS

The mean age of participants was 32.5 years and a standard deviation of 7.5 years, consisting of 120 male (60%) and 80 female (40%). Among the participants, 22.5% had hypertension, 25% had heart disease, and 27.5% had diabetes, while smoking status was nearly evenly split, with 50.5% smokers and 49.5% non-smokers. The participants were classified into three groups: 100 (50%) in the Microbial-Infectious diseases group (MID positive), 50 (25%) in the MID negative group, and 50 (25%) in the healthy control group, facilitating a comparative analysis of health outcomes across conditions (Table 1).

Table 1: Demographic characteristics of the study population

Characteristics	Total Number of Participants n= 200
Age	
20-45 Years	32.5±7.5 years
Gender	
Male	120 (60%)
Female	80 (40%)
Comorbidities	
Hypertension	45 (22.5%)
Heart Disease	50 (25%)
Diabetes	55 (27.5%)
Smoking Status	
Yes	101 (50.5%)

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No	99 (49.5%)
Sepsis Group	
Microbial-Infectious Diseases Group	100 (50%)
Microbial Non-Infectious Diseases Group	50 (25%)
Healthy Group	
Healthy control Group	50 (25%)

MID (Microbial infectious diseases) refers to participants with active infections, Non-infectious (MID negative) refers to those with microbial-related conditions that are not infectious

The analysis reveals that IL-6 and IL-8 levels are significantly elevated in the infectious group compared to the non-infectious and healthy control group, suggesting their potential as key biomarkers for identifying infection. IL-2, TNF, and IL-17A also show moderate differences, with higher levels in the infectious group, indicating some utility in distinguishing infection from non-infection. However, IL-4 and IFN-γ do not vary significantly across groups, suggesting limited diagnostic relevance in this context. These findings highlight IL-6 and IL-8 as primary indicators for infection, with other cytokines providing supplementary diagnostic value (Table 2).

Table 2: Different Cytokine Levels among study participants

Biomarker	Sepsis Group		Healthy Group	p-value (Kruskal-Wallis)
	Infectious Group (MDI Positive) (n=100) Median (IQR)	Non-Infectious Group (MDI Negative) (n=50) Median (IQR)	Healthy Control Group (n=50) Median (IQR)	
IL-2	5.7 (0-32)	5.0 (0-12)	3.4 (0-4)	0.03*
IL-4	3.9 (0-28)	3.0 (0-16)	3.7 (0-4)	0.07
IL-6	1677.3 (4-5000)	901.0 (4-5000)	4 (4-4)	<0.001**
IL-8	145.8 (0-1764)	110.4 (4-1372)	3.7 (0-4)	<0.001**
TNF	6.9 (0-48)	4.2 (0-20)	3.7 (0-4)	0.04*
IFN-γ	14.1 (0-148)	6.8 (0-28)	16.0 (0-36)	0.09
IL-17A	12.8 (0-92)	9.8 (0-44)	31.1 (4-48)	0.02*

Statistical; Mann-Whitney U test each cytokine comparison between two groups of sepsis (MDI positive, MDI negative) with a healthy group

With the greatest Area under the curve (AUC) value of 0.912 (95% CI: 0.853-0.971), according to the ROC analysis, IL-6 performed exceptionally well in differentiating between infected and non-infectious situations. Procalcitonin's AUC of 0.895 (p<0.001) demonstrated its great discriminative potential as well. The moderate AUC values of other cytokines, such as TNF, IL-2, IL-4, and IL-10, ranged from 0.678 to 0.756, indicating differing levels of efficacy in detecting infections. The clinical significance of these biomarkers in diagnostic contexts is further demonstrated by the sensitivity and specificity measurements (Table 3).

Table 3: Function of Cytokines with Procalcitonin

Cytokine/ Marker	AUC (95% CI)	p-value	Cut-off Value	TPR (Sensitivity, %)	FPR (1-Specificity, %)
IL-2	0.678 (0.578-0.778)	<0.001	5.5	70.0	20.0
IL-4	0.689 (0.600-0.778)	0.002	4.0	65.0	25.0
IL-6	0.912 (0.853-0.971)	<0.001	1000	85.0	10.0
IL-8	0.712 (0.618-0.806)	0.005	150	68.0	23.0
TNF	0.678 (0.578-0.778)	0.012	6.0	60.0	30.0
Pro-calcitonin	0.895 (0.820-0.970)	<0.001	0.5	90.0	15.0

The moderate AUC values of other cytokines, such as TNF, IL-2, IL-4, and IL-10, ranged from 0.678 to 0.756, indicating differing levels of efficacy in detecting infections (Figure 1).

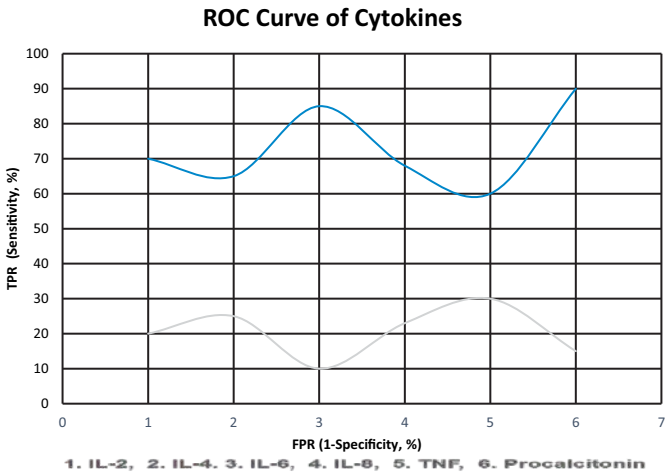

Figure 1: ROC Curves of the Activity of Cytokines

To visualize the ROC curve, plot FPR (x-axis) versus TPR (y-axis) for each cytokine/marker: X-axis: FPR (False Positive Rate, or 1 - Specificity). Y-axis: TPR (True Positive Rate, or Sensitivity). The ROC curve illustrates the diagnostic performance of cytokines and procalcitonin, with curves closer to the top left corner indicating better discriminative ability. IL-6 has the highest AUC at 0.912, followed closely by procalcitonin at 0.895. In contrast, other cytokines like IL-2, IL-4, IL-8, and TNF demonstrate lower AUC values, signifying reduced effectiveness in differentiating between groups.

DISCUSSION

Cytokines, which are repetitively secreted proteins, play significant roles in development, differentiation, and immune activation. These proteins regulate and specify immune responses, guide immune cell movement, and support cellular organization within immune organs [12]. The current study found that elevated levels of IL-2, IL-4, IL-6, IL-10, IFN-γ, TNF-α, and IL-17A correlate with severe

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infection and systemic inflammation in septic patients, with values above 100–300 pg/mL often indicative of sepsis. However, present results showed low specificity for procalcitonin (PCT) in differentiating gram-positive from gram-negative bacteria and reduced sensitivity in predicting infection severity compared to IL-6 and IL-10 [13, 14]. To measure cytokine levels, two widely used methods are Enzyme-Linked Immunosorbent Assay (ELISA) and Cytometry Bead Array (CBA). ELISA typically measures individual cytokines, while CBA allows simultaneous evaluation of multiple cytokines in a single sample, providing a broader cytokine profile. CBA uses fluorescent beads coated with specific antibodies, mixed with the sample, and analyzed via flow cytometry to quantify fluorescence emitted by the beads [15]. This method is particularly useful for studying cytokine interactions, as it is faster and more cost-effective, requiring a smaller sample volume compared to multiple ELISAs. However, CBA may have lower sensitivity than individual ELISAs, with detection limits varying by kit and cytokine [16]. In the current study, IL-6 and IL-10 were found to be more accurate sepsis biomarkers than PCT, with peak AUC values of 0.95 (0.75–0.97) and 0.90 (0.72–0.94) for IL-6 and IL-10, respectively [17]. Cytokine-based therapies hold potential for autoimmune diseases, cancer, and infections by either amplifying or dampening immune responses. Administering cytokines in combination with other treatments can maximize efficacy while reducing toxicity. Present findings suggest that while IL-6 and IL-10 effectively diagnose sepsis, PCT and IL-6 are particularly effective for sepsis severity, with PCT helping assess bacterial infection severity [18, 19]. PCT showed a robust ability to differentiate between infectious and non-infectious cases, with high AUC values in septic individuals. Early PCT measurement may improve the detection and follow-up of sepsis, making it an invaluable biomarker for identifying bacterial infections [20]. Additionally, curent study found that TNF-α and IFN-γ levels were significant in predicting infection severity, with AUCs of 0.85 (0.63–0.90) and 0.80 (0.66–0.91), respectively. This correlation could make them valuable markers during septic shock [21]. Research also shows that reactive oxygen and nitrogen species, generated by macrophages in response to IFN-γ, are critical in destroying intracellular pathogens like Mycobacterium tuberculosis. IFN-γ has shown potential in enhancing T-cell responses and antigen presentation, essential in treating drug-resistant tuberculosis. While not a first-line treatment, IFN-γ may be effective in cases where traditional therapies fail, though its usage requires careful evaluation due to cost, accessibility, and possible side effects.

CONCLUSIONS

It was concluded that IL-6 and IL-8 are strong biomarkers for diagnosing microbial infections in suspected sepsis cases, with IL-6 showing the highest diagnostic accuracy (AUC=0.912). Procalcitonin also demonstrated good discriminative power (AUC = 0.895). While cytokines like IL-2, TNF, and IL-17A showed moderate value, IL-4 and IFN-γ were less useful. These findings highlight the importance of IL-6 and IL-8 in infection diagnosis, enhancing clinical decision-making and potentially improving patient outcomes.

Authors Contribution

Conceptualization: AHP
Methodology: AHP, MK, AA, AQM, MAC, SAP
Formal analysis: AQM, MAC
Writing review and editing: AA, SAP

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] La Via L, Sangiorgio G, Stefani S, Marino A, Nunnari G, Cocuzza S, La Mantia I, Cacopardo B, Stracquadanio S, Spampinato S, Lavalle S. The global burden of sepsis and septic shock. Epidemiologia.2024 Jul 25;5(3):456-78. doi: 10.3390/epidemiologia5030032.

[2] Liu YC, Yao Y, Yu MM, Gao YL, Qi AL, Jiang TY *et al.* Frequency and Mortality of Sepsis and Septic Shock in China: A Systematic Review and Meta-Analysis. BioMed Central Infectious Diseases.2022 Jun; 22(1):564.doi: 10.1186/s12879-022-07543-8.

[3] Mulatu HA, Bayisa T, Worku Y, Lazarus JJ, Woldeyes E, Bacha D *et al.* Prevalence and Outcome of Sepsis and Septic Shock in Intensive Care Units in Addis Ababa, Ethiopia: A Prospective Observational Study. African Journal of Emergency Medicine.2021 Mar; 11(1): 188-95. doi: 10.1016/j.afjem.2020.10.001.

[4] Pfortmueller CA, Dabrowski W, Wise R, Van Regenmortel N,Malbrain ML.Fluid accumulation syndrome in sepsis and septic shock: pathophysiology,relevance and treatment—a comprehensive review. Annals of intensive care.2024 Jul 20;14(1):115. doi: 10.1186/s13613-024-01336-9.

[5] Kamath S, Hammad Altaq H, Abdo T. Management of sepsis and septic shock: what have we learned in the last two decades?. Microorganisms.2023 Sep

DOI:https://doi.org/10.54393/pjhs.v5i12.2348

4;11(9):2231. doi: 10.3390/microorganisms11092231.

[6] Dupuis C, Bouadma L, Ruckly S, Perozziello A, Van-Gysel D, Mageau A *et al.* Sepsis and Septic Shock in France: Incidences, Outcomes and Costs of Care. Annals of Intensive Care.2020 Dec; 10: 1-9. doi:10.1186/s13613-020-00760-x.

[7] Gavelli F, Castello LM, Avanzi GC. Management of Sepsis and Septic Shock in the Emergency Department. Internal and Emergency Medicine. 2021 Sep; 16(6): 1649-61. doi: 10.1007/s11739-021-02735-7.

[8] Li Y, Guo J, Yang H, Li H, Shen Y, Zhang D. Comparison of culture-negative and culture-positive sepsis or septic shock: a systematic review and meta-analysis. Critical Care.2021 May; 25(1): 167. doi: 10.1186/s13054-021-03592-8.

[9] Vermassen J, Decruyenaere J, De Bus L, Depuydt P, Colpaert K. Characteristics of Sepsis-2 septic Shock Patients Failing to Satisfy the Sepsis-3 Septic Shock Definition: An Analysis of Real-Time Collected Data. Annals of Intensive Care.2021 Dec; 11: 1-8. doi: 10.1186/s13613-021-00942-1.

[10] Rudd KE, Johnson SC, Agesa KM, Shackelford KA, Tsoi D, Kievlan DR *et al.* Global, Regional, and National Sepsis Incidence and Mortality, 1990–2017: Analysis for the Global Burden of Disease Study. The Lancet.2020 Jan; 395(10219): 200-11. doi: 10.1016/S0140-6736(19)32989-7.

[11] Kim YJ, Kim MJ, Kim YJ, Kim WY. Short and Long-Term Mortality Trends for Cancer Patients with Septic Shock Stratified by Cancer Type from 2009 to 2017: A Population-Based Cohort Study. Cancers.2021 Feb;13(4): 657. doi: 10.3390/cancers13040657.

[12] Rothrock SG, Cassidy DD, Barneck M, Schinkel M, Guetschow B, Myburgh C *et al.* Outcome of Immediate Versus Early Antibiotics in Severe Sepsis and Septic Shock: A Systematic Review and Meta-Analysis. Annals of Emergency Medicine.2020 Oct; 76(4): 427-41.doi: 10.1016/j.annemergmed.2020.04.042.

[13] Gorecki G, Cochior D, Moldovan C, Rusu E. Molecular Mechanisms in Septic Shock. Experimental and Therapeutic Medicine.2021 Oct; 22(4): 1-5. doi: 10.3892/etm.2021.10595.

[14] Rhee C, Chiotos K, Cosgrove SE, Heil EL, Kadri SS, Kalil AC *et al.* Infectious Diseases Society of America Position Paper: Recommended Revisions to the National Severe Sepsis and Septic Shock Early Management Bundle (SEP-1) Sepsis Quality Measure. Clinical Infectious Diseases.2021 Feb; 72(4):541-52.doi:10.1093/cid/ciaa059.

[15] Cui N, Zhang H, Chen Z, Yu Z. Prognostic Significance of PCT and CRP Evaluation for Adult ICU Patients with Sepsis and Septic Shock: Retrospective Analysis of 59 Cases.Journal of International Medical Research. 2019 Apr; 47(4): 1573-9. doi: 10.1177/0300060518822404.

[16] La Via L, Sangiorgio G, Stefani S, Marino A, Nunnari G, Cocuzza S *et al.* The Global Burden of Sepsis and Septic Shock. Epidemiology.2024 Jul; 5(3): 456-78. doi:10.3390/epidemiologia5030032.

[17] Sankar J, Garg M, Ghimire JJ, Sankar MJ, Lodha R, Kabra SK. Delayed Administration of Antibiotics Beyond the First Hour of Recognition Is Associated with Increased Mortality Rates in Children with Sepsis/Severe Sepsis and Septic Shock. The Journal of Pediatrics.2021 Jun; 233: 183-90. doi: 10.1016/j.jpeds.2020.12.035.

[18] Chiscano-Camón L, Ruiz-Sanmartin A, Bajaña I, Bastidas J, Lopez-Martinez R, Franco-Jarava C et al. Current Perspectives in the Management of Sepsis and Septic Shock. Frontiers in Medicine. 2024 Aug; 11: 1431791. doi: 10.3389/fmed.2024.1431791.

[19] Cinel I, Kasapoglu US, Gul F, Dellinger RP. The Initial Resuscitation of Septic Shock. Journal of Critical Care. 2020 Jun; 57: 108-17. doi:10.1016/j.jcrc.2020.02.004.

[20]Kamath S, Hammad Altaq H, Abdo T. Management of Sepsis and Septic Shock: What Have We Learned in the Last Two Decades? Microorganisms. 2023 Sep; 11(9): 2231. doi: 10.3390/microorganisms11092231.

[21] Van Der Velden FJ, Gennery AR, Emonts M. Biomarkers for Diagnosing Febrile Illness in Immunocompromised Children: A Systematic Review of the Literature. Frontiers in Pediatrics.2022 Mar; 10: 828569. doi: 10.3389/fped.2022.828569.

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Assessment of Husbands' Knowledge on Antenatal Care in a Tertiary Care Hospital, Karachi

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ABSTRACT

The husband's involvement during pregnancy was considered very disappointing earlier. As a result, women did not inform their husbands about their troubles and concerns during pregnancy. In some cases, the severity of complications leads to the death of the fetus and mother. However, with time, husbands now take responsibility for their wives during pregnancy and antenatal care. The involvement of husbands in antenatal care visits reduces the risk of maternal mortality. **Objective:** To evaluate the level of knowledge regarding antenatal care among husbands of pregnant women attending a tertiary care hospital in Karachi. **Methods:** A cross-sectional research design was selected and conducted with 360 husbands who accompanied their wives for the antenatal services at the Outpatient Gynecology and Obstetrics Department of Dow University of Health Sciences (DUHS) Ojha Campus Karachi. The study questionnaire comprised twenty questions about the husband's knowledge of antenatal care. Data were analyzed by using SPSS version 21.0. **Results:** The study findings showed that (57.5%) husbands felt that antenatal care was valuable, the majority of the husbands (95.6%) felt that it was not necessary to go for antenatal care if there was no complication, and (32.2%) husbands were considered to believe that a minimum of three antenatal visits were enough for the care. More than half were aware of the danger signs of pregnancy, and they knew that a pregnant woman should deliver her baby in the health care facility. **Conclusions:** The current research study concluded that a large number of husbands felt that antenatal care was valuable, but still a lack of knowledge was found in different antenatal care components. There was a need for awareness of all the components of antenatal care among husbands of pregnant women.

INTRODUCTION

Antenatal Care (ANC) is among the essential interventions in the effective continuum of care for the enhancement of maternal health. Antenatal Care (ANC) aims to provide safe and secure health services to both mother and child. The high maternal mortality in developing countries has shown a significant association with non-utilization of Antenatal Care (ANC). The world's maternal and neonatal morbidities can be improved if Antenatal Care (ANC) interventions are executed and operated [1]. The World Health Organization (WHO) has suggested antenatal education as a significant intervention to improve Maternal Mortality Ratio, especially in developing countries. In Pakistan, there is no standard antenatal education program exists. Factors such as low literacy, poor economic conditions, and cultural practices are the main hindrances in antenatal education programs. There is a need to establish a standard educational program to improve decision-making among parents regarding pregnancy and childbirth [2]. A research study conducted in India highlighted the importance of husband participation in Antenatal Care (ANC); the research also found that men with awareness of pregnancy-related problems and their wives are more approachable to

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utilizing services of maternal health. Hence, educating and authorizing men regarding pregnancy complications will play vital parts in lessening ongoing maternal and neonatal deaths [3]. The husband's support during and after pregnancy plays an important role in the mother's health and safe childbirth. The literature also showed that the women who lived away from their spouse during pregnancy are at more risk of having complications and may lose their pregnancies [4]. Moreover, a community survey at the Pakistan Institute of Medical Sciences Islamabad revealed a strong association between fathers' connection to maternal health with factors like fathers' education, age, criteria of income, and approach [5]. The stages of active involvement of men in antenatal care are different because of socio-cultural issues and work obligations. The majority of men showed adequate knowledge of antenatal care, mainly about the danger signs, and were involved in decision-making [6]. The male participation in antenatal services may encourage enhanced and efficient care, the knowledge of husband regarding antenatal services will also help in detecting and considering for health care in case of danger signs of pregnancy. The involvement of husband in antenatal services have a strong impact on both mother and child health outcomes [7].The cross-sectional study conducted in India reported that majority of husbands had sufficient knowledge about antenatal care, while only 4.7% did not have sufficient knowledge, the level of education was found to be significantly associated with the involvement of male partner in antenatal care [8].Furthermore the research study revealed that negative attitude of husbands towards antenatal care was due to social stigma and cultural hindrances, as many communities believed that it's the women's obligations and male has nothing to do with antenatal care [9]. The lack of husband support and involvement in antenatal care process were the leading barriers in achieving the antenatal care goal [10]. The results of research study conducted in Kenya indicated that 50% of the husbands knew about antenatal care, but only 31.8% were aware that ANC should be started in first trimester of pregnancy. Surprisingly no significant associations were found between demographic variables and husbands' attitude towards antenatal care [11]. Furthermore the study conducted in India also showed that the majority of the husbands had satisfactory knowledge regarding ANC, similarly no associations were found between knowledge score and demographic characteristics [12].Three major factors were identified in the study conducted in Uganda that are directly linked with the maternal death during pregnancy, the first factor was the poor decision making regarding health care facility for receiving care, second factor was the delay in transferring to health care setting due to lack of transport and third factor was the delay treatment at the health care setting.. At least two factors can be prevented by better male involvement in antenatal care [13]. Increased husband attendance in antenatal care was significantly associated with the factors such as, being married at 18years and older, better knowledge of pregnancy-related issues, higher education level and high economic status [14]. Furthermore many research studies from developing countries revealed that less than 50% of husband attended at least one antenatal care session [15].The objective of study is to evaluate the level of knowledge regarding antenatal care among husbands of pregnant women attending a tertiary care hospital in Karachi.

METHODS

The study design was cross-sectional. The current study was conducted at the OPD of Gynecology and Obstetrics Department, Dow University of Health Sciences Karachi. The study population was the husbands of pregnant women. The study was conducted from December 2020 to May 2021. The sample was selected using a consecutive sampling technique. The sample size of 360 participants was calculated using Open Epi Software with a 95% confidence interval, 80% power of test, and 5% margin of error. Inclusion criteria involve husbands and wives who visit their doctor and were willing to give their personal opinions on the research questionnaire. Exclusion criteria were based on age factors; less than 18-year-old and more than 47-year-old women were not added to this research. The study permission letter for data collection was taken from the university and the hospital's Medical Superintendent of DUHS with reference number (DUHS/ION/MSN/2020/405/18). Study approval was taken from the research committee of Dow University with reference number (DIONAM/MSN/2020/404-1). Each individual filled out the informed consent before the data collection. Data were collected using a questionnaire comprised of 20 questions. Data were collected on various factors, including age, family income, educational level, and husband's concern for their wives during pregnancy. The structured research questionnaire of 360 individuals was taken during DHUS OPD department visits with husbands and wives. This questionnaire was translated to those husbands who could not read English. The statistical package of the SPSS version 21.0 was used for data analysis. The percentage of the knowledge of the husbands was measured during this research questionnaire. Descriptive statistics such as percentages and frequency tables were used to display the results.

RESULTS

Table 1 presented a summary of the socio-demographic characteristics of a sample of 360 individuals. In terms of women's age, a greater number of individuals fall within the

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18-34 age category (83.3%), followed by the 35-50 age category (16.7%). Family types were mainly extended (56.4%), while nuclear families comprised (43.6%). Family income was different, with (13.6%) earning between 10,000–20,000 rupees, (38.6%) earning between 21,000-30,000 rupees and (47.8%) earning above 30,000 rupees. The educational status of husbands showed that (38.6%) were uneducated, (11.2%) completed primary school, (9.4%) completed secondary school and (40.8%) graduated high school.

Table 1: Socio Demographic Variables (n = 360)

Socio-Demographic Variables	Characteristics	N (%)
Age of Pregnant Women	18 - 34	300 (83.3%)
	35 - 50	60 (16.7%)
Type of Family	Nuclear	157 (43.6%)
	Extended	203 (56.4%)
Family Income Per Month	10,000 – 20,000	49 (13.6%)
	21,000 – 30,000	139 (38.6%)
	Above 30,000	172 (47.8%)
Educational Status of Husband	Uneducated	139 (38.6%)
	Middle	40 (11.2%)
	Matric	34 (9.4%)
	Intermediate	147 (40.8%)

The results of table 2 showed that (57.5%) of husbands felt that antenatal care was valuable, the majority of the husbands (95.6%) felt that it was not necessary to go for antenatal care even if there was no complication, and (32.2%) husbands were considered that minimum 3 antenatal visits were enough for the care. The knowledge regarding the importance of tetanus injection, vitamin supplements, and Iron /folic acid supplements during pregnancy among husbands was found to be below (50%). A large number of husbands (67.2%) believed that pregnant women need extra food compared to non-pregnant women, while (52.2%) felt that pregnant women should continue to do household jobs during pregnancy. Ultrasound test during antenatal care was not considered significant by the majority of husbands (53.3%), similarly more than (50%) were unaware of the importance of monitoring blood pressure and weight at every antenatal visit. In contrast more than (50%) of the husbands have good knowledge regarding Blood screening for HIV, Hepatitis, and Thyroid during antenatal care. In terms of laboratory tests, (72.5%) of individuals were aware of sugar testing, while only (12.5%) had knowledge of haemoglobin measurement, and (37.8%) knew about urine testing during antenatal care. Alarming results were found in terms of alcohol consumption and smoking by pregnant women, (80%) husbands assumed that alcohol consumption and smoking were not harmful for the fetus. More than half were aware of the danger signs of pregnancy and they knew that pregnant women should deliver their baby in the health care facility.

Table 2: Knowledge of Husbands Regarding Antenatal Care

Questions Asked	Response	
	Yes N (%)	No N (%)
Do you think Antenatal Care is Valuable or not?	207 (57.5%)	153 (42.5%)
Is it Necessary to go for ANC Even if there is no Complication?	16 (4.4%)	344 (95.6%)
Are Minimum 3 Antenatal Visits Required?	116 (32.2%)	244 (67.8%)
Is Injection TT Required to be given During Pregnancy?	37 (10.3%)	323 (89.7%)
Does a Pregnant Woman Need Vitamin Supplements?	170 (47.2%)	190 (52.8%)
Does a Pregnant Woman Need Iron /Folic Acid Supplements?	167 (46.4%)	193 (53.6%)
Does Pregnant Woman Need Extra Food Compared to Non-Pregnant Woman?	242 (67.2%)	118 (32.8%)
Is Alcohol Consumption/ Smoking by Pregnant Woman Harmful for Fetus?	72 (20%)	288 (80%)
Should USG be done to Assess Fetal Wellbeing?	168 (46.7%)	192 (53.3%)
Is Weight Measurement Required During Every Antenatal Visit?	163 (45.3%)	197 (54.7%)
Is BP Measurement Necessary During Every ANC Visit?	44 (12.2%)	316 (87.8%)
Is Haemoglobin Measurement During Pregnant Required?	45 (12.5%)	315 (87.5%)
Is Blood Sugar Testing Required?	261 (72.5%)	99 (27.5%)
Is Urine Test Required?	136 (37.8%)	224 (62.2%)
Is Blood Screening for HIV Required?	215 (59.7%)	145 (40.3%)
Is Blood Screening for Hepatitis Required?	188 (52.2%)	172 (47.8%)
Is Blood Screening for Thyroid Necessary?	220 (61.1%)	140 (38.9%)
Should Pregnant Women Continue to do Household Jobs?	188 (52.2%)	172 (47.8%)
Are You Aware of Danger Signs of Pregnancy?	224 (62.2%)	136 (37.8%)
Where Should a Pregnant Woman Deliver her Baby? Health Care Facility	302 (83.9%)	58 (16.1%)

DISCUSSION

The research aims to find the impact of husbands' involvement in anti-natal care on maternal and child health outcomes. The objectives of the research were to find out the perceptions of husbands towards ANC and the effects of husband's involvement in ANC on maternal and child health. The result of current study reveals that majority of the husbands (57.5%) believed that Antenatal Care is valuable .Comparable results were found in the study conducted in Nigeria, the (63%) of the husbands had good knowledge of antenatal care [16].The findings of present study showed that majority of the participant thought that minimum 3 Antenatal visits were not enough. Similar results were found in the research study in Yangon, Myanmar showed that the antenatal hospital visits were more likely to have more than four during pregnancy [17]. Moreover the result of this study showed that (62.2%) of the respondents were aware of danger signs of the pregnancy. Similarly the results of cross-sectional study surveyed 150 husbands in India showed that the majority of husbands exhibited sufficient knowledge of antenatal care, particularly regarding identifying danger signs [18]. This

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similar comparison may be due to the geographical location, as both countries are neighboring countries. In contrast a study conducted in Bangladesh found that one quarter of males could recall three or more delivery-related risk signs, even though most husbands were aware of prenatal danger indications [19].The complications can be prevented by the early detection of danger signs. Furthermore the current study revealed that (59.7%) husband reported blood screening for HIV is necessary during pregnancy, while 52.2% believed that blood screening for hepatitis is mandatory during ante-natal period. The contradictory results were found in the cross-sectional study conducted in Swat, Pakistan, the study results indicated that majority of husband (60.5%, 57.5%) were not aware of importance of screening of HIV and hepatitis [20]. This study further revealed that only (10.3%) respondents had the knowledge of importance of tetanus toxoid injection during pregnancy and less than half of the respondents were aware of supplements required in pregnancy. The much healthier results were reported in the study conducted in Mumbai, India, where (45%) of individuals had knowledge of importance of tetanus toxoid injection during pregnancy and more than half of the respondents were aware of supplements required during pregnancy [21]. This study further discovered that (37.8%) respondents assumed that urine analysis is required during pregnancy, which is consistent with the study findings of India, where (17.1%) of individuals thought that urine test is necessary during antenatal period [22]. Additionally the present study showed that (46.7%) of participants reported that ultrasound should be done to assess fetal well-being. Less than (50%) of participants had the knowledge regarding importance of blood pressure and weight measurement during antenatal visits. In contrast the results of study conducted in India reported that (72%) respondents considered ultrasound measurement is essential during pregnancy and (50%) had the knowledge regarding importance of blood pressure and weight measurement during antenatal visits [23].The findings of current study revealed that only (20%) of the respondents reported that smoking and alcohol consumption by pregnant women is harmful for the growth of fetus. In contrast the results of cross-sectional descriptive researched conducted in India showed that (58%) of the husbands considered smoking and alcohol consumption harmful for the fetal growth [24].

CONCLUSIONS

Knowledge of the husband about antenatal care was essential because it was helpful for pregnant women during pregnancy and childbirth. Pregnant women easily communicate and discuss their problems and complications with their husbands, so the husband's training was beneficial. Socio-demographic factors and antenatal care develop the husband's ability to make treatment decisions and proper health care. Any complication during pregnancy was timely observed and treated effectively. This study can further identify the husband's interest and help improve ANC according to the need.

Authors Contribution

Conceptualization: MA, SNZ
Methodology: MA, NAM
Formal analysis: MA, SNZ, DAS
Writing, review and editing: MA, DAK, FS, N

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Khan A, Hamid S, Reza TE, Hanif K, Emmanuel F. Assessment of effective coverage of antenatal care and associated factors in squatter settlements of Islamabad Capital Territory, Pakistan: an analytical cross-sectional study. Cureus. 2022 Aug; 14(8). doi: 10.7759/cureus.28454.

[2] Abbas M, Bhamani S, Kanjani Y, Sheikh L. Enhancing antenatal education in Pakistan: an audit and recommendations. Biomed Central Women's Health. 2023 Dec; 23(1): 645. doi: 10.1186/s12905-023-02799-x.

[3] Jungari S and Paswan B. What he knows about her and how it affects her? Husband's knowledge of pregnancy complications and maternal health care utilization among tribal population in Maharashtra, India. Biomed Central Pregnancy and Childbirth. 2019 Dec; 19: 1-2. doi: 10.1186/s12884-019-2214-x.

[4] Atif M, Farooq M, Shafiq M, Ayub G, Ilyas M. The impact of partner's behavior on pregnancy related outcomes and safe child-birth in Pakistan. Biomed Central Pregnancy and Childbirth. 2023 Jul; 23(1): 516. doi: 10.1186/s12884-023-05814-z.

[5] Maken ZH, Nasir Idrees I, Zahid A, Zulfiqar A, Munib A, Hassan F *et al.* Factors influencing father's antenatal and perinatal involvement in maternal health care. The Journal of Maternal-Fetal & Neonatal Medicine. 2018 Oct; 31(19): 2569-75. doi: 10.1080/14767058.2017.1347920.

[6] Shaad S, Pervez S, Jaiswal P, Hamid S, Jain M, Rekha T *et al.* IJCM_70A: Husband's knowledge regarding antenatal care of pregnant women and their involvement in the antenatal care of their wives.

DOI: https://doi.org/10.54393/pjhs.v5i12.2197

Indian Journal of Community Medicine. 2024 Apr; 49(1): S20-1. doi: 10.4103/ijcm.ijcm_abstract70.

[7] Aminat Omolara Akinyemi, Elhakim Adekunle Ibrahim. Prevalence and predictors of men's involvement in pregnancy care in Modakeke, Southwest Nigeria. Frontiers in global women's health. 2024 Mar 14; 5. doi.org/10.3389/fgwh.2024.1337094

[8] Gupta I, Mandal A. Assess the knowledge and attitude regarding antenatal care among spouses of pregnant women attending antenatal OPD in selected tertiary care hospital Bhubaneswar, Odisha. International Journal of Community Medicine and Public Health. 2021 Mar 25; 8(4):1757. doi.org/10.18203/2394-6040.ijcmph20211229

[9] Omayma M, Goda H, Osman N, Hanan El-Sayed. Assessment of Cultural and Socio-economic Factors Affecting the Involvement of Husbands in Antenatal Care from Wives' Point of View. Mansoura Nursing Journal. 2022 Jul 1; 9(2):151–61. doi:10.21608/mnj.2022.293718

[10] Laksono AD, Wulandari RD, Widya Sukoco NE, Suharmiati S. Husband's involvement in wife's antenatal care visits in Indonesia: What factors are related? Journal of Public Health Research. 2022 Apr; 11(2):227990362211041. doi.org/10.1177/22799036221104156

[11] Kinoti F, Fava S. Knowledge and Perceptions on Antenatal Care among Men in Embakasi South Sub County, Nairobi, Kenya. Journal of Maternal and Child Health. 2022; 7(2):171–82. doi.org/10.26911/thejmch.2022.07.02.06

[12] Regina. Knowledge assessment About Antenatal Care and Common Complications of Pregnancy among Husband of Pregnant Women in A Selected Rural Area of Erumapetty Gramapanchayat, Thrissur District. Journal of Survey in Fisheries Sciences. 2023; 10(4S):2420–6. doi.org/10.17762/sfs.v10i4S.1569

[13] Singh S, Powwattana A, Munsawaengsub C, Siri S. Factors Influencing Husband's Involvement during Antenatal Care in Lalitpur District of Nepal. Thai Journal of Public Health. 2022; 52(1).

[14] Paul PL, Pandey S. An examination of the factors associated with male partner attendance in antenatal care in India. BMC Pregnancy and Childbirth. 2023 Jul 22; 23(1). doi.org/10.1186/s12884-023-05851-8

[15] Daniele MAS. Male partner participation in maternity care and social support for childbearing women: a discussion paper. Philosophical Transactions of the Royal Society B: Biological Sciences. 2021 May 3; 376 (1827). doi.org/10.1098/rstb.2020.0021

[16] Falade-Fatila O, Adebayo AM. Male partners' involvement in pregnancy related care among married men in Ibadan, Nigeria. Reproductive Health. 2020 Jan 28; 17(1). doi.org/10.1186/s12978-020-0850-2

[17] Suandi D, Williams P, Bhattacharya S. Does involving male partners in antenatal care improve healthcare utilization? Systematic review and meta-analysis of the published literature from low- and middle-income countries. International Health. 2019 Oct 15; 12(5). doi: 10.1093/inthealth/ihz073.

[18] Shaad S, Pervez S, Jaiswal P, Hamid S, Jain M, Rekha T, *et al.* IJCM_70A: Husband's knowledge regarding antenatal care of pregnant women and their involvement in the antenatal care of their wives. Indian Journal of Community Medicine [Internet]. 2024 Apr; 49(Suppl 1):S20–1. doi: 10.4103/ijcm.ijcm_abstract70

[19] Rahman AE, Perkins J, Islam S, Siddique AB, Moinuddin M, Anwar MR, *et al.* Knowledge and involvement of husbands in maternal and newborn health in rural Bangladesh. BMC Pregnancy and Childbirth. 2018 Jun 18; 18(1). doi: 10.1186/s12884-018-1882-2.

[20] Younas M, Parpio Y, Tazeen Saeed Ali, Awan S. Male partners' knowledge and practices of antenatal care in district Swat, Khyber Pakhtunkhwa, Pakistan: A cross-sectional study. Journal of midwifery and reproductive health. 2020 Jan 1; 8(1):2005–15. doi: 10.22038/jmrh.2019.33935.1369

[21] Dahake S, Shinde R. Exploring husband's attitude towards involvement in his wife's antenatal care in urban slum community of Mumbai. Indian Journal of Community Medicine. 2020; 45(3):320. doi: 10.4103/ijcm.IJCM_344_19

[22] Nega Degefa, Dure A, Getahun D, Bukala Z, Tariku Bekelcho. Male partners' involvement in their wives' antenatal care and its associated factors in southern Ethiopia. A community-based cross-sectional study. Heliyon. 2024 Mar 1; e28276–6. doi.org/10.1016/j.heliyon.2024.e28276

[23] Pruthi N, Bacchani S, Singh V. Knowledge, attitude and practice regarding antenatal care among husbands attending antenatal clinic in a tertiary care hospital. International Journal of Community Medicine and Public Health. 2016; 1741–4.doi.org/10.18203/2394-6040.ijcmph20162035

[24] Col Geeta L, Singh M, Kumari M, Mathew S, Divya C, Martina S, *et al.* Antenatal Care-Knowledge of Spouses of Pregnant Women. International Journal of Science and Research (IJSR) Research Gate Impact Factor. 2018 [cited 2024 Dec 30].doi.10.21275/ART20203994

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Original Article

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Advancing Diagnosis: The Role of Imaging Modalities in Accurate Assessment of Skull Base ENT Pathologies

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ABSTRACT

The skull base was a multifaceted anatomical region where important structures unite, including major blood vessels and cranial nerves. Precise diagnosis of Ear, Nose, and Throat disorders in this area was critical for effective treatment planning, but conventional diagnostic methods often lack the required detail. **Objective:** To determine the efficiency of Computed Tomography and Magnetic Resonance Imaging in correctly diagnosing skull base Ear, Nose, and Throat pathologies. **Methods:** A comparative study was carried out at Shahida Islam Medical Complex, Lodhran, from September 2023 to February 2024. A purposive sampling technique was used to select 100 patients who underwent Computed Tomography and Magnetic Resonance Imaging for suspected skull base Ear, Nose, and Throat pathologies. Imaging results were compared against final clinical diagnoses confirmed through biopsy. Diagnostic accuracy was measured using sensitivity, specificity, Positive Predictive Value, and Negative Predictive Value. Statistical analysis was performed using SPSS version 25.0. **Results:** Magnetic Resonance Imaging showed higher sensitivity (85.7%) and specificity (87.7%) compared to Computed Tomography (sensitivity 73.0%, specificity 82.0% respectively). Diagnostic accuracy of Magnetic Resonance Imaging for specific pathologies included meningioma (sensitivity 93.52%, specificity 87.32%), chordoma (sensitivity 79.92%, specificity 95.72%), and nasopharyngeal carcinoma (sensitivity 86.62%, specificity 83.12%). **Conclusions:** It was concluded that Magnetic Resonance Imaging demonstrated higher diagnostic accuracy compared to Computed Tomography in the diagnosis of Ear, Nose, and Throat pathologies of skull base due to having greater sensitivity and specificity. These findings indicate that Magnetic Resonance Imaging is a superior diagnostic tool for early detection of skull base disorders.

INTRODUCTION

Lesions originating from the bony-cartilaginous structures of the skull base or neighbouring regions either the extra-cranial head and neck below or the intracranial compartment above can significantly impact the central skull base. This region serves as a critical boundary between the intracranial compartment and extracranial structures of the head and neck, making its evaluation complex and essential. Clinical assessment of the skull base is often limited, necessitating the use of imaging techniques for accurate diagnosis, planning, and follow-up in patients with skull base lesions [1, 2]. The rationale for this study lies in addressing the diagnostic challenges posed by skull base Ear, Nose, and Throat (ENT) pathologies. Cross-sectional imaging, including Computed Tomography (CT) and Magnetic Resonance Imaging (MRI), has emerged as a cornerstone for overcoming these limitations by providing detailed visualization of both bony and soft tissue structures. Imaging plays a pivotal role

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when clinical findings are inconclusive or when complications like intracranial spread or bone involvement are suspected [3]. For example, imaging is often critical in determining the need for surgery when conservative treatment fails. Experts recommend imaging in ENT patients under specific conditions to rule out clinically silent issues [4]. Contrast-enhanced high-resolution CT is widely regarded as the gold standard for detecting bone loss caused by inflammation [5]. However, contrast-enhanced MRI has demonstrated greater sensitivity for identifying cerebral infections and evaluating soft tissue involvement [6]. In many cases, both CT and MRI are employed to achieve a comprehensive understanding of the pathology [6, 7]. Cross-sectional imaging techniques provide detailed definitions of bony structures and tumor boundaries, allowing clinicians to assess the relationship between a lesion and its surrounding tissues [8]. This detailed evaluation aids in establishing differential diagnoses based on the lesion's origin and nature. The ongoing advancements in imaging technology have significantly transformed the diagnostic landscape in ENT. Techniques such as Positron Emission Tomography-Computed Tomography (PET-CT), CT, and MRI enable accurate localization and characterization of skull base lesions, offering insights that were previously unattainable [9]. MRI is particularly valuable for visualizing soft tissues, while CT excels in assessing bony structures. Endoscopic ultrasonography, a novel method combining endoscopy and ultrasonography, provides real-time imaging through the mouth or nose. This technique is particularly useful for biopsies and therapeutic interventions, offering precise lesion localization [10]. Conventional diagnostic approaches often fail to capture the complexity of the skull base region. In contrast, advanced imaging modalities provide unparalleled insights into both anatomical and pathological features, allowing for accurate detection and improved patient care [11]. Differentiating benign from malignant lesions, staging diseases, and planning treatments are increasingly dependent on these advanced technologies [12]. As imaging technology evolves, its role in diagnosing skull base ENT pathologies is expected to expand, further enhancing patient outcomes.

This study aims to clarify the key roles of different imaging modalities in accurately diagnosing selected ENT pathologies of the skull base. By exploring the strengths and limitations of these techniques, the study seeks to underscore their critical contributions to modern diagnostic strategies.

METHODS

This cross-sectional study was carried out at Shahida Islam Medical Complex, Lodhran, Pakistan, from September 2023 to February 2024. The patients undergoing CT and MRI imaging for suspected skull base ENT pathologies were selected according to the inclusion criteria set for the study. A purposive sampling technique was used to select 100 patients. The sample size was estimated on the base of power analysis ensuring statistical significance between different imaging modalities to detect ENT pathologies. The following formula was used to calculate the sample size for the study; $n=Z21-a/2\times Sn(1-Sn)/L2-P$. Where Sn was sensitivity; P was Prevalence; L was the margin of error (0.05) and Z1-α/2 was the confidence interval (1.96 at α=0.05). All the values were taken according to the estimated results of sensitivity and prevalence of neurodegenerative diseases at Shahida Islam Medical Complex, Lodhran, Pakistan and previous reported studies [13]. The inclusion criteria included patients of 20 to 70 years of age of any gender having clinical symptoms indicating Meningioma, Chordoma or Nasopharyngeal Carcinoma in the skull base and had experienced any of the two imaging modalities (CT and MRI) or both, at Shahida Islam Medical Complex, Lodhran. The patients having incomplete medical records, and those who had undergone imaging for non-ENT-related conditions or having contraindications for CT scan or MRI were excluded from the study. For detailed soft tissue contrast, the imaging modalities comprised of Computed Tomography (CT) for high-resolution bone detail assessment and Magnetic Resonance Imaging (MRI) were applied. Collection of a detailed medical history, including allergies and contraindications to differentiate agents, disclosure of implanted devices, and removal of metallic objects before MRI procedures were involved in the patient's preparation. Image interpretation involves a mutual effort among the radiology and ENT experts. CT scans were measured for fractures, calcifications, and bone integrity, while MRI provided detailed soft tissue evaluation for identifying tumors, inflammation, and vascular abnormalities. For the patient records, correct documentation and reporting were maintained, where radiologists were formulating comprehensive reports with the location and size of the ENT pathology, and associated findings. The diagnostic accuracy of each one of the imaging modalities was evaluated by evaluating imaging findings and the final diagnosis which were confirmed through biopsy. Statistical analysis was carried out using SPSS version 25.0, employing techniques such as sensitivity, specificity, Positive Predictive Value (PPV), and Negative Predictive Value (NPV) measurements [14]. The study was conducted as per the ethical standards of the Institutional Ethical Committee, Shahida Islam Medical Complex, Lodhran, (SIMC/H.R./7725/23) with written informed consent obtained from all patients or their guardians prior to inclusion.

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RESULTS

The mean age of the patients was 44.31 years, along with a standard deviation of 9.17 years. This showed that most of the patients were in their mid-40s, with the ages ranging from 35 to 53 years. The results showed that most of the patients in the study were from rural areas (62%), whereas 38% from urban areas (Table 1).

Table 1: Socio-Demographic Characteristics of Patients (n=100)

Variables	Frequency (%)/ (Mean ± SD)
Age	44.31 ± 9.17
Gender	
Male	58 (58%)
Female	42 (42%)
Residence	
Urban	38 (38%)
Rural	62 (62%)

MRI (85.7%) has a better level of sensitivity as compared with the results of CT (73.0%), which means MRI was a more beneficial technique for diagnosing pathologies in their early stages due to being precise in identifying positive cases. Additionally, the specificity of MRI (87.7%) was a little higher than CT's (82.0%), which showed that MRI can also be used to rule out the presence of certain diseases when they were not present (Table 2).

Table 2: Diagnosis Accuracy of MRI in selected ENT Pathologies of Skull Base

Pathology	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)	True Positive	False Positive	True Negative	False Negative
Meningioma	93.52	87.32	90.72	91.22	43	4	31	3
Chordoma	79.92	95.72	88.22	91.32	30	4	37	8
Nasopharyngeal Carcinoma	86.62	83.12	80.82	88.32	39	5	30	6
Total	86.72	88.72	86.62	90.32	-	-	-	-

As compared to MRI, CT scans displayed a little lower sensitivity and specificity. Although CT supports detecting structural abnormalities, its reduced sensitivity may increase the possibility of overlooking some of the subtle or early-stage diseases. On the other hand, CT showed improved specificity as compared to MRI, which showed its ability to spot the instances lacking these diseases. These findings highlight MRI's advantage in diagnosing ENT disorders of the skull base. Because of its high sensitivity, it can recognize and discover things at an early stage, which is important for medical intervention at an initial level. Even though CT scans have a high specificity, and can be suitable in situations where the pathology was clear from more subtle alterations (Table 3).

Table 3: Diagnosis Accuracy of CT in Selected ENT Pathologies of Skull Base

Pathology	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)	True Positive	False Positive	True Negative	False Negative
Meningioma	82.22	79.52	73.82	86.32	37	6	25	8
Chordoma	65.72	93.12	84.62	79.92	27	3	37	14
Nasopharyngeal Carcinoma	73.82	76.62	69.42	80.32	34	7	27	12
Total	74.02	83.02	75.92	82.12	-	-	-	-

DISCUSSION

This study highlights the strengths and limitations of CT scans and MRI in diagnosing skull base ENT pathologies, focusing on their effectiveness in various conditions. The results of our study showed that CT scans have an 82.22% sensitivity in diagnosing meningiomas compared with MRI, which has a 93.52% sensitivity and an overall positive predictive value of 92.72%. This demonstrates MRI's superior sensitivity in identifying meningiomas. Ren *et al.*, conducted a study on 153 patients to diagnose different ENT pathologies using MRI, CT scans, and PET, concluding that while MRI produced better accuracy, combining all three modalities provided the most comprehensive understanding of the disease [14]. However, previous studies reveal conflicting results. For instance, Jans *et al.*, found that CT scans performed better in diagnosing structural lesions in patients suspected of having sacroiliitis compared to MRI [15]. CT scans excel in detecting bone-related abnormalities, such as tumors, erosions, and fractures, but are limited in evaluating non-bony lesions due to their lower soft tissue resolution [16, 17]. On the other hand, MRI is a powerful technique for evaluating soft tissue features in the skull base. Techniques like Diffusion-Weighted Imaging (DWI) enhance MRI's ability to detect detailed changes in tumors and surrounding tissues [18]. In this study, MRI was generally more sensitive than CT in detecting skull base disorders, including meningioma, chordoma, and nasopharyngeal carcinoma. This sensitivity is critical for early diagnosis and timely medical intervention. Kalita and Misra studied Japanese Encephalitis (JE) patients,

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comparing MRI and CT for diagnosing JE. They found that thalamic and extrathalamic abnormalities were detected more easily by MRI than by CT [19]. Similarly, Kidwell *et al.*, compared MRI and CT in identifying acute intracerebral hemorrhage in patients with acute focal stroke symptoms, concluding that MRI was superior for detecting persistent intracerebral bleeding [20]. Despite its advantages, CT remains an essential diagnostic tool due to its cost-effectiveness and widespread availability, particularly in resource-limited settings. This makes CT an invaluable first-line imaging modality in many healthcare contexts, especially for detecting bone-related pathologies and structural abnormalities. Its accessibility and rapid imaging capabilities further enhance its utility in urgent clinical scenarios. Combining imaging techniques, such as CT, MRI, and PET scans, provides a more comprehensive diagnosis by overcoming the limitations of individual modalities [21, 22]. By integrating multiple imaging approaches, clinicians can achieve a more precise understanding of complex conditions.

CONCLUSIONS

The results of this study show that MRI is a better imaging modality compared to CT scans for diagnosing skull base ENT pathologies. However, the importance and accessibility of CT scans, especially in resource-limited settings, should not be overlooked. Combining results from multiple imaging techniques improves the accuracy of diagnosing conditions such as meningioma, chordoma, and nasopharyngeal carcinoma.

Authors Contribution

Conceptualization: AH
Methodology: JH, ABM
Formal analysis: SA
Writing, review and editing: JH, TZS, MA

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Urbančič J, Vozel D, Battelino S, Bošnjak R, Kokošar Ulčar B, Matos T *et al.* Atypical skull-base osteomyelitis: comprehensive review and multidisciplinary management viewpoints. Tropical Medicine and Infectious Disease.2023 Apr; 8(5): 254. doi: 10.3390/tropicalmed8050254.

[2] Ahmed AN. Preoperative Magnetic Resonance Elastography (MRE) of Skull Base Tumours: A Review. Indian Journal of Otolaryngology and Head & Neck Surgery. 2023 Dec; 75(4): 4173-8. doi: 10.1007/s12070-023-03955-3.

[3] Agarwal A, Murray J, Sandhu SJ. Image-Guided Biopsies of Superficial and Deep Head and Neck and Skull-Base Lesions. Oral and Maxillofacial Surgery Clinics.2023 Aug; 35(3): 451-68. doi: 10.10 16/j.coms. 20 23.02.006.

[4] Fang Y, Peng Z, Wang Y, Yuan X, Gao K, Fan R *et al.* Improvements and challenges of tissue preparation for spatial transcriptome analysis of skull base tumors. Heliyon. 2023 Mar; 9(3). doi: 10.1016/j. heliyon .2023.e14133.

[5] Bartolucci ML, Incerti Parenti S, Alessandri-Bonetti G, Marini I. Unusual Presentation of Juvenile Rhabdomyosarcoma in the Temporomandibular Area: A Case Report. Applied Sciences.2023 May; 13(10): 59 2 6. doi: 10.3390/app13105926.

[6] Luna LP, Kamel P, Nadgir R. Radiologic Evaluation of Skull Base Masses. Cerebrospinal Fluid Rhinorrhea: Comprehensive Guide to Evaluation and Management. 2023 Jan: 179. doi: 10.1016/B978-0-323-87072-6 .000 3 6-3.

[7] Zhan Y, Wang P, Wang Y, Wang Y, Tang Z. Dual-energy CT for the detection of skull base invasion in nasopharyngeal carcinoma: comparison of simulated single-energy CT and MRI. Insights into Imaging.2023 May; 14(1): 95. doi: 10.1186/s13244-023-01444-3.

[8] Kim SY, Beer M, Vogel DW. Imaging in head and neck cancers: Update for non-radiologist. Oral oncology. 2021 Sep 1;120:105434. 10.1016/j. oralonco logy .202 1.1 05434

[9] Mehmood A, Anjum Hameed DA, Kousar H, Khan ZG, Shahzad K, Asif M, Gulzada M, Lodhi K. Analysis on accurate diagnosis of skull base ear, nose, and throat (ENT) pathologies holds paramount importance in guiding effective treatment strategies and ensuring optimal patient outcomes. Eur. Chem. Bull. 2023, 12(Regular Issue 12),4404–4411.10.53555/ecb/2023.12. 12.322

[10] Erdem H, Tekeli M, Çevik Y, Şafak NK, Kaya Ö, Boyan N *et al.* Quantitative assessment of the pharyngeal recess morphometry in anatolian population using 3D models generated from multidetector computed tomography images. Medical Records. 2023 Jun; 5(3): 507-12. doi: 10.37990/medr.1305549.

[11] Baba A, Kurokawa R, Kurokawa M, Reifeiss S, Policeni BA, Ota Y *et al.* Advanced imaging of head and neck infections. Journal of Neuroimaging. 2023 Jul; 33(4): 477-92. doi: 10.1111/jon.13099.

DOI: https://doi.org/10.54393/pjhs.v5i12.2075

[12] Bryanskaya EO, Dremin VV, Shupletsov VV, Kornaev AV, Kirillin MY, Bakotina AV et al. Digital diaphanoscopy of maxillary sinus pathologies supported by machine learning. Journal of Biophotonics.2023 Sep; 16(9): e20 2300138. doi: 10.1002/jbio.202300138.

[13] qbal A, Khursheed S, Ibrahim M, Ali R, Munir SB, Khan TH *et al*. Comparative analysis of diagnostic accuracy between MRI and CT scans in detecting skull base ENT pathologies.Cardiometry.2023 Nov; 1(29): 103-10. doi: 10.18137/cardiometry.2023.29.103110.

[14] Ren J, Eriksen JG, Nijkamp J, Korreman SS. Comparing different CT, PET and MRI multi-modality image combinations for deep learning-based head and neck tumor segmentation. Acta Oncologica. 2021 Nov; 60(11): 1399-406. doi: 10.1080/02841 86X.2021.194 9034.

[15] Jans LB, Chen M, Elewaut D, Van den Bosch F, Carron P, Jacques P *et al*. MRI-based synthetic CT in the detection of structural lesions in patients with suspected sacroiliitis: comparison with MRI. Radiology. 2021 Feb; 298(2): 343-9. doi: 10.1148/radiol .2020201537.

[16] Rowse BM, Yu AC, Faulkner H, Sandler G, Howle JR, Ch'ng S *et al*. Does preoperative imaging for scalp non-melanocytic skin cancer accurately predict invasion of the cranial vault? A systematic review and meta-analysis. ANZ Journal of Surgery. 2023 Jul; 93(7-8): 1970-7. doi: 10.1111/ans.18566.

[17] Qureshi MF, Usmani A, Mehwish A, Rehman F, Ahmed RR. Use of Computed Tomography for Nasal and Paranasal Anatomic Variants. Pakistan Journal of Medicine and Dentistry. 2023; 12(3). doi: 10.362 83 /PJ MD12-3/010.

[18] Kuan EC, Tajudeen BA, Djalilian HR, Lin HW, editors. Skull Base Reconstruction: Management of Cerebrospinal Fluid Leaks and Skull Base Defects. Springer Nature; 2023 May 25. doi: 10.1007/978-3-031-27937-9.

[19] Kalita J and Misra UK. Comparison of CT scan and MRI findings in the diagnosis of Japanese encephalitis. Journal of the neurological sciences. 2000 Mar; 174(1): 3-8. doi: 10.1016/S0022-510X(99)00318-4.

[20] Kidwell CS, Chalela JA, Saver JL, Starkman S, Hill MD, Demchuk AM *et al*. Comparison of MRI and CT for detection of acute intracerebral hemorrhage. Journal of the American Medical Association.2004Oct;292(15) : 1823-30. doi: 10.1001/jama.292.15.1823.

[21] Mohammadzadeh M, Erfanian R, Rezaeian S, Batavani N, Amirzargar B. Jugular foramen versus hypoglossal canal in axial CT scan. BioMedicine. 2023; 13(1): 46. doi: 10.37796/2211-8039.1393.

[22] Hasan Z, Key S, Habib AR, Wong E, Aweidah L, Kumar A *et al*. Convolutional neural networks in ENT radiology: systematic review of the literature. Annals of Otology, Rhinology & Laryngology. 2023 Apr; 132(4): 417-30. doi: 10.1177/00034894221095899.

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Tool Development for Parental Reviews of Cochlear Implanted Children in Urdu

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ABSTRACT

The treatment of profound hearing loss and the adjustment of a child after this is a critical task for parents. Presently, cochlear implantation is the most common and effective treatment for profound hearing loss. However, navigating the decision-making process can be overwhelming for families. Currently, there is no standardized tool available in Urdu to help parents before taking the decision of cochlear implantation. **Objective:** To develop a tool to assess parental reviews of cochlear-implanted children in Urdu. **Methods:** This descriptive research conducted at Riphah International University (Sept. 2020-February 2021) utilized a sample of 20 parents of cochlear implanted children, aged 6 to 15 5 years. Parents included either gender aged 29 to 59 years. A semi-structured questionnaire was developed using interviews and existing literature. Themes from interviews and existing literature were used to develop items. Content validity was assessed by 5 expert speech and language pathologists. For the meaningfulness of each item, a cognitive debriefing interview was conducted with the parents. Each item was reviewed and modified as per suggestion and pre-tested. **Results:** A 92-item tool was developed with 07 subsections related to i) Decision of Cochlear Implantation, ii) Process of Cochlear Implantation, iii) Effects of Cochlear Implantation, iv) General Functioning of Child, v) Self-Reliance and QoL, vi) Education of Child and vii Communication. The tool revealed good reliability and content validity SCVI=0.94. **Conclusion:** The developed 92-item Parental Reviews of Cochlear-Implanted Children in Urdu (PRCIC-U) tool is a reliable and valid tool review of different stages of the cochlear implantation procedure for the Urdu-speaking population.

INTRODUCTION

Cochlear implantation is a surgical procedure of implantation of a neuroprosthetic hearing device that improves the sense of sound [1]. It is possible for the deaf person to understand speech and improve the sensitivity of sound [2]. Studies indicate that children implanted by 12 months of age are more likely to achieve education levels necessitating implantation before the age of 4 years in the case of congenital hearing loss [3, 4]. Literature suggests that approximately five percent of the world population (around 32 million adults and 34 children and adolescents) are hearing impaired. The degree of their hearing loss is moderate to severe, which is 40 dB for the good hearing ear of adults and 30 dB for the good hearing ear of children [5], with those in underdeveloped countries being most affected [6]. The benefits of implantation can also be measured in social terms, such as how the implantation helps in decreasing the educational cost and an aware life in the long run [7]. Literature reveals tools that may assist or influence the parental decision of cochlear implantation [8]. The data that parents give in the form of their reviews and experiences can be beneficial for the professional teams of implantation of the concerned parents and also for clinical usage [9]. However, no such tool in Urdu language exists. In academic achievement, it is significant that deaf children who have been implanted show considerably better results [10].

The vital impact of cochlear implantation is that it gave positive outcomes when the implanted child is grown up

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and able to go for employment, the same as the other of his peer groups.

METHODS

To develop a tool to assess parental reviews of cochlear-implanted children in Urdu (PRCIC-U), the current study utilized a descriptive research design with convenient sampling. The study was conducted at Riphah College of Rehabilitation Sciences, Riphah International University, Islamabad, over 6 months from 1st September 2020 to 28th February 2021. This study was initiated after obtaining ethical approval of the study from the Research Ethical Committee of Riphah International University vide Reference no. Riphah/RCRAHS/ISB/REC/00801 and informed consent of the parents of children. The confidentiality of participants was preserved. Though, convenience sampling can result in bias in research like selection and sampling bias, however since a special category of parents had to be selected carefully to obtain their ideas of their special experience. Hence using convenience sampling, the study recruited a sample of N=20 parents of cochlear-implanted children of Bahria Special Children College, Islamabad for pilot testing. The sample included both mothers and fathers, aged 29 to 59 years of whom 08 were permanent residents of the twin city of Islamabad and Rawalpindi while the remaining 12 were temporary residents. Only parents of children having experienced the procedure of cochlear implantation of their respective child with a child's age range 6-15 years and both genders were included. Parents of children having associated syndrome along with hearing impairment were excluded from the study. An inform consent was taken from the parents of children below 10 years of age, and children above the age of 10 after obtaining permission from the involved institution. Sample of Expert SLPs include n=5 SLPs of female gender and any age group with minimum PGD in speech language pathology and at least 5 years experience(table 1)

A detailed literature search was conducted to find existing tools and research articles related to parental review of cochlear implants. Semi-structured questions were used to ask parents about their experiences and problems faced by them during and after cochlear implant surgery. A list of items (95 questions) was generated by reviewing interviews and existing literature. The tool was categorized into different subparts of the cochlear implant procedure. The responses were calculated through a Likert Scale including 1= Strongly Agree, 2= Agree, 3= Neither agree nor disagree, 4= Disagree, 5=Strongly Disagree. The tool was developed by following the following protocols(figure 1).

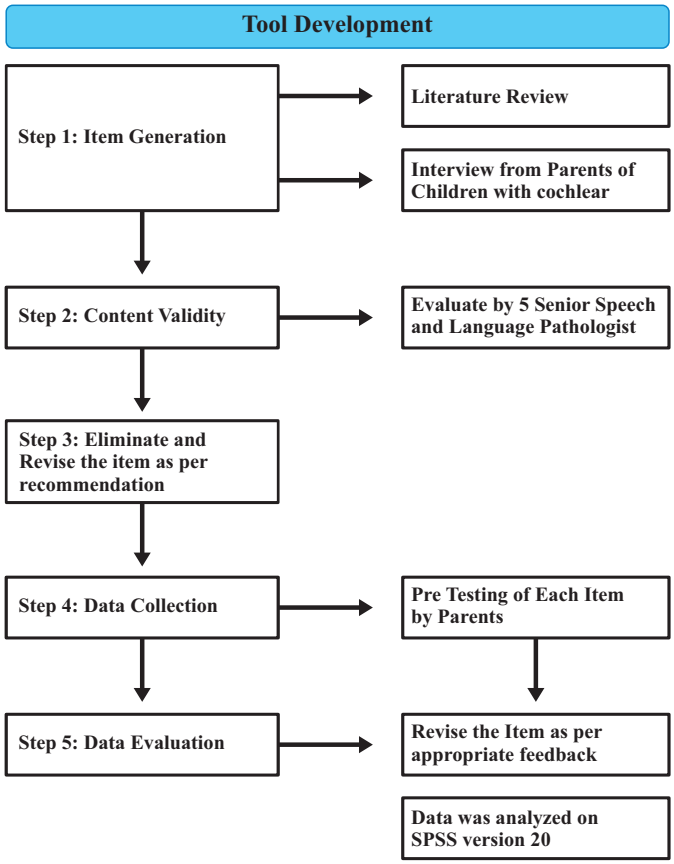

Figure 1: Consolidated Standards of Reporting Trials

Step 1: Generation of Items: Both inductive and deductive methods were used for generation of 95 item. Themes from interviews with parents and existing literature and existing scales on Parental reviews and experiences of children with Cochlear Implantation were used to develop items. Step 2: Content Validity: Assessed by 5 expert senior SLPs. The validity of content was also checked by the reviews and suggestions of five parents of cochlear-implanted children. Each item was reviewed and changed according to the suggestions of experts. Each item was rated by 5-experts on 4-point rating scale. Out of which the relevant rating was 3 or 4 which was scored as 5 and the non-relevant rating was 1 or 2 which was scored as 0. Content validity index I-CVI for items was calculated by the respective formula that expert in agreement divided by the number of experts for each item. Such items for which the result of I-CVI was less than 0.8, were considered to be revised according to expert advice. For the item that showed the I-CVI result 0, such an item was eliminated from the questionnaire as per expert opinion leaving behind 92 items. Step 3: Pre-testing of items: To check and ensure the meaningfulness of each item, a cognitive debriefing interview was conducted with the parents. Each item was reviewed and modified as per suggestion. Data analysis was performed using Statistical Package for Social Sciences (SPSS) version 20. Descriptive statistics was run

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to calculate the frequencies and percentages for demographics. The content validity index for items and the scale of the developed tool was also calculated.

RESULTS

The sample (N=20) of the current study revealed a mean age of 42.9 ± 7.67 years with the majority being females 15 (75%) and housewives 11 (55%) (Table 1).

Table 1: Demographic Characteristics of Sample

Variables	Group	N (%)
Sample of Parents (n=20)		
Gender	Male	5 (25%)
	Female	15 (75%)
Occupation	House Wife	11 (55%)
	Government Job	5 (25%)
	Business Personal	4 (20%)
Total		20 (100%)
Sample of Expert SLPs (n=5)		
S. No.	**Qualification**	**Experience**
1	MS (SLP)	5 Years
2	PhD	8 Years
3	PGD (SLP)	7 Years
4	MS (SLP)	6 Years
5	MS (SLP)	7 Years

Results revealed 92 items of different sections of the cochlear implant procedure. Initially, 95 items were generated. Seven sub-sections labeled as A to G were arranged to distribute all the items according to their respective sections. Each of these items was rated by 5 expert judges on 4-point rating scale. Out of which the relevant rating was 3 or 4 which was scored as 5 and the non-relevant rating was 1 or 2 which was scored as 0 (Table 2).

Table 2: Responses of Experts for Content Validity Assessment

Items Related To	Items	Experts in Agreement
A) Decision of Cochlear Implantation	1	5
	2	5
	3	5
	4	5
	5	5
	6	5
	7	5
	8	5
	9	5
	10	5
	11	5
	12	5
	13	5
	14	0
B) Process Of Cochlear Implantation	1	0
	2	5
	3	4
	4	5
	5	5
	6	5
	7	4
	8	5
	9	5
	10	5
	11	4
	12	5
	13	5
	14	5
	15	4
	16	5
	17	5
	18	5
	19	1
	20	5
	21	5
	22	5
	23	5
	24	5
C) Side Effects Of Cochlear Implantation	1	5
	2	5
	3	5
	4	5
	5	5
	6	1
	7	5
	8	5
	9	5
	10	5
	11	5
	12	5
D) General Functioning of Child	1	5
	2	5
	3	5
	4	5
	5	5
	6	5
	7	5
	8	5
E) Quality of Life	1	5
	2	5
	3	5
	4	5
	5	4
	6	5
	7	4
	8	4
	9	5

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	10	5
	11	5
	12	2
	13	0
	14	4
F) Education of Child	1	5
	2	5
	3	5
	4	5
	5	5
	6	5
	7	5
	8	5
	9	5
	10	5
	11	0
	12	5
G) Communication	1	5
	2	5
	3	1
	4	5
	5	5
	6	5
	7	5
	8	5
	9	5
	10	5
	11	5

Content validity index I-CVI for items was calculated by the respective formula that expert in agreement divided by the number of experts for each item. Such items for which the result of I-CVI was less than 0.8, was considered to be revised according to expert advice. For the item that showed the I-CVI result 0, such item was eliminated from the questionnaire as per expert opinion (Table 3).

Table 3: Content Validity of Tool Items

Sections	Items No.	Relevant (Rating 3 or 4)	Not-relevant (Rating 1 or 2)	I-CVI	Interpretation
A) Decision of Cochlear Implantation	1 to 14	5	0	1	Appropriate
B) Process of Cochlear Implantation	1	0	5	0	Eliminated
	19	1	4	0.2	Needs Revision
	2-18, 20-24	5	0	1	Appropriate
C) Effects of Cochlear implantation	1-5, 7-12	5	0	1	Appropriate
	6	1	4	0.2	Needs Revision
D) General Functioning of Child	1 to 8	5	0	1	Appropriate
E) Self-Reliance and QoL	1 to 11	5	0	1	Appropriate
	5,7,8,14	4	1	0.8	Appropriate
	12	2	3	0.4	Needs Revision
	13	0	5	0	Eliminated
F) Education of Child	1-10,12	5	0	1	Appropriate
	11	0	5	0	Eliminated
G) Communication	1-2,4-11	5	0	1	Appropriate
	3	1	4	0.2	Needs Revision

As a result of I-CVI, all 14 items of section A were considered to be appropriate, from section B out of 24 items, item 19: کا کلئیر امپلانٹ کے عمل حکومتی میسر ہونا ہماری مشکل آسان کر سکتا تھا was revised and 1 items was suggested to be eliminated. From section C out of 12 items, item 6: سطح پر سہولت کا شروع میں ہماری توقعات یہ بھی تھی کہ ہمارا بچی فوری طور پر ساری آوازوں سے آشنا ہو جائے گا was revised, in section D all 8 items were considered to be appropriate, in section E out of 14 items item 12: کا کلئیر امپلانٹ سے پہلے اس میں اعتماد، تحفظ اور یقین کا فقدان تھا وہ امپلانٹیشن سے پہلے ہم پر بہت انحصار :13 was revised and item مین اسٹریم :11 was eliminated, from section F item اسکولوں میں اسپیچ تھراپیسٹ کا ہونا ضروری ہے تا کہ امپلانٹیشن والے بچے اٹریم میں تعلیم حاصل کر سکیں اور اسپیچ تھراپیسٹ سے فائدہ اٹھا سکیں was eliminated out of 12, and from section G out of 11 items item 3 اس کا بولنے کا معیار تشویش کا باعث تھا was revised. A total of 3 items were eliminated and 4 items were considered to be revised according to expert advice of all judges. Hence 92 items are considered to be appropriate after elimination and revision with SCVI of 0.93. Table 4 showed the frequencies of reliability of items. Responses for each item were checked in Yes and No by debriefing interviews with parents. Yes, indicates that the item is reliable, no indicates that the item is not reliable. Only responses for important items are mentioned below with concerned statements (Table 4).

Table 4: Frequency of Reliability of Items checked by pilot testing by debriefing interview with parents

Variables	Categories	N (%)
اس بات کا فیصلہ کرنا کہ آیا ہمیں امپلانٹ کروانا چاہیے یا نہیں، یہ ایک سب سے بڑا مشکل مرحلہ تھا۔	Yes	20 (100%)
	No	0
امپلانٹ کروانا کس عمر میں فائدہ مند ہوگا اس بات نے ہمیں پریشان کیا۔	Yes	18 (90%)
	No	2 (10%)
ہمیں کاکلیئر امپلانٹیشن سے قبل، متعلقہ ماہرین تک رسائی نہ ملنے کے باعث پریشانی کا سامنا کرنا پڑا۔	Yes	19 (95%)
	No	1 (5%)
ہم دونوں میاں بیوی میں سے اگر کوئی بھی امپلانٹیشن کی مخالفت کرتا تو بچے پر اسکے منفی اثرات مرتب ہونے کا کلیئر امپلانٹیشن کا عمل والدین کے لئے تحفظات دینے والا عمل ہے۔	Yes	19 (95%)
	No	1 (5%)
امپلانٹ کرانے سے پہلے کسی دوسرے ایسے خاندان سے ملنا بہت مفید ہے جو۔	Yes	19 (95%)
	No	1 (5%)
کلیئر امپلانٹ کروانے کا تجربہ رکھتے ہوں۔	Yes	19 (95%)
	No	1 (5%)
مجھے اُمید ہے کہ امپلانٹ سینٹر ہمیں امپلانٹ کے بعد پیش آنے والی مشکل میں مدد کرے گا۔	Yes	19 (95%)
	No	1 (5%)
شروع میں ہماری توقعات یہ بھی تھی ہمارا بچہ اپنی امپلانٹیشن کے فوری بعد سننے کے ساتھ ساتھ بولنا بھی جاری کر دے گا۔	Yes	18 (90%)
	No	2 (10%)

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امپلانٹیشن کی وجہ سے اسے دوسری طبعی مشکلات کا سامنا کرنا پڑا۔	Yes	17 (85%)
	No	3 (15%)
چونکہ اب یہ اپنے اردگرد کی آوازوں سے واقف ہے اس لیے میں اب اسکو کھیلنے دیتی ہوں۔	Yes	19 (95%)
	No	1 (5%)
امپلانٹیشن کے بعد بھی یہ مین اسٹریم اسکول کا مقابلہ کرنے سے قاصر ہے۔	Yes	19 (95%)
	No	1 (5%)
امپلانٹیشن سے قبل یہ سکول میں محض وقت گزار رہا تھا۔	Yes	19 (95%)
	No	1 (5%)

DISCUSSION

The decision for the Cochlear Implantation (CI) procedure is difficult and stressful for the parents [11]. Due to non-availability of tool to determine the parental view and experiences of children with cochlear implantation, this study aimed to develop a tool that can assess the parental views and experiences of children with a cochlear implantation because this can benefit many other parents who are going for their child's implantation. Inspired by the literature, a study conducted in the United Kingdom indicated that there was a need to assess parental views for future ease [12]. The currently developed tool was categorized into parts. Each part comprises steps of the implantation procedure and the pros and cons of implantation on a child's mental health, quality of life, and parental experiences. The initiative behind these items was taken from the literature and a few existing tools which indicated the importance of assessment of parental experiences [13]. The purpose of developing this tool in the Urdu language was to facilitate the Pakistani population and parents from all backgrounds. As Urdu is the national language of the majority of Pakistani people these items in Urdu would be easy and readable for all the parents who can read and understand Urdu language. Keeping in view that content validity of a new developed tool should be assessed since it is essential hence, the overall Content validity index (SCVI) was assessed and it was 0.93, which is appropriate to support the literature which is more than 0.8 [14-16]. In a study related to the development of a content-valid scale, the investigator evaluated the outcomes of the content validity of the scale [14]. Certain steps should be followed while developing a tool these steps include identification of the area that needs to be measured. This is done by reviewing already existing literature, scales, and interviews [15], as done in the current study. The study suggests protocols for checking the content validity of the developed tool [14]. in which the experts mark each item for relevancy, clarity, reliability, and ambiguity. According to the content validity of each part, most of the experts have given the score of 1, 0.93, and 0.91, which is appropriate to support the content validity according to the literature [14]. The items below 0.8 were revised, and the items which were indicated as 0, were eliminated from the questionnaire. In the current study, frequencies of parental feedback were evaluated on each item related to the cochlear implant decision. Many researchers suggested that the most stressful phase is to decide on implantation [3, 16], indicating the need to cater to stressors [17]. In this tool, items were developed regarding the complications and concerns of parents while deciding on a cochlear implantation. The frequencies of feedback indicate that the reliability of the decision of cochlear implantation is the most important concern of parents [18]. In Urdu PRCIC-U, the items related to financial burden were also added, since this is an important aspect of parents' concern [,]. Studies suggest that, in underdeveloped countries, the prevalence of hearing loss is a huge burden on the economy [4]. Items regarding the expense related to cochlear implantation provide very clear results that parents need financial consultancy before proceeding toward the implant which is the significance of this tool because in existing tools there were no items related to financial constraints. Financial aspects in developing countries like Pakistan need to be catered since this makes implantation difficult [21, 22]. Items related to education of children were generated after the theme that was extracted from the parental interviews. Many studies suggest that parents are worried about the post-surgery improvement and the quality and performance in the field of education were their great concern [7]. The results of parental feedback indicate that the education of a child is the second major concern of parents after cochlear implant surgery, though implanted children hear better in daily life [22]. Parents gave this feedback that the availability of this tool enabled them to take an interest in participating of this study. The results of debriefing interviews show the parental feedback regarding feasibility and quick understanding of items in Urdu. Parents also suggested a few items to be added to the tool in future research. Many parents report that they were worried about the limited resources in their city and from where they should avail the facility of cochlear implantation. In debriefing interviews, parents acknowledge the development of tools in their familiar language. This study can benefit the future research due to the fact that this tool can inform parents and caregivers what they should expect at different stages of the cochlear implantation process. This is very important since there is no such tool available in Urdu language in Pakistan. This tool is also very important for future research in the area.

CONCLUSIONS

The developed 92-item Parental Reviews of Cochlear-Implanted Children in Urdu (PRCIC-U) tool is a reliable and valid tool review of different stages of the cochlear implantation procedure, for Urdu speaking population. It is

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recommended that more items can be generated from the diverse population across the country. Secondly, it is also suggested that parental views should be analyzed across different cities to check the availability of the quality of resources in the country. Due to the Covid-19 pandemic, and traveling limitations small sample was utilized with generalizability limitations. Also, convenience sampling may result in research bias.

Authors Contribution

Conceptualization: RM
Methodology: RS
Formal analysis: RS
Writing, review and editing: GS, WAA

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Hwang CF, Chen Y, Lin HC, Narayanan P, Oh SH, Truy E. Cochlear implant and its related science. BioMed Research International. 2015 Jul; 2015: 683967. doi: 10.1155/2015/683967.

[2] Suárez H and Ferreira E. Rol de la información auditiva en el control motor del sistema del equilibrio en pacientes con implantes cocleares. InAnales de la Facultad de Medicina. 2019 Dec; 6(2): 8-24. doi: 10.25184/anfamed2019v6n2a10.

[3] Dev AN, Adhikari S, Lohith U, Dutt CS, Dutt SN. Assessment of quality of life outcomes with the Glasgow Children's Benefit Inventory following cochlear implantation in children. The Journal of Laryngology and Otology. 2019 Sep; 133(9): 759-63. doi: 10.1017/S0022215119001555.

[4] Dhanasingh A and Jolly C. Cochlear Implants: Recent Advances and New Horizons. Cochlear Implants: New and Future Directions. 2022 Jul: 501-14. doi: 10.1007/978-981-19-0452-3_24.

[5] Yan F, Li J, Xian J, Wang Z, Mo L. The cochlear nerve canal and internal auditory canal in children with normal cochlea but cochlear nerve deficiency. Acta Radiologica. 2013 Apr; 54(3): 292-8. doi: 10.1258/ar.2012.110596.

[6] Dettman SJ, Dowell RC, Choo D, Arnott W, Abrahams Y, Davis A *et al.* Long-term communication outcomes for children receiving cochlear implants younger than 12 months: A multicenter study. Otology and Neurotology. 2016 Feb; 37(2): e82-95. doi: 10.1097/MAO.0000000000000915.

[7] Russell JL, Pine HS, Young DL. Pediatric cochlear implantation: expanding applications and outcomes. Pediatric Clinics. 2013 Aug; 60(4): 841-63. doi: 10.1016/j.pcl.2013.04.008.

[8] Warner-Czyz AD, Nelson JA, Kumar R, Crow S. Parent-reported quality of life in children with cochlear implants differs across countries. Frontiers in Psychology. 2022 Oct; 13: 966401. doi: 10.3389/fpsyg.2022.966401.

[9] Louw C, Swanepoel DW, Eikelboom RH, Hugo J. Prevalence of hearing loss at primary health care clinics in South Africa. African Health Sciences. 2018 Jun; 18(2): 313-20. doi: 10.4314/ahs.v18i2.16.

[10] Sterkers O, Mosnier I, Ambert-Dahan E, Herelle-Dupuy E, Bozorg-Grayeli A, Bouccara D. Cochlear implants in elderly people: preliminary results. Acta Oto-Laryngologica. 2004 Apr; 124(552): 64-7. doi: 10.1080/03655230410017184.

[11] Zamanzadeh V, Ghahramanian A, Rassouli M, Abbaszadeh A, Alavi-Majd H, Nikanfar AR. Design and implementation content validity study: development of an instrument for measuring patient-centered communication. Journal of Caring Sciences. 2015 Jun; 4(2): 165. doi: 10.15171/jcs.2015.017.

[12] Sarant J and Garrard P. Parenting stress in parents of children with cochlear implants: Relationships among parent stress, child language, and unilateral versus bilateral implants. Journal of Deaf Studies and Deaf Education. 2014 Jan; 19(1): 85-106. doi: 10.1093/deafed/ent032.

[13] Schmucker C, Kapp P, Motschall E, Löhler J, Meerpohl JJ. Prevalence of hearing loss and use of hearing aids among children and adolescents in Germany: a systematic review. BioMed Central Public Health. 2019 Dec; 19: 1-0. doi: 10.1186/s12889-019-7602-7.

[14] Shi J, Mo X, Sun Z. Content validity index in scale development. Zhong nan da xue xue bao. Yi xue ban= Journal of Central South University. Medical Sciences. 2012 Feb; 37(2): 152-5. doi: 10.3969/j.issn.1672-7347.2012.02.007.

[15] Patrick DL, Burke LB, Gwaltney CJ, Leidy NK, Martin ML, Molsen E et al. Content validity-establishing and reporting the evidence in newly developed patient-reported outcomes (PRO) instruments for medical product evaluation: ISPOR PRO Good Research Practices Task Force report: part 2-assessing respondent understanding. Value in Health. 2011 Dec; 14(8): 978-88. doi: 10.1016/j.jval.2011.06.013.

[16] Hyde M, Punch R, Komesaroff L. Coming to a decision about cochlear implantation: parents making choices for their deaf children. Journal of Deaf

DOI: https://doi.org/10.54393/pjhs.v5i12.2167

Studies and Deaf Education. 2010 Mar; 15(2): 162-78. doi: 10.1093/deafed/enq004.

[17] Zaidman-Zait A. Parenting a child with a cochlear implant: A critical incident study. Journal of Deaf Studies and Deaf Education. 2007 Mar; 12(2): 221-41. doi: 10.1093/deafed/enl032.

[18] Sud P, Munjal SK, Panda N. Challenges faced by Indian parents in raising a child with a cochlear implant-Impact on communication outcomes. International Journal of Pediatric Otorhinolaryngology. 2023 Sep; 172: 111695. doi: 10.1016/j.ijporl.2023.111695.

[19] Khan MI, Mukhtar N, Saeed SR, Ramsden RT. The Pakistan (Lahore) cochlear implant programme: issues relating to implantation in a developing country. The Journal of Laryngology and Otology. 2007 Aug; 121(8): 745-50. doi: 10.1017/S0022215107007463.

[20] Bodington E, Saeed SR, Smith MC, Stocks NG, Morse RP. A narrative review of the logistic and economic feasibility of cochlear implants in lower-income countries. Cochlear Implants International. 2021 Jan; 22(1): 7-16. doi: 10.1080/14670100.2020.1793070.

[21] Alkhamra R, Al-Omari HM, Hani HA. Reliability and validity assessment of a survey: Measuring satisfaction with cochlear implant rehabilitation services for children in Jordan. PLOS One. 2023 Dec; 18(12): e0295939. doi: 10.1371/journal.pone.0295939.

[22] Sultana H, Mumtaz N, Saqulain G. Parental Perspective on Impact of Hearing Assistive Devices on Children with Hearing Impairment: Parental Perspective on Impact of Hearing Assistive Devices. Pakistan Journal of Health Sciences. 2023 Oct; 4(10): 93-8. doi: 10.54393/pjhs.v4i10.1080.

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Epstein Barr Virus Positivity and Behavioral Patterns in Nasopharyngeal Cancer Patients Presenting in Oncology Ward at JPMC, Karachi

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ABSTRACT

Immunohistochemistry tests for the presence of the Epstein-Barr virus latent membrane protein (EBV-LMP), which can be used to diagnose non-Hodgkin's lymphoma. Tumors expressing high amounts of latent membrane protein 1(LMP-1) provide more evidence that EBV is an etiologic agent in the development of non-Hodgkin lymphoma. **Objective:** To investigate the association between Epstein-Barr Virus infection and Nasopharyngeal Cancers within a cohort of 131 patients. **Methods:** A prospective, observational approach was employed, gathering demographic data, addiction profiles, clinical stages, histopathological types, and Epstein-Barr Virus status through patient interviews and medical records review. Polymerase chain reaction assisted in the detection of the Epstein Barr Virus in paraffin-embedded tissue slices that had been treated with formalin. **Results:** Among the participants, 92 (70.2%) tested positive for Epstein-Barr Virus infection. Notably, 49.6% of Epstein-Barr Virus-positive individuals were active smokers, and 64.9% were treatment-naive. Epstein-Barr Virus positivity was prevalent in stage II (40.5%) and stage III (35.1%) nasopharyngeal cancer patients. **Conclusions:** It was concluded that understanding the role of the Epstein-Barr Virus and associated risk factors in nasopharyngeal cancer development is crucial for targeted interventions and preventive measures. Further research could enhance our understanding of Epstein-Barr Virus-associated cancers and inform prospective intervention methods.

INTRODUCTION

Twenty percent of all malignancies in humans, or around 2 million cases annually, have an infectious origin [1]. More and more, research into the connection between infections and cancer is illuminating potential therapeutic and preventative measures by revealing the processes that drive the oncogenic process. Being the first human tumor virus to be identified, the Epstein-Barr virus (EBV) has provided valuable information on the development of cancer and the course of chronic herpesvirus infection [2, 3]. Despite being uncommon internationally, Nasopharyngeal Cancers (NPC) is a hotspot in southern China and Southeast Asia. The male infection rate can exceed 25 cases per 100,000 in many southern Chinese cities, including Zhong Shan City, Zhuhai, and Jiangmen. There may be a mix of genetic predisposition and environmental variables that make people living in these regions more prone to developing non-small cell lung cancer (NPC) [4, 5]. Type I keratinizing squamous cell carcinoma and types II and III non-keratinizing epithelial cell carcinoma are the two main histological forms of NPC recognized by the World Health Organization (WHO) based on the light-microscopically seen tumor cell characteristics. Subtypes of non-keratinizing carcinoma include type II differentiated non-keratinizing carcinoma & type III undifferentiated carcinoma; tumors of types II and III are more likely to be EBV positive [6, 7]. While unique

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keratinizing NPC (type I) accounts for fewer than 20% of all NPC cases worldwide and is relatively rare in southern China, EBV has been linked to the more distinct WHO type I NPC, particularly in regions where undifferentiated NPC is widespread [7, 8]. It is common to associate EBV infection with NPC in regions where the virus is common, such as Southern China and Southeast Asia. The prognostic value and prevalence of EBV and HPVs in NPC tumors identified in Finland were investigated in research by Ruuskanen et al., [9]. Although 93 out of 150 NPC patients tested positive for EBV and 21 out of 150 patients tested positive for HPV, the study found that none of these patients had coinfections. When tested for both viruses, 36 tumors (or 24% of the total) came out negative. The percentage of patients with disease-specific survival after 5 years was 69% for those whose cancers tested positive for EBV, 63% for those who tested positive for HPV, and 39% for those who tested positive for both. Individuals diagnosed with cancer who tested positive for both HPV and EBV had a better chance of overall survival in a multivariable-adjusted study than those whose tumors tested negative for both viruses [9]. Therefore, it is essential to determine whether the patient with NPC has EBV infection or not. This could potentially change the outcome of the disease. However, very little literature is currently available from Pakistan, thus the present study was undertaken to highlight the burden of EBV associated with NPC in a tertiary care hospital.

This study aims to evaluate EBV infection in patients with nasopharyngeal carcinoma (NPC) in a tertiary care center in Karachi, Pakistan.

METHODS

A cross-sectional, observational study was conducted after receiving approval from the Institutional Review Board (IRB Ref No. F.2-81/2022-DENL/116/JPMC) of Jinnah Postgraduate Medical Center, Karachi, Pakistan from the period 1st August 2023 to 30th June 2024. The research was carried out at the Department of Medical Oncology, Jinnah Postgraduate Medical Center, Karachi, Pakistan, within six months of obtaining IRB approval. The sampling technique was non-probability purposive. We estimated the sample size using a prevalence of 18% of Epstein-Barr Virus, a margin of error of 10%, and a confidence interval of 95% [10]. The formula was used: $n=Z^2P(1-P)/d^2$, where n=Sample size, Z=Z statistic for a level of confidence (1.96 for 95% confidence level), P=Expected prevalence or proportion, and d=Precision. Patients aged 18 years or older and those diagnosed with nasopharyngeal carcinoma on histopathology were included. All samples were checked for EBV status on histopathology. Adults who did not consent and cases where EBV status was not mentioned in histopathology were excluded. To collect data, all eligible participants were given both verbal and written informed consent. Patients were enrolled based on these criteria. Data regarding the patient's socio-economic and demographic (SED) factors, along with other clinical variables were recorded in a predefined pro forma including gender, residence (rural/urban), education level, employment status, income level (low, medium, and high), spouse's occupation, ethnicity (Pashtun, Sindhi, Punjabi), marital status (married, single, divorced, or widowed), parity and gravidity, and age (below 50 years vs. 50 and above), menopausal status (pre, peri, and post-menopausal), symptoms with duration in months, stage at diagnosis (TNM), and grade. EBV viral load was also determined, maintaining patient anonymity throughout the process. As per the instructions provided by the manufacturer, the QIAamp® DNA FFPE Tissue kit was used to extract EBV DNA from tissue blocks (QIAGEN, Hilden, Germany, cat # 56404). After DNA was extracted, it was eluted in a final volume of 50 µL and its concentration was measured with a Nano-Drop spectrometer (Nano-Drop™ 2000/2000c Spectrophotometers). 131 NPC patients' EBV status (positive or negative) was determined from diagnostic laboratory pathology findings. The findings of variables as mentioned above were entered in predesigned proforma. The Statistical Package for the Social Sciences (IBM, IL, version 23.0) was used to analyze the data. All continuous variables, including age at presentation, mean duration of disease, viral loads, etc., were presented as mean and standard deviation. The frequency distribution for categorical variables like the presence of EBV infection and stage, gender etc. were calculated. Vaccination status was also determined among all cases by using the chi-square test. After post-stratification, the impact of sociodemographic parameters on EBV positivity and the stage of nasopharyngeal carcinoma was determined using the Chi-square test. Statistical significance was defined at a p-value<0.05.

RESULTS

The study included 131 participants, with a mean age of 41.82 years. Demographics comprised 61.8% male and 38.2% female participants. Ethnically, 46.6% were Urdu-speaking, and common comorbidities were diabetes mellitus (25.2%) and hypertension (29.0%). Residentially, 59.5% were urban. Socioeconomic status distribution was 42.0% lower, 43.5% middle, and 14.5% upper. Educational background included 45.8% illiterate and 43.5% with matriculation (Table 1).

Table 1: Demographic Characteristics of Study Participants (n=131)

Variables	Mean ± SD	95% C. I
Age in Years	41.82 ± 14.33	39.35-44.30
Age Group		
18-40 Years	58 (44.3)	

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>40 Years	73 (55.7)
Gender	
Male	81 (61.8)
Female	50 (38.2)
Ethnicity	
Urdu	61 (46.6)
Sindhi	38 (29.0)
Punjabi	13 (9.9)
Push toons	8 (6.1)
Balochi	11 (8.4)
Comorbidities	
Diabetes Mellitus	33 (25.2)
Hypertension	38 (29.0)
Ischemic Heart Disease	16 (12.2)
Residential Status	
Urban	78 (59.5)
Rural	53 (40.5)
Socioeconomic Status	
Lower	55 (42.0)
Middle	57 (43.5)
Upper	19 (14.5)
Educational Status	
Illiterate	60 (45.8)
Matric	57 (43.5)
Postgraduate	3 (2.3)
Professional	11 (8.4)

The addiction profile of the participants revealed that 31.3% used Betel Nut, 13.7% used Gutka, 32.1% used Pan, and 3.1% used Naswar. Physical activity was categorized into house chores, inactive lifestyle, regular exercise, and exercise once a week. House chores showed (45) EBV-positive and (13) EBV-negative cases, while an inactive lifestyle had (31) EBV-positive and (15) EBV-negative cases. Regular exercise revealed (3) EBV-positive and (1) EBV-negative cases, and exercise once a week had (13) EBV-positive and (10) EBV-negative cases (Figure 1).

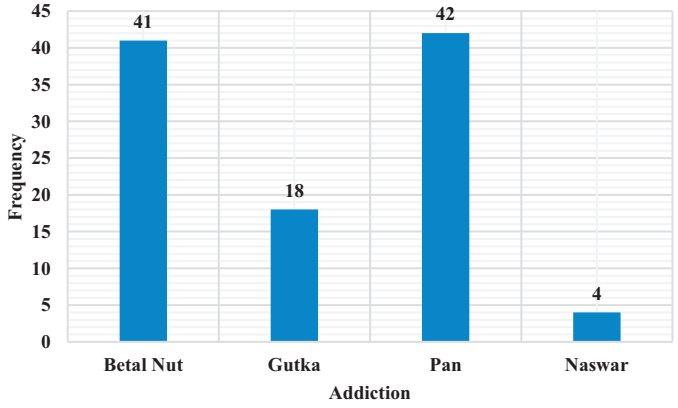

Figure 1: Substance Use among Participants

Physical activity was categorized into house chores, inactive lifestyle, regular exercise, and exercise once a week (Figure 2).

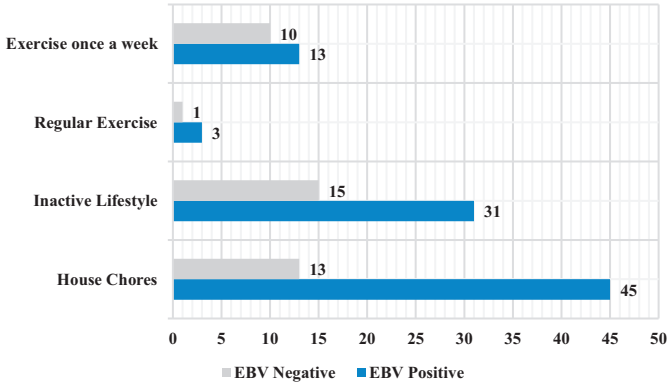

Figure 2: Physical Activity Between EBV Positive & Negative

The relationship between clinical stage, histopathological types according to the WHO classification, and viral status (EBV positive or negative) in 131 patients. Clinical stage distribution includes 5 cases (3.8%) in Stage I, 53 cases (40.5%) in Stage II, 46 cases (35.1%) in Stage III, and 27 cases (20.6%) in Stage IV. Regarding histopathological types, Type I is observed in 62 cases (47.3%), Type II in 14 cases (10.7%), and Type III in 55 cases (42.0%) (Table 2).

Table 2: Relationship Between Clinical Stage and Histological Types According to the WHO Classification and Viral Status (n=131)

Variables	All Patients	EBV Positive (n=92)	EBV Negative (n=39)	p-Value
Clinical Stage				
Stage I, n (%)	5 (3.8)	4 (3.1)	1 (0.8)	<0.001
Stage II, n (%)	53 (40.5)	44 (33.6)	1 (0.8)	
Stage I, n (%)	5 (3.8)	4 (3.1)	1 (0.8)	
Stage III, n (%)	46 (35.1)	33 (25.2)	13 (9.9)	
Histopathological Type				
Type I, n (%)	62 (47.3)	58 (44.3)	4 (3.1)	<0.002
Type II, n (%)	14 (10.7)	11 (8.4)	3 (2.3)	
Type III, n (%)	55 (42.0)	23 (17.6)	32 (24.4)	

EBV (Epstein-Barr virus) and vaccination status against measles and chickenpox in a cohort of 131 patients. Among the vaccinated group (n=57), 39 (29.8%) were EBV-positive, and 18 (13.7%) were EBV-negative. In the non-vaccinated group (n=74), 53 (40.5%) were EBV-positive, and 21 (16.0%) were EBV-negative. The p-value for the comparison is 0.691, indicating no statistically significant difference in EBV status based on vaccination against measles and chickenpox (Table 3).

Table 3: Comparison Between EBV and Vaccination Status Against Measles & Chicken Box (n=131)

Variables	Vaccinated (n=57)	Non-Vaccinated (n=74)	p-Value
Vaccination Status Against Measles & Chicken Box			
EBV Positive, n (%)	39 (29.8)	53 (40.5)	0.691
EBV Negative, n (%)	18 (13.7)	21 (16.0)	

Applied Chi-Square test, EBV (Epstein Barr Virus)

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The relationship was analyzed between EBV (Epstein-Barr virus) status and numerous risk factors in 131 individuals, including smoking, alcohol intake, family history of cancer, cancer therapy, oral contraception, steroid use, and eating habits. Among the EBV-positive group (n=92), 49.6% were active smokers, 13.0% consumed alcohol, 64.9% were treatment-naive, and 59.5% had a family history of cancer and other factors. In the EBV-negative group (n=39), the corresponding percentages were lower. Each risk factor is given an odds ratio (OR), a 95% confidence interval (CI), and a p-value to indicate the intensity and significance of the association with EBV status (Table 4).

Table 4: EBV, Risk Factor with Smoking, Alcohol, Family History of Cancer, Treatment Uses and Eating Habits (n=131)

Variable	EBV Positive (n=92)	EBV Negative (n=39)	OR	95% CI	p-Value
Smoking Status					
Active Smoker	65 (49.6)	33 (25.2)	0.429	(0.18-1.00)	0.105
Passive Smoker	19 (14.5)	6 (4.6)			
Non-Smoker	8 (6.1)	0 (0.0)			
Alcohol Consumption					
Yes	17 (13.0)	10 (7.6)	0.657	(0.27-1.60)	0.354
No	75 (57.3)	29 (22.1)			
Treatment-Naïve					
Yes	85 (64.9)	33 (25.2)	2.208	(0.69-7.05)	0.173
No	7 (5.3)	6 (4.6)			
Family History of Cancer					
Yes	78 (59.5)	32 (24.4)	1.219	(0.45-3.30)	0.697
No	14 (10.7)	7 (5.3)			
Any Other Cancer					
Yes	3 (2.3)	1 (0.8)	1.281	(0.12-12.71)	0.656
No	89 (67.9)	38 (29.0)			
Oral Contraception					
Yes	14 (10.7)	7 (5.3)	0.821	(0.30-2.22)	0.697
No	78 (59.5)	32 (24.4)			
Uses of Steroids					
Yes	43 (32.8)	22 (16.8)	0.678	(0.31-1.44)	0.311
No	49 (37.4)	17 (13.0)			
Eating Habit (Salt Cured Fish)					
Yes	39 (29.8)	17 (13.0)	0.952	(0.44-2.02)	0.899
No	53 (40.5)	22 (16.8)			
Eating Habit (Salt Cured Meat)					
Yes	42 (32.1)	18 (13.7)	0.980	(0.46-2.07)	0.958
No	50 (38.2)	21 (16.0)			

Applied Chi-Square test, EBV (Epstein Barr Virus), OR (Odd Ratio), CI (Confidence Interval)

DISCUSSION

This prospective, observational study underscores the association between Nasopharyngeal Cancers (NPC) and Epstein-Barr Virus (EBV), revealing that among 131 NPC patients, 92 tested positive for EBV infection. Furthermore, this research sheds light on the addiction profile, elucidating the connection between EBV status and various risk factors. Within the EBV-positive group, 49.6% were active smokers, 13.0% consumed alcohol, 64.9% were treatment-naive, and 59.5% had a family history of cancer, among other factors. A similar study on the aetiology of NPC found that the homogeneous histopathological type of NPC, which is frequent in southern China and Southeast Asia, had the strongest relationship between EBV infection and human tumors [11]. It also states that risk factors for NPC include genetic predisposition, dietary factors (salt-cured meat and fish), and EBV infection. In contrast, our findings showed that salt-cured meat and fish were not related to the development of NPC. Sharif *et al.*, mentioned in their research on Focus on NPC that the WHO classification categorizes NPC into three histopathological types, distinguishing them based on the degree of differentiation. Type I NPC is keratinizing squamous cell carcinoma (SCC), similar to other head and neck malignancies; Type II is differentiated non-keratinizing carcinoma; and Type III is undifferentiated carcinoma [12]. In regions with a high prevalence, such as Southern China, more than 97% of nasopharyngeal carcinoma cases are classified as World Health Organization (WHO) Type III, which represents undifferentiated carcinoma. Conversely, keratinizing squamous cell carcinoma (SCC) is more prevalent in Western countries. There are many other similar studies supporting this evidence [13, 14]. In the local context, a study by Su et al, found non-keratinizing NPC was the most prevalent subtype, constituting 92% (92 cases) while keratinizing squamous cell carcinoma (KSCC) accounted for 8% (8 cases) [15]. However, in our study, most of the patients of NPC were found to have histopathology Type I (n=62) of which 58 patients were EBV-positive. Though an EBV infection may increase the likelihood of developing undifferentiated carcinoma of the n (NPC), it is not a necessary condition for the development of this cancer [16]. In addition to EBV, other variables, such as environmental hazards and genetic predisposition, may combine with EBV to cause NPC. Factors that increase the likelihood of developing Type III nasopharyngeal carcinoma (NPC) include being of Cantonese ethnicity, being male, having Epstein-Barr virus (EBV) infection, having a personal or family history of NPC, eating too much salt-preserved fish, not getting enough fresh produce, smoking, and having specific human leukocyte antigen (HLA) class I alleles [10]. Similarly, in this study, it was observed that 61.8% of male were affected and a positive familial history (OR=1.219) is associated with the development of NPC. In the local context, research conducted on the clinical presentation of NPC at Jinnah Hospital Lahore revealed that 76% of male are affected [17]. Another study by Al-Anazi *et al.*, revealed the link between nasopharyngeal carcinoma (NPC) risk and cigarette smoking which

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appeared more pronounced for non-keratinizing carcinoma compared to keratinizing squamous cell carcinoma (KSCC), while a family history of cancer showed a stronger association with KSCC. The study did not find an association between NPC risk and alcohol consumption. The findings indicate that cigarette smoking and a family history of cancer can both operate as risk factors for NPC aetiology, potentially impacting the risk of different histopathological types of NPC in distinct ways. Internationally, previously reported that 75% and 75.5% of their NPC patients presented with neck mass respectively [18], which is only slightly more than our study whereas one study reported neck swellings in 80.8% of patients which could be due to loco-regional difference in presentation of NPC [19]. Globally, neither type I nor type II has been linked to a specific disease. For example, in Hau et al., a study from China, EBV type I dominated in patients with leukemia as well as those with myelodysplastic syndrome [21]. Likewise, in a study conducted on healthy blood donors from different nationalities in Qatar, EBV genotype I also predominated [20]. It is worth noting in our study that thirteen samples could not be genotyped because the PCR reaction yielded insufficient amplicon. One possible explanation could be the degradation or fragmentation of the viral DNA inside the block, possibly due to a stringent paraffin fixation procedure or long-term storage. Prolonged formalin fixation causes proteins as well as nucleic acid crosslinking. This understanding may contribute to a better comprehension of NPC aetiology overall and within each histologic type, offering insights that could enhance preventive efforts. Further information on the function of EBV and related risk factors in the onset and advancement of NPC is provided by the latest research. To establish a robust correlation between EBV and NPC subtypes across various ethnic groups, as well as to provide novel prospective therapeutic approaches for this EBV-associated malignancy, more study is necessary.

CONCLUSIONS

It was concluded that this study highlighted a significant association between Epstein-Barr Virus (EBV) infection and nasopharyngeal carcinoma (NPC) revealing that 70.2% of NPC patients were EBV-positive. Notably, EBV positivity was linked with higher stages of NPC. These findings highlight the importance of EBV in NPC's aetiology and progression, suggesting that understanding these relationships could lead to more effective screening, prevention, and treatment strategies. Future research should focus on revealing the complex interactions between EBV, genetic predispositions, and environmental factors in NPC development, providing a foundation for innovative therapeutic interventions and improved patient outcomes.

Authors Contribution

Conceptualization: SN
Methodology: SN, ZM, TBK
Formal analysis: MJ, AS, BR, SS
Writing review and editing: SN, GH, MJ, SZ

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Salahuddin S, Khan J, Azhar J, Whitehurst CB, Qadri I, Shackelford J *et al.* Prevalence of Epstein–Barr Virus Genotypes in Pakistani Lymphoma Patients. Asian Pacific Journal of Cancer Prevention.2018; 19(11): 3153. doi: 10.31557/APJCP.2018.19.11.3153.

[2] Chan AT, Hui EP, Ngan RK, Tung SY, Cheng AC, Ng WT *et al*. Analysis of Plasma Epstein-Barr Virus DNA in Nasopharyngeal Cancer After Chemoradiation to Identify High-Risk Patients for Adjuvant Chemotherapy: A Randomized Controlled Trial. Journal of Clinical Oncology.2018 Nov; 36(31): 3091-100 . doi: 10.1200/JCO.2018.77.7847.

[3] Salano VE, Mwakigonja AR, Abdulshakoor A, Kahinga AA, Richard EM. Epstein-Barr Virus Latent Membrane Protein-1 Expression in Nasopharyngeal Carcinoma. Journal of Global Oncology.2021 Sep; 7: 1406-12. doi: 10.1200/GO.21.00120.

[4] Chen YP, Chan ATC, Le QT, Blanchard P, Sun Y, Ma J. Nasopharyngeal carcinoma.Lancet.2019; 394 (1):6 4–80. doi: 10.1016/S0140-6736(19)30956-0

[5] Tsang CM, Lui VW, Bruce JP, Pugh TJ, Lo KW. Translational Genomics of Nasopharyngeal Cancer. In Seminars in Cancer Biology.2020 Apr; 61: 84-100. doi: 10.1016/j.semcancer.2019.09.006.

[6] Pathmanathan R, Prasad U, Chandrika G, Sadler R, Flynn K, Raab-Traub N. Undifferentiated, nonkeratinizing, and squamous cell carcinoma of the nasopharynx. Variants of Epstein-Barr virus neoplasia. Am J Pathol. 1995;146(6):1355–1367.

[7] Ayee R, Ofori ME, Tagoe EA, Languon S, Searyoh K, Armooh L *et al.* Genotypic Characterization of Epstein Barr Virus in Blood of Patients with Suspected Nasopharyngeal Carcinoma in Ghana. Viruses.2020 Jul; 12(7): 766. doi: 10.3390/v12070766.

[8] Xuemei J, Weidong Z, Conghua X, Bicheng W, Gong Z, Fuxiang Z. Nasopharyngeal carcinoma risk by histologic type in central China: impact of smoking,

DOI: https://doi.org/10.54393/pjhs.v5i12.2072

alcohol and family history. Int J Cancer. 2011; 129(3):724–732.doi:10.1002/ijc.25696

[9] Ruuskanen M, Irjala H, Minn H, Vahlberg T, Randen-Brady R, Hagström J *et al*. Epstein-Barr Virus and Human Papillomaviruses as Favorable Prognostic Factors in Nasopharyngeal Carcinoma: A Nationwide Study in Finland. Head & Neck.2019 Feb; 41(2): 349-57. doi: 10.1002/hed.25450

[10] Rafiq F, Rehman A, Khan AA. Clinical Presentation of Nasopharyngeal Carcinoma Experience at ENT Department, Jinnah Hospital, Lahore.Headache.2018 Jul; 15: 30.

[11] Abbott RJ, Pachnio A, Pedroza-Pacheco I, Leese AM, Begum J, Long HM *et al*. Asymptomatic Primary Infection with Epstein-Barr Virus: Observations on Young Adult Cases. Journal of Virology.2017 Nov; 91(21) : 10-128. doi: 10.1128/JVI.00382-17.

[12] Sharif SE, Zawawi N, Yajid AI, Shukri NM, Mohamad I. Pathology Classification of Nasopharyngeal Carcinoma. In an Evidence-Based Approach to the Management of Nasopharyngeal Cancer.2020 Jan: 73-92. doi: 10.1016/B978-0-12-814403-9.00005-7.

[13] Fierti AO, Yakass MB, Okertchiri EA, Adadey SM, Quaye O. The Role of Epstein-Barr Virus in Modulating Key Tumor Suppressor Genes in Associated Malignancies: Epigenetics, Transcriptional, And Post-Translational Modifications. Biomolecules. 2022 Jan; 12(1): 127. doi: 10.3390/biom12010127.

[14] Chan JY and Wong ST. The Role of Plasma Epstein-Barr Virus DNA in the Management of Recurrent Nasopharyngeal Carcinoma. The Laryngoscope.2014 Jan; 124(1): 126-30. doi: 10.1002/lary.24193.

[15] Su ZY, Siak PY, Leong CO, Cheah SC. The Role of Epstein–Barr Virus in Nasopharyngeal Carcinoma. Frontiers in Microbiology.2023 Feb; 14: 1116143. doi: 10.3389/fmicb.2023.1116143.

[16] Wu L, Li C, Pan L. Nasopharyngeal Carcinoma: A Review of Current Updates. Experimental and Therapeutic Medicine.2018 Apr; 15(4): 3687-92. doi: 10.3892/etm.2018.5878.

[17] Vasudevan HN and Yom SS. Nasopharyngeal Carcinoma and Its Association with Epstein-Barr Virus. Hematology/Oncology Clinics.2021 Oct; 35(5): 963-71. doi: 10.1016/j.hoc.2021.05.007.

[18] Al-Anazi AE, Alanazi BS, Alshanbari HM, Masuadi E, Hamed ME, Dandachi I *et al*. Increased Prevalence of EBV Infection in Nasopharyngeal Carcinoma Patients: A Six-Year Cross-Sectional Study. Cancers.2023 Jan; 15(3): 643. doi: 10.3390/cancers15030643.

[19] Hau PM, Lung HL, Wu M, Tsang CM, Wong KL, Mak NK *et al*. Targeting Epstein-Barr virus in Nasopharyngeal Carcinoma. Frontiers in Oncology.2020 May; 10: 600. doi: 10.3389/fonc.2020.00600.

[20] Leong MM and Lung ML. The Impact of Epstein-Barr Virus Infection on Epigenetic Regulation of Host Cell Gene Expression in Epithelial and Lymphocytic Malignancies. Frontiers in Oncology.2021 Feb; 11: 629780. doi: 10.3389/fonc.2021.629780.

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Association of Peripheral Artery Disease with Obesity

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ABSTRACT

Obesity has emerged as a significant contributor to the development and progression of Peripheral Artery Disease (PAD) which has significant impact on local population as the frequency of obesity is high. **Objective:** To determine the association between obesity and the development of Peripheral Artery Disease in patients attending General Medicine clinics. **Methods:** This cross-sectional study using non-probability convenient sampling was done to investigate association of obesity on the development of peripheral artery disease for six months. The study population consisted of adult patients (aged 18 and above) attending cardiovascular and metabolic clinics at Al-Tibri Medical Hospital. Inclusion criteria included patients with PAD confirmed by ankle-brachial index (ABI) of less than 0.90 into mild, moderate and severe. Patients with acute infections, malignancies were excluded. Hypothesis of the study stated that whether there was an association between obesity and development of PAD or not. Statistical analysis done using SPSS version 23.0, involved association between BMI and PAD using chi-square tests keeping $p<0.05$ statistically significant. **Results:** The mean age of participants was 50.87 ± 8.32 years. Mean ABI was 1.02 ± 0.12. Individuals having normal BMI (18-22.99 kg/m^2), 6 had PAD. In the overweight category (23-24.99 kg/m^2), 8 had PAD. In the Obese I category (25-26.99 kg/m^2), 11 had PAD. In the Obese II category (27-29.99 kg/m^2), 20 had PAD. In the Obese III category (>30 kg/m^2), 24 had PAD. A significant association between BMI and PAD was observed between both groups (p-0.01). **Conclusion:** A significant association between obesity and PAD development was observed in this study. Obesity was a significant factor in the development of PAD. The significant association between obesity and PAD observed in this study underscores the need for public health interventions aimed at weight management.

INTRODUCTION

Peripheral artery disease (PAD) is frequently reported circulatory problem characterized by narrowed arteries, reducing blood flow to limbs [1]. This condition primarily results from atherosclerosis, where fatty deposits build up in the artery walls. Among various risk factors, obesity is regarded as significant contributor in developing and progressing of PAD [2]. Obesity, is a growing global health issue [3]. It is established that obesity is a major risk factor for cardiovascular diseases, including PAD. Interplay between obesity and PAD is multifaceted, involving metabolic, inflammatory, and hemodynamic mechanisms [4]. Metabolic dysfunction is one of mechanism by which obesity primarily influences PAD. It is seldom linked to hyperglycemia, insulin resistance and dyslipidemia [5]. The metabolic alterations tend to cause dysfunction of endothelium, which is a precursor of atherosclerosis. Elevated levels of blood glucose and resistance to insulin can both lead to endothelial damage, which consequently causes deposition of fats in arterial walls [6]. In addition, obesity associated dyslipidemia, observed in terms of high triglycerides and low-density lipoprotein (LDL) levels. They further accelerate formation of atherosclerotic plaques [7]. Another vital link between PAD and obesity is inflammation. Adipose tissue, especially visceral fat, secretes multiple pro-inflammatory cytokines [8]. Such mediators cause chronic low-grade inflammatory conditions and promote atherosclerosis and subsequently lead to development of PAD. Oxidative stress can also occur because of chronic inflammation, thereby exacerbating plaque instability and endothelial dysfunction [9]. In the development of PAD, obesity associated hemodynamic changes also play a pivotal role.

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High body weight raises mechanical load on the heart which causes hypertension [10]. It is a well-known risk factor for atherosclerosis since it leads to stressed arterial walls and also promotes injury to endothelium. Furthermore, obesity alters dynamics of blood flow, as in increase in blood viscosity and alterations in shear stress which can further lead to damage to vascular endothelium and formation of plaque [11]. Researchers have continuously reported strong link between PAD and obesity. Research studies have observed obesity to be strongly associated with PAD when compared to individuals with normal weight [12]. Furthermore, PAD severity is often correlated with degree of obesity. For example, high BMI is linked to severe occlusion of arteries and increased risk for adverse cardiovascular event [13]. Obesity impacts PAD beyond development of disease, influencing clinical outcome of obese patients with PAD. This leads to complications, often whose rates tend to be high [14]. PAD patients who are obese tend to experience severe symptoms like resting pain and claudication, having higher risk for amputation of limb. In addition, even treatment of complications can sometimes be of limited help, wherein obesity can cause limited effectiveness of revascularization techniques, for instance bypass surgery or angioplasty. Factors associated with limited effectiveness amongst obese individuals are increase in peri-operative risks and technical challenges [15]. There to prevent and manage PAD, it is crucial to address obesity in terms of reduction of weight via modification in lifestyles, (dietary alterations and increased physical activity). Both have been reported to improve metabolic alterations, reducing inflammation and enhancing vascular function [16]. Peripheral Artery Disease (PAD) is a significant public health concern associated with considerable morbidity and mortality, yet the role of obesity in its development remains underexplored. Obesity, a global epidemic, is linked to systemic inflammation, endothelial dysfunction, insulin resistance, and pro-atherogenic metabolic disturbances, all of which contribute to vascular injury and atherosclerosis. While traditional risk factors like smoking, diabetes, and hypertension are well-established, obesity's independent role as a PAD risk factor is less clearly defined. This study aims to determine association between obesity and development of PAD in patients attending General Medicine clinics.

METHODS

This cross-sectional analytical study using non-probability convenient sampling was carried out on adult patients (18 years and above) attending medical out-patient department at Al-Tibri Medical Hospital, Karachi for a period of six months after approval from the Institutional Review Board (Ref no: ATMC/IERC/13th (01-2023)/15). Patients with clinical diagnosis of PAD confirmed by an ankle-brachial index (ABI) of less than 0.90 or imaging studies were included in the research. Patients having acute infections, malignancies, or conditions that might have confounded relationship between obesity and PAD (e.g., vasculitis) were excluded. A sample size calculation was performed based on the expected prevalence of PAD in obese population. Assuming a prevalence of PAD of 20% in the obese, with a power of 80% and a significance level of 5%, sample size was estimated at around 200 participants [13]. After ethical approval from Institutional Review Board (IRB) of hospital, data were collected through structured interviews, clinical examinations, and review of medical records. Informed consent was sought from each patient prior to inclusion in the study. The following information was gathered; demographic data included age, gender and BMI (kg/m2). Clinical data included ABI measurement and presence or absence of PAD. Initially 200 participants were included in the study but 10 had missing data, therefore a total of 190 participant's data were then processed. The data were collected on a pre-designed proforma, and data consistency were maintained by using the same proforma for all patients. All statistical analysis were carried out by SPSS version 23.0. Descriptive statistics was presented as frequency and percentage for gender while mean and standard deviation for age and BMI. Statistical analysis involved association between BMI and PAD using chi-square tests keeping $p<0.05$ as statistically significant.

RESULTS

The included participants had mean age of 50.87 ± 8.32 years. The Ankle Brachial Index (ABI), a measure used to assess peripheral arterial disease, had a mean value of 1.02 ± 0.12 (Table 1).

Table 1: Age and Ankle Brachial Index (ABI) of Patients Included (n=190)

Variable	Mean ± SD
Age	50.87 ± 8.32
ABI	1.02 ± 0.12

The gender distribution of the sample consisted of 88 male (46.3%) and 102 female (53.7%). The BMI categorization of the participants was as follows: 30 individuals (15.8%) had a normal BMI, 30 individuals (15.8%) were classified as Obese I, 55 individuals (28.9%) were classified as Obese II, 50 individuals (26.3%) were classified as Obese III, and 25 individuals (13.2%) were overweight. Regarding the Ankle Brachial Index (ABI) groups, 112 individuals (58.9%) had normal ABI values, 43 individuals (22.6%) were classified as having acceptable ABI values, 29 individuals (15.3%) had some arterial disease, 5 individuals (2.6%) had moderate arterial disease, and 1 individual (0.5%) had severe arterial disease (Table 2).

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Table 2: Baseline Demographics of Categorical Variables

Variable		Frequency (%)
Gender	Male	88 (46.3)
	Female	102 (53.7)
BMI	Normal	30 (15.8)
	Obese I	30 (15.8)
	Obese II	55 (28.9)
	Obese III	50 (26.3)
	Overweight	25 (13.2)
Ankle Brachial Index Groups	Normal	112 (58.9 %)
	Acceptable	43 (22.6 %)
	Some AD	29 (15.3 %)
	Moderate AD	05 (2.6 %)
	Severe AD	01 (0.5 %)

Figure 1 shows that 69 patients included in this study were reported to have PAD.

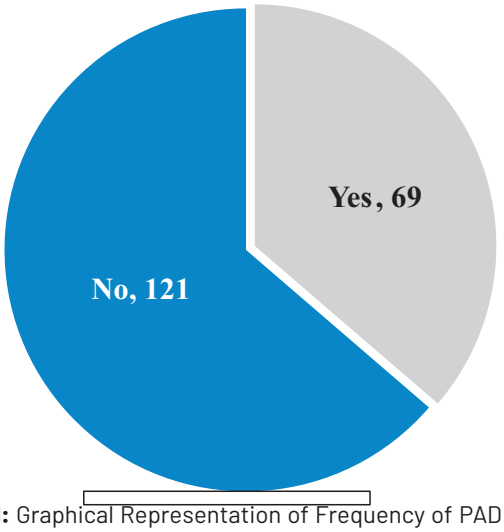

Figure 1: Graphical Representation of Frequency of PAD Among Patients Included in The Study (N=190)

Among individuals with a normal BMI (18-22.99 kg/m^2), 6 had PAD and 24 did not, out of a total of 30 individuals. In the overweight category (23-24.99 kg/m^2), 8 had PAD and 17 did not, out of a total of 25 individuals. In the Obese I category (25-26.99 kg/m^2), 11 had PAD and 19 did not, out of a total of 30 individuals. In the Obese II category (27-29.99 kg/m^2), 20 had PAD and 35 did not, out of a total of 55 individuals. In the Obese III category (>30 kg/m^2), 24 had PAD and 26 did not, out of a total of 50 individuals. A significant association between BMI and PAD was observed between both groups (p-0.01)(Table 3).

Table 3: Association between BMI and PAD (n=190)

Laterality of Eye		PAD		p-value	Proportion	95 % CI Lower	95 % CI Upper
		Yes	No				
BMI (kg/m^2)	Overweight (23-24.99)	06	24	0.01	0.20	0.057	0.343
	Overweight (23-24.99)	08	17		0.32	0.137	0.503
	Obese I (25-26.99)	11	19		0.367	0.194	0.539
	Obese II (27-29.99)	20	35		0.364	0.237	0.491
	Obese III (>30)	24	26		0.48	0.342	0.618

DISCUSSION

This study highlighted the association between Body Mass Index (BMI) and Peripheral Arterial Disease (PAD) which observed in this study aligns with findings from other research, highlighting the significant role that obesity plays in the development of PAD. Numerous research has established obesity as significant risk factor for PAD. For instance, a study published demonstrated that higher BMI was associated with higher risk of developing PAD [17]. The study found that individuals with a BMI ≥30 kg/m^2 had a significantly higher prevalence of PAD in comparison to BMI <30 kg/m^2. Similarly, the findings from the Framingham Heart Study highlighted that obesity, defined by a BMI ≥30 kg/m^2, was strongly associated with the incidence of PAD in either gender [18]. Current study, reporting higher BMI categories (Obese I, II and Obese III) are associated with a higher prevalence of PAD, are consistent with previous research. For example, a large cohort study reported individuals classified as obese had two-fold increased risk of PAD in comparison to those with normal weight [19]. Obesity seldom is linked with chronic low-grade inflammation which mainly contributes to pathogenesis of PAD and atherosclerosis [20]. Pro-inflammatory cytokines are secreted by adipose tissues that increase vascular inflammation, contributing towards PAD development [21]. Risk factors for PAD and atherosclerosis include hyperglycemia and resistance to insulin, both of which are closely linked to obesity [22]. Dyslipidemia is mostly observed in patients with a high BMI. Characteristic feature of dyslipidemia included elevated lipid levels overall. It is a well-known risk factor for PAD and atherosclerosis [23]. The findings of this research underscore the importance of managing weight for prevention and management of PAD. Clinicians should focus on signifying maintenance of healthy BMI via lifestyle modifications, dietary control and physical exercises. This should be practiced in patients which PAD or at-risk of PAD. Public health awareness programs ought to target weight reducing interventions in obese individuals for decreasing PAD burden. In order to achieve optimal health, nutritional counseling, weight loss programs and community-based activities should be promoted [24]. It should be routinely practiced that adult patients presenting to General Medicine clinics with obesity ought to be ruled out for peripheral arterial disease (PAD) by using Ankle Brachial Index (ABI). Patients presenting with any other complaint could possibly be diagnosed with PAD as an incidental finding. This study was

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not free from limitations. A single centered study with limited sample size cannot be used for generalization of the results. Moreover, BMI was recorded as a sole measure for obesity and no differentiation was made based on obesity types (central or peripheral) or through any laboratory investigations. Further multi-centered studies with greater sample size would be enlightening to the findings reported in this study.

CONCLUSIONS

Obesity was a significant factor in the development of PAD. The significant association between obesity and PAD observed in this study is consistent with previous research, highlighting the need for effective weight management strategies to mitigate the risk of PAD. Future research should explore the longitudinal impact of weight loss on the incidence and progression of PAD, as well as the underlying mechanisms linking obesity with peripheral arterial disease. The significant association between obesity and PAD observed in this study underscores the need for public health interventions aimed at weight management.

Authors Contribution

Conceptualization: HZ
Methodology: TA, AK
Formal analysis: HA
Writing review and editing: HA, SI, NAM

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

The authors declare no conflict of interest.

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REFERENCES

[1] Golledge J. Update on the Pathophysiology and Medical Treatment of Peripheral Artery Disease. Nature reviews cardiology.2022 Jul; 19(7): 456-474. doi: 10.1038/s41569-021-00663-9.

[2] Lempesis IG, Varrias D, Sagris M, Attaran RR, Altin ES, Bakoyiannis C, *et al.* Obesity and Peripheral Artery Disease: Current Evidence and Controversies. Current Obesity Reports.2023 Sep; 12(3): 264-279. doi: 10.1007/s13679-023-00510-7.

[3] Chooi YC, Ding C, Magkos F. The Epidemiology of Obesity. Metabolism.2019 Mar; 92:6-10. doi: 10.1016/j.metabol.2018.09.005.

[4] Keller K, Hobohm L, Geyer M, Münzel T, Lavie CJ, Ostad MA, *et al.* Obesity Paradox in Peripheral Artery Disease. Clinical Nutrition.2019 Oct; 38(5): 2269-2276. doi: 10.1016/j.clnu.2018.09.031.

[5] Heffron SP, Dwivedi A, Rockman CB, Xia Y, Guo Y, Zhong J, *et al.* Body Mass Index and Peripheral Artery Disease.Atherosclerosis.2020 Jan; 292:31-6. doi: 10.1016/j.atherosclerosis.2019.10.017.

[6] Kanegusuku H, Cucato GG, Domiciano RM, Longano P, Puech-Leao P, Wolosker N, *et al.* Impact of Obesity on Walking Capacity and Cardiovascular Parameters in Patients with Peripheral Artery Disease: A Cross-Sectional Study. Journal of Vascular Nursing.2020 Jun; 38(2): 66-71. doi: 10.1016/j.jvn.2020.02.004.

[7] Miao Y, Wang Y, Wang Y, Yan P, Chen Z, Wan Q. The Association Between Triglyceride-Glucose Index and Its Combination with Obesity Indicators and Lower Extremity Peripheral Artery Disease in Patients with Type 2 Diabetes Mellitus: A Cross-Sectional Study. Diabetes, Metabolic Syndrome and Obesity.2024 Dec: 2607-2617. doi: 10.2147/DMSO.S469692.

[8] Yadav U, Kumar N, Sarvottam K. Role of Obesity-Related Inflammation in Pathogenesis of Peripheral Artery Disease in Patients with Type 2 Diabetes Mellitus. Journal of Diabetes & Metabolic Disorders. 2023 Jun; 22(1): 175-88. doi: 10.1007/s40200-023-01221-5.

[9] Darvall KA, Sam RC, Silverman SH, Bradbury AW, Adam DJ. Obesity and Thrombosis. European Journal of Vascular and Endovascular Surgery.2007 Feb; 33(2): 223-33. doi: 10.1016/j.ejvs.2006.10.006.

[10] Maksimovic M, Vlajinac H, Radak D, Marinkovic J, Maksimovic J, Jorga J. Association of Overweight and Obesity with Cardiovascular Risk Factors in Patients with Atherosclerotic Diseases. Journal of Medical Biochemistry.2020 Jan; 39(2): 215. doi: 10.2478 /jomb-2019-0027.

[11] Li J, Yu S, Zhou W, Zhu L, Wang T, Bao H, *et al.* U-Shaped Association of Body Mass Index with the Risk of Peripheral Arterial Disease in Chinese Hypertensive Population. International Journal of General Medicine. 2021 Jul; 3627-3534. doi: 10.2147/IJGM.S323769.

[12] Lin DS, Lo HY, Yu AL, Lee JK, Chien KL. Mortality Risk in Patients with Underweight or Obesity with Peripheral Artery Disease: A Meta-Analysis Including 5,735,578 Individuals. International Journal of Obesity.2022 Aug; 46(8): 1425-1434. doi: 10.1038/s41366-022-01143-x.

[13] Zierfuss B, Höbaus C, Herz CT, Pesau G, Koppensteiner R, Schernthaner GH. Predictive Power of Novel and Established Obesity Indices for Outcome in PAD During a Five-Year Follow-Up. Nutrition, Metabolism and Cardiovascular Diseases.2020 Jun; 30(7): 1179-87. doi: 10.1016/j.numecd.2020.03.019.

[14] Haider R. Peripheral Vascular Disease. Cardiology Research and Reports. 2023; 5(4). doi: 10.31579/2692-

DOI: https://doi.org/10.54393/pjhs.v5i12.2086

9759/104.
[15] Bianchettin RG, Lavie CJ, Lopez-Jimenez F. Challenges in Cardiovascular Evaluation and Management of Obese Patients: JACC State-of-the-Art Review. Journal of the American College of Cardiology. 2023 Feb; 81(5): 490-504.
[16] Acosta S, Johansson A, Drake I. Diet and Lifestyle Factors and Risk of Atherosclerotic Cardiovascular Disease—A Prospective Cohort Study. Nutrients.2021 Oct; 13(11): 3822. doi: 10.3390/nu13113822.
[17] Aday AW and Matsushita K. Epidemiology of Peripheral Artery Disease and Polyvascular Disease. Circulation Research.2021 Jun; 128(12): 1818-32. doi: 10.1161/ CIR CRESAHA.121.318535.
[18] Fox CS, Massaro JM, Schlett CL, Lehman SJ, Meigs JB, O'Donnell CJ, *et al*. Periaortic Fat Deposition Is Associated with Peripheral Arterial Disease: The Framingham Heart Study. Circulation: Cardiovascular Imaging.2010 Sep; 3(5): 515-519. doi: 10.1161/ CIRCI MAG ING.110.958884.
[19] Lin DS, Lo HY, Yu AL, Lee JK, Yang WS, Hwang JJ. A Dose-Response Association Between Body Mass Index and Mortality in Patients with Peripheral Artery Disease: A Meta-Analysis Including 5,729,272 Individuals. European Journal of Vascular and Endovascular Surgery.2022 Mar; 63(3): 495-502. doi: 10.1016/j.ejvs.2021.11.016.
[20] Kawai T, Autieri MV, Scalia R. Adipose Tissue Inflammation and Metabolic Dysfunction in Obesity. American Journal of Physiology-Cell Physiology.2021 Mar; 320(3): 375-91. doi: 10.1152/ajpcell.00379.2020.
[21] Yadav U, Kumar N, Sarvottam K. Role of Obesity-Related Inflammation in Pathogenesis of Peripheral Artery Disease in Patients with Type 2 Diabetes Mellitus. Journal of Diabetes & Metabolic Disorders. 2023 Jun; 22(1): 175-88. doi: 10.1007/s40200-023-01221-5.
[22] Huang Y, Xu M, Xie L, Wang T, Huang X, Lv X, Chen Y, *et al*. Obesity and Peripheral Arterial Disease: A Mendelian Randomization Analysis. Atherosclerosis. 2016 Apr; 247: 218-24. doi: 10.1016 /j.ather oscler osis .2015.12.034.
[23] Aday AW, Everett BM. Dyslipidemia Profiles in Patients with Peripheral Artery Disease. Current Cardiology Reports.2019 Jun; 21:1-9. doi: 10.1007/s11886-019-1129-5.
[24] Heffron SP, Dwivedi A, Rockman CB, Xia Y, Guo Y, Zhong J, *et al*. Body Mass Index and Peripheral Artery Disease. Atherosclerosis.2020 Jan; 292: 31-6. doi: 10.1016/j.atherosclerosis.2019.10.017.

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Comparative Outcomes of Open Prostatectomy and Transurethral Resection of the Prostate for Benign Prostatic Hyperplasia

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ABSTRACT

The urinary function and comfort are substantially impacted by Benign Prostatic Hyperplasia (BPH), common in aging men. Moderate to severe cases frequently necessitate surgical interventions. Both Transurethral Resection of the Prostate (TURP) and Open Prostatectomy (OP) are well-established surgical procedures. **Objective:** To evaluate the efficacy, safety and patient outcomes of OP and TURP in the treatment of BPH. **Methods:** This quasi experimental study included 288 male patients diagnosed with BPH, allocated in the groups to undergo either OP (n=144) or TURP (n=144). The primary outcomes assessed were postoperative International Prostate Symptom Score (IPSS), maximal urinary flow rate (Qmax) and postvoid residual volume (PVR). Operative time, blood loss, hospital stay, complication rates and reoperation rates were secondary outcomes. **Results:** IPSS (at 1 month and 6 months), Qmax (at 1 month and 6 months) and PVR (at 6 months) were significantly improved in TURP patients ($P < 0.05$). OP patients encountered longer operative times ($P < 0.05$) and higher intraoperative blood loss ($P < 0.05$). Although trends favored the TURP group, there were non-significant differences between the groups regarding complications viz urinary incontinence and erectile dysfunction. Postoperatively, TURP also led to reduced analgesic needs and shortened hospital stays. **Conclusion:** TURP is the preferred treatment for most patients with BPH due to its faster recuperation, reduced complications and enhanced urinary function in comparison to OP. However, OP continues to be the valuable procedure for individuals with larger prostate volumes or specific clinical scenarios in which TURP may be insufficient.

INTRODUCTION

Benign Prostatic Hyperplasia is a prevalent urological condition that is associated with non-malignant enlargement of the prostate organ. It is most prevalent among the aging male population. Approximately 50% of male are affected by BPH by age of 60 and prevalence increases significantly with age, reaching up to 90% by the age of 85 [1-2]. This condition can result in lower urinary tract symptoms (LUTS), which can substantially reduce life comfort. These symptoms include urinary frequency, urgency, nocturia, weak stream and incomplete bladder emptying [3-4]. The management of BPH has undergone significant changes over the years, with the variety of therapeutic options available, including conservative management, pharmacotherapy and various surgical interventions [5]. When symptoms are moderate to severe, medical management fails or complications such as recurrent urinary tract infections, bladder stones or renal impairment develop, surgical treatment becomes a consideration [6]. Various factors, such as the size of prostate, specific symptoms, presence of comorbid conditions and preferences of the patient and clinician, influence the selection of the surgical technique. The TURP

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has been the conventional gold standard for surgical intervention. TURP has a long history of providing effective symptom relief; however, it is also linked to risks such as infection, bleeding and the rare but severe complication of TURP syndrome, which is characterized by diluted hyponatremia and hypertension [7, 8]. The popularity of alternative surgical methods has increased in recent years as a result of technological advancements and pursuit of procedures with shorter recovery periods and fewer complications [9]. Transurethral microwave thermotherapy, prostatic urethral lift systems and laser therapies (e.g., Holmium Laser Enucleation of Prostate - HoLEP) are minimally invasive techniques that have the potential to achieve comparable efficacy to TURP, with the potential for shorter convalescence and fewer adverse effects [10]. Each technique possesses a distinctive set of advantages and limitations that warrant a thorough examination [11-14].

This study aimed to investigate and evaluate efficacy, safety and patient outcomes of various surgical techniques as they pertain to the treatment of BPH.

METHODS

From May 2023 to April 2024, a quasi-experimental study was conducted at Gomal Medical College in Dera Ismail Khan to compare the complications and outcomes of TURP and OP for treating BPH. Using convenient sampling technique, the study encompassed 288 male patients, who were diagnosed with moderate to severe BPH. The sample size was calculated by the mean maximal urinary flow rate (Qmax), between OP (16.4 + 2.3) and TURP (13.3 + 1.5), by taking 80% power of test and 95% confidence interval, the sample size was 14, which was too small to perform statistical test with good efficiency, so we increase our sample size upto 288(144 in each group) [15]. Participants were required to meet the following eligibility criteria: having over 50 years age, diagnosed with BPH through clinical examination, prostate-specific antigen (PSA) levels, digital rectal examination and prostate ultrasonography. Patients with severe cardiovascular conditions, severe respiratory disorders, significant coagulopathies or any other health issues that would pose a high-risk during surgery were excluded from the study. In our study, we utilized a consecutive sampling technique for sample selection. All eligible patients presenting with moderate to severe BPH at our institution during the study period were included, provided they met the inclusion criteria and consented to participate. The participants were allocated as follows.

1.Transurethral Resection of the Prostate group (TURP Group)

2.Open Prostatectomy group (OP Group)

Efficacy was assessed using the following primary outcome variables: International Prostate Symptom Score (IPSS), maximal urinary flow rate (Qmax) and postvoid residual volume (PVR). These were measured at baseline, 1 month, 3 months, and 6 months postoperatively to evaluate improvements in urinary function which were the primary outcomes. Pertaining to our statistical analysis, quantitative variables included age, prostate volume, International Prostate Symptom Score (IPSS), maximal urinary flow rate (Qmax), postvoid residual volume (PVR), operative time, estimated blood loss and length of hospital stay. The qualitative variables included the presence of comorbidities, complication types and need for reoperation. SPSS version 25.0 was employed to conduct the statistical analysis. Odds Ratios (ORs) were calculated using logistic regression analysis to assess the association between the type of surgical procedure (TURP vs. OP) and occurrence of postoperative complications. For continuous outcome variables, such as IPSS, Qmax and PVR, ANOVA was used to compare the means between the OP and TURP groups at each time point. Effect sizes (Cohen's d) were calculated to assess the magnitude of differences between groups. Chi-square tests was employed for categorical variables. Statistical significance was defined as a p-value of less than 0.05. Institutional Review Board of Gomal Medical College authorized the study protocol vide Notification No. 35/GJMS//JC, dated May 21, 2023. Prior to enrollment in the investigation, each participant was granted informed consent. The investigation was conducted in compliance with the ethical standards outlined in the Declaration of Helsinki.

RESULTS

A thorough comparison of TURP and Open Prostatectomy in terms of numerous postoperative outcomes was conducted. Several critical findings regarding patient demographics, intraoperative metrics and postoperative outcomes were identified during the comparative analysis of TURP and OP. The baseline characteristics of the two groups did not exhibit any significant differences in prevailing hypertension and diabetes, baseline IPSS scores, BMI or age ($P > 0.05$). Thus, the groups were well-matched for the robust comparison. However, the prostate volume was considerably higher in OP group than TURP group (55 ± 10 cc vs. 30 ± 8 cc, $P < 0.01$)(Table 1).

Table 1: Baseline Characteristics and Demographics

Variables	OP Group (n=144)	TURP Group (n=144)	p-value
Age (Year)	68 ± 8 (65-71)	67 ± 7 (64-70)	0.451
BMI (kg/m^2)	29 ± 4 (27-31)	28 ± 3 (26-30)	0.379
Prostate Volume (cc)	55 ± 10 (50-60)	30 ± 8 (25-35)	0.001*
Baseline IPSS Score	22 ± 5 (20-24)	20 ± 4 (18-22)	0.153
Baseline Qmax (mL/sec)	8 ± 2 (7-9)	10 ± 3 (9-11)	0.028

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Baseline PVR (mL)	50 ± 20 (45-55)	45 ± 15 (40-50)	0.284
Comorbidities n (%)			
Hypertension	80 (55.9)	82 (56.9)	0.852
Diabetes	30 (21)	28 (19.4)	0.747

The OP group experienced longer operative times (90 ± 20 vs. 60 ± 15 minutes, P < 0.05) and greater blood loss (400 ± 150 vs. 200 ± 100 mL, P < 0.05) intraoperatively, which highlighted the more invasive character of open surgery in comparison to the transurethral approach. The rate of conversion to another method was low and did not differ substantially between the groups, despite these differences. The hospital stay duration was significantly longer in the OP group (7.5 ± 2.1 days) compared to the TURP group (4.2 ± 1.6 days) (p<0.01). The OP group had a higher overall complication rate, but it was not significantly higher (12.6 vs. 8.3%, P > 0.05)(Table 2).

Table 2: Intraoperative Data among study participants

Variables	OP Group (n = 144)	TURP Group (n = 144)	p-value
Operative Time (Minutes)	90 ± 20	60 ± 15	0.033*
Estimated Blood Loss (mL)	400 ± 150	200 ± 100	0.006*
Conversion to Another Method n (%)	2 (1.4%)	0 (0%)	0.157
Hospital Stay (Days)	7.5 ± 2.1	4.2 ± 1.6	0.001*
Complications n (%)	18 (12.6%)	12 (8.3%)	0.221
Urinary Incontinence n (%)	6 (4.2%)	3 (2.1%)	0.28
Erectile Dysfunction n (%)	7 (4.9%)	4 (2.8%)	0.31
Bleeding n (%)	3 (2.1%)	2 (1.4%)	0.47
Infection n (%)	2 (1.4%)	3 (2.1%)	0.58

The TURP group generally demonstrated superior outcomes, with significantly lower IPSS scores at 1 month (8 ± 2 vs. 10 ± 3) and higher Qmax at both 1 month (18 ± 4 vs. 15 ± 5 mL/sec) and 6 months (21 ± 3 vs. 19 ± 3 mL/sec)(P < 0.05). The effect size calculations implied that TURP may be more effective in short to medium term in alleviating urinary symptoms and improving flow rates, as they indicated a moderate to strong effect in favor of TURP for both IPSS scores and Q-max. Furthermore, efficacy of TURP in reducing urinary retention postoperatively was further supported by the fact that postvoid residual volume (PVR) was substantially lower in the TURP group at 6 months (10 ± 5 vs. 15 ± 7 mL, P < 0.05)(Table 3).

Table 3: Postoperative Outcomes at 1 and 6 Months

Outcome Measure	Time Point	OP Group	TURP Group	p-value
IPSS Score	1 Month	15 ± 5 (14-16)	8 ± 2 (7-9)	0.04*
	3 Months	9 ± 2 (8-10)	7 ± 2 (6-8)	0.05
	6 Months	7 ± 2 (6-8)	0 (0%)	0.09
Qmax (mL/sec)	1 Month	15 ± 5 (14-16)	18 ± 4 (17-19)	0.01*
	3 Months	19 ± 3 (18-20)	21 ± 3 (20-22)	0.03*
PVR (mL)	6 Months	15 ± 7 (14-16)	10 ± 5 (9-11)	0.02*

Repeated Measures ANOVA

The IPSS of both groups demonstrated progressive improvement from 1 to 6 months post-surgery as time progressed. The TURP group consistently revealed lower IPSS scores at each time point, implying more favorable outcome in terms of symptom relief than OP group (Figure 1).

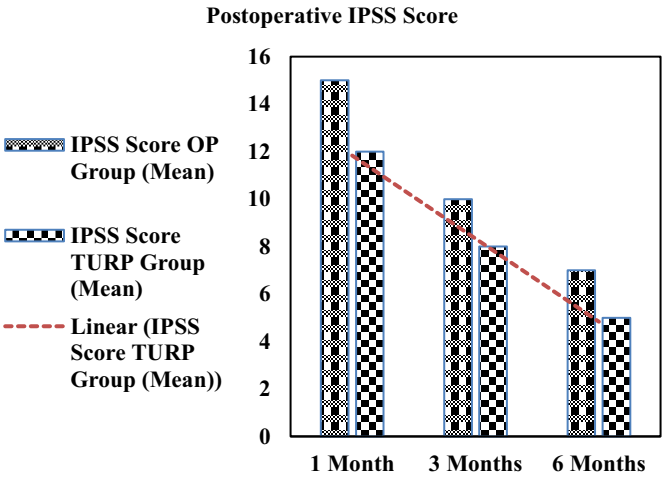

Figure 1: Postoperative IPSS Score Trends over Time

The postoperative challenges associated with each surgical approach were emphasized, while the observed odds ratios indicated trend toward the higher incidence in OP group, the differences in rates of urinary incontinence and erectile dysfunction between the two groups at 6 months were not statistically significant (P > 0.05). In particular, the more invasive nature of OP was indicative of potential hazards, as the incidence of urinary incontinence and erectile dysfunction in OP group was approximately twice that of TURP group and 1.6 times that of the TURP group, respectively (Table 4).

Table 4: Complications and Reoperation Rates at 6 Months

Complication Type	Severity	Time Point	OP Group n (%)	TURP Group n (%)	p-value	Odds Ratio (95% CI)
Urinary Incontinence	Mild	6 Months	6 (4.2)	3 (2.1)	0.28	2.0 (0.5-6.8)
	Moderate	6 Months	3 (2.1)	2 (1.4)	0.47	1.5 (0.3-7.5)
	Severe	6 Months	1 (0.7)	0 (0)	0.32	1.0 (0.2-5.8)
Erectile Dysfunction	Mild	6 Months	7 (4.9)	4 (2.8)	0.31	1.8 (0.5-6.1)
	Moderate	6 Months	6 (4.2)	4 (2.8)	0.39	1.5 (0.4-5.6)
	Severe	6 Months	2 (1.4)	2 (1.4)	1.00	1.0 (0.2-5.4)
Reoperation Rate	-	6 Months	5 (3.5)	3 (2.1)	0.45	1.7 (0.4-7.1)

The immediate postoperative period demonstrated that OP group experienced substantially higher pain scores and analgesic use at both 24- and 72-hours post-operation. These results were statistically significant, with p-values less than 0.01 and substantial effect sizes. The 72-hour

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period was particularly noteworthy with Cohen's d value of 2.0, indicating that OP is more invasive and associated with higher requirement for pain management and greater immediate postoperative discomfort (Table 5).

Table 5: Postoperative Pain and Analgesic Requirement

Outcome	Time Point	Measurement	OP Group	TURP Group	p-value	Effect Size (Cohen's d)
Pain Score (VAS)	24 Hours	Mean ± SD (95% CI)	7 ± 2 (6-8)	4 ± 1 (3-5)	0.003*	1.5
	72 Hours	Mean ± SD (95% CI)	4 ± 1 (3-5)	2 ± 1 (1-3)	0.007*	2.0
Analgesics Used	24 Hours	Number of Doses	3 ± 1	2 ± 1	0.018*	1.0
	72 Hours	Number of Doses	2 ± 1	1 ± 0.5	0.028*	1.0

DISCUSSION

The comparative analysis of TURP and Open Prostatectomy revealed substantial differences in outcomes that are essential for the rationale of clinical decisions regarding the management of BPH. Effective surgical interventions are necessary to alleviate the symptoms and enhance quality of life, as BPH remains the prevalent issue, particularly in elderly male population. The findings of this investigation are crucial in elucidating the extent to which each procedure influences recovery, symptom alleviation and long-term satisfaction [16-18]. TURP has been regarded as the gold standard for surgical treatment of BPH for an extended period due to its effective relief of symptoms and minimal invasive nature. In this investigation, patients who underwent TURP demonstrated consistently superior outcomes in terms of IPSS scores over the six-month period in comparison to those who underwent OP. Christidis *et al*. have reported in 2017 that TURP has superior outcomes in terms of both efficacy and recovery time, which is consistent with the results of other studies [19]. Lin *et al*. advocated for using TURP in clinical practice, particularly for patients with moderate prostate enlargement, due to the gradual improvement in urinary symptoms and reduced IPSS scores that are associated with it [20]. However, OP continues to be a viable option for patients with larger prostate volumes or when other complicated factors are present. Even though OP is more invasive, it can be particularly effective in patients with substantially enlarged prostates, where TURP may not be as efficient or feasible. In this context, our results suggested that OP can provide significant symptom relief, albeit at the delayed recovery pace and with higher complication rates, including increased pain and greater need for analgesics post-surgery, these findings are also supported by the literature [17, 21]. The pain management findings are particularly noteworthy, as OP patients exhibited substantially higher pain scores and greater analgesic requirements within an initial 72 hours following surgery. Beilstein *et al*. (2022) also observed that patients who undertake more invasive prostate procedures typically require more intensive postoperative pain management strategies, which these results corroborate [22]. It is imperative to implement effective pain management, as it has the potential to substantially impact patient satisfaction and recovery. Consequently, the selection of the surgical technique should take into account the potential for the more difficult recuperation period and increased postoperative discomfort, despite the fact that OP can be effective for large prostates. The reoperation rates and extended hospital stays that are linked to OP emphasize the personal and economic expenses of this method. In addition to the impact on healthcare costs, patients' comfort is also affected by the extended institutionalization, as it delays the return to normal activities [23]. In healthcare environments where resource allocation and patient throughput are critical considerations, it is necessary to balance these factors against the advantages of OP. Although there was no statistically significant difference between the groups in terms of urinary incontinence and erectile dysfunction, there was trend toward higher rates in OP group. These findings are consistent with the study suggesting more extensive surgical interventions may bear higher risk of such adverse events, which is consistent with potentially long-term complications associated with the more invasive nature of OP [24]. The study's implications are not limited to clinical outcomes; they also extend to the development of policy and practice guidelines. In the context of overall healthcare efficacy, patient satisfaction and cost-effectiveness, healthcare providers and policymakers must take these findings into account to facilitate the most effective surgical techniques and optimize resource utilization.

CONCLUSIONS

This comparative study of Open Prostatectomy and TURP established that, even though TURP provides less invasive alternative with the faster recovery, improved symptom management and fewer complications, OP continues to be significant surgical option for patients with significantly larger prostate volumes or when TURP is not suitable. The indications, benefits and drawbacks of each surgical method are distinct. Consequently, selection of the surgical procedure should be customized to unique characteristics of each patient, ensuring that the potential for symptom relief and quality of life enhancement is balanced against the invasive nature of the procedure and the corresponding recovery challenges to BPH patients.

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Authors Contribution

Conceptualization: IUR
Methodology: IUR, MF
Formal analysis: NA, MLJ, MF
Writing, review and editing: KK, MLJ, IUR, RN

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

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REFERENCES

[1] Roehrborn CG. Benign Prostatic Hyperplasia: An Overview. Reviews in Urology.2005; 7(9). doi: 10.1016/S1569-9056(04)90343-0.

[2] Moin AM and Nagarjuna M. Exploring Sensitivity and Significance of Tamsulosin as Modified Release in Benign Prostatic Hyperplasia. Saudi Journal of Medical and Pharmaceutical Sciences.2024; 10(3): 179-183. doi: 10.36348/sjmps.2024.v10i03.007.

[3] Lepor H. Pathophysiology of Lower Urinary Tract Symptoms in the Aging Male Population. Reviews in Urology. 2005; 7(7): 3.

[4] Kant P, Inbaraj LR, Franklyn NN, Norman G. Prevalence, Risk Factors and Quality of Life of Lower Urinary Tract Symptoms (LUTS) among Men Attending Primary Care Slum Clinics in Bangalore: A Cross-Sectional Study. Journal of Family Medicine and Primary Care. 2021 Jun; 10(6): 2241-2245. doi: 0.4103/jfmpc.jfmpc_2316_20.

[5] Miernik A and Gratzke C. Current Treatment for Benign Prostatic Hyperplasia. Deutsches Arzteblatt International.2020 Dec; 117(49): 843. doi: 10.3238/arztebl.2020.0843.

[6] Elterman DS, Barkin J, Kaplan SA. Optimizing the Management of Benign Prostatic Hyperplasia. Therapeutic Advances in Urology.2012 Apr; 4(2): 77-83. doi: 10.1177/1756287212437361.

[7] Xia E, Valle RF, Huang X, Yu D, Liu Y, Lin B, et al. Complications of Hysteroscopic Surgery. Practical Manual of Hysteroscopy.2022 Aug; 1: 365-420. doi: 10.1007/978-981-19-1332-7_12.

[8] Palaniappan S, Kuo TL, Cheng CW, Foo KT. Early Outcome of Transurethral Enucleation and Resection of the Prostate Versus Transurethral Resection of the Prostate. Singapore Medical Journal.2016 Dec; 57(12): 676-680. doi: 10.11622/smedj.2016026.

[9] Nimeh T, Magnan B, Almallah YZ. Benign Prostatic Hyperplasia: Review of Modern Minimally Invasive Surgical Treatments. Seminars in Interventional Radiology.2016 Sep; 33(3): 244-250. doi: 10.1055/s-0036-1586148.

[10] Fogaing C, Alsulihem A, Campeau L, Corcos J. Is Early Surgical Treatment for Benign Prostatic Hyperplasia Preferable to Prolonged Medical Therapy: Pros and Cons. Medicina.2021 Apr; 57(4): 368. doi: 10.3390/medicina57040368.

[11] Chen F, Chen Y, Zou Y, Wang Y, Wu X, Chen M. Comparison of Holmium Laser Enucleation and Transurethral Resection of Prostate in Benign Prostatic Hyperplasia: A Systematic Review and Meta-Analysis. Journal of International Medical Research. 2023 Aug; 51(8). doi: 10.1177/03000605231190763.

[12] Bharadwaj HR, Wireko AA, Adebusoye FT, Ferreira T, Pacheco-Barrios N, Abdul-Rahman T, et al. Challenges and Opportunities in Prostate Cancer Surgery in South America: Insights into Robot-Assisted Radical Prostatectomies—A Perspective. Health Science Reports. 2023 Aug; 6(8): 1519. doi: 10.1002/hsr2.1519.

[13] Liu S and Hemal A. Techniques of Robotic Radical Prostatectomy for the Management of Prostate Cancer: Which One, When and Why. Translational Andrology and Urology.2020 Apr; 9(2): 906. doi: 10.21037/tau.2019.09.13.

[14] Mian AH, Tollefson MK, Shah P, Sharma V, Mian A, Thompson RH, *et al.* Navigating Now and Next: Recent Advances and Future Horizons in Robotic Radical Prostatectomy. Journal of Clinical Medicine.2024; 13(2): 359. doi: 10.3390/jcm13020359.

[15] Sofimajidpour H, Khoshyar A, Zareie B, Sofimajidpour H, Rasouli MA. Comparison of the Effectiveness and Safety of Transvesical Open Prostatectomy Versus Transurethral Resection of the Prostate in Patients with Benign Prostatic Hyperplasia with a Prostate Weight of 65-40 Gram. Urology journal.2020 Nov; 18(03): 289-294.

[16] Eraky AM, Rubenstein SC, Khan A, Mokhtar Y, Gregorich NM. Non-Surgical Bleeding and Transurethral Resection of the Prostate (TURP) Syndrome after TURP Surgery: A Case Report and Literature Review. Pathophysiology.2024 Jul; 31(3): 367-375. doi: 10.3390/pathophysiology31030027.

[17] Fogaing C, Alsulihem A, Campeau L, Corcos J. Is Early Surgical Treatment for Benign Prostatic Hyperplasia Preferable to Prolonged Medical Therapy: Pros and Cons. Medicina.2021 Apr; 57(4): 368. doi: 10.3390/medicina57040368.

[18] Kaltsas A, Kratiras Z, Zachariou A, Dimitriadis F, Sofikitis N, Chrisofos M. Evaluating the Impact of Benign Prostatic Hyperplasia Surgical Treatments on Sexual Health. Biomedicines. 2024 Jan; 12(1): 110. doi:

DOI: https://doi.org/10.54393/pjhs.v5i12.1991

10.3390/biomedicines12010110.

[19] Christidis D, McGrath S, Perera M, Manning T, Bolton D, Lawrentschuk N. Minimally Invasive Surgical Therapies for Benign Prostatic Hypertrophy: The Rise in Minimally Invasive Surgical Therapies. Prostate International.2017 Jun; 5(2): 41-46. doi: 10.1016/j.prnil. 2017.01.007.

[20]Lin YH, Hou CP, Chen TH, Juang HH, Chang PL, Yang PS, *et al*. Transurethral Resection of the Prostate Provides More Favorable Clinical Outcomes Compared with Conservative Medical Treatment in Patients with Urinary Retention Caused by Benign Prostatic Obstruction. BMC geriatrics.2018 Dec; 18: 1-7. doi: 10.11 86/s12877-018-0709-3.

[21] Zeng XT, Jin YH, Liu TZ, Chen FM, Ding DG, Fu M, *et al*. Clinical Practice Guideline for Transurethral Plasmakinetic Resection of Prostate for Benign Prostatic Hyperplasia. Military Medical Research. 2022 Apr; 9(1): 14.

[22]Beilstein CM, Huber M, Furrer MA, Löffel LM, Wuethrich PY, Engel D. Impact of Analgesic Techniques on Early Quality of Recovery after Prostatectomy: A 3-Arm, Randomized Trial. European Journal of Pain.2022 Oct; 26(9): 1990-2002. doi: 10.1002/ejp.2020.

[23]Franco JV, Tesolin P, Jung JH. Update on the Management of Benign Prostatic Hyperplasia and the Role of Minimally Invasive Procedures. Prostate International.2023 Mar; 11(1): 1-7. doi: 10.1016/j. prnil. 20 23.01.002.

[24]Ng M, Leslie SW, Baradhi KM. Benign Prostatic Hyperplasia. StatPearls. 2024 Jan; 1.

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Original Article

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Frequency of Different Patterns of Fractures Presented in Accidents and Emergency Department of Mayo Hospital Lahore

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ABSTRACT

Emergency departments encounter various fracture patterns that are influenced by factors such as age, injury mechanism, and underlying health conditions. **Objectives:** To investigate the frequencies of different fracture types and patterns, and thus assess the work burden observed in the emergency departments of Mayo Hospital, Lahore. **Methods:** This study was conducted at the Orthopedic Section of the Emergency Department of Mayo Hospital, Lahore between 1st January to 31st December 2022. Data were obtained from registers used to make entries of the patients in the Orthopedic section. All patients were divided into a pediatrics group (up to 12 years of age) and an adult group (above 12 years of age). The adult group was further divided into male and female groups. **Results:** 29190 (85.03%) were adults and 5136 (14.97%) were pediatric patients. Among the adult patients, 21048 (72.11%) were males and 8142 (27.89%) were females while in the pediatrics age group, 3378 (65.78%) were boys and 1758 (34.22%) were girls. Overall, the lower limb was more commonly fractured than the upper limb (52.88 % versus 32.16%) and the most frequently fractured bone was the tibia (19.99%). The leading cause of injury is Road Traffic Accidents (64.21%) followed by machine injuries (9.28%) and falls (7.85%). Patients aged 21 to 30 years were frequently affected (19.77%). **Conclusions:** It was concluded that daily, nearly one hundred fractures were reported to the Emergency department of Mayo Hospital Lahore. Resources need to be improved to cope with continuous quality care for these patients.

INTRODUCTION

Bone fractures, characterized by disruptions in bone continuity, pose a substantial threat to global musculoskeletal health. The reported incidence of fractures in the general population varies across studies. It ranges from 3.21 to 22.8 per 1000 annually [1]. In England, a self-report survey estimated an overall annual fracture incidence of 3.6 per 100 people [2]. This suggests fractures may be more common than previously thought. A study in Leicestershire, England found an estimated annual incidence of 100 per 10,000 for males and 81 per 10,000 for females across all fracture types [2]. In southern Sweden, the overall incidence rate of distal radius fractures was 26 per 10,000 person-years [3]. A study in South Wales found a much higher fracture rate of 36.1 per 1,000 children. [4]. The reasons for this higher rate require further investigation. Additionally, fracture incidence appears to vary geographically, with lower rates reported in Britain compared to North America and some Scandinavian countries. The occurrence of different fracture patterns in Emergency departments varies considerably based on factors like age, gender, and mechanism of injury [5]. A thorough review of various studies as mentioned above reveals distinct trends in fracture types and associated demographics. Fractures in healthy bones typically result from high-energy impacts or repetitive stress, whilst bones weakened by disease may fracture under normal loads or minor injuries [6]. The external causes of limb fractures, such as motor vehicle collisions, falls, sports

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injuries, and assaults, are generally similar worldwide. However, the distribution of these etiological factors varies between and within countries, depending on demographic profiles, socioeconomic conditions, and environmental factors [7]. Some studies indicate a predominance of falls as the external cause of fractures among pediatric and geriatric populations, as well as in regions with hilly terrain [8]. Other reports suggest that motor vehicle collisions are the primary external cause of fractures, particularly in areas where road traffic injuries are a neglected epidemic [9-11]. The type and pattern of limb fractures also vary with age, injury mechanism and severity, and involvement of surrounding tissues. The characteristics of limb fractures and the affected population have implications for treatment strategies and outcomes. Detailed information on etiological factors and characteristics of limb fractures in a specific setting can facilitate preventive and treatment strategies. However, data on limb fractures are limited. Recent reports indicate that limb fractures constitute 82.1%–94.7% of all fractures by anatomical region distribution [12, 13]. Cant *and* Faergemann, reported a total incidence of physical fractures of lower limbs in children as 35 per 100000 person-years [14]. The lack of comprehensive data and the diverse patterns of limb fractures in terms of types, causes, and demographic characteristics across sub-regions emphasize the importance of conducting this research. The rationale for this study was that understanding the frequencies of different fractures would provide better insight into fracture patterns, which can inform community health initiatives, especially in resource-limited settings. Future research should focus on validating fracture classifications and exploring the implications of an ageing population on fracture incidence.

This study aims to investigate the frequencies of different fracture types and patterns, and thus assess the work burden observed in the Emergency Departments of Mayo Hospital, Lahore.

METHODS

This cross-sectional analysis was conducted in the Orthopedic Section of the Emergency Department at Mayo Hospital, Lahore, Pakistan. Ethical approval was taken from the Institutional Review Board of King Edward Medical University Lahore vide letter number 182/RC/KEMU. Taking reference of the previous study [15], a minimum sample size of 2341 was calculated using World Health Organization (WHO) calculator 1.1 with a confidence level of 99 %, anticipated population proportion of 83% and absolute precision of 2%. A convenient sampling technique was used. Informed consent was taken. The study examined records of patients who presented with bone fractures between 1st January 2022 and 31st December 2022. Patients with soft tissue injuries, infections, and dislocations were excluded. The subjects were categorized into pediatric (up to and including 12 years) [16] and adult (over 12 years) groups. Adult patients were further subdivided by gender, affected region and bone, and age. Pediatric patients were classified based on the fractured bone and gender. The compiled data were analyzed using SPSS version 23.0, with frequencies and percentages calculated and illustrated using pie charts and graphs.

RESULTS

The study encompassed 34326 patients, comprising 29190 (85.03%) adults and 5136 (14.97%) children (Figure 1).

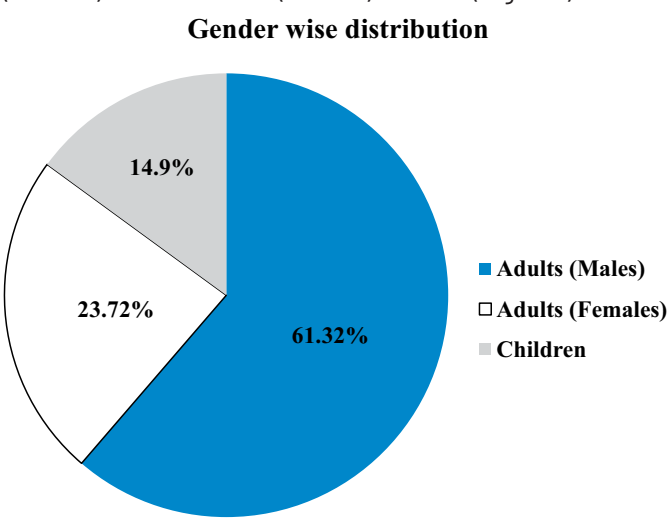

Figure 1: Gender Wise Distribution of the Patients

Among adults, 21048 (72.11%) were male and 8142 (27.89%) females, while the pediatric group consisted of 3378 (65.78%) boys and 1758 (34.22%) girls. Lower limb fractures were more prevalent than upper limb fractures (52.88% versus 32.16%). In adults, the most common lower limb fractures were the shaft of the tibia (2645, 7.71%), shaft of the femur (1994, 5.81%), and trochanteric (1661, 4.84%) (Table 1).

Table 1: Different Fractures and Their Frequencies in the Pelvic Girdle and Lower Limb (Adults)

Lower Limb Fractures	Frequency (%)
Pelvic, Acetabular ± HOF	724 (2.11%)
Neck of Femur	988 (2.88%)
Pertrochenteric and Sub-Trochenteric	1661(4.84%)
Shaft of Femur	1994 (5.81%)
Distal Femur (Intra-Articular)	1156 (3.37%)
Patella	1407 (4.10%)
Proximal Tibia (Intra-Articular)	1558 (4.54%)
Shaft of Tibia	2645 (7.71%)
Isolated Shaft of Fibula	81 (0.24%)
Distal Tibia (Intra-Articular)	943 (2.75%)
Single Malleolar	706 (2.06%)
Bi-Malleolar	1198 (3.49%)

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Tri-Malleolar	198 (0.58%)
Calcaneal	767 (2.23%)
Talar	84 (0.24%)
Jones / Pseudojones	113 (0.33%)
Metatarsal Shaft	184 (0.54%)
Lis' Franc Injuries	109 (0.32%)
Pharyngeal	387 (1.13%)
Multiple Fractures	1249 (3.64%)
Total Fractures of Lower Limb	18152 (52.88%)

For adult upper limb fractures, Distal Radius was most frequent (1708, 4.98%), followed by pharyngeal (1617, 4.71%) and metacarpals (1622, 4.22%) (Table 2).

Table 2: Different Fractures and Their Frequencies in Shoulder Girdle and Upper Limb (Adults)

Upper Limb Fractures	Frequency (%)
Clavicle	1034 (3.01%)
Scapula	16 (0.05%)
Proximal Humerus	678 (1.98%)
Shaft of Humerus	908 (2.65%)
Distal Humerus (Intra-Articular)	409 (1.19%)
Olecranon	414 (1.21%)
Radial Head	76 (0.22%)
Radius and Ulna	1385 (4.03%)
Distal Radius	1708 (4.98%)
Nightstick	762 (2.22%)
Scaphoid	87 (0.25%)
Carpels Other Than Scaphoid	9 (0.03%)
Metacarpals	1448 (4.22%)
Phalangeal	1617 (4.71%)
Total Fractures of Upper Limb	10551 (30.74%)
Maxillofacial, Head, Ribs and Spine Fractures	487(1.42%)

In children, supracondylar fracture was predominant (1332, 3.88%), followed by shaft of radius and ulna (945, 2.75%) and shaft of femur (565, 1.65%) (Table 3).

Table 3: Different Fractures and their Frequencies in the Pediatric Population

Pediatric Fractures	Frequency (%)
Facial Bones and Head Injuries	79 (0.23%)
Shaft of Humerus	97 (0.28%)
Supracondylar	1332 (3.88%)
Lateral Condyle	102 (0.30%)
Medial Condyle	7 (0.02%)
Shaft of Radius and Ulna	945 (2.75%)
Distal Radius	479 (1.40%)
Radial Head Subluxation	456 (1.33%)
Metacarpals And Phalanges	73 (0.21%)
Pelvic	3 (0.01%)
Neck Of Femur	96 (0.28%)
Shaft Of Femur	565 (1.65%)
Distal Femur	26 (0.08%)
Tibia	512 (1.49%)
Metatarsals And Pharyngeal	43 (0.13%)
Total Fractures In Pediatric Population	5136 (14.96%)
Total Number of Fractures of All Categories in the Year 2022	34526

Multiple bone fractures occurred in 1249 (3.64%) patients, while 487 (1.42%) had maxillofacial, head, ribs, and spine fractures. Tibia was the most frequently fractured bone in adults, accounting for 5146 cases (14.99% of all fractures), including proximal intra-articular (1558, 4.54%), shaft (2645, 7.71%), and distal intra-articular (924, 2.75%) fractures. The least common fractures in adults were metacarpals other than scaphoid (9 cases, 0.03%), while in children, pelvic bone fractures were rarest (3 cases, 0.01%). The most commonly affected age group was between 21 to 30 years with 6785 (19.77%) documented cases while the least frequently involved age group was above 80 years, having 256 (0.75%) patients. Most importantly, 16874 patients (49.15%) were from the earning population between 21 and 50 years of age (Table 4).

Table 4: Age Wise Frequency of fractures and Their Percentages

Age Category	Frequency (%)
Up to 12 Years	5136 (14.96%)
13-20 Years	3956 (11.52%)
20-30 Years	6785 (19.77%)
31-40 Years	5728 (16.69%)
41-50 Years	4361 (12.70%)
51-60 Years	3516 (10.24%)
61-70 Years	2921 (8.51%)
71-80 Years	1667 (4.86%)
>80 Years	256 (0.75%)
Total	34326 (100.00%)

Road Traffic Accidents (RTA) were the primary cause of injury, accounting for 22040 (64.21%) cases, followed by machine injuries (3185, 9.28%) and falls (2693, 7.85%), (Figure 2).

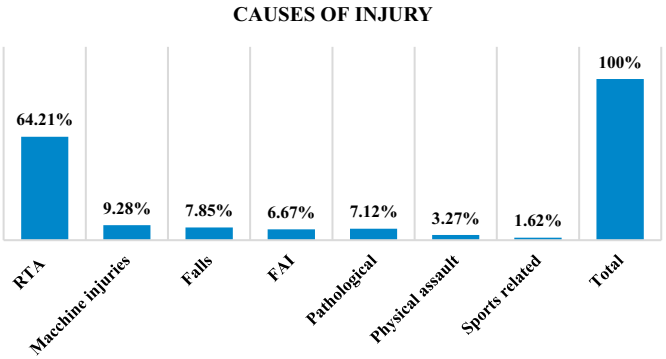

Figure 2: Causes of Injury among study participants

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DISCUSSION

This study encases the data of 34326 patients sustaining different types of fractures, of which more than twenty-nine thousand were adults and more than five thousand were children. More than two-thirds of the adult population were males and near one-third were females. Nearly similar trend was observed in pediatric population regarding gender. This doubled number of males is due to the more earning responsibilities over males in our society. Almigdad et al., also reported that male had more fractures than female [17]. Contrary to our study Reider *et al.*, observed that more women were involved in sustaining extremity fractures as compared to men [18]. A large number of patients had Road Traffic Accidents (RTAs), in which motorcycle was most frequently involved and almost all the cases of bike accidents were males. Omoke *et al.*, also found that RTA was the leading cause of fractures in Emergency department [19]. In more than half of the cases lower limb fractured was observed. Omoke also observed more fractures in lower limb than upper limb. Tibia was the most commonly fractured bone in lower limb, that is, every fifth or sixth patient had fracture of tibia and majority of these patients were younger than 50 years old. This high incidence of tibial fractures may be attributed to RTAs secondary to motorbike injuries and the working population [19]. Chaibi *et al.*, also reported a high incidence of 38% in tibia [20]. This is contrary to the results of a study published by Bergh *et al.*, which states that the proximal femur was the most frequent lower limb fracture [21]. The second and third most frequently fractured regions in lower limb bones were the shaft of the femur and peri-trochanteric (intertrochanteric and sub-trochanteric) region respectively. In the upper limb, the distal radius was the most commonly fractured bone with 1708 cases (4.98%). This is because distal radius fracture has a bimodal distribution. In young adults, it occurs from high energy trauma in active working males with fall on outstretched hand. In the elderly majority of distal radius fractures occur due to osteoporosis after trivial trauma. Bergh et al also reported distal radius fractures as high as 16.4% which is almost quadrupled as compared to our study [21]. Phalanx and metacarpal fractures were the second and third most frequent injuries of the upper limb in adults. More than 90% of these fractures were open and due to machine injuries including industrial machinery and grass cutters. Unfortunately, a wide majority of these victims were young males with ages below 30 years. The main reason for these injuries is the large number of press machinery in the vicinity of Mayo Hospital Lahore. Most of these patients had some degree of traumatic amputation at presentation with contaminated wounds. A vicious triad of poverty, disability and illiteracy was observed in these young patients which in turn increased the burden on the hospitals with negative income effect on the economic health of the country. Therefore, the government should make and implement proper legislation ensuring the safety protocols and compensation mechanism, in case of injury, of these poor industrial-machines workers. We observed more than twelve hundred multiple bone fractures. Unlike adults, children had more fractures in the upper limb as compared to the lower limb. Supracondylar fracture is the most frequent followed by both bone fractures of the forearm and shaft of femur in children. Merckaert *et al.*, also published that the pediatric population more frequently had upper extremity fractures but contrary to our study they found that the radius was the most frequently fractured bone in children [22]. Metacarpals (other than scaphoid) were the least commonly reported fractured bones. This is due to the relative stability of these small bones and the less expertise to diagnose their fracture with low-quality emergency department X-rays. Similarly, pediatric pelvic bone fractures were seen only in three patients. Regarding the cause of injury, it was RTA in about two-thirds of the cases followed by machine injuries (in every tenth patient) and falls in about every fourteenth or fifteenth patient. Algahtany, [23] also documented RTA as the leading cause of fractures but Rundgren *et al.*, reported simple falls as the most common cause of fractures [24]. This implies that strict compliance with the traffic rules should be ensured to avoid RTAs and proper legislation and protection should be ensured for machinery workers as discussed earlier. As far as the age group is concerned, the most affected age group was between 21 to 30 years and the least affected was above 80 years' age-group. Fayyaz *et al.*, also found that the peak age for fracture is between 15 and 44 years [25].

CONCLUSIONS

It was concluded that a total of 34326 patients with orthopedic fractures were recorded who visited the Emergency Department of Mayo Hospital in the year 2022 with about one hundred patients entertained daily. Every sixth patient is younger than 12 years. More than half of patients are from the earning age group, that is, between 21 and 50 years of age. The tibia is the most frequently fractured lower limb bone and distal radius in the upper limb in the adults while the supracondylar fracture is more frequently fractured in children. It is recommended that all tertiary care hospitals should be provided with enough human resources and equipment to cope with such a high burden of trauma and fractures. In this era of social media, awareness campaigns should be communicated to the public for their safety.

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Authors Contribution

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Methodology: MKN, KUI, MSN
Formal analysis: MSN, FM
Writing review and editing: MKN, KUI, SMRN, SNKN, AHS

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

The authors declare no conflict of interest.

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REFERENCES

[1] Qiu X, Deng H, Su Q, Zeng S, Han S, Li S *et al*. Epidemiology and Management of 10,486 Pediatric Fractures in Shenzhen: Experience and Lessons to Be Learnt. BioMed Central Pediatrics. 2022 Mar; 22(1): 161. doi: 10.1186/s12887-022-03199-0.

[2] Shah A, Judge A, Griffin XL. Incidence and Quality of Care for Open Fractures in England Between 2008 and 2019: A Cohort Study Using Data Collected by the Trauma Audit and Research Network. The Bone and Joint Journal.2022 Jun; 104(6): 736-46. doi: 10.1302/0301-620X.104B6.BJJ-2021-1097.R2.

[3] Ali M, Eiriksdottir A, Murtadha M, Åkesson A, Atroshi I. Incidence of Distal Radius Fracture in a General Population in Southern Sweden in 2016 Compared with 2001. Osteoporosis International. 2020 Apr; 31: 715-20. doi: 10.1007/s00198-020-05282-7.

[4] Doshi RP, Carpenter C. Pediatric Femoral Diaphyseal Fractures in a South Wales Tertiary Centre: An Account of Trend in Management and Complications Over 16 Years. Cureus.2022 Oct; 14(10). doi: 10.77 59/cureus.30917.

[5] Khurana B, Hines DA, Johnson BA, Bates EA, Graham-Kevan N, Loder RT. Injury Patterns and Associated Demographics of Intimate Partner Violence in Men Presenting to US Emergency Departments. Aggressive Behavior.2022 May; 48(3): 298-308. doi: 10.1002/ab.22007.

[6] Wilson-Barnes SL, Lanham-New SA, Lambert H. Modifiable Risk Factors for Bone Health and Fragility Fractures. Best Practice and Research Clinical Rheumatology.2022 Sep; 36(3): 101758. doi: 10.1016 /j.berh.2022.101758.

[7] Wu AM, Bisignano C, James SL, Abady GG, Abedi A, Abu-Gharbieh E *et al*. Global, Regional, and National Burden of Bone Fractures in 204 Countries and Territories, 1990–2019: A Systematic Analysis from the Global Burden of Disease Study 2019. The Lancet Healthy Longevity.2021 Sep; 2(9): e580-92. doi: 10.1016/S2215-0366(21)00395-3.

[8] Hikichi T, Takata M, Horii T, Shimanuki K, Suganuma S, Toratani T *et al*. Epidemiology of Trauma-Related Pediatric Limb Fracture Using A Unique Classification: A 10-Year Retrospective, Single-Center Study. Injury. 2022 Jun; 53(6): 2074-80. doi: 10.1016/j.injury. 2022. 02.012.

[9] Nutbeam T, Fenwick R, Smith J, Bouamra O, Wallis L, Stassen W. A Comparison of the Demographics, Injury Patterns and Outcome Data for Patients Injured in Motor Vehicle Collisions Who Are Trapped Compared to Those Patients Who Are Not Trapped. Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine.2021 Dec; 29: 1-7. doi: 10.1186/s13049-020-00818-6.

[10] Gidion F, Carroll J, Lubbe N. Motorcyclist Injuries: Analysis of German In-Depth Crash Data to Identify Priorities for Injury Assessment and Prevention. Accident Analysis and Prevention.2021 Dec; 163: 106463. doi: 10.1016/j.aap.2021.106463.

[11] Petit L, Zaki T, Hsiang W, Leslie MP, Wiznia DH. A Review of Common Motorcycle Collision Mechanisms of Injury. European Federation of National Associations of Orthopedics and Traumatology Open Reviews.2020 Sep; 5(9): 544-8. doi: 10.1302/2058-5241.5.190090.

[12] Khurana B, Raja A, Dyer GS, Seltzer SE, Boland GW, Harris MB *et al*. Upper Extremity Fractures Due to Intimate Partner Violence Versus Accidental Causes. Emergency Radiology.2021 Oct: 1-9. doi: 10.1007/s10140-021-01972-9.

[13] Erivan R, Carrie N, Descamps S, Caputo T, Boisgard S, Villatte G. Epidemiology of Limb Trauma Interventions in France: Current State and Future Projections. Orthopedics and Traumatology: Surgery and Research. 2024 Apr; 110(2): 103793. doi: 10.1016/j.otsr.2023.103793.

[14] Cant DA and Faergemann C. The Incidence of Physeal Fractures in the Lower Limb and the Frequency of Premature Physeal Closure: A Cohort Study of 236 Patients. Acta Orthopaedica.2023; 94: 289. doi: 10.2340/17453674.2023.13429.

[15] Lakho MT, Raza A, Qadir A, Kumar D, Khanzada A, Muzzammil M. To Assess the Frequency of Common Fractures Secondary to Motorcycle Accident in Patients Admitted to the Orthopedic Department of a Tertiary Care Hospital, Pakistan. International Journal of Medical Research and Health Sciences. 2019; 8(7): 74-9.

[16] Stracciolini A, Casciano R, Levey Friedman H, Meehan III WP, Micheli LJ. Pediatric Sports Injuries: An Age

DOI: https://doi.org/10.54393/pjhs.v5i12.2463

Comparison of Children Versus Adolescents. The American Journal of Sports Medicine.2013 Aug; 41(8): 1922-9. doi: 10.1177/0363546513490644.

[17] Almigdad A, Mustafa A, Alazaydeh S, Alshawish MM, Bani Mustafa M, Alfukaha H. Bone Fracture Patterns and Distributions According to Trauma Energy. Advances in Orthopedics.2022; 2022(1): 8695916. doi: 10.1155/2022/8695916.

[18] Reider L, Pollak A, Wolff JL, Magaziner J, Levy JF. National Trends in Extremity Fracture Hospitalizations among Older Adults Between 2003 and 2017. Journal of the American Geriatrics Society. 2021 Sep; 69(9): 2556-65. doi: 10.1111/jgs.17281.

[19] Omoke NI and Ekumankama FO. Incidence and Pattern of Extremity Fractures Seen in Accident and Emergency Department of a Nigerian Teaching Hospital. Nigerian Journal of Surgery. 2020; 26(1): 28-34. doi: 10.4103/njs.NJS_42_19.

[20] Chaibi E, Zambelli PY, Merckaert S. Epidemiology of Pediatric Lower Extremity Fractures in a Tertiary Care Center in Switzerland. European Journal of Trauma and Emergency Surgery.2022 Oct; 48(5): 3449-59. doi: 10.1007/s00068-020-01400-6.

[21] Bergh C, Wennergren D, Möller M, Brisby H. Fracture Incidence in Adults About Age and Gender: A Study of 27,169 Fractures in the Swedish Fracture Register in a Well-Defined Catchment Area. PloS one. 2020 Dec; 15(12): e0244291. doi: 10.1371/journal.pone.0244291.

[22] Merckaert S, Chaibi E, Meriem S, Kwiatkowski B, Divjak N, Zambelli PY. Epidemiology of Pediatric Upper Extremity Fractures in a Tertiary Care Center in Switzerland. Pediatric Emergency Care. 2021 Dec; 37(12): e825-35. doi: 10.1097/P EC.0 00 000 0 0 0 0 0 0 2 047.

[23] Algahtany MA. Association Between Orthopedic Fractures and Traumatic Spinal Injury Due to Road Traffic Accidents. European Review for Medical and Pharmacological Sciences.2021 Dec; 25(24). doi: 10. 1155/2021/2430090.

[24] Rundgren J, Bojan A, Mellstrand Navarro C, Enocson A. Epidemiology, Classification, Treatment and Mortality of Distal Radius Fractures in Adults: An Observational Study of 23,394 Fractures from the National Swedish Fracture Register. BioMed Central Musculoskeletal Disorders.2020 Dec; 21: 1-9. doi: 10.1186/s12891-020-3097-8.

[25] Fayyaz J, Wadhwaniya S, Shahzad H, Feroze A, Zia N, Mir MU *et al*. Pattern of Fall Injuries in Pakistan: The Pakistan National Emergency Department Surveillance (Pak-NEDS) Study. BioMed Central Emergency Medicine.2015 Dec; 15: 1-7. doi: 10.11 86/ 1471-227X-15-S2-S3.

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Original Article

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Comparison of Outcome between Limberg Flap and Karydakis Flap in Pilonidal Sinus Disease

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ABSTRACT

There was controversy regarding the treatment options for pilonidal sinus disease (PSD). Even though a number of techniques were used, such as Karydakis flap, Limberg flap, Bascom cleft lip treatment, and marsupialization, the most effective technique was still up for debate with lower rate of wound infection and recurrence of disease. **Objective:** To compare the outcome between the Karydakis flap (KF) and the Limberg flap (LF) for the treatment of PSD in terms of infection, wound dehiscence, and recurrence. **Methods:** This quasi-experimental study was conducted after the approval of the Ethical Committee Board of the Surgery Department, PAF Hospital Mushaf, and Fazaia Ruth Pfau Medical College from May 2021 to February 2022. A total 54 patients with PSD were selected and divided into two groups. The KF and the LF procedure was performed. Outcomes assessed included wound infection, wound dehiscence, and recurrence over a 1-year follow-up. **Results:** All patients were male in both groups. Wound infection occurred in 6 patients (22.2%) in group KF compared to 1 patient (3.7%) in group LF (p = 0.049). Wound dehiscence was noted in 4 patients (14.8%) in group KF but was absent in group LF (p = 0.039). Recurrence occurred in 3 patients (11.1%) in group KF, while no recurrence was observed in group LF during the follow-up period (p = 0.046). Overall, group LF proved statistically significant superior outcomes compared to group KF. **Conclusions:** Despite requiring demanding surgical skills, the Limberg Flap proved to be a preferred and reliable technique in the treatment of primary and recurrent sacrococcygeal PSD. It revealed lower rates of wound infection, dehiscence, and recurrence, making it an effective surgical treatment for natal cleft PSD.

INTRODUCTION

The PSD (pilonidal sinus disease) is present in the natal cleft that overlies the tail bone called the "coccyx". It consists of single or more midline openings that are often non-infected and connect to the fibrous tract lined by granulation tissue and contain loosely lying hair inside the lumen. According to reports, there are 25 cases of PSD for every 100,000 individuals [1]. Previously, PSD was considered congenital. But this paradigm shift was largely credited with the work of Georgios Karydakis, who identified three primary acquired variables that contribute to PSD: an external force that favors hair insertion into the skin, loose hair, and an underlying vulnerability of natal cleft skin [1]. Men are often two to four times more likely to get this disease. For women, the typical age of onset is 19, while for men, it is 21 [2]. A painful, small swelling, sinus-drained purulent, mucus or/and bloody discharge can be found in patients with chronic or acute illness [2]. En-bloc excision of whole pilonidal sinuses and it's all tracts; the affected sinus epithelized tracts are identified down to the sacrococcygeal fascia by using methylene blue, is the cornerstone of surgery for chronic or persistent PSD [2]. Numerous surgical and non-surgical treatments exist. The optimal course of treatment should result in a full recovery, a quick return to normal activities, cosmetic satisfaction, and minimal morbidity [3]. To treat PSD, surgical treatment is preferred, and various techniques have been developed;

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KF (Karydakis flap), LF (Limberg flap), the Dufourmentel flap, the modified LF, and additional advancement and Z-plasty flap operation are a few examples [4]. Despite the widespread and successful use of flap methods, recurrence still occurs more frequently than intended. It is necessary to mention that choosing a procedure wisely is cost-effective and post-operative care is easy. Therefore, it was designed to see and compare the outcome of two different common surgical procedures in the management of PSD in this study. Two flap procedures, the Limberg flap and the Karydakis flap, were compared in terms of outcome (infection, wound dehiscence, and PSD recurrence). There are few non-surgical approaches for treating PSD that are still being practiced. Silver nitrate and alcohol phenol intracavitary injection are non-surgical techniques with a high failure rate. So, nowadays these techniques are not recommended or reserved for very few non-complicate cases or those cases where surgical procedures are not opting due to any restriction [5]. Unfortunately, because there are many different types of interventions and inconsistent results to lower recurrence-related morbidity, no single method has been generally accepted as the gold standard [6]. The above-described surgical and non-surgical methods have been linked to varying rates of wound dehiscence, postoperative discomfort, surgical site infection, longer hospital stays, higher treatment costs, and, above all, recurrence rates [6, 7]. It is necessary to mention that natal cleft creates a plausible milieu for continued irritation, and profound natal cleft combined with an apparent negative pressurizing environment is highlighted as a key etiological feature. The primary step is removing the factors that cause PSD and avoiding a recurrence, lateralizing the surgical scar away from the midline, and straightening the natal cleft. This has led to the development of several lateralizing meticulous flap techniques, such as the KF, the LF, the modified LF, and several other progression flaps [7, 8].

METHODS

This quasi-experimental study was conducted in the General Surgery Department of PAF Hospital Mushaf from May 2021 to February 2022, after obtaining approval from the Ethical Committee Ref no: FRPMC/ERB014/21. The sample size was calculated using the Health Studies version 2.0.21 WHO formula, which kept a study power of 90% and a significance level of 5%.

The sample size equation was

$$\frac{\left(Z_{1-a/2}\sqrt{2\bar{p}\,(1-\bar{p})}+Z_{1-\beta}\sqrt{p_1\,(1-p_2)p_2\,(1-p_2)}\right)^2}{\text{Where } \bar{p}=\left(\frac{p_1+p_2}{2}\right)^{(p_1-p_2)^2}}$$

P1: Anticipated proportions of LF= 3.4%, P2: Anticipated proportions of KF = 38.0%, p1 – p2 : The proportion difference = 34.6%, Z 1 – β: The desired study power = 90%, Z 1-α/2 : the desired significance level = 5%, P^1 = percentage of complications in PSD patient treated with LF procedure, P^2 = percentage of complications in PSD patient treated with KF procedure, 54 patients in this study with PSD fulfilled the inclusion criteria admitted through the outpatient department were enrolled and divided into two groups. The inclusion criteria were patients aged >14 years having primary or recurrent unilateral PSD. Exclusion criteria were patients with ASA grades 4 and 5 who refused to become part of the study, acute pilonidal abscess, bilateral PSD, and patients with uncontrolled diabetes mellitus, chronic renal failure, steroid intake, and immunosuppression. Every patient underwent general physical and local examination and investigations to verify the diagnosis. A thorough informed consent was obtained after all patients were made aware of the procedure's risks. Pre-operative anesthesia evaluation was done. The demographic data was noted. The patient's hair was clipped the night before the surgery. Half an hour before the procedure, a prophylactic dose of 2 grams of ceftriaxone was given intravenously. All surgeries were performed under spinal anesthesia by a consultant anesthetist in Jack prone knife position. The surgical area was cleansed by wiping it at least twice with polyvinyl iodine. With a sterile pen, the borders of the incision, including the sinus, were delineated before the procedure began. Methylene blue injections into the sinus cavity were used to delineate all sinus tracts. Standard operating procedure performed by same consultant general surgeon with his experienced assistant. In KF, excision of sinus tract and associated tissue in an elliptical shape, create a flap on one side of incision, ensuring large enough to cover the excised area without tension. In LF, rhomboid shape excision with four equal sides, two 60^0 and two 120^0 angles, forms a parallelogram. Extend one 1200 angle outward to create a flap. The flap should match the size of defect to ensure tension free closure. All wounds closed primarily with suction drain placement and aseptic dressing. Drain removed on 3rd post-operative day and stitch removed after 10 days. Patients were assessed for wound infection and dehiscence on the 3^{rd} and 10^{th} postoperative days and followed for 1 year to monitor recurrence. All findings were recorded on a predesigned proforma and postoperative results compared between both groups. Data entry and analysis was performed using SPSS version 25.0. The quantitative variables such as age were expressed as mean ± SD. Categorical data for infection, wound dehiscence and recurrence of PSD were represented as frequency percentage. Comparison of recurrence and complications according to group was performed using chi-square test. Statistical significance was defined as $p<0.05$

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RESULTS

The demographic characteristics of the patients are summarized in Table 1. The average age of the LF group was 26 ± 4.99 years, while the KF group had a mean age of 28.40 ± 6.96 years. All patients in both groups were male (100%).

Table 1: Demographic Data of Both Groups (N=54)

Variables	Limberg Flap (LF) Procedure Group	Karydakis Flap (KF) Procedure Group
Age Distribution (Years)		
16 – 25	11 (40.7%)	10 (37.0%)
26 – 35	11 (40.7%)	10 (37.0%)
36 – 45	11 (40.7%)	10 (37.0%)
Mean ± SD	26 ± 4.99	28.40 ± 6.96

The postoperative outcomes, including wound healing, wound dehiscence, and recurrence rate, are detailed in Table 2. In the LF group, 96.3% of patients had uneventful wound healing, while 3.7% experienced wound infection with no cases of wound dehiscence or recurrence. In the KF group, 92.6% of patients had normal healing, 7.4% developed wound infections, 3.7% experienced wound dehiscence, and one patient (3.7%) had disease recurrence during the 1-year follow-up. The rates of wound infection, wound dehiscence, and recurrence between the two groups were compared using the chi-square test. There was no statistically significant difference in wound healing (infection and dehiscence rates) or recurrence rates between the groups ($p > 0.05$).

Table 2: Outcomes of Procedures in Both Groups (N=54)

Variables	Limberg Flap (LF) Procedure Group	Karydakis Flap (KF) Procedure Group	p-Value (Chi-Square Test)
Wound Healing			
Normal Healing (%)	96.3	92.6	0.513
Wound Infection (%)	3.7	7.4	
Wound Dehiscence (%)	0	3.7	
Recurrence Rate			
Recurrence (%)	0	3.7	1.0
No Recurrence (%)	100	96.3	

The Limberg Flap procedure confirms slightly better outcomes compared to the Karydakis Flap, with lower rates of wound infection and no cases of wound dehiscence or recurrence. However, the differences were not statistically significant ($p > 0.05$).

DISCUSSION

Anderson published a paper titled "Hair extracted from an ulcer" in 1847. Later, in 1880 Hodges first time used the term "Pilonidal Sinus" [9]. It was a benign, often chronic condition mostly affecting the male gender and involving the intergluteal region. [10]. Prior to World War II, the majority of PSD research came from the military and was skewed toward male patients, with no females included in the research. Similarly, our study was conducted in a military setup, and all our patients were male. Female PDS incidence may be underreported as a result of this gender bias [11]. Infection following surgery and recurrence of PSD were the main causes of morbidity in young people. In our study, the rate of infection is less in LF group. Similarly, Ashraf MN *et al.*, study discusses an infection rate of flap procedure, 4% in the Limberg and 22% in the Karydakis (P 0.039) [10]. To prevent hair entrapment, both approaches KF and LF includes closing the natal cleft away from the midline [9, 17]. Antony AM *et al.*, discussed an observational study on 30 patients who stated no recurrence among 15 patients who underwent the LF, and recurrence was noted in 6 patients of the KF group [12] as in our study no recurrence in LF and only 3.7% in KF. Another study by Turan stated complication rates of Limberg Flap and Karydakis Flap groups were 10.5 % and 12.2%, respectively [13] but they preferred only flap techniques over others. Destek S *et al.*, compare postoperative satisfaction between KF and LF groups; the mean psychosocial evaluation scores for the KF group were 70.3 (57.5-88.7), while the LF group's scores were 73.4 (53.5-87.5). This difference was statistically significant [14]. Elhiny AA *et al.*, evaluate feasibility and effectiveness in recurrent and complicated PSD; 40.7% of the Karydakis group's wound dehiscence occur, compared to 11.1% in Limberg group. In Karydakis group, there were six cases of recurrence while there were none in Limberg group. Eight patients in the Karydakis group and a single case in Limberg group were infected. All these variations were statistically significant [15] we also add participants with recurrent disease and almost similar result recorded. Complicated operations encourage quick recovery, early healing, and stop recurrence. That's why some studies discourage simple excision and primary closure in PSD [16, 17] as in our study we only prefer flap procedures. Ekici U *et al.*, compare the Karydakis and Limberg procedures to the lay-open and marsupialization approaches, the former was seen to be safer. The recurrence rate in the primary closure approach was found to be statistically considerably greater than in the other procedures ($p = 0.009$) [18]. In another study, they also compared LF and KF, two most widely used methods and also noticed less pain in post postoperative and early return to work which was the additional benefit of these complex procedures [19]. The vast variety in the PSD treatment options and patient results for a pilonidal disease was evident. A meta-analysis compared flap techniques; there were a total of 951 patients across six RCTs (five of which included Karydakis flaps and one using a Bascom cleft lip flap in comparison to Limberg flaps). No

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significant difference was seen between either group in terms of disease recurrence, SSI, or wound dehiscence rates [20]. A recent advance in the treatment of PSD includes the use of autologous adipose tissue or platelet-rich plasma, fibrin glue, endoscopic procedures, and laser treatment in trail. None of them were recommended because there was a lack of evidence that was reliable [21].

CONCLUSIONS

It is concluded that the Limberg flap technique yields better results than the Karydakis flap approach in terms of infection, wound dehiscence, and PSD recurrence. Therefore, this study recommended the Limberg flap surgery as the best off-midline treatment for primary and recurrent PSD.

Authors Contribution

Conceptualization: MS
Methodology: NQ
Formal analysis: MS
Writing, review and editing: MK, SZ, SS, AR

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Gavriilidis P and Bota E. Limberg flap versus Karydakis flap for treating pilonidal sinus disease: a systematic review and meta-analysis. Canadian Journal of Surgery. 2019 Apr; 62(2): 131. doi: 10.1503/cjs.003018.

[2] Alvandipour M, Zamani MS, Ghorbani M, Charati JY, Karami MY. Comparison of Limberg flap and Karydakis flap surgery for the treatment of patients with pilonidal sinus disease: a single-blinded parallel randomized study. Annals of Coloproctology.2019 Dec; 35(6): 313. doi: 10.3393/ac.2018.09.27.

[3] Botrous AM, Akhnoukh SG, Mikhaiel E. Comparative Study between Excision of Pilonidal Sinus Via Lay Open Technique Versus Closed Technique and between Karydakis Technique Versus Limberg Technique: Meta-Analysis. The Medical Journal of Cairo University. 2022 Dec; 90(12): 2601-16. doi: 10.21608/mjcu.2022.295337.

[4] Mohamed Abd-Elfattah AM, Elsayed Fahmi KS, Eltih OA, Abd-Elhady WA. The Karydakis Flap Versus the Limberg Flap in the treatment of pilonidal sinus disease. Zagazig University Medical Journal. 2020 Nov; 26(6): 900-7.

[5] Alkurt EG, Vardar YM, Tüzün İS. Comparison of Limberg flap and Karydakis flap repair in pilonidal sinus surgery: a prospective case-control study. Cureus. 2022 Sep; 14(9). doi: 10.7759/cureus.28933.

[6] Ray K, Albendary M, Baig MK, Swaminathan C, Sains P, Sajid MS. Limberg flap for the management of pilonidal sinus reduces disease recurrence compared to Karydakis and Bascom procedure: a systematic review and meta-analysis of randomized controlled trials. Minerva Chir.2020 Oct; 75(5): 355-64. doi: 10.23736/S0026-4733.20.08362-5.

[7] Ahmad N, Prakash P, Pawar SS, Baitha KS. Comparative study of limberg's rotation flap versus karydakis procedure in pilonidal sinus surgery. International Journal of Health and Clinical Research. 2022 Jan; 5(01): 365-9.

[8] Nawar AM, Mansour MA, Hanna GS, Fadey MA. Comparative study between Limberg technique and Karydakis procedure in surgical treatment of sacrococcygeal pilonidal sinus. Benha Medical Journal.2023 May; 40(1): 216-25. doi: 10.21608/bmfj.2023.195845.1766.

[9] Khan N, Singhal P, Chandrashekhar S, Goel D, Patel K, Deshpande N. Is limberg flap better than excision and primary closure for treatment of sacrococcygeal pilonidal sinus: a prospective randomised study of 30 cases. International Surgery Journal. 2021 Jan; 8(2): 699-703. doi: 10.18203/2349-2902.isj20210388.

[10] Ashraf MN, Azhar M, Akhtar N, Afzal K. Outcome of modified limberg flap with karydakis flap in treatment of pilonidal diseases. Isra Medical Journal.2019 Nov; 11(6).

[11] Chiu B, Abrajano C, Shimada H, Yousefi R, Dalusag K, Adams M, *et al*. Differences between male and female patients with pilonidal disease. Journal of Pediatric Surgery Open. 2024 Apr;6:100132. http://doi.org/10.1016/j.yjpso.2024.100132

[12] Antony AM, Ilango SP, Kiranraj R, Nathan S, Madhivanan S. Surgical outcome between Karydakis flap and Limberg flab in pilonidal sinus: A comparative study. International Journal of Surgery. 2022; 6(01): 13-7. doi: 10.33545/surgery.2022.v6.i1a.810.

[13] Turan U. Modified Limberg flap versus modified Karydakis flap in pilonidal sinus disease: single surgeon experience. International Surgery Journal. 2019 Aug; 6(9): 3069-73. doi: 10.18203/2349-2902.isj20194035.

[14] Destek S, Bektaşoğlu HK, Kunduz E, Akyüz MN. Comparison of postoperative quality of life of Limberg flap and Karydakis flap in pilonidal sinus operations. Turkish Journal of Surgery.2020 Mar; 36(1): 59. doi: 10.5578/turkjsurg.4598.

DOI: https://doi.org/10.54393/pjhs.v5i12.2037

[15] Elhiny AA, Saad DA, Farahat MS. Effectiveness and feasibility of Limberg and Karydakis flap in recurrent and complicated pilonidal sinus disease. Indian Journal of Surgery.2021 Feb; 83: 55-60. doi: 10.1007/s12262-020-02236-5.

[16] El Hadidi A, Negm A, Abdelhalim M, Taha A, Noaman N, Dawoud I. Karydakis versus Limberg flap reconstruction for the treatment of recurrent pilonidal disease: a prospective randomized controlled trial. The Egyptian Journal of Surgery. 2019 Apr; 38(2): 369-75. doi: 10.4103/ejs.ejs_107_18.

[17] Anwar A, Ahmad HN, Kamal M, Zaman M, Naz H. Off-midline closure techniques in the treatment of pilonidal sinus disease; Karydakis vs Limberg flap procedure. Rawal Medical Journal. 2021 Oct; 46(4): 902-.

[18] Ekici U, Kanlıöz M, Ferhatoğlu MF, Kartal A. A comparative analysis of four different surgical methods for treatment of sacrococcygeal pilonidal sinus. Asian Journal of Surgery. 2019 Oct; 42(10): 907-13. doi: 10.1016/j.asjsur.2018.12.011.

[19] S B, M A. Modified Limberg flap Versus Karydakis Flap Operations in Pilonidal Sinus Surgery. IOSR Journal of Dental and Medical Science.Volume 20(Issue 4, Ser.14):43-7. Available from: http://www.iosrjournals.org. doi: 10.9790/0853-2004144347.

[20]Harries RL, Alqallaf A, Torkington J, Harding KG. Management of sacrococcygeal pilonidal sinus disease. International Wound Journal. 2019 Apr; 16(2): 370-8. doi: 10.1111/iwj.13042.

[21] Iesalnieks I, Ommer A, Herold A, Doll D. German National Guideline on the management of pilonidal disease: update 2020. Langenbeck's Archives of Surgery. 2021 Dec; 406(8): 2569-80. doi: 10.1007/s00423-020-02060-1.

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Prognostic Significance of Serum C-Reactive Protein Levels Among Operable Breast Cancer Patients

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ABSTRACT

Serum C-Reactive Protein (CRP) levels, an indicator of systemic inflammation, are increasingly recognized for their prognostic value in cancer. In operable breast cancer, elevated CRP levels may correlate with tumor progression, treatment outcomes, and survival. **Objective:** To determine the outcome of the raised serum CRP among operable breast cancer patients. **Methods:** This prospective cohort study was conducted on 126 women of 20-60 years of age with a lump in the breast, bloody or serous nipple discharge ≥ 6-week duration and diagnosed as a case of operable breast cancer on histopathology and were selected for modified radical mastectomy. Patients were divided into 2 groups according to CRP levels (Raised; Group A vs normal; Group B). **Results:** In Group A (17.5%) cases had wound infections, 16 cases (25.4%) of seroma, and 10 cases (15.9%) of flap necrosis. In contrast, Group B had a lower incidence of these complications, with 4 cases (6.3%) of wound infections, 8 cases (12.7%) of seroma, and 5 cases (7.9%) of flap necrosis. In terms of pain severity, all 63 patients (100.0%) in Group A reported moderate pain, with no cases of severe pain and in Group B, 48 patients (76.2%) experienced moderate pain, and 15 patients (23.8%) reported severe pain (p-0.004). Prolonged Hospital stay was (25.4%) cases of group A and in Group B (49.2%) cases had prolonged hospital stays. **Conclusion:** Patients with elevated CRP levels are more likely to experience postoperative complications, such as wound infection, seroma formation, and flap necrosis, compared to patients with normal CRP levels.

INTRODUCTION

There is a notable increase in breast cancer cases among Asian women as it occupies 22% of the population as the second most persistent disease [1, 2]. Furthermore, it has also remained the second most lethal form of cancer among women [3]. As advancements go, this means breast cancer is one of the curable diseases, given the fact that it is detected at an early stage. The number of cases of breast cancer is rapidly increasing associated with various factors like sex, age, genetic predisposition, childlessness, breastfeeding, hormones, and lifestyle [4]. The diagnosis of breast cancer is based on a triple assessment including clinical examination along with imaging (ultrasonography is preferred for younger patients and mammography is for older age group) and is confirmed by the pathological assessment on biopsy with receptor status (ER, PR, Her 2neu) [5]. The mammogram will be done to have Breast Imaging-Reporting and Data System (BIRADS) scoring for both breasts to rule out the status of the contralateral breast as well. An ultrasound / contrast Computed Tomography (CT) scan of the chest, abdominal and bone scan can be considered for the staging of the disease to plan the treatment accordingly [6]. The surgical treatment options are multiple including breast saving procedures and breast scarifying procedures. Simple mastectomy with

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or without axillary sampling, radical mastectomy, and Modified Radical Mastectomy (MRM) are the options for breast scarifying procedures. Skin-sparing mastectomy, Breast Conservation Surgery (BCS) with or without sentinel lymph node biopsy is the options of breast conserving procedures. Surgery is concomitant with neoadjuvant or adjuvant chemo-radiotherapy according to the stage of the disease. Cancer antigen 153 (CA153), Cancer antigen 125 (CA-125), and Carcinoembryonic Antigen (CEA) are the most commonly used serum markers in the management of breast cancer but the debate on its specificity is still going on [6]. Inflammation is the seventh hallmark of cancer. Nowadays it is thought that cancer should be considered in patients with raised inflammatory markers. However, inflammatory markers have poor sensitivity for cancer diagnosis but they can lead us towards the path of the prognosis [7]. As the pathogenesis behind the cancer is molecular events include angiogenesis on the top and its association with the inflammatory process, to contribute to its further progression [3, 8]. As systemic inflammatory markers play an important role in cancer progression, they also act as the prognostic indicator including C-Reactive Protein (CRP) [9, 10]. Though CRP is a sensitive, reliable biomarker of systemic inflammation and its prognosis can be measured easily [11]. There is an increased association of CRP with breast cancer among the post-menopausal group due to differences in the site of estrogen production. While serum concentrations of CRP were shown to positively correlate with estrone, total estradiol and free estradiol, SHBG level was negatively correlated. Furthermore, breast density has been shown to correlate with a reduction in CRP levels, whereby lower CRP levels were observed in those with greater breast density [12]. Lowering agents of CRP like COX inhibitors, platelet aggregation inhibitors, lipid lowering agents, angiotensive converting enzymes inhibitors, antioxidants and antibiotics appear to be effective management strategies as accompanying treatments alongside breast cancer chemotherapy, into improving treatment and survival prognosis of such patients. Clinically elevated levels of C-reactive protein suggest that there is more likely to be a deleterious relationship between inflammatory response mechanisms and breast cancer that will more often than not poor patient outcome as well [13]. However, the existing literature on the elevated CRP levels in breast cancer patients in the local setting is scanty and thin.

Consequently, this study seeked to investigate in what way the elevated biomarkers namely CRP in operable breast cancer patients would lead to accelerated appearance of early postoperative complications as well as prolonged hospital stay in the population.

METHODS

This Prospective-Cohort study was done from Jan 2023 - June 2023, at the Department of Surgery, Liaquat University Hospital, Hyderabad, on 126 patients, who were divided into two groups. Group A (n=63) with elevated serum CRP (>0.37 mg/dl) and Group B (n=63) with normal serum CRP levels. Women aged 20-60 years with operable breast cancer (stage II or early III), verified by histopathology, with a period of at least 3-months after diagnosis and CT staging, and scheduled for modified radical mastectomy were included. Informed written consent was taken from each participant before enrolment into the study. Exclusion criteria encompassed patients with chronic liver disease, those on immunosuppressive therapy, pregnant or lactating women, stage IV breast cancer patients, and those who previously received non-adjuvant therapy. Patients were chosen via purposive sampling. Sample size was calculated via WHO software with frequency of raised serum CRP level among breast cancer patients as 9% with 5% margin of error and 95% confidence interval [9]. The study was approved by Ethical Review Committee of Liaquat University of Medical and Health Sciences, Jamshoro vide letter no. LUMHS/REC/-187. Data collection involved CRP measurement, clinical examination, and a detailed history of each patient. Outcomes assessed included early postoperative complications (e.g., seroma, flap necrosis, wound infection within five days' post-surgery), pain severity, and prolonged hospital stay (defined as >5 days postoperatively). Data analysis was performed using SPSS version 22.0. Chi-square test was used to analyse the association between different qualitative variables.

RESULTS

Patients in Group A (raised CRP) had a mean age of 41.60 ± 10.16 years, whereas those in Group B (normal CRP) averaged 45.53 ± 14.59 years. Average BMI and lump size were similar between groups, with no significant differences observed in height, weight, or lump dimensions. Group A had a slightly higher proportion of urban residents (49.2%) compared to Group B (25.4%), while rural residency was more common in Group B (74.6%). The right breast was more frequently affected in Group A (74.6%) and left breast in Group B (50.8%). The presence of pain was reported in 38.1% of Group A and 25.4% of Group B patients, with most lumps persisting for 7-12 months in both groups (Table 1).

Table 1: Descriptive Statistics (n=126)

Variables	Group A Raised CRP Mean ± SD / N (%)	Group B Normal CRP Mean ± SD / N (%)
Age (Years)	41.60 ± 10.16	45.53 ± 14.59
Height (cm)	177.49 ± 5.33	177.67 ± 6.65

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Weight (Kg)	63.84 ± 4.37	65.33 ± 6.76
BMI (Kg/m^2)	20.48 ± 1.15	20.68 ± 2.22
Lump Size (cm)	3.30 ± 2.13	3.22 ± 2.08
Serum CRP (mg/dL)	0.64 ± 0.21	0.21 ± 0.12
Residence		
Urban	31 (49.2%)	16 (25.4%)
Rural	32 (50.8%)	47 (74.6%)
Site of Lump		
Right	47 (74.6%)	31 (49.2%)
Left	16 (25.4%)	32 (50.8%)
Lump Pain Status		
With Pain	24 (38.1%)	16 (25.4%)
Without Pain	39 (61.9%)	47 (74.6%)
Duration of Lump		
≤ 6 Months	0 (0.0%)	24 (38.1%)
7-12 Months	48 (76.2%)	39 (61.9%)
> 12 Months	15 (23.8%)	0 (0.0%)

Complication rates were higher in Group A, with wound infections occurring in 17.5% compared to 6.3% in Group B (p=0.004). Group A also experienced more cases of seroma (25.4% vs. 12.7%) and flap necrosis (15.9% vs. 7.9%). Pain severity was notable, with all Group A patients reporting moderate pain, while 23.8% of Group B reported severe pain (p=0.0001). Prolonged hospital stay was required by 25.4% of Group A patients, compared to 49.2% in Group B (p=0.006)(Table 2).

Table 2: Postoperative Outcomes at the Time of Discharge (n=126)

Variables	Group A Raised CRP N (%)	Group B Normal CRP N (%)	p-Value
Postoperative Complications			
Wound Infection	11 (17.5%)	4 (6.3%)	0.004
Seroma	16 (25.4%)	8 (12.7%)	
Flap Necrosis	10 (15.9%)	5 (7.9%)	
No Complications	26 (41.3%)	46 (73.0%)	
Pain Severity			
Moderate Pain	63 (100.0%)	48 (76.2%)	0.0001
Severe Pain	0 (0.0%)	15 (23.8%)	
Prolonged Hospital Stay			
Yes	16 (25.4%)	31 (49.2%)	0.006
No	47 (74.6%)	32 (50.8%)	

Group A had a higher incidence of postoperative complications (30.2%) than Group B (11.1%), and fewer patients in Group A (66.7%) experienced no complications compared to Group B (87.3%)(p=0.006). A small percentage of patients were lost to follow-up in both groups (3.2% in Group A and 1.6% in Group B)(Table 3).

Table 3: Postoperative Outcomes at 1-Month Follow Up (n=126)

Variables	Group A Raised CRP N (%)	Group B Normal CRP N (%)	p-Value
No Complication	42 (66.7%)	55 (87.3%)	0.006
With Complication	19 (30.2%)	7 (11.1%)	
Lost Follow-up	2 (3.2%)	1 (1.6%)	

DISCUSSION

Breast cancer is one of the most prevalent cancers among women, and its prognosis is determined by various factors, including the stage at diagnosis, tumor characteristics, and response to treatment. In recent years, researchers have been exploring the potential role of C-Reactive Protein (CRP) as a prognostic marker in breast cancer. In Group A, the mean age was 41.60 years with a standard deviation of 10.16, whereas in Group B, the mean age was 45.53 years with a standard deviation of 14.59. Comparatively in the study by Badar F et al, four-thousand, three-hundred and sixty-six female breast malignancies were recorded, their mean age at presentation was 48.6 ± 12.2 years and mean Body Mass Index (BMI) was 29.0 ± 5.7 kg/m2 [14]. On the other hand, study by Sajid MT et al reported that the mean age of the patients of breast cancer was 52.90 ± 9.78 years [15]. Breast cancer risk generally increases with age, particularly in postmenopausal women. Therefore, when the mean age of breast cancer patients is over 40, it reflects the expected rise in breast cancer cases in this age group. In this study the mean BMI in Group A was 20.48 kg/m2 and in Group B, it was 20.68 kg/m2, p-value for BMI suggested no significant difference between the both groups (p=0.541). These findings were supported by the Badar F et al. [14]. In this study group A had more rural resident (50.8%) than Group B (74.6%), while Group A had fewer urban residents (49.2%) compared to Group B (25.4%). In Group A, 74.6% had right-sided lumps, while in Group B, 49.2% had right-sided lumps. For left-sided lumps, 25.4% in Group A had them, compared to 50.8% in Group B. In Group A, no individuals had lumps for over 6 months, 76.2% had lumps for 7-12 months, and 23.8% for more than 12 months. In Group B, 38.1% had lumps for over 6 months, 61.9% for 7-12 months, and none for more than 12 months. These findings regarding residential status were supported by the Moss JL et al., and Sprague BL et al., while findings regarding site of lump not found in their studies [16, 17]. In this study, Group A experienced higher rates of postoperative complications, including wound infections (17.5%), seroma (25.4%), and flap necrosis (15.9%). In contrast, Group B had lower complication rates: wound infections (6.3%), seroma (12.7%), and flap necrosis (7.9%). Pain severity was also higher in Group A, with all patients reporting moderate pain, while Group B had 76.2% with moderate pain and 23.8% with severe pain. The p-value of 0.004 indicates a significant difference in complication rates between the two groups. Additionally, Group B had a larger proportion of patients with prolonged hospital stays (49.2%) compared to Group A (25.4%). The possible explanation of association of elevated CRP levels with prolonged hospital stay lies in development of systemic inflammation, which can compromise wound healing by impairing the immune response, increasing

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vascular permeability, and promoting tissue damage. This pro-inflammatory state may predispose patients to complications such as seroma, infection, and necrosis. Chronic inflammation may exacerbate comorbid conditions, contributing to delayed recovery and prolonged hospital stays. Most patients in both groups (87.3%) recovered without complications by the 30th postoperative day. Along the same lines, Dahri FJ et al., reported that seroma formation was the most common complication encountered in 50 (33.3%) of cases, wound infection in 15 (10%) and flap necrosis in 4 (2.6%) cases [18]. Comparatively Shah S et al., reported that the frequency of early postoperative complications [19]. Seroma formation observed in 9 patients (15%) and wound infection seen in 5 cases (8.3%) were the commonest complications [20]. This study uniquely focused on the impact of preoperative CRP levels on early postoperative outcomes, such as seroma formation, wound infection, and hospital stay, among operable breast cancer patients undergoing modified radical mastectomy. Unlike prior studies, the study strengthened lies in context-specific insights for a local population of Pakistan and controls for confounders like prior systemic therapy, ensuring robust and actionable findings.

CONCLUSIONS

Elevated CRP levels are a valuable predictor of poor outcomes in operable breast cancer patients, linked to higher chances of postoperative-complications like wound infections, and flap necrosis. Enhanced perioperative care and close monitoring are essential for patients with elevated CRP to minimize complications and support recovery. Incorporating preoperative CRP assessments into routine practice could enable clinicians to optimize perioperative care and consider targeted interventions for high-risk patients to improve surgical outcomes.

Authors Contribution

Conceptualization: NA
Methodology: NA
Formal analysis: ZY, ZK
Writing, review and editing: AIM, SK, AMB, ZY, ZK

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Lin CH, Yap YS, Lee KH, Im SA, Naito Y, Yeo W *et al.* Contrasting epidemiology and clinicopathology of female breast cancer in Asians vs the US population. JNCI: Journal of the National Cancer Institute. 2019 Dec; 111(12): 1298-306. doi: 10.1093/jnci/djz090.

[2] Ghoncheh M, Pournamdar Z, Salehiniya H. Incidence and mortality and epidemiology of breast cancer in the world. Asian Pacific Journal of Cancer Prevention. 2016; 17(sup3): 43-6. doi: 10.7314/APJCP.2016.17.S3.43.

[3] Angahar LT. An overview of breast cancer epidemiology, risk factors, pathophysiology, and cancer risks reduction. MedCrave Online Journal Biology and Medicine. 2017 Jun; 1(4): 92-6. doi: 10.15406/mojbm.2017.01.00019.

[4] Usmani A and Lateef M. Evaluation of C-reactive protein in breast cancer by enzyme linked immunoassay technique. Journal of the Pakistan Medical Association. 2021 Feb; 71: 424-8. doi: 10.47391/JPMA.297.

[5] Cardoso F, Kyriakides S, Ohno S, Penault-Llorca F, Poortmans P, Rubio IT *et al.* Early breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology. 2019 Aug; 30(8): 1194-220. doi: 10.1093/annonc/mdz173.

[6] Lian M, Zhang C, Zhang D, Chen P, Yang H, Yang Y *et al.* The association of five preoperative serum tumor markers and pathological features in patients with breast cancer. Journal of Clinical Laboratory Analysis. 2019 Jun; 33(5): e22875. doi: 10.1002/jcla.22875.

[7] Watson J, Salisbury C, Banks J, Whiting P, Hamilton W. Predictive value of inflammatory markers for cancer diagnosis in primary care: a prospective cohort study using electronic health records. British Journal of Cancer. 2019 May; 120(11): 1045-51. doi: 10.1038/s41416-019-0458-x.

[8] Shimura T, Shibata M, Gonda K, Murakami Y, Noda M, Tachibana K *et al.* Prognostic impact of interleukin-6 and C-reactive protein on patients with breast cancer. Oncology Letters. 2019 Jun; 17(6): 5139-46. doi: 10.3892/ol.2019.10183.

[9] Takeuchi H, Kawanaka H, Fukuyama S, Kubo N, Hiroshige S, Yano T. Comparison of the prognostic values of preoperative inflammation-based parameters in patients with breast cancer. PLOS One. 2017 May; 12(5): e0177137. doi: 10.1371/journal.pone.0177137.

[10] Jung SY, Papp JC, Sobel EM, Pellegrini M, Yu H, Zhang ZF. Genetically predicted C-reactive protein associated with postmenopausal breast cancer risk:

DOI: https://doi.org/10.54393/pjhs.v5i12.2578

interrelation with estrogen and cancer molecular subtypes using Mendelian randomization. Frontiers in Oncology. 2021 Feb; 10: 630994. doi: 10.3389/fonc.2020.630994.

[11] Ravishankaran P, Karunanithi R. Clinical significance of preoperative serum interleukin-6 and C-reactive protein level in breast cancer patients. World Journal of Surgical Oncology. 2011 Dec; 9: 1-6. doi: 10.1186/1477-7819-9-18

[12] Fang CY, Egleston BL, Byrne C, Bohr GS, Pathak HB, Godwin AK *et al.* Inflammation and breast density among female Chinese immigrants: exploring variations across neighborhoods. Cancer Causes & Control. 2019 Oct; 30: 1113-26. doi: 10.1007/s10552-019-01206-x.

[13] Kaur RP, Banipal RP, Vashistha R, Dhiman M, Munshi A. Association of elevated levels of C-reactive protein with breast cancer, breast cancer subtypes, and poor outcome. Current problems in Cancer. 2019 Apr; 43(2): 123-9. doi: 10.1016/j.currproblcancer.2018.05.003.

[14] Badar F, Mahmood S, Faraz R, Yousaf A, Quader AU, Asif H. Epidemiology of breast cancer at the Shaukat Khanum memorial cancer hospital and research center, Lahore, Pakistan. Journal of College of Physicians and Surgeons Pakistan. 2015 Oct; 25(10): 738-42. doi: 10.2015/JCPSP.738742.

[15] Allin KH, Nordestgaard BG, Flyger H, Bojesen SE. Elevated pre-treatment levels of plasma C-reactive protein are associated with poor prognosis after breast cancer: a cohort study. Breast Cancer Research. 2011 Jun; 13: 1-3. doi: 10.1186/bcr2891.

[16] Moss JL, Liu B, Feuer EJ. Urban/rural differences in breast and cervical cancer incidence: the mediating roles of socioeconomic status and provider density. Women's Health Issues. 2017 Nov; 27(6): 683-91. doi: 10.1016/j.whi.2017.09.008.

[17] Sprague BL, Ahern TP, Herschorn SD, Sowden M, Weaver DL, Wood ME. Identifying key barriers to effective breast cancer control in rural settings. Preventive Medicine. 2021 Nov; 152: 106741. doi: 10.1016/j.ypmed.2021.106741.

[18] Dahri FJ, Awan MS, Qazi AR, Khaskheli NM, Soomro IA. Early wound complications following modified radical mastectomy with axillary clearance. Journal of Surgery Pakistan (Int). 2011 Oct; 16: 4.

[19] Shah S, Shah RU, Badar A, Shah M, Ahmad S, Muhammad H. Frequency of Early Post-Operative Complications following Modified Radical Mastectomy (MRM) in patients with Breast Carcinoma. Pakistan Journal of Medical and Health Sciences. 2021; 15(6): 1623-5. doi: 10.53350/pjmhs211561623.

[20] Sicking I, Edlund K, Wesbuer E, Weyer V, Battista MJ, Lebrecht A,. Prognostic influence of pre-operative C-reactive protein in node-negative breast cancer patients. PloS one. 2014 Oct; 9(10): e111306. doi: 10.1371/journal.pone.0111306.

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Knowledge, Attitude, and Practices of Practicing Dental Surgeons Towards Forensic Dentistry

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ABSTRACT

Forensic dentistry and dental records are essential to the legal system and healthcare because they support human identification, individualized patient care, and court cases. **Objective:** To assess the knowledge, attitude, and practices of dental surgeons in Karachi towards forensic dentistry. **Methods:** A cross-sectional study was conducted among 227 practicing dental surgeons in Karachi, Pakistan. A purposive sampling technique was used to recruit dentists. Hence by obtaining informed consent participants' privacy was assured. The sample size was calculated using Open-Epi Software with an aim of 18% knowledge among practicing dental surgeons. Descriptive statistics were used for data analysis methods by using SPSS version 24.0. **Results:** The study's findings showed that of the 227 participants, 38.7% were female practicing dental surgeons and 61.3% were male. About 91.1% of active dental surgeons acknowledged the value of keeping dental records, 35% said that gender, and 20% said that race could be determined from dental records. **Conclusions:** The results of the study concluded that there was a favorable attitude toward forensic dentistry and its inclusion in the curriculum. Hence, further workshops, need to be conducted among practicing dental surgeons.

INTRODUCTION

Teeth have been used as identifying techniques for a long time, with the first recorded court case reaching back to 1849. The term "forensic" is derived from Latin and refers to a forum or place for legal deliberations [1]. In the legal environment, dentistry is referred to as forensic dentistry or forensic odontology [2, 3]. The primary principle of forensic dentistry is that each individual's oral structure is unique [4]. Essentially, it is applying dental knowledge to legal systems. According to the Federation Dentaire International (FDI), it is the "field of dentistry focused on the correct management, examination, and evaluation of dental evidence in the pursuit of justice." This area of work involves a range of duties, such as bite mark analysis, human identification, investigating cases of abuse (of children, spouses, or elderly people), and evaluating medicolegal situations [5]. Forensic dentistry places great emphasis on teeth and other dental tissues for several reasons. First of all, there is a consistent aging pattern for teeth and the structures that support them. Because of this predictability, forensic specialists may determine an individual's age from the state of their teeth, which helps with identification and creating a timeline of events. Secondly, teeth have distinguishing characteristics that help in comparative identification. In cases involving

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unknown remains or victims, distinctive dental traits such as tooth morphology, dental restorations, and wear patterns can aid forensic investigators in differentiating between individuals and aid in the identification process [6]. In addition, the toughest tissue in the human body is found in the enamel that covers teeth. Compared to other body tissues, it is more resilient and can resist a wider range of traumas such as desiccation, submersion in water, burns, and chemical erosion. Because of this, dental evidence like enamel can frequently withstand adverse circumstances, offering crucial hints for forensic examination [7]. In addition, the dental pulp which is found in the tooth's center is a rich source of DNA. Enamel shielding the dental pulp allows genetic material to be preserved in challenging environments. As a result, forensic specialists can identify people implicated in criminal investigations or large-scale disasters by obtaining DNA from tooth pulp samples [8, 9]. Teeth and dental tissues are consequently essential tools in forensic science, aiding in both person identification and case resolution due to their special qualities and durability. Evaluating dental surgeons' forensic dentistry knowledge, attitudes, and practices residing in Karachi was the main objective of the study. A thorough analysis of the body of research indicates a sizable knowledge vacuum on the attitudes, behaviors, and knowledge of practicing dental surgeons employed by Karachi's dental facilities with regard to forensic dentistry.

The was to assess the level of knowledge, attitude, and practices of practicing dental surgeons of Karachi towards forensic dentistry

METHODS

A cross-sectional study was conducted from July till November 2024 among 227 practicing dental surgeons in Karachi, Pakistan. A purposive sampling technique was used to recruit the participants. A comprehensive list of practicing dental surgeons employed at these hospitals was obtained from the administrative departments before initiating the study. The inclusion criteria included practicing dental surgeons working in dental hospitals in Karachi with a recognized degree of at least one year of work experience and giving voluntary consent to participate. In contrast, those who had worked for less than six months or who had been very ill for three months were excluded. Permission was granted from the administrative department of the hospital and ethical approval was received from the Ethical Review Board (ERB) of Karachi Medical and Dental College (Reference No: ERB/KMDC/Approval/2024/067). All the participants were informed regarding the objective of the study and informed consent was taken from all recruited participants. They were also informed that they could withdraw from the study whenever they wanted to without excising pressure from the researchers. Open Epi software was used to determine the sample size, which was based on an estimated 18% prevalence of knowledge, attitude, and practices among dental surgeons, with a 95% confidence level and a 5% margin of error. This produced a sample size of 227 people, which was the minimum necessary. SPSS version 24.0 was used to analyze the data, and descriptive statistics were used to summarize the demographic data.

RESULTS

The results of the study revealed that the mean age was 37.5 years. The male participants made up the majority 61.3%, with female participants making up 38.7% of the group as shown in table 1.

Table 1: Demographic Characteristics of the Practicing Dental Surgeons

Variables	N (%)
Gender	
Male	139 (61.3%)
Female	88 (38.7%)

Almost 91.1% of participants showed that they understood the need to keep dental records in terms of their knowledge and abilities. Fewer participants, however, demonstrated specialized skills; only 32% were aware of distinguishing rugae patterns, 20% could identify race from teeth, and 35% could identify gender from teeth as shown in table 2.

Table 2: Knowledge of Forensic Dentistry of Practicing Dental Surgeons

Variables	N (%)
Understanding of Maintaining Dental Records	207 (91%)
Ability to Determine Gender by Teeth	81 (35%)
Ability to Determine Race by Teeth	47 (20%)
Forensic Dentistry Adopted as a Separate Subject	81 (35%)
Awareness of Distinctive Rugae Pattern	73 (32%)

Dental surgeons in Karachi have little experience and training in forensic dentistry, according to an evaluation of their knowledge, attitudes, and practices. Just 6.5% of respondents said they knew enough about the topic, and only 14.4% said they had received formal schooling in it. 49.3% of respondents were ignorant of the function that dental records play in identifying people, while 33.2% acknowledged its significance. Teeth were recognized as a feasible source for DNA extraction by more than half (57.5%). However, only 26.5% of them were aware of their prospective function as expert witnesses in court, and only 12.7% had received training in managing and presenting dental evidence. Despite this lack of readiness, a resounding 75% of respondents thought forensic dentistry ought to be taught as a distinct subject in undergraduate programs, underscoring the necessity for more focus as shown in table 3.

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Table 3: Assessment of Knowledge and Attitude of Dental Surgeons Working in Public and Private Dental Hospitals of Karachi Towards Forensic Dentistry

Item	Variables (Knowledge/Attitude)	Yes	No	Not Sure
1	Have you Received Formal Education in Forensic Dentistry in your Course?	14.4	84.4	1.2
2	Do you think you have adequate Knowledge about Forensic Dentistry?	6.5	91.2	2.3
3	Are you aware of how important Dental Records are for Identifying the Deceased and Charged with a Crime?	33.2	49.2	17.6
4	Do you believe that Teeth are an Appropriate Source for the Extraction of DNA?	57.5	10	32.5
5	Do you believe that a Court may Summon you at any Moment to Testify as an Expert Witness on Dental Evidence?	30.7	66.1	3.2
6	Do you Possess any Training in Obtaining, Assessing, and Presenting Dental Evidence?	12.7	79.3	8.0
7	Are you aware that you can Provide Forensic Dental Evidence in Court by Testifying as an Option Expert Witness?	26.5	69.3	4.2
8	Do you think Forensic Dentistry to be Included as a Separate Subject in the Undergraduate Curriculum?	75	23.2	1.8

The table 4 presented responses from male and female participants regarding their knowledge and awareness of forensic dentistry. It includes the distribution of responses (Yes, No, Not Sure) for various questions, along with the corresponding p-values for gender-based comparisons. The questions assess whether participants have received formal education in forensic dentistry, their self-perception of knowledge, their awareness of the importance of dental records, and their opinions on whether teeth are an appropriate source for DNA extraction. Additionally, the table examines participants' beliefs about their potential role as expert witnesses in court, their training in forensic dental evidence, and their awareness of the option to provide forensic dental testimony in court. The final question evaluates the respondents' opinion on whether forensic dentistry should be included as a separate subject in the undergraduate curriculum. Statistically significant differences are indicated by p-values marked with an asterisk (*), suggesting gender-based differences in knowledge or opinions on certain topics (Table 4).

Table 4: Comparison of Gender with Knowledge, Attitudes, Or Practices Regarding Forensic Dentistry

Variables	Yes	No	Not sure	p-value
Have you received formal education in forensic dentistry?				
Male	12 (8.6%)	123 (88.5%)	4 (2.9%)	0.045*
Female	21 (23.9%)	64 (72.7%)	3 (3.4%)	
Do you think you have adequate knowledge?				
Male	7 (5.0%)	128 (92.1%)	4 (2.9%)	0.098
Female	8 (9.1%)	78 (88.6%)	2 (2.3%)	
Are you aware of how important dental records are?				
Male	50 (36.0%)	64 (46.0%)	25 (18.0%)	0.022*
Female	25 (28.4%)	48 (54.5%)	15 (17.1%)	
Do you believe that Teeth are an Appropriate Source for the Extraction of DNA?				
Male	82 (59.0%)	10 (7.2%)	47 (33.8%)	0.310
Female	48 (54.5%)	13 (14.8%)	27 (30.7%)	
Do you believe that a Court may Summon you at any Moment to Testify as an Expert Witness on Dental Evidence?				
Male	82 (59.0%)	83 (59.7%)	6 (4.3%)	0.036*
Female	48 (54.5%)	67 (76.1%)	1 (1.2%)	
Do you Possess any Training in Obtaining, Assessing, and Presenting Dental Evidence?				
Male	18 (12.9%)	110 (79.1%)	11 (8.0%)	0.512
Female	11 (12.5%)	71 (80.7%)	6 (6.8%)	
Are you aware that you can Provide Forensic Dental Evidence in Court by Testifying as an Option Expert Witness?				
Male	37 (26.6%)	96 (69.1%)	6 (4.3%)	0.089
Female	37 (26.6%)	61 (69.3%)	4 (4.5%)	
Do you think Forensic Dentistry to be Included as a Separate Subject in the Undergraduate Curriculum?				
Male	106 (76.3%)	30 (21.6%)	3 (2.2%)	0.411
Female	65 (73.9%)	23 (26.1%)	0 (0.0%)	

* A statistically significant difference between genders is shown by a p-value < 0.05.

DISCUSSION

A branch of dentistry utilized in court cases was called forensic dentistry. This topic needs increased attention because crime, terrorism, and natural catastrophes have all been increasing globally over time. The majority of the time, forensic dentists were asked to assist with catastrophe victim identification, which helps identify victims' malformed corpses that were difficult for family members to recognize [9, 10]. Hence, similar to results in Lahore, where the same low level of awareness was seen [11]. The study's conclusions show that practicing dental surgeons in Karachi have a severe lack of knowledge, attitudes, and practices around forensic dentistry. Comparisons with both domestic and foreign research help to put these findings in a broader context and emphasize the need for better forensic dental education and training globally. In Lahore, Pakistan, similar research found that 87% of dental practitioners did not know the importance of forensic dentistry in identifying individuals, and just 16% had received basic training in preserving dental records. This was in line with these finding that 84.4% of participants had no formal training in forensic dentistry, indicating a widespread lack of foundational knowledge in Pakistan's biggest cities. Additionally, just 33.2% of participants recognized the need for dental records for identification, which was Despite being aware that dental surgeons could be called at any time in the court, unfortunately, the majority of dental surgeons had never submitted any dental evidence which was similar to a study

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conducted by Prakash P *et al.*, in Punjab of India [12]. Another study unequivocally demonstrates that dental professionals in India generally lack forensic odontology understanding and practice. Few universities provide formal instruction in forensic odontology. The majority of practitioners lacked formal education [13]. Dental schools in Canada, Japan, Norway, and the neighboring nations, including India and Nepal, have incorporated the subject into their undergraduate curriculum [14-16]. There aren't many universities that provide forensic odontology courses. Most practitioners have no formal schooling [14]. The topic has been included in the undergraduate dental curricula of dental schools in Canada, Japan, Norway, and the neighboring countries, such as India and Nepal [15-17]. Most participants did not know that forensic dentistry was taught in undergraduate programs as required by the Pakistan Medical and Dental Council [17]. Although 45% of dentists were aware of the function teeth play in DNA extraction, only 19% of them were able to accurately describe the process, according to a survey done in Rawalpindi by Shoro S *et al.*, 2020. However, this poll found that while 57.5% of respondents believed teeth may be a source of DNA, a significant 32.5% were not convinced, suggesting that while there was some information, a comprehensive understanding was still lacking [18]. Due to their lack of education and experience, the majority of respondents believed they were not qualified to offer an opinion in medico-legal cases requiring forensic dentistry [19]. This field has been ignored in the modern world. It was strongly recommended that more studies be conducted in this area in Pakistan. As a result, the focus should be placed on enhancing the curriculum by offering dental professionals specialized seminars and training courses, as well as raising awareness of forensic dentistry procedures in dental offices and financing them [19]. Due to their lack of education and experience, the majority of respondents believed they were not qualified to offer an opinion in medico-legal cases requiring forensic dentistry [20]. This area of study has been overlooked in the modern world. Additional research in this area was required in Pakistan. As a result, the focus should be placed on enhancing the curriculum by offering dental professionals specialized seminars and training courses, as well as raising awareness of forensic dentistry procedures in dental offices and financing them.

CONCLUSIONS

The field of forensic dentistry has not gained acceptance among the masses. It has been discovered that there were gaps in knowledge and practice, although practicing dental surgeons have expressed support for the inclusion of forensic dentistry as a course in the dental curriculum.

Authors Contribution

Conceptualization: NK
Methodology: NK, AA, SB, SN, MUH, NS
Formal analysis: SB
Writing, review and editing: NK, AA, MUH, NS

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

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REFERENCES

[1] Ireland CA, Chu S, Ireland JL, Hartley V, Ozanne R, Lewis M. Extreme stress events in a forensic hospital setting: Prevalence, impact, and protective factors in staff. Issues in Mental Health Nursing. 2022 May; 43(5): 418-33. doi: 10.1080/01612840.2021.2003492.

[2] Hachem M, Mohamed A, Othayammadath A, Gaikwad J, Hassanline T. Emerging applications of dentistry in medico-legal practice-forensic odontology. International Journal on Emerging Technologies. 2020; 11(2): 66-70.

[3] Mânica S, Gorza L. Forensic odontology in the 21st century–Identifying the opinions of those behind the teaching. Journal of forensic and legal medicine. 2019 May; 64: 7-13. doi: 10.1016/j.jflm.2019.03.006.

[4] Mohammed F, Fairozekhan AT, Bhat S, Menezes RG. Forensic odontology. 2019.

[5] Tahir F, Raja HZ, Saleem MN, Iqbal A, Ullah MS, Yasser F. Awareness of forensic odontology among dentists in Pakistan and its impact on dental record keeping. Pakistan Journal of Medical & Health Sciences. 2022 Sep; 16(08): 92-. doi: 10.53350/pjmhs2216892.

[6] Kundu A. Forensic Odontology: Bridging the Gap between Dental Science and Criminal Investigation. International Journal Of Ethics, Trauma & Victimology. 2024 Aug; 10(01): 18-27.

[7] Saxena V, Datla A, Bhargava A, Deheriya M. Forensic Dentistry in Disaster Management A Comprehensive Literature Review and Case Study Analysis. 2023.

[8] Qadri AW, Yadav S, Jain A, Shetty DC, Gulati N. Tooth as a vital source of DNA in forensic odontology: Recent perspective. Journal of Academy of Dental Education. 2023 Dec; 9(2): 73-9.

[9] Ketsekioulafis I, Katsos K, Kolentinis C, Kouzos D, Moraitis K, Spiliopoulou C *et al.* Humanitarian forensic medicine: a systematic review. International Journal of Legal Medicine. 2024 Dec: 1-5. doi: 10.1007/s00414-024-03381-2.

DOI: https://doi.org/10.54393/pjhs.v5i12.2419

[10] Lessig R, Prinz M. Mass Disaster Victim Identification. Handbook of Forensic Medicine. 2022 Jun; 1: 291-309.
[11] Zaheen U and Khan HA. Unlocking Clues Through Dental Records: A Descriptive Analysis of Dentists'role in Forensic Investigations. Pakistan Journal of Physiology. 2024 Jun; 20(2): 61-4. doi: 10.69656/pjp.v20i2.1576.
[12] Prakash P, Singh K, Bhandari SK. Forensic odontology: The prosthetic ID. Journal of Forensic Dental Sciences. 2019 Sep; 11(3): 113-7. doi: 10.4103/jfo.jfds_91_19.
[13] Isher DK, Isher PP, Kaur N, Rakhra J. Knowledge, awareness and practice of forensic odontology among the dentists of Punjab. Journal of Indian Academy of Oral Medicine and Radiology. 2019 Jul; 31(3): 239-45. doi: 10.4103/jiaomr.jiaomr_108_19.
[14] Monsy M, Thomas KS, Jijin MJ, Sanaka SR, Tiwari RV, Tiwari H. Knowledge and Awareness of Forensic Odontology amongst Dental Graduates: An Original Research. Journal of Advanced Medical and Dental Sciences Research. 2020 May; 8(5): 112-5. doi: 10.21276/jamdsr.
[15] Akram S, Arif Z, Khan S, Tauheed S. Knowledge, awareness and practice of forensic odontology among dental practitioners in Karachi, Pakistan. Pakistan Journal of Medicine and Dentistry. 2019 Apr; 8(1): 4.
[16] Hortsch M, Girão-Carmona VC, de Melo Leite AC, Nikas IP, Koney NK, Yohannan DG, et al. Teaching cellular architecture: the global status of histology education. In: Biomedical Visualisation: Volume 17-Advancements in Technologies and Methodologies for Anatomical and Medical Education. Cham: Springer International Publishing; 2023 Aug. 177-212. doi: 10.1007/978-3-031-36727-4_9.
[17] Wass V, Ng V, editors. Family Medicine in the Undergraduate Curriculum: Preparing medical students to work in evolving health care systems. CRC Press; 2023 Oct.
[18] Shoro S, Syed FM, Mânica S. Awareness and importance of forensic odontology amongst faculty members and students of dental institutes in Pakistan. Forensic Science International: Reports. 2020 Dec; 2: 100116. doi: 10.1016/j.fsir.2020.100116.
[19] Savić Pavičin I, Jonjić A, Maretić I, Dumančić J, Zymber Çeshko A. Maintenance of dental records and forensic odontology awareness: a survey of Croatian dentists with implications for dental education. Dentistry Journal. 2021 Mar; 9(4): 37. doi: 10.3390/dj9040037.
[20] Alamoudi RA and Alghamdi NS. Awareness of forensic dentistry among dental professionals in western Saudi Arabia: A knowledge, attitude, and practice-based cross-sectional study. Medicine. 2024 Apr; 103(14): e37738. doi: 10.1097/MD.0000000000037738.

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Original Article

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Effectiveness of Probiotics and Standard Therapy Versus Standard Therapy Alone in Patients of Mild to Moderate Rheumatoid Arthritis

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ABSTRACT

Analgesics, steroids and disease modifying anti-rheumatic drugs (DMARDs) are the cornerstone of treatment in rheumatoid arthritis (RA). **Objective:** To determine effectiveness of probiotics, introduced to standard treatment, in improving Disease Activity Score 28 (DAS-28) in patients with mild to moderate rheumatoid arthritis, when given for a period of three months. **Methods:** This randomized controlled trial registered under ClinicalTrials.gov ID: NCT06594822, was conducted on diagnosed cases of rheumatoid arthritis presenting to Mayo hospital, Lahore from 24th August 2023 till 23rd February 2024. Eighty-eight patients were recruited employing simple random sampling techniques and were categorized into two groups. Group A received standard therapy along with probiotics whereas Group B received standard therapy alone. DAS-28 score was assessed at baseline, at 45 and 90 days. **Results:** Patients in Group A showed an effective reduction in DAS-28 of 22.7% compared to 6.8% in group B (p=0.035). DAS-28 score in group A and B at baseline was 3.67 ± 0.61 vs 3.63 ± 0.52, p=0.708, after 45 days was 3.15 ± 0.63 vs 3.49 ± 0.56, p=0.010 and after 90 days was 2.93 ± 0.75 vs 3.27 ± 0.52, p=0.015. During treatment at days 45 and 90, group A patients showed a greater decrease from baseline i.e., -0.52 ± 0.63 vs -0.14 ± 0.56, p<0.010 and -0.74 ± 0.75 vs 0.36 ± 0.52, p<0.015 than group B patients. Group A also had a significant improvement in mean DAS-28 score at days 45 and 90 (p<0.05). **Conclusion:** Daily supplementation of probiotics with standard treatment is effective for the alleviation of symptoms and disease severity in patients having mild to moderate rheumatoid arthritis.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic, immune-mediated, progressive inflammatory disorder that causes joint pain, peri-articular soft tissue swelling, morning stiffness, reduced functional status, with osteoporosis and cartilage destruction leading to profound disability [1]. The worldwide prevalence of RA ranges from a mean point prevalence of 0.56% (SD 0.51) to a mean period prevalence of 0.51% (SD 0.35). A higher point to period prevalence is reported in the urban setting (0.69% vs 0.48%) compared to 0.54% vs 0.25% in the rural settings [2]. The age group affected is 20-40 years with increased susceptibility in the 75 and older individuals [3]. Female tend to have three to four times higher preponderance compared to male [4]. Apart from synovial joint inflammation, bone and cartilage deformities, there is production of antibodies namely Rheumatoid Factor (RF) and anti-cyclic citrullinated protein/peptide (Anti- CCP) antibodies [5]. Being a systemic disorder, inflammation tends to affect the heart, lungs, skeletal tissue and bone. Higher mortality is attributed to the increased risk of diabetes, asthma, bronchogenic carcinoma, chronic obstructive pulmonary disease, hypertension, cardiac and renal problems [6]. Although the exact etiopathogenesis of RA remains obscure, there appears to be a complex interaction of genetic, environmental, socioeconomic factors, dietary influences and imbalance of gut microbiota [7]. The current treatment recommendations for RA range from the simpler non-steroidal anti-inflammatory drugs (NSAIDs),

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corticosteroids mainly glucocorticoids like prednisone, conventional disease modifying anti-rheumatic drugs (DMARDs) like methotrexate, leflunomide, hydroxychloroquine, sulfasalazine, to more advanced biologic agents like infliximab, anakinra, abatacept, adalimumab to name a few and newer targeted synthetic DMARDs like baricitinib, tofacitinib etc. All these drugs mainly work my reducing inflammation and pain thereby leading to a reduction in tissue degradation and cellular damage and slowing the advancement of the disease [8]. The pathogenesis of RA involves cellular activation leading to autoimmunity in joints and other organs manifesting as synovial inflammation and joint injury with fibroblast-like synoviocytes (FLS) playing a key role in the inflammatory process [9-11]. People with RA have intestinal inflammation leading to changes in the gastrointestinal homeostasis and enhanced gut permeability causing leakage of harmful bacteria from the gut to the rest of the body [12]. Cytokines are released due to proinflammatory responses generated by the increased number of bacterial lipopolysaccharides present in the bloodstream as well as their build-up in the synovial joints [13]. A normal gut bacteria *Prevotella* spp. which is an anaerobic, non-spore forming bacteria, also constitutes an etiological factor for RA. By activating Toll-Like Receptors-2 (TLR-2) receptors in the intestinal epithelium and stimulating the secretion of proinflammatory cytokines like Interleukin-1β (IL-1β), IL-6 and IL-23, it produces inflammation and initiates RA by causing cartilage destruction and bone damage attributed to increased TNF-α [14]. Probiotics, the living organisms responsible for improving host microbiota and imparting health benefit when taken orally, have the potential to treat immune-mediated forms of arthritis by preserving equilibrium between beneficial and pathogenic bacteria in the body [15]. Numerous clinical trials have demonstrated the anti-inflammatory effects of probiotics supplementation in alleviating the symptoms of RA [16]. Various species of probiotics namely Lactobacillus spp. and Bifidobacterium spp. have been widely investigated. Owing to their anti-inflammatory effects on the intestines, probiotics mixture reduces IL-6 and TNF-α levels, nitric oxide metabolites and improved total antioxidant capacity thereby leading to alleviation of the symptoms of RA [17]. *Lactobacillus casei* 01 has been used in several randomized clinical trials and has shown to decrease proinflammatory cytokines, reduce global wellness score (gauged by visual analogue scale VAS), improve DAS-28 score and tender and swollen joint counts [18]. The addition of *Lactobacillus* and *Bifidobacterium* to diet produces anti-inflammatory short-chain fatty acids (SCFAs) which are beneficial to the gut [19].

This study aims to utilize *Bacillus clausii* in addition to DMARDs in patients having mild to moderate RA. The objective was to document symptom improvement in terms of reduction in DAS-28 score of ≥0.6 from baseline by recording symptoms on basis of European League Against Rheumatism (EULAR) response rates.

METHODS

This randomized controlled trial recruited patients presenting to the Rheumatology out-patients department of the Department of Medicine, King Edward Medical University, Mayo hospital, Lahore from 24th August 2023 till 23rd February 2024. The study was registered with ClinicalTrials.gov Identifier as NCT06594822, and approval was taken from Institutional Review Board (IRB) of King Edward Medical University vide No. 169/RC/KEMU. A sample size of 88 (44 in each group) was calculated by taking confidence level of 95%, absolute precision as 10% and expected percentage of efficacy in probiotic group as 20.11% and in standard therapy as 7.22% [20]. A total of 88 patients of both genders, between the age range of 18 to 70 years and having an established diagnosis of rheumatoid arthritis (proven on history, X-rays and biologic markers like RF and Anti-CCP antibodies, ESR) and having mild to moderate disease activity (DAS-28 score between 2.6 to <5.1) were selected via simple random sampling. Patients treated previously for RA with probiotics and those with a history of allergy to probiotics, patients with mixed connective tissue disorder and overlap syndrome as per history and labs, those with a history of gastrectomy, renal failure and liver cirrhosis, patients with recent or current use of antibiotics, pregnant patients and lactating mothers were excluded from the study. After approval, all patients conforming to the selection criteria were registered for the study. Informed written and verbal consent was obtained from all the participants. Patient's demographic data were obtained and recorded in a predesigned proforma. Patients were divided into two groups by computer generated method. Group A comprised 44 patients who received standard therapy (analgesics mainly diclofenac sodium 50mg thrice a day, glucocorticoids i.e., prednisone 10mg daily, DMARD mainly methotrexate 10mg weekly but sulfasalazine 1g twice a day in child- bearing age female) along with probiotic (*Bacillus clausii* in ampoule form containing 2 billion per 5ml once daily), whereas Group B also comprising 44 patients received standard therapy alone. Lab investigations like complete blood counts (CBC), Erythrocyte Sedimentation Rate (ESR), liver function tests (LFTs) and renal function tests (RFTs) were done at baseline and on follow up visits at 45 and 90 days. Disease activity score (DAS-28) consisting of 28 tender joint count (range 0-28), 28 swollen joint count (range 0-28), ESR and patient global assessment based on a visual analog scale (range 0-100) was assessed at baseline then on each subsequent visit to monitor response to treatment. Effectiveness was

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defined in terms of reduction of DAS-28 score of ≥0.6 from the baseline based on European League against Rheumatism(EULAR)response rates as given in Table 1.

Table 1: : Improvement in DAS-28 Score among study participants

Present DAS-28 Score	Improvement in DAS-28 Score		
	>1.2	>0.6 and ≤1.2	≤0.6
≤3.2	Good Response	Good Response	No Response
>3.2 and ≤5.1	Moderate Response	Moderate Response	No Response

Pancytopenia, derangement in LFTs and RFTs twice from the baseline because of treatment resulted in exclusion from the study. Data were interpreted using computer software Statistical Package for Social Sciences (SPSS) version 26.0. Mean ± SD were used for the calculation of quantitative variables including age and DAS-28 score. Qualitative variables including gender were expressed in the form of frequency and percentages. Chi- square test was employed to compare response between the two groups. p-value≤0.05 was considered statistically significant.

RESULTS

Out of a total of 88 enrolled patients, 44 were assigned to each group. The mean age of patients in group A was 56.64 ± 6.80 years and in group B, 58.07 ± 7.40 years with a p-value of 0.348. A female preponderance was observed in both the study groups. In group A, male comprised 15(34.1%) of the patients whereas 29(65.9%) of the patients were female and in group B, male patients constituted 13(29.5%) and female 31(70.5%) with a p-value of 0.647. The male to female ratio in group A was 1:1.93 and in group B it was 1:2.39. The mean DAS-28 score in group A and B at baseline was 3.67 ± 0.61 and 3.63 ± 0.52 with a p-value of 0.708. During follow-up at 45 days, it was reported to be 3.15 ± 0.63 and 3.49 ± 0.56 in Group A and B respectively with a p-value of 0.010 and at the end of treatment at 90 days, mean DAS-28 scores were 2.93 ± 0.75 in Group A and 3.27 ± 0.52 in Group B with a p-value of 0.015. The p-values calculated during follow-up and end of treatment were both found to be statistically significant indicating effective treatment response in the probiotic group, i.e., Group A as depicted in Table 2.

Table 3: Results of DAS-28 Score in Study Groups

DAS-28 scores	Group	N	Mean ± SD	Mean Difference	p-value
At Baseline	Group A	44	3.67 ± 0.61	-	0.708
	Group B	44	3.63 ± 0.52	-	
After 45 Days	Group A	44	3.15 ± 0.63	-0.52	0.010
	Group B	44	3.49 ± 0.56	-0.14	
After 90 Days	Group A	44	2.93 ± 0.75	-0.74	0.015
	Group B	44	3.27 ± 0.52	-0.36	

Group A: Standard treatment plus probiotic; Group B: Standard treatment alone

Effectiveness monitored in terms of a reduction in DAS-28 score of ≥0.6 was noted in 10 (22.7%) patients in Group A while it was observed in only 3 (6.8%) patients in Group B. This is given in a tabulated form in Table 3. A graphical representation of treatment response in both the groups is given in Figure 1.

Table 3: Effectiveness of Treatment in Study Groups

Effectiveness	Groups		Total	p-value
	Group A (Standard Therapy Plus Probiotic)	Group B (Standard Therapy)		
Yes	10	3	13	0.035
	22.7%	6.8%	14.8%	
No	34	41	75	
	77.3%	93.2%	85.2%	
Total	44	44	75	
	100.0%	100.0%	100.0%	

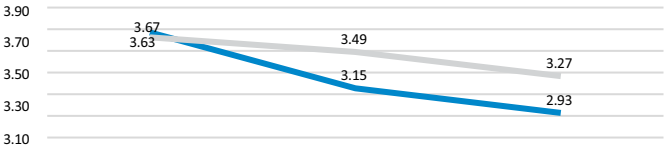

Figure 1: Comparison of DAS-28 Scores in Response to Treatment

DISCUSSION

Rheumatoid arthritis, a disease that not only affects the joints leading to bone and cartilage destruction, it also markedly reduces the overall functional capacity. A higher mortality rate in RA patients is attributed to an increased likelihood of other co-morbidities like diabetes, hypertension, lung, kidney diseases, psychological problems and cancer [6]. Keeping the complex pathogenesis in mind involving the genetic, immunologic and environmental factors, research has continuously been searching for novel therapeutic options [7]. Although the early initiation of DMARDs as soon as the diagnosis of RA is established has proven beneficial, but the variable progressive nature of the disease warrants a more aggressive treatment approach that not only controls the symptoms but also decelerates the advancement of the disease. Biologic agents like TNF inhibitors, IL-6 inhibitors, Janus kinase inhibitors, all specifically target the molecules implicated in the inflammatory cascade. These agents have demonstrated significant effectiveness but at the expense of being very costly and having numerous side effects that demand careful observation and hematological tests. This high cost and adverse effect profile has intrigued the researchers to utilize a more comprehensive and holistic approach and devise supplementary therapies that are both cost-effective and have a better safety profile. As RA causes significant alterations in the gut microbiota, the use of probiotics as complementary therapy emerged. Literature search

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revealed various studies mainly conducted on laboratory rats and demonstrated the beneficial role of probiotics in rheumatoid arthritis. Rudbane *et al.*, conducted a systematic review and meta-analysis and demonstrated the role of *L. caseii* when given as an adjuvant to standard therapy in patients of active RA and showed a considerable improvement in CRP levels in these patients [20]. No effect on improvement in DAS-28 score was reported in this meta-analysis. A study conducted in Brazil on 42 patients used a combination of probiotics namely *Lactobacillus casei, Lactobacillus acidophilus, Lactococcus lactis, Bifidobacterium lactis* and *Bifidobacterium bifidum* for a period of 60 days. They concluded that probiotic combination led to a significant reduction in white cell count, TNF-α, IL-6 and NO metabolites and an increase in antioxidant parameters [21]. Alipour *et al* showed a significant improvement in DAS-28 score as well as EULAR response rates in patients who received probiotics [22]. A study undertaken by Zamani *et al*. administered 3 different strains of probiotics namely *Lactobacillus acidophilus, Lactobacillus caseii* and *Bifidobacterium bifidum* to a group of 30 RA patients and compared it with a placebo. After 8 weeks of intervention, he observed a significant improvement in DAS-28 score (-0.3 ± 0.4 vs -0.1 ± 0.4, p=0.01) and high sensitivity C- reactive protein (hsCRP) concentrations (-6.66 ± 2.56 vs. +3.07 ± 5.53mg/L, p<0.001) [23]. The results of this study were congruent with current results as 22.7% of patients taking a probiotic with standard therapy showed an improvement in DAS-28 score compared to only 6.8% of the patients taking standard therapy alone. The effectiveness of probiotics in treating RA was also shown by Yuan *et al* [9]. According to their research, probiotics improve DAS-28 score in RA patients but have limited impact on IL-6, IL-10, and ESR. All these studies, systematic reviews and meta-analyses have not yet provided sufficient data that can help the healthcare policy makers to formulate recommendations for regular use of probiotics in RA patients. Selection of the probiotic, using the optimal dose and appropriate treatment duration are all crucial and case-specific and demand extensive workup when considering their role in the management of RA. To gauge and assess treatment response, we also recommend easy availability and routine monitoring of immunologic markers like cytokines. Although probiotics cannot replace the standard treatment for RA but if proved effective on a large scale, they can be recommended as an adjunct to standard therapy in treating RA patients. There were certain limitations of current study like small sample size, use of only one type of probiotic, shorter duration of therapy and no use of assays for cytokine measurements.

CONCLUSIONS

It was concluded that the addition of probiotics to standard therapy in the treatment of mild to moderate RA patients is effective in terms of improving DAS-28 score, reducing pain, swelling and tenderness of joints. Therefore, it leads to improved quality of life and functional status.

Authors Contribution

Conceptualization: GI
Methodology: TN
Formal analysis: BA, YI
Writing review and editing: TN, TF, AI

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

The authors declare no conflict of interest.

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REFERENCES

[1] Gravallese EM and Firestein GS. Rheumatoid Arthritis-Common Origins, Divergent Mechanisms. The New England Journal of Medicine.2023; 388(6): 529-542. doi: 10.1056/NEJMra2103726.

[2] Almutairi KB, Nossent JC, Preen DB, Keen HI, Inderjeeth CA. The Prevalence of Rheumatoid Arthritis: A Systematic Review of Population-Based Studies. The Journal of Rheumatology.2021; 48(5): 669-676. doi:10.3899/jrheum.200367.

[3] Sepriano A, Kerschbaumer A, Smolen JS, Van Der Heijde D, Dougados M, Van Vollenhoven R, *et al*. Safety of Synthetic and Biologic DMARDs: A Systematic Literature Review Informing the 2019 Update of the EULAR Recommendations for the Management of Rheumatoid Arthritis. Annals of Rheumatic Diseases. 2020; 79(6): 760-770. doi: 10.1136/annrheumdis-2019-216653.

[4] Schrezenmeier E and Dȍrner T. Mechanisms of Action of Hydroxychloroquine and Chloroquine: Implications for Rheumatology. Nature Reviews Rheumatology. 2020; 16: 155-166. doi: 10.1038/s41584-020-0372-x.

[5] Van Delft MAM and Huizinga TWJ. An Overview of Antibodies in Rheumatoid Arthritis. Journal of Autoimmunity.2020;110:102392.doi:10.1016/j.jaut .2019. 102392.

[6] Reis ETd, Kakehasi AM, Pinheiro MdM, Ferreira GA, Marques CDL, Mota LMH, *et al*. Revisiting Hydroxychloroquine and Chloroquine for Patients with Chronic Immunity-Mediated Inflammatory Rheumatic Diseases. Advances in Rheumatology.2020; 60:32.

DOI: https://doi.org/10.54393/pjhs.v5i12.2241

doi: 10.1186/s42358-020-00134-8.

[7] Scherer HU, Haupl T, Burmester GR. The Etiology of Rheumatoid Arthritis. Journal of Autoimmunity. 2020; 110: 102400. doi: 10.1016/j.jaut.2019.102400.

[8] Rai V, Patel N, Mammen SR, Chaudhary SM, Arshad S, Munazzam SW. Futuristic Novel Therapeutic Approaches in the Treatment of Rheumatoid Arthritis. Cureus.2023; 15(11): e49738. doi:10.7759/cureus.49738.

[9] Yuan Y, Ji W, Lin Z, Gan K. Benefits of Probiotics in Rheumatoid Arthritis Patients: A Systematic Review and Meta Analysis. Tropical Journal of Pharmaceutical Research. 2023; 22(2): 399-406.

[10] Weyand CM and Goronzy JJ. The Immunology of Rheumatoid Arthritis. Nature Immunology.2021; 22(1): 10-18. doi: 10.1038/s41590-020-00816-x.

[11] Nygaard G and Firestein GS. Restoring Synovial Hemostasis in Rheumatoid Arthritis by Targeting Fibroblast-like Synoviocytes. Nature Reviews Rheumatology.2020; 16(6): 316-333. doi:10.103 8/s41 584-020-0413-5.

[12] Gomaa EZ. Human Gut Microbiota/Microbiome in Health and Diseases: A Review. Antonie Van Leeuwenhoek.2020; 113(12): 2019-2040. doi:10.1007/s10482-020-01474-7.

[13] Lin L, Zhang K, Xiong Q, Zhang J, Cai B, Huang Z, *et al.* Gut Microbiota in Pre-Clinical Rheumatoid Arthritis: from Pathogenesis to Preventing Progression. Journal of Autoimmunity.2023 Dec; 141: 103001. doi:10.1016/j.jaut.2023.103001.

[14] Santos-Sierra S. Targeting Toll-like Receptor (TLR) Pathways in Inflammatory Arthritis: Two Better Than One? Biomolecules.2021; 11(9): 1291. doi: 10.3390/ biom 11091291.

[15] Yang Y, Hong Q, Zhang X, Liu Z. Rheumatoid Arthritis and the Intestinal Microbiome: Probiotics as A Potential Therapy. Frontiers in Immunology. 2024 Mar; 15: 1331486. doi: 10.3389/fimmu.2024.1331486.

[16] Bungau SG, Behl T, Singh A, Sehgal A, Singh S, Chigurupati S, *et al*. Targeting Probiotics in Rheumatoid Arthritis.Nutrients.2021; 13(10): 3376.doi :10.3390/nu13103376.

[17] Cannarella LAT, Mari NL, Alcantara CC, Iryioda TMV, Costa NT, Oliveira SR, *et al.* Mixture of Probiotics Reduces Inflammatory Biomarkers and Improves the Oxidative/Nitrosative Profile in People with Rheumatoid Arthritis. Nutrition.2021;89:111282.doi :10.1016/j.nut.2021.111282.

[18] Harden RN, McCabe CS, Goebel A, Massey M, Suvar T, Grieve S, *et al.* Complex Regional Pain Syndrome: Practical Diagnostic and Treatment Guidelines, 5th Edition. Pain medications.2022 Jun; 23(1): S1-S53. doi: 10.1093/pm/pnac046.

[19] Li N, Li X, Su R, Wu R, Niu HQ, Luo J, *et al*. Low-Dose Interleukin-2 Altered Gut Microbiota and Ameliorated Collagen-Induced Arthritis. Journal of Inflammation Research.2022; 15: 1365-1379. doi:10.214 7/JIR.S34 4 3993.2.

[20] Rudbane ASM, Rahmdel S, Abdollahzadeh SM, Zare M, Bazrafshan A, Mazloomi SM. The Efficacy of Probiotic Supplementation in Rheumatoid Arthritis: A Meta-Analysis of Randomized Controlled Trials. Inflammopharmacology.2018; 26(1): 67-76. doi: 10.10 0 7/s10787-017-0436-y.

[21] Cannarela LAT, Mari NL, Alcantara CC, Iryioda TMV, Costa NT, Oliveira SR, *et al*. Mixture of Probiotic Reduces Inflammatory Biomarkers and Improves the Oxidative/Nitrosative Profile in Patients with Rheumatoid Arthritis. Nutrition. 2021; 89: 111282. doi: 10.1016/j.nut.2021.111282.

[22] Alipour B, Homayouni-Rad A, Vaghef-Mehrabany E, Sharif SK, Vaghef-Mehrabany L, Asghari-Jafarabadi M, *et al.* Effects of Lactobacillus casei Supplementation on Disease Activity and Inflammatory Cytokines in Rheumatoid Arthritis Patients: A Randomized Double-Blind Clinical Trial.International Journal of Rheumatic Diseases. 2019; 17(5): 519-527.

[23] Zamani B, Golkar HR, Farshbaf s, Emadi-Beygi M, Tajabadi-Ebrahimi M, Jafari P, *et al.* Clinical and Metabolic Response to Probiotic Supplementation in Patients with Rheumatoid Arthritis: A Randomized, Double-Blind, Placebo Controlled Trial. International Journal of Rheumatic Diseases.2016; 19(9): 869-879. doi: 10.1111/1756-185X. 12888.

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B12 Deficiency: Hidden Player in Dengue-Induced Thrombocytopenia

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ABSTRACT

Dengue fever is a significant health challenge in tropical and subtropical countries. Because it increases the likelihood of thrombocytopenia with hemorrhagic symptoms, treating thrombocytopenia is a serious clinical concern. According to some studies, certain vitamin status may impact platelet deficiency and hence the clinical outcome of the disease. **Objectives:** To determine the association between the severity of thrombocytopenia, bleeding manifestations, and the severity of Dengue fever with Vitamin B12 deficiency. **Methods:** It was a prospective cohort study carried out over 4 months. A total of 139 patients were included in the study. Serial blood counts and Vitamin B12 were checked. Patients were observed for any bleeding manifestations and need for transfusion of Blood components. **Results:** Among 139 patients, 46% exhibited moderate thrombocytopenia, 30.9% showed severe thrombocytopenia and 5.8 % had a very severe drop in platelet count. A large proportion (82.7%) had normal B12 levels and cross-tabulation between serum B12 levels and severity of thrombocytopenia was not significant (p-value=0.34). **Conclusion:** It was concluded that the severity of thrombocytopenia was not associated with underlying Vitamin B12 deficiency.

INTRODUCTION

Dengue Virus is an enveloped RNA, a single-stranded virus that belongs to the flavivirus group. There are four different serotypes. Dengue Virus is responsible for causing Dengue Fever, a vector-borne disease spread by mosquitoes [1]. High-grade fever, retro-orbital discomfort, headache, joint pain, vomiting, abdominal pain, and bleeding manifestations are the hallmarks of dengue fever. Dengue infection can occasionally result in harmful symptoms like dengue shock syndrome and dengue hemorrhagic fever [2, 3]. Recent studies show Pakistan has an endemic Dengue Virus infection, most prevalent during the monsoon season. During 2022, around 78,554 confirmed cases of dengue fever were reported in Pakistan. Three large outbreaks of Dengue Fever in Pakistan in 2006, 2010, and 2011 affected almost 40,000 people [4]. Thrombocytopenia and leucopenia are significant laboratory markers of Dengue Fever. Several mechanisms, including bone marrow suppression, antibody-mediated destruction, and peripheral platelet consumption, have been suggested as potential causes of thrombocytopenia [5]. Platelet counts show a sharp decline during the early days of Dengue infection leading to mucosal bleeding and may need transfusion of platelets or RCC (red cell concentrate) occasionally. Hemorrhagic manifestations are one of the most common serious complications which are associated with high morbidity and mortality in Dengue Hemorrhagic

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Fever and Dengue Shock Syndrome [6, 7]. Interestingly the degree of thrombocytopenia in Dengue Fever is correlated with Vitamin B12 deficiency. Several studies have demonstrated a link between marked thrombocytopenia with bleeding symptoms and a prolonged hospital stay with Vitamin B12 deficiency [8]. Vitamin B12 is essential for DNA synthesis and cellular proliferation, particularly in hematopoietic cells of the bone marrow. Animal-based meals can provide Vitamin B12, which is primarily stored in the liver of humans [9]. Before signs of Vitamin B12 insufficiency appear, liver reserves are adequate for three to five years. Dietary insufficiency, chronic gastritis, particularly Helicobacter-associated gastritis, terminal ileum surgery, intrinsic factor deficiency, pancreatitis, and fish tapeworm infestation are a few of the reasons for Vitamin B12 deficiency [10, 11]. In processes necessary for pyrimidine and purine biosynthesis, including the production of DNA nucleotides, folate and cobalamin are both necessary to maintain one-carbon metabolism. Therefore, a deficiency in vitamin B12 leads to a disruption in DNA synthesis, which is followed by less significant alterations in RNA and protein synthesis, which finally results in disturbed cell division and unbalanced cellular proliferation. [12]. Nutritional deficiency of Vitamin B12 is prevalent in the subcontinent and is predominantly caused by poor nutrition or malabsorption [11]. A recent study revealed that a lack of vitamin B12 is the third most common cause of pancytopenia in children in Pakistan [13]. The clinical manifestations of Vitamin B12 deficiency are varied including hematological, gastrointestinal, and neurological. Severe Vitamin B12 deficiency can lead to pancytopenia due to bone marrow suppression [10]. Vitamin B12 deficiency reduces platelet production by about 10% in individuals, mostly due to impaired thrombopoiesis and aberrant platelet function [14]. Several studies have suggested that Vitamin B12 deficiency may have a role in the development of severe thrombocytopenia in people who have Dengue Fever, particularly in the subcontinent [15]. Thrombocytopenia results in mucosal membrane bleeding is the main concern with dengue fever. With Dengue Fever looming around the corner, there are many herbal treatments available to treat thrombocytopenia, which may lead to irrational drug and platelet product use due to a fear of bleeding. In Pakistan, a third-world nation, health facilities are few and inaccessible. Products made from platelets are expensive and not widely accessible for many people.

This study aims to determine whether severe thrombocytopenia in dengue fever patients is caused by concomitant Vitamin B12 insufficiency. If a link exists between Serum Vitamin B12 levels and the degree of thrombocytopenia, treating Vitamin B12 deficiency will prevent marked thrombocytopenia and the subsequent requirement for platelet transfusions.

METHODS

This prospective cohort study was carried out in Department of Medicine Units 1 and 2 of Pakistan Air Force (PAF) Hospital Islamabad from July 2023 to October 2023 over 4 months. Necessary ethical approval was taken before the start of the study with reference number 230601. The study included all individuals with dengue fever who were older than 13 and who visited the PAF hospital's outpatient department or emergency room. Dengue fever was confirmed by non-structural protein 1 (NS1) Antigen and Immunoglobulin M (IgM) serology. Patients with strong clinical suspicion were included in the study in some cases. All individuals with underlying liver disease, malignancy, sepsis, hematological disorders, and those who were using any drugs that could lead to thrombocytopenia were excluded from the study. Following informed consent, demographic data were acquired. All confirmed cases of Dengue Fever fulfilling the admission criterion were admitted and their serum vitamin B12 was checked. Serial blood counts were performed and a baseline complete blood count (CBC) was obtained. The minimum platelet count, length of hospital stay, any bleeding manifestations requiring blood products transfusion, and any complications from Dengue Hemorrhagic Fever and Dengue Shock Syndrome were evaluated for the patient. For Outpatient Department (OPD) cases, Vitamin B12 was checked at presentation. CBC was done initially and patients were called for follow-up with serial CBC. Patients were divided into four groups according to the severity of thrombocytopenia where mild was defined as a platelet count of more than 1 lacx10^9/L, moderate was a platelet count of 50,000 to 1 lacx10^9, severe 20,000-50,000 and very severe with platelet count less than 20,000x109/L. The WHO sample size calculator calculated the sample size; keeping the percentage positivity of the study outcome at 52%, a confidence interval of 90%, and 7.1% precision, a Sample size of 139 participants was considered adequate [16]. Participants were included using non-probability convenient sampling. Data were entered and analyzed using SPSS version 23.0. While mean and standard deviation were used to summarize continuous variables, frequencies, and percentages were used to characterize categorical variables. Cross-tabulation was done between vitamin B12 levels and several patient groups based on the decrease in platelets. A p-value of less than 0.05 was deemed noteworthy.

RESULTS

A total number of 139 patients were included, with a mean age of 36.6 + 1.4 years. Among them, 68.3% were male, while 31. 7% were female. Out of 139, the majority 76.3% of

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the patients had no co-morbid. Dengue was confirmed by NS1 antigen in 89%. Only 15.8% of patients had a history of prior dengue infection. The majority of patients, (82.7%) had normal Serum B12 levels. The demographics of participants are shown in Table 1.

Table 1: Demographic Characteristics of study participants

Demographics	Mean+ SD/ n=139 (%)
Age	36.6 + 1.4 Years
Up To 35 Years	83 (59.7)
Gender	
Male	95 (68.3)
Female	44 (31.7)
Comorbidities	
None	106 (76.3)
Diabetes	17 (12.2)
Hypertension	6 (4.3)
COPD	3 (2.2)
Others	7 (5)
Diagnostic Test	
NS1 Antigen	125 (89.9)
IGM Serology	9 (6.5)
Clinical Diagnosis	5 (3.6)
History of Previous Dengue Fever	
Yes	22 (15.8)
No	117 (84.2)
Serum Vitamin B12 Levels	
Normal	115 (82.7)
Deficient	24 (17.3)
Thrombocytopenia	
Mild	23 (16.5)
Moderate	65 (46.8)
Severe	43 (30.9)
Very Severe	8 (5.8)
Dengue Hemorrhagic Fever	
Yes	17 (12.2)
No	122 (87.8)
Bleeding Manifestation	
None	116 (83.4)
Petechial Hemorrhages	14 (10.1)
Nasal/ Gum Bleed	3 (2.2)
GI Bleed (Melena)	4 (2.9)
Hematuria	2 (1.4)
Transfusion (Platelet/RCC)	
Yes	5 (3.6)
No	134 (96.4)
Outcome Of Dengue Fever	
Recovered	138 (99.3)
Died	1 (0.7)

COPD: Chronic Obstructive Pulmonary Disease

The mean duration of hospital stay was 4.24 + 1.75 days. Among 139 patients with dengue fever, 16.5% exhibited mild (>100,000x109 /L) thrombocytopenia. Moderate (50,000-100,000x109/L) thrombocytopenia had been observed in 46.8% of patients. However, 30.9% experienced severe (20,000-50,000x109/L) and only 5.8% expressed very severe (<20,000x109/L) thrombocytopenia. Out of 139, 12.2% suffered from Dengue hemorrhagic fever, and only 23 (16.6%) exhibited bleeding manifestations, amongst them 10.1% showed petechial hemorrhages and 2.9% had a Gastrointestinal (GI) bleed. However, only 5 (3.6%) required transfusion of blood product (RCC/Platelet). Only one patient died due to arrhythmia secondary to viral myocarditis. The characteristics of Dengue fever are shown in Table 2.

Table 2: Course of Dengue Fever

Characteristics	Mean+ SD/ n=139 (%)
Length of Hospital Stay	4.24 + 1.75
1-3 Days	70 (50.4)
4-7 Days	56 (40.3)
More Than 7 Days	13 (9.4)

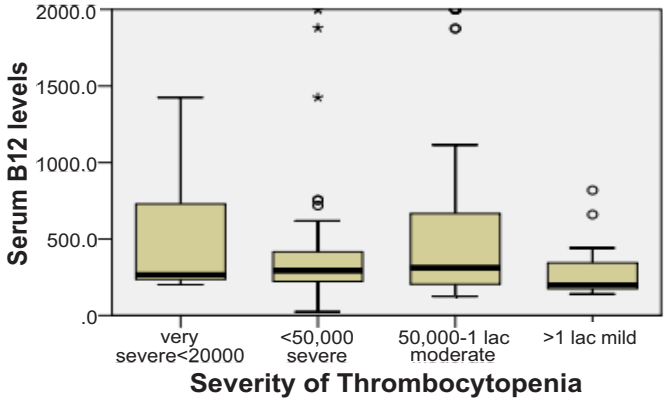

Figure: 1 Association of Thrombocytopenia with Serum B12 Level in Patients with Dengue Fever

However, the study results show that the severity of thrombocytopenia in dengue patients was significantly associated with their comorbid, occurrence of dengue hemorrhagic fever and need for transfusion with p-value <0.00. However, age, gender, previous dengue infection, bleeding manifestations, and duration of illness were not found to be significantly associated with the severity of thrombocytopenia as shown below in Table 3.

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Table 3: Association of Severity of Thrombocytopenia in Patients with Dengue Fever

Variables	n=139 (%)	Mild n (%)	Moderate n (%)	Severe n (%)	Very Severe n (%)	p-value
Age						
Up to 35 Years	83 (59.7)	17 (12.2)	39 (28)	23 (16.5)	4 (2.9)	0.272
36 Years or Above	56 (40.3)	6 (4.3)	26 (18.7)	20 (14.4)	4 (2.8)	
Gender						
Male	95 (68.3)	14 (10.1)	45 (32.4)	28 (20.1)	8 (5.7)	0.210
Female	44 (31.7)	9 (6.5)	20 (14.4)	15 (10.8)	0 (0)	
Comorbid						
None	106 (76.3)	21 (15.1)	48 (34.5)	35 (25.2)	2 (1.4)	<0.00
Diabetes	17 (12.2)	1 (0.7)	12 (8.6)	3 (2.2)	1 (0.7)	
Hypertension	6 (4.3)	1 (0.7)	3 (2.2)	1 (0.7)	1 (0.7)	
COPD	3 (2.2%)	0 (0)	0 (0)	1 (0.7)	2 (1.4)	
Other	7 (5)	0 (0)	2 (1.4)	3 (2.2)	2 (1.4)	
History of Previous Dengue Fever						
Yes	22 (15.8)	7 (5)	7 (5)	6 (4.3)	2 (1.4)	0.136
No	117 (84.2%)	16 (11.5%)	58 (41.7%)	37 (26.6%)	6 (4.3%)	
Dengue Hemorrhagic Fever						
Yes	17 (12.2)	2 (1.4)	4 (2.9)	6 (4.3)	5 (3.6)	<0.00
No	122 (87.8)	21 (15.1)	61 (43.9)	37 (26.6)	3 (2.2)	
Bleeding Manifestation						
None	116 (83.5)	21 (15.1)	55 (39.6)	35 (25.2)	5 (3.6)	0.489
Petechial Hemorrhages	14 (10.1)	1 (0.7)	5 (3.6)	6 (4.3)	2 (1.4)	
Nasal/ Gum Bleed	3 (2.2)	1 (0.7)	1 (0.7)	1 (0.7)	0 (0)	
GI bleed (Melena)	4 (2.9)	1 (0.7)	2 (1.4)	1 (0.7)	0 (0)	
Hematuria	2 (1.4)	0 (0)	2 (1.4)	0 (0)	0 (0)	
Transfusion (Platelet/RCC)						
Yes	5 (3.6)	0 (0)	0 (0)	2 (1.4)	3 (2.2)	<0.00
No	134 (96.4)	23 (16.5)	65 (46.8)	41 (29.5)	5 (3.6)	
Serum Vitamin B12 Levels						
Normal	115 (82.7)	17 (12.2)	53 (38.1)	37 (26.6)	8 (5.8)	0.345
Deficient	24 (17.3)	6 (4.3)	12 (8.6)	6 (4.3)	0 (0)	
Duration of Illness						
1-3 Days	70 (50.4)	8 (5.8)	41 (29.5)	17 (12.2)	4 (2.9)	0.010
4-7 Days	56 (40.3)	9 (6.5)	23 (16.5)	21 (15.1)	3 (2.2)	
More Than 7 Days	13 (9.4)	6 (4.3)	1 (0.7)	5 (3.6)	1 (0.7)	

DISCUSSION

The Discussion section of this study engages deeply with the complex interrelationship between thrombocytopenia severity in dengue fever patients and their serum vitamin B12 levels. Thrombocytopenia, marked by a substantial reduction in platelet count, stands as a defining feature of dengue fever, often contributing to bleeding complications that can significantly impact patient prognosis and recovery [16]. The role of vitamin B12 in cellular proliferation and DNA synthesis, particularly in hematopoiesis, emerges as a crucial factor in understanding the potential exacerbation of thrombocytopenia severity among dengue patients [17]. Emerging evidence suggests that a deficiency in this essential vitamin may exacerbate thrombocytopenia, thereby worsening clinical outcomes in dengue fever patients [8]. This holds particular significance in regions like the Indian subcontinent, where vitamin B12 deficiency is prevalent and may compound the challenges posed by dengue fever [15]. The results of current study provide an overview of various demographic and clinical characteristics among the 139 dengue fever patients. These findings offer valuable insights into the complexities surrounding thrombocytopenia severity, and serum B12 level and their interplay within the context of dengue fever [18]. Notably, a substantial proportion (82.7%) of patients exhibited normal serum vitamin B12 levels. Cross tabulation between the drop in platelets and underlying serum B12 was not significant. These findings underscore the complex multifactorial nature of thrombocytopenia in dengue fever, suggesting that factors beyond nutritional

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deficiencies may contribute to its pathogenesis [3]. However, this is in contrast to many studies done by Sagar *et al.*, [15] and Kansara and Sharma [17] in India previously which showed a positive association between the severity of platelet drop and underlying B12 deficiency. Numerous Indian studies revealed a favourable correlation between thrombocytopenia and B12 deficiency. However, what current research showed was the exact reverse. This could be explained by the fact that the majority of Indians are likely vegetarians, and vitamin B12 deficiency is common, thus the association may be coincidental. The demographic profile of patient cohort reveals a predominant representation of younger individuals (59.7%) affected by dengue. This distribution underscores the susceptibility of younger populations to dengue fever, aligning with the known epidemiological patterns of the disease [19]. Furthermore, gender distribution shows a higher prevalence among males, accounting for 68.3% of the patients, consistent with existing literature documenting a slightly increased risk of dengue fever among male [7]. Among the patients, the majority (76.3%) presented with no premorbid conditions, while a small proportion had pre-existing medical conditions such as diabetes mellitus (12.2%), hypertension (4.3%) and chronic obstructive pulmonary disease (COPD) (2.2%). 5% of patients have other premorbid like Interstitial lung disease or hypothyroidism etc. Interestingly the drop in platelets was more severe in patients with comorbid conditions and that relationship was significant. The diagnosis of dengue fever was predominantly confirmed by NS1 antigen testing (89.9%), highlighting the reliability of this diagnostic modality in identifying acute dengue infections. Additionally, a noteworthy proportion of patients (6.5%) were diagnosed based on IgM serology, with a small subset (3.6%) diagnosed based on typical clinical symptoms supported by the blood CP report characteristic of bi-cytopenia. This underscores the importance of utilizing multiple diagnostic approaches to ensure accurate and timely diagnosis, particularly in resource-constrained settings where access to laboratory testing may be limited [4]. Evaluation of platelet counts revealed varying degrees of thrombocytopenia severity among patients, but the incidence of severe bleeding manifestations was relatively low, with only a small percentage of patients experiencing petechial hemorrhage (10.1%) or more severe bleeding such as melena or upper gastrointestinal bleeding 2.9% (4 patients). Out of 139 patients, only 17 (12.2 %) went into DHF (dengue hemorrhagic fever). Importantly, no cases of intracranial hemorrhage were reported, highlighting the overall manageable nature of bleeding complications in current patient cohort. In present study, the average duration of hospital stay was five days, with the majority of patients experiencing a favourable clinical course. However, one unfortunate fatality occurred due to dengue myocarditis with associated arrhythmia, emphasizing the importance of vigilant monitoring for cardiac complications in dengue patients [20]. Greater severity of thrombocytopenia was significantly associated with longer hospital stays. Similar findings are supported by various studies done in India [15, 16]. In summary, we studied the relationship of underlying B12 and folate deficiency with the severity of thrombocytopenia in dengue patients which turned out to be non-significant. The findings emphasize the necessity for further investigation into the mechanisms driving thrombocytopenia in dengue fever and suggest the potential for developing tailored therapeutic interventions to improve patient outcomes in this prevalent disease.

CONCLUSIONS

It was concluded that the severity of thrombocytopenia is not associated with underlying serum B12 deficiency and the relationship is not significant.

Authors Contribution

Conceptualization: UB
Methodology: UB, AS, AA, BR, RA
Formal analysis: AA, BR, RA, TZ
Writing review and editing: TZ

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Murhekar M, Joshua V, Kanagasabai K, Shete V, Ravi M, Ramachandran R *et al.* Epidemiology of Dengue Fever in India, Based On Laboratory Surveillance Data, 2014–2017. International Journal of Infectious Diseases. 2019 Jul; 84: S10-4.doi:10.1016/j.ijid.2019. 01. 004.

[2] Majeed MA, Shafri HZ, Zulkafli Z, Wayayok A. A Deep Learning Approach for Dengue Fever Prediction in Malaysia Using LSTM with Spatial Attention. International Journal of Environmental Research and Public Health.2023 Feb; 20(5): 4130. doi: 10.339 0/ije rp h20054130.

[3] Salam MA, Shah SA, Zafar F, Naseer M, Irshad I, Shoukat S *et al.* Dengue Fever Epidemiological Investigation in the District of Rawalpindi, Punjab, Pakistan. Journal of Pharmaceutical Negative

DOI: https://doi.org/10.54393/pjhs.v5i12.2378

Results.2023 Feb; 14(2): 2648-55. doi: 10.47750/ pnr. 2023.14.S02.311.

[4] Rehman AU, Anwar F, Tayyab M, Haq I, Haq M, Ahmed A *et al*. Incidence of Dengue Fever, Serotypes, Clinical Features, and Laboratory Markers: A Case Study of 2019 Outbreak at District Shangla, KP, Pakistan. African Health Sciences.2022 Apr; 22(1): 521-31. doi: 10.4314/ahs.v22i1.61.

[5] Castilho BM, Silva MT, Freitas AR, Fulone I, Lopes LC. Factors Associated with Thrombocytopenia in Patients with Dengue Fever: A Retrospective Cohort Study. British Medical Journal Open.2020 Sep; 10(9): e035120. doi: 10.1136/bmjopen-2019-035120.

[6] Wayez A, Zafar L, Aijaz M, Afroz N. Study of Platelet Indices in Dengue Fever with Thrombocytopenia and Correlation of Immature Platelet Fraction (IPF) with Platelet Recovery. Archives of Hematology Research Articles and Reviews.2020 Jan; 5(1): 001-5. doi: 10.173 52/ ahcrr.000021.

[7] Tulara NK. Dengue Fever and Thrombocytopenia–A Prospective Observational Study at Tertiary Care Centre. Eastern Journal of Medical Sciences.2019; 4(1): 45-8. doi: 10.32677/EJMS.2019.v04.i01.009.

[8] Paliwal HP, Mittal C, Kalia A, Jain M, Choudhary S, Rijhwani P *et al*. Correlation of Vitamin B12 Levels with Degree of Thrombocytopenia in Dengue Patients. Journal of Mahatma Gandhi University of Medical Sciences and Technology.2022 Aug; 7(1): 1-3. doi: 10. 5 005/jp-journals-10057-0190.

[9] Butola LK, Kute PK, Anjankar A, Dhok A, Gusain N, Vagga A. Vitamin B12-Do You Know Everything. Journal of Evolution of Medical and Dental Sciences. 2020 Oct; 9(42): 3139-47. doi: 10.14260/ jemds/ 202 0/ 688.

[10] Khazali AS, Hadrawi WH, Ibrahim F, Othman S, Rashid NN. Thrombocytopenia in Dengue Infection: Mechanisms and A Potential Application. Expert Reviews in Molecular Medicine. 2024 Jan; 26: e26. doi: 10.1017/erm.2024.18.

[11] Gupta P, Chaurasia AK, Mall AP, Mathur MK, Gautam AK. Correlation of Vitamin B12 Levels with Clinical Manifestations, Thrombocytopenia, Hospital Stay, and Platelet Recovery in Dengue Patients. SN Comprehensive Clinical Medicine.2024 Aug; 6(1): 88. doi: 10.1007/s42399-024-01717-y.

[12] Lyon P, Strippoli V, Fang B, Cimmino L. B Vitamins and One-Carbon Metabolism: Implications in Human Health and Disease. Nutrients.2020 Sep; 12(9): 2867. doi: 10.3390/nu12092867.

[13] Tahir MN, Athar H, Shahid M, Umer R. Frequency of Vitamin B12 Deficiency in Patients of Pancytopenia. Pakistan Journal of Medical & Health Sciences. 2022; 16(12): 40-. doi: 10.53350/pjmhs2022161240.

[14] Ramalingaiah MT, Mood JK, Narayanashetty S, Bhuvaneshappa RM. The Study of Clinical Profile and Vitamin B12 in Dengue Fever Patients. Asian Journal of Medical Sciences.2021 Jul; 12(7): 47-51. doi: 10.3126/ ajms.v12i8.36311.

[15] Sagar V, Kumar M, Rawat R, Kumar P, Kumar G, Yadav SK. To Determine the Correlation of Severity of Thrombocytopenia, with Vitamin B12 Deficiency in Patients of Dengue Fever. International Journal of Health Sciences.2022(II): 5579-90. doi: 10.5373 0/ijhs .v6nS2.6379.

[16] Wagh TI, Mahajan SD, Mahajan SV, Patil JS. The Role of Vitamin B12 in the Management of Dengue Fever. International Journal of Progressive Research in Engineering Management and Science.2023 Oct; 3(10) : 209-211.

[17] Kansara YK and Sharma E. To Study the Correlation between Vitamin B12 Level and Thrombocytopenia in Dengue Fever and Malaria. East African Scholars Journal of Medical Sciences.2022; 5(2): 29-34. doi: 10 .36349/easms.2022.v05i02.001.

[18] Khan MN. Thrombocytopenia in Dengue Fever and Its Correlation with Serum Vitamin B12 Level. Liaquat National Journal of Primary Care. 2024; 6(2): 108-112.

[19] Jing Q, Wang M. Dengue Epidemiology. Global Health Journal.2019 Jun; 3(2): 37-45. doi: 10.1016/ j.glohj .201 9.06.002.

[20] Kukkar A, Kumar Y, Sandhu JK, Kaur M, Walia TS, Amoon M. Dengue Fog: A Fog Computing-Enabled Weighted Random Forest-Based Smart Health Monitoring System for Automatic Dengue Prediction. Diagnostics.2024 Mar; 14(6): 624. doi:10.3390/diagn ostics14060624.

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A Comparative Study of Perioperative Blood Loss in Monopolar Versus Bipolar Transurethral Resection of the Prostate: Quasi Experimental Study

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ABSTRACT

Transurethral Resection of the Prostate (TURP) is frequently performed for Benign Prostatic Hyperplasia (BPH), and the choice between monopolar and bipolar diathermy influences blood loss. Minimizing blood loss is crucial for reducing complications and improving recovery, with bipolar diathermy generally offering better hemostasis than monopolar diathermy. **Objective:** To compare perioperative blood loss in monopolar versus bipolar transurethral resection for benign prostatic hyperplasia. **Methods:** Quasi experimental study was conducted at the Department of Urology and Renal Transplantation, DHQ Hospital Gujranwala, from December 11, 2018, to June 11, 2019. Patients were assigned to either Group A, which received monopolar diathermy, or Group B, which received bipolar diathermy, using convenience sampling technique. Each group comprised 40 patients. Hematocrit levels were assessed 24 hours' post-surgery; hematocrit, the proportion of blood volume occupied by red blood cells, serves as an indirect measure of blood loss. Blood loss during surgery was estimated by comparing pre-operative and post-operative hematocrit readings, and the data were analyzed using SPSS version 23. **Results:** Perioperative blood loss was significantly higher in patients who underwent monopolar diathermy compared to those treated with bipolar diathermy (monopolar: 325.22 ml vs. bipolar: 240.0 ml, p-value = 0.0001). Similar findings were observed when stratifying by age and prostate size, indicating that bipolar TURP consistently resulted in less perioperative blood loss. **Conclusions:** A significant reduction in perioperative blood loss with bipolar TURP compared to monopolar TURP in BPH patients. Reduction is clinically relevant, as it may lead to lower morbidity and improved recovery times.

INTRODUCTION

BPH, also known as benign prostatic hyperplasia, affects elderly men and causes lower urinary tract symptoms due to increase in smooth muscle and epithelial cells in the urinary tract [1, 2]. Men aged 40–50 have a 20% increased risk of developing BPH, men aged 50–60 a 50% increased risk, and men aged 80+ have a 90% increased risk [3]. Goal of therapy is around three features: eradicate the LUTS, hinder disease development, and to decrease complications. Surveillance, medication therapy, and surgical management are all viable options for treating BPH [4]. Moderate to severe LUTS and individuals who have acquired problems owing to BPH are evaluated for surgical treatment [5]. In view of long-term findings from randomized control studies, transurethral monopolar resection of the prostate has become the gold standard for the surgical care of BPH. The diathermy unit is used endoscopically to remove the inner prostate gland [6]. Retrograde ejaculation, transurethral resection syndrome, peri- and post-operative bleeding, erectile dysfunction and urinary incontinence are among complications that might arise from this procedure despite its usefulness in enhancing urine flow rate, symptom score, and other

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metrics [7]. Recently, several minimally invasive techniques have been developed such as photosensitive vaporization, holmium laser enucleation of the prostate, and plasma kinetic bipolar loop resection. These methods seek to minimize the dangers linked to TURP and, although similar to monopolar techniques, they differ in their rates of complications [4]. In the technique called bipolar resection of the prostate gland, a specific resectoscope loop is utilized. This loop comprises both active and return electrodes, and the pattern of current flow that results from its use mitigates the potentially damaging effects of continuous current flow [8]. Normal saline is used as the irrigation fluid in bipolar TURP, offering potential benefits such as reducing TUR syndrome and minimizing blood loss. In contrast, monopolar TURP has historically been associated with severe bleeding, often requiring frequent blood transfusions [9]. Numerous studies have shown that patients undergoing bipolar TURP experience significantly less intraoperative blood loss compared to those receiving monopolar TURP, with findings indicating blood loss of 238.5 ml versus 289.6 ml, and 300.0 ml versus 349.0 ml, respectively [10, 11]. While the introduction highlights the advantages of both techniques, it does not sufficiently emphasize the importance of blood loss as a key outcome measure. Blood loss is critical in surgical procedures, as it directly impacts patient morbidity, recovery time, and overall surgical success; excessive bleeding can lead to complications such as transfusions, longer hospital stays, and heightened postoperative risks [2]. By prioritizing blood loss as an outcome, this study seeks to provide valuable insights into the safety and effectiveness of each technique, which is essential for optimizing surgical strategies and enhancing patient care in the treatment of BPH [7]. Bipolar TURP has gained global popularity as a preferred surgical method for BPH due to its potential for reduced perioperative blood loss. However, a critical gap in the literature exists, as there is currently no data directly comparing blood loss between bipolar and monopolar TURP techniques. This research aims to address this gap by determining whether there is a significant difference in blood loss between the two methods. Establishing this difference could position bipolar TURP as a safer option for patients at higher risk of bleeding with monopolar diathermy. Group A and Group B were selected based on the surgical technique employed: Group A received monopolar diathermy, while Group B received bipolar diathermy. This distinction allowed for a direct comparison of perioperative blood loss between the two techniques, which is critical to understanding the safety and efficacy of each method in the treatment of BPH.

This study hypothesized that bipolar TURP will demonstrate significantly lower perioperative blood loss compared to monopolar TURP.

METHODS

A quasi-experimental study was conducted at the Department of Urology and Renal Transplantation, DHQ Hospital Gujranwala, from December 11, 2018, to June 11, 2019. Following approval from the Institutional Review Board (IRB) (Reference no: Admn.105/GMC), written informed consent was obtained from all patients. Patient confidentiality was ensured by anonymizing all data and securely storing it in password-protected files. Only authorized personnel had access to the data, and the consent form outlined the voluntary nature of participation and the option to withdraw at any time. A total of 80 male patients, age 55-75 years, with diagnosed Benign Prostatic Hyperplasia (BPH) were enrolled using a 95% confidence level and 80% statistical power, based on an anticipated mean blood loss of 238.5 ± 69.43 ml for bipolar TURP and 289.6 ± 89.47 ml for monopolar TURP using OpenEpi [5]. Group A (monopolar diathermy) and Group B (bipolar diathermy) each consisted of 40 patients. Exclusion criteria were patients with diabetes mellitus (FBS >240), chronic liver disease (ALT & AST >40 IU/L), bleeding disorders (PT, INR > 1.5), and uncontrolled hypertension (≥140/90). All patients underwent preoperative assessment, including demographic data, a full blood count, urinalysis, and abdominal and pelvic ultrasound to confirm Benign Prostatic Hyperplasia (BPH) symptoms and prostate size (>30 ml). Hematocrit levels were measured preoperatively and 24 hours' post-surgery to estimate blood loss. The hematocrit-based measurement is an indirect blood loss assessment, calculated by comparing the pre-and post-operative hematocrit values. The study's data collection process was standardized, with all researchers using an approved data collection form to ensure consistency. SPSS version 23.0 was used for data analysis, presenting quantitative data on prostate size, blood loss, age, and duration as means and standard deviations. Preoperative blood loss comparisons between groups were conducted using the T-test, with age, duration of BPH, and prostate volume as additional stratification factors. Statistical significance was defined as a p-value of less than 0.05. Ethical considerations were upheld throughout the study, guided by the four principles of ethics: beneficence (maximizing benefits), non-maleficence (minimizing harm), autonomy (respecting patient choices), and justice (ensuring fair treatment). Handling of missing data and potential confounders was addressed through statistical techniques, although further details on these methodologies could enhance clarity.

RESULTS

Mean age of patients in Group-A and Group-B was 62.42 ± 5.27 and 62.27 ± 4.86 years, respectively. Mean duration of BPH was 3.28 ± 1.66 months for Group A and 3.70 ± 1.84

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months for Group B. Comparison of perioperative blood loss describe in Table 1. Group A showed a mean value of 325.22 (SD = 49.56), and the scores ranged from a minimum of 221 to a maximum of 390. In contrast, Group B had a mean value of 240 (SD= 37.36), with scores ranging from 171 to 307. An independent T-test was used to compare blood loss between the groups. Assumptions of normality and homogeneity of variance were confirmed through Shapiro-Wilk and Levene's tests, respectively. A significant difference between the two groups, yielding a t-value of 8.684 and a p-value of 0.0001.

Table 1: Comparison of Perioperative Blood Loss (ml) in Both Groups

Group	N (Participants)	Mean Blood Loss Mean ± SD	Minimum (mL)	Maximum (mL)
Monopolar Diathermy	40	325.22 ± 49.56	171	307
Bipolar Diathermy	40	240.0 ± 37.36	221	390

Group-A: Monopolar Diathermy; Group-B; Bipolar Diathermy; N= Number of participant's Independent sample t-test= 8.684; p-value= 0.0001

The comparison of perioperative blood loss (in milliliters) between Group A (Monopolar Diathermy) and Group B (Bipolar Diathermy) is presented, stratified by age in Table 2. For the 55-60 years' age group, Group A recorded a mean blood loss of 317.94 ml with a standard deviation of 60.45, while Group B had a mean of 243.12 ml and a standard deviation of 36.01, resulting in a p-value of 0.000. In the 61-65 years' age group, Group A had a mean of 314.14 ml (SD = 50.02) compared to Group B's mean of 222.44 ml (SD = 38.45), with a p-value of 0.001. For the 66-70 years' age group, Group A recorded a mean blood loss of 337.81 ml (SD = 34.64), while Group B had a mean of 247.20 ml (SD = 37.27), again showing a significant difference with a p-value of 0.000. These results indicate that Monopolar Diathermy consistently leads to higher perioperative blood loss across all age groups compared to Bipolar Diathermy.

Table 2: Comparison of Perioperative Blood Loss (mL) in both Groups Stratified for Age

Age Group (Years)	Group A Mean ± SD (mL)	Group B Mean ± SD (mL)	p-Value
55-60	317.94 ± 60.45	243.12 ± 36.01	0.000
61-65	314.14 ± 50.02	222.44 ± 38.45	0.001
66-70	337.81 ± 34.64	247.20 ± 37.27	0.000

In the analysis of perioperative blood loss based on the duration of Benign Prostatic Hyperplasia (BPH), the results in table 3 revealed that for patients with BPH duration of 1-3 months, Group A (Monopolar Diathermy) had a mean blood loss of 325.10 ml (SD = 54.14), while Group B (Bipolar Diathermy) had a mean of 238.00 ml (SD = 36.44), with a significant p-value of 0.000. For patients with BPH duration of 4-6 months, Group A recorded a mean of 325.37 ml (SD = 45.45), compared to Group B's mean of 241.81 ml (SD = 38.99), also showed a significant difference with a p-value of 0.000. These findings indicated that monopolar diathermy results in significantly higher perioperative blood loss across both durations of BPH.

Table 3: Comparison of Perioperative Blood Loss (mL) in both Groups Stratified for duration of BPH

BPH Duration (Months)	Group A Mean ± SD (mL)	Group B Mean ± SD (mL)	p-Value
1-3	325.10 ± 54.14	238.00 ± 36.44	0.000
46	325.37 ± 45.45	241.81 ± 38.99	0.000

The comparison of perioperative blood loss by prostate size further supported these findings in table 4. For patients with prostate sizes of 33-36 mm, Group A had a mean blood loss of 311.66 ml (SD = 51.13), while Group B had a mean of 240.06 ml (SD = 39.02), yielding a significant p-value of 0.000. In the 37-40 mm size category, Group A recorded a mean of 343.77 ml (SD = 35.77) compared to Group B's mean of 241.09 ml (SD = 41.82), with a p-value of 0.000. For prostate sizes of 41-45 mm, Group A showed a mean of 325.00 ml (SD = 53.48) against Group B's mean of 239.00 ml (SD = 34.26), again demonstrating significance with a p-value of 0.000. Overall, these results indicated that monopolar diathermy consistently leads to greater perioperative blood loss across all examined prostate sizes.

Table 4: Comparison of Perioperative Blood Loss (mL) in both Groups Stratified for Prostate Size

Prostate Size (mm)	Group A Mean ± SD (mL)	Group B Mean ± SD (mL)	p-Value
33-36	311.66 ± 51.13	240.06 ± 39.02	0.000
37-40	343.77 ± 35.77	241.09 ± 41.82	0.000
41-45	325.00 ± 53.48	239.00 ± 34.26	0.000

DISCUSSION

One of the results of having LUTS or BPO is BPH. Treatment options include radical prostatectomy, observation, drug treatment, and TURP, a minimally invasive therapy. In the field of BPO, the most effective surgical treatment is considered to be monopolar TURP due to its established track record of long-lasting effectiveness. Despite significant technological advancements over the past few decades, concerns still remain over complications such as transurethral resection syndrome, bleeding, and urethral strictures, which have decreased in frequency but are still considered problematic [12, 13]. Mortality and morbidity after TURP have decreased (0.1% and 11.1%, respectively), according to a prospective, large-scale, multicenter observational study [14]. Recent advancements in bipolar technology have significantly improved TURP outcomes. Notably, bipolar TURP can be performed in normal saline, which addresses a major shortcoming of monopolar TURP. This study found a notable increase in perioperative blood loss in patients receiving monopolar diathermy compared to those treated with bipolar diathermy (monopolar: 325.22

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vs. bipolar: 240.0, p-value=0.000). Stratification by age and prostate size showed similar findings, indicating that bipolar TURP consistently results in significantly less perioperative blood loss [15]. Several studies corroborate these findings, indicating that monopolar TURP results in greater blood loss [16-18]. Tawfik A *et al.*, demonstrated that bipolar TURP results in less intraoperative blood loss compared to monopolar TURP (238.5 ± 69.43 ml versus 309.62 ± 89.47 ml) [10]. Similarly, Nour and colleagues prospective randomized controlled trial showed less blood loss with bipolar TURP (300.0 ± 2.47 ml versus 349.0 ± 43.5 ml) [11]. These findings suggest that bipolar TURP is linked to significantly reduced blood loss during surgery, attributed to improved hemostasis from the bipolar technique's lack of a returning current [17]. Research by Bashir S and Swami G *et al.*, in an isolated blood-perfused pig kidney model indicated that bipolar devices result in significantly less bleeding (15.16 g/min) compared to monopolar devices (20.78 ± 1.52 g/min) [18]. Additionally, in canine prostates, the coagulation zones were statistically deeper with bipolar devices (237.73 ± 20.12 m) compared to monopolar devices (200.75 ± 19.34 m) [19]. This suggested that bipolar technology is more effective at closing major blood vessels. Furthermore, study demonstrated that bipolar cutting produced a deeper coagulation zone (236.25 ± 36.69 m) compared to monopolar cutting (216.00 ± 42.24 m) [20]. The enhanced coagulation ability of bipolar devices may be linked to a unique cutting method and higher initial power levels. In contrast, conventional monopolar devices primarily generate heat to eliminate tissue, with much of the heat lost as steam, resulting in minimal effective tissue coagulation [21]. The power level for cutting with bipolar devices is set at 175 W, while the coagulation setting is 75 W. The plasma effect is crucial for cutting tissue with bipolar devices. High-frequency energy is transmitted from the active pole to the conductive fluid (NaCl 0.9%), which then returns to the return pole. Charged ions in the fluid facilitate the breaking of bonds in organic compounds [21]. The study adds valuable insight into the benefits of bipolar TURP, but it is important to acknowledge several limitations. Sample size may restrict the generalizability of study findings, and potential confounding factors could influence the outcomes. Biases in patient selection or surgical technique may also affect results. Future research should address these limitations and explore how these findings can impact clinical practice, particularly in optimizing surgical approaches for patients with BPH. By highlighting the advantages of bipolar TURP over monopolar techniques, to better inform clinical decision-making and enhance patient care.

CONCLUSIONS

In conclusion, this study demonstrated a significant reduction in perioperative blood loss with bipolar TURP compared to monopolar TURP for patients with Benign Prostatic Hyperplasia (BPH). Bipolar diathermy consistently resulted in less blood loss across various stratifications, including age, duration of BPH, and prostate size. This finding suggested that bipolar TURP is a superior option, offering better hemostasis and potentially leading to lower morbidity, faster recovery, and reduced transfusion needs. Future research should explore long-term outcomes and how bipolar TURP impacts complications in diverse patient populations.

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Authors Contribution

Conceptualization: RNA
Methodology: AM, SI
Formal Analysis: MI
Writing, review and editing: RNA, MZA, SS

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REFERENCES

[1] Gomes CM, Moromizato JK, Brandão TB. Bipolar and monopolar transurethral resection of the prostate are equally effective and safe in this high quality randomized controled trial. International Brazilian Journal of Urology.2020 Nov; 47(1): 145-8. doi: 10.1590/s1677-5538.ibju.2019.0766.1.

[2] Srinivasrao P and Shashidhar M. Bipolar versus monopolar transurethral resection for benign prostatic hypertrophy: a prospective comparative study. International Surgery Journal.2022 Apr; 9(5): 1016-8. doi: 10.18203/2349-2902.isj20221035.

[3] Shao WH, Zheng CF, Ge YC, Chen XR, Zhang BW, Wang GL *et al.* Age-related changes for the predictors of benign prostatic hyperplasia in Chinese men aged 40 years or older. Asian Journal of Andrology.2023 Jan; 25(1): 132-6. doi: 10.4103/aja202223.

[4] Murad L, Bouhadana D, Nguyen DD, Chughtai B, Zorn KC, Bhojani N *et al.* Treating LUTS in men with benign prostatic obstruction: a review article. Drugs & Aging.

DOI: https://doi.org/10.54393/pjhs.v5i12.1863

2023 Sep;40(9): 815-36. doi: 10.1007/s40266-023-01054-0.

[5] Rieken M, de Nunzio C, Cornu JN, Ramasamy R, Misrai V, Malde S *et al.* Medical treatment incidence and persistence after surgical relief of lower urinary tract symptoms suggestive of benign prostatic obstruction: a critical analysis of the literature. European Urology Focus. 2024 May; 10(3): 421-31. doi: 10.1016/j.euf.2023.08.013.

[6] Vanderbruggen W, Brits T, Tilborghs S, Derickx K, De Wachter S. The effect of tranexamic acid on perioperative blood loss in transurethral resection of the prostate: A double-blind, randomized controlled trial. The Prostate.2023 Dec; 83(16): 1584-90. doi: 10 .1002/pros.24616.

[7] Alexander CE, Scullion MM, Omar MI, Yuan Y, Mamoulakis C, N'Dow JM *et al.* Monopolar transurethral resection of the prostate for lower urinary tract symptoms secondary to benign prostatic obstruction: A Cochrane review. Canadian Urological Association Journal. 2020 Dec; 14(12): 423. doi: 10.54 8 9/cuaj.6464.

[8] Coman, R.A., Coman, R.T., Popescu, R.I., Leucuta, D.C., Couți, R., Coman, I. and Al Hajjar, N., 2024. Multimodal Approach Combining Thulium Laser Vaporization, Bipolar Transurethral Resection of the Prostate, and Bipolar Plasma Vaporization versus Bipolar Transurethral Resection of the Prostate: A Matched-Pair Analysis. Journal of Clinical Medicine.2024 Aug; 13(16): 4863. doi: 10.3390/jcm13164863.

[9] Kretzmer L, Damola A, Sandher MJ, Martin W, Ehsanullah SA, Jones A et al. A ten-year observational study of the use of two-way catheters post-transurethral resection of the prostate without the use of post-op irrigation. Journal of Clinical Urology. 2024 May; 17(3): 295-302. doi: 10.1177/20 514158 22 108 1815.

[10] Tawfik A, Soliman M, Aboelenen M. 971 Can transrectal intraprostatic injection of local vasoconstrictor reduces blood loss during transurethral resection of moderately enlarged prostate: A randomized controlled trial. European Urology Supplements. 2016 Mar; 3(15): e971. doi: 10.1016/S1569-9056(16)60972-7.

[11] Nour HH, Elkady HW, Hussein M, Kamal AM, Elganzoury HM, Elbaz AG. Bipolar Transurethral Resection of the Prostate: Perioperative Safety and Functional Outcome: Prospective Randomized Study. World Journal of Medical Sciences. 2014 Jan; 11(4): 439-44.

[12] Boukhlifi Y. Comparison of Bipolar and Monopolar Transurethral Resection of the Prostate, Functional Outcomes and Analysis of Factors Predictive of Complications: A Prospective Study. Scholars Journal of Applied Medical Sciences.2024 Feb; 2: 102-6. doi: 10.36347/sjams. 2024.v12i02.001.

[13] Kervancioglu E, Hasirci E, Salgur F, Cicek Z, Doruk H. Evaluation of the Efficacy and Safety of Bipolar and Monopolar Transurethral Prostate Resection in Geriatric Patients. Nigerian Journal of Clinical Practice. 2024 Aug; 27(8): 1020-6. doi: 10.4103/njcp .njcp_869_23.

[14] Reich O, Gratzke C, Bachmann A, Seitz M, Schlenker B, Hermanek P *et al.* Urology Section of the Bavarian Working Group for Quality Assurance†. Morbidity, mortality and early outcome of transurethral resection of the prostate: a prospective multicenter evaluation of 10,654 patients. The Journal of Urology. 2008 Jul; 180(1): 246-9. doi: 10.1016/j. juro.20 08. 03. 058.

[15] Kim LH and Patel MI. Transurethral resection of bladder tumour (TURBT). Translational andrology and Urology.2020Dec;9(6):3056.doi:10.21037/tau.2019 .09.38.

[16] Pastore AL, Salhi YA, Fuschi A, Petrozza V, Maurizi A, Illiano E *et al.* Prospective randomized study comparing monopolar with bipolar transurethral resection of prostate in benign prostatic obstruction: 36-month outcomes. World Journal of Urology. 2017 Oct; 35(10): 1595-601. doi: 10.1007/s00345-017-2023-7.

[17] Sharma K and Kumar D. Ligation versus bipolar diathermy for hemostasis in tonsillectomy: a comparative study. Indian Journal of Otolaryngology and Head & Neck Surgery.2011 Jan; 63: 15-9. doi: 10.10 07/s12070-010-0094-5.

[18] Bashir S and Swami G. Comparative Study of Bipolar Electrocautery Versus Silk Ligation for Hemostasis During Tonsillectomy. Indian Journal of Otolaryngology and Head & Neck Surgery.2023 Sep; 75(3): 2025-8. doi: 10.1007/s12070-023-03778-2.

[19] Huang X, Wang XH, Wang HP, Qu LJ. Comparison of the microvessel diameter of hyperplastic prostate and the coagulation depth achieved with mono-and bipolar transurethral resection of the prostate A pilot study on hemostatic capability. Scandinavian Journal of Urology and Nephrology.2008 Jan; 42(3): 265-8. doi: 10.1080/00365590701702168.

[20]Lumen N, Wang Z, Waterschoot M, Tailly T, Turchi B, Verla W. Robot-assisted T-plasty for recalcitrant bladder neck stenosis: description of technique and initial results. Minerva Urology and Nephrology. 2024 Oct. doi: 10.23736/S2724-6051.24.05872-5.

[21] Castellani, D., Tramanzoli, P., Chiacchio, G., Cormio, A., Rubino, A., Nedbal, C., *et al.* Reoperation Rate for Residual/Regrowth Adenoma Following Transurethral Interventions for Benign Prostatic Enlargement:

DOI: https://doi.org/10.54393/pjhs.v5i12.1863

Results from a Systematic Review and Meta-Analysis of Comparative Randomized Studies. Journal of Endourology. 2024 Jun; 38(6): 605-628. doi: 10.1089/end.2023.0766.

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Prenatal Detection of Placenta Accreta: A Comparison of Doppler Ultrasound and MRI

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ABSTRACT

Placenta accreta is a severe maternal complication where the placenta abnormally attaches to the uterine wall, causing significant maternal and neonatal morbidity. **Objectives:** To compare the effectiveness of Doppler ultrasound and magnetic resonance imaging in the early detection of placenta accreta and their impact on maternal and fetal outcomes. **Methods:** Using purposive sampling, 150 high-risk pregnant women were screened with Colour Doppler Ultrasonography and magnetic resonance imaging. Findings were confirmed at delivery. Maternal outcomes included blood transfusion, emergency hysterectomy, intensive care unit admission, and hospital stay. Fetal outcomes included preterm birth, low birth weight, and neonatal intensive care unit, admission. Sensitivity, specificity, positive, and negative predictive values were calculated. Mc-Nemar's test compared modalities. **Results:** Of 150 patients, 74 had placenta accreta. Colour-Doppler ultrasonography had a sensitivity of 86.5% and specificity of 89.1%, diagnosing 64 cases. Magnetic resonance imaging showed 79.7% sensitivity and 83.3% specificity, identifying 59 cases. Colour-Doppler ultrasonography was linked to fewer emergency hysterectomies (p=0.032) and shorter intensive care unit stays (p=0.045). Preterm birth (p=0.028) and low birth weight (p=0.037) were higher in placenta accreta cases diagnosed with antepartum, though neonatal intensive care unit, admissions did not differ (p=0.451). Magnetic resonance imaging helped in inconclusive Colour-Doppler ultrasonography cases. **Conclusions:** It was concluded that Colour-Doppler ultrasonography is more effective than magnetic resonance imaging for early Placenta accreta detection, offering better diagnostic accuracy and improved outcomes. The findings highlight its value in the clinical management of high-risk pregnancies.

INTRODUCTION

A pregnancy issue known as placenta accreta (PA) arises when the chorionic villi intrude into the myometrium. It is linked to severe peripartum hemorrhage-related maternal morbidity and mortality [1]. The two primary risk factors for PA are placenta previa and a history of caesarean birth; the prevalence of PA rises exponentially with the number of caesarean sections performed [2, 3]. It has been demonstrated that if PA is diagnosed before delivery, morbidity can be considerably decreased [4, 5]. Using magnetic resonance imaging (MRI) or ultrasound as a means of systematic screening and diagnosis of PA would enable high-risk pregnant women to be referred to tertiary hospitals that have specialized multidisciplinary teams with experience managing pregnancies affected by PA [6]. Additionally, thromboembolism and hospitalisation to the critical care unit are risks that are higher for patients with PA. It has been estimated that 7% of maternal deaths are related to PA [7]. Utilising methods like magnetic resonance imaging (MRI) and ultrasound to check the foetus can help prevent issues connected to PA by facilitating safe delivery and surgical planning [8]. One useful tool for diagnosing PA is ultrasound. Pregnancy-related PA monitoring and prompt identification of placental invasion are made possible by the non-invasive ultrasound examination, which can be done multiple times. The placenta's posterior positioning and the patient's body

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composition can both have an impact on the ultrasound examiner's performance, which is dependent on their prior experience [9, 10]. MRI can be used in place of or in addition to ultrasound for the diagnosis and monitoring of PA [11] to get around some of the limitations of ultrasound. With MRI, permanent digital images can be acquired without the real-time execution issues that are usually present with ultrasound. Still, there are ongoing worries about fetal safety, and a contrast medium might be needed. Despite these reservations, MRI has become more often utilized in prenatal care for patients with PA, especially to assess the depth of invasion and disease extent [12]. Although PA has been diagnosed in utero using both MRI and ultrasound, the precision of these two imaging modalities is yet unknown. There are still several unsolved questions concerning the use of MRI and ultrasonography in PA patients. As an example, reports on their diagnostic accuracy vary [13]. The use of MRI or ultrasound in PA has since been the subject of reports from several different research groups [14]. The woman is more likely to experience potentially fatal bleeding and surgical complications, such as damage to the ureters and bladder, if placenta accreta is not diagnosed during pregnancy [15].

This study aims to assess the early diagnosis of PA using MRI and ultrasonography and its impact on fetal and maternal outcomes.

METHODS

This cross-sectional study was carried out over one year, from January 2023 to December 2023, and enrolled a total of 150 pregnant women considered at high clinical risk for placenta accreta. The study was taken place at Social Security Teaching Hospital Lahore after getting approval from the Institutional Review Board (Reference number: 16/2022). The sample size was calculated to achieve adequate power for comparing the diagnostic sensitivity and specificity of prenatal Doppler ultrasound and MRI. The sample size was calculated using the following formula for diagnostic test studies: $n=Z2a/2\times P\times(1-P)/d2$. Where: $Z\alpha/2$ the critical value corresponding to the desired confidence level (1.96 for 95% confidence), P is the expected prevalence or sensitivity of the diagnostic test (assumed to be 90% for Doppler ultrasound and MRI based on previous studies) [16], d is the desired precision or margin of error (set at 5%). The calculation yielded a minimum sample size of approximately 138 participants. To account for potential dropouts and incomplete data, the sample size was increased to 150 participants, in line with dropout rates of 5–8% reported in similar studies [17]. Inclusion criteria comprised of pregnant women between 20 and 36 weeks of gestation, identified as high-risk for placenta accreta based on clinical factors such as prior cesarean sections, uterine surgeries, or presence of placenta previa on ultrasound. Women with contraindications to MRI or pregnancies with severe fetal anomalies were excluded. Each participant after taking a written informed consent for the inclusion in study, underwent both Doppler ultrasound and MRI for prenatal screening. Doppler ultrasound was performed using a Philips Enterprise Platform for Integrated Quality (EPIQ) 7 system, employing grayscale imaging and colour Doppler to assess placental anatomy, vascularity, and myometrial thickness. MRI scans were performed using a 1.5-T MRI scanner (Philips Ingenia), acquiring T2-weighted images in sagittal, coronal, and axial planes, with a focus on detecting abnormal placental invasion. MRI sequences were interpreted by a radiologist with 10 years of experience. Maternal outcomes, including blood transfusion requirements, emergency hysterectomy, intensive care unit (ICU) admission, and duration of postpartum stay, were recorded. Fetal outcomes such as preterm birth, low birth weight, and neonatal intensive care unit (NICU) admission were also documented. Placenta accreta, increta, or percreta were confirmed at delivery and/or through histopathological examination. SPSS version 25.0 was used for data analysis. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for Doppler ultrasound and MRI and compared using the McNemar test. Potential confounders, including gestational age, parity, and prior uterine surgeries, were controlled through multivariate logistic regression. Maternal and fetal outcomes were analyzed using independent t-tests for continuous variables and chi-square tests for categorical variables, ensuring that assumptions for the McNemar test were met.

RESULTS

The diagnostic performance of Doppler ultrasound and MRI is summarized. Doppler ultrasound demonstrated a sensitivity of 86.5% and specificity of 89.1%, correctly identifying 64 of the 74 confirmed cases of placenta accreta. MRI, in comparison, showed a sensitivity of 79.7% and specificity of 83.3%, accurately diagnosing 59 cases. Doppler ultrasound had 10 false-negative and 8 false-positive cases, whereas MRI had 15 false-negative and 13 false-positive cases. P-values for the comparison of sensitivity (p=0.041) and specificity (p=0.036), along with 95% confidence intervals to enhance interpretability (Table 1).

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Table 1: Diagnostic Performance Metrics of Doppler Ultrasound and MRI

Diagnostic Modality	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	True Positives (n)	True Negatives (n)	False Positives (n)	False Negatives (n)	p-Value	95% CI (Sensitivity, Specificity)
Doppler Ultrasound	86.5	89.1	88.2	87.5	64	68	8	10	0.041	(80.2–91.7, 83.7–93.2)
MRI	79.7	83.3	81.9	81.2	59	63	13	15	0.036	(72.3–85.4, 77.0–89.0)

Maternal outcomes showed significant differences between cases diagnosed via Doppler ultrasound and MRI. Doppler ultrasound was associated with a lower incidence of emergency hysterectomy (12 cases vs. 19 cases in the MRI group; p=0.032) and shorter ICU stays (mean of 3.5 days vs. 5.1 days; p=0.045). There was no significant difference in blood transfusion rates (p=0.283) (Table 2).

Table 2: Maternal Outcomes Based on Diagnostic Modality

Outcome	Doppler Ultrasound (n=64)	MRI (n=59)	p-Value
Emergency Hysterectomy	12	19	0.032
Average ICU Stay (Days)	3.5 ± 1.2	5.1 ± 1.6	0.045
Blood Transfusion (≥2 units)	24	26	0.283

Preterm births were more frequent in cases diagnosed with antepartum (p=0.028), with 38 cases in the Doppler ultrasound group and 42 in the MRI group. Similarly, low birth weight infants (<2,500 grams) were more common in the Doppler ultrasound group (p=0.037). NICU admission rates did not significantly differ between the two groups (p=0.451) (Table 3).

Table 3: Fetal Outcomes Based on Diagnostic Modality

Fetal Outcome	Doppler Ultrasound (n=64)	MRI (n=59)	p-Value
Preterm Birth (<37 Weeks)	38	42	0.028
Low Birth Weight (<2,500 g)	36	33	0.037
NICU Admission	29	27	0.451

DISCUSSION

In this study, we compared the diagnostic efficacy of Doppler ultrasound and MRI for the early detection of PA and its impact on maternal and fetal outcomes. Our findings highlight the superior sensitivity and specificity of Doppler ultrasound, underscoring its role as the primary diagnostic tool for PA. Beyond numerical comparisons, Doppler ultrasound offers advantages in terms of accessibility, cost-effectiveness, and ease of use in routine clinical settings, particularly in resource-limited environments. It also showed reduced maternal complications such as emergency hysterectomy and ICU stays. These results align with prior research that highlights the risk factors associated with diagnosing PA using imaging modalities and the importance of early detection to improve clinical outcomes [18]. The values of sensitivity and specificity found in our study for both modalities are slightly lower than those reported in earlier research. However, due to the risks associated with gadolinium in pregnancy, particularly nephrogenic systemic fibrosis, its use remains controversial. Our findings reinforce the importance of optimizing non-contrast MRI techniques to minimize fetal risks while maintaining diagnostic accuracy. The presence of low-signal-intensity intra-placental bands on MRI, a key marker of abnormal placentation, was detected in 78% of true-positive cases in our study, similar to findings from previous research [19, 20]. These bands likely represent areas of placental hemorrhage and infarction, as suggested by histologic examination [21, 22]. Quantifying the association between these MRI findings and histological outcomes could help refine diagnostic criteria in future studies. Despite the overall effectiveness of Doppler ultrasound, our study identified 10 false-negative cases and 8 false-positive cases with ultrasound, compared to 15 false-negative and 13 false-positive cases with MRI. The false-negative cases in both modalities were often attributed to posterior placentas or placentas interpreted as mature but later found to have abnormal placentation upon histologic examination. This highlights the need for tailored protocols for posterior placentas, potentially incorporating both modalities to improve diagnostic accuracy. Future research should focus on refining imaging protocols for Doppler ultrasound to minimize false-negative cases and on developing cost-effective strategies for integrating MRI in high-risk or complex cases. Studies examining the economic burden of PA diagnosis and management could guide resource allocation, especially in low- and middle-income countries. This approach allows for a more reliable comparison of diagnostic accuracy between the two modalities. However, our study has some limitations, which include a small sample size and potential bias due to the retrospective analysis. The sample was restricted to the patients who undertook both MRI and ultrasound, which may not fully reflect the broader population of high-risk pregnancies. Additionally, the prior knowledge of imaging results might have influenced subsequent interpretations. Further prospective, multicenter studies with relatively large sample sizes and people from different regions are suggested to validate our findings. Integrating subgroup analyses based on placental location, gestational age, and other confounding factors could provide deeper insights into diagnostic performance.

CONCLUSIONS

It was concluded that Doppler ultrasound is a better modality for early detection of PA as compared with MRI, having more sensitivity and specificity. It also

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demonstrated superior maternal and fetal outcomes, making it the preferred first-line diagnostic tool in most clinical scenarios. Given its accessibility and cost-effectiveness, Doppler ultrasound should be prioritized for routine screening of high-risk pregnancies. MRI, while less sensitive, remains a valuable adjunct, particularly in complex cases or when ultrasound findings are inconclusive. Prospective trials are also warranted to evaluate the long-term clinical implications of early PA detection on maternal and fetal health.

Authors Contribution

Conceptualization: ZEH
Methodology: ZEH, HN, MA, UA, SJ
Formal analysis: ZEH
Writing review and editing: RAA

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Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Arakaza A, Zou L, Zhu J. Placenta Accreta Spectrum Diagnosis Challenges and Controversies in Current Obstetrics: A Review. International Journal of Women's Health. 2023 Dec; 15: 635-54. doi: 10.2147/IJWH.S395271.

[2] Tinari S, Buca D, Cali G, Timor-Tritsch I, Palacios-Jaraquemada J, Rizzo G *et al.* Risk factors, histopathology and diagnostic accuracy in posterior placenta accreta spectrum disorders: systematic review and meta-analysis. Ultrasound in obstetrics and Gynaecology. 2021 Jun; 57(6): 903-9. doi: 10.1002/uog.22183.

[3] Ogawa K, Jwa SC, Morisaki N, Sago H. Risk Factors and Clinical Outcomes for Placenta Accreta Spectrum with or Without Placenta Previa. Archives of Gynaecology and Obstetrics. 2022 Mar; 305(3): 607-15. doi: 10.1007/s00404-021-06189-2.

[4] Fonseca A and de Campos DA. Maternal Morbidity and Mortality Due to Placenta Accreta Spectrum Disorders. Best Practice and Research Clinical Obstetrics and Gynaecology. 2021 Apr; 72: 84-91. doi: 10.1016/j.bpobgyn.2020.07.011.

[5] Morlando M and Collins S. Placenta Accreta Spectrum Disorders: Challenges, Risks, and Management Strategies. International Journal of Women's Health. 2020 Nov; 12: 1033-45. doi: 10.2147/IJWH.S224191.

[6] Cheng C, Ramsey PS, Byrne JJ, Katabathina VS, Ireland KE, Munoz JL. Factors Limiting Magnetic Resonance Imaging Diagnosis of Placenta Accreta Spectrum. American Journal of Perinatology. 2023 Oct; 40(13): 1398-405. doi: 10.1055/a-2099-4542.

[7] De Oliveira Carniello M, Oliveira Brito LG, Sarian LO, Bennini JR. Diagnosis of Placenta Accreta Spectrum in High-Risk Women Using Ultrasonography or Magnetic Resonance Imaging: Systematic Review and Meta-Analysis. Ultrasound in Obstetrics and Gynaecology. 2022 Apr; 59(4): 428-36. doi: 10.1002/uog.24861.

[8] Oliveira GF, Diego RP, Oliveira AC. Applicability of the Magnetic Resonance Technique during the Gestational Period: a narrative review. Brazilian Journal of Clinical Medicine and Review. 2023 Jan; 1(1): 7-23. doi: 10.52600/2965-0968.bjcmr.2023.1.1.7-23.

[9] Hernandez-Andrade E, Huntley ES, Bartal MF, Soto-Torres EE, Tirosh D, Jaiman S *et al.* Doppler Evaluation of Normal and Abnormal Placenta. Ultrasound in Obstetrics and Gynaecology. 2022 Jul; 60(1): 28-41. doi: 10.1002/uog.24816.

[10] Abinader RR, Macdisi N, El Moudden I, Abuhamad A. First-Trimester Ultrasound Diagnostic Features of Placenta Accreta Spectrum in Low-Implantation Pregnancy. Ultrasound in Obstetrics and Gynaecology. 2022 Apr; 59(4): 457-64. doi: 10.1002/uog.24828.

[11] Sun X, Ren R, Yu X, Peng F, Gao X. Application of Colour Doppler Ultrasound Combined with Magnetic Resonance Imaging in Placenta Accreta. Scanning. 2022 July; 2022(1): 1050029. doi: 10.1155/2022/1050029.

[12] Kapoor H, Hanaoka M, Dawkins A, Khurana A. Review of MRI Imaging for Placenta Accreta Spectrum: Pathophysiologic Insights, Imaging Signs, and Recent Developments. Placenta. 2021 Jan; 104: 31-9. doi: 10.1016/j.placenta.2020.11.004.

[13] Ishibashi H, Miyamoto M, Shinmoto H, Soga S, Matsuura H, Kakimoto S *et al.* The use of magnetic resonance imaging to predict placenta previa with placenta accreta spectrum. Acta Obstetricia et Gynecologica Scandinavica. 2020 Dec;99(12):1657-65. doi: 10.1111/aogs.13937.

[14] Faralli I, Del Negro V, Chinè A, Aleksa N, Ciminello E, Piccioni MG. Placenta Accreta Spectrum (PAS) Disorder: Ultrasound Versus Magnetic Resonance Imaging. Diagnostics. 2022 Nov; 12(11): 2769. doi: 10.3390/diagnostics12112769.

[15] Guo P, Wu Y, Yuan X, Wan Z. Clinical Diagnostic Value and Analysis of MRI Combined with Ultrasound in

DOI: https://doi.org/10.54393/pjhs.v5i12.2445

Prenatal Pernicious Placenta Previa with Placenta Accreta. Annals of Palliative Medicine. 2021 Jun; 10(6): 6753759-6759. doi: 10.21037/apm-21-1285.

[16] Inayat K, Saifullah S, Nelofer T, Jadoon H, Danish N, Ali N. Evaluating the Effectiveness of Various Prenatal Screening Methods and Diagnostic Tools for Early Detection of Placenta Accreta and Their Impact On Maternal and Fetal Outcomes. Health Affairs. 2024; 12(4).

[17] Barzilay E, Brandt B, Gilboa Y, Kassif E, Achiron R, Raviv-Zilka L *et al*. Comparative Analysis of Ultrasound and MRI in the Diagnosis of Placenta Accreta Spectrum. The Journal of Maternal-Fetal and Neonatal Medicine. 2022 Nov; 35(21): 4056-9. doi: 10.1080/14767058.2020.1846699.

[18] Hong S, Le Y, Lio KU, Zhang T, Zhang Y, Zhang N. Performance Comparison of Ultrasonography and Magnetic Resonance Imaging in Their Diagnostic Accuracy of Placenta Accreta Spectrum Disorders: A Systematic Review and Meta-Analysis. Insights into Imaging. 2022 Mar; 13(1): 50. doi: 10.1186/s13244-022-01192-w.

[19] Abdel-Aziz S, El-Goly NA, Maged AM, Bassiouny N, El-Demiry N, Shamel A. Diagnostic Accuracy of Magnetic Resonance Imaging in the Diagnosis of Placenta Accreta Spectrum: A Systematic Review and Meta-analysis. Maternal-Fetal Medicine. 2023 Jan: 10-97. doi: 10.1097/FM9.0000000000000241.

[20] Srisajjakul S, Prapaisilp P, Bangchokdee S. Magnetic Resonance Imaging of Placenta Accreta Spectrum: A Step-By-Step Approach. Korean Journal of Radiology. 2020 Dec; 22(2): 198. doi: 10.3348/kjr.2020.0580.

[21] Romeo V, Verde F, Sarno L, Migliorini S, Petretta M, Mainenti PP *et al.* Prediction of Placenta Accreta Spectrum in Patients with Placenta Previa Using Clinical Risk Factors, Ultrasound and Magnetic Resonance Imaging Findings. La Radiologia Medica. 2021 Sep; 126(9): 1216-25. doi: 10.1007/s11547-021-01348-6

[22] Araujo Júnior E, Caldas JV, Sun SY, Castro PT, Passos JP, Werner H. Placenta Acrreta Spectrum First Trimester, 2D and 3D Ultrasound, and Magnetic Resonance Imaging Findings. Journal of Clinical Ultrasound. 2024 Mar; 52(3): 321-30. doi: 10.1002/jcu.23627.

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Original Article

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Efficacy of Collagen Resorbable Membrane after Surgical Extraction of Impacted Mandibular Third Molar

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ABSTRACT

Impacted teeth, particularly mandibular third molars, can cause complications like pain, infection, and periodontal issues in adjacent teeth. Surgical management strategies, including the use of collagen-resorbable membranes, may improve healing and minimize postoperative complications. **Objectives:** To evaluate the effectiveness of a collagen-resorbable membrane following surgical extraction of impacted mandibular third molars, focusing on pain severity, bone status, and periodontal ligament status adjacent to the second molar. **Methods:** The quasi-experimental study utilized a non-probability sampling technique for 6 months. Patients were equally divided into three groups: A (primary closure), B (secondary closure), and C (collagen membrane-based primary closure). Pain severity, bone status, and periodontal ligament status adjacent to the second molar were evaluated clinically and via post-operative radiographs postoperatively at the 2nd, 4th, 6th, and 12th weeks. **Results:** The study involved participants with an average age of 28.51 ± 7.53 years and an unequal gender distribution across all groups. Initially, Group C experienced higher moderate to severe pain levels. Group A had the longest surgery duration at 41.89 ± 14.10 minutes. By the second week of follow-up, pain significantly decreased in all groups, with no significant differences between them. By the fourth and sixth weeks, pain levels continued to decrease, with only mild pain observed in one patient each in Groups B and C. **Conclusions:**. There is no evidence to suggest that collagen resorbable membrane it is more effective than primary or secondary closure techniques

INTRODUCTION

Third molars typically emerge between 17 and 21 years of age [1, 2]. When they're obstructed by adjacent structures, they become impacted. Around 73% of European young adults are affected and this is a common developmental issue [3]. Impacted third molars often result from inadequate space in the mandible. Surgery to remove them can lead to various complications, including nerve damage, dry sockets, pain, swelling, and infection [4]. After extraction, the alveolar socket undergoes natural resorption and remodeling, reducing its size. Techniques like socket preservation and guided tissue regeneration aim to mitigate this process, using resorbable membranes to prevent unwanted tissue growth [5, 6]. Membranes, leveraging their mechanical and physiological properties, facilitate optimal bony healing by preventing soft tissue ingress in extraction sockets. Collagen, pivotal in wound healing, imbues membranes with guiding, chemotactic, and hemostatic properties, while resisting masticatory forces [7]. Kilinc et al., found that post-surgical placement of resorbable membranes after impacted lower third molar

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extraction could enhance attachment levels, probing depths, and bone fill of adjacent molars [8]. Guided tissue regeneration, a technique developed to address intraosseous defects, employs biocompatible membranes—resorbable or non-resorbable—as barriers to epithelial migration, promoting periodontal tissue repair [9]. This technique is particularly effective in managing deep periodontal pockets following surgical extraction of impacted third molars [10]. Wound closure methods in third molar surgery are debated: primary closure involves complete flap closure, while secondary closure leaves a gap for healing. Secondary closure may reduce pain and swelling, but primary closure promotes comfort and healing [11]. However, recent reviews found no significant outcome differences, prompting further research [11]. Partially erupted molars pose risks with primary closure due to flap tension. Collagen membranes aid wound healing by promoting clot stabilization, hemostasis, and fibroblast attraction [7]. Yet, research on their use post-impacted third molar removal primarily focuses on periodontal health and bone regeneration, overlooking postoperative morbidity and wound healing evaluation. Studies on resorbable collagen membrane use post-extraction have shown conflicting results [9]. The application of resorbable collagen membrane following surgical extraction of impacted mesioangular lower third molars enhances bone regeneration, improving attachment levels and bone fill distal to the lower second molar. It reduces the distal probing depth and accelerates recovery.

This study aims to evaluate the effectiveness of collagen membrane placement after surgery for partially impacted mandibular third molars.

METHODS

This quasi-experimental study utilized a non-probability sampling technique after the approval of the synopsis and was conducted at the Department of Oral and Maxillofacial Surgery, Liaquat University of Medical and Health Sciences, Jamshoro/Hyderabad from January 2020 to December 2020. A total of 87 patients were enrolled and sample size was calculated via the Epi-tools online calculator. Participants were further divided into three groups: primary closure (PC) (n=29), secondary closure (SC) (n=29), and collagen membrane-based primary closure (CMBPC) (n=29). The study included participants of both genders aged between 18 and 50 years who required surgical extraction of impacted (mesioangular) mandibular third molars. Exclusion criteria comprised patients with pericoronitis, periapical infections or lesions related to impacted third molars, traumatic occlusion or upper third molars impingement, smokers, alcoholics, and individuals with systemic diseases. The sample size was calculated to be 57 (19 per group) using Open Epi with 80% power and a 95% confidence interval, based on the mean pain score on day 3, which was 3.93 (3.72) for primary closure and 6.72 (2.22) for membrane-based primary closure from a previous study [12]. To further increase the power of the study, we included 87 available cases. Every patient who met the inclusion criteria and gave their written consent was recruited. After getting approval from the Liaquat University of Medical and Health Sciences Ethical Review Committee in Jamshoro, Pakistan (no.LUMHS/REC-819), data were collected. Patients were categorized into three groups: A (primary closure), B (secondary closure), and C (collagen membrane-based primary closure). Data, including age, gender, clinical history, and impaction diagnosis via clinical examination and orthopantomogram, were recorded. Surgery was performed by the principal investigator at the Department of Oral and Maxillofacial Surgery, Liaquat University Hospital, using local anesthesia (2% xylocaine with 1: 100,000 epinephrine). Standard incisions and flap techniques were employed, with tooth sectioning and extraction conducted as needed. Wound closure methods varied by group: Group A received interrupted sutures (3-0 vicryl), Group B underwent secondary closure with flap repositioning and suturing, and Group C received membrane-based primary closure using a resorbable collagen membrane (Lyoplant, USA). Postoperative care included antibiotics, metronidazole, nonsteroidal anti-inflammatory drugs, and mouthwash, with suture removal after 7 days. Luckily no loss to follow up was there. Patient assessment was done by pain, bone, and periodontal ligament (PDL) status distal to the second molar were assessed clinically and via post-operative radiographs at the 2nd, 4th, 6th, and 12th weeks. Pain was measured pre- and post-operatively utilizing the Wong-Baker FACES Pain Rating Scale (0-10). Periodontal status was recorded using a Williams Probe. (1) Using a Michigan "O" probe with Williams markings, the probing depth was determined. Up until a small amount of resistance is encountered, the probe tip is introduced into the gingival sulcus parallel to the tooth's long axis. (2) The gingival margin to the cement-enamel junction at the second molar's distal surface (lingual and labiolingual) was the measurement point for gingival recession. (3) Gingival recession plus probing depth was used to record attachment loss. The bone defect was measured using orthopantomograms (OPGs), with a standardized radiographic calibration technique. Measurements were taken from the crest of the alveolar bone adjacent to the second molar to the deepest point of the surgical defect. This assessment was performed immediately after surgery and at follow-up intervals to monitor bone healing over time. To evaluate the bone state (defect size and fill), measurements from pre- and post-periapical radiographs were taken using a ruler and documented on a preform to show the healing process and bone regeneration. The data were analyzed using SPSS version 20.0, a statistical

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software program. Mean and standard deviation were calculated for age and frequency with percentages for qualitative variables. A one-way ANOVA test was run to compare age, Pocket depth (PD), gingival recession and attachment loss among three interventions and the chi-square/Fisher exact test for pain at various time points. p-values were regarded as statistically significant if they were less than 0.05.

RESULTS

A total 87 number of patients were enrolled which were divided equally into three groups named A, B and C respectively. The mean age of patients in the primary closure group was 27.03 ± 4.66 years, in the secondary closure group it was 30.03 ± 9.24 years, and in the collagen membrane-based primary closure group, it was 28.48 ± 7.92 years. The overall mean age across all groups was 28.51 ± 7.53 years. However, there was no statistically significant difference in the mean age among the patients across the study groups (p=0.321) (Table 1).

Table 1: Descriptive Statistics of the Age of Study Groups (n=87)

Variables	Age (yrs)				p-value*
	n	Mean ± SD	Minimum	Maximum	
Primary Closure	29	27.03 + 4.66 Years	18 Years	40 Years	
Secondary Closure	29	30.03 + 9.24 Years	18 Years	55 Years	0.321
Collagen Membrane -Based Primary Closure	29	28.48 + 7.92 Years	18 Years	47 Years	

*ANOVA test

Pre-operative pain assessment showed no significant differences among groups (p=0.581). In Group A, 4 (13.8%) reported "No Hurt," 10 (34.5%) "Hurts a Little Bit," and 10 (34.5%) "Hurts a Little More." Group C had more participants, 13 (44.8%), in "Hurts a Little More." By the second postoperative week, pain reduced significantly across groups (p=0.400). "No Hurt" was reported by 19 (65.5%) in Group A, 16 (57.1%) in Group B, and 12 (42.9%) in Group C. By the fourth and sixth weeks, nearly all reported "No Hurt," except 1 (3.4%) in Groups B and C (p=0.599). By the twelfth week, all participants were pain-free (p=1.000). (Table 2).

Table 2: Pre and Post-Operative Pain Assessment

Assessments	Study Groups	Levene's Test for Equality of Variances						
		No Hurt	Hurts Little Bit	Hurts Little More	Hurts Even More	Hurts Whole Lot	Total	p-value
Pre-Operative Pain	A	4 (13.8%)	10 (34.5%)	10 (34.5%)	4 (13.8%)	1 (3.4%)	29 (100%)	0.581
	B	4 (13.8%)	8 (27.6%)	9 (31.0%)	6 (20.7%)	2 (6.9%)	29 (100%)	
	C	0	7 (24.1%)	13 (44.8%)	7 (24.1%)	2 (6.9%)	29 (100%)	
Post-Operative Pain 2nd Week	A	19 (65.5%)	10 (34.5%)	0	0	-	29 (100%)	0.400
	B	16 (57.1%)	12 (42.9%)	1 (3.4%)	0	-	29 (100%)	
	C	12 (42.9%)	16 (57.1%)	1 (3.4%)	0	-	29 (100%)	
Post-Operative Pain 4th Week	A	29 (100%)	0	0	0	-	29 (100%)	0.599
	B	28 (96.6%)	1 (3.4%)	0	0	-	29 (100%)	
	C	28 (96.6%)	1 (3.4%)	0	0	-	29 (100%)	
Post-Operative Pain 6th Week	A	29 (100%)	0	0	0	-	29 (100%)	0.599
	B	28 (96.6%)	1 (3.4%)	0	0	-	29 (100%)	
	C	28 (96.6%)	1 (3.4%)	0	0	-	29 (100%)	
Post-Operative Pain 12th Week	A	29 (100%)	0	0	0	-	29 (100%)	1.000
	B	29 (100%)	0	0	0	-	29 (100%)	
	C	29 (100%)	0	0	0	-	29 (100%)	

Further results show the average probing depth was 5.41 ± 1.82 in Group A, 5.41 ± 1.82 in Group B, and 6.17 ± 1.33 in Group C (p=0.157). The mean gingival recession was 3.79 ± 1.83 in Group A, 2.96 ± 1.42 in Group B, and 3.48 ± 1.37 in Group C (p=0.132). Average attachment loss was 9.20 ± 3.02 in Group A, 8.58 ± 2.21 in Group B, and 9.65 ± 2.31 in Group C (p=0.281). However, these findings were statistically insignificant across study groups (Table 3).

Table 3: PDL Status Distal to 2nd Molar According to Study Groups (n=87)

Variables		Statistics		p-value
		n	Mean + SD	
Probing Depth (PD)	Primary Closure	29	05.41 ±1.82	0.157
	Secondary Closure	29	05.62 ± 1.39	
	Collagen Membrane-Based Primary Closure	29	6.17 + 1.33	

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Gingival Recession (GR)	Primary Closure	29	03.79 + 1.83	0.132
	Secondary Closure	29	02.96 + 1.42	
	Collagen Membrane-Based Primary Closure	29	03.48 + 1.37	
Attachment Loss	Primary Closure	29	09.20 + 3.02	0.281
	Secondary Closure	29	08.58 + 2.21	
	Collagen Membrane-Based Primary Closure	29	09.65 + 2.31	

Findings show the mean duration of surgery was 41.89 ± 14.10 minutes in Group A, 36.20 ± 12.07 minutes in Group B, and 31.89 ± 9.00 minutes in Group C, with a significantly lower duration observed in Group C (p=0.008). Surgery duration differed significantly among the groups (p=0.008). The longest mean duration was observed in the Primary Closure group at 41.89 ± 14.10 minutes (range: 18–75 minutes), followed by the Secondary Closure group at 36.20 ± 12.07 minutes (range: 21–60 minutes). The shortest mean duration was in the Collagen Membrane-Based Primary Closure group at 31.89 ± 9.00 minutes (range: 25–50 minutes). (Table 4).

Table 4: Descriptive Statistics of Surgery Duration According to Study Groups (n=87)

Study Groups	Statistics				p-value
	n	Mean ± SD	Minimum	Maximum	
Primary Closure	29	41.89 + 14.10 minutes	18 minutes	75 minutes	0.008
Secondary Closure	29	36.20 + 12.07 minutes	21 minutes	60 minutes	
Collagen Membrane -Based Primary Closure	29	31.89 + 9.00 minutes	25 minutes	50 minutes	

Further findings clearly show the bone defect was early normalized in Group C as compared to Groups A and B, while results were statistically insignificant, p-values were quite insignificant (p=>0.05) (Table 5).

Table 5: Descriptive statistics of post-operative bone defect after immediate post-operative to 12th week according to study groups (n=87)

Post-Operative Bone Defect	Study Groups	Statistics		p-value
		n	Mean ± SD	
Immediately After Surgery	Group A	29	9.62 + 4.78mm	0.419
	Group B	29	18.48 + 4.97mm	
	Group C	29	16.89 + 2.80mm	
After 2nd Week	Group A	29	16.44 + 5.07mm	0.961
	Group B	29	14.58 + 3.60mm	
	Group C	29	14.74 + 2.78mm	
After 4th Week	Group A	29	11.67 + 22.91mm	0.573
	Group B	29	9.50 + 3.79mm	
	Group C	29	5.67 + 2.24mm	
After 6th Week	Group A	29	2.32 + 0.45mm	0.296
	Group B	29	02.11 + 0.32mm	
	Group C	29	01.03 + 0.41mm	
After 12th Week	Group A	29	1.37 + 0.04mm	0.082
	Group B	29	01.39 + 0.09mm	
	Group C	29	0.44 + 0.33 mm	

DISCUSSION

Mandibular third molar (3M) surgery often results in postoperative complications such as pain, swelling, trismus, and periodontal destruction in adjacent second molars [1, 2]. Techniques to categorize tooth impaction commonly consider factors like the degree of impaction, angulation, and the molar's position relative to the anterior boundary of the mandibular ramus [13]. Factors contributing to impaction include crowding, ectopic tooth germ location, extra teeth, hereditary susceptibility, and soft tissue or bone lesions [14, 15]. Impacted third molars are frequently associated with conditions such as pericoronitis, incisor crowding, resorption of adjacent tooth roots, and temporomandibular joint dysfunction [16]. This study observed mean ages for the primary closure group was little higher than secondary closure group with no significant differences across groups (p=0.321). Similarly, gender distribution was comparable across groups (p=0.723). Postoperative assessments of probing depth, gingival recession, and attachment loss also revealed no statistically significant differences). These findings align partially with Camps-Font *et al.* [17], who reported significant gains in clinical attachment level (CAL) and reductions in probing depth, highlighting potential differences in study methodologies, sample characteristics, or follow-up durations. Postoperative pain reductions across all groups, with the collagen membrane-based group showing a slight advantage by the second week, though the differences were not statistically significant (p=0.400). This finding is consistent with Kilinc *et al.* [9], who also observed no significant pain differences among groups over a 7-week follow-up period. The similarity may stem from comparable surgical techniques or pain management protocols. However, Jim-Charm Kim [21] emphasized that collagen membrane placement after third molar extraction effectively reduced early-stage postoperative complications and enhanced gingival and periodontal repair.The difference could be due to variations in membrane properties, surgical skills, or postoperative care strategies. These findings underscore the potential benefits of collagen membranes in managing postoperative pain and promoting soft tissue healing. Surgery duration, was significantly shorter in the collagen membrane group compared to primary and secondary closure methods (p=0.008). The shorter operative time in the collagen membrane group might be attributed to its ease of application and reduced surgical manipulation. Differences in operator experience and procedural protocols could also contribute to this variation. These

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findings align with Aimetti *et al.*[18], who reported significant bone gain with membrane placement, and Sammartino *et al.* [19], who demonstrated effective healing outcomes with collagen membranes combined with platelet-rich plasma.The efficiency of collagen membranes in promoting faster wound healing and reducing surgical complexity is evident from these studies. Periodontal outcomes, with statistically insignificant differences in probing depth, gingival recession, and attachment loss across groups. Korkmaz *et al.* [20] similarly reported no significant changes in periodontal pocket depth around second molars in either primary or secondary closure groups at the three-month follow-up. The lack of significant findings in this study might result from shorter follow-up durations or the absence of advanced adjunctive techniques. However, Aimetti *et al.* [18] and Sammartino *et al.* [19] emphasized significant bone gain and periodontal improvements with membrane-based techniques,suggesting that longer follow-up durations or different patient populations might yield more pronounced differences. Differences in patient oral hygiene, surgical protocols, or membrane properties might also account for the contrasting results.

CONCLUSIONS

While the use of a collagen-resorbable membrane following the surgical extraction of impacted mandibular third molars was associated with reduced severe pain, shorter surgery duration, and improved healing with prevention of periodontal defects, there is no evidence to suggest that it is more effective than primary or secondary closure techniques. The results indicate that the collagen-resorbable membrane offers similar outcomes to traditional closure methods.

Authors Contribution

Conceptualization: RI
Methodology: RI, MO, SKP, TA
Formal analysis: MAS
Writing review and editing: MAC

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Lamichhane NS, Sigdel B, Lamichhane S, Tripathi R, Koirala U, Bajgai DP. Mandibular Third Molar Impaction among Patients Visiting Outpatient Dental Department of a Tertiary Care Centre. Journal of the Nepal Medical Association.2023 Oct; 61(266): 769. doi :10.31729/jnma.8295.

[2] Matzen LH, Schropp L, Spin-Neto R, Wenzel A. Use of Cone Beam Computed Tomography to Assess Significant Imaging Findings Related to Mandibular Third Molar Impaction. Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology.2017 Nov; 124(5): 506-16. doi: 10.1016/j.oooo.2017.07.007.

[3] Juodzbalys G and Daugela P. Mandibular Third Molar Impaction: Review of Literature and a Proposal of a Classification. Journal of Oral and Maxillofacial Research. 2013 Apr; 4(2). doi: 10.5037/jomr.2013.4201.

[4] Chen YW, Chi LY, Lee OK. Revisit Incidence of Complications After Impacted Mandibular Third Molar Extraction: A Nationwide Population-Based Cohort Study. Plos One.2021 Feb; 16(2): e0246625. doi : 10.1371/journal.pone.0246625.

[5] Movaniya PN, Makwana TR, Desai NN, Makwana KG, Patel HB. Efficacy of Collagen Membrane Graft in Intraoral Surgery-An Evaluative Study. Annals of Maxillofacial Surgery.2021 Jan; 11(1): 42-8. doi: 10.4103/ams.ams_192_20.

[6] El Masri M, Shokry M, Attia N, Ramal A. Comparison of PRF Versus Collagen Membrane On Healing of Socket and Bone Formation (Randomized Split Mouth Design). Acta Scientific Dental Sciences.2018; 2: 13-22.

[7] Kim JW, Seong TW, Cho S, Kim SJ. Randomized Controlled Trial On the Effectiveness of Absorbable Collagen Sponge After Extraction of Impacted Mandibular Third Molar: Split-Mouth Design. BioMed Central Oral Health.2020 Dec; 20: 1-9. doi: 10.1186/s12903-020-1063-3.

[8] Kilinc A and Ataol M. Effects of Collagen Membrane On Bone Level and Periodontal Status of Adjacent Tooth After Third Molar Surgery: A Randomized Controlled Trial. Head and Face Medicine.2023 Mar; 19(1): 13. doi: 10.1186/s13005-023-00351-8.

[9] Kokash M, Darwich K, Ataya J. The Effect of Hyaluronic Acid Addition to Collagen in Reducing the Trismus and Swelling After Surgical Extraction of Impacted Lower Third Molars: A Split-Mouth, Randomized Controlled Study.Clinical Oral Investigations.2023 Aug; 27(8): 4659-66. doi: 10.1007/s00784-023-05092-1.

[10] Elsayed SA, Gawish AS, Khalifa A. Management of Periodontal Defect After Mandibular Third Molar Extraction. International Journal of Clinical Oral and Maxillofacial Surgery. 2015; 1(1): 4-10. doi: 10.11648/j.ijcoms.20150101.12.

DOI: https://doi.org/10.54393/pjhs.v5i12.1914

[11] Azab M, Ibrahim S, Li A, Khosravirad A, Carrasco-Labra A, Zeng L *et al.* Efficacy of Secondary Vs Primary Closure Techniques for the Prevention of Postoperative Complications After Impacted Mandibular Third Molar Extractions: A Systematic Review Update and Meta-Analysis. The Journal of the American Dental Association. 2022 Oct; 153(10): 943-56. doi: 10.1016/j.adaj.2022.04.007.

[12] Kilinc A and Ataol M. How Effective Is Collagen Resorbable Membrane Placement After Partially Impacted Mandibular Third Molar Surgery On Postoperative Morbidity? A Prospective Randomized Comparative Study. BioMed Central Oral Health. 2017 Dec; 17: 1-8. doi: 10.1186/s12903-017-0416-z.

[13] Kumari B, Punjabi SK, Mustafa N, Iqbal R, Shams S. Comparison between Modified Triangular Flap and Envelop Flap Techniques for Surgical Removal of Impacted Mandibular Third Molar.Journal of Pharmaceutical Research International.2022 Feb; 34(14A): 58-66. doi: 10.9734/jpri/2022/v34i14A35649.

[14] Panyasakulwong M. Prevalence and Pattern of Impacted Third Molar as Assessed by Panatomic Radiographs in Patients Admitted to Rajavithi Hospital. Journal of The Department of Medical Services. 2022 Dec; 47(4): 92-100.

[15] Braimah RO, Ali-Alsuliman D, Agbaje HO, Alsalah Y, Sharma HK, Alsawas NM. Prevalence, Sociodemographics, and Indications for Extraction of Impacted Mandibular Third Molar in Najran, a Southern Saudi Arabian City. Saudi Journal of Oral Sciences. 2021 May; 8(2): 75-80. doi: 10.4103/sjos.SJOralSci_27_20.

[16] Ramamurthy A, Pradha J, Jeeva S, Jeddy N, Sunitha J, Kumar S. Prevalence of Mandibular Third Molar Impaction and Agenesis: A Radiographic South Indian study. Journal of Indian Academy of Oral Medicine and Radiology.2012 Jul; 24(3): 7. doi: 10.4103/0972-1363.166268.

[17] Camps-Font O, Caro-Bonfill C, Sánchez-Garcés MÀ, Gay-Escoda C. Periodontal Regenerative Therapy for Preventing Bone Defects Distal to Mandibular Second Molars After Surgical Removal of Impacted Third Molars: A Systematic Review and Meta-Analysis of Randomized Clinical Trials. Journal of Oral and Maxillofacial Surgery.2018 Dec; 76(12): 2482-514. doi: 10.1016/j.joms.2018.07.025.

[18] Kumari CB, Ramakrishnan T, Devadoss P, Vijayalakshmi R, Alzahrani KJ, Almasri MA *et al.* Use of Collagen Membrane in the Treatment of Periodontal Defects Distal to Mandibular Second Molars Following Surgical Removal of Impacted Mandibular Third Molars: A Comparative Clinical Study. Biology. 2021 Dec; 10(12): 1348. doi: 10.3390/biology10121348.

[19] Sammartino G, Tia M, Gentile E, Marenzi G, Claudio PP. Platelet-rich plasma and Resorbable Membrane for Prevention of Periodontal Defects After Deeply Impacted Lower Third Molar Extraction. Journal of Oral and Maxillofacial Surgery. 2009 Nov; 67(11): 2369-73. doi: 10.1016/j.joms.2009.04.093.

[20] Korkmaz YT, Mollaoglu N, Ozmeriç N. Does Laterally Rotated Flap Design Influence the Short-Term Periodontal Status of Second Molars and Postoperative Discomfort After Partially Impacted Third Molar Surgery? Journal of Oral and Maxillofacial Surgery. 2015 Jun; 73(6): 1031-41. doi: 10.1016/j.joms.2015.01.005.

[21] Nguyen NT, Le SH, Nguyen BL. The Effect of Autologous Demineralized Dentin Matrix On Postoperative Complications and Wound Healing Following Lower Third Molar Surgery: A Split-Mouth Randomized Clinical Trial. Journal of Dental Sciences. 2024 May. doi: 10.1016/j.jds.2024.04.026

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Effectiveness of Bupivacaine Infiltration in Reducing Postoperative Pain in Patients Undergoing Percutaneous Nephrolithotomy

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ABSTRACT

Percutaneous Nephrolithotomy is a standard way to treat large renal calculi because it is slightly invasive. One big problem with normal percutaneous nephrolithotomy, though, is that patients often have discomfort and pain at the nephrostomy place after the surgery. **Objective:** To evaluate the effectiveness of bupivacaine infiltration in reducing postoperative pain in patients undergoing percutaneous nephrolithotomy. **Methods:** The quasi-study lasted for six months at Liaquat National Hospital in Karachi. A total of 60 patients were recruited as Group A=30 patients (20ml/50mg of 0.25% bupivacaine) and Group B=30 patients (20ml of normal saline). All the patients had percutaneous nephrolithotomy and at the end of the operation; a 12 Fr nephrostomy tube was put in place. All patients were carefully watched, and their pain levels were measured using a visual analogue scale and computed as mean ± SD. **Results:** Group A had a mean age of 39.9 ± 12.9 years, and Group B had a mean age of 39.4 ± 11.2 years. There were 16 men (53.3%) and 14 women (46.7%) in Group A, and 20 men (66.7%) and 10 women (33.3%) in Group B. The average amount of pain after surgery was 2.07 ± 0.78 in Group A and 4.80 ± 0.92 in Group B. The p-value was found to be extremely significant, which means it was 0.0001. **Conclusion:** It was concluded that the postoperative pain score was significantly better in bupivacaine infiltration as compared to placebo in percutaneous nephrolithotomy.

INTRODUCTION

Nephrolithiasis, also known as renal stones, is a urological disorder characterized by the formation of stones within the kidneys due to the crystallization of substances from urine [1]. Crystallization can occur within the urinary system due to either an abundance of stone-forming materials or a lack of chemicals that inhibit stone formation [2]. Notably, bilateral renal stones are linked to life-threatening problems like obstructive uropathy and kidney failure, so it's important to think about any kind of immediate action [3]. Risk factors for these problems include urinary tract obstruction and metabolic disorders.

These past few years, the side with symptoms or more stones has usually had the treatment of choice, which is surgical removal or percutaneous nephrolithotomy (PCNL) [4]. Percutaneous nephrolithotomy (PCNL) is a well-known way to eliminate big, complicated kidney stones. The main goal of medical treatment is to get rid of as many stones as possible with as little harm to the patient as possible [5]. It is less painful for patients to have a smaller nephrostomy tube put in at the end of a percutaneous nephrolithotomy [6]. Applying local anesthetics directly to the surgical site has been shown to help reduce pain after several surgeries

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[7]. Putting bupivacaine along the nephrostomy tube after PCNL dramatically lowers the need for painkillers and peritubular infiltration [8]. A visual analogue scale was used to measure the amount of pain two hours after PCNL [9]. In real life, nerve function loss happens in this order: (1) pain, (2) temperature, (3) touch, (4) proprioception, and (5) leg muscle tone [10]. With bupivacaine, the anesthesia lasts a lot longer than with any other widely used local anesthetic. Some people have also noticed that there's a period of pain relief that lasts after the feeling is restored. During this time, strong painkillers are not needed as much [11]. A former study compared the average pain after surgery between people who had bupivacaine injected into their nephrostomy tube before surgery and people who had a placebo [12]. Analgesia given before the onset of pain, that is, pre-emptive analgesia, prevents the plasticity of the central nervous system and hence gives more effective pain relief. The local infiltration bupivacaine at the surgical site has become relatively common for several surgical procedures and can produce effective analgesia and has the advantage of relative simplicity compared with other regional anesthesia techniques.

This study aims to find out how much pain patients who had bupivacaine injected into their nephrostomy tube before surgery had compared to patients who had a placebo before percutaneous nephrolithotomy for symptomatic nephrolithiasis. This will help researchers understand the situation in the area better as in critical patient care, lowering pain after surgery is a primary goal. The study's results would also let current and local data know which strategy is better than another and suggest the first choice of treatment to lower pain, morbidities, and complications. Ultimately, this would ease the patients' clinical outcomes.

METHODS

The six-month comparative quasi-study was conducted in the Department of Urology at Liaquat National Hospital in Karachi, from January 27, 2021, to July 26, 2021. The study used a sample size of 60 people, with 30 in each group. WHO software was used to determine the sample size; non-probability, convenience sampling was used to pick the samples. The study included patients who had percutaneous nephrolithotomy for pain in the flanks radiating to the groin (Visual Analogue Scale (VAS)>4) for more than 24 hours, were of either gender, had an American Society of Anesthesiologists (ASA) level of less than 2, and were between the ages of 20 and 60. Patients who refused to participate had a nephrostomy tube size greater than 12 Fr, had a history of Hepatitis C, B, or human immunodeficiency virus (HIV) infection, had a history of cancer, had a history of hypo or hyperthyroidism, or were pregnant were excluded or the study. Before the study was carried out, the institutional ethics review committee asked for and granted permission (R.C-LNH-Urology-12/2021/151). A brief account of each patient's background was gathered. Patients were given group A (20ml/50mg of 0.25% bupivacaine) or B (20ml of normal water) in a sealed, opaque envelope. The percutaneous nephrolithotomy was done on all of the patients while they were under general anesthesia. At the end of the operation, a 12 Fr nephrostomy tube was put in place. All surgeries in both groups were carried out by a single urologist who was an expert and had more than ten years of expertise. After surgery, every patient was carefully watched for six hours, and the researcher checked their pain status by using a visual analogue scale [13]. The patient was told that the visual analogue scale measured different types of pain on a scale from zero to ten, where zero means no pain and ten means the worst pain possible. The patient was then asked to mark the number that best described their pain. A wall-mounted scale was used to measure each participant's height in meters, and a weighing machine was used to measure their weight to the nearest kilogram. Before the process, their Body Mass Index (BMI) was also calculated. The results of the quantitative variables (age, height, weight, size of stone, VAS pain score, and length of surgery) and qualitative variables (gender, diabetes mellitus type II, high blood pressure, BMI>30 kg/m2, side of stone, and smoking status) are presented as mean ± SD, frequencies and percentages while the diabetes mellitus, hypertension and smoking was explored by taking clinical history, the BMI was estimated by measuring height and weight whereas the site of the stone was identified by ultrasound findings. SPSS Version 20.0 was used to look at the data for quantitative factors like their ages, height, weight, stone size, VAS pain score, and surgery length; the mean and standard deviation were found. For qualitative factors like gender, type II diabetes, high blood pressure, BMI>30 kg/m2, side of stone and smoking status, rates and proportions were found. Various factors like age, gender, diabetes mellitus, hypertension, BMI greater than 30 kg/m2, smoking, side of the stone, and length of surgery were controlled to see how they affected the results. After sorting, an independent sample t-test was used for quantitative data while chi-square for qualitative data and a p-value of ≤0.05 was considered statistically significant.

RESULTS

60 patients with symptomatic nephrolithiasis were split into two equal groups: Group A (20ml/50mg of 0.25% bupivacaine) and Group B (20 of normal saline). Group A's mean age was 39.9 ± 12.9 years, and Group B's was 39.4 ± 11.2 years. Group A's mean height was 1.69 ± 0.08 meters, and Group B's was 1.68 ± 0.08 meters. The mean weight for group A was 75.4 ± 8.6 kg and for group B it was 76.7 ± 9.3 kg. The mean body mass index for Group A was 26.5 ± 3.3 kg/m2

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and for Group B it was 27.3 ± 3.5 kg/m2. Group A had 16 men (53.3%) and 14 women (46.7%), while Group B had 20 men (66.7%) and 10 women (33.3%). The average stone size in Group A was 2.7 mm, and the average stone size in Group B was 2.5 mm, with a standard deviation of 0.4 mm. Surgery took 1.74 ± 0.35 hours on average for Group A and 1.58 ± 0.42 hours on average for Group B (Table 1).

Table 1: Descriptive Statistics of Study Population

Groups [A=30] [B=30]	Mean ± SD
Age (Years)	
Group A	39.9 ± 12.9
Group B	39.4 ± 11.2
Height (m)	
Group A	1.69 ± 0.08
Group B	1.68 ± 1.55
Weight (Kg)	
Group A	75.4 ± 8.6
Group B	76.7 ± 57
BMI (kg/m^2)	
Group A	26.5 ± 3.3
Group B	27.3 ± 3.5
Stone Size (mm)	
Group A	2.7± 0.7
Group B	2.5± 0.4
Duration of Surgery (Hours)	
Group A	1.74 ± 0.35
Group B	1.58 ± 0.42

The body mass index showed that 25 (83.3%) patients were between 20 to 30 kg/m2 and 5 (16.7%) patients were >30 kg/m^2 were included in group A while 21 (70.0%) and 9 (30.0%) patients between 20 to 30 and >30 kg/m^2 were included in group B respectively. The frequency distribution of diabetes mellitus, hypertension, body mass index, side of stone and smoking is analyzed (Table 2).

Table 2: Frequency Distribution of Diabetes Mellitus, Hypertension, Body Mass Index, Side of Stone and Smoking (n=60)

Variables	Group A n=30	Group B n=30	p-value
Diabetes Mellitus			
Yes	13 (43.3%)	10 (33.3%)	0.03
No	17 (56.7%)	20 (66.7%)	
Hypertension			
Yes	15 (50.0%)	10 (33.3%)	0.12
No	15 (50.0%)	20 (66.7%)	
Body Mass Index (kg/m^2)			
20-30	25 (83.3%)	21 (70.0%)	0.05
>30	5 (16.7%)	9 (30.0%)	
Side of Stone			
Right Side	20 (66.7%)	16 (53.3%)	0.24
Left Side	10 (33.3%)	14 (46.7%)	
Smoking			
Yes	9 (30.0%)	10 (33.3%)	0.41
No	21 (70.0%)	20 (66.7%)	

In the group-wise distribution of the side of the stone, 20 (66.7%) patients had a stone on the right side and 10 (33.3%) had a stone detected on the left side in Group A while 16 (53.3%) and 14 (46.7%) had stone was detected in right and left side respectively in Group B. Out of 60 patients, 9 (30.0%) and 10 (33.3%) patients were smokers in Group A and B while 21 (70%) and 20 (66.7%) were non-smokers in Group A and B respectively. In a comparison of both groups, mean post-operative pain was noted as 2.07 ± 0.78 in Group A whereas 4.80 ± 0.92 in Group B and the p-value was found to be significant i.e. (p<0.01) whereas the statistics for postoperative pain (in terms of mean ± SD) with age group, gender, diabetes mellitus, hypertension, BMI, side of the stone, smoking status and duration of surgery were also seen to be significant (Table 3).

Table 3: Stratification of Study Variables with Post-Operative Pain Between Groups (A and B)

Variables	Group	Post-Operative Pain Mean ± SD	*p-value
Age Group (In Years)			
21-40 (n=31)	Group A	2.00 ± 0.73	<0.01
	Group B	5.02 ± 0.04	
>40 (n=29)	Group A	2.14 ± 0.86	<0.01
	Group B	5.01 ± 1.01	
Gender			
Male (n=36)	Group A	2.00 ± 0.73	<0.01
	Group B	4.31 ± 0.92	
Female (n=24)	Group A	2.14 ± 0.86	<0.01
	Group B	4.52 ± 0.62	
Diabetes Mellitus			
Yes (n=23)	Group A	2.15 ± 0.98	<0.01
	Group B	4.73 ± 0.82	
No (n=37)	Group A	2.00 ± 0.61	<0.01
	Group B	4.30 ± 0.91	
Hypertension			
Yes (n=25)	Group A	2.06 ± 0.70	<0.01
	Group B	5.21± 1.10	
No (n=35)	Group A	2.06 ± 0.88	<0.01
	Group B	5.42 ± 0.71	
Body Mass Index [Kg/M^2]			
20 - 30 (n=46)	Group A	2.12 ± 0.78	<0.01
	Group B	5.41 ± 1.04	
>30 (n=14)	Group A	1.80 ± 0.83	<0.01
	Group B	5.52 ± 0.86	
Side of Stone			
Right Side (n=36)	Group A	2.05 ± 0.82	<0.01
	Group B	4.94 ± 1.31	
Left Side (n=24)	Group A	2.10 ± 0.73	<0.01
	Group B	4.62 ± 1.22	
Smoking Status			
Smoker (n=19)	Group A	2.00 ± 0.86	<0.01
	Group B	4.52 ± 1.42	
Non-Smoker (n=41)	Group A	2.09 ± 0.76	<0.01
	Group B	4.86 ± 1.23	

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Duration (In Hours)			
1 – 1.5 (n=31)	Group A	2.38 ± 0.76	<0.01
	Group B	5.11 ± 1.05	
>1.5 (n=29)	Group A	1.82 ± 0.72	<0.01
	Group B	5.31 ± 1.31	

*Applied Independent T-Test

DISCUSSION

Percutaneous nephrolithotomy (PCNL) is the best way to treat large renal calculi because it is minimally invasive and has few side effects [14]. In normal PCNL, a nephrostomy tube is put in to help with drainage, tamponade, and second-look surgery [15]. However, one of the biggest problems with standard PCNL patients is pain and discomfort at the nephrostomy site after surgery. This makes them stay in the hospital longer and need more painkillers, which slows their total recovery. Each of the painkillers has its side effects and restrictions. [16]. Individuals who have had PCNL have said that there isn't a set way to handle pain after surgery [17]. However, different ways of treating it have been offered, such as painkillers (narcotic and non-narcotic), patient-controlled analgesia pumps, single-dose subarachnoid anesthesia, and local absorption of anesthetic substances [18]. Even though using a small nephrostomy tube has led to less painkiller use, it doesn't help the patient and makes it harder for them to heal smoothly after surgery. Some studies have shown that bupivacaine infiltrated at the nephrostomy site reduced the need for painkillers after surgery [19, 20]. Over the past 30 years, the way kidney stones are treated has changed from open surgeries to silent methods like extracorporeal shockwave lithotripsy, as well as less invasive methods like PCNL. The PCNL procedure is a safe and successful way to treat patients with renal calculi, and it is less invasive than open surgery. This PCNL method has been used for a long time because it has high rates of tone-free hearing and very few problems. It is expected to be put in a nephrostomy tube 48 hours after PCNL to stop bleeding, make sure there is enough drainage, and allow for more endoscopic treatments. In recent years, tubeless PCNL has become popular, and it has been shown to significantly reduce pain in some patients after surgery. But a nephrostomy tube can't be given out when there are complicated stones, perforations, or too much blood. Not giving enough painkillers after surgery can make it take longer to move around, make breathing harder, and keep a person in the hospital longer. Painkillers like opioids and non-steroidal anti-inflammatory drugs have side effects that make it hard for people who might have kidney problems to use them. Anesthesiologists know how important it is to control pain well, which is one of their main goals. Our study's findings agree with those of many other studies done worldwide by different researchers. We discuss some of them here, along with our results. The people in Group A were 39.9 ± 12.9 years, and the mean age in Group B was 39.4 ± 11.2 years. Khan et al., found that out of 94 cases, the average age was 37.23 ± 11.31 years [12]. When the mean ages of the cases were compared to those from other studies, there were no significant differences. In the present research, 53.3% of the people in group A were men and 46.7% were women. Most people in Group B were men (66.7%), while only 33% were women. Honey *et al.*, found that 60.6% of the control group patients were men and 39.4% were women [20]. The current study found that the mean BMI for Group A was 26.5 ± 3.3 kg/m2, and the mean BMI for Group B was 27.3 ± 3.5 kg/m^2. The mean body mass index (BMI) for the control group was 28.2 kg/m^2 (4.6 kg/m^2), and for the bupivacaine group it was 28.1 kg/m2 (5.4 kg/m^2) [20]. The BMI figure was the same as what had been found before. Researchers found that the average stone dimension in the Group A case was 2.7 mm, with an error of 0.7 mm. The control group had a mean thickness of 28.3 mm [21]. According to Khan *et al.*, the average VAS pain score for patients in group A was 5.22 ± 0.76, and for patients in group B, it was 7.85 ± 0.78 [12]. Andreoni and colleagues noted that a single preoperative dose of subarachnoid spinal analgesia with morphine along with infiltration of the nephrostomy tract with bupivacaine was a statistically significant decrease in the requirement of postoperative parenteral pain medication [22]. Jonnavithula *et al.*, conducted a study on subcutaneous infiltration of bupivacaine versus saline after PCNL and showed reduced rescue analgesic requirement in the bupivacaine group [23].

CONCLUSIONS

It was concluded that postoperative pain score was significantly better in bupivacaine infiltration (Group A) as compared to placebo (Group B) in patients undergoing percutaneous nephrolithotomy for symptomatic nephrolithiasis. To confirm the results of this study, further studies with a large sample size and more parameters in multidisciplinary settings are needed.

Authors Contribution

Conceptualization: AR, WA, RK
Methodology: AR, SK, WA, NS, RK
Formal analysis: AR, ZHR, NS, RK
Writing review and editing: SK, WA, SZAS

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

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REFERENCES

[1] Khan TM, Anwar MS, Shafique Z, Nawaz FK, Karim MS, Saifullah D *et al.* Risk Factors of Nephrolithiasis in A Tertiary Care Hospital in Rawalpindi: A Descriptive Cross-Sectional Study.Cureus.2022 Jun; 14(6):e2 6274. doi: 10.7759/cureus.26274. PMID: 35898378.

[2] Khan SR, Pearle MS, Robertson WG, Gambaro G, Canales BK, Doizi S *et al.* Kidney stones. Nat Rev Dis Primers. 2016 Feb 25;2:16008. doi: 10.1038/ nrdp. 2016. 8. PMID: 27188687.

[3] Arrabal-Martín M, Cano-García MC, Arrabal-Polo MÁ, Dominguez-Amillo A, Canales-Casco N, de la Torre-Trillo J *et al.* Etiopathogenic Factors of the Different Types of Urinary Litiasis.Arch Esp Urol.2017 Jan;70(1):40-50. PMID: 28221141.

[4] Giusti G, Maugeri O, Taverna G, Benetti A, Zandegiacomo S, Peschechera R *et al.* Tubeless Percutaneous Nephrolithotomy: Our Experience. Archivio Italiano Di Urologia E Andrologia. 2010 Mar; 82(1): 34-6. doi: 10.1016/S1569-9056(10)60013-9.

[5] Darabi MR, Soltani S, Rezayat AA, Yousefi M, Kashefi M, Tavakkoli M *et al.* Clinical Outcomes of the Simultaneous Bilateral Percutaneous Nephrolithotomy (PCNL) in Patients With Kidney Stones: A Prospective Cohort Study.Electronic Physician. 2018 Feb; 10(2): 6377. doi: 10.19082/6377.

[6] Shah HN, Sodha HS, Khandkar AA, Kharodawala S, Hegde SS, Bansal MB. A Randomized Trial Evaluating Type of Nephrostomy Drainage After Percutaneous Nephrolithotomy: Small Bore V Tubeless. J Endourol. 2008 Jul;22(7):1433-9. doi: 10.1089/end.2007.0350. PMID: 18690809.

[7] Shah HN, Shah RH, Sodha HS, Khandkar AA, Gokhale A. A Randomized Control Trial Evaluating Efficacy of Nephrostomy Tract Infiltration with Bupivacaine After Tubeless Percutaneous Nephrolithotomy. Journal of Endourology.2012 May; 26(5): 478-83. doi: 10.10 89/ end.2011.0465.

[8] Gokten OE, Kilicarslan H, Dogan HS, Turker G, Kordan Y. Efficacy of Levobupivacaine Infiltration to Nephrosthomy Tract in Combination with Intravenous Paracetamol On Postoperative Analgesia in Percutaneous Nephrolithotomy Patients. Journal of Endourology. 2011 Jan 1;25(1):35-9. doi: 10.1089/ end. 2010.0346.

[9] Haleblian GE, Sur RL, Albala DM, Preminger GM. Subcutaneous Bupivacaine Infiltration and Postoperative Pain Perception After Percutaneous Nephrolithotomy. The Journal of Urology.2007 Sep; 178(3): 925-8. doi: 10.1016/j.juro.2007.05.025.

[10] Sajedi P, Yaraghi A, Zadeh MT. Comparison of Pre-Vs. Post-Incisional Caudal Bupivacaine for Postoperative Analgesia in Unilateral Pediatric Herniorrhaphy: A Double-Blind Randomized Clinical Trial. Saudi Journal of Anaesthesia.2011 Apr; 5(2): 157-61. doi: 10.4103/ 1658 -354X.82783.

[11] Khan SA, Khalid S, Effendi F, Mithani MH, Awan AS, Mugal T. Postoperative Pain Score of Bupivacaine Versus Placebo in Patients Undergoing Percutaneous Nephrolithotomy. Journal of the College of Physicians and Surgeons Pakistan.2018 Nov; 28(11): 858-61. doi: 10.29271/jcpsp.2018.11.858.

[12] Khan MK, Ullah A, Rahman AU. Effect of Preoperative Bupivacaine Infiltration of Nephrostomy Tract on Post-Operative Pain in Patients Undergoing Percutaneous Nephrolithotomy: A Randomized Controlled Trial.Khyber Medical University Journal. 2013 Jun; 5(2).

[13] Delgado DA, Lambert BS, Boutris N, McCulloch PC, Robbins AB, Moreno MR *et al.* Validation of Digital Visual Analog Scale Pain Scoring with A Traditional Paper-Based Visual Analog Scale in Adults. J Am Acad Orthop Surg Glob Res Rev. 2018 Mar 23;2(3):e088. doi: 10.5435/JAAOSGlobal-D-17-00088. PMID: 30211382; PMCID: PMC6132313.

[14] Karaduman I, Karasu D, Yilmaz C, Oner S, Erdem Solak H, Korfali G.The Effect of Peritubal Infiltration with Bupivacaine and Morphine on Postoperative Analgesia in Patients Undergoing Percutaneous Nephrolithotomy.Pain Research and Management. 2017; 2017(1): 2454267. doi: 10.1155/2017/2454267.

[15] Sofer M, Lidawi G, Keren-Paz G, Yehiely R, Beri A, Matzkin H. Tubeless Percutaneous Nephrolithotomy: First 200 Cases in Israel. Isr Med Assoc J. 2010 Mar ;12(3):164-7. PMID: 20684181.

[16] Pietrow PK, Auge BK, Lallas CD, Santa-Cruz RW, Newman GE, Albala DM *et al.* Pain After Percutaneous Nephrolithotomy: Impact of Nephrostomy Tube Size. J Endourol. 2003 Aug;17(6):411-4. doi: 10.108 9/08 92 77 903767923218. PMID: 12965069.

[17] 1Kirac M, Tepeler A, Bozkurt OF, Elbir F, Ozluk C, Armagan A *et al.* The Efficacy of Bupivacaine Infiltration on the Nephrostomy Tract in Tubeless and Standard Percutaneous Nephrolithotomy: A Prospective, Randomized, Multicenter Study. Urology. 2013 Sep; 82(3): 526-31. doi: 10.1016/j. urology. 2013 .02. 083.

[18] Ugras MY, Toprak HI, Gunen H, Yucel A, Gunes A. Instillation of Skin, Nephrostomy Tract, and Renal Puncture Site with Ropivacaine Decreases Pain and

DOI: https://doi.org/10.54393/pjhs.v5i12.1505

Improves Ventilatory Function After Percutaneous Nephrolithotomy. J Endourol. 2007 May;21(5):499-503. doi: 10.1089/end.2006.0335. PMID: 17523902.

[19] Alam K, Biyabani R, Ather MH. 573 The Impact of Nephrostomy Tube Size on Post-Operative Pain and Perinephric Collection After Percutaneous Nephrolithotomy. A Randomized Controlled Trial. Eur Urol Suppl 2009;8(4):264.doi: 10.1016/S1569-90 56 (09)60568-6.

[20] Honey RJ, Ghiculete D, Ray AA, Pace KT. A Randomized, Double-Blinded, Placebo-Controlled Trial of Intercostal Nerve Block After Percutaneous Nephrolithotomy. J Endourol.2013 Apr;27(4):415-9. doi: 10.1089/end.2012.0418. PMID: 23445266.

[21] Parikh GP, Shah VR, Vora KS, Modi MP, Mehta T, Sonde S. Analgesic Efficacy of Peritubal Infiltration of Ropivacaine Versus Ropivacaine and Morphine in Percutaneous Nephrolithotomy Under Ultrasonic Guidance. Saudi J Anaesth. 2013 Apr;7(2):118-21. doi: 10.4103/1658-354X.114046. PMID: 23956707.

[22] Andreoni C, Olweny EO, Portis AJ, Sundaram CP, Monk T, Clayman RV. Effect of Single-Dose Subarachnoid Spinal Anesthesia on Pain and Recovery After Unilateral Percutaneous Nephrolithotomy.J Endourol.2002 Dec;16(10):721-5.doi:10.1089/08927 79 0260472863. PMID: 12542874.

[23] Jonnavithula N, Pisapati MV, Durga P, Krishnamurthy V, Chilumu R, Reddy B. Efficacy of Peritubal Local Anesthetic Infiltration in Alleviating Postoperative Pain in Percutaneous Nephrolithotomy. J Endourol. 2009 May;23(5):857-60. doi: 10.1089/end.2008.0634. PMID: 19397429.

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Assessment of Risk Factors Causing Oral Cancer among Patients Visiting Dental OPD

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ABSTRACT

In Pakistan, oral cavity cancer incidence rates are increasing making it the most common cancer, numbered as the second cancer in the list of cancers among males as well as females. Oral cancer is diagnosed frequently and is one of the leading causes of death in Pakistan. Worldwide, oral cancer is 6th most common cancer; in developing countries like Pakistan, India, and Sri Lanka incidence is very high. **Objective:** To examine the risk factors causing oral cancer among patients visiting the dental Out Patients Department of Liaquat University of Medical and Health Science, Jamshoro/Hyderabad. **Methods:** A cross-sectional study was done at the Department of Oral and Maxillofacial Surgery Department, Liaquat University of Medical and Health Science, Jamshoro/Hyderabad over a six-month duration. The data were analyzed by using SPSS version 26 employing Pearson's chi-square test. **Results:** Male were mostly affected as compared to female (76%). The mean age of the patients was noted as 46.62 years. Buccal mucosa was the most common site affected (45.5%). Smokeless tobacco products and smoking have a significant association with oral cancer (p-value=0.000). **Conclusions:** It was concluded that smokeless products are used more frequently than smoking and have more risk of increasing the incidence of oral cancer. Among all participants, 115 patients were diagnosed with squamous cell carcinoma.

INTRODUCTION

Oral cancer is well-defined as, the neoplasm of a malignant nature raised in the mouth, lips and anterior two of three equal parts of the whole of the tongue involving the lining mucosa [1]. Globally it is among the most common cancers, almost 300,000 cases are diagnosed yearly, due to very poor prognosis it is a serious global health problem [2]. it is a common cancer number as a sixth of cancer all over the globe. In Pakistan, the frequency rates of cancer of mouth are increasing making it the most common cancer, ranked as the second cancer in the list of cancers among male as well as female. Oral cancer estimation in the year 2020 was in 16th rank in incidence and global death caused across much of South and Southeast Asia and the Western Pacific [3, 4]. Differences in mortality were seen among countries, developing countries result from more involvement of around two-thirds of the population and in South Asia approximately half [5]. Oral cancer is diagnosed frequently and is one of the leading causes of death in Pakistan. It has a multifactorial etiology. The most common risk factors in Pakistan are: Tobacco in its multiple forms smokeless

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tobacco and smoking [6]. Smokeless tobacco products are substances used without combustion, they contain many toxic products, and nicotine and tobacco-specific nitrosamines are present in them and may lead to many health hazards local as well as systemic [7]. In Pakistan, rates of smokeless tobacco consumption are higher than cigarette use, and oral cancer rates are increasing to the highest, significantly higher than in other countries of the Region. The cause of this increasing habit is the misconception that tobacco products such as smokeless tobacco are less harmful to health than smoking cigarettes, the health dangers of smokeless tobacco use are less understood by users [8, 9]. Two main types of Smokeless tobacco are broadly categorized as: Tobacco in chewing form and snuff, availability of chewing tobacco is commonly in the form of cut, loose and ragged leaves and snuff is available as tobacco that is finely ground packaged in sachets can be dry, moist in consistency. These products are available in the market with different names such as Naswar, Gutka, Betel Quid, Supari, Manipuri, Mawa, Khaini, Qiwam, Zarda, Nass, Mishri, Gul, Shammah plug, Gudakhu, highly reactive electrophiles are released by smokeless tobacco products because nitrosamines are present in them and as a result, free radicals develop oxidative stress [10, 11], damage of DNA, lipid peroxidation level increase and levels of antioxidant enzymes altered are harmful changes produced by the generation of these free radicals [12]. The very initial line of defence against damage by any free radical are these antioxidant enzymes, alterations in their levels affect their function of defence [13]. The common clinical features are unhealing ulcers in the mouth, persistent swellings in the oral cavity, chewing difficulty, limited mouth opening, and swelling to the advanced stages [14]. A complete history of the patient with a history of tobacco use by either means of tobacco, smokeless tobacco or smoking along with Clinical examination and Biopsy are keys for diagnosis for effective planning and promoting cancer awareness programs, prevention and visit programs, it is very critical to have an eye on available information analyzing, investigating the background of top risk factors causing oral cancer in different locations. This study will add to existing knowledge on the major cause of a rise in the incidence of oral cancer in a population of Jamshoro/Hyderabad city, Pakistan.

This study aimed to examine the risk factors causing oral cancer among patients visiting the dental outpatient department of Liaquat University of Medical Health Science, Jamshoro/Hyderabad.

METHODS

A cross-sectional study was conducted at the Department of Oral and Maxillofacial Surgery department Liaquat University of Medical and Health Sciences (LUMHS), Jamshoro/Hyderabad in the time frame of six months (December 2020 to May 2021) by non-probability convenience sampling technique after the approval by Ethical review committee of LUMHS (NO.LUMHS/REC/-974) on dated. The sample size was calculated by Raosoft online calculator using the Margin of error=5%, Confidence interval= 95%, and Response distribution/ Prevalence= 8.6% [3]. The total sample size calculated was 121. Inclusion criteria consisted of patients aged between 20 to 72 years, either gender with a histopathological confirmed diagnosis of oral cancer, a history of tobacco use minimum from 2 years either using consuming smokeless tobacco products or smoking, cases visiting the hospital during the study period, patient having oral cancer with history of smokeless tobacco use or smoking or both of them, patients having history of tobacco smokeless/ smoking were included and patients were not willing to participate in the study, mentally retarded patients and pregnant women were excluded. Data were collected from the patients after getting a signed written informed consent form. Demographic details like age and gender were noted. All information about patients was kept confidential. After complete history and examination, the patients fulfilling inclusion criteria were included in the study. A biopsy procedure was performed for the patients including injection of 2% xylocaine anaesthesia and then tissues were packed in 10% formalin solution for the diagnosis in the histopathological laboratory. Instructions and medication were prescribed after the procedure. The data were analyzed by using the software SPSS version 26.0. The frequency and percentages were calculated for categorical variables like gender, oral hygiene practices, smoking and smokeless tobacco. The mean and standard deviation (SD) was calculated for continuous variables like age. The Pearson's chi-square ($\chi 2$) test with the level of significance set as $p<0.05$ was applied to check the statistical significance.

RESULTS

Age of patients is divided into groups where the majority of patients belong to age group 31-40 and 41-50 years 37 (30.5%) followed by age group 51-60 years 26 (21.4%), 61-72 years 11 (9.09%) respectively and mean age of patients was 46.62 + 11.35 years. Whereas gender distribution shows that male was in predominance 92 (76%) and female were 29 (24%) as shown in table 1.

Table 1: Demographic Information of Patients

Variables	Frequency (%)
Age	
20-30	10 (8.26%)
31-40	37 (30.5%)

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41-50	37 (30.5%)
51-60	26 (21.4%)
61-72	11 (9.09%)
Gender	
Male	92 (76.0%)
Female	29 (24.0%)

Table 2 demonstrates the stratification of brushing habit, and duration time of smokeless tobacco use. Brushing habit indicates that out of 121 just 1 had brushed in past before acquiring oral cancer, all others admitted that neither they did at the current point time due to oral lesions nor before the lesion, they admitted to never brushing habit. 93 patients (76.9%) used tobacco for more than 20 years, 23 patients (19%) used tobacco for more than 5 years and 5 patients (4.1%) admitted the use of tobacco products for less than 3 years. 46 patients (38%) had use of smoking for 1-5 years while 75 patients (62%) agreed to use smoking for more than 5 years. Regarding the site of complaint lesion which later proved as oral cancer as indicated in this study buccal mucosa was the most common site affected at 45.5% (n=55), 20.7% (n=25) had lesion at retro molar trigon, 18.2% (n=22), complaint the presence of lesion at the lateral border of tongue respectively and the least site documented was the palate 5.8% (n=7) as presented in table 2.

Table 2: Stratification of Brushing Habit, Duration Time of Smokeless Tobacco Use

Variables		Frequency (%)
Brushing Habit	No Brushing Habit	120 (99.2%)
	Daily Brushing	1 (0.8%)
Duration of Smokeless Tobacco Use	More Than 5 Years	23 (19.0%)
	More Than 20 Years	93 (76.9%)
	Less Than 3 Years	5 (4.1%)
Duration of Smoking	1-5 Years	46 (38.0%)
	More Than 5 Years	75 (62.0%)
Site Involved	Retro-molar-trigon	25 (20.6%)
	Buccal Mucosa	55 (45.5%)
	The Lateral Border of the Tongue	22 (18.2%)
	Lip	12 (9.9%)
	Palate	7 (5.8%)

Tobacco type use by patients and the status of biopsy results. The Majority of patients were using smokeless tobacco products 36 patients used Naswar as the most common type followed by 26 patients with complaints of lesions were users of Mainpuri, and 18 patients were habitual of betel nuts respectively. 30 patients were using both smokeless tobacco products as well as smoking and they all were found to have squamous cell carcinoma and results are shown in table 3.

Table 3: Tobacco Type Use by Patients and Status of Biopsy Results

Type of Tobacco Use	Number of Patients	Biopsy Proved Squamous Cell Carcinoma		p-Value
		Yes	No	
Smokeless Tobacco				0.000
Mainpuri	26	25	1	
Gutka	3	3	0	
Naswar	36	34	2	
Betal nut	18	17	1	
Pan	3	2	1	
Nas	1	0	1	
Only smoking				
Smokers	4	4	0	
Smokeless Tobacco and Smoking				
Total	30	30	0	
	121	115	6	

DISCUSSION

Oral cancer is a multifactorial disease and one of the most common malignancies globally. Indian studies report that the site of oral cancer is most often found in the tongue and buccal mucosa, among those sites involvement of buccal mucosa, was on top [18]. Another study in Chennai reports that oral cancer is reported to peak at the base of the tongue and mouth with an increased metastasis rate [12]. Another study reports that buccal mucosa, alveolus, and the base of the oral cavity were mostly involved sites [13]. Current study resulted out of 121 patients 45.5% (n=55) had lesions at the buccal mucosa, 20.7% (n=25) patients had lesions at the retro-molar trigone area, 18.2% (n=22) patients given the complaint of the presence of lesion at the lateral border of the tongue, 12 patients had lip lesion, 7 patients sited lesion at the palate. In the present study, it was observed that men were more commonly affected and found habitual of smoking and smokeless products. During the whole study time, none of the Lesbian, Gay, Bisexual, Transgender, Queer, Intersex, or Asexual (LGBTQ) (Transgender persons) patients came with clinical symptoms of oral cancer, this is the point for further research that either they are resistant to the disease or have no habit of ST or it was just a time blink in which they could not approach to hospital for the subjected reason. The World Health Organization (WHO) estimations recorded that about 58% of world oral and oropharyngeal cancer-reporting patients belong to South and Southeast Asia, Indonesia [15]. Education plays a key role in society and self-hygiene maintenance. Developed countries of the World are so self-esthetic conscious and our people are unfortunately very backwards, almost all the patients with oral cancer have a habit of ST consumption too, and reported that they never do tooth brushing. This point should be considered for future developmental plans to ignite more light of awareness and raise educational plans

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for future generations. As for disease of oral cancer is observed in people of more anxiety-bearing poor and Labourers, farmers and drivers by occupation, this group of people undergo more physical and mental workload and anxiety thoughts so as anxiety was relevant they use smokeless tobacco, more use of the masticatory system as in bruxism during the night during sleep is seen in anxious people likewise overuse of masticatory system by whole day chewing of smokeless tobacco products can be correlated for future researches. Various surgical groups and treatment guidelines suggest that appropriate treatment can only be selected by appropriate Knowledge of the extent of the disease and it plays a key. Impacts of efforts for early detection, diagnosis, clinical studies which are required for stratification of patients, and appropriate treatment selection require knowledge and information that can be obtained by identifying the anatomic extent, histology of a neoplasm, topography, and Cancer staging [16]. One study suggests diagnosis by nano biosensors, in that proteases, transmembrane receptors, adhesion molecules and tetraspanins are enriched on phosphatidyl serine, cholesterol and ceramide all together compose exosomes. Some proteins that have an association with cancer are also expressed on exosome surfaces in high concentrations that can also be used as differentiation markers among cancers. human epidermal growth factor receptor 2 (HER2), Mucin 18 (MUC18), and Latent Membrane Protein 1 (LMP1) are Proteins that can be used as exosome detectors, these are found in biosensors development for total. A particular nucleic acid, miR-24-3P (miRNA) found in the saliva, is expressed in high amounts in Oral Squamous Cell Carcinoma (OSCC) patients. Based on this, recently, a potential biosensor has been developed that prefers miRNA as a target for the diagnosis of oral cancer [17]. Diagnostics by Nano-biosensors-based lateral flow immune sensing is a revolution in the field of oral cancer early diagnosis [18-20] that needs to be common in Pakistan that until is not as frequent as in other developed countries Pakistan yet needs to work more for enhancement in oral cancer diagnostics at very early stages. Indicates cancer-causing bad habits increase the risk of oral cancer in the community, risky habits include betel nut chewing, alcohol consumption, and smoking, hypothesis is that practicing these may be influencing salivary profiles as well and having a worse impact on oral health [21, 22].

CONCLUSIONS

It was concluded that regarding gender, male was more affected than female, the use of Naswar was found at peak level and the second leading habit was Manipuri. The buccal mucosa was the most commonly involved site. There is a strong association between smokeless tobacco product use and oral cancer. There is a close relationship between poverty, stress and the use of such products, further studies should be conducted to confirm the relationship of such habits.

Authors Contribution

Conceptualization: MM
Methodology: BC, SUUB, MS
Formal analysis: BC, AS, RK
Writing review and editing: MAP, RK

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Liu H, Huang Y, Huang M, Huang Z, Wang Q, Qing L *et al.* Current Status, Opportunities, and Challenges of Exosomes in Oral Cancer Diagnosis and Treatment. International Journal of Nano-Medicine. 2022 Jun: 2679-705. doi: 10.2147/IJN.S365594.

[2] Sari EF, Johnson NW, McCullough MJ, Cirillo N. Prevalence and Risk Factors of Oral Potentially Malignant Disorders in Indonesia: A Cross-Sectional Study Undertaken in 5 Provinces. Scientific Reports. 2024 Mar; 14(1): 5232. doi: 10.1038/s41598-024-54410-4.

[3] Warnakulasuriya S and Kerr AR. Oral Cancer Screening: Past, Present, and Future. Journal of Dental Research. 2021 Nov; 100(12): 1313-20. doi: 10.1177/00220345211014795.

[4] Xu W, Li C, Liu Q, Liu W, Wang X. A Scientometric Study of Oral Cancer Research in South and Southeast Asia with Emphasis On Risk Factors Control. Journal of Dental Sciences. 2024 Mar; 19(4): 2157-2162. doi: 10.1016/j.jds.2024.03.014.

[5] Saglam G and Dag A. Evaluation of Oral Cancer Knowledge and Awareness among Patients at a Periodontology Clinic. Journal of Clinical Trials and Experimental Investigations. 2024 Mar; 3(1): 1-9. doi: 10.5281/zenodo.10871099.

[6] Bile KM, Shaikh JA, Afridi HU, Khan Y. Smokeless tobacco use in Pakistan and its association with oropharyngeal cancer. EMHJ-Eastern Mediterranean Health Journal. 2010; 16 (Supp.): 24-30. doi: 10.26719/2010.16.Supp.24.

[7] Rai P, Goh CE, Seah F, Islam I, Chia-Wei WW, Mcloughlin PM *et al.* Oral Cancer Awareness of Tertiary Education Students and General Public in

DOI: https://doi.org/10.54393/pjhs.v5i12.2550

Singapore. International Dental Journal. 2023 Oct; 73(5): 651-8. doi: 10.1016/j.identj.2022.11.021.

[8] Chou CW, Lin CR, Chung YT, Tang CS. Epidemiology of Oral Cancer in Taiwan: A Population-Based Cancer Registry Study. Cancers. 2023 Apr; 15(7): 2175. doi: 10.3390/cancers15072175.

[9] Heller MA, Nyirjesy SC, Balsiger R, Talbot N, VanKoevering KK, Haring CT *et al.* Modifiable Risk Factors for Oral Cavity Cancer in Non-Smokers: A Systematic Review and Meta-Analysis. Oral Oncology. 2023 Feb; 137: 106300. doi: 10.1016/j.oraloncology.2022.106300.

[10] Uqaili AA, Shah R, ul Hussain A, Kumar N. Oral Cancer Awareness and Prevalence of Betel Nuts, Pan and Ghutka in School Children of Rural Areas of Sindh, Pakistan. International Journal of Medicine and Medicinal Sciences. 2014; 4(6): 178-82.

[11] Singh V, Singh AK, Dutta KD, Kumar N, Kumari A. Evaluation of Quality of Life and the Nutritional Status of Oral Cancer Treated Patients as Compared with the Control Group in Varanasi District: A Cross-Sectional Study. International Journal. Community Medicine and Public Health. 2019 Nov; 6: 4804. doi: 10.18203/2394-6040.ijcmph20195059.

[12] Thavarool SB, Muttath G, Nayanar S, Duraisamy K, Bhat P, Shringarpure K *et al.* Improved Survival among Oral Cancer Patients: Findings from a Retrospective Study at a Tertiary Care Cancer Centre In Rural Kerala, India. World Journal of Surgical Oncology. 2019 Dec; 17: 1-7. doi: 10.1186/s12957-018-1550-z.

[13] Bhosle P, Pathan H, Tapadiya G, Alam MI. Case Study On Oropharyngeal Cancer Prediction and Diagnosis and Management Based Upon Mri, Ct Scan Imaging Techniques. In Disruptive Developments in Biomedical Applications. 2022 Dec: 91-106. doi: 10.1201/9781003272694-8.

[14] Rochefort J, Karagiannidis I, Baillou C, Belin L, Guillot-Delost M, Macedo R *et al.* Defining Biomarkers in Oral Cancer According to Smoking And Drinking Status. Frontiers in Oncology. 2023 Jan; 12: 1068979. doi: 10.3389/fonc.2022.1068979.

[15] Kadashetti V, Shivakumar KM, Choudhary M, Patil S, Gawande M. Awareness and Knowledge of Tobacco Associated Risk of Development of Oral Cancer and Oral Potentially Malignant Disorders among Patients Visiting a Dental College. Journal of Family Medicine and Primary Care. 2020 May; 9(5): 2244-7. doi: 10.4103/jfmpc.jfmpc_181_20.

[16] Sassi LM, Guebur MI, Melzer RS, Dissenha JL, Schussel JL, Zanferrari F et al. Smoking as a Risk Factor for Oral Cancer and 30 Years of Prevention Campaigns in the State of Paraná, Brazil. Brazilian Journal of Health Review. 2024 Jul; 7(4): e71268-. doi: 10.34119/bjhrv7n4-091.

[17] Ghasemian A, Sargeran K, Khami MR, Shamshiri AR. Effects of Educational Interventions Based On the Theory of Planned Behavior On Oral Cancer-Related Knowledge and Tobacco Smoking in Adults: A Cluster Randomized Controlled Trial. BioMed Central cancer. 2024 Jan; 24(1): 45. doi: 10.1186/s12885-024-11845-2.

[18] Amarasinghe H, Rathnapriya M, Abeysundara A, Jayaweera S, Jayathilake A, Jayasinghe R. Assessment of the Oral Cancer Control Activities Through Care Seeking Behavior of Hospital Attendees and Their Level of Awareness. Journal of Oral Biology and Craniofacial Research. 2021 Oct; 11(4): 536-40. doi: 10.1016/j.jobcr.2021.07.009.

[19] Das H and Motghare S. India as "The Oral Cancer Capital of the World": The Rising Burden of Oral Malignancies Across the Nation. International Journal of Science and Health Research. 2021; 6: 99-107. doi: 10.52403/ijshr.20210419.

[20] Srivastava R, Jyoti B, Pradhan D, Siddiqui Z. Prevalence of Oral Submucous Fibrosis in Patients Visiting Dental OPD of A Dental College in Kanpur: A Demographic Study. Journal of Family Medicine and Primary Care. 2019 Aug; 8(8): 2612-7. doi: 10.4103/jfmpc.jfmpc_465_19.

[21] Sun R, Dou W, Liu W, Li J, Han X, Li S *et al.* Global, Regional, and National Burden of Oral Cancer and Its Attributable Risk Factors from 1990 to 2019. Cancer Medicine. 2023 Jun; 12(12): 13811-20. doi: 10.1002/cam4.6025.

[22] Barsouk A, Aluru JS, Rawla P, Saginala K, Barsouk A. Epidemiology, Risk Factors, And Prevention of Head and Neck Squamous Cell Carcinoma. Medical Sciences. 2023 Jun; 11(2): 42. doi: 10.3390/medsci11020042.

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Original Article

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Comparison of Accuracy of WHARFE Assessment and Pederson Difficulty Index for Predicting Surgical Difficulty in Patients with Impacted Mandibular Third Molar Surgery

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ABSTRACT

The extraction of a mandibular impacted third molar was a highly prevalent oral surgical procedure. Assessing the surgical difficulty of impacted mandibular third molar extraction was crucial for planning and executing successful procedures. Various assessment tools, such as the WHARFE Assessment and Pederson's Difficulty Index, have been developed to aid clinicians in predicting the complexity of these surgeries. **Objective:** To determine the accuracy of the WHARFE assessment and Pederson's difficulty index for predicting surgical difficulty in patients with impacted mandibular third molar surgery. **Methods:** A descriptive cross-sectional study was conducted at the department of Oral and maxillofacial surgery, Dow university of health sciences, Karachi, Pakistan. Data were collected in time duration of six months by employing non-probability convenience sampling technique. SPSS version 26.0 was used for data analysis. Chi-square test was applied with a significant level of p value <0.05. **Results:** The WHARFE assessment demonstrated an accuracy of 60.0% in predicting surgical difficulty, with a corresponding p-value of (p=0.001). Similarly, Pederson's difficulty index assessment showed an accuracy of 54.5% in predicting surgical difficulty, with a p-value of (p=0.232). **Conclusion:** Both assessments showed some ability to predict surgical difficulty, WHARFE assessment demonstrated a strong predictive accuracy, and the differences observed did reach statistical significance(p-value 0.001).

INTRODUCTION

One of the teeth that gets impacted the most often is the lower third molar. Around the world, its prevalence varies from 30.3% to 68.6% [1, 2]. A tooth that has been impaction is a pathological condition in which the tooth does not erupt normally, that is, within the anticipated time frame. Due to postural instability and aberrant position brought on by the impaction, the impacted tooth becomes non-functional [3]. Numerous local and systemic factors influence the natural eruption of teeth. A nearby tooth, an excessive amount of soft tissue nearby, or solid bone above can all affect a normal eruption. Also influencing or changing the impaction rate are race and ethnicity [4]. One of the most frequent surgical procedures carried out in dental clinics on a daily basis is the extraction of the wisdom tooth [5-7]. No grading system or scale is thought to be adequate to anticipate the degree of difficulty of this

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surgery for impacted lower third molars; that is, each scale considers some characteristics while leaving out others, making it clinically not very reliable. Here are a few suggested scales or models that are currently being used in therapeutic settings: The models of WHARFE, Pederson, winter, Pell, and Gregory [8-10]. A popular classification/method for determining the degree of difficulty while organizing the extraction of a third mandibular molar tooth is WHARFE's grading system. WHARFE is an acronym for Winter's lines, mandibular height, angulation, root, follicular size, shape and morphology, and tooth exit path [11]. Prior to organizing any third-molar intervention, this approach aids in a more thorough examination of the tooth and its radiological condition. Pederson's difficulty assessment scale, however, is used to forecast the level of pre- and post-operative difficulty associated with extracting the third mandibular molar tooth [12]. Patients who have impacted third molars surgically extracted may have severe pain, swelling, and trismus as a consequence of the inevitable stress to soft and hard tissues. They frequently suffer from severe postoperative discomfort and a reduction in their Quality of Life (QoL) [13-15]. The impaction of the third molar, commonly known as wisdom tooth impaction, can lead to various dental issues. Some of the notable problems associated with third molar impaction include: pain, infection, cyst formation, misalignment of teeth, stiffness, damage to adjacent teeth, orthodontic issues etc [16]. Therefore, the purpose of this study was to evaluate these systems' believability. In addition, this research will investigate if these systems are reliable enough to be used in the (intelligent) planning of interventions for patients who present with lower third-molar impaction. It will undoubtedly aid in expanding one's knowledge base and offer some recommendations for better clinical practice when caring for these individuals. In the end, this will bring the clinical strategy and body of knowledge for treating oral and maxillofacial surgeries up to date.

METHODS

Descriptive cross sectional study was conducted at Department of Oral and Maxillofacial Surgery Dow university of health sciences Karachi by employing non probability consecutive sampling technique in time frame of six months (from 19 October 2022 to 18 April, 2023) with approval of research ethics committee (IRB-2502/DUHS/Approval/2022/848) on dated (30th April, 2022) after getting the written consent from the patients. Sample size was calculated from online calculator (from www.openepi.com) keeping confidence intervals of 95% and 44% accuracy of the Pederson Scale index, with a 7% margin of error it yields sample of 194, in case of a drop out failure to follow up and also enhance the study's strength, total sample size was 200 [12].

Inclusion criteria was based on patients having age of 18 to 35 years with either gender. Patients having impacted 3rd mandibular molar according to Winter's classification and patients with no evidence of dental caries or restoration in the past were included. Patients with history of orthodontic treatment or periodontal surgery, having craniofacial anomalies, congenital deformities or syndromes, with evidence of cyst or tumor in the molar area and pregnant women were excluded from the study. Demographic details like age, gender were noted. All information about patients was kept confidential.

After complete history and examination, the patients fulfilling inclusion criteria were picked for the study. Pre-operative analysis with OPG radiograph tracing, the difficulty was determined by Pederson's and WHARFE's indices, and the surgical procedure was planned in the light of the modified parent scale. Intra operatively, the application of preoperative assessment observations by the pre-planned surgical procedure and the actual difficulty was analyzed with the variable of time to justify the effectiveness of a particular scoring system. The primary outcomes include the accuracy of both systems compared to the pre-operative measure of Pederson's and WHARFE'S systems with the actual intra-operative difficulty faced, by filling a developed proforma. The secondary outcome variable was the time taken of the surgical procedure which was recorded by a stopwatch from the start of the procedure i.e. administration of local anesthetic to the end i.e. packing of the extraction site. SPSS version 26.0 was used as a tool for data analysis. The quantitative variables like age, time, and scoring of the WHARFE and Pederson's systems were represented in Mean ± SD or median. The qualitative variables like gender and the percentage of accuracy were represented in frequencies and percentages. Effective modifiers such as age, gender and the percentage of accuracy were controlled through stratification. Fischer exact test/Chi square test was applied, taking a p-value of <0.05 as significant.

RESULTS

Table 1 indicated demographic information of patients where Mean ± SD of age was 28.43 ± 5.13 with a median of 29. Among the gender distribution, there were 101 individuals, constituting 50.5% of male, whereas 99 individuals, making up 49.5% as female. The duration of procedure of the patients ranged from 4 to 30 minutes with a median of 8 and Mean ± SD of 13.97 ± 8.19 (Table 1).

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Table 1: Demographic Characteristics and Duration of Procedure of Patients

Variables	Mean ± SD	Median	
Age	28.43 ± 5.13	29.00	
Gender	**Male N (%)**	**Female N (%)**	
	101 (50.5%)	99 (49.5%)	
Duration of Procedure (Minutes)	**Mean ± SD**	**Minimum**	**Maximum**
	13.97 ± 8.19	4.00	30.00

Table 2 showed descriptive statistics of WHARFE score, Pederson's difficulty index score and surgical difficulty score where the WHARFE score of the patients ranged from 2 to 12 with a median of 5 and with a Mean ± SD of 5.45 ± 2.40 with difficult score of 3 and 197 was recorded as easy score. The Pederson's difficulty index score of the patients ranged from 3 to 9 with a median of 6 and a Mean ± SD of 6.27 ± 1.46 with difficult score of 96 and 104 was easy score. Surgical difficulty score of patients ranged from 1 to 4 with a median of 2.00 and with a Mean ± SD of 2.44 ± 1.07 with difficult score of 83 and 117 was recorded as easy score(Table 2).

Table 2: Assessment of WHARFE Score, Pederson's Difficulty Index Score and Surgical Difficulty Score

Variables	Categories	Statistics Mean ± SD
WHARFE Score	Mean ± SD	5.45 ± 2.40
	Median	5.0000
	Minimum	2.00
	Maximum	12.00
	Difficult	3
	Easy	197
Pederson's Difficulty Index Score	Mean ± SD	6.27 ± 1.46
	Median	6.0000
	Minimum	3.00
	Maximum	9.00
	Difficult	96
	Easy	104
Surgical Difficulty Score	Mean ± SD	2.44 ± 1.07
	Median	2.0000
	Standard Deviation	1.07366
	Minimum	1.00
	Maximum	4.00
	Easy	117
	Difficult	83

Table 3 demonstrated accuracy of WHARFE assessment and Pederson's difficulty index assessment for predicting surgical difficulty. WHARFE assessment demonstrated an accuracy rate of 60.0% in predicting surgical difficulty, along with a p-value of (p=0.001) and Pederson's difficulty index assessment achieved an accuracy rate of 54.5% in predicting surgical difficulty, did not reach statistical significance along with Chi square test with a p-value of (p=0.232)(Table 3).

Table 3: Accuracy of WHARFE Assessment and Pederson's Difficulty Index Assessment

WHARFE Assessment	Surgical Difficulty N (%)		p-Value
	Difficult	Easy	
Difficult	3 (100.0%)	0 (0.0%)	0.001
Easy	80 (40.6%)	117 (59.4%)	
Pederson's Difficulty Index Assessment			
Difficult	44 (45.8%)	52 (54.2%)	0.232
Easy	39 (37.5%)	65 (62.5%)	

DISCUSSION

Assessing the complexity of third molar surgery was crucial for developing an effective treatment plan that minimizes potential complications. To estimate the time needed for tooth removal accurately, it was essential to gather both clinical and radiological data. Over time, numerous attempts have been made to establish a reliable model for this assessment, with several proposed but none universally accepted [17, 18]. Several other notable models have been proposed over time, including those by Winter, Pell and Gregory, Pederson, and the WHARFE classification or scoring systems. These models encompass various criteria, such as Winter's classification, mandible height, second molar angulation, root shape and morphology, follicle development, and exit path. These adopted quantitative scores for each of the parameters and difficulty was estimated based on the total radiographic scoring of the impacted tooth [19, 20]. The findings of this study were comparable with multiple studies conducted worldwide. This study evaluated the predictive accuracy of the WHARFE assessment and Pederson's Difficulty index in a cohort of patients aged 18 to >30. A study by Sekhar, MR *et al.*, had a mean age of 27.04 years (19–49 years) [21]. Demographically, this study represented a diverse patient group, with a median age of 29 years, aligning with previous research on this surgical population. Before extraction, the Pederson index can be used to assess the level of difficulty. In terms of accuracy and usability, a modified parent scale with a postoperative index was thought to be a superior substitute for the Pederson scale [22]. According to results of this study the median surgical procedure duration of 8 minutes fell within the expected range. The mean duration of the procedure of the study was 13.97±8.1. The WHARFE assessment achieved an accuracy rate of 60.0% in predicting surgical difficulty, but a closer look revealed a p value of 0.001. While the accuracy may seem promising on the surface, the p-value suggests a statistical significance. These results have raised concerns about the predictive efficacy of the WHARFE assessment. Pederson's difficulty index, on the other hand, yielded an accuracy rate of 54.5% in predicting surgical difficulty, with a p-value of 0.232. According to study by Janjua OS *et al.*, 44% accuracy of Pederson scale index in assessing third molar surgery [11].

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Numerous indices have been introduced and were employed by clinicians to categorize the complexity of removing impacted third molars. Among these indices, the Pederson and WHARFE indices were commonly used for pre-extraction assessments. However, their effectiveness was constrained, as multiple studies have revealed [23]. In practice, experienced oral and maxillofacial surgeons often consider multiple factors and use their clinical judgment to assess the difficulty of a particular case. This holistic approach takes into account patient-specific characteristics, anatomical variations, and other clinical factors that may affect the surgical procedure's outcome. It's important for clinicians to be aware of the limitations of any assessment tool or index and to use them as a part of a broader clinical evaluation rather than as definitive predictors of surgical difficulty [20]. Nevertheless, the study demonstrates specific limitations that require further examination. An important drawback was the possible restriction imposed by the study's sample size, which could undermine the strength of the results. The relatively moderate accuracy ratings of 60.0% for WHARFE and 54.5% for Pederson's difficulty index indicate that these evaluation tools have only limited predictive powers. This suggests that there was potential for development in these instruments. Moreover, the lack of substantial disparities detected between the evaluations, as evidenced by the p-values, prompts inquiries regarding the therapeutic importance of the identified distinctions.

CONCLUSIONS

It was to be concluded that both assessments showed some ability to predict surgical difficulty, whereas WHARFE assessment demonstrated a predictive accuracy of 60% (p-value 0.001) and the differences observed did reach statistical significance. Study has discovered WHARFE assessment to be a more consistent and reliable measure for the evaluation of surgical difficulty over the Pederson difficulty index.

Authors Contribution

Conceptualization: GR
Methodology: GR, AA, R
Formal analysis: SK
Writing, review and editing: SNI, DS, R

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Jaroń A and Trybek G. The pattern of mandibular third molar impaction and assessment of surgery difficulty: A Retrospective study of radiographs in east Baltic population. International Journal of Environmental Research and Public Health. 2021 Jun; 18(11): 6016. doi: 10.3390/ijerph18116016.

[2] McCarthy C. Comparison between local anaesthetic agents, lidocaine and bupivacaine, in patients undergoing third molar extraction in terms of patient satisfaction. 2020 Oct; 24(10): 3539-3546. doi: 10.1007/s00784-020-03224-5.

[3] Rezaei F, Imani MM, Khavid A, Nabavi A. Patterns of mandibular third molar impaction in an Iranian subpopulation. Pesquisa Brasileira em Odontopediatria e Clínica Integrada.2020 Jul; 20: e5411. doi: 10.1590/pboci.2020.099.

[4] Gupta V and Singh A. Comparing the predictability of surgical outcomes: Wharfevs Pederson in third molar impactions. International Journal of Oral Surgery. 2023 Dec; 76(4): 400-8. doi: 10.7759/cureus.50816.

[5] Roy I, Baliga SD, Louis A, Rao S. Importance of clinical and radiological parameters in assessment of surgical difficulty in removal of impacted mandibular 3rd molars: a new index. Journal of Maxillofacial and oral Surgery. 2015 Sep; 14: 745-9. doi: 10.1007/s12663-014-0731-8.

[6] Chen Y, Zhang K, Liu X. Wharfe assessment and Pederson index: Predictive accuracy in surgical outcomes. Journal of Dental Research.2021 Sep; 100(10): 1200-6. doi: 10.1007/s12663-020-01362-7.

[7] Zhang X, Wang L, Gao Z, Li J, Shan Z. Development of a new index to assess the difficulty level of surgical removal of impacted mandibular third molars in an Asian population.Journal of Oral and Maxillofacial Surgery.2019 Jul; 77(7): 1358-e1. doi: 10.1016/j .joms. 2019.03.005.

[8] Hyam DM. The contemporary management of third molars. Australian Dental Journal. 2018 Mar; 63: S19-26. doi: 10.1111/adj.12587.

[9] Juodzbalys G and Daugela P. Mandibular third molar impaction: review of literature and a proposal of a classification. Journal of Oral & Maxillofacial Research. 2013 Apr; 4(2). doi: 10.5037/jomr.2013.4201.

[10] Varghese G. Management of impacted third molars. Oral and Maxillofacial Surgery for the Clinician. 2021 Feb: 299-328. doi: 10.1007/978-981-15-1346-6_14.

[11] Janjua OS, Baig Z, Manzoor A, Abbas T. Accuracy of Pederson and modified Parant scale for predicting difficulty level of mandibular third molars. Archives Orofacial Science. 2013 Jan; 8(1): 9-13.

DOI: https://doi.org/10.54393/pjhs.v5i12.2444

[12] Menon RK, Gopinath D, Li KY, Leung YY, Botelho MG. Does the use of amoxicillin/amoxicillin-clavulanic acid in third molar surgery reduce the risk of postoperative infection? A systematic review with meta-analysis. International Journal of Oral and Maxillofacial Surgery. 2019 Feb; 48(2): 263-73. doi: 10.1016 /j.ijom .2018. 08. 002.

[13] Kim T, Wang J, Zhao L. Predictive factors of third molar surgery difficulty: A review of the Wharfe and Pederson scales. International Journal Oral Maxillofacial Surgery. 2022; 51(5): 520-6.

[14] Lim S, Chong H, Park J. Wharfevs Pederson: Assessment accuracy in mandibular third molar extractions. Journal of the Korean Association of Oral and Maxillofacial Surgeons. 2021; 47(4): 287-94.

[15] Ahmed N, Rahman F, Aziz M. Comparing surgical difficulty assessments: Wharfe Assessment and Pederson Index in mandibular third molar surgery. Oral Surgery Oral Medicine Oral Pathology and Oral Radiology. 2022; 134(6): 745-51.

[16] Rodriguez E and Silva D. Predictive value of Wharfe and Pederson indices in surgical removal of impacted third molars. Journal of Stomatology Oral and Maxillofacial Surgery. 2023 Sep; 54(2): 103-9. doi: 10.1007/s12663-012-0435-x.

[17] Huang Z, Lee C, Wong S. Comparison of Wharfe and Pederson indices for predicting surgical outcomes of impacted third molars. British Journal of Oral and Maxillofacial Surgery. 2024; 62(1): 15-21.

[18] Kumar P, Patel A, Roy D. Accuracy of the Wharfe Assessment compared with the Pederson Index in mandibular third molar surgeries: A prospective study. Journal of Oral & Maxillofacial Research.2021 Sep; 12(3): e13. doi: 10.1007/s12663-020-01362-7.

[19] Crowley M. Evaluation of the effect of submucosal dexamethasone injection on pain in patients undergoing third molar removal: a randomised controlled trial. PhD Thesis, University College Cork 20 21.

[20] O'Sullivan F and Byrne M. A clinical evaluation of the Wharfe and Pederson scales in predicting third molar surgery complexity. Irish Journal of Medical Science. 2022; 191(4): 1457-63.

[21] Sekhar MR, Singh S, Valluri R. Correlation of variables for WHARFE Assessment and Pederson difficulty Index for impacted mandibular third molar surgery-a prospective clinical study. Journal of Maxillofacial and Oral Surgery. 2021 Sep; 20: 502-6. doi: 10.1007/s12663-020-01362-7.

[22] Cotrin P, Freitas KM, Freitas MR, Valarelli FP, Cançado RH, Janson G. Evaluation of the influence of mandibular third molars on mandibular anterior crowding relapse. Acta Odontologica Scandinavica. 2020 May; 78(4): 297-302. doi: 10.1080 /000 163 57. 201 9.1703142.

[23] Sousa M, Lima R, Costa F. Efficacy of Wharfe Assessment versus Pederson Index in third molar extractions: A randomized study. Revista Brasileira Cirurgia Craniomaxilofacial. 2023; 38(2): 120.

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Original Article

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Role of CA 19-9/CRP Ratio as A Predictor for Malignancy in Obstructed Jaundice Patient

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ABSTRACT

The cancer-antigen-19-9 tumor marker, increases during biliary and pancreatic malignancy. **Objectives:** To determine diagnostic accuracy and role of cancer-antigen-19-9 and C-reactive-protein ratio as a predictor for malignancy in obstructive jaundice patients taking a Computed Tomography scan as the gold standard. **Methods:** A total of 158 patients were admitted with obstructive jaundice in Al-Tibri Hospital. Cancer-antigen-19-9 was adjusted by dividing it with the C-reactive-protein value. Malignancy was considered based on computed tomography scan findings. Specificity, sensitivity, negative predictive value, positive predictive value, and diagnostic accuracy of cancer antigen-19-9 to C-reactive protein ratio were calculated. **Results:** There were 57.6% male and 42.4% female patients. The mean cancer antigen-19-9 and C-reactive-protein ratio was 51.39 ± 69.40 U/ml. The significant p-values (<0.001) confirm meaningful differences in CA19-9/CRP ratios between benign and malignant cases, but low sensitivity (63.2%) and negative predictive value (46.8%) limit its clinical utility as a standalone tool. A total of 50% of patients were diagnosed as benign and 50% as malignant by cancer antigen-19-9 and C-reactive-protein ratio. However, 27.8% of patients were diagnosed as benign and 72.2% as malignant by computed tomography scan. Sensitivity, Specificity, positive predictive value, negative predictive value and accuracy were 63.2%, 84.1%, 91.1%, 46.8%, and 68.98% respectively. **Conclusions:** It was concluded that the cancer-antigen-19-9/CRP ratio while exhibiting moderate overall diagnostic accuracy (68.98%), provides significant diagnostic specificity (84.1%) and positive predictive value (91.1%). These characteristics make it a valuable supplemental tool for confirming malignancy in obstructive jaundice patients, particularly when used alongside other diagnostic modalities.

INTRODUCTION

Obstructive jaundice, a common clinical condition, results from the blockage of bile flow due to benign or malignant causes, including pancreatic and biliary cancers. Differentiating between these etiologies is critical for timely diagnosis and management, as malignant causes require prompt intervention to improve prognosis. Biomarkers like Cancer Antigen (CA) 19-9 have been widely used in diagnosing malignancies associated with obstructive jaundice, but their diagnostic accuracy is often limited by elevated levels in benign inflammatory conditions such as pancreatitis or cholangitis [1-3]. These limitations necessitate the exploration of novel diagnostic approaches to enhance specificity and sensitivity in detecting malignancy. CA19-9, a carbohydrate antigen, is a tumor marker commonly elevated in pancreatic biliary malignancies. Despite its utility, studies have highlighted its nonspecific elevation in benign conditions, reducing its reliability as a standalone diagnostic tool [4-6]. Similarly, inflammatory markers like C-reactive protein (CRP) have demonstrated limited specificity when used independently. The combination of these markers, however, offers a promising avenue for improving

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diagnostic accuracy. Emerging evidence suggests that the CA19-9/CRP ratio may help differentiate between malignant and benign causes by integrating tumor marker levels with systemic inflammatory responses [7]. This study aims to evaluate the diagnostic utility of the CA19-9/CRP ratio in predicting malignancy in obstructive jaundice. By analyzing its diagnostic accuracy, sensitivity, specificity, and predictive value, the study seeks to address the limitations of standalone biomarkers and contribute to the development of more effective diagnostic strategies. Previous research has underscored the need for innovative biomarker combinations to improve diagnostic precision, particularly in resource-constrained settings where advanced imaging modalities may not be readily available [8]. Understanding the clinical implications of the CA19-9/CRP ratio could significantly impact the management of patients with obstructive jaundice. By providing a supplemental diagnostic tool, this study aims to aid clinicians in stratifying patients for further evaluation, reducing diagnostic delays, and improving outcomes in malignancy-associated cases. The findings will also contribute to the growing body of literature advocating for integrative biomarker approaches in oncology diagnostics. This study aims to determine diagnostic accuracy and the role of CA19-9 and CRP ratio as a predictor for malignancy in obstructive jaundice patients taking computed tomography (CT) scans as a gold standard.

METHODS

The cross-sectional validation study was conducted by enrolling the obstructive jaundice patients, admitted to Al-Tibri Hospital, Karachi by the approval of the institutional ethical review committee via approval number IERC/ATMC/14(01-2024)/20. This research was carried out from 27 May to 21 September 2024. The sample size was 158 calculated by using a sample size calculator for sensitivity and specificity, taking the prevalence of malignancy in obstructive jaundice as 29.8%, sensitivity 82.3%, specificity 45% with a margin of error of 11% for sensitivity and 10% for specificity at a confidence interval of 95% [9], non-probability consecutive sampling was used. Patients having a value of total bilirubin >1.2 mg/dl and alkaline phosphatase >136 U/L were considered obstructive jaundice patients. The standard cutoff CRP value for this research was considered 1.5 mg/L, and the nominal cut-off threshold level for CA19-9 was 32 U/mL. Patients with obstructive jaundice as per operational definition with no CBD or gallstones on ultrasound and age of 30 to 70 years were included in the study. Patients with cause of jaundice other than obstruction, non-consenting patients and those already diagnosed with malignancy were excluded from this study. The CA19-9 and CRP ratio was calculated. The patients were declared as malignant jaundiced patients based on a CT scan abdomen with pancreatic protocol findings. All the data were noted on a structured questionnaire after obtaining consent. Data were entered and analyzed by using SPSS version 22.0. Mean and standard deviation were computed for quantitative variables. Frequency and percentage were calculated for categorical variables. A table was made for calculating diagnostic accuracy, sensitivity, specificity, NPV and PPV of CA19-9 to CRP ratio taking CT scan as the gold standard.

RESULTS

A total of 158 patients with obstructive jaundice, aged 30 to 70 years, were included in the study. Of these, 50% were classified as benign and 50% as malignant based on the CA19-9 and CRP ratio. Table 1 presents the descriptive statistics of CA19-9 and CRP ratio values for each group. The mean CA19-9/CRP ratio in malignant cases (94.05 ± 76.99 U/mL) was significantly higher than in benign cases (8.73 ± 9.06 U/mL). Similar trends were observed for other metrics, such as median and range, indicating that CA19-9 and CRP ratios differ markedly between benign and malignant cases, reinforcing their potential diagnostic relevance (Table 1).

Table 1: Descriptive Statistics of CA 19-9 And CRP Ratio (U/Ml) among Benign and Malignant Patients Diagnosed by CA 19-9 and CRP Ratio (n=158)

Variables	Benign (79)	Malignant (79)
Mean + SD	8.73 ± 9.06	94.05 ± 76.99
Median	4.20	78.20
Range	30.98	621.80
Minimum	0.02	36.40
Maximum	31.00	658.20

Among patients diagnosed as benign or malignant based on CT scan findings, the CA19-9/CRP ratio showed marked differences between the two groups. Malignant cases had a significantly higher mean CA19-9/CRP ratio (66.54 ± 75.34 U/mL) compared to benign cases (12.14 ± 22.04 U/mL). The median CA19-9/CRP ratio for malignant cases (56.70 U/mL) was also substantially higher than that for benign cases (3.41 U/mL), with a wide range observed in both groups (Table 2).

Table 2: Descriptive Statistics of CA 19-9 and CRP Ratio (U/Ml) among Benign and Malignant Patients Diagnosed by CT Scan Findings (n=158)

Variables	Benign (44)	Malignant (114)
Mean + SD	12.14 ± 22.04	66.54 ± 75.34
Median	3.41	56.70
Range	92.90	658.18
Minimum	0.10	0.02
Maximum	93.00	658.20

Among patients who were diagnosed benign and malignant by CT scan findings, the mean CA19-9 was 139.65 ± 253.78

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U/ml and 949.20 ± 1065.54 U/ml respectively. The mean CRP was 14.36 ± 13.26 U/ml and 25.92 ± 35.29 U/ml respectively. Here too, the CA19-9/CRP ratio was significantly higher in malignant cases compared to benign cases (p<0.001) (Table 3). The ratio demonstrated high specificity (84.1%) and positive predictive value (PPV) (91.1%), indicating its strong ability to correctly identify benign cases and confirm malignancy in positive cases, respectively. However, its sensitivity (63.2%) and negative predictive value (NPV) (46.8%) were moderate to low, suggesting it misses a proportion of true malignancy cases and has limited reliability in ruling out malignancy. The overall diagnostic accuracy was moderate at 68.98%, and the observed differences between diagnostic classifications based on the CA19-9/CRP ratio and CT scan findings were statistically significant (p<0.001).

Table 3: Diagnostic Accuracy of CA 19-9 and CRP Ratio for Predicting Malignancy in Obstructive Jaundice Patients with CT Scan Findings as Gold Standard (n=158)

CA 19-9 and CRP Ratio	CT Scan Findings		Total CA19-9 and CRP Ratio	p-value
	Malignant n (%)	Benign n (%)		
Malignant	72 (91.1)	7 (8.9)	79	<0.001*
Benign	42 (53.2)	37 (46.8)	79	
Total CT scan	114	44	158	
Sensitivity	Specificity	PPV	NPV	Accuracy
63.2%	84.1%	91.1%	46.8%	68.98%

*p-value <0.001 indicates a highly significant difference as determined by the Chi-square test

DISCUSSION

This study evaluates the CA19-9/CRP ratio as a diagnostic marker for malignancy in patients with obstructive jaundice. Despite showing potential as an adjunct tool with advanced imaging and histopathology, the diagnostic accuracy of 69% indicates significant limitations, suggesting its inadequacy as a standalone diagnostic test. The sensitivity and specificity of the CA19-9/CRP ratio highlight its moderate ability to distinguish between benign and malignant causes of obstructive jaundice. While such markers can aid in stratifying patients for further diagnostic evaluation, their relatively low accuracy underscores the risk of false positives or negatives. This aligns with previous findings that inflammatory biomarkers, while supportive, often lack sufficient reliability to independently guide clinical decision-making [10, 11]. Previous research has extensively explored the utility of CA19-9 and CRP as standalone markers in diagnosing malignancy, particularly in pancreatic and biliary diseases. Studies such as Zhou *et al.*, and Lyu *et al.*, highlighted the diagnostic limitations of CA19-9 due to its nonspecific elevation in benign inflammatory conditions like pancreatitis or cholangitis [11, 12]. Similarly, CRP has been examined for its role in malignancy detection but is hampered by its broad response to inflammatory stimuli regardless of malignancy status [13]. This study is innovative in its evaluation of the CA19-9/CRP ratio, offering an integrative approach that compensates for the shortcomings of standalone markers. Unlike earlier studies that analyzed these biomarkers individually, this research highlights the utility of their combined use to improve diagnostic precision. This is consistent with trends in oncology diagnostics that favoured multidimensional approaches, as reflected in recent meta-analyses advocating for composite biomarker strategies [14, 15]. The specificity observed in this study was notably high, at 84.1%, underscoring the CA19-9/CRP ratio's ability to effectively rule out non-malignant conditions. Furthermore, the positive predictive value (PPV) of 91.1% highlights its clinical relevance by accurately identifying cases more likely to be malignant. These high values reinforce the potential of the CA19-9/CRP ratio as a supplemental diagnostic tool, particularly in settings where diagnostic resources are constrained. By leveraging a novel metric and achieving high specificity and PPV, this study provides a valuable addition to the existing literature. It aligns with the growing interest in refining diagnostic methodologies to balance accuracy with resource efficiency, thus setting a foundation for further exploration and validation in broader clinical settings. Given the suboptimal accuracy observed, the CA19-9/CRP ratio cannot be recommended as a primary diagnostic tool for malignancy in obstructive jaundice. Instead, it should be considered a supplementary marker within a multimodal diagnostic framework. Combining it with imaging techniques, histopathology, and other advanced biomarkers could enhance overall diagnostic accuracy [16, 17]. Efforts should focus on refining biomarker panels and integrating them into a multimodal diagnostic approach to improve clinical outcomes. Investigating additional inflammatory markers or genetic and proteomic profiles may provide more comprehensive diagnostic tools for malignancies in obstructive jaundice [18-20].

CONCLUSIONS

It was concluded that while the CA19-9 and CRP ratio show potential in enhancing the specificity (84.1%) and positive predictive value (91.1%) for malignancy detection in obstructive jaundice, its overall diagnostic accuracy remains moderate (68.98%). The sensitivity (63.2%) and negative predictive value (46.8%) suggest limited reliability in ruling out malignancy. This suggests that the CA19-9/CRP ratio can be a valuable adjunct in diagnostic frameworks, particularly when used in combination with other diagnostic modalities like imaging and histopathology.

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Authors Contribution

Conceptualization: RK, MM
Methodology: AA, RK, MF, MM
Formal analysis: RK, MF
Writing review and editing: WA

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

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REFERENCES

[1] Lee T, Teng TZ, Shelat VG. Carbohydrate Antigen 19-9—Tumor Marker: Past, Present, And Future. World Journal of Gastrointestinal Surgery.2020 Dec; 12(12): 468. doi: 10.4240/wjgs.v12.i12.468.

[2] Mittal D, Singh J, Kaur M, Kumar A, Kaur A. To Estimate the Levels of Ca19-9 and Its Significance in the Diagnosis and Treatment of Pancreatic Biliary and Gastrointestinal Malignancies. Asian Journal of Pharmaceutical and Clinical Research.2022;15(5):125-7. doi: 10.22159/ajpcr.2022.v15i5.44365.

[3] Ghallab M, Abosheaishaa H, Gupta I, Abdelmoteleb S, Stern R. A Case of Choledocholithiasis and Obstructive Jaundice with A Very High Serum Carbohydrate Antigen 19-9(CA 19-9)Level: A Case Report and Review of Literature. Cureus.2022 Dec;14(12).doi:10.7759/cureus.32447.

[4] Zhao B, Cheng Q, Cao H, Zhou X, Li T, Dong L *et al.* Dynamic Change of Serum CA19-9 Levels in Benign and Malignant Patients with Obstructive Jaundice After Biliary Drainage and New Correction Formulas. BioMed Central Cancer.2021 May; 21(1): 517. doi: 10.1186/s12885-021-08204-w.

[5] Utsumi M, Inagaki M, Kitada K, Tokunaga N, Kondo M, Yunoki K *et al*. Preoperative C-Reactive Protein-To-Albumin Ratio as a Prognostic Factor in Biliary Tract Cancer: A Systematic Review and Meta-Analysis. Medicine.2023 Jun; 102(22): e33656. doi: 10.1097/MD.0000000000033656.

[6] Ghallab M, Abosheaishaa H, Gupta I, Abdelmoteleb S, Stern R. A Case of Choledocholithiasis and Obstructive Jaundice with A Very High Serum Carbohydrate Antigen 19-9(Ca 19-9)Level: A Case Report and Review of Literature. Cureus.2022 Dec;14(12).doi:10.7759/cureus.32447.

[7] Giron F and Alcantar D. Looks Can Be Deceiving: A Case Report On the Clinical Value of CA 19-9 in Obstructive Jaundice. Cureus.2020 Jan; 12(1).doi: 10.7759/cureus.6637.

[8] Shah M, Gonzalez F, Chernyavsky S. S1650 Severely Elevated CA19-9: Benign or Malignant? Official Journal of the American College of Gastroenterology.2021 Oct; 116:S739-40.doi:10.14309/01.ajg.0000780132.29425.af.

[9] La Greca G, Sofia M, Lombardo R, Latteri S, Ricotta A, Puleo S *et al.* Adjusting CA19-9 Values to Predict Malignancy in Obstructive Jaundice: Influence of Bilirubin and C-Reactive Protein. World Journal of Gastroenterology.2012 Aug;18(31):4150.doi:10.3748/wjg.v18.i31.4150.

[10] Kim HS, Han Y, Kang JS, Kang YH, Lee M, Sohn HJ *et al.* Serum Carcinoembryonic Antigen and Carbohydrate Antigen 19-9 As Preoperative Diagnostic Biomarkers of Extrahepatic Bile Duct Cancer. British Journal of Surgery Open.2021 Nov;5(6):zrab127.doi:10.1093/bjsopen/zrab127.

[11] Zhou X. Meta-Analysis of the Diagnostic Performance of Serum Carbohydrate Antigen 19-9 for diagnosing Gallbladder Cancer. The International Journal of Biological Markers.2022 Mar; 37(1): 81-9. doi: 10.11 77/17246008211068866.

[12] Lyu SC, Wang J, Huang M, Wang HX, Zhou L, He Q *et al.* CA19-9 Level to Serum γ-Glutamyl-transferase as a Potential Prognostic Biomarker in Patients with Pancreatic Head Carcinoma. Cancer Management and Research.2021 Jun: 4887-98. doi: 10.2147/ CMAR. S313517.

[13] Ghosh S, Baruah M, Yadav AK, Das AK. Role of CA 19-9 and its Ratio with CRP and Total Bilirubin in Differentiating Malignant from Benign Obstructive Jaundice. Journal of Clinical and Diagnostic Research. 2019 Jan; 13(1). doi: 10.7860/JCDR/2019/38019.12477.

[14] Azam MG, Chowdhury AA, Sajjad SM, Datta IK, Rahman MA, Rowshon AH. Diagnostic Role of CA19-9, CA19-9/CRP Ratio and CA19-9/Total Bilirubin Ratio in Differentiating Benign and Malignant Obstructive Jaundice. Bangladesh Journal of Medicine.2023 May; 35(2): 165-6. doi: 10.3329/bjm.v35i20.73261.

[15] Boyd LN, Ali M, Leeflang MM, Treglia G, de Vries R, Le Large TY *et al.* Diagnostic Accuracy and Added Value of Blood-Based Protein Biomarkers for Pancreatic Cancer: A Meta-Analysis of Aggregate and Individual Participant Data. E Clinical Medicine.2023 Jan; 55: 101747. doi: 10.1016/j.eclinm.2022.101747.

[16] Liu W, Liu Q, Wang W, Wang P, Chen J, Hong T *et al.* Differential diagnostic roles of the Serum CA19-9, Total Bilirubin (TBIL) and the Ratio of CA19-9 To TBIL for Benign and Malignant.Journal of Cancer.2018; 9(10) : 1804. doi: 10.7150/jca.25093.

DOI: https://doi.org/10.54393/pjhs.v5i12.2123

[17] Zhang W, Wang Y, Dong X, Yang B, Zhou H, Chen L *et al.* Elevated serum CA19-9 indicates severe liver inflammation and worse survival after curative resection in hepatitis B-related hepatocellular carcinoma. Bio-Science Trends.2021 Dec; 15(6): 397-405. doi: 10.5582/bst.2021.01517.

[18] Wu Z, Zhao P, Wang Z, Huang X, Wu C, Li M *et al.* Adjusting CA19-9 Values with Clinical Stage and Bilirubin to Better Predict Survival of Respectable Pancreatic Cancer Patients: 5-Year-Follow-Up of A Single Center. Frontiers in Oncology.2022 Jul; 12: 966256. doi: 10.3389/fonc.2022.966256.

[19] Sayed MM, Elshafie AI, Lotfy M, Abdelhakam SM, Rushdy M. Clinical Significance of Serum CA 19-9, CA 19-9/CRP Ratio and CA19-9/Total Bilirubin Ratio in Differentiation Between Malignant and Benign Obstructive Jaundice. European Academic Research. 2017; 12: 10271-91.

[20] Huang X, Lu Z, Zhang K, Wang G, Cai B, Wu P *et al.* Prognostic Impact of the Ratio of Preoperative CA19-9 to Liver Enzyme Levels in Pancreatic Cancer Patients with Jaundice (Predictability of Combined CA19-9/AST and CA19-9/γ-GGT for Jaundiced PDAC Patients). Pancreatology.2021 Sep; 21(6): 1092-101. doi: 10.1016/j.pan.2021.05.300.

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Understanding the Interplay of Perceived Stress, Perceived Social Support and Quality of Life in Pregnant Females

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ABSTRACT

The journey of pregnancy or motherhood is transformative, offering fulfillment and joy alongside natural concerns. This phase entails both physiological and emotional shifts, impacting quality of life. Social support enhances the quality of life by improving coping abilities to effectively deal with prenatal stress. **Objective:** To assess predictive association of perceived stress, perceived social support, and quality of life of pregnant women; and the mediating role of perceived social support in pregnant women's perceived stress and quality of life. **Methods:** This correlational cross-sectional study was conducted from December-2022 to January-2023 upon 150 pregnant females (x̄-age 26.5 years) selected from gynae OPDs of different hospitals in Karachi, Pakistan through purposive sampling. Urdu versions of Perceived Stress Scale, Multidimensional Scale of Perceived Social Support and the Quality-of-Life questionnaire were used to collect the data. **Results:** The significant predictive association was found between perceived stress and quality of life (R^2= .17, β=-.108, p=<.001), and perceived social support and quality of life of pregnant women (R^2=.036, β=-.189, p<.001). Furthermore, Mediation analysis showed that perceived social support partially mediated the association between perceived stress and QoL of pregnant women (R^2=.164, F= 15.64, p<.001). **Conclusions:** It may be concluded that perceived social support positively predicts QOL, while perceived stress negatively predicts QOL in pregnant females. Moreover, PSS mediate the relationship between PS and QOL in this population. Policy making, targeted intervention and support from family, and health practitioners would help reduce the distress level and enhance QoL of pregnant females.

INTRODUCTION

Pregnancy is acknowledged as a challenging journey in the life of a woman navigating productivity, demanding substantial psychological adjustments [1]. Yet, it is frequently presented as an exciting time along with the distress [2]. Expectant mothers often experience apprehension about the uncertainties surrounding childbirth, parenthood, financial and professional adjustments, emotional challenges, and relationship with their partner [3]. These initial changes render them susceptible, both physically and mentally. Even during an uncomplicated pregnancy, these transformations can hinder a woman's capacity to fulfill her regular responsibilities [4]. QOL is a crucial concept that effectively captures both positive and negative elements contributing to the well-being of a population or individual at a precise point in time. Perceived quality of life among women is crucial in the realm of perinatal well-being that covers physical, mental health, and societal aspects. PSS pertains to how individuals perceive the presence and sufficiency of their social connections as perception of social support during stressful periods can positively influence health by reshaping insights of risk, reducing anxiety, and enhancing managing skills [5]. Furthermore, the cognitive facets of social support might act as a protective barrier, mitigating the physiological response to stress [6]. The primary foundations of assistance for a pregnant woman, involving her partner, spouse, family, friends, midwife, and doctor, play a pivotal role in delivering essential aid. Numerous pregnant mothers encounter significant stress, often representing one of the most

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profound challenges they will ever confront. Perceived stress refers to the emotions or mental perceptions a person experiences concerning the intensity of stress from a particular occasion or condition, either at an exact instant or in a period of time [7]. There is a complex and crucial link between pregnant women's social support and their quality of life throughout pregnancy. Pregnant women find solace in the supportive embrace of social networks, which have an impact on more than just companionship; it permeates the domains of emotional HEALTH, mental wellness, and general happiness. Both the mother's and the unborn child's well-being are impacted by the complex web of variables that is revealed when one examines the relationship between PSS and pregnancy QOL. Studies showed that when pregnant women have more social support, they have a better QOL in terms of their health [8]. Considering the notable prevalence of elevated stress levels reported among surveyed women, it is noteworthy to highlight that pregnancy necessitates a range of adjustments and encounters that contribute to heightened emotional susceptibility to psychosocial factors [7]. Stress manifests in daily life and is observable in regular interpersonal interactions. Numerous studies have individually investigated the connections between PSS, PS, and the QOL among pregnant women. However, this study stresses the position of examining collective impact of these variables within the context of this research. Furthermore, the study exclusively focuses on women experiencing their first pregnancies, as this cohort offers a diverse range of experiences within the interplay of these variables. As the literature on this specific intersection of PS, PSS, and QOL among pregnant women is relatively limited, so this research intends to fill this gap and provide significant new information to what is already known.

The study designed to investigate predictive relationship among PSS, PS, and QOL. It was hypothesized that PSS would act as a mediator of PS and QOL.

METHODS

The correlational cross-sectional study was carried out from December 2022 to January 2023 upon 150 pregnant females with aged between 18-37 years (M=26.5; SD=4.5). The sample size was estimated through G*power software, which revealed a mandatory sample size of 150 participants to detect a medium effect size ($f^2 = 0.15$) with 80% power at α= 0.05. Participants were approached from obstetric departments of various private and Government hospitals in the city of Karachi by using purposive sampling technique that was used to ensure the inclusion of participants with relevant experiences to address the study's objectives effectively. After getting endorsement from Ethical Review of Research Committee [Letter No: ICP-1(101) 5945] of the Institute of Clinical Psychology, University of Karachi. Participants involved in the study willingly provided their consent by signing a form indicating their consent to take part in the research and they were given the freedom and right to opt out at any given time without facing any repercussions. Furthermore, it was emphasized that all data gathered during the study would be handled with confidentiality. The inclusion criteria of study focused on first-time expectant mothers and all trimesters to gain a comprehensive understanding of their unique journey. Pregnant women with existing health issues, such as heart problems or anemia and those with known conditions or taking medications were excluded from the research to focus on the impact of pregnancy, on participants that are medically fit specifically selected from this group to explore the unique challenges of first-time pregnancy in this age bracket. This research involved the administration of informed consent form, demographic form, and urdu versions of PSS [9, 10], MSPSS [11, 12], and QOL of Physiological Pregnancy Scale [13]. The Perceived Stress Scale consists of 10 items that was applied in evaluating stress levels present in people. The marking was done on a 5-point Likert questionnaire where the participants can respond on a 0 representing 'Never" to a 4 representing "Very Frequently". The cronbach's alpha reliability of scale is 0.89. The sum score ranges from 0-40 and as would be expected, higher scores reflect greater levels of perceived stress. The MSPSS is a brief assessment measure called the Multidimensional Scale of Perceived Social Support and specifically designed for measuring people's appraisal of the adequacy of available social support with reference to the care from family members, friends and significant other. The MSPSS is made up of 12 items and assesses perception of support using the Likert rating that includes Very Strongly Agree (7), Strongly Agree (6) Agree (5), Moderately Agree (4), Neutral (3), Moderately Disagree (2) and Very Strongly Disagree (1). Cronbach's alpha reliability of scale is .78. QOL in pregnant females was assessed using QOL of the Physiological Pregnancy Scale. The 9-items questionnaire aims to capture the physical, psychological, and social experiences that significantly impact the QoL of pregnant women. Cronbach's alpha reliability was .80. SPSS version 25.0 was used to analyze the variables of the study.

RESULTS

Table 1 outlined the demographic information of the participants of the study. It shows that 41.3% of the participants had qualification post Masters, 32% hold Master's degree while 16.7% completed graduation. A significant portion of the data showed that the participants were homemaker (i.e., 76.7%) and belonged to Middle (42%) to lower middle socioeconomic status (40%). 88.7% of the participants were from joint family system, and had no

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history of abortions (i.e., 86.7%) and no miscarriages (i.e., 71.3%). 21.3% of the participants had their first trimester, 30.7% had second trimester, while 48% were in their third trimester of their pregnancies at the time of data collection. These demographic details offered a thorough insight into the characteristics of the individuals involved in the study.

Table 1: Demographic Characteristics of Participants (n=150)

Demographic Characteristics	N (%)
Education	
Middle	1 (0.7%)
Matric	4 (2.7%)
Intermediate	10 (6.7%)
Graduation	25 (16.7%)
Masters	48 (32.0%)
Post-Masters	62 (41.3%)
Occupation	
Student	9 (6.0%)
Govt-Employees	3 (2.0%)
Private job	20 (13.3%)
Homemaker	115(76.7%)
Other	3 (2.0%)
Socio-Economic Status	
Poor	11 (7.3%)
Lower middle	60 (40.0%)
Middle	63 (42.0%)
Upper Middle	16 (10.7%)
Family System	
Joint	133 (88.7%)
Nuclear	17 (11.3%)
Gestation Period	
First Trimester	32 (21.3%)
Second Trimester	46 (30.7%)
Third Trimester	72 (48.0%)
Planning	
Yes	94 (62.7%)
No	56 (37.3%)
Abortion Times	
No	130 (86.7)
Natural way	15 (10.0%)
Medical way	5 (3.3%)
Miscarriage Times	
No	107 (71.3%)
Naturally	31 (20.7%)
Medical way	12 (8.0%)

Table 2 showed perceived social support with data that indicates the mean score of the sample of study and good internal consistency of the scale.

Table 2: Descriptive Statistics and Reliability Analysis of Perceived Stress Scale (PSS) (n=150)

Variable	Minimum	Maximum	Mean ± SD	Cronbach's Alpha
PSS	16	95	64.09 ± 15.22	0.914

*PSS (Perceived Stress Scale)

Table 3 showed perceived stress with data that indicates the mean score of the sample of study and good internal consistency of the scale.

Table 3: Descriptive Statistics and Reliability Analysis of Pain Scale (PS) (n=150)

Variable	Minimum	Maximum	Mean ± SD	Cronbach's Alpha
PS	0	69	18.47 ± 9.96	0.677

*PS (Pain Scale)

Table 4 showed quality of life with the data that indicates the mean score of the sample of study and good internal consistency of the scale.

Table 4: Descriptive Statistics and Reliability Analysis of Quality of Life (QOL) (n=150)

Variable	Minimum	Maximum	Mean ± SD	Cronbach's Alpha
QOL	17	44	33.67 ± 5.94	0.872

*QOL (Quality of Life)

Table 5 resulted showed that PSS has been found a statistically significant predictor of perceived QOL of the research participants. PSS accounts for 36% of the variance in outcome variable i.e., quality of life, and model demonstrates significance as (R^2 = 0.036, β = 0.189) **p < 0.001.

Table 5: Linear Regression Analysis with the PSS as a Predictor of QOL of Pregnant Women (n=150)

Variable	Beta	SE	95% CI		B	p-Value
			LL	UL		
Constant	25.15	2.27	20.65	29.64	-	-
PSS	0.132	0.034	0.064	0.201	0.334	0.000**

**p < 0.001

* PSS (Perceived Stress Scale)

Table 6 resulted suggested that Perceived Stress (PS) has been found to be a statistically significant predictor of perceived QOL of the research participants. Perceived stress accounts for 17% of variance in outcome variable i.e., QOL, and the model demonstrates significance as (R^2 = 0.017, β = 0.108) **p < 0.001.

Table 6: Regression Analysis with the Perceived Stress as a predictor of Quality of Life of Pregnant Women (n=150)

Variable	Beta	SE	95% CI		B	p-Value
			LL	UL		
Constant	36.59	1.174	34.26	38.91	-	-
PSS	-0.146	0.054	-0.249	-0.042	-0.248	0.006*

*p < 0.001

* PS (Pain Scale)

Mediation analysis has been done with the Mediation Model (Model 4) using Hayes Process Macro to see mediation effect of PSS on association among PS and QOL. The indirect effect of PSS on QOL is significant; effect = -0.026, bootstrapped SE = 0.246, 95% CI [-0.0747 to -0.0024]. A direct effect of PS on QOL is also significant. This model

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says that PSS mediates partially the association among PS and QOL (Table 7).

Table 7: Summary of Mediation affects PSS on the Relationship between PS and QOL (n=150)

Path	Coefficient	SE	CI	p-Value
Path a (PS-PSS)	-0.2210	0.1242	-0.466 to -0.024	0.024
Path b (PSS-QOL)	0.121	0.031	-0.059 to 0.182	0.007
Total Effect (c: PS →QOL	-0.1894	0.049	-0.286 to -0.092	0.000
Direct Effect, c'(PS→QOL)	-0.162	0.048	-0.257 to -0.068	0.000
Indirect Effect: a*b (PS→QOL)	-0.026	0.019	-0.075 to -0.002	-

*p<0.001. Bootstrap Sample = 5000

*QOL (Quality of Life)

* PSS (Perceived Stress Scale)

* PS (Pain Scale)

Mediation analysis indicated the PSS is indirectly related to quality of life by its relationship with PS. As can be seen in Figure 1, perceived social support reported a high association with PS (a = -0.2210, p = 0.024) as compared to a lower relationship among PS and QOL (b = 0.121, p = 0.007). Based on 5000 bootstrap samples, a 95% bias-corrected confidence interval presented that the indirect effect (c' = -0.162) was entirely more than zero (-0.075 to - 0.002). Moreover, perceived social support reported a higher quality of life even after considering the indirect effect of PS (ab = -0.026, p = 0.000) (Figure 1).

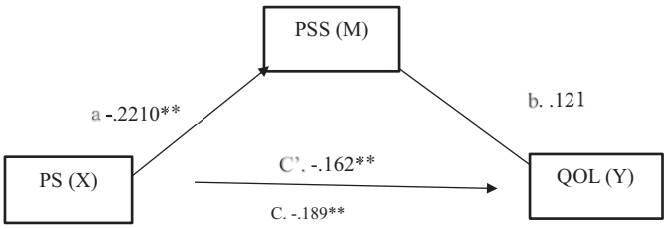

Figure 1: Mediation Model of PSS (M) on the Association between PS (X) and QOL (Y)

DISCUSSION

This study found predictive relationship of PSS and PS, on QOL and mediating effect of PSS on PS and QOL. The results revealed that PSS positively predicted QOL whereas perceived stress negatively predicted QOL. This indicated that pregnant ladies with high PSS will be able to reduce PS and have a better quality of physical, emotional, social, and functional life. The findings of this study is currently one of the few validations of this relationship as supported by the findings that pregnant women's PSS and QOL was measured and concluded that high social support enhances the health-related quality of life of women with pregnancy [8]. It further explored that pregnant women's observations of social support is found to be associated with lower levels of anxiety and other negative emotions while measuring life quality and satisfaction [14]. The research findings are aligned with the study in which they investigated the immediate impact of social support on Health-Related QOL and explore mediating role of social support in correlation between PS and health related QoL throughout pregnancy [15]. The study unveils significant findings with implications for understanding these interconnections in their correlational study found that stress was contrariwise and significantly connected with social support and QOL [16]. Also, social support had a direct and significant correlation with the QOL. The study of revealed a notable negative relationship among the level of PSS and the extent of PS as well as positive relationship with enhancement of QOL of pregnant women [17, 18]. PSS throughout pregnancy enhanced women's overall evaluation of their experiences, as found that the ratio of difficulties to improvements in one's quality of life on a daily basis is inversely correlated with substantial social support [15]. Uplifts and good experiences in QOL occurred more often in groups with high levels of social support, but hassles occurred less frequently in groups with low levels of support [15]. The results of study also align to the study of in which they investigate the immediate impact of social support on Health-Related Quality of Life and found mediating role of social support in correlation between PS and QoL throughout pregnancy [15]. The study unveils significant findings with implications for understanding these interconnections. Moreover, studies have also revealed that pregnant women who get sufficient social support are more likely to be attentive to pregnancy-related changes, motivating them to adopt beneficial maternity care behaviors [19]. Studies also revealed that provision of support from health care providers significantly reduce anxiety regarding child care after delivery [20]. The study's limitations include the cross-sectional design, which captures data at a single point, hindering the assessment of evolving relationships among variables. Cultural influences and purposive sampling may limit the generalizability of findings, as the results may not apply to diverse cultural contexts. Additionally, shifts in perceived support, stress, coping mechanisms, and quality of life throughout pregnancy remain unexplored, highlighting the need for longitudinal research.

CONCLUSIONS

To sum up, this study showed that expectant women experienced different QOL depending on their psychological well-being that PSS was a positive predictor of QOL, and PS was a negative predictor of QOL. Moreover, perceived social support played a mediating role between PS and QOL in females with pregnancy. The findings suggest that improving perceived social support and reducing stress perceptions can further enhance the QOL of pregnant women.

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Authors Contribution

Conceptualization: RM
Methodology: RM, AA
Formal Analysis: RM, AA
Writing, review and editing: RM, AA

All authors have read and agreed to the published version of the manuscript

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REFERENCES

[1] Khouj MA, Albasri S, Albishri AA, Softa SM, Almaslamani AS, Ahmad HM. Prevalence of stress, anxiety, and depression among pregnant women in Jeddah. Cureus.2022 Jul; 14(7).doi:10.775 9/ cureus.27174.

[2] Rabipoor S and Abedi M. Perceived stress and prenatal distress during pregnancy and its related factors. Journal of Research Development in Nursing and Midwifery.2020Apr;17(1):67-80.doi:10.29252/ jgbfnm .17.1.67.

[3] Skurzak A, Korżyńska-Piętas M, Kicia M, Iwanowicz-Palus GJ. Social support for pregnant women. General Medicine & Health Sciences/Medycyna Ogólna i Nauki o Zdrowiu. 2021 Jan; 27(1). doi: 10.26444/monz/131992.

[4] Boutib A, Chergaoui S, Marfak A, Hilali A, Youlyouz-Marfak I. Quality of life during pregnancy from 2011 to 2021: systematic review. International Journal of Women's Health.2022 Dec: 975-1005. doi: 10.2147 /IJW H.S361643.

[5] Eagle DE, Hybels CF, Proeschold-Bell RJ. Perceived social support, received social support, and depression among clergy. Journal of Social and Personal Relationships. 2019 Jul; 36(7): 2055-73. doi: 10.1177/0265407518776134.

[6] Gallagher S, O'Súilleabháin PS, Smith MA. The cardiovascular response to acute psychological stress is related to subjectively giving and receiving social support. International Journal of Psychophysiology. 2021Jun; 164:95-102.doi:10.1016/j.ijpsycho.2021.03. 004.

[7] Engidaw NA, Mekonnen AG, Amogne FK. Perceived stress and its associated factors among pregnant women in Bale zone Hospitals, Southeast Ethiopia: a cross-sectional study. BioMed Central Research Notes. 2019 Dec; 12: 1-6. doi: 10.1186/s13104-019-4383-0.

[8] Gul B, Riaz MA, Batool N, Yasmin H, Riaz MN. Social support and health related quality of life among pregnant women. The Journal of the Pakistan Medical Association. 2018 Jun; 68(6): 872-5.

[9] Cohen S and Wills TA. Stress, social support, and the buffering hypothesis. Psychological Bulletin.1985 Sep; 98(2): 310. doi: 10.1037//0033-2909.98.2.310.

[10] Mushtaq R and Ahmed R. Psychometric properties of Pakistani version of Perceived Stress Scale.Pakistan Journal of Psychology. 2020 Jun; 51(1).

[11] Zimet GD, Powell SS, Farley GK, Werkman S, Berkoff KA. Psychometric characteristics of the multidimensional scale of perceived social support. Journal of Personality Assessment.1990 Dec; 55(3-4): 610-7. doi: 10.1080/00223891.1990.9674095.

[12] Rizwan M and Aftab S. Psychometric properties of the multidimensional scale of perceived social support in Pakistani young adults. Pakistan Journal of Psychology. 2009 Jun; 40(1): 51-65.

[13] Ishaq R, Ishaque A, Iqbal Q, Shahzad F, Ahmed N, Saleem F. Translation and validation study of Quality of Life Questionnaire for Physiological Pregnancy at Sandeman Provincial Hospital, Quetta, Pakistan. The Journal of the Pakistan Medical Association. 2021 Nov; 71(11): 2582-8. doi: 10.47391/JPMA.012457.

[14] Yu M, Qiu T, Liu C, Cui Q, Wu H. The mediating role of perceived social support between anxiety symptoms and life satisfaction in pregnant women: a cross-sectional study. Health and Quality of Life Outcomes. 2020 Dec; 18: 1-8. doi: 10.1186/s12955-020-01479-w.

[15] Bedaso A, Adams J, Peng W, Sibbritt D. The direct and mediating effect of social support on health-related quality of life during pregnancy among Australian women. BioMed Central Pregnancy and Childbirth. 2023 May; 23(1): 372. doi: 10.1186/s12884-023-05708-0.

[16] Nazzal S, Ayed A, Zaben KJ, Abu Ejheisheh M, ALBashtawy M, Batran A. The Relationship between Quality of Life and Social Support among Pregnant Women: A Cross-Sectional Study. SAGE Open Nursing. 2024 Dec; 10: 23779608241301225. doi: 10.1177/23779608241301225.

[17] Nulufer Erbil RN and Ozlem Akin RN. The Effect of Perceived Social Support on Pregnancy Stress: A Descriptive and Cross-Sectional Study. International Journal of Caring Sciences. 2024; 17(1): 426-37.

[18] Martín-Vázquez C, Urchaga-Litago JD, García-Fernández R, Calvo-Ayuso N, Quiroga-Sánchez E, Liébana-Presa C. Quality of life and social support during pregnancy in Spanish population. A longitudinal study. Midwifery. 2024 Oct; 137: 104119. doi: 10.1016/j.midw.2024.104119.

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[19] Malik A, Park S, Mumtaz S, Rowther A, Zulfiqar S, Perin J *et al*. Perceived social support and women's empowerment and their associations with pregnancy experiences in anxious women: a study from urban Pakistan. Maternal and Child Health Journal. 2023 May; 27(5): 916-25. doi: 10.1007/s10995-023-03588-6.

[20] Hijazi HH, Alyahya MS, Al Abdi RM, Alolayyan MN, Sindiani AM, Raffee LA *et al*. The impact of perceived social support during pregnancy on postpartum infant-focused anxieties: A prospective cohort study of mothers in Northern Jordan. International Journal of Women's Health. 2021 Oct: 973-89. doi: 10.214 7/IJ WH.S329487.

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Sero-Prevalence of Hepatitis B and Hepatitis C in District Sialkot

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ABSTRACT

Hepatitis B and hepatitis C are peak overwhelming infectious conditions belonging to liver inflammation. According to the World Health Organization's hepatitis report, 96% of the 1.3 million hepatitis virus-related fatalities annually, of which 720,000 happened at the cirrhosis stage, were the result of chronic infections with the hepatitis B and hepatitis C viruses. **Objectives:** To assess the sero-prevalence of Hepatitis B and Hepatitis C in District Sialkot. **Methods:** A total of 1,737 blood samples were randomly collected from participants who visited the hospital for hepatitis screening from March 2018 to August 2018. All the samples were screened via Immune-chromatographic strip test. Statistical analysis was performed on data using IBM SPSS Statistics (Version 27). **Results:** A total of 15.5% samples tested positive, out of which 12.43% samples were hepatitis C viruses and 2.82% were hepatitis B viruses positive respectively. Overall prevalence was higher in male (16.60%) than female 14.19%. Sero-prevalence was high between the age group of 61-80 years. Likewise, among married persons (17.16%) as compared to unmarried (8.01%). **Conclusions:** It was concluded that a significant association of prevalence of hepatitis with both age and marital status ($p<0.001$) was observed, while no significant effect was on gender.

INTRODUCTION

Viral hepatitis is the most widely spread infectious condition of liver inflammation having a list of serotypes [1]. Both Hepatitis B virus (HBV) and Hepatitis C virus (HCV) infections are significant for causing chronic hepatitis and have become the chief cause of liver cirrhosis and hepatocellular carcinoma. Out of these two, hepatitis C had become severe sequelae. It can develop acute hepatitis, chronic hepatitis or a chronic carrier state and hepatocellular carcinoma [2]. Hepatitis B contamination is caused by the hepatitis B virus (HBV). It belongs to the Hepadenviridae family [3]. It is a member of the Orthohepadnavirus genus [4]. It is a partly double-stranded DNA virus. HBV have a constricted host range, which is restricted to humans and chimpanzees only. Out of these two, humans are the chief natural host for HBV [5]. HBV can cause tarnishing of hepatic cells of the liver and liver failure. At the late phase of infection, HBV may progress to hepatocellular carcinoma (HCC) and cirrhosis. There are two states of HBV infection, acute and chronic. Acute hepatitis frequently happens when the natural resistance is sound. Upon infection to liver cells, HBV has 4-6 weeks to an extensive 6-month incubation phase. Chronic Hepatitis B is the disease state if the perseverance of Hepatitis B (HB) antibodies and HBV exceeds 6 months [6]. It is related to a total 15-25% hazard of premature deaths from liver malignancy [7]. Hepatitis C virus (HCV) belongs to the family Flaviviridae and species of Hepacivirus [8]. It is a miniature, encapsulated virus of 55 nanometers. It is a single-stranded RNA virus and this strand is a positive sense strand [9]. HCV is accountable for liver scarring, liver cancer and liver failure after decades of infection. HCV move into the host cells via receptor-mediated endocytosis [10]. There are two states of hepatitis C first is Acute and second is chronic hepatitis. In the acute

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hepatitis C infection state, the onset of disease with clear symptoms ranges from 3-12 weeks after first exposure [11]. In chronic hepatitis C viral RNA remained persistent in blood. It occurs after at least 6 months or longer afterwards the inception of severe infection [12]. Approximately 2 to 10% of individuals with chronic HCV infection have co-infection with hepatitis B. This co-infection accelerates liver infection and increases the risk of liver cirrhosis, HCC, and even death [13]. Symptoms of HBV and HCV infection include jaundice, tiredness, anorexia, low appetite, malaise and severe weakness [11]. The basic treatment of HB viral infection is vaccination against the virus which has been accessible since 1982. This inoculation comprises a recombinant HBs Ag protein which is derived from yeast. This protein is effective in more than 95% of Immuno-competent receivers [14]. Up to now, the vaccine is not available for HCV [15]. Two commonly adopted HCV therapies are utilized for treating hepatitis. Firstly, is standard or PEGylated interferon Alfa and the second one is ribavirin. These two therapies ensure effectiveness in 40%–50% of treated suffering ones [16]. Among all the serotypes of hepatitis, HBV is the major necro-inflammatory agent in developing and under-developing countries. Approximately 248 million individuals are chronically septic by hepatitis B virus worldwide [17]. Around 780, 000 deaths occur per year due to HBV. Chronic infection is responsible for 650,000 deaths annually. Wisely, 130,000 deaths occur due to acute hepatitis [18]. There are about 370 million carriers of HBV [19]. The prevalence of Hepatitis B is at a peak of 6.2% in the Pacific Regions of West [7]. The World Health Organization has associated hepatitis C with a 'viral time bomb'. This time bomb could be the chief cause of billions of deaths around the world. About 350, 000 to 500, 000 individuals are expected to expire each year due to hepatitis C virus. WHO demonstrated that about 3% of the world's population, about 180 hundred thousand people is disease-ridden by HCV. HCV is accountable for 50-76% of entire liver malignancy cases [7]. Pakistan is currently facing the overwhelming infectious condition of hepatitis with a prevalence rate between 0.3-33 percent [20]. It is assessed that approximately 150, 000 individuals are world widely diseased with hepatitis C virus [21]. One study predicted 10% frequency of HBV and 6.7% of HCV among women in Pakistan [22]. Records from diverse regions of Pakistan revealed a 2.4% frequency of HBV. Temperate to the heavy dominance of HBV infection was observed in Punjab, Baluchistan, Sindh and (KPK) Khyber Pakhtunkhwa. About 29% of chronic liver disease cases and 8% of hepatocellular carcinoma cases are HCV seropositive in Pakistan [23]. This study aims to assess the sero-prevalence of Hepatitis B and Hepatitis C in District Sialkot.

METHODS

This cross-sectional study was conducted in district Sialkot, located at Latitude 32°30'N and Longitude 74°31'E in the northeast province of Punjab, Pakistan. From March 2018 to August 2018, 1,737 blood samples were randomly collected from Abdul-Sattar lab's free hepatitis screening camp. The minimum sample size (385) was calculated with the online tool "Sample Size Calculator" at 5% error. All Individuals from District Sialkot, both married and unmarried, infected with HBV+/HCV+, aged (0->80) years, and any gender (male and female) who visited Abdul-Sattar lab's free hepatitis screening camp. Patients with any other infection and having HAV+ were excluded. Distinct information including the history, sex, age and marital status of each patient was obtained by interviewing the patient via a questionnaire. For screening of Hepatitis, a standard diagnostic kit was used (Bioline kit). The presence of the control line and test line confirms a positive test. Faint test lines were regarded as weak positive. The presence of the control line alone confirms negative results. Statistical analysis (Chi-square) was applied to data using IBM SPSS Statistics (Version 27).

RESULTS

Out of 1,737 samples, 265 (15.25%) were positive for hepatitis B and C. While 49 (2.82%) were HBV positive and 216 were HCV positive (12.43%). Out of 765 males 127(16.60%) were positive for hepatitis. A total of 3.52% were HBV and 13.07% were HCV positive. Among 972 females 2.26% were HBV positive and 11.93% were HCV positive. Non-significant difference (p=0.204) was observed between the prevalence of hepatitis in two genders (Table 1).

Table 1: Gender Wise Prevalence of HBV+ and HCV + Patients

Gender	Total Patients	Positive Patients (%)	HBV+ Patients (%)	HCV+ Patients (%)	p-value*
Male	765	127 (16.60%)	27 (3.52%)	100 (13.07%)	0.204
Female	972	138 (14.19%)	22 (2.26%)	116 (11.93%)	
Total	1737	265 (15.25%)	49 (2.82%)	216 (12.43%)	

Distribution of HBV and HCV in different age groups from 0-20, 21-40, 41-60, 61-80 and above 80 years of age are mentioned in Table 2. The highest HBV and HCV were noted in the 61-80 years' age group. No positive patients above 80 years were noted for HBV infection while the lowest HCV infection was noted in the 0-20-year age group. The chi-square test showed a significant difference (p=0.0001) between the prevalence of hepatitis in different age groups (Table 2).

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Table 2: Age-Wise Distribution of HBV+ and HCV+ Patients

Age (Years)	Total Patients	Positive Patients	HBV+ Patients	HCV+ Patients	p-Value
0-20	151 (8.69%)	10 (6.62%)	4 (2.64%)	6 (3.97%)	0.0001
21-40	1,012 (58.26%)	127 (12.54%)	29 (2.86%)	98 (9.68%)	
41-60	452 (26.02%)	95 (21.01%)	12 (2.65%)	83 (18.36%)	
61-80	110 (6.33%)	30 (27.27%)	4 (3.63%)	26 (23.63%)	
>80	12 (0.69%)	3 (25%)	0 (0.00%)	3 (25%)	
Total	1737	265 (15.25%)	49 (2.82%)	216 (12.43%)	

Out of 1,375 married patients, 236 (17.16%) were positive overall. Among married positive patients 2.69% were HBV+ and 14.47% were HCV+. While unmarried patients were 8.01% positive, out of it 3.31% were HBV+ and 4.69% were HCV+. A significantly high (p=0.000016) prevalence of hepatitis was observed in married persons (Table 3).

Table 3: Prevalence of HBV+ and HCV+ According to Marital Status of Patients

Marital status	Total Patients	Positive Patients (%)	HBV+ Patients	HCV+ Patients	p-Value
Married	1,375 (79.15%)	236 (17.16%)	37 (2.69%)	199 (14.47%)	0.0-00016
Unmarried	362 (20.84%)	29 (8.01%)	12 (3.31%)	17 (4.69%)	
Total	1737	265 (15.25%)	49 (2.82%)	216 (12.43%)	

Among 765 male samples, 0.13% were weak HBV+ and 0.26% were HCV+. While in female samples 0.61% were weak positive only for HCV. No significant (p=0.516) difference was noted gender-wise in weak hepatitis-infected patients (Table 4).

Table 4: Gender-Wise Distribution of Weak HBV+ and HCV+

Gender	Total Patients	Weak +ve Patients (%)	Weak HBV+ Patients (%)	Weak HCV+ Patients (%)	p-Value
Male	765 (44.04%)	3 (0.39%)	1 (0.13%)	2 (0.26%)	0.516
Female	972 (55.95%)	6 (0.61%)	0 (0.00%)	6 (0.61%)	
Total	1737	9 (0.51%)	1 (0.05%)	8 (0.46%)	

There are some exceptional cases of showing weak positive results with testing regarding age. Among age groups of 0-20, 21-40, 41-60, 61-80 and above 80 years, weak HBV was noted only in the 61-80 years' age group. Likewise, weak HCV prevalence was in the age group of 0-20, 21-40, and 41-60 years. A significant difference (p=0.015) was observed between the prevalence of hepatitis in different age groups with weak infection (Table 5).

Table 5: Age-Wise Distribution of Weak HBV+ and HCV+ Patients

Age (Years)	Total Patients (%)	Weak +Ve Patients (%)	Weak HBV+ Patients (%)	Weak HCV+ Patients (%)	p-Value
0-20	151 (8.69%)	1 (0.66%)	0 (0.00%)	1 (0.66%)	0.015
21-40	1,012 (58.26%)	4 (0.39%)	0 (0.00%)	4 (0.39%)	
41-60	452 (26.02%)	3 (0.66%)	0 (0.00%)	3 (0.66%)	
61-80	110 (6.33%)	1 (0.90%)	1 (0.90%)	0 (0.00%)	
>80year	12 (0.69%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	
Total	1737 (100%)	9 (0.51%)	1 (0.05%)	8 (0.46%)	

According to the marital status, 9 samples showed weak positivity out of whom 8 were married and 1 was a bachelor. No significant (p=0.47) difference was noted in married and unmarried weak hepatitis-infected patients (Table 6).

Table 6: Prevalence of Weak HBV+ and Weak HCV+ Patients According to Martial Status of Patients

Marital status	Total Patients (%)	Weak Positive Patients (%)	Weak HBV+ Patients (%)	Weak HCV+ Patients (%)	p-Value
Married	1,375 (79.15%)	8 (0.58%)	1 (0.07%)	7 (0.50%)	0.47
Unmarried	362 (20.84%)	1 (0.27%)	0 (0.00%)	1 (0.27%)	
Total	1,737 (100%)	9 (0.51%)	1 (0.05%)	8 (0.46%)	

There were also some unique cases in which some patients were suffering from HBV and HCV at the same time. Out of 1,737 patients, 0.28% of samples had shown their positivity to both HBV and HCV screening tests. Among these 5 patients, 3 were male and 2 were female. All of these 5 patients belong to 21-40 years of age group and were married.

DISCUSSION

HBV and HCV viruses are widespread in South East Asia including Pakistan. It is expected that nearly 10,00, 000 people are living with hepatitis in Pakistan. Several studies have been conducted to estimate the seroprevalence of HBV and HCV in Pakistan and reported different rates of infection from different areas. In 2008, a report presented 7.3% HCV infection and 2.2% HBV infection at Sir Ganga Ram Hospital, Lahore [24]. In 2006, 1.7% to 5.5% HBV prevalence was reported among children of Karachi, Pakistan [25]. In 1996, 1.18% prevalence of HCV and 2.48% prevalence of HBV among blood donors in southern Pakistan was reported [26]. In the Punjab Regiment Centre Mardan, sero-prevalence of HCV reported was 3.69% and HBV was 3.24% [27]. Our study also reported a low prevalence of Hepatitis B (2.82%) in contrast to Hepatitis C (12.43%) indicating people are more susceptible to Hepatitis B or there may be differences in the mode of transmission of both type of infections. In a study, 7.56% Seroprevalence of HCV with a male predominance of 10.84% was reported in Fauji Foundation Hospital, Rawalpindi [28]. Our results are significant to these results with the predominant prevalence of HCV and HBV in males. In Rawalpindi and Islamabad, the dominance of HBV over HCV was reported as 2.6% [29]. These results of HBV prevalence are by our results showing 2.82% HBV prevalence but HCV is dominant in Sialkot as compared to the HBV in Rawalpindi and Islamabad. A study reported a 3.5% prevalence of HCV in District Mansehra. The incidence of HCV infection was high 4% in males as compared to females 2% [30]. These results of our study also show a higher prevalence of HCV among males. Gender-wise incidence was documented to be higher 19.1% in male than in female 12.7% from the district Peshawar is

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analogous to our results [31]. Our study shows high surveillance of HCV and HBV among males and married people. The main routes of transmission of HBV and HCV are blood transfusion and, the use of contaminated syringes, and razors. Males are more susceptible to infection due to having insecure sexual relationships with numerous partners and using contaminated syringes at barber shops.

CONCLUSIONS

It was concluded from this research work that there is an elevated incidence of HCV than HBV in District Sialkot, Pakistan. A high prevalence of HBV and HCV is seen in male, in people belonging to the 60-80 years' age group and in married ones. Massive caution should be employed regarding modes of transmission of HBV and HCV. Awareness campaigns for HBV and HCV should be conducted to control the infection.

Authors Contribution

Conceptualization: AWQ
Methodology: AWQ, FJ, MM
Formal analysis: AWQ
Writing review and editing: AWQ, FJ

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Weinbaum CM, Mast EE, Ward JW. Recommendations for Identification and Public Health Management of Persons with Chronic Hepatitis B Virus Infection. Hepatology.2009 May; 49 (S5): S35-44. doi: 10.1002/hep.22882.

[2] 2Basit A, Rahim K, Ahmad I, Shafiq M, Mushtaq S, Shaheen H *et al.* Prevalence of Hepatitis B and C Infection in Pakistan. Journal of Infection and Molecular Biology.2014 May; 2(3): 35-8. doi: 10.14737/jimb.2307-5465/2.3.35.38.

[3] Zanetti AR, Van Damme P, Shouval D. The Global Impact of Vaccination Against Hepatitis B: A Historical Overview. Vaccine.2008 Nov; 26(49): 6266-73. doi: 10.1016/j.vaccine.2008.09.056.

[4] Norder H, Couroucé AM, Coursaget P, Echevarria JM, Lee SD, Mushahwar IK *et al.* Genetic Diversity of Hepatitis B Virus Strains Derived Worldwide: Genotypes, Sub-Genotypes, and HBs Ag Subtypes. Intervirology.2004 Nov; 47(6): 289-309. doi: 10.1159/000080872.

[5] Rehermann B and Nascimbeni M. Immunology of Hepatitis B Virus and Hepatitis C Virus Infection. Nature Reviews Immunology. 2005 Mar; 5(3): 215-29. doi: 10.1038/nri1573.

[6] Seeger C and Mason WS. Molecular Biology of Hepatitis B Virus Infection. Virology. 2015 May; 479: 672-86. doi: 10.1016/j.virol.2015.02.031.

[7] World Health Organization. Global Health Sector Strategy On Viral Hepatitis 2016-2021. Towards Ending Viral Hepatitis. World Health Organization. 2016.

[8] Ferri C, Sebastiani M, Giuggioli D, Colaci M, Fallahi P, Piluso A *et al*. Hepatitis C Virus Syndrome: A Constellation of Organ and Non-Organ Specific Autoimmune Disorders, B-Cell Non-Hodgkin's Lymphoma, and Cancer. World Journal of Hepatology.2015 Mar; 7(3): 327. doi:10.4254/wjh.v 7. i3.327.

[9] Adams MJ, Lefkowitz EJ, King AM, Harrach B, Harrison RL, Knowles NJ *et al*. Changes to Taxonomy and the International Code of Virus Classification and Nomenclature Ratified by the International Committee on Taxonomy of Viruses (2017). Archives of virology.2017 Aug; 162(8): 2505-38. doi: 10.1007 /s0 0705-017-3358-5.

[10] Tang H and Grisé H. Cellular and Molecular Biology of HCV Infection and Hepatitis. Clinical Science.2009 Jul; 117(2): 49-65. doi: 10.1042/CS20080631.

[11] Thimme R, Oldach D, Chang KM, Steiger C, Ray SC, Chisari FV. Determinants of Viral Clearance and Persistence During Acute Hepatitis C Virus Infection. The Journal of Experimental Medicine.2001 Nov; 194 (10): 1395-406. doi: 10.1084/jem.194.10.1395.

[12] Alter MJ, Kruszon-Moran D, Nainan OV, McQuillan GM, Gao F, Moyer LA *et al*. The Prevalence of Hepatitis C Virus Infection in the United States, 1988 Through 1994. New England Journal of Medicine. 1999 Aug; 341(8): 556-62. doi: 10.1056/NEJM199908193410802.

[13] Jamma S, Hussain G, Lau DT. Current Concepts of HBV/HCV Coinfection: Coexistence, But Not Necessarily in Harmony. Current Hepatitis Reports. 2010 Nov; 9: 260-9. doi: 10.1007/s11901-010-0060-4.

[14] Sheldon J and Soriano V. Hepatitis B Virus Escape Mutants Induced by Antiviral Therapy. Journal of Antimicrobial Chemotherapy.2008 Apr; 61(4): 766-8. doi: 10.1093/jac/dkn014.

[15] Umar M and Bilal M. Hepatitis C, A Mega Menace: A Pakistani Perspective. Journal of Pioneering Medical Sciences.2012 Jun; 2: 68-72.

[16] Thomas DL, Astemborski J, Rai RM, Anania FA, Schaeffer M, Galai N *et al*. The Natural History of

DOI: https://doi.org/10.54393/pjhs.v5i12.990

Hepatitis C Virus Infection: Host, Viral, and Environmental Factors. Journal of American and Medical Association.2000 Jul; 284(4): 450-6. doi: 10.1001/jama.284.4.450.

[17] Schweitzer A, Horn J, Mikolajczyk RT, Krause G, Ott JJ. Estimations of Worldwide Prevalence of Chronic Hepatitis B Virus Infection: A Systematic Review of Data Published Between 1965 and 2013. The Lancet. 2015 Oct; 386(10003): 1546-55. doi: 10.1016/S0140-67 36(15)61412-X.

[18] Edmunds WJ, Medley GF, Nokes DJ, Hall AJ, Whittle HC. The Influence of Age On the Development of the Hepatitis B Carrier State. Proceedings of the Royal Society of London. Series B: Biological Sciences. 1993 Aug; 253(1337): 197-201. doi: 10.1098/ rspb .19 93 .0102.

[19] Bostan N, Naeem M, Afzal MS, Shah ZH, Mustafa I, Arshad M *et al*. Sero-Prevalence of Hepatitis B and C Virus from Rural Areas of Northern Punjab (Sargodha District), Pakistan. Tropical Biomedicine. 2016; 33(4): 599–607.

[20] Mahmood M, Anwar MA, Khanum A, Zaman N, Raza A. Distribution and Clinical Significance of Hepatitis B Virus Genotypes in Pakistan.BioMed Central Gastroenterology.2016 Dec; 16: 1-9. doi: 10.1186/s128 76-016-0513-5.

[21] Parlati L, Hollande C, Pol S. Treatment of Hepatitis C Virus Infection. Clinics and Research in Hepatology and Gastroenterology.2021 Jul; 45(4): 101578. doi: 10 . 1016/j.clinre.2020.11.008.

[22] Khan JK, Lone DS, Hameed A, Munim R, Bhatti M, Khattak AA *et al*. Evaluation of the Performance of Two Rapid Immune-Chromatographic Tests for Detection of Hepatitis B Surface Antigen and Anti-HCV Antibodies Using ELISA Tested Samples. Annals of King Edward Medical University.2010; 16(1 SI). doi: 10.21649/akemu.v16i1%20SI.166.

[23] Tong MJ, El-Farra NS, Reikes AR, Co RL. Clinical Outcomes After Transfusion-Associated Hepatitis C. New England Journal of Medicine.1995 Jun; 332(22): 1463-6. doi: 10.1056/NEJM199506013322202.

[24] Ali SA, Donahue RM, Qureshi H, Vermund SH. Hepatitis B and Hepatitis C in Pakistan: Prevalence and Risk Factors. International Journal of Infectious Diseases.2009 Jan; 13(1): 9-19. doi: /10.10 16/j. ijid. 20 08.06.019.

[25] Jafri W, Jafri N, Yakoob J, Islam M, Tirmizi SF, Jafar T *et al*. Hepatitis B and C: Prevalence and Risk Factors Associated with Sero-Positivity among Children in Karachi, Pakistan. BioMed Central Infectious Diseases. 2006 Dec; 6: 1-0. doi: 10.1186/1471-2334-6-101.

[26] Kakepoto GN, Bhally HS, Khaliq G, Kayani N, Burney IA, Siddiqui T *et al*. Epidemiology of Blood-Borne Viruses: A Study of Healthy Blood Donors in Southern Pakistan. The Southeast Asian Journal of Tropical Medicine and Public Health. 1996 Dec; 27(4): 703-6.

[27] Mirza IA, Mirza SH, Irfan S, Siddiqi R, Tariq WU, Janjua AN. Sero-Prevalence of Hepatitis B and C in Young Adults Seeking Recruitment in Armed Forces. Pakistan Armed Forces Medical Journal.2006 Jun; 56(2): 192-7.

[28] Chaudhary IA, Khan SS, Majrooh MA, Alvi AA. Sero-Prevalence of Hepatitis-B and C among the Patients Reporting in Surgical OPD at Fauji Foundation Hospital, Rawalpindi: Review of 5-Year Literature. Pakistan Journal of Medical Sciences.2007 Jul; 23(4): 514.

[29] Waheed Y, Shafi T, Safi SZ, Qadri I. Hepatitis C Virus in Pakistan: A Systematic Review of Prevalence, Genotypes and Risk Factors. World Journal of Gastroenterology.2009 Dec; 15(45): 5647. doi: 10.3 7 4 8/wjg.15.5647.

[30] Ali A, Ahmad H, Ali I, Khan S, Zaidi G, Idrees M. Prevalence of Active Hepatitis C Virus Infection in District Mansehra Pakistan. Virology Journal.2010 Dec; 7: 1-5. doi: 10.1186/1743-422X-7-334.

[31] Ilyas M and Ahmad I. Chemiluminescent Microparticle Immunoassay Based Detection and Prevalence of HCV Infection in District Peshawar Pakistan. Virology Journal.2014 Dec; 11: 1-5. doi: 10.1186/1743-422X-11-127.

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Diagnostic Accuracy of Spot Urine Protein-Creatinine Ratio for Pre-Eclampsia among Females Presented to Tertiary Level Hospital with Pregnancy-Induced Hypertension

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ABSTRACT

Preeclampsia is main cause of fetal, maternal and newborn death globally, particularly in low- and middle-income nations. It's usually diagnosed when a pregnant woman shows indicators of hypertension and proteinuria. **Objective:** To determine diagnostic accuracy of spot urine protein-creatinine ratio (P/C ratio) for pre-eclampsia in females presenting with pregnancy induced hypertension, using 24-hour urine protein as gold standard, and to look for a correlation between spot urine P/C ratio and 24-hour urine protein. **Methods:** This was cross sectional study carried out at Department of Obstetrics and Gynecology, Sughra Shafi Medical Complex, Narowal from February 2024 to August 2024. 451 pregnant females after 20 weeks till delivery were admitted through OPD in ward. Simple Random sampling technique was used to collect data. All information was recorded through pre-designed Proforma regarding 24-hour urine collection and spot urine to P/C ration. Data were entered and analyzed by SPSS version 23.0. Spearman's rank correlation coefficient was used to evaluate the relationship between the spot urine P/C ratio and 24-hour urine protein. A p-value <0.05 was considered statistically significant. **Result:** Spearman's correlation showed a strong positive correlation (r=0.82, p<0.05) between 24-hour protein and spot urine P/C ratio. Moreover, results showed a specificity of 87.8% (83.6%-91.9%), and sensitivity of 97.2% (94.9%-99.4%) based on clinical thresholds for proteinuria. **Conclusions:** The findings showed that urine P/C ratio might replace 24-hour urine protein for detecting proteinuria in preeclampsia. Additionally, it is a standardize, easy to execute and straightforward test and affordable with no requirement of systematic hospitalization.

INTRODUCTION

Approximately 5-8% of pregnancies are affected by pre-eclampsia, a hypertensive disorder [1]. It remains one of the leading cause of fetal and maternal morbidity and mortality around the globe [2, 3]. Pre-eclampsia, if not promptly diagnosed and managed, may result in serious complications, including intrauterine growth restriction, placental abruption, and progression to eclampsia, a life-threatening condition involving seizures [4]. Accurate and timely diagnosis of pre-eclampsia is extremely critical in ensuring maternal and fetal well-being. The traditional gold standard test to diagnose proteinuria, a key diagnostic criterion for pre-eclampsia, is 24-hour urine collection test [5]. This process is very accurate but time-consuming, burdensome, and often impractical for use in busy clinical

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settings [6]. Substantial compliance challenges are faced by the patients. To address these limitations, a faster and simpler diagnostic methods such as spot urine P/C ratio have been explored [7]. P/C ratio that involves measuring protein and creatinine concentration within a single sample spot urine, normalizing the level of protein to creatinine to account for changes in the urine concentration [8, 9]. It provides a reliable estimate of daily protein excretion and offers a very suitable substitute to 24-hour urine collection test. Several studies investigated the accuracy of the diagnostic P/C ratio to predict significant proteinuria in pregnant women, but the results have been varied across clinical context and populations [10]. However, this method shows promise as a fast and non-invasive tool for the identifying pre-eclampsia in women with Pregnancy-Induced Hypertension (PIH) [11]. PIH is characterized by elevation of blood pressure in pregnancy without any previous history hypertension [12]. While PIH may resolve postpartum, it can pose a substantial risk of progressing to pre-eclampsia. Thus, it is crucial to detect pre-eclampsia early on in hypertensive pregnant women to prevent any adverse outcomes [13]. There is growing interest to evaluate the diagnostic precision of the P/C ratio as a dependable alternative to the 24-hour urine collection, given the clinical importance of identifying pre-eclampsia early on in women with PIH [14]. If proven to be effective, it could enhance the efficiency of pre-eclampsia diagnosis and enable timely intervention, reducing the burden of complications [15].

This study aimed to assess and evaluate the diagnostic accuracy of the spot urine P/C ratio to detect pre-eclampsia in hypertensive women induced by pregnancy. By comparing the P/C ratio to the traditional 24-hour urine collection method, seeked to determine its utility as a screening tool for an early and efficient diagnosis of pre-eclampsia in clinical settings.

METHODS

This cross sectional study was carried out at Department of Gynecology and Obstetrics, Sughra Shafi Medical Complex, Narowal from February 2024 to August 2024. Study Population was pregnant females after 20 weeks till delivery were admitted through OPD in ward of Gynecology and Obstetrics, Sughra Shafi Medical Complex, Narowal. Simple random sampling technique was used to take data. Sample size of 451 females was collected using www.raosoft.com with the confidence level 99% and margin of error 5%. All females with age of 16-35 years having 1st time hypertension during pregnancy with Gestational age >20weeks (through LMP) and singleton pregnancy (through USG). PIH (BP≥140/90mmHg) having suspicion of pre-eclampsia (PIH + proteinuria ≥ +1 on dipstick) were included in study. While females with history of tuberculosis, Diabetes Mellitus (BSR >180mg/dl), Deranged LFTs (ALT > 40IU, AST > 40IU), Renal insufficiency (serum creatinine >1.2mg/dl), Chronic hypertension (through history and medical record or PIH before 20 weeks of gestation) and with history of urinary tract infection (detect from urine test) were excluded from study. After taking approval from the ethical review board (Ref: SMC/0108), 451 patients meeting the inclusion requirements were admitted from the OPD in ward of Gynecology and Obstetrics, Sughra Shafi Medical Complex, Narowal. Informed consent was taken from all participants. The descriptive data of subjects including sex, age, BMI, height and weight were obtained. 24-hour urine was collected from all patients. Patients were given instructions regarding collection of on-time spot urine on the next day after the 24-hour urine collection in hospital-provided sterile containers. Instructions were given to patients regarding proper sample collection to avoid contamination. Both spot urine and 24-hour samples were analyzed on same day in the hospital laboratory to ensure sample integrity. The analyses were performed using a fully automated biochemical analyzer. Creatinine concentration was determined using the Jaffe kinetic method (Roche) while protein concentration was measured using the immunoturbidimetric method (Roche). P/C ratio was calculated using formula: P/C ratio= Spot Urine Protein (mg) / Spot Urine Creatinine (mmol). All this data was taken through pre designed Proforma. Data were entered and analyzed by using SPSS version 23.0. Mean ± S.D was used for quantitative variables like age, height, weight, BMI, spot urine and 24-hour urine P/C ratio. Frequency and percentage were calculated for status (positive or negative) of spot and 24 hour's urine P/C ratio. To show correlation between the spot urine P/C ratio and 24-hour urine total protein Spearman's rank correlation coefficient was used to evaluate the relationship between the spot urine P/C ratio and 24-hour urine protein. The p-value for statistical significance was established at $p<0.05$. Specificity and Sensitivity were calculated to check the diagnostic performance of the spot urine P/C ratio in identifying substantial proteinuria. A 24-hour urine protein excretion >0.3 g/day and spot urine P/C ratio >30 mg/mmol was considered indicative of significant proteinuria.

RESULTS

Table 1 showed descriptive statistics of subjects. The mean maternal age was 31-years (range: 17-35 years), showing diversity in age group. The average BMI of females was 28.2kg/m^2, suggestive of being overweight, which may highlight an underlying risk factor for pre-eclampsia in this population. The mean gestational age at time of assessment was around 33.4 weeks. It demonstrates that study population was focused on women in third trimester of pregnancy.

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Table 1: Descriptive Statistics of Subjects

Variables	Mean ± SD	Median (Min-Max)
Mother Age (Years)	31.0 ± 8.2	30 (17-35)
Body Mass Index (BMI)	28.2 ± 7.7	28 (24-30)
Gestational Age (Weeks)	33.4 ± 8.7	33 (32-34)

Table 2 summarized data on urine protein analysis. The median spot urine P/C was 25 mg/mmol with broad range (0-105 mg/mmol). Likewise, the median of 24-hour urine protein was 1.4 g/day (range: 0.3-10.95 g/day). These findings in proteinuria levels among the pregnant females suggested varying severity of pre-eclampsia, emphasizing importance of accessible and reliable diagnostic tool.

Table 2: Descriptive Statistics of Urine Analysis

Variables	Median (Min-Max)
Spot Urine P/C Ratio (mg/mmol)	25 (0-105)
24 Hour Urine Protein (g/Day)	1.4 (0.30-10.95)

Table 3 classified participants based on proteinuria status using spot and 24-hour urine tests. Spot urine protein tests classified 47.7% as positive, while 52.3% were negative closely aligning with 24-hour urine results i.e. 47.2% negative and 52.8% positive. These results showed that the spot urine P/C ratio closely supports results of 24-hour urine collection, confirming its possibility as an alternative diagnostic mean.

Table 3: Urine Protein Quantification

Variables	Category	Median (Min-Max)
Spot Urine Protein (mg/mmol)	Positive	215 (47.7%)
	Negative	236 (52.3%)
24-Hour Urine Analysis (g/Day)	Positive	238 (52.8%)
	Negative	213 (47.2%

Sensitivity that is aptitude to spot true positives of the spot urine test was 97.2% (94.9%–99.4%), means it correctly identifies 97.2% of cases with proteinuria. The specificity which is ability to detect true negatives was 89.9% (83.6%–91.9%), showing that it successfully ruled out proteinuria in 89.9% of cases. The positive predictive value which is probability that positive result is truly positive was 87.7%, while negative predictive value that is probability that a negative result is truly negative was 97.2%. The accuracy of the test was 92.2%, representing that the spot urine protein-to-creatinine ratio is very effective diagnostic tool (Table 4).

Table 4: Specificity, Sensitivity, Positive and Negative Predicative Value and Accuracy

Variables	Category	Frequency (%)
-	True Positive (TP)	207 (45.9%)
	False Positive (FP)	29 (6.5%)
	False Negative (FN)	6 (1.3%)
	True Negative (TN)	209 (46.3%)
Sensitivity	TP/(TP + FN)	207/(207 + 6) = 97.2
Specificity	TN/(TN + FP)	209/(209 + 29) = 89.9
Positive Predictive Value	TP/(TP + FP)	207/(207 + 29) = 87.7
Negative Predictive Value	TN/(TN + FN)	209/(209 + 6) = 97.2
Accuracy	(TP+TN)/ (TP + TN + FP + FN)	(207 + 209)/(207+ 209+29+6) = 92.2

Table 5 showed that there is positive correlation between the spot urine P/C ratio and the 24-hour urinary protein, ($r=0.82$, $p< 0.05$). This strong correlation coefficient shows that the spot urine test aligns well with the results of 24-hour urine test in detecting proteinuria. So it supported use of spot urine P/C ratio as a diagnostic alternate for diagnosing significant proteinuria.

Table 5: Correlation between P/C Ratios Versus 24 hours Urinary Protein

Variables	Correlation Co-Efficient	p-Value
P/C Ratio Versus 24 hour Urinary Correlation	r = 0.82 (Strong Positive Correlation)	<0.05

DISCUSSION

The present study results reported the efficacy of spot urine P/C ratio in diagnosing pre-eclampsia, demonstrating a significant correlation ($r=0.82$) with 24-hour urine protein test. The median value of P/C ratio in current cohort was reported as 25 (0-105mg/mmol), reflecting a significant prevalence of proteinuria. Mdunge and Baloyi in 2021 carried out a prospective cross-sectional study and highlighted that spot urine P/C ratio is an effective alternative for 24-hour proteinuria with a correlation coefficient of $r=0.74$($p<0.001$). However, cut-off of 30mg/mmol and area under curve (AUC=0.8506) propose produces lower sensitivity of 81.4% and specificity of 77.7% compared to our findings. These variations may be due to population differences in clinical threshold. Though, it is concluded that spot urine P/C ratio shortens hospital stays and speed up treatment commencement, the lower specificity reported warrants caution in interpreting borderline results [16]. A study conducted by Talukdar DS *et al.*, in 2023 revealed that there was a significant association between abnormal serum lipid levels and higher P/C ratio values in females with gestational hypertension compared to pregnant females with normal blood pressure. The findings of present study showed that 52.8% of the participants tested positive for 24-hour urine protein test but did not find its association with serum lipid levels. Thus, their findings showed that serum lipid indicators such as cholesterol and triglycerides exhibited unique patterns in patients with gestational hypertension besides raised P/C ratio values. This suggest an opportunity for future research to check theses biomarkers along with P/C ratio to improve precision and prognostic value in PIH [17]. In present study a sensitivity of 97.2% closely aligns with findings from Nyota PK *et al.*, (96.6%) however specificity (89.9%) was slightly lower than

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Nayota PK *et al.*, at optimum threshold of 30.8mg/mmol. The low specificity in present study might highlight differences in proteinuria severity. Thus, it is established P/C ratio's role in reducing diagnostic delays and improving results, predominantly in developing countries with economic constraints [18]. Tian M *et al.*, carried out a study in 2021 to evaluate the PCR test diagnostic accuracy in detecting severe proteinuria in pre-eclamptic females. The findings of their study demonstrated significant correlation ($r = 0.802$, $p < 0.001$). The overall results support the use of the P/C ratio to predict clinically significant proteinuria in outpatient settings, even though the correlation was weak in cases with proteinuria < 300 mg ($r = 0.69$, $p = 0.044$). This method reduces unnecessary hospitalizations while offering a useful and less burdensome alternative to 24-hour urine collection. It also gives important information for monitoring renal function in pre-eclamptic women [19]. Similarly, cross-sectional study was carried out in 2021 by Bindu, which highlighted strong correlation ($r = 0.7$, $p < 0.001$), slightly lower than these results ($r=0.82$, $p<0.05$). Moreover, the findings of this study endorse the use of spot urine P/C ratio test as a quick, easy, valid, and time-efficient alternate for laborious 24-hour urine protein test, specifically in nations such as India where there is high patient to staff ratio [20]. Furthermore, the results of the present study demonstrated that in participants the value of median 24-hour urine protein was 1.4g/day; whereas, the median value of P/C ratio was found to be 25 mg/mmol. Kamińska J *et al.*, conducted a systematic review in 2020 to estimate the diagnostic value of the spot P/C ratio test regarding spectrum of clinical diseases, like kidney disease, hypertension, gestational hypertension, and preeclampsia. Their outcomes exhibited a significant correlation between the two tests, accentuating reliability and efficacy of spot urine P/C ratio. The recommended values of cut point such as 30 mg/mmol are crucial for precise diagnosis of preeclampsia. However, 24-hour urine protein test is gold standard test in doubtful cases as it increases the efficacy of patient care by accurately diagnosing proteinuria [14]. DEĞER SM *et al.*, carried out a study in 2023 reinforced spot urine P/C ratio validity and correlation with 24-hour urine protein [21]. Furthermore, they reported that this test in simple, quick, valid and convenient substitute of 24-hour urine protein test which is laborious and time consuming. Hence, their study mirrors our results further validating its reliability. The findings of this study have significant implications for clinical practice. The spot P/C ratio offer rapid and cost-effective choice mainly in resource limited settings. Moreover, Spot urine P/C ratio testing can aid in timely diagnosis, enabling early intervention and management of pre-eclampsia. Additionally, integrating P/C ratio with other biomarkers, such as lipid profiles, could improve diagnostic accuracy and offer a more comprehensive assessment of PIH risk.

CONCLUSIONS

In conclusion, these results showed that the spot urine P/C ratio is a highly specific, sensitive, and accurate method for diagnosing proteinuria in pre-eclampsia. Spot urine P/C ratio's strong correlation with 24-hour urine protein and high diagnostic accuracy makes it an effective alternative in both resource-rich and resource-limited settings.

Authors Contribution

Conceptualization: AA
Methodology: AA
Formal analysis: SA
Writing, review and editing: AK, MH, AH, SC, MN

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Lee CS, Choi EY, Lee M, Kim H, Chung H. Serous retinal detachment in preeclampsia and malignant hypertension.Eye. 2019 Nov; 33(11): 1707-14. doi: 10.1038/s41433-019-0461-8.

[2] Lewandowska M, Więckowska B, Sajdak S, Lubiński J. Pre-pregnancy obesity vs. other risk factors in probability models of preeclampsia and gestational hypertension. Nutrients.2020 Sep; 12(9): 2681. doi: 10.3390/nu12092681.

[3] Sarkar R, Rawat S, Sharma NR, Tiwari HC. A study of spot urine protein: creatinine ratio as an alternative to 24 hours proteinuria for the diagnosis of pre-eclampsia. International Journal of Reproduction, Contraception, Obstetrics and Gynecology. 2020 Jan; 9(1): 140-5. doi: 10.18203/2320-1770.ijrcog20196010

[4] Morikawa M, Mayama M, Noshiro K, Saito Y, Nakagawa-Akabane K, Umazume T *et al*. Earlier onset of proteinuria or hypertension is a predictor of progression from gestational hypertension or gestational proteinuria to preeclampsia. Scientific Reports. 2021 Jun; 11(1): 12708. doi: 10.1038/s41598-021-92189-w.

[5] Bartal MF, Lindheimer MD, Sibai BM. Proteinuria during pregnancy: definition, pathophysiology, methodology, and clinical significance. American Journal of Obstetrics and Gynecology. 2022 Feb; 226(2): S819-34. doi: 10.1016/j.ajog.2020.08.108.

DOI: https://doi.org/10.54393/pjhs.v5i12.2413

[6] Akin D and Ozmen S. An unresolved issue: The relationship between spot urine protein-to-creatinine ratio and 24-hour proteinuria. Journal of International Medical Research. 2019 Mar; 47(3): 1179-84. doi: 10.1177/0300060518819602.

[7] Rupakala BM and Hiremath AS. Comparative study of 24-hour urinary protein and spot urine protein creatinine ratio in pre-eclamptic women. International Journal of Reproduction, Contraception, Obstetrics and Gynecology.2021 Jul; 10(7): 2734-9. doi: 10.18203/2320-1770.ijrcog20212659.

[8] Nielsen LH, Jensen BL, Fuglsang J, Andersen LL, Jensen DM, Jørgensen JS *et al.* Urine albumin is a superior predictor of preeclampsia compared to urine plasminogen in type I diabetes patients. Journal of the American Society of Hypertension. 2018 Feb; 12(2): 97-107. doi: 10.1016/j.jash.2017.12.003.

[9] Ibrahimi L, Paçarada M, Hoxha SL, Bimbashi A, Ibishi VA. Role of calcium/creatinine ratio in urine compared with proteinuria and uric acid in predicting preeclampsia: a study from Kosovo. Medical Science Monitor Basic Research. 2021 Mar; 27: e929845-1. doi: 10.12659/MSMBR.929845.

[10] Teeuw HM, Amoakoh HB, Ellis CA, Lindsley K, Browne JL. Diagnostic accuracy of urine dipstick tests for proteinuria in pregnant women suspected of preeclampsia: A systematic review and meta-analysis. Pregnancy Hypertension. 2022 Mar; 27: 123-30. doi: 10.1016/j.preghy.2021.12.015.

[11] Creanga AA, Syverson C, Seed K, Callaghan WM. Pregnancy-related mortality in the United States, 2011-2013. Obstetrics & Gynecology.2017 Aug; 130(2): 366-73. doi: 10.1097/AOG.0000000000002114.

[12] Gudeta TA and Regassa TM. Pregnancy induced hypertension and associated factors among women attending delivery service at mizan-tepi university teaching hospital, tepi general hospital and gebretsadik shawo hospital, southwest, Ethiopia. Ethiopian Journal of Health Sciences. 2019 Jan; 29(1): 831-840. doi: 10.4314/ejhs.v29i1.4.

[13] Braunthal S and Brateanu A. Hypertension in pregnancy: Pathophysiology and treatment. SAGE Open Medicine. 2019 Apr; 7: 2050312119843700. doi: 10.1177/2050312119843700.

[14] Kamińska J, Dymicka-Piekarska V, Tomaszewska J, Matowicka-Karna J, Koper-Lenkiewicz OM. Diagnostic utility of protein to creatinine ratio (P/C ratio) in spot urine sample within routine clinical practice. Critical Reviews in Clinical Laboratory Sciences. 2020 Jul; 57(5): 345-64. doi: 10.1080/10408363.2020.1723487.

[15] Abdelazim IA, Amer OO, Shikanova S, Karimova B. Protein/creatinine ratio versus 24-hours urine protein in preeclampsia. Ginekologia Polska. 2022 Feb; 93(12): 975-9. doi: 10.5603/GP.a2021.0233.

[16] Mdunge BS and Baloyi SM. The accuracy of spot urine protein-to-creatinine ratio in diagnosis or exclusion of significant proteinuria in pre-eclampsia. InObstetrics and Gynaecology Forum. 2021 Jul; 31(1): 8-11. In House Publications.

[17] Talukdar DS, De PDJ, Saha3 DA, De DA. Assessment of Correlation of Serum Lipid Profile and Urinary Protein Creatinine Ratio with Occurrence of Gestational Hypertension in Pregnant Mothers in a Tertiary Care Hospital, Kolkata. Mediterranean Journal of Basic and Applied Sciences. 2023 Oct-Dec; 07(04): 51-66. doi: 10.46382/MJBAS.2023.7402.

[18] Nyota PK, Beya DT, Ngandu PC, Natuhoyila AN, Manzambi BS, Zita MN *et al*. Evaluation of the proteinuria-creatininuria ratio for the diagnostic confirmation of preeclampsia in Congolese pregnant women. Journal of Medical Research.2021 May-Jun; 7: 70-8. doi: 10.31254/jmr.2021.7303.

[19] Tian M, Chen M, Huang L, Liu Q. A meta-analysis on diagnostic accuracy of spot urinary protein to creatinine ratio versus 12-h proteinuria in preeclampsia. Iscience. 2024 Feb; 27(2). doi:10.1016/j.isci.2024.109026.

[20] Bindu KH. Correlation of 24-hour urinary protein excretion and spot urine protein-creatinine ratio in women with preeclampsia: A cross sectional study. Medpulse International Journal of Gynaecology. 2021 Feb; 17(3): 62-6. doi: 10.26611/10121736.

[21] DEĞER SM, GÜNGÖR Ö, DERİCİ Ü, editors. Hypertension and Kidney Diseases Studies and Reviews. Academician Bookstore; 2020 Feb 4.

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Original Article

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Knowledge and Practices of Oncology and Bone Marrow Transplant Nurses in the Management of Neutropenic Fever in Patients Undergoing Chemotherapy

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ABSTRACT

Febrile neutropenia is a significant complication from chemotherapy, often being the initial indication of infection in cancer patients. Neutropenic fever requires efficient management. **Objectives:** To determine knowledge and infection control practices of Oncology and Bone Marrow Transplant Nurses in managing Neutropenic Fever in Chemotherapy patients. **Methods:** A cross-sectional survey was conducted from April to June 2024 to assess nurses' knowledge and infection control practices regarding neutropenic fever. A sample of 105 oncology and bone marrow transplant nurses was recruited from four tertiary care hospitals in Rawalpindi and Islamabad. Convenient Sampling was employed for enrolling participants. The data were collected using a structured questionnaire comprising three sections: demographic information, a 30-item true/false neutropenia knowledge questionnaire, and a 16-item practice-based questionnaire developed. Data were analyzed using SPSS version 26.0. Results were presented as frequencies and percentages, and associations were tested using the chi-square test. **Results:** The study revealed a significant correlation between knowledge scores and infection control practices. Nurses had an average knowledge score of 23.04 ± 4.0, with 50.5% demonstrating good knowledge. Infection control adherence averaged 11.91 ± 2.37, with 44.8% showing good practices. The correlation was significant (Pearson Chi-Square=20.975, p<0.001). **Conclusions:** It was concluded that nurses showed a solid understanding of neutropenia and generally followed infection control procedures, though improvements in efficacy and consistency are needed. Targeted training, ongoing education, and regular workshops can reinforce knowledge and promote best practices among nursing staff, ultimately enhancing infection control measures and improving patient outcomes.

INTRODUCTION

Neutropenia is a common side effect of chemotherapy that compromises immune function and heightens infection risk among patients. Febrile neutropenia (FN) is a serious complication of chemotherapy treatment and may present as the only clinical sign of infection [1]. Patients with febrile neutropenia are more susceptible to life-threatening bacterial infections due to a lack of inflammatory response [2]. Effective management of neutropenic fever is essential for reducing serious infections and improving patient outcomes, especially given that cancer is the second leading cause of mortality worldwide [3]. Oncology-trained nurses play a critical role in diagnosing and managing neutropenic fever, necessitating a thorough understanding of the condition and its treatment [4]. Neutropenia is a major dose-limiting adverse effect associated with chemotherapy, radiation therapy, and various blood disorders. It markedly heightens the risk of infections, which can quickly worsen and result in sepsis, a potentially life-threatening condition if not addressed swiftly. In the management of FN, Nurses are essential in managing infections related to neutropenia by enforcing preventive strategies, educating patients and their caregivers about the signs of infection, and facilitating timely medical intervention when needed '. According to a

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study conducted in (2016), nurses are vital members of multidisciplinary teams and advocates for supportive patient care. Oncology nurses bridge the gap between oncologists and patients, positively influencing outcomes by educating patients on side effects and available therapies. They also relay patients' concerns to physicians and can enhance care quality by participating in continuous improvement initiatives and developing neutropenia management guidelines [6]. Despite advancements in cancer therapies, the fundamental principles for managing neutropenia have remained largely unchanged. As front-line healthcare providers, nurses are often the first to detect serious side effects, underscoring the need for continuous education to ensure adherence to evidence-based practices [7]. However, recent research reveals significant gaps in nursing practices and knowledge regarding infection control for neutropenic patients. Ayele *et al.*, found that 75% of nurses practiced infection prevention inconsistently, with only 60% demonstrating adequate awareness of protocols. This inconsistency highlights the urgent need for standardized infection control practices, as variations in care can lead to increased patient risk [8]. It is essential to ensure the proper handling, administration, and disposal of chemotherapy drugs (CDs) to safeguard patients and healthcare personnel from potential risks. Sargidy *et al.*, aimed to assess the knowledge of oncology nurses in Sudan regarding these practices [9]. A 2021 study indicated that Lebanese nurses had a moderate understanding of neutropenia but struggled to apply this knowledge effectively, revealing deficiencies in training and a lack of comprehensive, standardized protocols for managing these patients [10]. Further complicating care, a study in Iran found discrepancies between nurses' understanding and their actual practices in infection control [11]. Research in Pakistan similarly indicated that while nurses had moderate knowledge of infection prevention, their adherence to infection control procedures was high, emphasizing the need for standardized training to bridge the gap between knowledge and practice [12]. A study by Eskander *et al.*, revealed that fewer than 75% of participants demonstrated inadequate knowledge regarding infection prevention and control measures. [13]. Sadly, numerous research revealed a significant knowledge-practice gap concerning infection prevention procedures [14]. A thorough review of the literature indicated that there is little research on nurses' understanding of CIN and how it relates to patient care in Pakistan. Nursing administrators, nurses, clinical educators, and nursing scholars could all benefit from this kind of research. The results may serve as a starting point for developing policies and putting nursing education programs into action.

This study aims to evaluate the state of nurse preparedness and implement targeted interventions to enhance standardized practices in managing neutropenic fever. The outcomes could lead to improved educational programs and updated clinical protocols, ensuring consistent and effective care for patients undergoing chemotherapy and bone marrow transplants, ultimately reducing complications and improving prognoses.

METHODS

A quantitative cross-sectional study was used to assess the knowledge and practices of oncology and bone marrow transplant nurses in the management of neutropenic fever patients from April 2024 to June 2024. There are 210 nurses in the oncology and bone marrow transplant (BMT) setting in twin cities. Cochran formula is used to calculate sample size by taking the margin of error (e) 0.07, an estimated proportion of the population (p) 0.5, a population of 2100, and a Z(a/2) score from the Z table at 95% confidence interval which was 1.96. The final sample size, based on limited population was calculated to be 105 participants. All registered nurses who were currently practicing in oncology and bone marrow transplant (BMT) units were included in the study. Whereas nurses who were unavailable during the data collection period, were approached the next day and no one was excluded. The data collection tool for this study consists of three sections. The first section covered the demographic information of the participants, and the second part was the neutropenia knowledge questionnaire, which was used for the evaluation of the knowledge of nurses regarding the disease and the care of the patients suffering from neutropenia [15]. The set of questionnaires consisted of 30 true and false statements, and each correct answer was given a score of 1; otherwise, 0. The third section was related to the prevention practices of neutropenic fever. This tool was adapted from a previous study that was conducted in Lahore, Pakistan [12]. This section of the tool was made based on the site observation done by the researcher and includes 16 practice-based questions related to the prevention of the captioned infection with "Yes" and "No" as response options. The development of this section was done as per WHO/Centers for Disease Control (CDC) guidelines, and related items of literature were checked. Scoring was done by giving '1' points for 'Yes' and 0 for 'No'. The instrument was previously validated and used in multiple international and national studies, the reliability was checked by pilot testing and the calculated Cronbach alpha was 0.805, indicating good internal consistency. The scoring system was chosen based on Bloom's taxonomy to categorize knowledge and practice levels as follows; Poor knowledge: score <60% (<18 correct answers)(indicated an insufficient understanding of neutropenia and its management). Moderate knowledge: score 61-79% (18 to

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23) (indicated a basic understanding but lacking in depth and application). Good knowledge: score 80-100% (24 to 30) (indicated comprehensive understanding and ability to apply knowledge effectively). Poor Practices: score<60% (less than 10 out of 16 scores indicated poor practices). Moderate Practice: score 61-79% (10 to 13 score indicated moderate practices). Good Practices: score 80-100% (Score 13 to 16 indicated good practices). Ethical approval was obtained from the relevant institutional review board committee (Reference No: 412-AAA-ERC-AFPGMI), and the hospital site ensuring the protection of participants' rights and welfare. Informed consent has been obtained, confidentiality and anonymity have also been carried out and voluntary participation was focused on the research process. The entire data collection process was completed, entered and coded in SPSS version 26.0 for data analysis. Descriptive statistics were applied to calculate the frequency and percentages of questionnaire items, whereas the chi-square test was used to identify the association between variables.

RESULTS

The demographic analysis of 105 oncology and bone marrow transplant nurses reveals a predominantly experienced and well-educated workforce, with 47.6% aged 31–40 years and 89.5% being female. Most participants (57.1%) held a bachelor's degree, while 35.6% had over 15 years of nursing experience. However, training in chemotherapy preparation varied, with 30.5% receiving training only once and an equal percentage having no training, indicating potential gaps in professional development. Despite a strong awareness of antimicrobial policies (83.8%) and chemotherapeutic spill kits (96.2%), the presence of a minority lacking knowledge underscores the need for continuous education. Overall, while the nurses demonstrate significant knowledge and experience, standardized training and reinforcement of key policies are essential to enhance patient care and safety in oncology settings (Table 1).

Table 1: Descriptive Characteristics of Demographic Information of Oncology and BMT Nurses

Variable	Categories	Frequency (%)
Age	20 – 30 Years	18 (17.1%)
	31 -40 Years	50 (47.6%)
	41 -50 Years	32 (47.1%)
	Above 50 Years	5 (4.8%)
Gender	Male	11 (10.5%)
	Female	94 (89.5%)
Educational Level	Diploma	40 (38.1%)
	Bachelor Degree	60 (57.1%)
	Master Degree	05 (4.8%)
Experience	1 – 5 Years	16 (15.2%)
	6 -10 Years	17 (16.2%)
	11 – 15 Years	34 (32.7%)
	More Than 15 Years	37 (35.6%)
Experience in Chemotherapy Administration	6 Months – 11 Months	17 (16.2%)
	1 Year – 3 Years	36 (34.3%)
	4 Years – 7 Years	19 (18.1%)
	Above 7 Years	33 (31.4%)
Training for Chemotherapy Preparation	Once	32 (30.5%)
	Twice	18 (17.1%)
	More Than Twice	23 (21.9%)
	Never	32 (30.5%)
Awareness of Antimicrobial Policy and Barrier Nursing	Yes	88 (83.8%)
	No	17 (16.2%)
Awareness of Chemotherapy Spill Kit	Yes	101 (96.2%)
	No	04 (3.8%)

Despite significant individual differences, nurses showed a strong awareness of neutropenia, with an average knowledge score of 23.04 ± 4.0. The true average knowledge level most likely fell within this range, as the mean score's 95% confidence interval ranged between 22.25 and 23.82. Nurses usually adhered to infection control policies well, as seen by their average score of 11.91 ± 2.37 for these techniques. The confidence interval for this score, which ranged from 11.46 to 12.37, showed an average level of adherence to infection control protocols. 50.5% of surveyed nurses demonstrated good knowledge, while 36.2% had moderate knowledge, indicating acceptable understanding. The smallest group, at 13.3%, displayed inadequate knowledge, highlighting a limited comprehension of the issue among some staff (Figure 1).

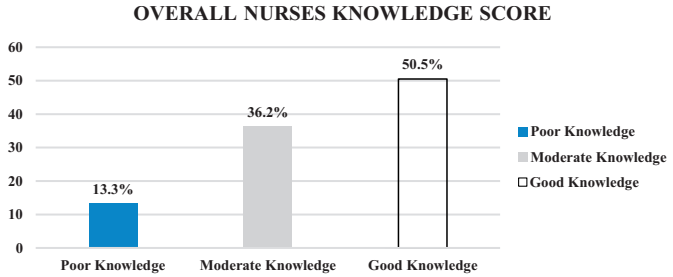

Figure 1: Overall Nurse's Knowledge Score among Study Participants

44.8% of nurses employed effective infection control practices for neutropenic patients, indicating adherence to appropriate protocols. Meanwhile, 36.2% demonstrated moderate practices, suggesting some good policies but scope for improvement. Conversely, 19.0% exhibited inadequate processes, highlighting a need for enhanced safety measures among a significant portion of staff (Figure 2).

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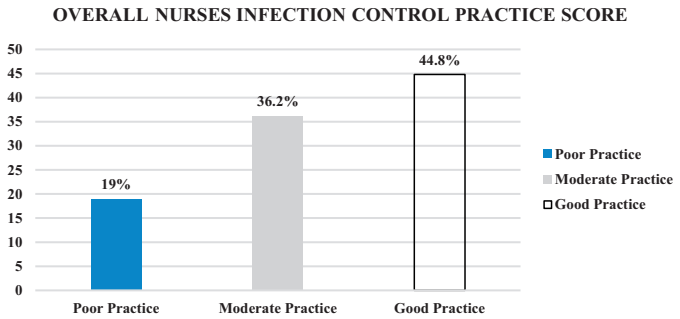

Figure 2: Overall Nurse's Infection Control Practice Score among Study Participants

Despite significant individual differences, nurses showed a strong awareness of neutropenia, with an average knowledge score of 23.04 ± 4.0. The true average knowledge level most likely fell within this range, as the mean score's 95% confidence interval ranged between 22.25 and 23.82. Nurses usually adhered to infection control policies well, as seen by their average score of 11.91 ± 2.37 for these techniques. The confidence interval for this score, which ranged from 11.46 to 12.37, showed an average level of adherence to infection control protocols. A clear correlation was studied between knowledge and practice scores among nurses managing neutropenic patients. In poor practice, 25% had poor knowledge, 60% moderate, and 15% good, suggesting that most had only moderate understanding. For moderate practice, 7.9% had poor, 47.4% moderate, and 44.7% good knowledge, indicating that better knowledge is associated with improved practices. In good practice, 12.8% had poor, 17.0% moderate, and 70.2% good knowledge, showing a strong link between high knowledge and effective practices. Higher practice levels are substantially correlated with higher knowledge scores, as indicated by the Pearson Chi-Square value of 20.975 and p-value of <0.001, which show a statistically significant association between practice and knowledge levels. This strong correlation between practice score and knowledge score is supported by the p-value (asymptotic significance) of 0.000, which is less than the conventional alpha threshold of 0.05 (Table 2).

Table 2: Contingency Table and Chi-Square Test Results

Category		Knowledge Score			
		Poor Knowledge	Moderate Knowledge	Good Knowledge	p-value
Practice Score	Poor Practice	5 (25%)	12 (60%)	3 (15%)	<0.001
	Moderate Practice	3 (7.9%)	18 (47.4%)	17 (44.7%)	
	Good Practice	6 (12.8%)	8 (17.0%)	33 (70.2%)	

DISCUSSION

This cross-sectional study assessed the knowledge and practice of the oncology and BMT nurses about neutropenic fever. The aims are to add to the body of literature concerning improving nursing education and training, and consequently patient care and outcomes. In the present study, the majority of participants were female (89.5%), with nearly half (47.6%) falling within the 31–40 age range. Similarly, a study conducted in Lebanon in 2021 reported that 77.8% of participants were female, with 44% in the 31 to 40 age range [10]. Additionally, another study in Ethiopia in 2022 found that 59.8% of participants were female, primarily in the 22 to 30 age range, further supporting the trend of a predominantly female nursing workforce in oncology [8]. In contrast, other studies reported that all participants in the oncology ward were female, suggesting a consistent female representation but differing age demographics within the nursing population [15, 16]. Regarding educational attainment, the current study revealed that 57.1% of participants held a bachelor's degree. Similarly, a study in Lahore, Pakistan, reported that 40% of participants had a bachelor's degree [12]. In contrast, a study in Turkey found that 100% of participants were with a bachelor's degree [15]. In the current study, the education and training provided to nurses for chemotherapy preparation showed notable variation. Specifically, 30.5% of respondents reported receiving training only once, while another 30.5% indicated they had never received any training at all. This aligns with findings from a 2022 study conducted in Muscat, which revealed that a significant majority of nurses had not participated in any educational programs related to oncology nursing (74.2%) or neutropenia (86.3%) [14]. The average knowledge score regarding neutropenia in the current study was 23.04 ± 4.0, indicating that nurses generally possess a good level of awareness. This is supported by a study [15]. that reported a mean knowledge score of 21.3 ± 2. In contrast, a study found a mean score of 16.3 out of 30 (SD=3.7), indicating moderate knowledge [14]. Another study reported a mean knowledge score of 15.9 (SD=1.72) [8]. Overall, more than half (64%) of the respondents in this study demonstrated poor knowledge regarding infection prevention for chemotherapy-induced neutropenia. Specific areas require targeted educational interventions, particularly in the management of stable patients and infection recognition. The current study found good adherence to infection control policies among nurses, with an average score of 11.91 ± 2.37, indicating substantial compliance with established protocols. However, identified gaps in infection control practices highlight the need for ongoing education and training to ensure comprehensive care for neutropenic patients. In contrast, a 2019 study on Iranian nurses' knowledge of neutropenia and their infection prevention practices reported only moderate practices, with just 19.2% demonstrating good practices [11]. This emphasizes the need for additional

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general education and training to enhance nurses' knowledge and clinical practices. Continuous education and training are recommended to better equip nurses with the knowledge and skills necessary for infection prevention. This is encouraging, as greater knowledge among nurses can lead to improved application of infection control measures. In the present study, 57.1% of nurses caring for neutropenic patients exhibited good hand hygiene practices, indicating strong adherence to infection control guidelines. However, 30.5% of practices were rated as moderate, and 12.4% were substandard, suggesting areas for improvement. These findings were supported by a study highlighting the role of comprehensive training programs in raising the level of knowledge and skills among nurses [5]. Hand hygiene is the most effective method for preventing healthcare-associated infections (HCAIs), yet compliance is often low, highlighting the need for effective improvement strategies [17]. In contrast, a study from Lahore found that only 44% of nurses demonstrated effective hand hygiene, highlighting a significant gap in infection prevention [12]. Another study's results showed, only 27.3% of nurses performed hand hygiene before patient contact, with 56.8% doing so afterwards [8]. These findings emphasize the need for targeted education and training to improve hand hygiene compliance, particularly before patient interactions, to better protect neutropenic patients and enhance treatment outcomes. Addressing these gaps is essential for enhancing infection control and protecting neutropenic patients, ultimately improving their treatment outcomes. In the current study, a significant positive relationship was observed between the knowledge and practices of oncology and BMT nurses in managing neutropenic patients. Chi-square analysis revealed p-values less than 0.001, indicating that as nurses' knowledge scores increased, their practice scores also improved. A study supports our finding which demonstrated a positive correlation between nurses' knowledge and their practices (r=0.75, p=0.001)[18]. Furthermore, our findings align with a qualitative study conducted in Norway, which found that oncology nurses with higher levels of cancer knowledge provided better nursing care, resulting in increased patient satisfaction [19]. However, contrary to our results, studies conducted in the USA and Iran reported no correlation between nurses' knowledge of neutropenia and their infection prevention practices [20]. This study has several limitations that should be considered when interpreting the results. The reliance on self-reported measures may have introduced response bias, as nurses might overstate their practices. Additionally, the census sampling method limits generalizability, as the sample was drawn from a single geographic area and may not represent other settings with different cultures and resources. Variability in institutional guidelines for managing neutropenic fever further complicates the ability to extrapolate best practices. Future research should employ observational methods for more reliable data and explore nurses' knowledge of chemotherapy-induced neutropenia (CIN), given the limited existing literature on this topic.

CONCLUSIONS

It was concluded that the research showed that, while there is some baseline knowledge about neutropenic fever among nurses, there are significant gaps in knowledge and practice. Continuous education and training programs would help the nurses learn from experts and keep themselves up-to-date regarding the changing guidelines and protocols on this very sensitive aspect of patient care. Such standardization of guidelines in all practice settings will minimize the variability in the practice and provide quality care. It is necessary to educate neutropenic fever to the patients and their families. Better quality educational literature may further engage the patients and family members in infection prevention and early symptom monitoring.

Authors Contribution

Conceptualization: SM
Methodology: SM, MAK, SB
Formal analysis: MAK, FK
Writing review and editing: SB

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Foley AM and Hoffman M. CE: Febrile Neutropenia in the Chemotherapy Patient. The American Journal of Nursing.2023 May; 123(5): 36-42.doi:10.1097/01.NAJ.00=00931888.96896.a1.

[2] Siddiqui B, Azmat R, Tikmani SS, Rafi S, Syed B, Khan MT *et al.* Frequency of Bloodstream Infection in Febrile Neutropenic Patients, Experience from A Developing Country. Annals of Medicine and Surgery.2018 Oct; 34: 71-4. doi: 10.1016/j.amsu.2018.09.004.

[3] Rehman SU and Khan AW. Febrile Neutropenia in Intensive Care: A Challenge for the Modern Day Intensivist. Anaesthesia, Pain and Intensive Care. 2018 Oct; 22: S102-5. doi: 10.35975/apic.v22i1.1114.

[4] Davis K and Wilson S. Febrile Neutropenia in Pediatric Oncology. Pediatrics and Child Health. 2020 Mar; 30(3):

DOI: https://doi.org/10.54393/pjhs.v5i12.2297

93-7. doi: 10.1016/j.paed.2019.12.002.
[5] Koirala S, Upreti S, Upadhyay HP. Nurses' Knowledge regarding Infection Prevention in Neutropenic Patients at Tertiary Cancer Hospital, Nepal. International Journal of Silkroad Institute of Research and Training.2024 Aug; 2(1): 16-21.doi: 10.3126 /ijsirt.v1i 2.68463.
[6] Teleb Osman SM, Mohamed Bayoumy HM. Effectiveness of a Nursing Intervention Protocol for Chemotherapy-Induced Neutropenia: Nurses and Patients' Related Outcome. Annals of Nursing and Practice. 2016; 3(1): 1038.
[7] Banegas S. Timing of Antibiotic Administration after First Fever in Blood and Marrow Transplant Patients. In Oncology Nursing Forum. 2023 Mar; 50(2): C5-C6.
[8] Ayele A, Tsige Y, Boka A. Nurses' Knowledge and Care Practices for Infection Prevention in Chemotherapy-Induced Neutropenic Patients. International Journal of Africa Nursing Sciences.2023Jan;19:100604. doi:10.1016/j.ijans.2023.100604.
[9] Sargidy AA, Yahia A, Ahmad M, Abdalla A, Khalil SN, Alasiry S *et al.* Knowledge of Safe Handling, Administration, and Waste Management of Chemotherapeutic Drugs among Oncology Nurses Working at Khartoum Oncology Hospital, Sudan. PeerJ. 2022 Oct; 10: e14173. doi: 10.7717/peerj.14173.
[10] Mortada M and Moussa S. Assessment of knowledge and Care Practices for Infection Prevention in Neutropenic Patients in Bekaa, Lebanon: A Descriptive Cross-Sectional Design. Beirut Arab University Journal-Health and Wellbeing.2021; 4(1): doi: 10.54729/2789-8288.1154.
[11] Naghdi H, Azizzadeh Forouzi M, Dehghan M. Iranian Nurses' Knowledge of Neutropenia and Their Practice for Infection Prevention in Patients with Cancer. Journal of Cancer Education. 2021 Jun; 36(3): 547-55. doi: 10.1007/s13187-019-01663-7.
[12] Khokhar N, Parveen K, Afzal M, Gilani SA. Assess the Nurse's Knowledge and Standard Practice Regarding the Prevention of Infection in Neutropenic Patients. Journal of Health, Medicine and Nursing.2020Jul;77 0): 28-41.
[13] Eskander HG, Morsy WY, Elfeky HA. Intensive Care Nurses' Knowledge and Practices Regarding Infection Control Standard Precautions at a Selected Egyptian Cancer Hospital. Prevention. 2013; 4(19): 160-74.
[14] Al Qadire M, Ballad CA, Aljezawi ME, Al Omari O, Alaloul F, Musa A *et al* Nurses' knowledge of Chemotherapy-Induced Neutropenia and Its Management: A Cross-Sectional Survey. Journal of Cancer Research and Clinical Oncology.2023 Jul; 149(7): 2893-901. doi: 10.1007/s00432-022-04140-9.
[15] Tarakcioglu Celik GH and Korkmaz F. Nurses' Knowledge and Care Practices for Infection Prevention in Neutropenic Patients. Contemporary Nurse.2017 Mar; 53(2): 143-55. doi: 10.1080/10376178.2 016.1254566.
[16] Silva RA, Ramos YT, Santiago MR, Lima MT, Souza NR, Barros MB *et al.* Evaluation of Nurses' Knowledge About Febrile Neutropenia in Children with Cancer. Health Care Sciences.2020 May; 19: e52839-.doi:10. 4025/cienccuidsaude.v19i0.52839.
[17] Abd El-Fattah MA, Hussein F, Mohamed GE, Ahmed RA. Nurses' Performance Regarding Care of Patients Undergoing Stem Cell Transplantation in Hematological Malignancies. Journal of Survey in Fisheries Sciences. 2023 Apr; 10(3S): 3874-89. doi: 10.17762/sfs.v10i3S.1391.
[18] Chui PL, Nasyrah NA, Nur Hazirah A. Nurses' Knowledge and Practice of Neutropenic Care for Infection Prevention in Patients with Cancer. International Conference in Cancer Nursing. 2022 Feb.
[19] Kvåle K. Patients' Perceptions of the Importance of Nurses' Knowledge About Cancer and Its Treatment for Quality Nursing Care. Number 4/July 2010. 2010 Jul; 37(4): 436-42. doi: 10.1188/10.ONF.436-442.
[20] An MB and Talks AH. The 49th Annual Meeting of the European Society for Blood and Marrow Transplantation: Nurses Group–Poster Sessions. Bone Marrow Transplantation. 2023 Nov; 58: 638–659. doi: 10.1038/s41409-023-02058-5.

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Correlation of Dual-Energy X-Ray Absorptiometry and Quantitative Computerized Tomography in Detection of Osteoporosis among Postmenopausal Women

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ABSTRACT

Osteoporosis is a serious health responsibility for clinicians, especially in postmenopausal patients. Dual-energy x-ray absorptiometry is currently the gold standard for the detection of osteoporosis, though its accuracy may be compromised due to concomitant degenerative changes. **Objectives:** To find out the detection rate of osteoporosis in women who have gone through menopause using both dual-energy X-ray absorptiometry and quantitative computerized tomography and to identify correlations between the two. To evaluate quantitative computerized tomography as a possible future imaging modality that can address the constraints of dual-energy x-ray absorptiometry. **Methods:** From June 2016 to July 2017, this cross-sectional study was carried out in the radiology Departments of Capital Hospital and Nuclear Medicine, Oncology and Radiotherapy Institute Hospital, Islamabad. With informed consent, seventy postmenopausal women participated. T-scores were calculated for quantitative computerized tomography and dual-energy x-ray absorptiometry, and data analysis, including the Pearson correlation coefficient, was conducted using SPSS-17. **Results:** The study included postmenopausal women aged 45–70, with menopause lasting over two years. The mean T-scores for quantitative computerized tomography and dual-energy x-ray absorptiometry were -2.4 ± 1.4 SD and -2.1 ± 1.3 SD, respectively. A strong positive correlation was established between quantitative computerized tomography and dual-energy x-ray absorptiometry T-scores ($r=0.808$; $p<0.05$). **Conclusions:** It was concluded that the study showed a constructive association between the T-scores obtained using quantitative computerized tomography and dual-energy x-ray absorptiometry, thus suggesting that quantitative computerized tomography can be used as an alternative to dual-energy x-ray absorptiometry in the detection of osteoporosis.

INTRODUCTION

Osteoporosis is a prevailing affliction condition mostly affecting older adults and women who have gone through menopause. It causes the strength of the bones to diminish, raising the risk of fracture. Reduced bone density and the bony microarchitecture breakdown, which leaves the bones porous or fragile, are the two main characteristics of osteoporosis [1]. The usual initial clinical presentation of osteoporosis is a fracture. Diagnosis and early management of osteoporosis is important as it has diverse clinical presentation; most patients with no symptoms wrongly believe that they may not be at risk for osteoporosis. Conversely, a lot of people who have widespread body pain mistakenly believe that osteoporosis is the cause of their symptoms. It is less likely to be true in the absence of fragility fracture. Without taking a bone mineral density (BMD) reading, one can make a clinical diagnosis of osteoporosis if a patient has a fragility fracture, especially in common places including the hip,

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wrist, humerus, ribs, and pelvis [2]. Future fractures of all kinds are strongly predicted by vertebral fractures [3]. Although fragility fractures (VFs) are the most prevalent form of fracture, only around two-thirds of vertebral fractures (VFs) are clinically recognized [4]. A method for looking at the spine to detect vertebral fractures (VFs) is called dual-energy x-ray absorptiometry (DXA) vertebral fracture assessment (VFA) [5]. Compared to traditional spine radiography, this may be completed during BMD testing, which offers more patient convenience, cheaper costs, and less radiation exposure [6]. The diagnosis of osteoporosis may only be considered final, by the classification by the World Health Organization (WHO), if the fragility fracture is missing and BMD can be determined by utilizing dual-energy x-ray absorptiometry (DEXA). The T-score of young people serves as a reference for the BMD threshold values that the WHO has supplied for osteoporosis and low bone mass. The difference in BMD between a patient and a young adult reference group, expressed as standard deviation (SD), is defined as T-score [7]. A T-score of 2.5 SD or below the mean BMD of the adult reference group specifies osteoporosis after controlling for other possible causes of reduced bone density and osteoporosis, such as osteomalacia [8]. The International Clinical Densitometry Society (ICDS) has created guidelines for applying WHO classification in clinical practice. The ICDS advises using the WHO recommendations for postmenopausal women and men over 50, but not for women before menopause and men under 50, due to variations in the relationship between BMD and fracture risk for younger women and men [9]. These days, there are several approaches available for determining bone mineral density. However, since DEXA provides the most exact and reliable estimation of BMD, it is the preferred approach for diagnostic categorization in clinical practice. However, some evidence suggests that there are still limitations to the clinical use of DXA. More than 80% of individuals with osteoporosis-related fragility fractures do not have comparable BMD levels, according to the research. Furthermore, DXA analysis relies on two-dimensional images and is unable to distinguish between cancellous and cortical bone. Furthermore, age-related degenerative changes such as the development of osteophytes, an increase in soft tissue density, and atherosclerosis can cause BMD measurements to be erroneously normal or high [10]. On the other hand, Quantitative Computerized Tomography (QCT) evaluates the hip and spine's volumetric bone density and separately examines cortical and trabecular bone. This method can be used to monitor therapy responses in people when notable progress might be observed [11]. As a result, noninvasive techniques to determine bone mineral density (BMD) are essential for monitoring the progression of osteoporosis and diagnosing it clinically. Dual X-ray absorptiometry (DEXA) and quantitative computed tomography (QCT) are frequently used techniques for calculating BMD. DEXA uses bi-dimensional analysis to evaluate bone mineral density (BMD), which includes both trabecular and cortical bone. In grams per square centimeter or areal density, the findings are shown. Without superimposing cortical bone and other tissues, volumetric trabecular bone density may be evaluated using QCT. In the 1970s, QCT was proposed as a method for assessing bone mineral density (BMD). However, CT technology was initially overlooked due to its limited development and the higher levels of radiation exposure. Recently, though, rapid advancements in CT technology have made it an effective tool for evaluating BMD [12]. DEXA is the primary method for diagnosing osteoporosis. However, its limitations—such as the inability to capture three-dimensional BMD measurements, inaccuracies from scanning artefacts, and BMD overestimation due to factors like aortic calcification, osteophytes, and other degenerative changes highlight the need for alternative imaging modalities that can address these issues. In our setting, we aim to compare QCT with the traditional DXA method for detecting osteoporosis in postmenopausal women. Since QCT is more accessible and less expensive than DEXA, it would be advantageous for patients if it could be demonstrated that its osteoporosis detection rate is equivalent to that of DEXA.

This study aims to find out the detection rates of osteoporosis in women who have gone through menopause using both DXA and QCT and to identify correlations between the two methods. The goal is to evaluate QCT as a possible future imaging modality that can address the limitations of dual-energy X-ray absorptiometry (DEXA).

METHODS

Imaging Radiology Departments of Capital and Nuclear Medicine, Oncology and Radiotherapy Institute (NORI) Hospital in Islamabad hosted this cross-sectional study from June 2016 to July 2017. Already diagnosed cases of multiple myeloma, rheumatoid arthritis, ankylosing spondylitis, connective tissue disease, metabolic or hormonal abnormalities, and primary or secondary skeletal cancers were excluded from the study. The sample size was determined using a sequential non-probability sampling approach, Level of significance=5%, using the WHO sample size calculator. After obtaining written informed consent on a structured form and ethical approval (IRB reference no. IRB-04-18-2-16), seventy postmenopausal women were included in the research following the exclusion of 40 patients. Patients meeting the criteria to be included in the study were selected from the outpatient Departments of Medicine, Gynaecology, and

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Radiology. Each participant received written information and was educated about the study's objectives and benefits before providing informed consent. Data pertinent to clinical presentation and demographic features of the selected patients was recorded. Both imaging procedures were performed by a skilled technician, under the supervision of the trainee researcher, with a one-month interval between them. Similar regions of interest (ROI) were drawn on the lumbar spine for both the techniques by trainee researcher. DXA T-scores were measured using the software, based on the Chinese reference database. Scans were performed on the left hip and supine vertebrae from L1 to L4 in post-anterior projections. QCT measurements were taken using a 64-slicer Toshiba-AQUILION multi-detector CT scan machine, incorporating the Mind-way QCT phantom. Scans of the L1 through L4 vertebrae were taken keeping the patient in the supine position. Mind-ways software analyzed the images by automatically placing elliptical regions of interest in the mid-plane of three vertebral bodies (L2–L4) in the region of trabecular bone, automatically avoiding cortical bone. Vertebrae with fractures were not included in the measurements. Both the International Society for Clinical Densitometry (2007) and the American College of Radiology (2008) thresholds were used for trabecular BMD for spine: 80 mg/cm^3 for osteoporosis (equal to a DXA T-score of -2.5 SD) and 120 mg/cm^3 for osteopenia (equal to a DXA T-score of -1.0 SD). A consultant radiologist verified the final reports, and T-scores were computed for both QCT and DXA. Data analysis was performed using SPSS-17. Continuous variables, including age, BMI, and BMD values from DXA and QCT, were reported as means and standard deviations. Pearson correlation coefficients were used to assess T-score correlations between QCT and DXA using a Bivariate correlation procedure. p-values were considered statistically significant if less than 0.05. Stratification by age, menopausal duration, and BMI were applied to control for confounding factors. Post-stratification analysis with Pearson correlation testing considered p-value=<0.05 as significant.

RESULTS

The mean value of T-scores obtained using QCT and DEXA methods was -2.4 ± 1.4 SD and -2.1 ± 1.3 SD, respectively. Assuming that both variables were approximately normally distributed, "The Bivariate Correlations procedure" in SPSS version 17 was used to correlate the two T-scores. The results of computing the pairwise associations for the set of both variables were shown in a matrix. T-scores determined by QCT and DEXA had a substantial and high positive connection (p<0.05), according to the computed correlation value of 0.808 (Table 1).

Table 1: Correlation Between the Whole Research Sample's Mean T-Scores as Determined by QCT and DEXA

Variables		T Score QCT	T Score DEXA
T-Score QCT	Pearson Correlation	1	0.808
	Sig. (2-Tailed)		0.0001
	n	70	70
T-Score DEXA	Pearson Correlation	0.808	1
	Sig. (2-Tailed)	0.0001	
	N	70	70

Age, BMI, T-scores and duration of menopause in the study population are tabulated (Table 2).

Table 2: Mean Age, BMI, T-Scores and Duration of Menopause in Study Sample

Variables	Mean + SD
Age (Years)	59.6 ± 6.9
BMI (Kg/M^2)	25.5 ± 8.7
T Score Qct	-2.4 ± 1.4
T Score Dexa	-2.1 ± 1.3
Duration of Menopause (Years)	14.9 ± 6.2

In the age group 45-55 years, the correlation coefficient calculated was 0.851, and in the age group 56-70 years, it was 0.751, suggesting that T-scores obtained by DEXA and QCT have a substantial and favourable connection (p<0.05) (Table 3).

Table 3: Correlation Between Mean T-Scores Measured Through QCT and DEXA in Age-Based Stratification

Age 45-55 Years		T Score QCT	T Score DEXA
T-Score QCT	Pearson Correlation	1	0.851
	Sig. (2-Tailed)	-	0.0001
	N	23	23
T-Score DEXA	Pearson Correlation	0.851	1
	Sig. (2-Tailed)	0.0001	-
	N	23	23
Age 55-70 Years			
T-Score QCT	Pearson Correlation	1	0.759
	Sig. (2-Tailed)	-	0.0001
	N	47	47
T-Score DEXA	Pearson Correlation	0.759	1
	Sig. (2-Tailed)	0.0001	-
	N	47	47

T-scores determined by QCT and DEXA show a high positive association (p<0.05) with a correlation coefficient of 0.866 in women who have gone through menopause for less than ten years and 0.760 in women who have gone through menopause for more than ten years (Table 4).

Table 4: Correlation Between Mean T-Scores Measured Through QCT and DEXA (Menopause)

Menopause of ≤10 Years		T Score QCT	T Score DEXA
T-Score QCT	Pearson Correlation	1	0.866
	Sig. (2-Tailed)	-	0.0001
	N	16	16

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T-Score DEXA	Pearson Correlation	0.866	1
	Sig. (2-Tailed)	0.0001	-
	N	16	16
Menopause Of >10 Years			
T-Score QCT	Pearson Correlation	1	0.760
	Sig. (2-Tailed)	-	-
	N	54	54
T-Score DEXA	Pearson Correlation	0.760	1
	Sig. (2-Tailed)	-	-
	N	54	54

DISCUSSION

An evaluation of bone mineral density can be used to speculate the likelihood of osteoporotic fractures. Dual-energy X-ray absorptiometry (DEXA) and quantitative computed tomography (QCT) are two extensively used techniques for diagnosing osteoporosis. In the mid-1970s, Quantitative Computed Tomography (QCT) saw the introduction of its initial iteration. This technique is usually used to measure the bone mineral density (BMD) in (mg/cm3) of the trabecular bone of the lumbar spine [13]. In contemporary diagnostic and therapeutic guidelines, DEXA is still assigned as the "gold standard" to identify osteoporosis and foresee fracture risk [14]. However, without using ionizing radiation, quantitative ultrasound (QUS) and quantitative magnetic resonance (QMR) offer novel methods to evaluate bone microarchitecture besides the density of bone minerals [15]. A special benefit of whole-body scanners for quantitative computed tomography (QCT) is the ability to pick the individual components of bone mineral density (BMD) including trabecular, cortical, and subcortical BMD most notably in the hip and spine, although the distal forearm may also be examined [16, 17]. Treatment effects have a greater impact on trabecular architectural parameters than BMD. It is appropriate for treated patients who follow their treatment plan to see stability or an increase in BMD. A study found that opportunistic QCT screening inhibited 2.6 further VFs for every 1,000 women and 2 extra VFs for every 1,000 males. The probabilistic sensitivity analysis showed that QCT screening remained economical in 90.0% of iterations for males and 88.3% for females [18]. Another study revealed that in individuals with fragility compression fractures of the vertebrae, DXA failed to detect osteoporosis [19]. A comparative study between DXA and QCT concluded that QCT is better in the evaluation of lumbar osteoporosis than DXA [20]. We conducted the current study because there is a dearth of evidence-based information about BMD assessment. In this work, we discovered a link between postmenopausal osteoporotic women's mean bone mineral density (BMD), as determined by dual-energy X-ray absorptiometry, and quantitative computed tomography. The T-scores acquired by QCT and DEXA demonstrated a mean value of -2.4 ± 1.4 SD and -2.1 ± 1.3 SD, respectively, based on our findings. A noteworthy and substantial positive correlation (r=0.808; p<0.05) was discovered between the T-scores derived by DEXA and QCT. A similar pattern was seen after stratification by age, BMI, and menopause duration.

CONCLUSIONS

It was concluded that QCT offers accurate osteoporosis detection comparable to DXA, showing a significant correlation between the two methods. Additionally, QCT can help prevent DXA from overestimating bone mineral density (BMD) when other sclerotic conditions are present, such as bone islands, spinal degeneration, and atherosclerosis. While QCT may be more sensitive in identifying osteoporosis, additional studies with high sample sizes are needed to confirm its effectiveness.

Authors Contribution

Conceptualization: SY
Methodology: SY, SBK, MAA, RMHK
Formal analysis: MAA, HR, RMHK
Writing review and editing: HR, RZ

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Langdahl BL. Overview of Treatment Approaches to Osteoporosis. British Journal of Pharmacology.2021 May; 178(9): 1891-906. doi: 10.1111/bph.15024.

[2] Dimai HP and Fahrleitner-Pammer A. Osteoporosis and Fragility Fractures: Currently Available Pharmacological Options and Future Directions. Best Practice and Research Clinical Rheumatology.2022 Sep; 36(3): 101780. doi: 10.1016/j.berh.2022.101780.

[3] Lorentzon M, Johansson H, Harvey NC, Liu E, Vandenput L, McCloskey EV *et al*. Osteoporosis and Fractures in Women: The Burden of Disease. Climacteric.2022Jan;25(1):4-10.doi:10.1080/13697137 .2021.1951206.

[4] Himič V, Syrmos N, Ligarotti GK, Kato S, Fehlings MG, Ganau M. The Role of Genetic and Epigenetic Factors in Determining the Risk of Spinal Fragility Fractures: New Insights in the Management of Spinal Osteoporosis. Quantitative Imaging in Medicine and Surgery. 2023 Nov; 13(11): 7632. doi: 10.21037/qims-23-513.

DOI: https://doi.org/10.54393/pjhs.v5i12.1811

[5] Khan AA, Slart RH, Ali DS, Bock O, Carey JJ, Camacho P *et al*. Osteoporotic Fractures: Diagnosis, Evaluation, and Significance from the International Working Group on DXA Best Practices. In Mayo Clinic Proceedings.2024Jul:99(7):1127-1141.doi:10.1016/j.mayocp.2024.01.011.

[6] Kennel KA and Drake MT. The Long and Winding Road to Improving Bone Mineral Density Testing and Reporting. In Mayo Clinic Proceedings. 2024 Jul; 99(7): 1027-1029. doi: 10.1016/j.mayocp.2024.05.008.

[7] Camacho PM, Petak SM, Binkley N, Diab DL, Eldeiry LS, Farooki A *et al*. American Association of Clinical Endocrinologists/American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis 2020 Update. Endocrine Practice.2020 May; 26: 1-46.doi:10.4158/GL-2020-0524SUPPL.

[8] LeBoff MS, Greenspan SL, Insogna KL, Lewiecki EM, Saag KG, Singer AJ *et al*. The Clinician's Guide to Prevention and Treatment of Osteoporosis. Osteoporosis International.2022Oct;33(10):2049-102. doi: 10.1007/s00198-021-05900-y.

[9] Amarnath SS, Kumar V, Das SL. Classification of Osteoporosis. Indian Journal of Orthopedics.2023 Dec; 57(Suppl 1): 49-54. doi: 10.1007/s43465-023-01058-3.

[10] Pu M, Zhang B, Zhu Y, Zhong W, Shen Y, Zhang P. Hounsfield Unit for Evaluating Bone Mineral Density and Strength: Variations in Measurement Methods. World Neurosurgery.2023Dec;180:e56-68.doi:10.1016/j.wneu.2023.07.146.

[11] Gruenewald LD, Koch V, Martin SS, Yel I, Eichler K, Gruber-Rouh T *et al*. Diagnostic Accuracy of Quantitative Dual-Energy CT-Based Volumetric Bone Mineral Density Assessment for the Prediction of Osteoporosis-Associated Fractures. European radiology. 2022 May; 32: 1-9. doi: 10.1007/s00330-021-08323-9.

[12] Alawi M, Begum A, Harraz M, Alawi H, Bamagos S, Yaghmour A *et al*. Dual-Energy X-Ray Absorptiometry (DEXA) Scan Versus Computed Tomography for Bone Density Assessment. Cureus.2021 Feb; 13(2). doi: 10.7759/cureus.13261.

[13] Fang Y, Li W, Chen X, Chen K, Kang H, Yu P *et al*. Opportunistic Osteoporosis Screening in Multi-Detector CT Images Using Deep Convolutional Neural Networks. European Radiology. 2021 Apr; 31: 1831-42. doi: 10.1007/s00330-020-07312-8.

[14] Do TD, Rahn S, Melzig C, Heußel CP, Stiller W, Kauczor HU *et al*. Quantitative Calcium-Based Assessment of Osteoporosis in Dual-Layer Spectral CT. European Journal of Radiology.2024 Sep; 178: 111606. doi: 10.1016/j.ejrad.2024.111606.

[15] Chen M, Gerges M, Raynor WY, Park PS, Nguyen E, Chan DH *et al*. State of the Art Imaging of Osteoporosis. In Seminars in Nuclear Medicine.2024 May;54(3):415-426. doi: 10.1053/j.semnuclmed.2023.10.008.

[16] Dheeraj D, Chauhan U, Khapre M, Kant R. Comparison of Quantitative Computed Tomography and Dual X-Ray Absorptiometry: Osteoporosis Detection Rates in Diabetic Patients.Cureus.2022Mar;14(3).doi:10.7759/cureus.23131.

[17] Cheng X, Zhao K, Zha X, Du X, Li Y, Chen S *et al*. Opportunistic Screening Using Low-Dose CT and the Prevalence of Osteoporosis in China: A Nationwide, Multicenter Study. Journal of Bone and Mineral Research.2020 Dec; 36(3): 427-35. doi:10.1002/jbmr.4187.

[18] Rühling S, Schwarting J, Froelich MF, Löffler MT, Bodden J, Hernandez Petzsche MR *et al*. Cost-Effectiveness of Opportunistic QCT-Based Osteoporosis Screening for the Prediction of Incident Vertebral Fractures. Frontiers in Endocrinology.2023 Jul; 14: 1222041. doi: 10.3389/fendo.2023.1222041.

[19] Paggiosi MA, Debono M, Walsh JS, Peel NF, Eastell R. Quantitative Computed Tomography Discriminates Between Postmenopausal Women with Low Spine Bone Mineral Density with Vertebral Fractures and Those with Low Spine Bone Mineral Density Only: The SHATTER Study. Osteoporosis International.2020 Apr; 31: 667-75. doi: 10.1007/s00198-020-05317-z.

[20] Lin W, He C, Xie F, Chen T, Zheng G, Yin H *et al*. Discordance in Lumbar Bone Mineral Density Measurements by Quantitative Computed Tomography and Dual-Energy X-Ray Absorptiometry in Postmenopausal Women: A Prospective Comparative Study. The Spine Journal.2023 Feb; 23(2): 295-304. doi: 10.1016/j.spinee.2022.10.014.

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Antimicrobial Activity of Azithromycin versus Ciprofloxacin in the Treatment of Uncomplicated Enteric Fever in Children and Adolescents: Preclinical Trial

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ABSTRACT

Typhoid fever, or enteric fever, is an infectious disorder particularly prevalent in Pakistan. Salmonella Typhi is the common and occasionally fatal cause of enteric fever. **Objective:** To compare the antimicrobial activity of Azithromycin versus Ciprofloxacin in the treatment of uncomplicated enteric fever in children. **Methods:** This was a comparative cross-sectional study conducted at the Department of Microbiology at Ziauddin University Hospital, Karachi. It lasted six months, from 3 January 2020 to 2 July 2020. There were 152 blood samples in all. According to Clinical and Laboratory Standards Institute guidelines, the antibiotic susceptibility of the isolates was assessed using the Modified Kirby Bauer disc diffusion method on Muller-Hinton agar. **Results:** When treating typhoid fever in children with simple enteric fever, the susceptibility pattern of Salmonella Typhi revealed that azithromycin was more efficient than ciprofloxacin in preventing the growth of Salmonella Typhi across all samples. Ciprofloxacin showed resistant bacteria. **Conclusion:** Azithromycin seems to be more clinically effective than ciprofloxacin in treating children's simple enteric fever when treating typhoid fever.

INTRODUCTION

Children are more prone than adults to the spread of infectious diseases because their immune systems are still developing [1]. Typhoid fever, or enteric fever, is one of these infectious disorders that is particularly prevalent in Pakistan. Salmonella Typhi is a common and occasionally fatal cause of enteric fever. Its feco-oral method of transmission and inadequate sanitation make it most common in impoverished nations [2]. Reported estimates of the annual incidence of enteric fever are global, ranging from 12 million to 27 million cases. The estimated death toll varied from 129,000 to 223,000 based on data from the year 2017, as per the epidemiological analyses [1, 2]. Interventions focusing on early diagnosis and appropriate clinical treatment, along with risk factor prevention, can improve the outcomes of enteric fever. Chloramphenicol used to be the recommended medication. however, it is no longer in use due to adverse effects, relapses, and widespread bacterial resistance. Next, co-trimoxazole and ampicillin were employed as suitable and efficient substitutes. However, in the 1980s, S. typhi developed

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resistance to ampicillin, co-trimoxazole, and chloramphenicol. As a result, fluoroquinolone use increased. Fluoroquinolone resistance also gradually emerged [3]. Multi-drug resistant bacteria, resistant to fluoroquinolones, ampicillin, co-trimoxazole, and chloramphenicol, increased in frequency from 19% in 1987 to 100% in 1993, declining to 5% by 2000 [4]. At present, azithromycin and extended-spectrum cephalosporins (ceftriaxone, cefixime) are being recommended as therapeutics for enteric fever [5]. When a single therapy fails to provide the desired results, a combination of these medications is required to potentially expand the antibacterial spectrum through pharmacological synergism. Azithromycin is more effective than many other competing medications in reducing recurrence, length of hospital stay, and clinical failure rate, according to many trials. It is also well tolerated [6]. Because of this, physicians are now using azithromycin and cephalosporins as the final treatments for which there is solid evidence from clinical trials. There is evidence of the introduction of a cephalosporin-resistant strain of Salmonella Typhi today, in addition to the bacterial burden of enteric fever that is currently prevalent in South Asia [7]. Fluoroquinolones, such as Ciprofloxacin, are being used as the first-line treatment due to the advent of multidrug-resistant strains (MDR) to first-line antibiotics including Chloramphenicol, Ampicillin, and Trimethoprim-sulfamethoxazole [8]. Although azithromycin and ciprofloxacin are among the oral antibiotics that are most frequently administered in our area as an empirical treatment for uncomplicated enteric fever, concerns about treatment response differences still exist. Recently, a significant typhoid outbreak in Pakistan has been linked to Salmonella typhi genetic variants that are highly resistant to drugs. Multiple cases of these strains have been documented [9]. Along with resistance, azithromycin and ciprofloxacin have been associated with varying fever clearance time (FCT), which averages 4-5 days. This has been connected to less-than-ideal therapeutic response, elevated morbidity, treatment expenses, and healthcare burden [10]. The best oral antimicrobial treatment for simple typhoid fever is unknown because of the constantly shifting pattern of microbial resistance and the inconsistent responses to medications.

This study aims to investigate the comparative efficacy of azithromycin and ciprofloxacin in our local community of children with uncomplicated enteric fever, as to our knowledge there is currently no data available on it.

METHODS

The comparative cross-sectional study was done by the microbiology Department of Ziauddin University Hospital in Karachi. The study was for six months from 3rd January 2020 to 2nd July 2020. After obtaining informed consent, all blood samples from inpatients and outpatients were taken for sensitivity and culture. Male and female participants in the study ranged in age from 1 to 20 years (Children and adolescents). Duplicate and repeat samples from the same patient, as well as blood samples for sensitivity and culture that showed growth other than bacteria, including yeast or fungus, were not included. The management of Ziauddin Hospital granted authorization, and the institutional ethics committee provided written approval IRB: 0611118ZIMIC. Using the WHO Sample size calculator and the Meropenem sensitivity statistics of 87% margin of error, 9%, and 95% confidence interval, the sample size was determined to be 54 per group. All blood cultures were obtained from a peripheral vein while adhering to the proper aseptic protocols before starting any antibiotic therapy, for the pediatric population, pediatric BACTEC bottles were used. The sample was cultured for five days at 35.5 °C ± 1.5°C in a BACTEC 9240 blood culture apparatus with a blood-to-broth ratio of 1:10. The BACTEC device uses fluorescence sensing technology to identify the growth of microorganisms. To evaluate the amount of microbiological development that the device's flag and audible sound could identify, a gram-stained smear of the broth was used. To isolate the bacteria, they were then sub-cultured on 5% sheep blood agar, chocolate, and Mac-Conkey agar plates and incubated at 37°C for 18 to 24 hours. Plates of sheep blood agar, chocolate and Mac-Conkey agar were pre-incubated to rule out any possibility of mishandling during plate preparation. Mac-Conkey agar plates were maintained in an aerobic incubator at 37°C, while sheep blood agar and chocolate agar were incubated in a capnophilic atmosphere with 5–10% CO2. Standard microbiological methods were used to identify the S. typhi clinical isolates, including gram staining, the oxidase and catalase tests, motility, triple-sugar iron (TSI) fermentation, colony morphology, and, for the final confirmation, biochemical tests of the analytical profile index (API 20 E) [10]. Following Clinical and Laboratory Standards Institute (CLSI) recommendations, the isolate's antibiotic susceptibility patterns were assessed in two treatment groups one getting azithromycin (Group A) and the other receiving ciprofloxacin (Group B) using the Modified Kirby Bauer disc diffusion method on Muller-Hinton agar. For 18–24 hours, the Muller-Hinton agar plates were kept in an aerobic environment at 35°C ± 2°C. Version 20 of the Statistical Package for the Social Sciences was used to enter and analyze the data. Data were shown as a percentage and as frequency. The Chi-square test was used. p-value less than 0.05 was regarded as significant.

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RESULTS

A total of 152 patients, aged 1 to 20 years, were enrolled in the study and randomly assigned to two treatment groups to compare the efficacy of Ciprofloxacin and Azithromycin in treating uncomplicated typhoid fever. Group A included patients receiving Azithromycin, while Group B comprised those treated with Ciprofloxacin. 38% of Group A samples exhibited sensitivity to Azithromycin across the 1–20-year age range. In Group B, 21% of samples showed sensitivity to Ciprofloxacin in the 1–10-year age group, while 79% were resistant. Among patients aged 10–20 years in Group B, 8% demonstrated sensitivity to Ciprofloxacin, while 92% were resistant Table 1.

Table 1: Antimicrobial Susceptibility Pattern According to Age

Age Group	Antimicrobial Susceptibility	Group A (Azith -15µg)	Group B (Cipro -5µg)	p-value
1-10 Years	Sensitive	38 (100%)	8 (21%)	0.01
	Resistant	0 (0%)	30 (79%)	
10-20 Years	Sensitive	38 (100%)	3 (8%)	0.02
	Resistant	0 (0%)	35 (92%)	
Total		76	76	152

Chi-Square Test was applied. p-value ≤0.05 is considered as Significant. Group A (Azith-Azithromycin 15µg): Refers to the antimicrobial susceptibility test using Azithromycin with a 15µg disc. Group B (Cipr-Ciprofloxacin 5µg): Refers to the antimicrobial susceptibility test using Ciprofloxacin with a 5µg disc.

Analysis based on gender revealed that 45 (90%) of male were sensitive to Azithromycin, while 5 (10%) were resistant. In comparison, 10 (17%) of male were sensitive to Ciprofloxacin, while 50 (83%) were resistant. Azithromycin was significantly more effective in male compared to Ciprofloxacin (p-value=0.001). For females, 7 (38%) were sensitive to Azithromycin, while 12 (62%) were resistant. Similarly, 9 (38%) of females were sensitive to Ciprofloxacin, while 14 (63%) were resistant. No significant difference in drug response was observed between Azithromycin and Ciprofloxacin in females (p-value=0.5). Azithromycin demonstrated greater efficacy compared to Ciprofloxacin in treating uncomplicated typhoid fever, particularly in younger age groups and male. The p-value for the 1–10-year age group was 0.01, for the 10–20-year age group was 0.02, for male was 0.001, and for female was 0.5 in table 2.

Table 2: Antimicrobial Susceptibility Pattern According to Gender

Gender	Susceptibility	Group A (Azith -15µg)	Group B (Cipro -5µg)	p-value
Male	Sensitive	45 (90%)	10 (17%)	0.001
	Resistant	5 (10%)	50 (83%)	
Female	Sensitive	7 (38%)	9 (38%)	0.5
	Resistant	12 (62%)	14 (63%)	
Total		69	83	152

The Chi-Square Test was applied. p-value ≤0.05 is considered as Significant. Group A (Azith-Azithromycin 15µg): Refers to the antimicrobial susceptibility test using Azithromycin with a 15µg disc. Group B (Cipr-Ciprofloxacin 5µg): Refers to the antimicrobial susceptibility test using Ciprofloxacin with a 5µg disc.

DISCUSSION

Young children in Pakistan are at risk of contact with typhoid infection due to improper hygiene. The increasing resistance to second-line anti-typhoid agents is a public health concern. The incidence of superbugs in children is a public health emergency. The current state of antimicrobial surveillance in Pakistan needs urgent attention to prevent antibiotic resistance and appropriate stewardship. In impoverished nations like Pakistan, enteric fever is a serious health issue that requires a treatment option that is both affordable and effective to be employed often with limited resources at our disposal [11]. Two typical antibiotics used to treat typhoid fever are azithromycin and ciprofloxacin. However, due to variations in pharmacodynamics, resistance patterns, and patient tolerability, these drugs' efficacy can vary, especially when administered in children. Azithromycin is a macrolide antibiotic that inhibits protein synthesis in bacteria, halting growth and exerting a bacteriostatic effect, particularly effective against Gram-positive and Gram-negative pathogens like Salmonella Typhi [12]. Ciprofloxacin, a fluoroquinolone antibiotic, inhibits DNA gyrase and topoisomerase IV, resulting in bactericidal activity, making it popular for treating typhoid fever due to its potent Gram-negative bacteria resistance [13]. This study, which compared azithromycin and ciprofloxacin for treating children's uncomplicated enteric fever, showed that azithromycin was highly responsive, with clinical efficacy of over 90% (p-value is significant), which is consistent with the findings of many other studies [14-16]. Azithromycin treatment was found to be effective in a small number of adult studies, but not significantly enough in children, despite our findings that the majority of children responded favourable to azithromycin [17]. In this investigation, azithromycin was able to limit growth by over 90%. Azithromycin's exceptional intracellular penetration, which produces potent therapeutic efficacy primarily against intracellular S. typhi, may account for its high responsiveness. The likelihood of Salmonella Typhi strains developing resistance to antibiotics is one of the most important factors affecting the selection of antibiotic treatment for typhoid fever. There is a growing demand for alternative antibiotics due to treatment failures caused by fluoroquinolone resistance, notably in South Asia, which includes ciprofloxacin. Mutations in the bacterial DNA gyrase and topoisomerase genes' quinolone resistance-

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determining regions (QRDR) are frequently the cause of this resistance [18]. Azithromycin has been shown in numerous studies to be clinically effective in treating pediatric typhoid fever. Numerous studies have also demonstrated that azithromycin is more effective than ciprofloxacin in treating typhoid fever in children [19]. When compared to ciprofloxacin, clinical investigations have shown that azithromycin had higher cure rates and a quicker time to defervescence, or the reduction of fever [20]. In addition, compared to ciprofloxacin, azithromycin is generally well-tolerated in children and causes fewer gastrointestinal adverse effects. Despite its effectiveness, ciprofloxacin can cause side effects in juvenile children, including tendinitis, gastrointestinal distress, and infrequently, arthropathy. In the case of young patients, azithromycin is a safer choice due to these possible side effects [21].

CONCLUSIONS

It was concluded that azithromycin seems to be more clinically effective than ciprofloxacin in treating children's simple enteric fever when treating typhoid fever. Because of its daily dosage, tolerability, and lower risks of resistance, azithromycin is a safer substitute. For management to be effective, resistance tendencies must be regularly monitored.

Authors Contribution

Conceptualization: ZI, YMP, FP
Methodology: ZI, YMP, FP
Formal analysis: SPS, HA
Writing review and editing: ZI, ANB, YMP, FP, SPS, HA

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

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REFERENCES

[1] Igiri B, Okoduwa SI, Munirat SA, Otu-Bassey IB, Bashir A, Onyiyioza OM *et al.* Diversity in Typhoid Diagnostic Protocols and Recommendation for Composite Reference Standard.2021 Jul.doi:10.20944/preprints 202107.0515.v1.

[2] Chand Y and Singh S. Prioritization of Potential Vaccine Candidates and Designing a Multiepitope-Based Subunit Vaccine Against Multidrug-resistant Salmonella Typhi Str. CT18: A Subtractive Proteomics and Immuno-Informatics Approach. Microbial Pathogenesis.2021 Oct;159:105150.doi:10.1016/j.micpath.2021.105150.

[3] Coates AR, Hu Y, Holt J, Yeh P. Antibiotic Combination Therapy Against Resistant Bacterial Infections: Synergy, Rejuvenation and Resistance Reduction. Expert review of Anti-infective therapy.2020 Jan; 18(1): 5-15. doi: 10.1080/14787210.2020.1705155.

[4] Konnur S. Antibiotic Usage, Resistance and Sensitivity Pattern in Paediatric Septicaemia in a Tertiary Care Hospital (Doctoral dissertation, Rajiv Gandhi University of Health Sciences(India)). 2019.

[5] Parry CM, Qamar FN, Rijal S, McCann N, Baker S, Basnyat B. What Should We Be Recommending for the Treatment of Enteric Fever? In Open Forum Infectious Diseases.2023 May; 10(Supplement_1): S26-S31. doi:10.1093/ofid/ofad179.

[6] Kobbernagel HE, Buchvald FF, Haarman EG, Casaulta C, Collins SA, Hogg C *et al.* Efficacy and Safety of Azithromycin Maintenance Therapy in Primary Ciliary Dyskinesia (BESTCILIA): A Multicenter, Double-Blind, Randomized, Placebo-Controlled Phase 3 Trial. The Lancet Respiratory Medicine.2020 May; 8(5): 493-505. doi: 10.1016/S2213-2600(20)30058-8.

[7] Carey ME, Dyson ZA, Ingle DJ, Amir A, Aworh MK, Chattaway MA *et al.* Global Diversity and Antimicrobial Resistance of Typhoid Fever Pathogens: Insights from 13,000 Salmonella Typhi Genomes. MedRxiv.2022 Dec: 2022-12.

[8] Almutairy B. Extensively and Multidrug-Resistant Bacterial Strains: Case Studies of Antibiotics Resistance. Frontiers in Microbiology.2024 Jul; 15:138 1511. doi: 10.3389/fmicb.2024.1381511.

[9] Zakir M, Khan M, Umar MI, Murtaza G, Ashraf M, Shamim S. Emerging Trends of Multidrug-Resistant (MDR) and Extensively Drug-Resistant (XDR) Salmonella Typhi in a Tertiary Care Hospital of Lahore, Pakistan. Microorganisms.2021 Nov;9(12):2484.doi:10.3390/microorganisms9122484.

[10] Hidayatallah Z. Comparative Analysis of Azithromycin and Cefixime in the Treatment of Typhoid Fever. Journal of Advanced Zoology.2024 Jan; 45. doi: 10.53555/jaz.v45iS2.3756.

[11] Ishtiaq A, Khalil S, Khalil S, Ahmed F, Ahmad B, Ghaffar A *et al.* Prevalence of Typhoid Fever among Different Socio-Demographic Groups in District Bahawalnagar, Pakistan: Prevalence of Typhoid Fever. Pakistan Journal of Health Sciences.2023 Nov: 138-43.doi:10.54393/pjhs.v4i11.1063.

[12] Paul D, Chawla M, Ahrodia T, Narendrakumar L, Das B. Antibiotic Potentiation as a Promising Strategy to Combat Macrolide Resistance in Bacterial Pathogens. Antibiotics.2023 Dec; 12(12): 1715. doi: 10.3390/antibiotics12121715.

[13] Chauhan N and Farooq U. Multidrug Resistance: A Challenge in Typhoid Treatment. Asian Journal of

DOI: https://doi.org/10.54393/pjhs.v5i12.2215

Microbiology Biotechnology Environmental Sciences. 2021; 23(2): 163-174.

[14] Raza SK, Javaid H, Bajwa H, Saleem K, Hashim M. Evaluation of Hematological Variables in Patients with Typhoid in Pakistan: Hematological Parameters in Patients with Typhoid. Pakistan Journal of Health Sciences.2022 Nov: 73-7. doi: 10.54 393/ pjhs. v3i06. 104.

[15] Jin C, Gibani MM, Pennington SH, Liu X, Ardrey A, Aljayyoussi G *et al*. Treatment Responses to Azithromycin and Ciprofloxacin in Uncomplicated Salmonella Typhi Infection: A Comparison of Clinical and Microbiological Data from A Controlled Human Infection Model. Plos Neglected Tropical Diseases. 2019 Dec;13(12):e0007955.doi:10.1371/journal.pntd. 0007955.

[16] McCann N, Scott P, Parry CM, Brown M. Antimicrobial Agents for the Treatment of Enteric Fever Chronic Carriage: A Systematic Review. PLoS One.2022 Jul; 17(7): e0272043. doi: 10.1371/journal.pone.0272043.

[17] Herka SN. A Thorough Systematic Review of the Diagnosis and Complication of Typhoid Fever in Children. The Indonesian Journal of General Medicine. 2024 Jun; 1(4): 44-58.

[18] Heidary M, Ebrahimi Samangani A, Kargari A, Kiani Nejad A, Yashmi I, Motahar M *et al*. Mechanism of Action, Resistance, Synergism, and Clinical Implications of Azithromycin. Journal of Clinical Laboratory Analysis.2022 Jun; 36(6):e24427.doi:10.1 002/jcla.24427.

[19] Uzair M, Wali S, Ur Rehman A, Ahmad A, Rafique MH, Nadeem MB. Clinical Efficacy of Oral Azithromycin Versus Other Antimicrobial Drugs in the Treatment of Typhoid Patients Across All Age Groups: A Systematic Review of Randomized Controlled Trials. Journal of Ayub Medical College Abbottabad-Pakistan.2024 Jul; 36(3). doi: 10.55519/JAMC-03-12881.

[20]Machakanur V and Rohit S. Azithromycin Versus Ceftriaxone—Which Is Better in Uncomplicated Typhoid Fever? A Clinical Trial in a Tertiary Care Hospital. Journal of Evolution of Medical and Dental Sciences.2019Apr;8(17):1394-9.doi:10.14260/jemds/ 2019/310.

[21] Rampedi PN, Ogunrombi MO, Adeleke OA. Leading Pediatric Infectious Diseases Current Trends, Gaps, and Future Prospects in Oral Pharmaco-therapeutic Interventions. Pharmaceutics.2024 Jun; 16(6): 712. doi: 10.3390/pharmaceutics16060712.

DOI: https://doi.org/10.54393/pjhs.v5i12.1939

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Original Article

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Efficacy of Membrane Sweeping in Primigravida and Effect on the Duration of Pregnancy

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ABSTRACT

Prolonged pregnancies, defined as those extending beyond 40 weeks of gestation pose increased risks to both maternal and fetal health, including higher rates of cesarean delivery, postpartum hemorrhage, and neonatal complications. Membrane sweeping is a non-pharmacological, mechanical method of labour induction that is often used to reduce the likelihood of post-term pregnancies and their associated risks. **Objectives:** To evaluate the efficacy of membrane sweeping in initiating spontaneous labour and its effect on the duration of pregnancy in women with term pregnancies. **Methods:** A Quasi-experimental study was conducted in the Department of Obstetrics and Gynecology, Lady Reading Hospital, Peshawar, from September 2023 to March 2024. One hundred and thirty-six primigravida women aged 40 to 42 weeks who underwent membrane sweeping for labour induction were selected. Effectiveness was assessed in terms of initiation of spontaneous labour. Other parameters considered were maternal and fetal outcomes. **Results:** Spontaneous labour was successfully initiated in 76.5% of patients and notably reduced the mean gestational age at delivery (40.49 ± 0.591 weeks) compared to those who did not achieve spontaneous labour (41.72 ± 0.581 weeks, p=0.0001). Most patients required one or two sweeps to achieve labour, demonstrating the effectiveness of membrane sweeping in reducing pregnancy duration. **Conclusions:** It was concluded that membrane sweeping is an effective and non-invasive method for initiating spontaneous labour and reducing pregnancy duration, minimizing the need for medical induction and preventing post-term pregnancies.

INTRODUCTION

Membrane sweeping is a procedure performed during vaginal examination in which the examiner inserts fingers into the cervical canal and rotates them to detach the amniotic membranes from the lower uterine wall [1, 2]. This process stimulates the release of prostaglandins, leading to cervical softening and the initiation of uterine contractions. Membrane sweeping is considered a minimally invasive technique for labour induction [3, 4]. A study recorded that membrane sweeping was effective in 87.06% for initiating the onset of labour, vaginal delivery in 83.53%, and cesarean observed in 16.47% [5]. Postdate pregnancies, defined as those extending beyond 40 weeks of gestation, pose risks to the fetus due to reduced placental function, which can lead to fetal mortality [6-8]. Early ultrasound for accurate pregnancy dating is recommended to reduce the incidence of postdate pregnancies, as relying solely on the last menstrual period is less precise [9, 10]. In a low-risk population, sweeping the membranes is a safe way to shorten a term pregnancy and lower the frequency of prolonged pregnancy [11]. Initiating labour before 42 weeks can reduce these risks, although it may impact the childbirth experience [12]. Membrane sweeping is a non-invasive procedure that involves separating the amniotic membranes from the cervix. It is suggested to be a safe and effective way to induce labour and reduce the risks associated with post-term pregnancies. However, the available evidence on its effectiveness and safety, particularly in first-time pregnant

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women, remains limited.

This study aims to assess the outcomes of membrane sweeping in primigravida with prolonged pregnancies.

METHODS

A quasi-experimental study was conducted at Lady Reading Hospital, Peshawar, from September 2023 to March 2024, after obtaining ethical approval from the hospital's ethical committee (REF: No.1/LRH/MTI). A total of 136 primigravida women aged 18 to 40 years, with a gestational age of 40-42 weeks, were included. Women with prior health issues, obstetrical complications, or those who declined participation were excluded. Each patient underwent membrane sweeping to initiate labour, membrane sweeping was performed by the researcher, a gloved finger was inserted in the cervix, and then the finger was moved around the inner cervical OS in a circular fashion separating the membranes from the lower uterine segment. If there was no response after 72 hours, the procedure was repeated, with up to four sweeps performed. Once uterine contractions began, no additional induction methods were used, and labour was managed accordingly. Data on the number of sweeps required, the interval from sweeping to delivery, mode of delivery, spontaneous delivery, maternal outcomes (including infection and postpartum hemorrhage), and fetal outcomes (birth weight, neonatal intensive care unit (NICU) admission, and APGAR score) were collected. Effectiveness was defined as the occurrence of spontaneous delivery, characterized by the initiation of labour naturally without medical induction and resulting in delivery before 42 weeks of gestation. Birth weight was measured using an analogue scale, birth weight of greater than or equal to 2.5 kg was considered normal. APGAR score was calculated at 1 minute and 5 minutes after birth, an APGAR score greater than or equal to 7 was considered normal. The sample size was calculated using Open-Epi, utilizing the previous frequency of spontaneous labour 88.3% [13], margin of error of 5.41% and a confidence interval of 95%. Patients were selected using a non-probability consecutive sampling technique. Data analysis was performed using SPSS version 23.0. Frequencies along with percentages were calculated for categorical variables such as spontaneous labour, comorbid condition, maternal and fetal outcome, means, and standard deviations were calculated for age, gestational age and time from membrane sweeping to the onset of labour. The consent form was taken Chi-Square test was applied to assess the association between spontaneous labour and frequency of membrane sweeping, while the independent samples T-test was used to assess the association between spontaneous delivery and gestational age. p-value <0.05 was considered significant.

RESULTS

The study included 136 patients with a mean age of 28.84 ± 4.83 years and a mean gestational age of 40.78 ± 0.78 weeks. The mean time from membrane sweeping to the onset of labour was 40.95 ± 19.14 hours. In our study, 41.9% of patients were literate, while 58.1% were illiterate (Figure 1).

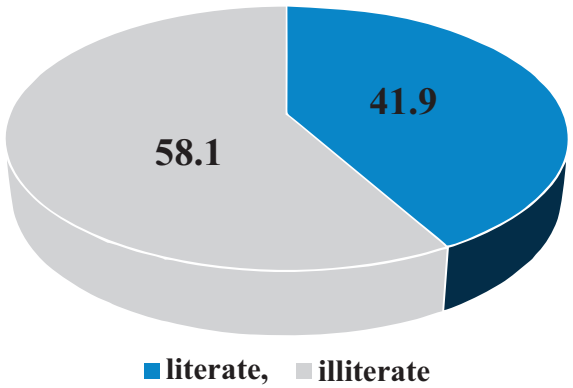

Figure 1: Age Distribution of selected Patients

Comorbid conditions included diabetes (8.1%), hypertension (13.2%), and obesity (10.3%) (Table 1).

Table 1: Comorbid Conditions among study participants

Comorbid Conditions	Frequency (%)
Diabetes	11 (8.1%)
Hypertension	18 (13.2%)
Obesity	14 (10.3%)

The frequency of membrane sweeps was performed (Table 2).

Table 2: Frequency of Membrane Sweeping among study participants

Membrane Sweeping	Frequency (%)
One Time	55 (40.4%)
Two Times	66 (48.5%)
>Two Times	15 (11.0%)
Total	136 (100%)

Results present the frequency of spontaneous delivery, which we considered effective in this study, we observed that 76.5% of patients achieved spontaneous delivery following membrane sweeping. This indicates that membrane sweeping effectively initiated labour naturally in a significant majority, reducing the dependency on medical induction methods. The observed spontaneous delivery rate suggests that the intervention helped avert post-term pregnancies by promoting timely labour onset (Figure 2).

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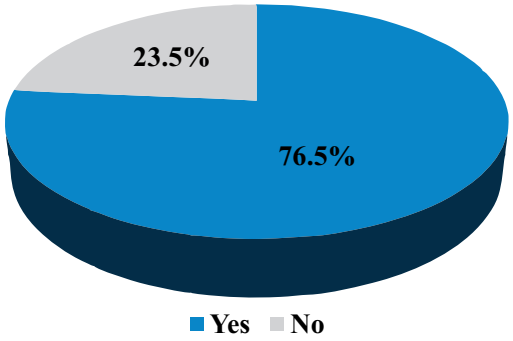

Figure 2: Spontaneous Delivery among study participants

In terms of maternal outcomes, normal vaginal delivery was achieved in 112 (82.4%) patients, while 24 (17.6%) underwent cesarean sections. Postpartum hemorrhage was observed in 6 (4.4%) patients, and infection in 2 (1.5%) (Table 3).

Table 3: Maternal Outcomes among study participants

Maternal Outcomes	Frequency (%)
Mode of Delivery	
Normal Vaginal Delivery	112 (82.4%)
Caesarean Section	24 (17.6%)
Postpartum Hemorrhage (PPH)	
Yes	6 (4.4%)
No	130 (95.6%)
Infection	
Yes	2 (1.5%)
No	134 (98.5%)

Fetal outcomes showed that 15 (11%) newborns required NICU admission. A birth weight ≥2.5 kg was observed in 119 (87.5%) newborns, and an APGAR score ≥ 7 was recorded in 129 (94.9%) newborns (Table 4).

Table 4: Fetal Outcomes among study participants

Fetal Outcomes	Frequency (%)
Admission to NICU	15 (11%)
Birth Weight ≥2.5 kg	119 (87.5%)
APGAR Score ≥7	129 (94.9%)

The effect of membrane sweeping on the duration of pregnancy is evident, as patients who experienced spontaneous labour had a mean gestational age of 40.49 ± 0.591 weeks, significantly lower than the 41.72 ± 0.581 weeks for those who did not achieve spontaneous labour (p=0.0001). This demonstrates that membrane sweeping effectively reduces the duration of pregnancy by promoting labour onset before post-term gestation (Table 5).

Table 5: Association of Spontaneous Delivery with Gestational Age

Maternal Outcomes	n	Mean ± S.D	p-value
Yes	104	40.49 + 0.591	0.0001
No	32	41.72 + 0.581	

Study shows the association of spontaneous labour with the frequency of membrane sweeping. Spontaneous labour was most common after a single membrane sweep, accounting for 50.0% of cases, followed by 40.4% after two sweeps, and only 9.6% after more than two sweeps. This association was statistically noteworthy (p=0.0001), suggesting that fewer sweeps are more effective in achieving spontaneous labour. These findings underscore the effectiveness of membrane sweeping in initiating spontaneous labour, particularly with fewer sweeps, and reducing the need for prolonged intervention (Table 6).

Table 6: Association of Spontaneous Delivery with Frequency of Membrane Sweeping

Spontaneous Labor	Membrane Sweeping			Total	p-value
	OneTime	Two Times	>Two Times		
Yes	52	52	52	104	0.0001
	50.0%	40.4%	9.6%	100.0%	
No	3	24	5	32	
	9.4%	75.0%	15.6%	100.0%	
Total	55	66	15	136	
	40.4%	48.5%	11.0%	100.0%	

DISCUSSION

Induction of labour (IOL) is a critical intervention in obstetrics, used to reduce risks associated with prolonged pregnancies. It is estimated that 20-30% of all pregnancies worldwide require IOL, particularly when the risks of continuing the pregnancy, such as fetal growth restriction, oligohydramnios, or preeclampsia, outweigh the benefits. The ARRIVE trial has further validated that IOL at 39 weeks in low-risk nulliparous women can be more beneficial than expectant management, leading to better maternal and fetal outcomes [14]. The success of IOL heavily depends on the cervical status, which is a significant determinant of whether labour induction will be effective. Prostaglandins play a pivotal role in the process of cervical ripening by promoting the softening, thinning, and dilatation of the cervix. This hormonal activity is crucial for initiating labour, and when cervical ripening does not occur naturally, prostaglandins can be used therapeutically. Mechanical methods such as membrane sweeping also facilitate labour induction by stimulating the local release of endogenous prostaglandins [15]. Previous studies have debated the effects and outcomes of starting membrane sweeping before 42 weeks of gestation. For instance, a randomized controlled trial (RCT) comparing the effects of membrane sweeping between 38-40 weeks versus only pelvic examination found that the median duration to delivery was significantly shorter in the membrane sweeping group. This result suggests that membrane sweeping is effective in reducing the time to delivery without compromising neonatal outcomes [16]. A similar outcome was observed in a trial that compared the initiation of membrane sweeping

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at 41 weeks of gestation with expectant management to prevent post-term pregnancy. The trial involved 742 cases considered to be at very low risk. Membrane sweeping performed sequentially at 41 weeks resulted in a reduced likelihood of post-date pregnancy without leading to any significant adverse neonatal outcomes [17]. In our study, we observed a high rate of successful vaginal deliveries (82.4%) among women who underwent membrane sweeping, with the majority requiring only one or two sweeps. This finding is consistent with previous research that has reported similar success rates with minimal adverse maternal outcomes [18]. In our study, the frequency of spontaneous delivery was 76.5%, indicating that membrane sweeping effectively initiated labour in a significant majority. This finding aligns closely with a study, where 88.3% of patients achieved spontaneous labour following membrane sweeping, demonstrating a similar efficacy in reducing the dependency on medical induction methods and preventing prolonged pregnancies [13]. Similarly, another study reported a spontaneous labour rate of 86.4%, further supporting the role of membrane sweeping in initiating natural labour and minimizing the need for additional interventions [19]. The effect of membrane sweeping on the duration of pregnancy in our study showed that patients who achieved spontaneous labour had a significantly lower mean gestational age (40.49 ± 0.591 weeks) compared to those who did not (41.72 ± 0.581 weeks, p=0.0001). This reduction in gestational duration mirrors the findings of a study, where membrane sweeping was associated with earlier labour onset in the majority of patients [19]. In the current study, it was found that spontaneous labour was most common after one sweep (50.0%), followed by two sweeps (40.4%) and more than two sweeps (9.6%), with a significant association (p=0.0001). This observation is supported by the aforementioned study, where most patients required only one or two sweeps to achieve labour, while only a minority needed more than two sweeps [19]. The maternal outcomes in our study were quite favourable, with only 4.4% of patients experiencing postpartum hemorrhage and just 1.5% developing infections. These findings are consistent with a study that reported no significant adverse outcomes associated with membrane sweeping [19]. Fetal outcomes in the present study were also favourable, with 94.9% of newborns achieving an APGAR score of ≥7, and only 11% requiring NICU admission. These results align with a study that reported low rates of neonatal complications associated with membrane sweeping [20]. However, despite the positive outcomes observed in our study, it is essential to acknowledge the limitations. Our study was conducted in a single tertiary care center with a specific population, which may limit the generalizability of the results. Additionally, the lack of a control group in our study design restricts our ability to make definitive conclusions about the efficacy of membrane sweeping compared to other labour induction methods. Further research with larger sample sizes and control groups across multiple centers is needed to confirm these findings and explore the broader implications of membrane sweeping in different populations and settings.

CONCLUSIONS

It was concluded that membrane sweeping effectively initiates spontaneous labour, with 76.5% achieving spontaneous labour, and notably reduces pregnancy duration by promoting timely labour onset. It is a practical, non-invasive intervention to prevent prolonged pregnancies and reduce reliance on medical induction. The minimal maternal and fetal risks observed in current study suggest that this procedure can be a valuable tool in obstetric practice, particularly in settings where more invasive or pharmacological methods may not be readily available.

Authors Contribution

Conceptualization: SS
Methodology: SS, S, NK
Formal analysis: QQ
Writing review and editing: SS

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Hong JG, Magalingam VD, Sethi N, Ng DS, Lim RC, Tan PC. Adjunctive Membrane Sweeping in Foley Catheter Induction of Labor After One Previous Cesarean Delivery: A Randomized Trial. International Journal of Gynecology and Obstetrics.2023 Jan; 160(1): 65-73. doi: 10.1002/ijgo.14166.

[2] Avdiyovski H, Haith-Cooper M, Scally A. Membrane Sweeping at Term to Promote Spontaneous Labour and Reduce the Likelihood of a Formal Induction of Labour for Post-maturity: A Systematic Review and Meta-Analysis. Journal of Obstetrics and Gynaecology.2019 Jan; 39(1): 54-62. doi: 10.1080/0 144 3615.2018.1467388.

[3] Spiby H, Roberts J, Evans K, Evans C, Pallotti P, Eldridge J. Women's Information Needs, Decision-Making and Experiences of Membrane Sweeping to

DOI: https://doi.org/10.54393/pjhs.v5i12.1939

Promote Spontaneous Labour. Midwifery.2020; 83. doi: 10.1016/j.midw.2019.102626.

[4] Tsakiridis I, Mamopoulos A, Athanasiadis A, Dagklis T. Induction of Labor: An Overview of Guidelines. Obstetrical and Gynecological Survey. 2020 Jan; 75(1): 61-72. doi: 10.1097/OGX.0000000000000752.

[5] Saeed F, Abbasi SE, Bano N, Khan S, Jabeen K, Faraz F. Comparison Between Expectant Management and Sweeping of Membranes for Spontaneous Onset of Labour and Subsequent Mode of Delivery. Journal of The Society of Obstetricians and Gynaecologists of Pakistan. 2023 Oct; 13(4): 355-9.

[6] Ehikioya E, Nwachukwu OB, Okobi OE. Effectiveness of Single Fetal Membrane Sweeping in Reducing Elective Labor Induction for Postdate Pregnancies (38+ 0 to 40+ 6 Weeks): A Randomized Controlled Trial. Cureus. 2024 Apr; 16(4). doi: 10.7759/cureus.58030.

[7] Twayana K, Tamrakar SR. Efficacy of Membrane Sweeping at Term Gestation to Prevent Post Term Pregnancy: A Comparative. Nepal Journal of Obstetrics and Gynaecology. 2024 Jun; 19(1): 21-6. doi: 10.70241/njog103.

[8] Pirzada H, Ehsan A, Tahir N, Fatima A. Sweeping of Membranes for Induction of Labour in Low Risk Term Pregnancy. Pakistan Armed Forces Medical Journal. 2022 May;72(2): 658-61.doi: 10.5125 3/pafmj .v72i 2.6644.

[9] Madugalle TM and Jayasundara DM. Comparative Effectiveness of and Maternal Acceptability with Cervical Ripening uSing cErvicaL Massage vErsuS Membrane Sweep (CEASELESS): A Randomized Controlled Trial. 2024. doi: 10.21203/rs.3.rs-126016/v1.

[10] TMSSB M, Jayasundara DM. Comparative Effectiveness of and Maternal Acceptability with Cervical Ripening Using Cervical Massage Versus Membrane Sweep (CEASELESS): A Randomized Controlled Trial. Archives of Clinical and Biomedical Research.2022;6(3): 587-99. doi: 10.2650 2/a cbr.50 170269.

[11] Ashmawy NE, Assar TM, Taha SM, Helmy EA. Original Article Effect of Membrane Sweeping on Induction of Labour a Randomized Controlled Trial. Benha Journal of Applied Sciences. 2020 Feb; 5(2 part (1)): 73-9. doi: 10.21608/bjas.2020.135448.

[12] Nilvér H, Lundgren I, Elden H, Dencker A. Women's Lived Experiences of Induction of Labour in Late-and Post-Term Pregnancy Within the Swedish Post-Term Induction Study–A Phenomenological Study. International Journal of Qualitative Studies On Health and Well-Being. 2022 Dec; 17(1): 2056958. doi: 10.1080/17482631.2022.2056958.

[13] Ali A, Iqbal S, Rashid T. The Effectiveness of Membrane Sweeping at Term and Clinical Effects On Duration of Pregnancy. Annals of King Edward Medical University. 2021 Jul; 27(2). doi: 10.21649/akemu.v27i2.4550.

[14] Grobman WA, Rice MM, Reddy UM, Tita AT, Silver RM, Mallett G *et al.* Labor Induction Versus Expectant Management in Low-Risk Nulliparous Women. New England Journal of Medicine.2018 Aug; 379(6): 513-23. doi: 10.1056/NEJMoa1800566.

[15] Bhatia A, Teo PL, Li M, Lee JY, Chan MX, Yeo TW *et al.* Dinoprostone Vaginal Insert (DVI) Versus Adjunctive Sweeping of Membranes and DVI for Term Induction of Labor. Journal of Obstetrics and Gynaecology Research.2021 Sep; 47(9): 3171-8. doi: 10.1111/ jog.1 49 07.

[16] Yildirim G, Güngördük K, Karadağ Öİ, Aslan H, Turhan E, Ceylan Y. Membrane Sweeping to Induce Labor in Low-Risk Patients at Term Pregnancy: A Randomised Controlled Trial. The Journal of Maternal-Fetal and Neonatal Medicine.2010 Jul; 23(7): 681-7. doi: 10.3109/ 14767050903387078.

[17] De Miranda E, Van Der Bom JG, Bonsel GJ, Bleker OP, Rosendaal FR. Membrane Sweeping and Prevention of Post-Term Pregnancy in Low-Risk Pregnancies: A Randomized Controlled Trial. An International Journal of Obstetrics & Gynaecology.2006 Apr; 113(4): 402-8. doi: 10.1111/j.1471-0528.2006.00870.x.

[18] Lella M, Shetty J, Kyalakond K, Pai MV. The Performance of Membrane Sweep in Conjunction with the Induction of Labor with Sublingual Misoprostol. Current Women's Health Reviews.2021 May; 17(2): 110-6. doi: 10.2174/1573404816999201123162640.

[19] Hassan AM. Membrane Sweeping to Induce Labor in Post-Term Pregnant Women: Success Rate and Outcomes.Cureus.2023 Mar;15(3). doi: 10.77 59/ cur eus .36942.

[20] Nyamzi MG, Isah DA, Offiong RA, Isah AY. Effectiveness of Sweeping of Membranes in Reducing the Incidence of Elective Induction of Labor for Postdate Pregnancies. Archives of Medicine and Surgery.2019 Jan; 4: 15-21. doi: 10.4103/archms.archms_36_18.

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Assessment of the Characteristics and Clinical Outcomes of Un-Booked Obstetric Patients at Tertiary Care Hospital of Southern Punjab

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ABSTRACT

Un-booked obstetric patients often lack adequate antenatal care, leading to increased risks of maternal and neonatal complications. Understanding the characteristics and clinical outcomes in this population is essential to improve healthcare delivery and reduce disparities **Objectives:** To analyze the characteristics and clinical outcomes of un-booked obstetric patients presented at Tertiary Care Hospital in Rahim Yar Khan. **Methods:** This cross-sectional study analyzed the outcomes of 384 un-booked obstetric patients presented at the Department of Obstetrics and Gynecology in a Tertiary Care Hospital, between July 2022 to June 2023 aged 18-35 years. obstetric outcomes including the type of labour, mode of delivery, premature rupture of membranes and postpartum hemorrhage were studied in enrolled patients. **Results:** The mean age and mean gestational age of un-booked obstetric patients were 27.08 ± 4.59 years and 36.31 ± 4.18 weeks respectively. Vaginal deliveries were 257 (66.9%) and C-section was performed in 127 (33.1%) patients. Regarding the type of labor, term and preterm deliveries were 312 (81.3%) and 72 (18.7%), similarly premature rupture of membranes and postpartum hemorrhage were noted in 42 (10.9%) patients and 30 (7.8%) patients. **Conclusion:** It was concluded that un-booked obstetric patients primarily experienced vaginal deliveries with a low incidence of complications such as premature rupture of membranes and postpartum hemorrhage. Parity significantly influenced delivery and labor outcomes, highlighting the need for targeted antenatal care for high-risk groups such as primiparous and nulliparous women. These findings emphasize the importance of improving access to antenatal care to optimize maternal and neonatal outcomes.

INTRODUCTION

In Pakistan and other countries of the world, un-booked obstetric patients are a big problem, especially in developing countries which do not have adequate facilities for antenatal care (ANC). This implies that there is a need to promote and establish maternal healthcare services for women across the world [1, 2]. The causes associated with this situation are therefore complex and include economic and social status, distance, education and culture. These are compounded by poor healthcare facilities, and cultural beliefs that may encourage normal birth practices as opposed to the recommended ones [3, 4]. ANC is significantly associated with an increased risk of maternal and neonatal complications [5, 6]. The women who do not attend antenatal clinics are not taught how to take care of themselves, they do not receive proper nutrition, and they are not checked for complications early. This puts the woman at a higher risk of suffering from serious conditions such as pre-eclampsia, gestational diabetes and preterm labour as well as low birth weight deliveries [2]. Also, these women have a higher risk of adverse neonatal outcomes including stillbirth and neonatal deaths this underlines the need for antenatal care for healthy pregnancy and

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childbirth [7]. Because of these factors, it is important to design interventions for increasing the uptake of antenatal care among women in Pakistan to better fit with their socio-cultural and economic environment. Indeed, strategies such as enhancing the provision of care facilities, and altering attitudes towards pregnancy and child-bearing are some of the few important ways of enhancing attendance to antenatal care [4, 6]. Moreover, it is important to ensure that all pregnant women regardless of their socio-economic or geographic status are provided with the required support for safe pregnancy and childbirth services by addressing the barriers to ANC uptake in the culturally ever-integrating modern healthcare approaches [8, 9]. Effects of un-booked pregnancies do not just remain limited to health issues but also include deep personal and grieving loss for family and society. They highlight the need to work together to make sure that pregnant women get basic essential ANC services in the larger context of improving maternal and neonatal health [10, 11]. Evaluating the characteristics and clinical outcomes of un-booked obstetric patients is crucial, as these individuals face a higher risk of adverse outcomes, including maternal and neonatal mortality, low birth weight, and preterm birth.

This study aims to guide health promotion efforts to increase antenatal care uptake and enhance healthcare facilities' readiness to manage pregnancy-related complications effectively, particularly in resource-limited settings where un-booked pregnancies remain a significant challenge.

METHODS

This prospective cross-sectional study conducted in the Department of Obstetrics and Gynecology, Tertiary Care Hospital, Rahim Yar Khan, from July 2022 to June 2023. The study population consisted of 384 un-booked obstetric patients, defined as those presenting for delivery or emergency obstetric care without any prior recorded antenatal visits. The sample size was calculated using a 49.3% prevalence rate for vaginal delivery in un-booked cases, with a 95% confidence level and a 5% margin of error. A non-probability consecutive sampling technique was employed for patient recruitment. Ethical approval was obtained from the Ethical Review Committee of the hospital (ERB No.CMH-RYK-00102). Written informed consent was secured from all participants before enrollment, ensuring adherence to ethical guidelines. Patients were prospectively recruited upon their admission to the hospital for delivery or emergency obstetric care. A structured proforma was used to record demographic and clinical data during the patient's stay in the hospital. Information collected included age, parity, mode of delivery, labor type (term or preterm), premature rupture of membranes (PROM), postpartum hemorrhage (PPH), income level, education status, and residential area. Data collection was conducted by trained medical personnel through direct interviews with patients and observation of clinical outcomes during labor and delivery. The inclusion criteria included obstetric patients aged 18 to 35 who presented directly to the hospital for delivery. Patients over 35 years, those with systemic diseases such as diabetes mellitus or hypertension, those with a history of uterine rupture, and patients with two or more prior cesarean sections were excluded. All the collected data were analyzed by using SPSS version 25.0. Descriptive statistics, including mean and standard deviation for continuous variables and proportions for categorical variables, were used to summarize patient characteristics and clinical outcomes. Stratification was done about age, gestational age, income status, education status, area of residence and parity. Post-stratification chi-square test was applied to detect the association of these variables with outcome variables i.e. Mode of Delivery, Type of labor, PROM, Maternal Death, and PPH. p-value≤0.05 was considered statistically significant.

RESULTS

A total of 384 un-booked obstetric patients were selected for this study. The mean age and mean gestational age were 27.08 ± 4.59 years and 36.31 ± 4.18 weeks, respectively. The analysis of delivery patterns revealed that vaginal births occurred in 257 (66.9%) patients, while 127 (33.1%) underwent cesarean sections. Most deliveries were at term (312, 81.3%), with 72 (18.7%) classified as preterm. In contrast, preterm deliveries were less common, occurring in 72 (18.7%). Prolonged rupture of membranes (PROM) was relatively rare, with only 42 (10.9%) of patients experiencing this condition. Similarly, the incidence of postpartum hemorrhage (PPH) was low, observed in 30 (7.8%) cases (Table 1).

Table 1: Delivery Outcomes and Complications in Un-booked Obstetric Patients

Variable	Category	Frequency (%)
Mode of Delivery (MOD)	Vaginal	257 (66.9%)
	C-Section	127 (33.1%)
Labor Type	Term	312 (81.3%)
	Preterm	72 (18.7%)
Prolonged Rupture of Membranes	Yes	42 (10.9%)
	No	342 (89.1%)
Postpartum Hemorrhage	Yes	30 (7.8%)
	No	354 (92.2%)

There was no statistically significant association between age group and mode of delivery (p=0.547). Vaginal deliveries were most common in the 18–24 years' age group, with 71 (68.9%), followed by the 25–29 years' group, with 113 (68.5%), and the 30–35 years' group, with 73 (62.9%).

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Cesarean sections accounted for 32 (31.1%), 52 (31.5%), and 43 (37.1%) of deliveries in the respective age groups. The association between gestational age and mode of delivery approached statistical significance (p=0.057). Vaginal deliveries were highest in the 28–31 weeks' group, with 28 (82.4%), followed by the <28 weeks' group, with 18 (78.3%), and the 32–36 weeks' group, with 59 (70.2%). In the 37–41 weeks' group, vaginal deliveries accounted for 152 (62.6%). Cesarean deliveries were most frequent in the 37–41 weeks' group, with 91 (37.4%), compared to 5 (21.7%) in the <28 weeks' group, 6 (17.6%) in the 28–31 weeks' group, and 25 (29.8%) in the 32–36 weeks' group. No significant association was found between income status and mode of delivery (p=0.646). Vaginal deliveries were reported in 91 (64.1%) of the low-income group, 116 (69.0%) of the middle-income group, and 50 (67.6%) of the high-income group. Cesarean deliveries occurred in 51 (35.9%), 52 (31.0%), and 24 (32.4%) of the respective groups. There was no significant association between education status and mode of delivery (p=0.758). Vaginal deliveries were highest among patients with no education, at 34 (73.9%), and lowest in patients with secondary education, at 93 (65.5%). Primary education and higher education groups had 71 (66.4%) and 59 (66.3%) vaginal deliveries, respectively. Cesarean deliveries ranged from 12 (26.1%) in the no-education group to 49 (34.5%) in the secondary education group. The association between residence and mode of delivery was not statistically significant (p=0.234). Vaginal deliveries were more frequent among urban residents, at 154 (69.4%), compared to rural residents, at 103 (63.6%). Cesarean deliveries were observed in 68 (30.6%) of urban residents and 59 (36.4%) of rural residents. A significant association was observed between parity and mode of delivery (p<0.001). Vaginal deliveries were most frequent among primiparous patients, at 143 (81.3%), followed by multiparous patients, at 54 (69.2%), and nulliparous patients, at 60 (46.2%). Cesarean deliveries were highest among nulliparous patients, at 70 (53.8%), followed by multiparous patients, at 24 (30.8%), and primiparous patients, at 33 (18.8%) (Table 2).

Table 2: Association of Mode of Delivery with Different Variables

Different Variables		MOD		Total	p-value
		Vaginal	C-section		
Age Group	18-24 Years	71 (68.9%)	32 (31.1%)	103	0.547
	25-29 Years	113 (68.5%)	52 (31.5%)	165	
	30-35 Years	73 (62.9%)	43 (37.1%)	116	
Gestational Age Group	<28 Weeks	18 (78.3%)	5 (21.7%)	23	0.057
	28-31 Weeks	28 (82.4%)	6 (17.6%)	34	
	32-36 Weeks	59 (70.2%)	25 (29.8%)	84	
	37-41 Weeks	152 (62.6%)	91 (37.4%)	243	
Income Status	Low	91 (64.1%)	51 (35.9%)	142	0.646
	Middle	116 (69.0%)	52 (31.0%)	168	
	High	50 (67.6%)	24 (32.4%)	74	
Education Status	No Education	34 (73.9%)	12 (26.1%)	46	0.758
	Primary Education	71 (66.4%)	36 (33.6%)	107	
	Secondary Education	93 (65.5%)	49 (34.5%)	142	
	Higher Education	59 (66.3%)	30 (33.7%)	89	
Residence	Urban	154 (69.4%)	68 (30.6%)	222	0.234
	Rural	103 (63.6%)	59 (36.4%)	162	
Parity	Nulliparous	60 (46.2%)	70 (53.8%)	130	0.000
	Primiparous	143 (81.3%)	33 (18.8%)	176	
	Multiparous	54(69.2%)	24 (30.8%)	78	

No statistically significant association was observed between age group and PROM (p=0.598). PROM was most frequent in the 18–24 years' group, with 3 (12.6%), followed by the 30–35 years' group, with 14 (12.1%), and the 25–29 years' group, with 15 (9.1%). Among those without PROM, the proportions were similar, with 90 (87.4%) in the 18–24 years' group, 150 (90.9%) in the 25–29 years' group, and 102 (87.9%) in the 30–35 years' group. There was no significant association between gestational age and PROM (p=0.701). PROM was most common in the 32–36 weeks' group, with 11 (13.1%), followed by the 37–41 weeks' group, with 27 (11.1%). PROM was less frequent in the <28 weeks' group, with 2 (8.7%), and in the 28–31 weeks' group, with 2 (5.9%). Most patients without PROM were in the 37–41 weeks' group, with 216 (88.9%). PROM showed no significant association with income status (p=0.848). PROM rates were highest among the low-income group, with 17 (12.0%), followed by the middle-income group, with 18 (10.7%), and the high-income group, with 7 (9.5%). Patients without PROM were predominantly in the middle-income group, with 150 (89.3%). Education status did not show a significant association with PROM (p=0.793). PROM was most frequent among patients with secondary education, with 18 (12.7%), and least frequent among those with no education, with 4 (8.7%). Patients without PROM were most common in the secondary education group, with 124 (87.3%). There was no significant association between residence and PROM (p = 0.368). PROM was more common in urban residents, with 27 (12.2%), compared to rural residents, with 15 (9.3%). Among those without PROM, 195 (87.8%) were urban residents, and 147 (90.7%) were rural residents. PROM showed no significant association with parity (p=0.848). PROM was most frequent among primiparous patients, with 22 (12.5%), followed by nulliparous patients, with 13 (10.0%), and multiparous patients, with 7 (9.0%). Among those without PROM, 154 (87.5%) were primiparous, 117 (90.0%) were nulliparous, and 71 (91.0%) were multiparous (Table 3).

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Table 3: Association of PROM with Different Variables

Different Variables		PROM		Total	p-value
		Yes	No		
Age Group	18-24 Years	3 (12.6%)	90 (87.4%)	103	0.598
	25-29 Years	15 (9.1%)	150 (90.9%)	165	
	30-35 Years	14 (12.1%)	102 (87.9%)	116	
Gestational Age Group	<28 Weeks	2 (8.7%)	21 (91.3%)	23	0.701
	28-31 Weeks	2 (5.9%)	32 (94.1%)	34	
	32-36 Weeks	11 (13.1%)	73 (86.9%)	84	
	37-41 Weeks	27 (11.1%)	216 (88.9%)	243	
Income Status	Low	17 (12.0%)	125 (88.0%)	142	0.848
	Middle	18 (10.7%)	150 (89.3%)	168	
	High	7 (9.5%)	67 (90.5%)	74	
Education Status	No Education	4 (8.7%)	42 (91.3%)	46	0.793
	Primary Education	12 (11.2%)	95 (88.8%)	107	
	Secondary Education	18 (12.7%)	124 (87.3%)	142	
	Higher Education	8 (9.0%)	81 (91.0%)	89	
Residence	Urban	27 (12.2%)	195 (87.8%)	222	0.368
	Rual	15 (9.3%)	147 (90.7%)	162	
Parity	Nulliparous	13 (10.0%)	117 (90.0%)	130	0.848
	Primiparous	22 (12.5%)	154 (87.5%)	176	
	Multiparous	7 (9.0%)	71 (91.0%)	78	

No statistically significant association was observed between age group and PPH (p=0.599). PPH was most frequent in the 18–24 years' age group, with 10 (9.7%), followed by the 25–29 years' group, with 13 (7.9%), and the 30–35 years' group, with 7 (6.0%). Among those without PPH, 93 (90.3%) were in the 18–24 years' group, 152 (92.1%) in the 25–29 years' group, and 109 (94.0%) in the 30–35 years' group. There was no significant association between gestational age and PPH (p=0.434). PPH was most frequent in the 32–36 weeks' group, with 10 (11.9%), followed by the 37–41 weeks' group, with 17 (7.0%). PPH was least frequent in the <28 weeks' group, with 1 (4.3%), and in the 28–31 weeks' group, with 2 (5.9%). Most patients without PPH were in the 37–41 weeks' group, with 226 (93.0%). Income status showed no significant association with PPH (p=0.908). PPH was observed in 12 (8.5%) of the low-income group, 12 (7.1%) of the middle-income group, and 6 (8.1%) of the high-income group. Patients without PPH were most common in the middle-income group, with 156 (92.9%). Education status did not show a significant association with PPH (p=0.395). PPH was most frequent among patients with secondary education, with 15 (10.6%), followed by those with primary education, with 8 (7.5%), and no education, with 3 (6.5%). Patients with higher education had the lowest PPH rate, at 4 (4.5%). Among those without PPH, 127 (89.4%) were in the secondary education group. There was no significant association between residence and PPH (p=0.159). PPH was more frequent among urban residents, with 21 (9.5%), compared to rural residents, with 9 (5.6%). Among those without PPH, 201 (90.5%) were urban residents, and 153 (94.4%) were rural residents. Parity showed a statistically significant association with PPH (p=0.007). PPH was most frequent among primiparous women, with 22 (12.5%), compared to nulliparous women, with 5 (3.8%), and multiparous women, with 3 (3.8%). Among those without PPH, 154 (87.5%) were primiparous, 125 (96.2%) were nulliparous, and 75 (96.2%) were multiparous (Table 4).

Table 4: Association of PPH with Different Variables

Different Variables		PPH		Total	p-value
		Yes	No		
Age Group	18-24 Years	10 (9.7%)	93 (90.3%)	103	0.599
	25-29 Years	13 (7.9%)	152 (92.1%)	165	
	30-35 Years	7 (6.0%)	109 (94.0%)	116	
Gestational Age Group	<28 Weeks	1 (4.3%)	22 (95.7%)	23	0.434
	28-31 Weeks	2 (5.9%)	32 (94.1%)	34	
	32-36 Weeks	10 (11.9%)	74 (88.1%)	84	
	37-41 Weeks	17 (7.0%)	226 (93.0%)	243	
Income Status	Low	12 (8.5%)	130 (91.5%)	142	0.908
	Middle	12 (7.1%)	156 (92.9%)	168	
	High	6 (8.1%)	68 (91.9%)	74	
Education Status	No Education	3 (6.5%)	43 (93.5%)	46	0.395
	Primary Education	8 (7.5%)	99 (92.5%)	107	
	Secondary Education	15 (10.6%)	127 (89.4%)	142	
	Higher Education	4 (4.5%)	85 (95.5%)	89	
Residence	Urban	21 (9.5%)	201 (90.5%)	222	0.159
	Rual	9 (5.6%)	153 (94.4%)	162	
Parity	Nulliparous	5 (3.8%)	125 (96.2%)	130	0.007
	Primiparous	22 (12.5%)	154 (87.5%)	176	
	Multiparous	3 (3.8%)	75 (96.2%)	78	

There was no statistically significant association between age group and type of labor (p=0.856). Term labor was most frequent in the 18–24 years' group, with 85 (82.5%), followed by the 30–35 years' group, with 95 (81.9%), and the 25–29 years' group, with 132 (80.0%). Preterm labor rates were similar across all age groups, ranging from 17.5% in the 18–24 years' group to 20.0% in the 25–29 years' group. Gestational age did not show a significant association with the type of labor (p=0.962). Term labor was highest in the <28 weeks' group, with 19 (82.6%), followed by the 37–41 weeks' group, with 199 (81.9%), and the 28–31 weeks' group, with 27 (79.4%). Preterm labor was most frequent in the 28–31 weeks' group, with 7 (20.6%), followed by the 32–36 weeks' group, with 17 (20.2%). No significant association was found between income status and type of labor (p=0.915). Term labor rates were similar across all income groups, with 114 (80.3%) in the low-income group, 138 (82.1%) in the middle-income group, and 60 (81.1%) in the high-income group. Preterm labor rates ranged from 17.9% in the middle-income group to 19.7% in the low-income

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group. Education status showed no significant association with the type of labor (p=0.799). Term labor was most frequent in patients with no education, with 39 (84.8%), followed by those with primary education, with 88 (82.2%), and higher education, with 73 (82.0%). Preterm labor rates were highest in the secondary education group, with 30 (21.1%). The residence was not significantly associated with the type of labor (p=0.716). Term labor was slightly more frequent among rural residents, with 133 (82.1%), compared to urban residents, with 179 (80.6%). Preterm labor rates were similar, with 43 (19.4%) in urban residents and 29 (17.9%) in rural residents. Parity showed a statistically significant association with the type of labor (p<0.001). Term labor was highest among nulliparous patients, with 117 (90.0%), and multiparous patients, with 70 (89.7%). Primiparous patients had the lowest term labor rate, with 125 (71.0%), and the highest preterm labor rate, with 51 (29.0%) (Table 5).

Table 5: Association of Type of Labor with Different Variables

Different Variables		Type of Labor		Total	p-value
		Term	Pre-Term		
Age Group	18-24 Years	85 (82.5%)	18 (17.5%)	103	0.856
	25-29 Years	132 (80.0%)	33 (20.0%)	165	
	30-35 Years	95 (81.9%)	21 (18.1%)	116	
Gestational Age Group	<28 Weeks	19 (82.6%)	4 (17.4%)	23	0.962
	28-31 Weeks	27 (79.4%)	7 (20.6%)	34	
	32-36 Weeks	67 (79.8%)	17 (20.2%)	84	
	37-41 Weeks	199 (81.9%)	44 (18.1%)	243	
Income Status	Low	114 (80.3%)	28 (19.7%)	142	0.915
	Middle	138 (82.1%)	30 (17.9%)	168	
	High	60 (81.1%)	14 (18.9%)	74	
Education Status	No Education	39 (84.8%)	7 (15.2%)	46	0.799
	Primary Education	88 (82.2%)	19 (17.8%)	107	
	Secondary Education	112 (78.9%)	30 (21.1%)	142	
	Higher Education	73 (82.0%)	16 (18.0%)	89	
Residence	Urban	179 (80.6%)	43 (19.4%)	222	0.716
	Rual	133 (82.1%)	29 (17.9%)	162	
Parity	Nulliparous	117 (90.0%)	13 (10.0%)	130	0.000
	Primiparous	125 (71.0%)	51 (29.0%)	176	
	Multiparous	70 (89.7%)	8 (10.3%)	78	

DISCUSSION

The investigation into the health trajectories of 384 un-booked obstetric patients not only sheds light on the ramifications of lacking antenatal care but also contextualizes these findings within a global landscape of similar challenges. With a demographic profile marked by a mean age of 27.08 ± 4.59 years and gestational age of 36.31 ± 4.18 weeks, this study aligns with global observations on the critical need for proactive maternal healthcare interventions. This analysis revealed a distinct preference for vaginal delivery among younger women in this cohort, with 68.9% of those aged 18–24 opting for this mode of birth. This trend is comparable to findings by Shaheen *et al.*, who reported that 39% of un-booked cases resulted in vaginal deliveries [12]. These similarities suggest a potential universal pattern in delivery modes among un-booked patients across different settings. However, in this study, cesarean section rates were higher among women aged 30–35 years, at 37.1%, underscoring the need for preventative health measures to address risk factors necessitating surgical interventions. Older women may prefer cesarean delivery due to a combination of medical, psychological, and social factors. Advanced maternal age is associated with a higher likelihood of pregnancy complications, including gestational diabetes, hypertensive disorders, and reduced uterine elasticity, which increase the risk of prolonged labor and adverse neonatal outcomes. Consequently, healthcare providers may recommend cesarean sections more often for older women to mitigate these risks. Additionally, older women are more likely to have had prior cesarean deliveries, leading to repeat cesareans due to concerns about uterine rupture or other complications associated with vaginal birth after cesarean (VBAC). Psychological factors, such as a preference for greater control over the timing and method of delivery, may also influence older women to opt for cesarean sections. The prevalence of PROM in this study, at 12.6% in the youngest age group, highlights the risks linked to un-booked pregnancies. This observation aligns with findings from Shaheen *et al.*, who noted that 61% of their patients required cesarean sections, often due to complications like PROM [12]. These findings emphasize the importance of antenatal care in mitigating such risks. Furthermore, this study observed postpartum hemorrhage (PPH) in 9.7% of patients aged 18–24 years, consistent with Latif *et al.*, who reported significant complications among both booked and un-booked patients, including anemia affecting 47.1% of their total population [13]. Interestingly, these results suggest that educational and socio-economic status did not significantly impact the mode of delivery. This observation contrasts with commonly held assumptions that higher socio-economic status and education levels equate to better maternal health outcomes. Qureshi *et al.*, similarly noted that while maternal age and socioeconomic backgrounds differed significantly between booked and un-booked patients, such differences did not always translate to disparities in delivery outcomes [14]. The findings of this study reinforce the critical importance of antenatal care. This is supported by Butt *et al.*, [15] and Ago *et al.*, who highlighted the role of regular antenatal visits in improving maternal and neonatal outcomes [15, 16]. Moreover, Baloch *et al.*, emphasized that un-booked pregnancies are more prevalent in lower socioeconomic groups, pointing to the urgent need to

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overcome barriers to accessing prenatal care in these populations [17]. Traditional and cultural norms also influence the health choices of pregnant women, particularly in rural areas. Studies by Barbi *et al.*, and Abbas *et al.*, reported that home births and reliance on traditional midwives remain common in certain cultures, contributing to the higher prevalence of un-booked cases [18, 19]. Addressing these cultural preferences by integrating traditional practices with medical services is critical. Suleiman and Pappan, found that community engagement and reliable communication channels significantly increase antenatal care utilization, thereby reducing unattended maternal health issues [20].

CONCLUSIONS

It was concluded that this study of 384 un-booked obstetric patients highlights the critical importance of antenatal care in reducing maternal and neonatal complications. This analysis evaluated the clinical characteristics and outcomes associated with un-booked pregnancies, revealing that younger women predominantly experienced vaginal deliveries, whereas older women were more likely to undergo emergency cesarean sections. Complications such as Premature Rupture of Membranes (PROM) and Postpartum Hemorrhage (PPH), though observed in a smaller proportion of cases, underscore the elevated risks linked to inadequate antenatal care. Addressing barriers to antenatal care such as socioeconomic disparities, limited education, and cultural norms is vital.

Authors Contribution

Conceptualization: UIK
Methodology: UIK, SG, FM, SSJ
Formal analysis: UIK, SU, ZS, SSJ
Writing review and editing: UIK, SU, ZS, SG, FM

All authors have read and agreed to the published version of the manuscript

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REFERENCES

[1] Escañuela Sánchez T, Linehan L, O'Donoghue K, Byrne M, Meaney S. Facilitators and Barriers to Seeking and Engaging with Antenatal Care in High-Income Countries: A Meta-Synthesis of Qualitative Research. Health and Social Care in the Community.2022 Nov; 30(6): e3810-28. doi: 10.1111/hsc.14072.

[2] Tessema ZT and Minyihun A. Utilization and Determinants of Antenatal Care Visits in East African Countries: A Multicountry Analysis of Demographic and Health Surveys. Advances in Public Health. 2021; 2021(1): 6623009. doi: 10.1155/2021/6623009.

[3] Diguisto C, Saucedo M, Kallianidis A, Bloemenkamp K, Bødker B, Buoncristiano M *et al.* Maternal Mortality in Eight European Countries with Enhanced Surveillance Systems: Descriptive Population-Based Study. British Medical Journal.2022 Nov; 379. doi: 10.1136/bmj-2022 -070621.

[4] Fleszar LG, Bryant AS, Johnson CO, Blacker BF, Aravkin A, Baumann M *et al.* Trends in State-Level Maternal Mortality By Racial and Ethnic Group in the United States. Journal of American Medical Association.2023 Jul; 330(1): 52-61. doi: 10.100 1/jama. 2023.9043.

[5] Kamal P, Kaur S, Kaur H, Nagpal M. Non-hemorrhagic causes of Obstetrical Intensive Care Unit Admissions in Tertiary Care Setting. International Journal of Reproduction, Contraception, Obstetrics and Gynecology.2020 Apr; 9(4): 1393. doi: 10.18203/2320-1770.ijrcog20201007.

[6] Memon FP. Maternal Outcome Among Women Undergoing Obstetric Massive Blood Transfusions. Annals of Punjab Medical College.2019 Jan; 13(2): 177-80. doi: 10.29054/apmc/2019.84.

[7] Bryant AS, Worjoloh A, Caughey AB, Washington AE. Racial/Ethnic Disparities in Obstetric Outcomes and Care: Prevalence and Determinants. American Journal of Obstetrics and Gynecology.2010 Apr;202 (4): 335-43. doi: 10.1016/j.ajog.2009.10.864.

[8] Johnson FA, Padmadas SS, Matthews Z. Are Women Deciding Against Home Births in Low and Middle-Income Countries? PLoS One.2013 Jun; 8(6): e65527. doi: 10.1371/journal.pone.0065527.

[9] Knight M, Nair M, Tuffnell D, Kenyon S, Shakespeare J, Brocklehurst P *et al.* Saving Lives, Improving Mothers' Care: Surveillance of Maternal Deaths in the UK 2012-14 and Lessons Learned to Inform Maternity Care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2009-14. Oxuniprint. 2016 Dec.

[10] Adenaya OR, Ibrahim AM, Ojo OO, Grillo EO, Ade-Onojobi AO, Odelola OI. Comparative Study of the Obstetric Outcome between Booked and Unbooked Mothers at the Federal Medical Centre, Abeokuta: A Two-Year Review. Western Journal of Medical and Biomedical Sciences. 2022 Feb; 3(1): 59-67.

[11] Anyigor-Ogah CS, Egede JO, Ogeh CO, Agunanne CC, Ozioko AI, Duru CC. Determinants and Outcomes of Pregnancies Among Booked Versus Unbooked Patients in A Tertiary Hospital South East, Nigeria. Open Journal of Obstetrics and Gynecology. 2024 Jan;

DOI: https://doi.org/10.54393/pjhs.v5i12.1834

14(1): 144-61. doi: 10.4236/ojog.2024.141014.
[12] Shaheen H, Khosa MS, Aslam H. Frequency of Un-Booked Obstetric Patients and Their Outcome. Pakistan Journal of Medical and Health Sciences. 2016 Oct; 10(4): 1268-71.
[13] Latif F, Ayub R, Javaid K. Comparison of Feto-Maternal Complications in Booked and Un-Booked Females Presenting at Time of Delivery in Sir Ganga Ram Hospital, Lahore. Pakistan Journal of Medical Health Sciences. 2014 Sep; 8(3): 595-599.
[14] Qureshi D, Abduljalil R, Nadham AN, Qureshi A. Effect of Booking Status on Mode of Delivery and Postnatal Maternal Outcome. Bahrain Medical Bulletin.2020 Mar; 42(1): 47-50.
[15] Butt S, Noreen M, Syed SZ, Mazhar A. Comparison of Maternal Outcome in Booked Vs Un-Booked Women in Lady Willingdon Hospital, Lahore. Pakistan Journal of Medical Health Sciences. 2018 Jul; 12: 969-71.
[16] Ago B and Ekanem E. Obstetric Outcome of Booked and Un-Booked Deliveries at the University of Calabar Teaching Hospital, Calabar, Nigeria. Qeios. 2022 Dec. doi: 10.32388/16JKEW.2.
[17] Baloch S, Siddique SM, Shams N, Ahuja KB, Sahito RM, Jan MM. A Study of Maternal Outcome of Booked and Unbooked Cases. Pakistan Journal of Medical and Health Sciences.2023 Oct; 17(04): 714-. doi: 10.5 3350/pjmhs2023174714.
[18] Barbi L, Cham M, Ame-Bruce E, Lazzerini M. Socio-Cultural Factors Influencing the Decision of Women to Seek Care During Pregnancy and Delivery: A Qualitative Study in South Tongu District, Ghana. Global Public Health. 2021 Apr; 16(4): 532-45. doi: 10.1080/17441692.2020.1839926.
[19] Abbas M, Bhamani S, Kanjani Y, Sheikh L. Enhancing Antenatal Education in Pakistan: An Audit and Recommendations. BioMed Central Women's Health. 2023 Dec; 23(1): 645. doi: 10.1186/s12905-023-0279x.
[20] Suleiman S and Pappan S. Assessment of Obstetric and Fetal Outcome among Un-Booked Mothers at Alqassimi Women's and Children Hospital, Sharjah. International Journal of Nursing Education. 2020 Jan; 12(1): 61-4.

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Primary Amenorrhea Due to Developmental Defects in Adolescent Girls in Faisalabad

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ABSTRACT

Understanding the frequency of developmental defects in adolescents presenting with primary amenorrhea is crucial for timely diagnosis and intervention, in order to preserve reproductive potential, and address psychosocial impacts. **Objective:** To determine the frequency of developmental defects in adolescent girls presenting with primary amenorrhea. **Methods:** This cross-sectional study was conducted from March 2021 to September 2021 after taking approval from ethical review committee of Faisalabad Medical University. 205 girls having primary amenorrhea were recruited from Obstetrics and Gynecology Department, Allied Hospital, Faisalabad. Non-probability consecutive sampling technique was used. After taking history and physical examination, patients were sent to the hospital Radiology department for transabdominal ultrasound and reported by senior Radiologist. Developmental defects were assessed and noted. Data analysis was done using SPSS version 26.0, quantitative data were presented as mean and standard deviation, while qualitative as frequency and percentages. **Results:** Frequency of developmental defects in adolescent girls presenting with primary amenorrhea was found in 23 (11.22%) participants; with imperforate hymen in 26.09%, Mayer-Rokitansky-Küster-Hauser syndrome in 21.74%, transverse vaginal septum in 8.70% and absent vaginal functioning uterus in 43.48%. **Conclusions:** This study concluded that the frequency of developmental defects in adolescent girls presenting with primary amenorrhea is quite high. It was recommended that public awareness programs should be arranged on national levels for women about primary amenorrhea and their causes through educational training and guidance to take proper and timely treatment in order to reduce the morbidity of these particular patients.

INTRODUCTION

Approximately 2-5% of adolescent girls presents with primary amenorrhea [1]. Its prevalence is rising, and this increase can be attributed to greater access to healthcare services, declining trend in child marriages, and enhanced awareness driven by social media [2]. Primary amenorrhea is a symptom indicative of an underlying condition affecting any part of the hypothalamic-pituitary-ovarian-uterine axis. The causes can be categorized as functional or anatomical defects in the hypothalamus, pituitary gland, uterus, or ovaries, as well as genetic abnormalities at the chromosomal or gene level [3]. Primary amenorrhea often involves developmental anomalies, or imperforate hymen [4]. Among developmental anomalies, Müllerian agenesis and gonadal dysgenesis being commonest [5]. While imperforate hymen may be identified during childhood, it can also remain undiagnosed and present in adolescence with cyclic abdominal pain and primary amenorrhea [6]. Another category of outflow tract anomalies involves absence of Müllerian structures, including Mayer-Rokitansky-Küster-Hauser syndrome (MRKH) and

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Androgen Insensitivity Syndrome (AIS). MRKH, commonly associated anomalies include skeletal, renal, and auditory defects [7]. Diagnosis is typically made using ultrasound or MRI [8]. AIS, arises from androgen resistance in genetic males with functional testes. Both MRKH and AIS share overlapping clinical features, but they are distinguished by karyotype analysis [9]. Primary amenorrhea is a challenging problem in developing countries like Pakistan due to society pressure and unknown fear. It affects physical, mental, psychological and social life of the patients and family and hence delayed diagnosis [10]. There is a misconception that the hormonal defects are the main cause of primary amenorrhea and treatment is given according to this concept.

So, this study was conducted to determine the frequency of developmental defects in adolescent girls presenting with primary amenorrhea in adolescent girls. Proper diagnosis can lead to appropriate treatment of the patients suffered from primary amenorrhea.

METHODS

This cross-sectional study was conducted at Obstetrics and Gynecology Department, Allied Hospital, Faisalabad, from 30th March 2021 to 29th September 2021. After obtaining approval from Faisalabad Medical University ethical review board (F.No.48-ERC/2020-21/PHRC/FMU/56), 205 eligible patients meeting the selection criteria were enrolled in the study. Informed consent was obtained from all participants. A sample size of 205 was calculated using the WHO sample size calculator with confidence level of 95%, an anticipated proportion 7%, and absolute precision 3.5%. A non-probability consecutive sampling technique was used [11]. Females aged 12–18 years, presenting with primary amenorrhea were included. Primary amenorrhea was defined as menstrual onset failure by the age of 14 in individuals without secondary sexual characteristics or absence of menstruation by the age of 16 despite normal growth and the development of secondary sexual characteristics. Females with hypopituitarism, weight loss, anorexia nervosa and isolated GnRH deficiency, constitutional delay of puberty, or chronic systemic disease /acute illness were excluded. A detailed history was taken, and physical examinations were conducted on all participants. Patients were referred to the hospital's Radiology Department for transabdominal ultrasound, which was interpreted by senior radiologist with minimum experience of 4 years in relevant filed. Developmental defects were assessed and noted including Imperforate hymen, MRKH syndrome, Transverse vaginal septum and Gonadal dysgenesis. Gonadal dysgenesis was labelled if; Ultrasound showed "streak" of fibrous tissue seen in the expected location of the ovaries and may contain no or very few ovarian follicles [12]. Transverse vaginal septum appears on ultrasound as a shortened, blind vaginal pouch with positive transillumination, septum can occur at any point along the vaginal cavity, although the vulva typically appears normal if the septum is located in the mid or upper vagina [13]. Imperforate hymen was labelled if; Presence of bluish bulging membrane at the entrance of vagina that allows positive transillumination at introitus on examination and confirmed on ultrasound as distended fluid-filled vagina and uterus with internal echoes [13]. Ultrasound findings of absent uterus and upper two-thirds of vagina, accompanied by normal ovaries and fallopian tubes, suggest Müllerian agenesis [14]. The study data were entered and analyzed by SPSS version 26.0. Quantitative variables, were presented as mean and standard deviation, while qualitative variables, as frequencies and percentages. Data were stratified for age, BMI and marital status, post stratification chi square was applied, p value ≤ 0.05 was taken as significant.

RESULTS

Table 1 shows demographic characteristics of study population. Mean age of 205 study participants noted was of 15.39 ± 1.83 years, among them majority of the patients 110 (53.66%) were between 16 to 18 years of age. Mean BMI noted was 27.31 ± 2.90 kg/m2. 188 (91.71%) participants found to be unmarried while only 17(8.29%) were married.

Table 1: Demographic Characteristics of Study Population (n=205)

Variables	Frequency (%)/Mean ± SD
Age	
12-15 (Years)	95 (46.34)
16-18 (Years)	110 (53.66)
Mean Age (Years)	15.39 ± 1.83
BMI (Kg/m^2)	27.31 ± 2.90
Marital Status	
Unmarried	188 (91.71)
Married	17 (8.29)

In current study, developmental defects in adolescent girls presenting with primary amenorrhea was found in 23 (11.22%) as shown in figure 1.

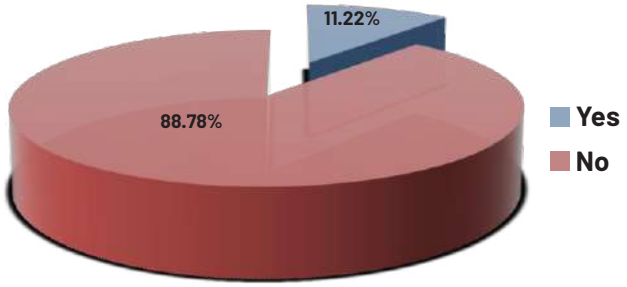

Figure 1: Frequency of Developmental Defects in Adolescent Girls Presenting with Primary Amenorrhea (n=205)

Among 23 patients found to have developmental defect, most common defect found was absent vaginal functioning uterus 43.48%, followed by imperforate hymen 26.09%,

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MRKH syndrome 21.74%, and transverse vaginal septum 8.70% as shown in table 2.

Table 2: Frequency Distribution Developmental Defect Etiology (n=23)

Types of Defects	Frequency (%)
Imperforate Hymen	06 (26.09%)
MRKH Syndrome	05 (21.74%)
Transverse Vaginal Septum	02 (8.70%)
Absent Vaginal Functioning Uterus	10 (43.48%)

Stratification of developmental defects with respect to age groups, BMI, and marital status is shown in Table 3 respectively, p-value >0.05 found to be statistically insignificant. In the age group of 12-15 years, 7.37% had developmental defects, compared to 14.55% in the 16-18 years' group, with a p-value of 0.105, suggesting a potential increase in prevalence with age despite the lack of statistical significance. For BMI, 13.86% of individuals with a BMI ≤27 kg/m^2 had developmental defects, while 8.65% of those with BMI >27 kg/m^2 did, with a p-value of 0.228 indicating no significant difference but suggesting a slight trend toward fewer defects in higher BMI individuals. Marital status showed that 12.23% of unmarried individuals had developmental defects, while none of the married individuals did, with a p-value of 0.126, suggesting no statistical association, though the absence of defects in married individuals might reflect other socio-economic factors.

Table 3: Data Stratification

Variables		Developmental Defects		p-value	CI
		Yes Frequency (%)	No Frequency (%)		
Age	12-15 (Years)	07 (7.37%)	88 (92.63%)	0.105	(-1.2% - 15.56%)
	16-18 (Years)	16 (14.55%)	94 (85.45%)		
BMI	≤27 (Kg/m^2)	14 (13.86%)	87 (86.14%)	0.228	(-3.45%- 13.87%)
	>27 (Kg/m^2)	09 (8.65%)	96 (91.35%)		
Marital Status	Unmarried	23 (12.23%)	165 (87.77%)	0.126	(7.84% - 16.62%)
	Married	00 (0.0%)	17 (100.0%)		

DISCUSSION

I have conducted this study to determine the frequency of developmental defects in adolescent girls presenting with primary amenorrhea. In current study, frequency of developmental defects in adolescent girls presenting with primary amenorrhea was found in 11.22% with imperforate hymen in 26.09%, MRKH syndrome in 21.74%, transverse vaginal septum in 8.70% and absent vaginal functioning uterus in 43.48%. In contrast to current results, study conducted by Kim *et al,* on 1060 females with primary ammenorrhea found higher frequency (30.96%) of outflow tract abnormality; among them Müllerian agenesis was most common cause (26.17%), followed by gonadal dysgenesis (22.4%), imperforate hymen (2.57%) and transverse vaginal septum (0.47%) [11]. This is further supported by another study conducted in Pakistan by Bibi *et al*, anatomical defect was noted in 60% females presenting with primary amenorrhea, and found Müllerian agenesis as most frequent cause (46%), followed by transverse vaginal septum and imperforate hymen (7% each)[15]. However, study conducted by Fowler *el al.*, found anatomical defect in only 1.5% participants [16]. In study conducted by Javed *et al.*, cases, most common anatomical defect found was gonadal dysgenesis (24%) followed by Mayer Rokistansky Kuster Hauser (21.9%), Imperforate hymen (8.5%), and vaginal septum (6.1%) [17]. These variances were found in results because factors including racial, genetic, and environmental seem to play a role in pathophysiology of primary amenorrhea [18]. The primary goals of treatment for young women with these anomalies are to alleviate obstructive symptoms, restore normal menstrual flow, and ensure sexual function while preserving reproductive potential [19]. It was proposed earlier that if regular menstruation has not commenced within two years after the onset of otherwise normal puberty, it is essential to rule out congenital absence of the uterus or vagina, provided this has not already been identified clinically [20]. In cases where puberty is atypical, or if abnormal gonadal tissue is identified before puberty, comprehensive investigations should be conducted promptly [21]. The clinical implications of these findings are significant for improving early detection, diagnosis, and treatment of primary amenorrhea, particularly among populations at higher risk for developmental defects. Health professionals should consider incorporating screening for developmental defects into routine evaluations for primary amenorrhea. Moreover, these findings highlight the need for targeted educational campaigns to raise awareness about primary amenorrhea, its causes, and available treatments. Furthermore, incorporating this data into treatment guidelines can help create a more personalized approach to care, ultimately enhancing the quality of life and reproductive health of affected girls. This study has certain limitations. It focused solely on structural anomalies and did not explore other potential etiologies of primary amenorrhea, such as endocrine abnormalities, genetic mutations, or environmental influences. Hormonal assessments and advanced genetic testing were not included, which may have provided a more comprehensive understanding of the condition. Additionally, the study relied on transabdominal ultrasound for diagnosis, which, while effective, may not capture subtle abnormalities detectable by more advanced imaging modalities like MRI.

CONCLUSIONS

This study concluded that the frequency of developmental defects in girls with primary amenorrhea is quite high. It

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was recommended that public awareness programs should be arranged on regional and national levels for educating women about primary amenorrhea and their causes through educational training and guidance to take proper and timely treatment in order to reduce the morbidity of these particular patients.

Authors Contribution

Conceptualization: SS
Methodology: SS, SH, NK, SNZ
Formal analysis: HR, SK
Writing, review and editing: HR, BZ, SNZ

All authors have read and agreed to the published version of the manuscript

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REFERENCES

[1] Gaspari L, Paris F, Kalfa N, Sultan C. Primary amenorrhea in adolescents: approach to diagnosis and management. Endocrines.2023 Jul; 4(3): 536-47. doi: 10.3390/endocrines4030038.

[2] Melnick A. Primary Amenorrhea. InProblem-Focused Reproductive Endocrinology and Infertility 2023 Feb: 25-31. doi: 10.1007/978-3-031-19443-6_4.

[3] Seppä S, Kuiri-Hänninen T, Holopainen E, Voutilainen R. Management of endocrine disease: diagnosis and management of primary amenorrhea and female delayed puberty. European Journal of Endocrinology. 2021 Jun; 184(6): R225-42. doi: 10.1530/EJE-20-1487.

[4] Kerns J, Itriyeva K, Fisher M. Etiology and management of amenorrhea in adolescent and young adult women. Current Problems in Pediatric and Adolescent Health Care.2022 May; 52(5): 101184. doi: 10.10 16/j. cppeds. 20 22.101184.

[5] Islam A, Zubair M, Wahid S, Noreen U. Aetiology and management of primary amenorrhoea. Journal of Ayub Medical College Abbottabad-Pakistan. 2021 Apr; 33(2): 262-266.

[6] Hamouie A and Dietrich JE. Imperforate Hymen: Clinical Pearls and Implications of Management. Clinical Obstetrics and Gynecology. 2022 Dec; 65(4): 699-707. doi: 10.1097/GRF.0000000000000703.

[7] Kapczuk K and Kędzia W. Primary amenorrhea due to anatomical abnormalities of the reproductive tract: Molecular insight. International Journal of Molecular Sciences. 2021 Oct; 22(21): 11495. doi: 10.33 90/ ijms2 22111495.

[8] Antari LP, Suadiatmika DG, Dewi PU. Magnetic Resonance Imaging Findings in Mayer-Rokitansky-Küster-Hauser (MRKH) Syndrome: A Report of Two Cases. Intisari Sains Medis.2023 Dec; 14(3): 1382-5. doi: 10.15562/ism.v14i3.1889.

[9] Pitts S, DiVasta AD, Gordon CM. Evaluation and management of amenorrhea. Journal of the American Medical Association.2021 Nov; 326(19): 1962-3. doi: 10.1001/jama.2021.13312.

[10] Rauf U, Zahid M, Ashiq F. Social Support, Quality Of Life and Mental Health Problems among Females with Menstruation Problems. Pakistan Journal of Social Research. 2023 May; 5(02): 1229-37. doi: 10.52 567 /pjsr .v5i02.1344.

[11] Kim H, Lee MH, Lee DY, Kim H, Lee HJ, Kim M *et al.* Etiology and Secular Trends in Primary Amenorrhea in 856 Patients: A 17-Year Retrospective Multicenter Study in Korea. Journal of Korean Medical Science. 2022 Jul; 37(29). doi: 10.3346/jkms.2022.37.e230.

[12] Jakovleva A and Kovalova Z. Complete gonadal dysgenesis analysis in the population of Latvia: malignant outcomes and a review of literature. Medicine and Pharmacy Reports. 2022 Jan; 95(1): 47. doi: 10.15386/mpr-2064.

[13] Wang YF, Kuo SM, Lin YC, Fang HH, Chu CH, Lin CM. Mimics of malignancy caused by concurrent imperforate hymen and transverse vaginal septum: an instructive case and review of the literature. Journal of International Medical Research. 2021 May; 49(5): 03000605211014797. doi: 10.1177/03000605211014797.

[14] Wu CQ, Childress KJ, Traore EJ, Smith EA. A review of Mullerian anomalies and their urologic associations. Urology. 2021 May; 151: 98-106. doi: 10.1016/j.urology. 2020.04.088.

[15] Bibi K, Azim P, Kifayatullah M, Shakeel F, Aamir M. Primary amenorrhea in females attending gynaecological outpatient of a tertiary care hospital at Peshawar. Journal of the American Medical Association.2020 May; 70(5): 888-91. doi: 10.5455/JP MA.24317.

[16] Fowler K, Josephson R, O'Brien KO, Pitera R. Updated Causes of Primary Amenorrhea [ID: 1381195]. Obstetrics & Gynecology. 2023 May; 141(5S): 92S. doi: 10.1097/01.AOG.0000931120.89215.39.

[17] Javed S, Nusheen B, Hussain K. Causes of Primary Amenorrhea among Patient Presenting At a Tertiary Care Hospital. 2024 Nov; 7(11): 573-578. doi: 10.36348/ sijog.2024.v07i11.007.

[18] Nappi L, Sorrentino F, Greco F, Vona L, Zullo FM, Bettocchi S. Pathophysiology of Female Reproduction and Clinical Management. InPractical Clinical Andrology. 2022 Oct; 213-226. doi: 10.1007/978-3-031-

DOI: https://doi.org/10.54393/pjhs.v5i12.2598

11701-5_16.
[19] Shoupe D, editor. Handbook of gynecology. Springer Nature;2023 Dec. doi: 10.1007/978-3-319-17002-2_89-2.
[20] Ansari NM, Chatur VM, Walode SG. Amenorrhea: a review. Medicine & Science in Sports & Exercise. 2021 Oct; 17(1): 56-72.
[21] Pergialiotis V and Antsaklis A. Primary and Secondary Amenorrhoea. The EBCOG Postgraduate Textbook of Obstetrics & Gynaecology: Gynaecology. 2021 Dec; 2: 91. doi: 10.1017/9781108582322.013.

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Prevalence of Dyslipidemia and the Role of ApoB and hsCRP in Acute Myocardial Infarction: A Comprehensive Analysis

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ABSTRACT

Dyslipidemia significantly contributes to AMI, with ApoB and hsCRP offering potential for improved risk prediction. **Objective:** To determine the prevalence of dyslipidemia and the role of ApoB and hsCRP in acute myocardial infarction in patients presenting to a tertiary care hospital in Lodhran, Punjab. **Methods:** A cross-sectional study was conducted at the Department of Medicine, Shahida Islam Medical College, Lodhran, from May 2023 to November 2023. A total of 187 AMI patients aged 30–90 years were included using non-probability consecutive sampling. Data were collected using structured clinical history forms and laboratory analysis of lipid profiles, ApoB, and hsCRP levels. Dyslipidemia was defined using standard lipid cutoff values. Statistical analysis was performed using SPSS version 25.0, employing Chi-square and logistic regression to explore associations and predictors of dyslipidemia, with a significance level of $p < 0.05$. **Results:** Dyslipidemia was highly prevalent, affecting 74.9% of patients. Hypertension was significantly associated with dyslipidemia (OR = 2.049, p = 0.042), indicating a potential need for combined management strategies. ApoB and hsCRP levels did not show significant differences between dyslipidemic and non-dyslipidemic patients, though total cholesterol and LDL levels were significantly higher in the dyslipidemic group ($p < 0.001$). **Conclusions:** This study revealed a high prevalence of dyslipidemia in AMI patients, with hypertension as a key predictor. While ApoB and hsCRP were not significant discriminators, their roles in cardiovascular risk assessment may complement traditional lipid profiles, supporting personalized management strategies to reduce cardiovascular risk.

INTRODUCTION

Dyslipidemia is a major modifiable risk factor for Cardiovascular Disease (CVD), a leading cause of morbidity and mortality worldwide. This lipid imbalance, significantly elevated Low-Density Lipoprotein Cholesterol (LDL-C) and Apolipoprotein B (ApoB), promotes atherosclerosis, a primary precipitant of Acute Myocardial Infarction (AMI) [1]. The accumulation of ApoB-containing lipoproteins in arterial walls triggers an inflammatory response, driving lesion progression and plaque formation [2]. Recent studies have established ApoB as a crucial marker of cardiovascular disease risk, as it reflects the count of atherogenic particles undetectable by standard lipid profiles [3]. The pathophysiology of AMI includes inflammation, which often coexists with lipid abnormalities. High-Sensitivity C-Reactive Protein (hsCRP), an inflammation biomarker, is independently associated with adverse cardiovascular outcomes [4]. Elevated hsCRP levels indicate systemic inflammation, suggesting that the formation and rupture of atheromatous plaques correlate with AMI events [5]. The integration of hsCRP measurement into cardiovascular risk assessment enhances the evaluation of the inflammatory component of atherosclerosis [6]. ApoB and hsCRP together provide a comprehensive picture of

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cardiovascular risk through their respective lipid and inflammatory mechanisms. This dual assessment offers insights into reducing the incidence of adverse cardiac events in high-risk populations [7]. Lipid-lowering therapies targeting ApoB-rich lipoproteins can dramatically reduce cardiovascular risk in ApoB-rich patients [8]. Similarly, anti-inflammatory interventions targeting hsCRP may serve as promising adjunctive therapies in managing cardiovascular disease [9]. Further research is needed to clarify the significance of ApoB and hsCRP in AMI, particularly in refining risk stratification models and optimizing treatment protocols based on individual risk profiles. These biomarkers could provide novel insights into the contributions of lipid abnormalities and inflammation to atherosclerotic disease, thereby improving clinical outcomes [10]. Although traditional lipid profiles are valuable, they may not fully capture the cardiovascular risk burden in AMI patients. Emerging evidence highlighted the complementary roles of ApoB, as a measure of atherogenic particles, and hsCRP, as an inflammatory marker, in risk stratification. In resource-limited settings, conventional risk stratification tools may not have effectively applied to AMI patients. Assessing these biomarkers alongside conventional lipid levels could enhance risk stratification and guide tailored interventions.

The purpose of this study was to determine the prevalence of dyslipidemia and evaluate the significance of ApoB and hsCRP levels in AMI patients, aiming to improve management strategies for cardiovascular complications in this high-risk population.

METHODS

This cross-sectional study was conducted at the Department of Medicine, Shahida Islam Medical College, Lodhran, between May 2023 and November 2023. A total of 187 patients with AMI, aged 30–90 years, either male or female, were included. The sample size was calculated using OpenEpi, an online epidemiological tool, based on a reported prevalence of dyslipidemia of 60.83%, a 95% confidence level, and a precision of 7% [11]. This method ensured an adequate sample size to detect meaningful associations in the study population. A non-probability consecutive sampling technique was employed. Patients taking lipid-lowering treatments before the study or those with incomplete medical records were excluded. Informed consent was obtained from all patients, and the ethical committee approved the study SIMC/ET.C./10010/23. Demographic data of all the patients were recorded. A comprehensive clinical history including BMI, smoking status, and comorbidities like hypertension, diabetes mellitus, and family history of cardiovascular disease were taken. Blood samples were taken within the first 24 hours of admission, before starting lipid-lowering treatments, and were sent to a laboratory for lipid profile, ApoB, and hsCRP levels. The lipid profile measured total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides, while ApoB levels indicated atherogenic lipoprotein particles, and hsCRP was measured as a marker of systemic inflammation. Each variable was carefully recorded to ensure data integrity and accuracy. Collected data were entered and analyzed using SPSS version 25.0. Mean and SD were calculated for age, total cholesterol, triglycerides, HDL cholesterol, LDL cholesterol, ApoB, and hsCRP. For categorical variables like dyslipidemia status (Yes/No), gender (Male/Female), obesity status (Obese/Non-obese), smoking status (Smoker/Non-smoker), hypertension status (Hypertensive/Normotensive), diabetes mellitus status (Diabetic/Non-diabetic), and family history of cardiovascular disease (Present/Absent) were present as frequencies and percentages. The Chi-square test was employed to assess associations between categorical variables. Logistic regression analysis was performed to adjust for potential confounding variables, including ApoB and hsCRP, with a significance level set at $p < 0.05$

RESULTS

A total of 187 AMI patients were included in the study. Smoking status showed a high prevalence of dyslipidemia in both smokers and non-smokers, with 76 out of 102 smokers (74.5%) and 64 out of 85 non-smokers (75.3%) identified as dyslipidemic. The p-value of 0.902 indicated no significant association, suggesting that smoking status may not notably influence dyslipidemia prevalence in this cohort. For hypertension status, dyslipidemia was observed in 76 out of 94 hypertensive patients (80.9%) and 64 out of 93 normotensive patients (68.8%), yielding a p-value of 0.058. Although this result did not reach statistical significance, it suggests a potential trend where hypertensive AMI patients might have a higher predisposition to dyslipidemia. Similarly, diabetes status did not show a significant association with dyslipidemia. Among diabetic patients, 69 out of 90 (76.7%) were dyslipidemic, compared to 71 out of 97 (73.2%) non-diabetic patients ($p = 0.585$), implying no notable difference in dyslipidemia prevalence based on diabetes status. Regarding family history of cardiovascular disease (CVD), dyslipidemia occurred in 79 out of 100 patients (79.0%) with a family history of CVD and 61 out of 87 patients (70.1%) without such history, resulting in a p-value of 0.162. This indicates no significant relationship between a family history of CVD and dyslipidemia. Analysis of gender showed that 66 out of 93 male patients (71.0%) and 74 out of 94 female patients (78.7%) were dyslipidemic, with a p-value of 0.222, suggesting no significant gender influence on dyslipidemia status among AMI patients in this study (Table 1).

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Table 1: Association between Dyslipidemia and Key Clinical Variables in Patients with Acute Myocardial Infarction (n = 187)

Variable Names	Status	Dyslipidemia N (%)	Dyslipidemia N (%)	Total	p-value
Smoking Status	Smokers	26 (25.5%)	76 (74.5%)	102	0.902
	Non-Smokers	21 (24.7%)	64 (75.3%)	85	
Hypertension Status	Hypertensive	18 (19.1%)	76 (80.9%)	94	0.058
	Normotensive	29 (31.2%)	64 (68.8%)	93	
Diabetes Status	Diabetic	21 (23.3%)	69 (76.7%)	90	0.585
	Non-Diabetic	26 (26.8%)	71 (73.2%)	97	
Family History of CVD	Present	21 (21.0%)	79 (79.0%)	100	0.162
	Absent	26 (29.9%)	61 (70.1%)	87	
Gender	Male	27 (29.0%)	66 (71.0%)	93	0.222
	Female	20 (21.3%)	74 (78.7%)	94	
ApoB Status	Normal	45 (25.4%)	132 (74.6%)	x	0.829
	Elevated	2 (22.2%)	7 (77.8%)	9	
hsCRP Status	Normal	13 (19.1%)	55 (80.9%)	68	0.152
	Elevated	34 (28.6%)	85 (71.4%)	119	

Novel markers ApoB and hsCRP were also examined. Among patients with normal ApoB levels, 132 out of 177 (74.6%) were dyslipidemic, while 7 out of 9 (77.8%) with elevated ApoB levels had dyslipidemia, resulting in a p-value of 0.829. For hsCRP, 55 out of 68 patients (80.9%) with normal hsCRP levels and 85 out of 119 (71.4%) with elevated hsCRP levels were dyslipidemic, with a p-value of 0.152. These findings indicate no statistically significant association between dyslipidemia status and either ApoB or hsCRP levels in this AMI cohort, suggesting that while ApoB and hsCRP are relevant cardiovascular markers, they may function independently of dyslipidemia in the context of AMI. Several key differences in clinical and metabolic parameters were noted in comparing patients with and without dyslipidemia. Total cholesterol and LDL cholesterol levels were significantly elevated in the dyslipidemic group, with mean values of 217.91 mg/dL (SD 40.921) for total cholesterol and 141.54 mg/dL (SD 31.376) for LDL, compared to 164.67 mg/dL (SD 27.457) and 110.81 mg/dL (SD 15.027) in the non-dyslipidemic group (both $p < 0.001$). These differences emphasize the substantially higher levels of atherogenic lipids in dyslipidemic patients, aligning with established roles of elevated total and LDL cholesterol in increasing cardiovascular risk and contributing to atherosclerosis. HDL cholesterol levels did not significantly differ between groups, with a mean of 46.53 mg/dL (SD 10.547) in dyslipidemic patients compared to 44.20 mg/dL (SD 11.391) in non-dyslipidemic patients ($p = 0.200$). ApoB and hsCRP levels also did not show significant differences between the groups: ApoB levels were 99.97 mg/dL (SD 19.449) in dyslipidemic patients and 99.27 mg/dL (SD 18.163) in non-dyslipidemic patients ($p = 0.827$), while hsCRP levels were 2.92 mg/L (SD 1.360) in dyslipidemic patients and 3.11 mg/L (SD 1.357) in non-dyslipidemic patients ($p = 0.414$). These findings suggest that while ApoB and hsCRP are valuable indicators of cardiovascular risk, they may act as independent risk factors rather than correlating directly with dyslipidemia status in AMI patients (Table 2).

Table 2: Comparison of Clinical and Metabolic Parameters between Patients with and without Dyslipidemia in Acute Myocardial Infarction

Variable	No Dyslipidemia (Mean ± SD)	Dyslipidemia (Mean ± SD)	p-Value
Age	58.45 ± 17.151	60.04 ± 18.320	0.600
BMI	24.69 ± 3.870	24.87 ± 4.613	0.812
Total Cholesterol	164.67 ± 27.457	217.91 ± 40.921	0.000
LDL	110.81 ± 15.027	141.54 ± 31.376	0.000
HDL	44.20 ± 11.391	46.53 ± 10.547	0.200
Triglycerides	160.91 ± 51.358	146.21 ± 50.981	0.089
ApoB	99.27 ± 18.163	99.97 ± 19.449	0.827
hs-CRP	3.11 ± 1.357	2.92 ± 1.360	0.414

Regression analysis identified hypertension as the only significant predictor of dyslipidemia among AMI patients, with hypertensive patients being twice as likely to have dyslipidemia (OR = 2.049, 95% CI: 1.027–4.086, p = 0.042). This aligns with established evidence linking hypertension to lipid abnormalities, highlighting the importance of managing both conditions to mitigate cardiovascular risk. Other variables, including age, BMI, smoking status, diabetes status, family history of CVD, ApoB, and hsCRP, did not show statistically significant associations with dyslipidemia in this cohort. The model fit was acceptable, with a Hosmer and Lemeshow test p-value of 0.720 and an overall classification accuracy of 74.9%, supporting the reliability of hypertension as an independent predictor in this population (Table 3).

Table 3: Logistic Regression Analysis for Predictors of Dyslipidemia in AMI Patients

Variables	B	S.E.	Wald	df	Significant (p-Value)	Exp (B) (Odds Ratio)	95% CI for Exp (B)
Age	0.007	0.010	0.476	1	0.490	1.007	0.987 – 1.027
BMI	-0.001	0.040	0.000	1	0.987	0.999	0.923 – 1.082
Smoking Status (1)	-0.067	0.353	0.036	1	0.850	0.936	0.469 – 1.868
Diabetes Status (1)	0.102	0.354	0.082	1	0.774	1.107	0.551 – 2.225
Family History of CVD (1)	0.578	0.360	2.570	1	0.109	1.782	0.882 – 3.601
ApoB	0.000	0.009	0.002	1	0.965	1.000	0.982 – 1.018
hs-CRP	-0.100	0.130	0.594	1	0.441	0.905	0.697 – 1.174
Constant	0.324	1.540	0.044	1	0.833	1.383	-

Notes: (1) Indicates the reference category for binary variables. Adjusted Odds Ratios (ORs) are provided with 95% Confidence Intervals (CI).

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DISCUSSION

The comprehensive analysis of dyslipidemia in patients presenting with Acute Myocardial Infarction (AMI) revealed significant findings that both align with and expand upon existing literature. The high prevalence of dyslipidemia observed in the cohort underscores the critical role of lipid abnormalities in the pathogenesis of AMI. The inclusion of biomarkers such as Apolipoprotein B (ApoB) and high-sensitivity C-reactive Protein (hsCRP) aimed to provide novel insights into cardiovascular risk profiles in dyslipidemic AMI patients. Although ApoB levels did not differ significantly between dyslipidemic and non-dyslipidemic patients, ApoB remains a well-recognized marker reflecting the total number of atherogenic particles, as highlighted by Kayani T et al [11]. The absence of significant differences in ApoB levels may suggest that while cholesterol levels are elevated, the atherogenic particle count itself does not vary notably, or that post-AMI metabolic changes influence these results. Similarly, hsCRP, a key inflammatory biomarker, showed no significant differences between groups. Nevertheless, hsCRP's role in cardiovascular risk is well-established, with Khan HA et al., reporting an inverse relationship between hsCRP and HDL cholesterol [12]. This relationship underscores inflammation's role as an independent contributor to cardiovascular risk, rather than solely through lipid dysregulation. Compared with Ali SN et al., who reported a 60.83% prevalence of dyslipidemia in young AMI patients, the higher rate may have suggested an upward trend in dyslipidemia or demographic differences in lipid profiles [13]. However, smoking status did not significantly impact dyslipidemia prevalence in the cohort, contrasting with findings by Iqbal MZ et al [14]. Differences in smoking intensity, genetic predispositions, or population characteristics may contribute to these varied results, indicating that smoking's impact on lipid levels may differ across populations. Morofuji Y et al., have also noted the influence of lifestyle-related factors, which may affect lipid levels independently of smoking in certain cohorts [15]. Hypertension was the only predictor that reached significance in the regression analysis and hypertensive patients were twice as likely to be dyslipidemic (OR = 2.049, p = 0.042) [16]. This association, in turn, underscores the importance of coordinating the treatment of hypertension and lipid abnormalities in AMI patients to contain cardiovascular risk. By comparing these findings of elevated total and LDL cholesterol in dyslipidemic patients with well-described atherogenic patterns associated with greater risk for cardiovascular disease, reflected the well-documented alterations. These findings emphasize the need to monitor these lipid parameters to better control cardiovascular health in AMI patients. In this study, ApoB and hsCRP be statistically significant predictors of dyslipidemia, but remain important risk assessment biomarkers independent of cardiovascular risk. As Kayani T et al., suggested, ApoB's predictive value for cardiovascular events may be stronger in larger studies [11]. Furthermore, hsCRP's functionality as an index of atherosclerotic inflammation lends it as one more tool enabling assessment of AMI risk that warrants further exploration. However, dyslipidemia and its cardiovascular risk in AMI patients can be further unraveled by incorporating genetic markers, as discussed by Pham-Thi NN et al [17]. Finding polymorphisms related to cardiovascular risk will make it possible to improve risk prediction and to provide personalized therapeutic strategies. The results of this study underline the importance of conducting comprehensive lipid profiling in AMI patients together with ApoB and hsCRP in the risk assessment of cardiovascular diseases. Considered together with hypertension, both dyslipidemia and its treatment were consistent with aggressive lipid-lowering and blood pressure control strategies, given the high prevalence of dyslipidemia. More often, gaps in dyslipidemia management are suggested by Talviste G et al., to be addressed in order to reduce recurrent cardiovascular events and improve the outcomes of patients with AMI [18]. Emerging research highlights the role of lipoprotein (a) [Lp (a)] as an independent cardiovascular risk factor, particularly in AMI patients with dyslipidemia. Elevated Lp (a) levels are associated with increased residual cardiovascular risk despite optimal LDL-C management, as demonstrated by Tsimikas S et al [19]. Moreover, recent advances in lipidomics have provided insights into specific lipid species contributing to cardiovascular events. Rhee EJ et al., reported that certain ceramide and sphingolipid profiles may serve as novel biomarkers for AMI risk stratification, offering new therapeutic targets for dyslipidemia management [20].

CONCLUSIONS

This study highlighted the high prevalence of dyslipidemia in AMI patients with its important role in cardiovascular risk. This powerful association of hypertension with dyslipidemia supports the idea that integrated hypertensive patient management is helpful for AMI in reducing cardiovascular risk by addressing both blood pressure and lipid abnormalities. Although novel biomarkers ApoB and hs-CRP did not significantly identify dyslipidemic versus non-dyslipidemic patients, they are important cardiovascular risk assessments and may also function independently of conventional lipid measures. Additionally, the reduction of the prevalence of dyslipidemia, among which approximately half of the population who do not achieve Lp (a) LDL goals, is a reflection of statin therapy's central role in the

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management of cardiovascular risk. Future research should be done with a larger, more diverse population exploring potential genetic, inflammatory, and lifestyle influences on dyslipidemia in AMI patients, which will support more personalized therapeutic approaches.

Authors Contribution

Conceptualization: AF
Methodology: ZI
Formal analysis: MAQ
Writing, review and editing: MAQ, BH, SAF, NA

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Arvanitis M and Lowenstein CJ. Dyslipidemia. Annals of internal medicine. 2023 Jun; 176(6): ITC81-96. doi: 10.7326/AITC202306200.

[2] Krintus M, Kozinski M, Stefanska A, Sawicki M, Obonska K, Fabiszak T *et al*. Value of C-reactive protein as a risk factor for acute coronary syndrome: A comparison with apolipoprotein concentrations and lipid profile. Mediators of Inflammation. 2012; 2012(1): 419804. doi: 10.1155/2012/419804.

[3] Leela P. Study of Serum Lipoprotein (a), Apolipoprotein B, hsCRP and Lipid Profile in Ischemic Heart Disease. [Doctoral dissertation]. Rajiv Gandhi University of Health Sciences(India). 2014.

[4] Quispe R, Martin SS, Michos ED, Lamba I, Blumenthal RS, Saeed A *et al*. Remnant cholesterol predicts cardiovascular disease beyond LDL and ApoB: a primary prevention study. European Heart Journal. 2021 Nov;42(42):4324-32.doi:10.1093/eurheartj/ehab432.

[5] Higashi Y. Endothelial Function in dyslipidemia: roles of LDL-cholesterol, HDL-cholesterol and triglycerides.Cells.2023May;12(9):1293.doi:10.3390/cells12091293.

[6] Rasouli M, Kiasari AM. Interactions of serum hsCRP with apoB, apoB/AI ratio and some components of metabolic syndrome amplify the predictive values for coronary artery disease. Clinical biochemistry.2006 Oct;39(10):971-7.doi:10.1016/j.clinbiochem.2006.07.003.

[7] Lin H, Wang L, Liu Z, Long K, Kong M, Ye D *et al*. Hepatic MDM2 Causes Metabolic Associated Fatty Liver Disease by Blocking Triglyceride-VLDL Secretion via ApoB Degradation. Advanced Science.2022 Jul; 9(20): 2200742. doi: 10.1002/advs.202200742.

[8] Chyu KY, Zhao X, Zhou J, Dimayuga PC, Lio NW, Cercek B *et al*. Immunization using ApoB-100 peptide-linked nanoparticles reduces atherosclerosis. JCI Insight. 2022 Jun; 7(11). doi: 10.1172/jci.insight.149741.

[9] Carrero JJ, Andersson Franko M, Obergfell A, Gabrielsen A, Jernberg T. hsCRP level and the risk of death or recurrent cardiovascular events in patients with myocardial infarction: a healthcare-based study. Journal of the American Heart Association.2019 Jun; 8(11): e012638. doi: 10.1161/JAHA.119.012638.

[10] Johannesen CD, Mortensen MB, Langsted A, Nordestgaard BG. ApoB and Non-HDL Cholesterol Versus LDL Cholesterol for Ischemic Stroke Risk. Annals of Neurology.2022 Sep; 92(3): 379-89.doi:10.1002/ana.26425.

[11] Kayani T, Ahmad B, Chang RS, Qian F, Sahinoz M, Rehan MW *et al*. Beyond Statins: Novel Lipid-Lowering Agents for Reducing Risk of Atherosclerotic Cardiovascular Disease. Pharmacoepidemiology. 2024 Mar; 3(1): 117-68. doi: 10.3390/pharma3010009.

[12] Khan HA, Alhomida AS, Sobki SH. Lipid profile of patients with acute myocardial infarction and its correlation with systemic inflammation. Biomarker Insights. 2013 Jan; 8: BMI-S11015. doi: 10.4137/BMI.S11015.

[13] Ali SN, Bashir M, Sherwani M. Pattern of dyslipidemia in young patients with acute ST elevation myocardial infarction. Journal Sheikh Zayed Medical College. 2016; 7(3): 998-1001.

[14] Iqbal MZ, Dogar LA, Rafiq Z. Association of Dyslipidemia with Acute Myocardial Infarction (CAD). Lateral. 2012; 25(10): 35.

[15] Morofuji Y, Nakagawa S, Ujifuku K, Fujimoto T, Otsuka K, Niwa M *et al*. Beyond lipid-lowering: effects of statins on cardiovascular and cerebrovascular diseases and cancer. Pharmaceuticals.2022Jan;15(2): 151. doi: 10.3390/ph15020151.

[16] Gupta MD, Girish MP, Sarkar PG, Gupta A, Kategari A, Bansal A *et al*. Role of ApoE gene polymorphism and nonconventional biochemical risk factors among very young individuals (aged less than 35 years) presenting with acute myocardial infarction. Indian Heart Journal. 2018 Dec; 70: S146-56. doi:10.1016/j.ihj.2018.08.013.

[17] Pham-Thi NN, Tran-Thi TL, Duong HQ, Do HL, Huynh TC, Le TS *et al*. Comprehensive Analysis of Demographic, Clinical, and Genetic Characteristics in Acute Myocardial Infarction Patients. F1000Research. 2024 Aug;13(937):937.doi:10.12688/f1000research.154230.1.

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[18] Talviste G, Leinsalu M, Ross P, Viigimaa M. Lipid-Lowering Treatment Gaps in Patients after Acute Myocardial Infarction: Using Global Database TriNetX. Medicina.2024 Sep;60(9):1433.doi:10.3390/medicina 60091433.

[19] Tsimikas S, Karwatowska-Prokopczuk E, Gouni-Berthold I, Tardif JC, Baum SJ, Steinhagen-Thiessen E *et al.* Lipoprotein (a) reduction in persons with cardiovascular disease. New England Journal of Medicine.2020 Jan; 382(3): 244-55.doi: 10.1056/NEJ Moa1905239.

[20] Rhee EJ, Kim HC, Kim JH, Lee EY, Kim BJ, Kim EM *et al.* 2018 Guidelines for the management of dyslipidemia in Korea. Journal of Lipid and Atherosclerosis. 2019 Sep; 8(2): 78-131. doi: 10.12997/jla.2019.8.2.78.

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Internet Addiction and Its Association with Personality Traits and Depression in Medical Undergraduates, A Cross-Sectional Study from Pakistan

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ABSTRACT

Internet usage has gained an essential role in modern-day life, leading to various undesirable behaviours. Unnecessary internet use can lead to dependence which poses significant mental health risks like depression and specific personality traits, particularly for university medical students, potentially impacting their education and future careers. **Objectives:** To examine Internet addiction among MBBS scholars and investigate the relationship between excessive internet use, depression, personality traits, and socio-demographic variables in this group. **Methods:** A cross-sectional survey was conducted with 206 medical undergraduates from the People's University of Medical and Health Sciences for Women, Nawabshah, Pakistan through convenience sampling by self-administered questionnaire. The Young's Internet Addiction Test assessed Internet addiction, the Patient Health Questionnaire-9 measured depression, and the Ten-Item Personality Inventory and a self-structured questionnaire evaluated personality traits and socio-demographic characteristics respectively. **Results:** The mean age of the female medical students was 21.72 ± 1.631 years. The majority were Sindhi Muslims and unmarried. In 68.3% of the participants, mild internet addiction was found, with a mean score of 40.76 ± 16.495. Approximately half of the participants experienced depression. Participants with conscientiousness (Type 3) and emotional stability (Type 4) personalities were negatively associated with Internet addiction and positively associated with depression, particularly among second-year students. **Conclusions:** It was concluded that internet addiction is an alarming issue in medical students, leading to negative outcomes like depression, poor conscientiousness, and emotional stability. Efforts should be made to raise awareness and develop alternatives.

INTRODUCTION

Incapability to control internet usage time is termed as internet addiction, leading to significant distress, mood changes, and social, occupational, and academic impairments. With the surge in global internet usage, especially in developing countries, nearly 5.45 billion people are now online, and young people, particularly university students, are increasingly showing signs of unnecessary and problematic internet use [1, 2]. Due to this unnecessary internet usage, psychologists and educators are increasingly concerned about the emotional, social, physical, and mental dysfunctions of the students resulting from excessive internet use [3, 4]. Diagnosis of internet addiction involves ascertaining specific criteria, which include spending significantly more time online than intended, being worried and depressed when unable to access the internet, damaging personal and social relationships or career obligations and using it as a coping mechanism [5]. The abundance of free time, the newfound freedom for young adults aged 18 to 22, unlimited internet access, and difficulties with socializing serve as the contributing factors which may cause students to retreat to the internet rather than form in-person connections. Though the Internet is a valuable academic tool and social platform it also poses the risk of dependence and addiction. By 2016, there were over 3.5 billion internet users, with Asia leading the statistics with 1.3 billion users. Research shows that internet addiction is more common in regions where dissatisfaction in life is more prevalent, and

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traffic congestion and pollution are common [6]. Studies also link internet use with certain personality traits, like extraversion, agreeableness, conscientiousness, neuroticism, and openness to experience [7]. University students rely heavily on the Internet for academic activities, entertainment, shopping, and gaming. However, this dependence leads to severe mental health issues, strongly linked to depression, despair, loneliness, and suicidal tendencies [8-10]. Medical students show particularly high rates of addiction, with one study reporting that 52.4% experienced moderate to severe Internet addiction [11]. Cultural norms like social restrictions for women contribute to higher addiction rates among female students. Surveys from various countries reveal a concerning increase in the frequency of internet usage from 1.5% to over 11% [12]. In Iran, 8.3% of high school girls, while South Korea, Finland, China, and Italy report similarly high rates of internet addiction [13]. In Nepal, over 40% of medical students were identified as moderate users, while 3% had severe addiction [14]. In India, a 2019 study found a prevalence of 61.4% [15]. In a meta-analysis of 12 studies the five main personality traits and internet addiction were found to be strongly correlated, particularly neuroticism [16]. In the same way in Iraq, studies have revealed a connection between internet addiction and personality traits [17]. A study from Pakistan in 2014 revealed that university students generally had positive attitudes toward internet use but felt dissatisfied when they could not access it [18]. Among medical students in Karachi, 85% were found to have some level of internet addiction, with females being disproportionately affected [9]. There is a paucity of research in Pakistan on the personality traits among medical students hence this needs to be explored. Literature There is a well-documented link between IA and depression, fretfulness, and even substance abuse. A systematic review of 20 studies reported (75%) a significant affiliation between internet addiction and depression [19, 20]. In Pakistan, a 2019 study on MBBS students in Azad Kashmir concluded that internet addiction was extremely prevalent. (52.4%) and a minor positive association with depression [11]. Neuroticism and aggression, have been shown to correlate with internet addiction [21]. In particular, the Big Five Model has been extensively studied, with neuroticism being positively linked to addiction, while traits like openness, conscientiousness, extraversion, and agreeableness tend to be negatively associated [22]. Nearly 45% of medical students in China's three medical schools participated in a cross-sectional study in 2017 that revealed internet addiction; neuroticism was favourable connected with the condition, while conscientiousness and agreeableness were adversely associated [23, 24].

This study aims to examine Internet addiction among medical students and explore the association between excessive internet use, depression, personality traits, and socio-demographics in this group.

METHODS

The study design was cross-sectional and descriptive. A convenience sampling strategy was employed to collect data from MBBS scholars at the People University of Medical and Health Sciences for Women in Nawabshah, Pakistan, spanning their first to final academic year. The sample size was calculated using Open Epi software, with a 95% confidence interval, a 5% margin of error, and an 85% frequency of internet dependence grounded on a former study. The minimum sample size was 196, with an additional 5% included to enhance the study's power. The projected sample size was 206. The study commenced in September 2021 and continued for one year. Ethical approval was attained from the Peoples University of Medical and Health Sciences for Women, Nawabshah, Pakistan, and the Malaysian Allied Health Sciences Academy University Ethics Committee (RMC/ EC04/ 2020). Informed consent was attained. The questionnaire comprised four sections 1. Socio-demographics, 2. Internet Addiction Test (IAT), 3. Ten- Item Personality Inventory (TIPI), and 4. Patient Health Questionnaire (PHQ-9) for depression. Internet addiction (IA) is characterized as inordinate or inadequately regulated prepossessions, urges, or actions related to computer use and Internet access that lead to impairment or anguish. The IAT consists of 20 questions, each with 5 response druthers (1=Rare to 5=Always) to assess the impacts of the internet on daily life, particular effectiveness, emotional well-being, and sleep habits. Scores vary from a minimum of 20 to a max of 100. Scores between 20 and 49 denote minimum users, scores from 50 to 79 signify moderate, and scores ranging from 80 to 100 represent insane users. Cronbach's Alpha equals 0.899. Psychologists assert that personality is innovated on five top traits openness, meticulousness, extraversion, agreeability, and neuroticism inclusively appertained to as the Big-Five dimensions. The reverse-scored particulars on the Ten-point Personality Inventory (TIPI) were quantified by recoding values (e.g., a score of 7 was converted to 1, 6 to 2, 5 to 3, and so on). Particulars 2, 4, 6, 8, and 10 are reverse-scored. Calculating the mean of the two factors comprising each scale (the traditional item and the recoded reverse-scored item). Participants estimate the particulars using a 7- 7-point scale, ranging from 1 (strongly disagree) to 7 (strongly agree). Urdu interpretation created by Fareeha Arshad, flaunting Cronbach's Alpha of 0.62 for English and 0.63 for Urdu. Depression is characterized by feelings of dejection, melancholy, and a lack of interest in daily activities. Measurement was conducted exercising the Patient Depression Questionnaire (PHQ-9). It was

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innovated on nine top symptoms of the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) depression disorder and their circumstance throughout the anteceding two weeks. Responses are estimated on a scale of 0 to 27, with scores assigned as follows 0 for not at all, 1 for some days, 2 for more than half the days, and 3 for nearly every day. Scores below 10 signify the absence of depression, but scores of 10 or over indicate the presence of depression. The data were analyzed exercising the Statistical Package for Social Sciences (SPSS 23.0). Descriptive statistics were conducted for socio-demographics, internet dependence, depression, and personality factors. Mean and standard deviation (SD) were calculated for all continuous data, while frequencies and percentages were determined for categorical variables. The correlation between internet dependence and personality traits, as well as the age of scholars, was examined using the Pearson Correlation Coefficient test to assess the strength and relationship between variables at a statistically significant position (p-value≤0.05). The T-test was employed to estimate the mean score of online dependence between groups with two categorical factors, whereas the ANOVA test was employed to compare the mean score of internet dependence among groups with more than two categorical variables. A multivariate regression analysis was performed to identify the elements that most significantly contribute to internet dependence among scholars.

RESULTS

The study participants' mean age was 21.72 + 1.631 years. More than half of the students were Sindhi (55.3%). 90.9% were unmarried and 90% of them were Muslims. The income of 68.9 % of respondents was >50000pkr (179.7 USD) which comes under the average salary range in Pakistan. Only 2.7% of the student's family income was <15000pkr(54 USD)(Table 1).

Table 1: Socio-Demographic Traits of the Study Participants (n=206)

Variable	Min-max	Mean ± SD
Age in Years	19-27	21.72 +1.631
Variable		**Frequency (%)**
Ethnicity	Punjabi	22 (11%)
	Sindhi	114 (55.3%)
	Muhajir	46 (22.4%)
	Others	24 (11.4%)
Marital Status	Married	19 (9%)
	Unmarried	187 (91%)
Year of Study	Academic Year 1	44 (21.5%)
	Academic Year 2	38 (18.3%)
	Academic Year 3	50 (24.2%)
	Academic Year 4	36 (17.8%)
	Final Academic Year	38 (18.3%)
Religion	Muslims	185 (90%)
	Non-Muslims	21 (10%)
Total Family Income	<Rs 15,000Pkr	6 (2.7%)
	Rs 15,000 - 30,000Pkr	13 (6.4%)
	Rs 30,000 - 50,000Pkr	45 (21.9%)
	>Rs 50,000Pkr	142 (68.9%)

IA was identified as mild in 68.3% of cases, moderate in 31.2%, and severe in 0.5%. The total internet addiction score varies from 3 to 83, with a mean of 40.76 + 16.49. The mean IA score was high in 2nd year MBBS students, 48.4% of the participants had depression which is nearer to the no depression found in 51.6% of the participants. The students with type 2 personality show the highest mean value and students with type 1 personality show the lowest mean value among all other personality traits (Table 2).

Table 2: Internet Addiction, Depression and Personality Traits (n=206)

Category	Min-max	Mean ± SD	Frequency (%)
Internet Addiction			
1st Year	6-74	40.77±17.307	--
2nd Year	6-83	46.80±15.008	
3rd Year	6-77	43.51±16.206	
Final Year	11-75	39.18±15.593	
Total IAT Score	3-83	40.76±16.495	
Mild Internet Addiction	-	-	141 (68.3%)
Moderate Internet Addiction	-	-	64 (31.2%)
Severe Internet Addiction	-	-	1 (0.5 %.)
Depression (PHQ-9)			
Yes	-	-	100 (48.4%)
No	-	-	106 (51.6%)
Ten Item Personality Measure (TIPI)			
Extraversion	1-7	3.65 +1.405	-
Agreeableness	2-7	4.97+1.281	
Conscientiousness	1-7	4.70+1.642	
Emotional Stability	1-7	4.19+1.432	
Openness	1-7	4.62+1.390	

0-20=no internet addiction, 21-49= mild internet addiction, 50-79=moderate internet addiction, 80-100= severe internet addiction. <10 is no depression, >=10 is depression. Personality type 1=Extraversion, Personality type 2=Agreeableness, Personality type 3=Conscientiousness, Personality type 4=Emotional Stability, Personality type 5=Openness

The results of the Pearson coefficient test indicated a strong negative association between IA and personality trait 3 (conscientiousness) and personality trait 4 (emotional stability). This means participants with higher conscientiousness and emotional stability showed less internet addiction. Whereas no relation was found between IA and the age of the students. Before applying the t-test and One-way ANOVA assumptions of normality and homogeneity of variances (tested by Levene's T-test and

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Levene's F-test) were fulfilled. High internet addiction was found in depressed students with a mean value of 48.12 ± 14.583 and a significant difference was seen between groups on applying a one-way ANOVA test. Post-HOC using least significant difference (LSD) statistics was utilized to explore the difference between groups (Table 3).

Table 3: Association of Internet Addiction with Personality Traits, Depression and Socio-Demographics (n=206)

Variable	Internet Addiction	Mean ± SD	T-value (df)	f-value (df)	p-value
Correlation Analysis					
Age	-0.086	-	-	-	-
Personality 1 (Extraversion)	-0.075	-	-	-	-
Personality 2 (Agreeableness)	-0.099	-	-	-	-
Personality 3 (Conscientiousness)	-0.166*	-	-	-	-0.086
Personality 4 (Emotional Stability)	-0.196**	-	-	-	-0.075
Personality 5 (Openness)	-0.075	-	-	-	-
T-Test Analysis					
Depression	-	48.12 ± 14.583	-7.085 (217)	-	0.000
Marital Status	-	41.25 ± 16.527	0.140 (217)	-	0.889
Religion	-	40.55 ± 16.527	-0.549 (217)	-	0.584
One-Way ANOVA Analysis					
Ethnicity	-	2.34 ± 0.822	-	0.888 (3)	0.448
Year of Study	-	46.80 ± 15.008	-	4.520 (4)	0.002
Total Family Income	-	3.57 ± 0.735	-	1.982 (3)	0.118

The multi-collinearity assumption was evaluated using the Tolerance statistic and Variance Inflation Factor (VIF) across all conducted regressions. All tolerance values were above 0.10, and the VIF did not surpass 10. The Durbin-Watson statistic was employed to evaluate independent errors. The Durbin-Watson coefficient in the present study was 1.7, falling within the range of 1.50 to 2.50. This signifies the absence of autocorrelation in the analysis of multiple linear regression data. In the multiple regression analysis, the results indicated that the predictors accounted for 25.1% of the variance (R^2=0.251, F (7, 211) =10.126, p<0.01). A positive correlation between internet addiction and depression was observed, alongside a negative correlation between internet addiction and both Conscientiousness and emotional stability, when considering explanatory power. Correlation coefficient (r=0.501; **p<0.01). Internet addiction has a negative association with personality trait 3 (conscientiousness) and personality trait 4 (emotional stability), whereas year 2 depression has a favourable correlation with internet addiction. Among these characteristics, depression (p=0.000) and year 2 (p=0.001) were substantially correlated with IA (Table 4).

Table 4: Multiple Regression Analysis for Variables Association to Internet Addiction (n=206)

Variables	B	SE b	β	p-value
Constant	40.833	5.035	-	0.000
Depression	11.341	2.117	0.344	0.000
Conscientiousness	-1.343	0.618	-0.134	0.031
Emotional Stability	-1.377	0.758	-0.120	0.071
Year 1	6.701	3.289	0.167	0.043
Year 2	10.686	3.307	0.251	0.001
Year 3	8.089	3.299	0.211	0.010
Year 4	6.607	3.299	0.154	0.046

R^2 =0.251 Adjusted R^2 =0.2227

DISCUSSION

Given the participants' age, the Internet has overtaken our routine life from learning to research, and information sharing to social networking, particularly for medical students [25]. This study focused exclusively on female medical students, as previous research has demonstrated that female students exhibit higher rates of internet addiction [26]. The mean age of the participants (21.72 ± 1.631 years) aligns with findings from similar research. Additionally, the majority of participants were Sindhi Muslims, reflecting the demographic composition of the university, which is located in the Sindh province of Pakistan and primarily enrolls students from the region. In this study, the overall mean IA score of the participants was 40.76 ± 16.495. In 2019, a descriptive cross-sectional study among 210 MBBS students at Poonch Medical College, Azad Kashmir, reported a high prevalence of internet addiction (52.4%) [11]. Similarly, another prevalent study at the Northwest School of Medicine in Peshawar, Pakistan, reported a total mean Internet Addiction score of 50.52 ± 18.8, with the mean score for female students being 45.37 ± 18.74 slightly higher than the findings in our study [27]. In contrast, a 2016 cross-sectional observational study in India, involving 140 medical students, reported a mean IA score of 33.94 ± 13.592, which is slightly lower than our results. This difference may be attributed to variations in cultural context and gender dynamics between the two countries [25]. Approximately 48.4% of the medical undergraduates experienced depression, a finding

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consistent with previous research [28, 29]. A cross-sectional study in the Faculty of Medicine, Ramathibodi Hospital in Thailand, reported a lower prevalence of depression at 28.8% among medical students [30]. In contrast, a 2018 study in medical colleges of the Kingdom of Saudi Arabia identified a higher prevalence of depression, with 55.9% of students affected, particularly among first-year students [31]. Depression is more prevalent among pre-clinical students, likely due to the increased academic pressure they face during the early stages of their education, where achieving a high grade point average is a primary concern. This contrasts with students in their final years, who may feel more confident in their knowledge. Furthermore, hostile students exhibited elevated levels of depression relative to their peers residing with family, potentially attributable to insufficient social support. We identified two negatively significant personality traits among medical students: conscientiousness and emotional stability. Numerous studies have highlighted the impact of higher levels of neuroticism and lower levels of conscientiousness, which supports our findings that neuroticism is a predominant personality trait in medical students. While there has been no research specifically examining personality traits among medical students in Pakistan, limited studies from other countries provide relevant insights. For instance, a 2014 cross-sectional study conducted in Malaysia found significant variability in personality traits among medical students, with higher levels of extroversion, conscientiousness, agreeableness, and openness, and lower levels of neuroticism [25]. These findings are similar to our study. The heightened stress and emotional burden experienced by medical students due in part to their distance from family and limited social interaction likely contribute to the prominence of neuroticism in this population. A study conducted at Bolan University of Medical and Health Sciences, Pakistan found higher levels of internet addiction among 2nd and 3rd-year MBBS students, which aligns with our study's findings [32]. Medical students experience greater psychological stress compared to students in other disciplines, and research has shown that unnecessary internet use, which disrupts normal life, also increases the risk of depression. In our study, we identified a significant positive association between IA and depression (48.4%). [11, 27]. Additionally, we observed a statistically significant negative association between IA and the personality traits of conscientiousness and emotional stability. To alleviate the detrimental consequences of excessive internet usage among medical students, awareness campaigns should be implemented in universities and colleges to promote early detection of warning signs and establish healthy internet use boundaries. Encouraging students to engage in alternative healthy activities can help reduce the impact of IA.

CONCLUSIONS

It was concluded that the study concluded and revealed a significant Internet addiction (IA) among medical students, highlighting an alarming future trend. A strong positive association between IA and depression suggests that depression may predispose medical students to IA, as they might use the internet to cope with their sadness. Additionally, the study identified a negative significant link between IA, conscientiousness, and emotional stability, suggesting that personality traits influence Internet addiction. Addictive behaviours are associated with personality characteristics such as high emotional reactivity, stress proneness, and impulsivity.

Authors Contribution

Conceptualization: FR, NA
Methodology: FR, MZ, NA
Formal analysis: FR
Writing review and editing: MZ

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Ismail N, Tajjudin AI, Jaafar H, Nik Jaafar NR, Baharudin A, Ibrahim N. The Relationship Between Internet Addiction, Internet Gaming and Anxiety among Medical Students in a Malaysian Public University During COVID-19 Pandemic. International Journal of Environmental Research and Public Health. 2021 Nov; 18(22): 11870. doi: 10.3390/ijerph182211870.

[2] Niemz K, Griffiths M, Banyard P. Prevalence of Pathological Internet Use among University Students and Correlations with Self-Esteem, The General Health Questionnaire (GHQ), and Disinhibition. Cyber-psychology and Behavior.2005 Dec; 8(6): 562-70. doi: 10.1089/cpb.2005.8.562.

[3] Saleem M, Owaisi AM, Tufail MW. Internet Addiction: Its Impact On Procrastination of Higher Learning Students in Pakistan. The Sindh University Journal of Education. 2015 Dec; 44(2).

[4] Soleymani MR, Garivani A, Zare-Farashbandi F. The Effect of Internet Addiction on the Information-Seeking Behavior of the Postgraduate Students. Materia socio-medica.2016 Jun; 28(3): 191. doi: 10.5455/msm.2016.28.191-195.

[5] Kassiani K, Evanthia P, Rafailia-Iro V, Aspridis G, Nikolaos B, Tselios D. A Study About Internet Addiction

DOI: https://doi.org/10.54393/pjhs.v5i12.2230

of University Students. Journal of Educational and Social Research.2018 Jan; 8. doi: 10.2478/jesr-2018-0003.

[6] Shao YJ, Zheng T, Wang YQ, Liu L, Chen Y, Yao YS. Internet Addiction Detection Rate among College Students in the People's Republic of China: A Meta-Analysis. Child and Adolescent Psychiatry and Mental Health.2018 Dec; 12: 1-0. doi: 10.1186/s13034-018-0231-6.

[7] McAdams DP. The Five-Factor Model in Personality: A Critical Appraisal. Journal of Personality.1992 Jun; 60(2): 329-61. doi: 10.1111/j.1467-6494.1992.tb00976.x.

[8] Carli V, Durkee T, Wasserman D, Hadlaczky G, Despalins R, Kramarz E *et al*. The Association Between Pathological Internet Use and Comorbid Psychopathology: A Systematic Review. Psychopathology.2012 Jul; 46(1): 1-3. doi: 10.1159/000337971.

[9] Ahmer Z and Tanzil S. Internet Addiction Among Social Networking Sites Users: Emerging Mental Health Concern Among Medical Undergraduates of Karachi. Pakistan Journal of Medical Sciences.2018 Nov; 34(6): 1473. doi: 10.12669/pjms.346.15809.

[10] Zaffar M, Mahmood S, Saleem M, Zakaria E. Facebook Addiction: Relation with Depression, Anxiety, Loneliness and Academic Performance of Pakistani Students. Science International(Lahore).2015; 27(3): 2469-75.

[11] Javaeed A, Bint Zafar M, Iqbal M, Ghauri SK. Correlation Between Internet Addiction, Depression, Anxiety and Stress Among Undergraduate Medical Students in Azad Kashmir. Pakistan Journal of Medical Sciences. 2019 Mar; 35(2): 506. doi: 10.12669/pjms.35.2.169.

[12] Cash H, D. Rae C, H. Steel A, Winkler A. Internet Addiction: A Brief Summary of Research and Practice. Current Psychiatry Reviews. 2012 Nov; 8(4): 292-8. doi: 10.2174/157340012803520513.

[13] J Kuss D, D Griffiths M, Karila L, Billieux J. Internet Addiction: A Systematic Review of Epidemiological Research for the Last Decade. Current Pharmaceutical Design.2014 Aug; 20(25): 4026-52. doi :10.2174/13816128113199990617.

[14] Shakya R and Sharma P. Problematic Internet Use–An Introduction and Current Status in Nepal. Journal of Psychiatrists' Association of Nepal.2015; 4(2): 4-9. doi: 10.3126/jpan.v4i2.18316.

[15] Asokan AG, Varghese VA, Rajeev A. Internet Addiction among Medical Students and Its Impact On Academic Performance: An Indian Study. Journal of Medical Sciences and Clinical Research.2019 Mar; 7(3): 670-. doi: 10.18535/jmscr/v7i3.122.

[16] Kayiş AR, Satici SA, Yilmaz MF, Şimşek D, Ceyhan E, Bakioğlu F. Big Five-Personality Trait and Internet Addiction: A Meta-Analytic Review. Computers in Human Behavior.2016 Oct; 63: 35-40. doi: 10.1016/j.chb.2016.05.012.

[17] Alfadhul SA. Ghazi hameed H, Mohammed SJ (2018). Internet Addiction Disorder among Medical Students in University of Kufa: A Cross-Sectional Study. Journal of General Practice. 2018; 6: 369.

[18] Azher M, Khan RB, Salim M, Bilal M, Hussain A, Haseeb M. The Relationship Between Internet Addiction And Anxiety Among Students of University of Sargodha. International Journal of Humanities and Social Science. 2014 Jan; 4(1): 288-93.

[19] Rabadi L, Ajlouni M, Masannat S, Bataineh S, Batarseh G, Yessin A *et al*. The Relationship Between Depression and Internet Addiction Among University Students in Jordan. Journal of Addiction Research Therapy.2017; 8(6): 1-8. doi: 10.4172/2155-6105.1000349.

[20] Günay O, Öztürk A, Arslantas E, Sevinc N. Internet Addiction and Depression Levels in Erciyes University Students. Dusunen Adam-Journal of Psychiatry and Neurological Sciences.2018; 31(1). doi: 10.5350/DAJPN2018310108.

[21] Othman Z, Lee CW, Kueh YC. Internet Addiction and Personality: Association with Impulsive Sensation Seeking and Neuroticism-Anxiety Traits. International Medical Journal. 2017 Oct; 24(5): 375-8.

[22] Hsiao KL, Shu Y, Huang TC. Exploring the Effect of Compulsive Social App Usage On Technostress and Academic Performance: Perspectives from Personality Traits. Telematics and Informatics.2017 May; 34(2): 679-90. doi: 10.1016/j.tele.2016.11.001.

[23] Shi M and Du TJ. Associations of Personality Traits with Internet Addiction in Chinese Medical Students: The Mediating Role of Attention-Deficit/Hyperactivity Disorder Symptoms. BioMed Central psychiatry.2019 Dec; 19: 1-8. doi: 10.1186/s12888-019-2173-9.

[24] Chang YH, Lee YT, Hsieh S. Internet Interpersonal Connection Mediates the Association Between Personality and Internet Addiction. International Journal of Environmental Research and Public Health. 2019 Oct; 16(19): 3537. doi: 10.3390/ijerph16193537.

[25] Saini VK, Baniya GC, Verma KK, Soni A, Kesharwani S. A Study On Relationship of Internet Addictive Behavior with Personality Traits among Medical Students. Journal of Mental Health and Human Behaviour.2016 Jul; 21(2): 108-11. doi: 10.4103/0971-8990.193429.

[26] Haroon MZ, Zeb Z, Javed Z, Awan Z, Aftab Z, Talat W. Internet Addiction in Medical Students. Journal of Ayub Medical College Abbottabad.2018 Oct; 30(4): S659-63.

[27] Ansar F, Ali W, Zareef A, Masud N, Zahab S, Iftekhar H. Internet Addiction and Its Relationship with Depression and Academic Performance: A Cross-

DOI: https://doi.org/10.54393/pjhs.v5i12.2230

Sectional Study at A Medical School in Pakistan. International Journal of Medical Students.2020 Dec; 8 (3): 251-6. doi: 10.5195/ijms.2020.740.

[28] Ali R, Mohammed N, Aly H. Internet Addiction Among Medical Students of Sohag University, Egypt. Journal of Egyptian Public Health Association. 2017 Jun; 92(2): 86-95. doi: 10.21608/EPX.2018.8946.

[29] Kumari U, Dawani N, Devnani J, Qureshi MF, Soleja FK, Mohammad D *et al*. Depression Among Medical Students of Karachi A Cross-Sectional Study. MedEdPublish.2019; 8. doi: 10.15694/ mep.2019.000 18 1.1.

[30] Boonvisudhi T and Kuladee S. Association between Internet addiction and depression in Thai medical students at Faculty of Medicine, Ramathibodi Hospital. PloS One.2017 Mar; 12(3): e0174209. doi: 10.13 71/journal.pone.0174209.

[31] Alharbi H, Almalki A, Alabdan F, Haddad B. Depression among Medical Students in Saudi Medical Colleges: A Cross-Sectional Study. Advances in Medical Education and Practice.2018 Dec: 887-91. doi: 10.2147/ AMEP.S182960.

[32] Khosa Z, Bazai MY, Khosa AZ, Sana H. Medical Students and Internet Addiction: A Study at Bolan University of Medical and Health Sciences Quetta, Pakistan. Journal of Advances in Medical and Pharmaceutical Sciences. 2020; 22(3): 31-40. doi: 10.9734/ jamps/ 2020/ v22 i33 0162.

DOI: https://doi.org/10.54393/pjhs.v5i12.1958

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Effectiveness and Clinical Outcomes of Long-Term Rifaximin in Cirrhotic Patients with Hepatic Encephalopathy

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ABSTRACT

Rifaximin has emerged as a new primary intervention for the treatment and management of hepatic encephalopathy in cirrhosis patients. **Objective:** To evaluate the efficacy of long-term rifaximin therapy and its clinical effects on hepatic encephalopathy in patients with liver cirrhosis. **Methods:** A retrospective cohort study was conducted in the Hepatology and Medicine Department of Bakhtawar Amin Hospital, Multan, from May 2022 to May 2024. A total of 100 liver cirrhosis patients were selected for the study by consecutive sampling. The patients were divided into two groups: the rifaximin group, including 50 patients who were administered rifaximin for 6 months at this hospital, and the control group, including 50 patients who were not administered rifaximin. The primary end point of our analysis was to assess the effectiveness of long-term rifaximin therapy. **Results:** The baseline serum ammonia was 105 (60-296) µg/dL in the rifaximin group, which decreased to 83 (33-152) µg/dL after 14 days and 83 (44-190) µg/dL after 60 weeks (p=0.001). Adverse effects of rifaximin were presented in one patient (2%) in the form of diarrhea only. The patients with stents smaller than 8 mm had pretreatment ammonia of 100 (60-182) µg/dL and 65 (42-145) µg/dL post-treatment (P=0.040). **Conclusions:** Rifaximin was an effective and safe treatment regimen for the long-term treatment of hepatic encephalopathy in patients with liver cirrhosis. It reduces the serum ammonia levels and prevents E. coli infections, increasing survival. Ineffective rifaximin treatment was associated with portosystemic shunt diameter ≥ 8.

INTRODUCTION

Liver cirrhosis is a frequent condition caused by permanent scarring and damage to the liver tissue leading to impaired liver function [1]. Since it is stage 3 of liver disease, it progresses to liver failure and increases the risk of mortality. Cirrhosis also presents as complications such as ascites, hepatic encephalopathy, variceal bleeding, and jaundice. Hepatic encephalopathy is a common complication in cirrhotic patients, occurring in 30-45% of patients [2]. He is the gradual or sudden onset of neurological and psychological dysfunction that can range from changes in behavior (stage I) and lethargy (stage III) to a comatose state (stage IV) [3]. Stage IV HE, also known as overt HE, indicates poor patient prognosis with a mortality rate of 65% in one year and 85% in a five-year analysis. Minimal HE can also affect prognosis and increase the risk of morbidity. The primary treatment of hepatic encephalopathy is antibiotic treatment with lactulose or rifaximin [4]. However, literature in the U.S. and Europe has recommended rifaximin over lactulose since, due to its long-term effects, it prevents the incidence and recurrence of overt hepatic encephalopathy and decreases the risk of morbidity [5, 6]. Studies have also reported an excellent efficacy of the combined use of lactulose and rifaximin in complete recovery, decreasing the risk of morbidity and mortality [7]. He is pathophysiological related to gut-derived toxins that accumulate and cause cerebral edema. As a result, liver function decreased, and portosystemic shunts developed,

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hindering the removal of toxins from blood. The incidence of overt HE after shunt development is 10-50% in a 1-year follow-up. Rifaximin has been proven to be superior to placebo or lactulose treatment for the prevention of overt HE after shunts [8, 9]. The 5-year survival outcomes are also significantly higher, up to 60% as compared to 10-13% in controls [10]. In Pakistan, the short-term use of rifaximin has shown positive results [11]. However, no study has yet been conducted to assess the long-term clinical use and impact of rifaximin and its association with spontaneous portosystemic shunts. In this study, it was reported that the results of its long-term administration and impact on shunts, incidence of infections, and prognosis of liver cirrhosis in comparison to a pair-matched control group.

It was conducted that this study used to evaluate the efficacy of long-term rifaximin therapy and its clinical effects on hepatic encephalopathy in patients with liver cirrhosis.

METHODS

A retrospective cohort study was conducted in the Hepatology and Medicine Department of Bakhtawar Amin Hospital, Multan, from May 2022 to May 2024. The population consists of 200 units, and a total of 100 liver cirrhosis patients were selected for the study by consecutive sampling. The sample size was calculated by keeping a 95% CI, 5% margin of error, and 50% population proportion (of patients presenting in the hepatology department) and 60% predictive effectiveness of rifaximin in Epi Info software. The test statistic *Z* for evaluating the population proportion requires a sufficiently large sample size; therefore, 50% of the population was used as a reference proportion. All patients provided their informed consent to become a part of the study. The ethical committee approved the study by Ref No. RL/C.12/BATH. The patients were divided into two groups: the rifaximin group, including 50 patients who were administered rifaximin for 6 months at our hospital, and the control group, including 50 patients who were not administered rifaximin. The primary end-point of the analysis was to assess the effectiveness of long-term rifaximin therapy, and the secondary end-points were the effect of shunts and Escherichia coli infection. The clinical outcomes between both groups were evaluated by measuring liver stiffness by magnetic resonance elastography using age, Child-Pugh score, incidence of hepatocellular carcinoma, and magnetic resonance elastography (MRE) as covariables. MRE was measured at the start of rifaximin therapy by using 3.0-T imagers. It was classified that shunts larger than 8 mm in the large group and shunts smaller than 8 mm in the small group to evaluate the effect of the size of the shunt. Shunts were assessed during hepatocellular carcinoma follow-up by contrast-enhanced CT images. In the case of more than one shunt, the diameter of the largest shunt was considered. All data were analyzed by SPSS version 24.0. Categorical variables were compared by Fisher's exact test and were presented in percentages. Continuous variables were presented as medians and were compared by the Mann-Whitney U test, and paired variables were compared by the Wilcoxon rank test. Overall survival between both groups was measured by comparing measures of MRE.

RESULTS

A total of 100 patients with liver disease were included for analysis among which 50 were administered rifaximin for 6 months. In rifaximin treated patients, 30% had a history of overt HE, 24% had hepatocellular carcinoma and 70% had esophageal varices. In 76% of patients, lactulose was administered in combination with lactulose, and in 64% of patients BCAA was administered in combination with rifaximin. The baseline characteristics of patients of both groups were shown in Table 1. The baseline Serum ammonia was 105 (60-296) µg/dL in the rifaximin group which decreased to 83 (33-152) µg/dL after 14 days and 83 (44-190) µg/dL after 60 weeks (p=0.001). Overt HE recurred in 2 patients during pleural drainage and self-interruption of the drug. Albumin, platelet count, total bilirubin, and prothrombin time did not change significantly after treatment. Adverse effects of rifaximin were presented in one patient (2%) in the form of diarrhea only.

Table 1: Patients' Baseline Variables Compared Between Study Groups (n=100)

Variables	Rifaximin Group Frequency (%)	Control Group Frequency (%)	p-value
Median Age	70 (39-85)	70.5 (41-89)	0.929
Gender	-	-	0.240
Male	23 (46%)	15 (30%)	-
Female	27 (54%)	35 (70%)	
Median BMI	25.82 (19.70-34.91)	24.3 (16.6-29.8)	0.039
Etiology of Liver Cirrhosis	-	-	0.110
Viral hepatitis B	20 (40%)	10 (20%)	-
Viral hepatitis C	16 (32%)	25 (50%)	
Non-alcoholic Fatty Liver Disease	4 (8%)	15 (30%)	
Child-Pugh Classification	-	-	0.048
A	20 (40%)	27 (54%)	-
B	20 (40%)	21 (42%)	
C	10 (20%)	2 (4%)	
Albumin-Bilirubin Grade	-	-	< 0.001
1	2 (4%)	29 (58%)	-
2	35 (70%)	20 (40%)	
3	13 (26%)	1 (2%)	
MELD Score	7 (3-18)	10 (0-23)	0.211
ALT	25.3 (9-106)	32.4 (9-1489)	0.112

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AST	40.1 (21-135)	44 (16-1039)	0.432
Gamma-Glutamyl Transpeptidase	36.6 (12-560)	65 (15-505)	0.063
Serum Ammonia	105 (60-296)	53 (24-90)	<0.001
Albumin	3 (2.5-4.6)	4.01 (2.7-5.0)	<0.001
Total Bilirubin	1.70 (0.6-5.0)	1 (0.6-8.8)	0.001
Platelet Count	9.0 (5.1-28.3)	12.6 (2.7-31.4)	0.025
Prothrombin Activity	61 (39-135)	70 (15-110)	0.070
AFP	5.6 (1-3380)	7.19 (1.5-390.2)	0.069
DCP	38 (16-2180)	26 (10-11690)	0.378
Fibrosis 4 Index	6.58 (1.67-14.9)	5.11 (1.5-34.7)	0.120
MRE	6.05 (4-10.10)	5.92 (4.45-11.8)	0.750
SWE	5.6 (1-3380)	7.19 (1.5-390.2)	<0.001
History of Overt Hepatic Encephalopathy	15 (30%)	-	<0.001
Hepatocellular Carcinoma	12 (24%)	15 (30%)	0.439
Ascites	15 (30%)	13 (26%)	0.828
Esophageal Varices	35 (70%)	30 (60%)	0.474
Max Diameter of portosystemic Shunts	7.8 (2.0-17.4)	5.1 (1.9-11.1)	<0.001
Number of Shunts	-	-	0.001
0,1	11 (22%)	32 (64%)	-
2 or more	39 (78%)	18 (36%)	
Administration of Lactulose	38 (76%)	8 (16%)	<0.001
Branched-chain Amino Acid	32 (64%)	18 (36%)	0.040
Sarcopenia	23 (46%)	23 (46%)	1
Follow-up	62 (23-90)	90 (6-119)	<0.001

*AFP: Alpha-Feto Protein, MRE: Magnetic Resonance Elastography, DCP: Des-Gamma Carboxyprothrombin, SWE: Shear Wave Elastography, ALT: Alanine Aminotransferase.

A total of 23 patients (46%) had shunts larger than 8mm with pretreatment ammonia of 110 (92-295) µg/dL and 83 (52-148) µg/dL after 6 months (p=0.001). The patients with stunts smaller than 8 mm had pretreatment ammonia of 100 (60-182) µg/dL and 65 (42-145) µg/dL post-treatment (P=0.040). 39 patients (78%) patients had two or more shunts with pretreatment ammonia of 102 (70-295) µg/dL and 81.2 (42-149) after treatment (p<0.001). A less improvement in ammonia levels after treatment was related to shunt diameter and ALBI score. However multivariable analysis showed that insufficient improvement in ammonia was independently related to shunt length equal to or longer than 8 mm (Table 2).

Table 2: Risk Factors of Insufficient Improvement in Serum Ammonia after Treatment

Variables	Hazards Ratio (95% CI)	p-value
Univariable Analysis		
≥ 70 Years Old	1.9 (0.61-8.9)	0.28
Male Gender	0.489 (0.130-1.91)	0.32
BMI ≥ 28	0.38 (0.090-1.88)	0.27
AST ≥ 36	0.367 (0.090-1.53)	0.15
ALT ≥ 30	0.36 (0.08-1.9)	0.20
GGTP ≥ 42	0.66 (0.22-2.94)	0.62
Albumin < 3.0	3.6 (0.77-14)	0.089
Total Bilirubin ≥ 1.4	4 (0.78-13)	0.09
Platelet Count < 6.8	3.9 (0.73-24)	0.10
Prothrombin ≥ 58	2.7 (0.68-12)	0.10
AFP ≥ 6.5	3.11 (0.61-18)	0.18
DCP ≥ 18	3.8 (0.62-22)	0.14
Presence of Ascites	2.3 (0.68-9.0)	0.15
Presence of Esophageal Varices	2.0 (0.46-7.8)	0.39
History of HE	3.8 (0.81-15)	0.08
Presence of HCC	0.77 (0.20-3.5)	0.67
Presence of Sarcopenia	1.60 (0.35-6.4)	0.51
Child-Pugh Score ≥ 7	4.1 (0.96-15)	0.058
ALBI ≥ -1.6	5.5 (1-24)	0.029
MELD ≥ 12	2.8 (0.69-12)	0.09
Fibrosis 4 Index ≥ 8.3	0.38 (0.097-2.1)	0.28
MRE ≥ 5.0	1.60 (0.36-8.5)	0.40
SWE ≥ 17.7	2.7 (0.68-13)	0.18
Diameter of Shunt ≥ 8	7.2 (1.6-32)	0.020
2 or More Shunts	1.40 (0.35-6.0)	0.71
Multi-Variable Analysis		
Diameter of shunt ≥ 8	5.8 (1.0-27)	0.040
ALBI ≥ -1.6	3.0 (0.56-17)	0.18

The mean follow-up was 62 weeks in rifaximin group and 90 weeks in controls. Six patients (12%) died in the rifaximin group by liver failure or pleurodesis. Patients with Child-Pugh C had the shortest survival span (Figure 1).

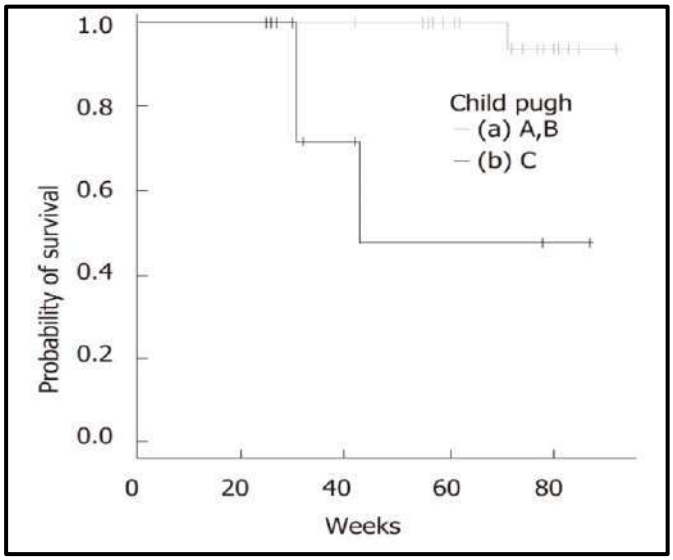

Figure 1: Comparison of Survival between Child Pugh A and B Patients and Child Pugh C

Seven patients (14%) died in the control group due to hepatic insufficiency, cardiovascular disease, or disseminated intravascular coagulation The difference in survival rate between both groups was insignificant (p=0.890)(Figure 2).

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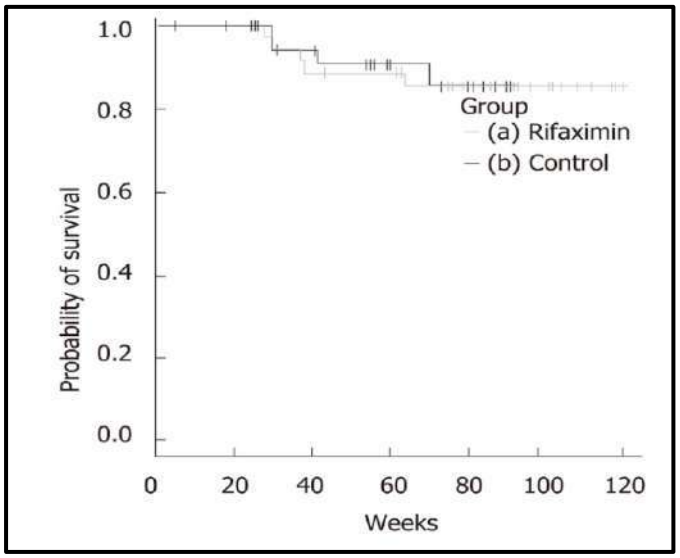

Figure 2: Comparison of Survival Outcomes between Study Groups

DISCUSSION

Hepatic encephalopathy was a common complication occurring in up to 45% of cirrhotic patients. Rifaximin has emerged as a new primary treatment for the treatment and management of HE. We conducted this study to test the 6-month efficacy and clinical effects of rifaximin in cirrhosis patients and its association with shunts and E. coli infection. The results revealed that a decline in ammonia levels occurred 14 days after treatment and remained significantly lower up to 6 months. The recurrence was only reported in 2 patients (4%), and diarrhea as an adverse effect was seen in 1 patient only. These results suggest that rifaximin was an effective and safe regimen for long-term treatment of HE. The efficacy and safety of rifaximin were also reported by previous studies conducted in Europe and the Americas [12-14]. The HE recurrence in our study occurred due to pleural drainage, which may be due to dehydration, infections, or intestinal hemorrhage. He was assessed by the West Haven criteria and the Trail Making test; however, the latter was not performed in our study. The shunts larger than 8 mm were 50% in the rifaximin group and 12% in controls, which indicated a strong correlation between hepatic encephalopathy and the development of shunts. Other studies also concluded that portosystemic shunts were significantly associated with ammonia levels [15, 16]. This finding was also reported in the present study. No studies have been previously conducted to evaluate the relationship between shunts and rifaximin treatment. However, the findings of our study showed that rifaximin can help reduce ammonia levels for up to 6 months and improve encephalopathy, especially in patients who developed large shunts (≥ 8 mm). Ammonia levels did not decline in some patients, which was independently related to large shunt diameter. This finding suggests that overt HE was improved by rifaximin therapy, but this treatment may not be effective for minimal HE patients with large shunts, and the shunt diameter was associated with ammonia levels. Previous literature also backs this finding [17-19]. Surgery or interventional radiology was recommended for whom rifaximin was not effective. It has been reported previously that cirrhosis alters the function of the gut microbiome, which increases the risk of mortality [20, 21]. In our study, one patient died due to an intestinal bacterial infection, although no patients had spontaneous bacterial peritonitis. This indicates that rifaximin prevents Escherichia coli infections. Both groups also did not differ significantly with respect to survival rates, but the shortest survival was observed in cohort patients with Child C, suggesting that rifaximin has limited efficacy in treating cirrhosis itself. Our study has some limitations. We did not diagnose minimal HE, so the effectiveness of rifaximin for it could not be found. Secondly, there was no protocol for starting treatment other than the instinct of the physicians. Thirdly, we did not assess the incidence of HCC, cardiovascular disease, infection, and malnutrition as causes of mortality in patients.

CONCLUSIONS

Rifaximin was an effective and safe treatment regimen for the long-term treatment of hepatic encephalopathy in patients with liver cirrhosis. It reduces the serum ammonia levels and prevents *Escherichia coli* infections, increasing survival. Ineffective rifaximin treatment was associated with portosystemic shunt diameter ≥ 8.

Authors Contribution

Conceptualization: NU
Methodology: AR, RK
Formal analysis: HA
Writing, review and editing: SM, NU, HNS

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Ginès P, Krag A, Abraldes JG, Solà E, Fabrellas N, Kamath PS. Liver cirrhosis. The Lancet.2021 Oct; 398(10308):1359-76. doi:10.1016/S0140-6736(21)01374-X.

DOI: https://doi.org/10.54393/pjhs.v5i12.1958

[2] Butterworth RF. Hepatic encephalopathy in cirrhosis: pathology and pathophysiology.Drugs.2019 Feb;79(1): 17-21.doi: 10.1007/s40265-018-1017-0.

[3] Montagnese S and Bajaj JS. Impact of hepatic encephalopathy in cirrhosis on quality-of-life issues. Drugs.2019Feb;79:11-6.doi:10.1007/s40265-018-1019y.

[4] Moran S, López-Sánchez M, del Pilar Milke-García M, Rodríguez-Leal G. Current approach to treatment of minimal hepatic encephalopathy in patients with liver cirrhosis. World Journal of Gastroenterology.2021 Jun; 27(22): 3050. doi: 10.3748/wjg.v27.i22.3050.

[5] Hudson M and Schuchmann M. Long-term management of hepatic encephalopathy with lactulose and/or rifaximin: a review of the evidence. European Journal of Gastroenterology & Hepatology. 2019Apr;31(4):434-50.doi:10.1097/MEG.0000000000001311.

[6] Moon AM, Kim HP, Jiang Y, Lupu G, Bissram JS, Barritt IV AS *et al.* Systematic review and meta-analysis on the effects of lactulose and rifaximin on patient-reported outcomes in hepatic encephalopathy. Official Journal of the American College of Gastroenterology. 2023 Feb;118(2):284-93.doi:10.14309/ajg.0000000000002008.

[7] Fu J, Gao Y, Shi L. Combination therapy with rifaximin and lactulose in hepatic encephalopathy: A systematic review and meta-analysis. PLOS One. 2022 Apr;17(4):e0267647.doi:10.1371/journal.pone.0267647.

[8] Razzack AA, Hussain N, Hassan SA, Gulzar R, Karam A, Panday P *et al.* Rifaximin for prophylaxis of post-TIPPS hepatic encephalopathy-a meta-analysis.InJournal of Hepatology 2021 Jul; 75: S383-S383.

[9] Gairing SJ, Müller L, Kloeckner R, Galle PR, Labenz C. post-TIPSS hepatic encephalopathy-current knowledge and future perspectives. Alimentary Pharmacology & Therapeutics. 2022 May; 55(10): 1265-76. doi: 10.1111/apt.16825.

[10] Wang LJ, Yao X, Qi Q, Qin JP. Prevention and treatment of hepatic encephalopathy during the perioperative period of transjugular intrahepatic portosystemic shunt. World Journal of Gastrointestinal Surgery. 2023 Aug; 15(8): 1564. doi: 10.4240/wjgs.v15.i8.1564.

[11] Saleem MZ, Saleem MH, Saleem H, Aasil MA. Rifaximin Effectiveness in Preventing the Recurrence Of Hepatic Encephalopathy Among Patients With Liver Cirrhosis. Pakistan Armed Forces Medical Journal. 2021Aug;71(4):1296-99.doi:10.51253/pafmj.v71i4.2481.

[12] Bureau C, Thabut D, Jezequel C, Archambeaud I, D'alteroche L, Dharancy S *et al.* The use of rifaximin in the prevention of overt hepatic encephalopathy after transjugular intrahepatic portosystemic shunt: a randomized controlled trial. Annals of Internal Medicine. 2021 May; 174(5): 633-40. doi: 10.7326/M20-0202.

[13] Suzuki H, Sezaki H, Suzuki F, Kasuya K, Sano T, Fujiyama S *et al.* Real-world effects of long-term rifaximin treatment for Japanese patients with hepatic encephalopathy. Hepatology Research. 2019 Dec; 49(12): 1406-13. doi: 10.1111/hepr.13415.

[14] Han X, Luo Z, Wang W, Zheng P, Li T, Mei Z *et al.* Efficacy and safety of rifaximin versus placebo or other active drugs in critical ill patients with hepatic encephalopathy. Frontiers in Pharmacology.2021 Oct; 12: 696065. doi: 10.3389/fphar.2021.696065.

[15] Sarwar S, Muhyuddin B, Aleem A, Nadeem MA. Primary prophylaxis of hepatic encephalopathy in decompensated cirrhosis: low dose vs. full dose rifaximin. Pakistan Journal of Medical Sciences. 2019 Sep; 35(5): 1446. doi: 10.12669/pjms.35.5.549.

[16] Kawaratani H, Kondo Y, Tatsumi R, Kawabe N, Tanabe N, Sakamaki A *et al.* Long-term efficacy and safety of rifaximin in Japanese patients with hepatic encephalopathy: A multicenter retrospective study. Journal of Clinical Medicine.2022 Mar; 11(6): 1571. doi: 10.3390/jcm11061571.

[17] Zacharias HD, Kamel F, Tan J, Kimer N, Gluud LL, Morgan MY. Rifaximin for prevention and treatment of hepatic encephalopathy in people with cirrhosis. Cochrane Database of Systematic Reviews.2023 Jul; 7(7): CD011585. doi: 10.1002/14651858.CD011585.pub2.

[18] Torre A, Córdova-Gallardo J, Frati Munari AC. Rifaximin alfa and liver diseases: more than a treatment for encephalopathy, a disease modifier. Therapeutics and Clinical Risk Management.2023 Dec: 839-51.doi:10.2147/TCRM.S425292.

[19] Hiramine Y, Uto H, Mawatari S, Kanmura S, Imamura Y, Hiwaki T *et al.* Efficacy of rifaximin, a poorly absorbed rifamycin antimicrobial agent, for hepatic encephalopathy in Japanese patients. Hepatology Research. 2021 Apr; 51(4): 445-60. doi: 10.1111/hepr.13622.

[20] Yu X, Jin Y, Zhou W, Xiao T, Wu Z, Su J *et al.* Rifaximin modulates the gut microbiota to prevent hepatic encephalopathy in liver cirrhosis without impacting the resistome. Frontiers in Cellular and Infection Microbiology. 2022 Jan; 11: 761192. doi: 10.3389 /fcimb.2021.761192.

[21] Zheng R, Wang G, Pang Z, Ran N, Gu Y, Guan X *et al.* Liver cirrhosis contributes to the disorder of gut microbiota in patients with hepatocellular carcinoma. Cancer Medicine. 2020 Jun; 9(12): 4232-50. doi: 10.1002 /cam4.3045.

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Original Article

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Visual Outcomes and Postoperative Complications of ACIOL vs. SFIOL: A Prospective Comparative Study

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ABSTRACT

Anterior chamber intraocular lens and scleral fixated intraocular lens are key options for patients without capsular support, necessitating a comparison of their visual outcomes and complications. **Objectives:** To analyze and contrast the postoperative visual results and complications amongst patients who underwent cataract surgery or secondary lens implantation and received either an anterior chamber intraocular lens or a scleral fixated intraocular lens. **Methods:** The total number of participants was n=120: Group I involved 60 eyes that received an anterior chamber intraocular lens while Group II involved 60 eyes that were given a scleral fixated intraocular lens. The primary outcomes measured were best-corrected visual acuity before the procedure and then at 1-, 3-, and 6-months post-op, whereas secondary outcomes included complications such as inflammation, elevated intraocular pressure, dislocation of the artificial intraocular lens, as well as other postoperative adverse events. SPSS 23 was used. **Results:** At the 6-month mark, both groups demonstrated significant improvement in best-corrected visual acuity compared to pre-op levels, with no noteworthy difference in final visual acuity between those who received an anterior chamber intraocular lens versus a scleral fixated intraocular lens. The mean best-corrected visual acuity for Group I was 6/9 whereas Group II presented with a mean best-corrected visual acuity of 6/12 ($p>0.05$). No significant discrepancies in complication rates were observed between the two procedures. **Conclusions:** It was concluded that anterior chamber intraocular lens implantation and scleral fixated intraocular lens implantation can yield positive visual outcomes for patients undergoing cataract surgery or secondary lens implantation.

INTRODUCTION

One of the most commonly performed ophthalmic procedures worldwide is cataract surgery in which patients who have lens opacities or lens disorders can attain clear vision again. For many patients, with complicated cases, this will require replacing the natural lens with an artificial intraocular lens (IOL) to restore the clarity of vision [1,]. Specifically, common solutions for aphakia, subluxated lenses, as well as complexities due to intraoperative and post-operative cataract challenges include the use of anterior chamber intraocular lenses (ACIOLs) and porous and suture-less scleral fixated intraocular lenses (SFIOLs) [2]. ACIOLs (anterior chamber intraocular lenses) are placed in the anterior chamber of the eye and are commonly preferred when there is no supporting area for these lenses in the posterior capsule [3]. They are used in primary and secondary implants, especially in posterior capsular rupture and insufficient capsular support. However, associated complications have been reported, including loss of corneal endothelial cells, raised intraocular pressure, and greater risk of ocular inflammation [4]. SFIOLs are inserted when both anterior segment and posterior segment support are lacking. These lenses are anchored to the sclera with sutures for a durable, long-lasting placement. Although good anatomical positioning and lower risks of anterior segment complications are advantages of SFIOLs, they still need

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advanced surgical skills which carry risks like suture-related problems, scleral thinning, scleral perforation, and retinal detachment [5, 6]. The two types of IOLs each have their advantages and disadvantages, and we must compare both the visual results and any subsequent complications in surgery that each monitor might create so that the two can be clinically compared with one another for the more challenging types of cataracts [7, 8]. The effectiveness of ACIOL and SFIOL by determining best-corrected visual acuity (BCVA) improvement and incidence of complications [lens dislocation, inflammation in anterior segment and intraocular pressure (IOP) changes] [9].

This study aims to analyze and contrast the postoperative visual results and complications amongst patients who underwent cataract surgery or secondary lens implantation and received either an Anterior Chamber Intraocular Lens (ACIOL) or a Scleral Fixated Intraocular Lens(SFIOL).

METHODS

This retrospective cohort study was conducted from April 2022 to September 2022 at the Department of Ophthalmology at Arif Memorial Teaching Hospital/Rashid Latif Medical College, Lahore. Inclusion criteria: included adults aged 41 to 74 who had inadequate posterior capsule backing requiring an alternative lens placement following extraction. Exclusion criteria: comprised of active ocular disease, uncontrolled glaucoma, or systemic conditions that may interfere with surgery or recovery. The formula for sample size calculation was $n=2(Z\alpha/2+Z\beta)2\cdot\sigma2/\Delta2$. The required sample size was approximately 120 participants to estimate the power 80%, confidence level 95%, standard deviation (σ\sigma) 0.3 and clinically significant difference (Δ\Delta) 0.2 [10]. Patient data were gathered from medical records, covering demographic information, preoperative and postoperative visual acuity (VA), refractive error, and complication rates. A thorough eye exam was conducted before and after surgery, with patients monitored for at least six months. For ACIOL implantation, the lens was positioned in the anterior chamber, either in the angle or using a secured system, with the choice of a single-piece or multi-component design left to the surgeon's preference. In SFIOL implantation, the lens was affixed to the sclera employing 10-0 nylon or polypropylene sutures, with or without the utilization of a glued arrangement. The surgeries addressed conditions such as aphakia, subluxated lenses, and posterior capsular tears. Patients with exclusions like glaucoma, iritis, amblyopia, and poor vision unrelated to cataracts were omitted. The sampling technique employed in this study was consecutive sampling, where all eligible patients presenting during the study period who met the inclusion criteria were enrolled. Preoperative and postoperative best-corrected visual acuity (BCVA) were documented. Follow-ups at one, three, and six months recorded BCVA and any complications included ACIOL group, complications included corneal decompensation, glaucoma, and cystoid macular oedema. In the SFIOL group, retinal detachment, suture-related issues, and hypotony were observed. The data were analyzed using SPSS version 23.0 to gain insights. Visual outcomes and intraocular pressure were recorded before surgery and at various intervals afterwards for patients receiving either ACIOL or SFIOL implants. Paired t-tests internally compared each group's results over time. Independent t-tests distinguished the groups' performances at each checkpoint. Postoperative complications were also tracked using Chi-square tests to categorize outcomes. Informed consent was obtained from all participants, and approval from the Institutional Review Board (IRB) was secured for the study. This study was approved by the institutional review board (IRB/2023/205) of Rashid Latif Medical College, Lahore.

RESULTS

The preoperative characteristics of the ACIOL and SFIOL groups were comparable, with no significant differences in age, gender, or indications for implantation. Both groups had a mean age of 65 years, and a balanced gender distribution (50% male and 50% female). Statistical analysis revealed no significant differences between the two groups in terms of these factors, indicating that the groups were similar at baseline (Table 1).

Table 1: : Preoperative Characteristics of the Study Population

Preoperative Characteristics	ACIOL Group (n=60)	SFIOL Group (n=60)	Total (n=120)	Statistical Analysis
Mean Age (Years)	65 ± 10	65 ± 12	65 ± 11	>0.005
Gender Distribution				
Male (%)	30 (50%)	30 (50%)	60 (50%)	Chi-square =0.0, p=1.0
Female (%)	30 (50%)	30 (50%)	60 (50%)	

In both arms, ACIOL and SFIOL caused significant enhancement in best-corrected visual acuity (BCVA) at all time intervals. The preoperative baseline visual acuity was 6/60 in most patients in both groups. At 1-month postoperatively both groups showed early gains with more patients achieving 6/6-6/9 vision. At 3 months, there was an additional rise in the proportion of patients in the 6/6-6/9 category for both groups and by 6 months, the vast majority of patients from both groups had achieved 6/6-6/9 vision, while only a small subset of patients from either group remained in the 6/60 and worse category. Both types of IOLs provided clinically significant visual benefits ($p<0.001$)(Table 2).

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Table 2: Distribution of BCVA Categories Preoperative and Postoperative at 1 Month, 3 Months, and 6 Months

BCVA Category	Preoperative (ACIOL Group, n=60)	1 Month Postoperative (ACIOL Group, n=60)	3 Months Postoperative (ACIOL Group, n=60)	6 Months Postoperative (ACIOL Group, n=60)	Preoperative (SFIOL Group, n=60)	1 Month Postoperative (SFIOL Group, n=60)	3 Months Postoperative (SFIOL Group, n=60)	6 Months Postoperative (SFIOL Group, n=60)	Chi-Square Test	p-value
6/6 - 6/9	5 (8.3%)	15 (25%)	30 (50%)	45 (75%)	4 (6.7%)	12 (20%)	32 (53.3%)	43 (71.7%)	62.5	p<0.001
6/12 - 6/18	15 (25%)	25 (41.7%)	20 (33.3%)	10 (16.7%)	10 (16.7%)	20 (33.3%)	18 (30%)	12 (20%)	15.2	p<0.001
6/60 and worse	40 (66.7%)	20 (33.3%)	10 (16.7%)	5 (8.3%)	46 (76.7%)	28 (46.7%)	10 (16.7%)	5 (8.3%)	122.8	p<0.001

There were no statistically significant differences in the analysis of postoperative complications between ACIOL and SFIOL groups. Complication rates, such as postoperative inflammation, endothelial cell loss, glaucoma, hyphemia, IOL displacement, and vitreous hemorrhage were similar between both groups. In particular, although the rate of postoperative inflammation was 8.3% for the ACIOL group and 13.3% for the SFIOL group, the difference was not significant (p=0.092). Other adverse events including loss of endothelial cells, glaucoma, hyphema, and IOL dislocation occurred at a similar frequency between the two groups (p>0.05, symbolically indicating that there was not a significant difference). Vitreous hemorrhage was uncommon with only one case occurring in the SFIOL group (statistically insignificant, p=0.420). Conclusions POSTCOMP, the study suggests that ACIOL and SFIOL implants are equally safe about postoperative complications (Table 3).

Table 3: Postoperative Complications in ACIOL and SFIOL Groups

Complication	ACIOL Group (n=60)	SFIOL Group (n=60)	Chi-Square Test	p-value
Postoperative Inflammation	5 (8.3%)	8 (13.3%)	2.85	p=0.092
Endothelial Cell Loss	10 (16.7%)	12 (20%)	0.45	p=0.503
Glaucoma	3 (5%)	4 (6.7%)	0.18	p=0.670
Hyphema	2 (3.3%)	3 (5%)	0.13	p=0.711
IOL Displacement	1 (1.7%)	2 (3.3%)	0.28	p=0.595
Vitreous Hemorrhage	0 (0%)	1 (1.7%)	0.65	p=0.420

When comparing the IOP between the ACIOL and SFIOL groups, no significant differences were observed at the preop level or 1, 3, and 6 months postoperatively. Table II shows that both groups had similar IOP throughout the study, with p values being larger than 0.05 at all-time points, which indicates that IOP was not significantly different between the two groups. That means ACIOL and SFIOL have a more or less similar effect on IOP after a period (Table 4).

Table 4: Comparison of Intraocular Pressure (IOP) Preoperative and Postoperative (1 Month, 3 Months, and 6 Months) in ACIOL and SFIOL Groups

Time Point	ACIOL Group (n=60)	SFIOL Group (n=60)	Chi-Square Test	p-value
Preoperative IOP (mmHg)	14.5 ± 2.3	14.2 ± 2.1	0.46	p=0.647
1 Month Postoperative IOP	15.2 ± 2.6	15.8 ± 2.4	1.23	p=0.219
3 Months Postoperative IOP	16.1 ± 2.7	16.4 ± 2.5	0.43	p=0.669
6 Months Postoperative IOP	16.3 ± 2.5	16.7 ± 2.6	0.53	p=0.597

DISCUSSION

It was done to compare the visual outcome and complications of implantation of the Anterior Chamber Intraocular Lens (ACIOL) and Scleral Fixated Intraocular Lens (SFIOL). Significantly improved best corrected visual acuity (BCVA) for both groups was evident during a follow-up of 6 months with no statistically significant differences between the groups. Both ACIOL and SFIOL implants were equally safe in regards to postoperative complications and intraocular pressure (IOP) stable over time in both groups [11, 12]. Also, there is a great improvement in the visual equity of both ACIOL and SFIOL groups in our study and in a time comparison at the 6th month postoperatively; 71% of the patients of the ACIOL group and 67% of the SFIOL group could see 6/6-6/9 vision. This result is in concordance with the previous studies. This is consistent with other studies, which also found significant visual improvement post-ACIOL and SFIOL implantation [13]. On the contrary, there are several studies noted the superiority of incomplete exposure of SFIOLs in providing comparable initial BCVA due to reduced problems with decentration and glare or corneal endothelial cell loss resulting from SFIOLs by stable slit-lamp patterns over time, which our study did not demonstrate [14]. The current study aligned with previous studies that ACIOLs have more immediate visual improvement after surgery, however, they can have higher rates of post-operative complications such as corneal endothelial cell loss and post-operative IOP spikes although these have not been statistically significant in our results [15]. The lack of clinically relevant differences in visual function between the two lens types suggests that lens selection may be better guided by the relevant clinical situation, and any anatomical considerations, than expected differences in visual outcomes [16, 17]. As for complications, there was no difference in postoperative inflammation, endothelial cell loss, glaucoma, hyphema, IOL dislocation, and vitreous hemorrhage between ACIOL and SFIOL. Complications seen were consistent with other studies. For instance, this group found a higher risk of endothelial cell loss for ACIOLs compared to other IOLs given the closeness of ACIOLs to the cornea [19]. Patients

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with ACIOLs were also found to have a higher risk of glaucoma, especially in those with pre-existing ocular conditions. Nevertheless, we found no significant difference in the incidence of these complications, possibly due to the selective patient population and the management protocols [20]. Liang et al., the relatively better stability of the IOLs in the long term due to SFIOLs, although they may be complicated by scleral perforation or IOL dislocation as a consequence of insufficiently secured scleral fixation. We found only 1 IOL dislocation in the ACIOL group and 2 in the SFIOL group, and this difference was not statistically significant. These conclusions are consistent with earlier research showing that SFIOLs are safer about corneal complications, while, on the other hand, SFIOLs may cause surgical technique issues and posterior segment complications [21]. Concerning glaucoma, the current study found low incidences of this complication in both groups as reported previously by Kim et al (who introduced a new pragmatic 6-standardised classification of glaucomas in ACIOL eyes. In the previous study, Megevand et al., found that ACIOLs (anterior chamber intraocular lenses) cause a shunt to an elevated IOP more frequently than posterior chamber IOLs because they occupy a space in the anterior chamber. In our study, however, IOP remained stable at all postoperative time points in both groups, suggesting that neither lens type may carry a risk advantage over another with modern surgical techniques [22]. We did not observe any significant difference in IOP between groups as the IOP was similar in both groups both preoperatively and on 1, 3 and 6 months post-operatively. The findings of this study corroborate the report by McGhee et al., that an earlier rise in the IOP post-operatively was linked with ACIOL as anterior chamber angle gets involved causing a possible angle-closure glaucoma [23]. Nevertheless, the fact that IOP remained stable in both groups, and the lenses could be implanted without the occurrence of complications, could indicate that the risk related to both lenses might have been offset by other improvements in surgical techniques, optimal placement of insertion of the lens and postoperative management. In addition, Pinto et al also reported similar results with our findings. Hecht et al., demonstrated insignificant differences in IOP between ACIOL and SFIOL groups after 6 months [24].

CONCLUSIONS

It was concluded that both lens types led to a notable upgrade in visual sharpness, without substantial differences between the groups. Both implants likewise exhibited comparable complication profiles, and internal eyeball pressure stayed balanced over the long run in both assemblages.

Authors Contribution

Conceptualization: FM
Methodology: FM, SMA
Formal analysis: NF
Writing review and editing: MAA

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Pershing S, Lum F, Hsu S, Kelly S, Chiang MF, Rich III WL *et al.* Endo-Phthalmitis After Cataract Surgery in the United States: A Report from the Intelligent Research in Sight Registry, 2013–2017. Ophthalmology.2020 Feb; 127(2): 151-8. doi: 10.1016/j.ophtha.2019.08.026.

[2] Narayan A, Evans JR, O'Brart D, Bunce C, Gore DM, Day AC. Laser-Assisted Cataract Surgery Versus Standard Ultrasound Phacoemulsification Cataract Surgery. Cochrane Database of Systematic Reviews. 2023 Jun. doi: 10.1002/14651858.CD010735.pub3.

[3] Naderi K, Gormley J, O'Brart D. Cataract Surgery and Dry Eye Disease: A Review. European Journal of Ophthalmology.2020 Sep; 30(5): 840-55. doi: 10.1177/1120672120929958.

[4] Hashemi H, Pakzad R, Yekta A, Aghamirsalim M, Pakbin M, Ramin S *et al.* Global and Regional Prevalence of Age-Related Cataract: A Comprehensive Systematic Review and Meta-Analysis. Eye.2020 Aug; 34(8): 1357-70. doi: 10.1038/s41433-020-0806-3.

[5] Miura M, Inomata T, Nakamura M, Sung J, Nagino K, Midorikawa-Inomata A *et al.* Prevalence and Characteristics of Dry Eye Disease After Cataract Surgery: A Systematic Review and Meta-analysis. Ophthalmology and Therapy. 2022 Aug; 11(4): 1309-32. doi: 10.1007/s40123-022-00513-y.

[6] Shimabukuro M, Maeda N, Koh S, Abe K, Kobayashi R, Nishida K. Effects of Cataract Surgery On Symptoms and Findings of Dry Eye in Subjects with and Without Preexisting Dry Eye. Japanese Journal of Ophthalmology.2020Jul;64:429-36.doi:10.1007/s10384-020-00744-1.

[7] Villani E, Catania AG, Luccarelli SV, Magnani F, Martone G, Zanzottera E *et al.* Dry Eye and Cataract Surgery: Narrative Review and Recommendations for Management. European Journal of Ophthalmology. 2023 May: 11206721231174060. doi: 10.1177/11206721231174060.

DOI: https://doi.org/10.54393/pjhs.v5i12.2712

[8] Auffarth GU, Gerl M, Tsai L, Janakiraman DP, Jackson B, Alarcon A *et al.* Clinical Evaluation of a New Monofocal IOL with Enhanced Intermediate Function in Patients with Cataracts. Journal of Cataract and Refractive Surgery.2021 Feb; 47(2): 184-91. doi: 10.1097/j.jcrs.0000000000000399.

[9] Ang MJ and Afshari NA. Cataract and Systemic Disease: A Review. Clinical and Experimental Ophthalmology.2021Mar;49(2):118-27.doi:10.1111/ceo.13892.

[10] Zhang W. Samp Size Cal the Platform-Independent Computational Tool for Sample Sizes in the Paradigm of New Statistics. Network Biology. 2024 Jun; 14(2): 100.

[11] Mahapatra SK and Mannem N. Anterior Chamber Intraocular Lens-An Effective Alternative in Traumatic and Surgical Aphakia in the Era of Scleral-Fixated Intraocular Lens. Indian Journal of Ophthalmology. 2021 Jun; 69(6): 1404-8. doi: 10.4103/ijo.IJO_2192_20.

[12] Shen JF, Deng S, Hammersmith KM, Kuo AN, Li JY, Weikert MP *et al.* Intraocular Lens Implantation in the Absence of Zonular Support: An Outcomes and Safety Update: A Report by the American Academy of Ophthalmology. Ophthalmology.2020Sep;127(9):1234-58. doi: 10.1016/j.ophtha.2020.03.005.

[13] Kanekar PS, Patare S, Naik R. Comparative Analysis of Secondary Implantation of Iris Claw Intraocular Lens (ICIOL) and Scleral Fixated Intraocular Lens (SFIOL) in Terms of Visual Outcome and Complications. VIMS Health Science Journal.2020 Dec; 7(4): 110-7. doi: 10.46858/vimshsj.7404.

[14] Shuchi TK, Hafiz SA, Danny AS, Aktar N, Raihan MH, Afrin H. Visual Outcome After Scleral Fixation of Intraocular Lens (SFIOL) Implantation Following Pars Plana Vitrectomy (PPV) and Removal of Dropped Intra-Ocular Lens (IOL). Journal of National Institute of Ophthalmology.2022 Dec; 5(1): 27-31.doi:10.3329/jnio.v5i1.63150.

[15] Bulbanat A, Alqabandi Y, Kankoni M, Aljassar F. Compare the Outcome of Different Scleral Fixation (SFIOL) and Retropupillary Iris-Claw Intraocular Lens (RPICIOL) in Correcting Aphakia: A Meta-Analysis. 2024 May. doi: 10.21203/rs.3.rs-4394649/v1.

[16] Warren A, Kemp PS, Coussa RG, Cheng L, Boldt HC, Russell SR *et al.* Comparative Long-Term Outcomes of Vitrectomy Combined with Anterior Chamber Intraocular Lens to Intra-Scleral Haptic Fixation of Posterior Chamber Intraocular Lens. International Journal of Retina and Vitreous.2024 Aug; 10(1): 59. doi: 10.1186/s40942-024-00572-2.

[17] Shahid SM, Flores-Sánchez BC, Chan EW, Anguita R, Ahmed SN, Wickham L *et al.* Scleral-Fixated Intraocular Lens Implants—Evolution of Surgical Techniques and Future Developments. Eye. 2021 Nov; 35(11):2930-61. doi: 10.1038/s41433-021-01571-5.

[18] Garg A, Lau TH, Popovic MM, Kertes PJ, Muni RH. Sutured Scleral-Fixated Versus Anterior Chamber Intraocular Lens Implantation: A Meta-Analysis. Ophthalmic Surgery, Lasers and Imaging Retina. 2022 Jan; 53(1): 12-21. doi: 10.3928/23258160-20211213-01.

[19] Kaur M and Mohindra VK. Comparison of Visual Outcome and Complications Between Scleral Fixated Intraocular Lens and Anterior Chamber Intraocular Lens in Aphakes. Journal of Advanced Medical and Dental Sciences Research. 2019 May; 7(5): 59-62.

[20] Kumari N, Anand A, Sinha R, Ali M, Sinha S, Sinha B. Factors Affecting Visual Outcomes Following Scleral-Fixated Intraocular Lens Implantation at a Tertiary Care Center in Eastern India. Cureus. 2024 Dec; 16(12). doi: 10.7759/cureus.76154.

[21] Liang IC, Chang YH, Hernández Martínez A, Hung CF. Iris-Claw Intraocular Lens: Anterior Chamber or Retropupillary Implantation? A Systematic Review and Meta-Analysis. Medicina.2021 Jul; 57(8): 785. doi: 10.3390/medicina57080785.

[22] Megevand GS and Bron AM. Personalizing Surgical Treatments for Glaucoma Patients. Progress in Retinal and Eye Research.2021 Mar; 81: 100879. doi: 10.101 6/j.preteyeres.2020.100879.

[23] McGhee CN, Zhang J, Patel DV. A Perspective of Contemporary Cataract Surgery: The Most Common Surgical Procedure in the World. Journal of the Royal Society of New Zealand.2020 Apr; 50(2): 245-62. doi: 10.1080/03036758.2020.1714673.

[24] Hecht I, Kanclerz P, Tuuminen R. Secondary Outcomes of Lens and Cataract Surgery: More Than Just "Best-Corrected Visual Acuity". Progress in Retinal and Eye Research.2023Jul;95:101150.doi:10.1016/j.preteyeres.2022.101150.

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Obstetrical Outcomes in Primigravida with Engaged Versus Unengaged Fetal Head during Spontaneous Labor

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ABSTRACT

When the fetal head's widest diameter fits into the pelvic inlet, it is referred to as engaged. When a primigravida's labor begins with the fetal head still not engaged, she was most likely to experience an obstructed labor. This study was conducted at a large tertiary care center with adequate sample size to determine the study outcomes. **Objective:** To compare the obstetrical outcomes in primigravida with engaged versus unengaged fetal head at the onset of spontaneous labor in terms of delivery methods and associated risks. **Methods:** This was a case control study. Study was conducted at Department of Obstetrics and Gynecology National Hospital Defence, Lahore. One hundred thirty patients through non-probability consecutive sampling. Demographic data like name, age was recorded for participants. Data were analyzed using SPSS version 22.0. RR was calculated for two groups. **Results:** Mean age of patients was 22.4 ± 2.6 years. Total 44.7% patients had C-section. When comparison of engaged and unengaged fetal head, 49 patients out of 88 i.e. 55.68% patients had engagement of head in vaginal delivery group and 16 patients out of 42 i.e. 38% patients had engagement of fetal head in C-section group. Relative risk among two group was 1.2564 and z score was 1.847 and p value was 0.0648. **Conclusion:** Relative risk of primigravida getting C-section was high with un-engaged fetal head compared to primigravida who has engaged fetal head.

INTRODUCTION

The start of regular contractions in the uterus, gradual cervical dilatation, effacement, and descent of the presenting portion are all signs of labor. Primagravidae have considerably different normal labor than multigravidae due to the uterus's physiological inefficiency and the possibility of irregular or hypotonic contractions, which can delay the onset of labor 37% of primigravidae are diagnosed with dystocia, or difficult labor [1-3]. When the fetal head's widest diameter fits inside the pelvic inlet, it is considered to be engaged. When a primigravida's labor begins with the fetal head still not engaged, she is most likely to experience an obstructed labor [4, 5]. In some situations, labor lasts longer and may call for further intervention. For a long time, unengagement of the head has been linked to cephalopelvic disproportion. It corresponds to an increased chance of challenging delivery [6]. Anomalies like as dystocia, dysfunctional labor, inability to descend, and failure to progress are

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typically the cause of abnormal labor. It's debatable when aberrant labor progress warrants a caesarean delivery. It is evident that there is still some leeway for clinical judgement when determining what is deemed normal and enough abnormal to require surgical intervention [7]. Primigravidas who have not engaged their heads are more likely to experience obstructed labor and all of the associated morbidity and mortality. For delivery, they ought to be referred to a health facility with professional staff and amenities. In Pakistan, Home birth is very common so it increases the chances of obstructed labor. Majority of the studies so far have studied management of primigravida with unengaged head at term with very few looking at comparing the outcomes in primigravida with unengaged vs engaged fetal head at term [8]. Cephalopelvic disproportion is a subjective clinical assessment based on physical examination and course of labour. In a prospective study of nulliparous women in active labour, a persistently floating head at 7 cm dilation was predictive of eventual cesarean delivery in 100 percent of cases [9]. Antepartum, the clinician is generally unable to predict maternal pelvis-fetal size/position discordance leading to arrest of labour requiring cesarean delivery. Clinical and radiologic assessments of the maternal pelvis and fetal size (ie, pelvimetry) are inexact and poorly predict the course and outcome of labour [10]. Normal delivery happens in 46%, assisted vaginal in 14% and caesarian section in 40% of primigravida with caesarian section rates ranging from 21.73% to 90% depending on engagement. Fetal station at full cervical dilation tends to be higher in multiparous women than in nulliparous women, and descent tends to be faster [11]. However, in select scenarios where the probability of a vaginal delivery appears to be low and a woman has been pushing effectively without descent, it is reasonable to make a diagnosis of arrest of descent and proceed with cesarean prior to these upper limits. Factors such as the fetal station, estimated fetal weight, obstetric history, fetal status, maternal pelvis, and adequacy of maternal pushing should all be considered [12]. The time to dilate 1 cm in latent phase (defined as dilation <6 cm) is significantly longer in women undergoing induction than in those in spontaneous labour and can take many hours [13, 14]. The active phase (time to dilate from 6 to 10 cm) is similar in both induced and spontaneous labors and is more rapid. In the preterm induction study above, the median (95th percentile) time for dilation from 6 to 10 cm was approximately 0.3 hours (2 hours) for both nulliparous and multiparas [15].

This study was therefore meant to determine the obstetrical result for a primigravida who's delivery began autonomously and whose fetal head was involved or not using a sizable sample size at a tertiary care center.

METHODS

This was case control study, conducted at Department of Obstetrics and Gynecology National Hospital, Lahore. The study was conducted over six months, from January 27, 2020, to July 26, 2020, with a 95% power of the test. The expected frequency of C-sections was 19% for cases with fetal head engagement and 39% for cases with unengaged fetal heads [5]. Sample size was estimated to be 130 in exposed/case group and 65 in unexposed or control group. Non-probability consecutive sampling was used [3]. Inclusion criteria was all primigravida between the ages of 18 and 28 who had spontaneous labor onset, a cephalic presentation, and a singleton pregnancy while exclusion criteria were patients not willing to participate in the study. Excluded cases included numerous pregnancies, fetal growth retardation, cephalopelvic imbalance, and placenta Previa. This was determined from history, medical record and examination. Diagnosed medical conditions like diabetes mellitus (BSL >200 mg/dl) and hypertension (BP >160/90) as per medical record were excluded. The present study was carried out prospectively at Gynecology department with 130 study participants (65 in exposed group and 65 in unexposed group) selected based on criteria. Recorded were demographic details such as name, age, and address. Informed consent was obtained after patients were reassured about the expertise and confidentiality. Every piece of information was input into pre-made proforma. Every patient's labor progress was documented. According to the operational definition, a caesarean section was performed if labor did not proceed or the fetal head did not descend following observation. Patients were managed as per protocol for any complications. Statistical analysis was done using Statistical Package for Social Sciences (SPSS) version 22.0. Quantitative data i.e., age, cesarean section rate was presented as means and standard deviations. Data were stratified for age, gestational age and birth weight to control for effect modifier. Post stratification chi square test was employed with p value <0.05 considered statistically significant.

RESULTS

This study involved a total of 130 patients, 65 of whom were in the exposed group and 65 of whom were not. 40% of the patients in this study were between the ages of 24 and 28, whereas 60% of the patients were between the ages of 18 and 23. The patients' average age was 22.4 ± 2.6 years. In terms of caesarean section rates, 55.3% of patients had a normal delivery, while 44.7% of patients had a C-section. Comparing engaged and unengaged foetal heads, it was found that 16 out of 42 patients, or 38% of the total, had engaged fetal heads in the C-section group, while 49 out of 88 patients, or 55.68% of the total, had engaged fetal heads

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in the vaginal delivery group. Given that the p-value was 0.0648, there was no discernible difference between the engagement and unengagement groups in the normal delivery and C-section groups. There was no significant difference between age groups, patient occupations, educational levels, or engagement versus unengagement of the fetal head (p-value < 0.05) when stratified this data for engagement and unengagement between normal delivery and C-section for various age groups, occupations, and educational levels. In this study, 60% patients were between the ages of 18-23 years whereas 40% patients were between the ages of 24-28 years. Mean age of patients was 22.4 ± 2.6 years (Table 1).

Table 1: Age of Study Participants

Age (Years)	Number of Patients N (%)
18-23	78 (60.0%)
24-28	52 (40.0%)
Total	130 (100%)

Regarding rate of caesarian section, 44.7% patients had C-section whereas 55.3% patients had normal delivery (Table 2).

Table 2: Rate of C-Section among Study Participants

Cesarean Section	Number of Patients N (%)
Yes	42 (44.7%)
No	88 (55.3%)
Total	130 (100%)

When engaged and unengaged fetal head were compared, 49 patients out of 65 i.e. 55.68% patients had engagement of head in vaginal delivery group and 16 patients out of 65 i.e. 38% patients had engagement of fetal head in C-section group (Table 3).

Table 3: Comparison of Engaged and Unengaged Group

Engagement of Fetal Head	Outcome		
	Vaginal Delivery (N)	Cesarean Section (N)	Total (N)
Yes	49	16	65
No	39	26	65
Total	88	42	130

Stratified data for engagement and unengagement between normal delivery and C-section for different age groups, 18-23 years, vaginal delivery for engaged was 26, for C-section was 13 while the vaginal delivery for unengaged was 27 and for C-section was 12 (Table 4).

Table 4: Stratification of study Patients by Age (n=130)

Age	Groups	Outcome			p-Value
		Vaginal Delivery (N)	Cesarean Section (N)	Chi-Square	
18-23 Years	Engaged	26	13	0.058	0.80
	Unengaged	27	12		
18-23 Years	Engaged	18	8	0.087	0.767
	Unengaged	17	9		
Total	130	88	42	-	-

The data for stratification of patients by gestational age was for up to 38 weeks' vaginal delivery for engaged was 17, for C-section was 9 while for unengaged was 18 and 8 respectively. The stratification of patients by gestational age was for more than 38 weeks' vaginal delivery for engaged was 26, for C-section was 13 while for unengaged was 27 and 12 respectively (Table 5).

Table 5: Stratification of study Patients by Gestational Age (n=130)

Gestational Age	Groups	Outcome		Chi-Square	p-Value
		Vaginal Delivery (N)	Cesarean Section (N)		
Upto 38 Weeks	Engaged	17	9	0.087	0.767
	Unengaged	18	8		
>38 Weeks	Engaged	26	13	0.058	0.80
	Unengaged	27	12		
Total	130	88	42	-	-

The stratification of patients by birth weight was for upto 2.75kg, the vaginal delivery for engaged was 24, for C-section was 10 while for unengaged was 22 and 11 respectively. The stratification of patients by birth weight was for more than 2.75kg, the vaginal delivery for engaged was 22, for C-section is 9 while for unengaged was 20 and 12 respectively (Table 6).

Table 6: Stratification of Patients by Birth Weight (n=130)

Birth Weight	Groups	Outcome		Chi-Square	p-Value
		Vaginal Delivery (N)	Cesarean Section (N)		
Upto 2.75 Kg	Engaged	24	10	0.001	0.965
	Unengaged	22	11		
> 2.75Kg	Engaged	22	9	0.508	0.475
	Unengaged	20	12		
Total	130	88	42	-	-

DISCUSSION

When the fetal head's widest diameter fits into the pelvic inlet, it was referred to as engaged. When a primigravida's labor begins with the fetal head still not engaged, she was most likely to experience an obstructed labor. With a big enough sample size, this study was carried out in a tertiary care center to check the study results. Regarding rate of Cesarean section, 44.7% patients had C-section whereas 55.3% patients had normal delivery. Rate of C-section in various studies has been comparable to present study. According to World Health Organization report between 2007 and 2008, rate of C-section in China was 46%. In one study conducted at Iran, prevalence of C-section was 48% [16]. In another study, rate of C-section was slightly higher i.e. 54.90% [17]. Other similar studies showed variable rates

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of caesarian section in different countries. One study conducted at Ethiopia showed that prevalence of C-section was 27.6% [18]. Another study from Brazil showed that prevalence of C-section was 55.5% [19]. Similarly, a study conducted at Cyprus showed prevalence of C-section as high as 52.2% [20]. One study conducted at Rawanda showed very high rate of C-section i.e. 62.4% [21]. When engaged and unengaged fetal head were compared, 49 patients out of 88 i.e. 55.68% patients had engagement of head in vaginal delivery group and 16 patients out of 42 i.e. 38% patients had engagement of fetal head in C-section group. Relative risk among two group was 1.2564 and z score was 1.847. There was no significant difference between engagement and unengagment in normal delivery and C-section groups as p value was 0.0648. These results were comparable to the results of other studies. In one study conducted by Sirisha VS *et al.*, it was seen that unengaged head was found in 31% of primigravida. It was also found that out of which 82.9% were delivered through vagina and 17.1% had abdominal delivery (p value <0.0001) [22]. A study conducted in Pakistan reported that 19% of patients with engaged fetal heads and 39% with unengaged fetal heads underwent cesarean delivery. In the same study, vaginal delivery occurred in 65% of the engaged group and 42% of the non-engaged group [1-3]. Similarly, a study by Shrivastava and colleagues found that vaginal delivery occurred in 46% of cases, assisted vaginal delivery in 14%, and cesarean section in 40% of primigravida, with cesarean rates varying between 21.73% and 90%, depending on the engagement of the fetal head. When stratified this data for engagement and unengagment between normal delivery and C-section for different age groups, occupation and education level, there was no significant difference between different. The study's goals were explained to the participants, and written informed consent was obtained. There were no competing ideas declared by the authors. The study's findings were given simply and honestly, with no exaggeration, manipulation, or improper deletion of information.

CONCLUSIONS

Compared to primigravida with an engaged fetal head, those with an unengaged fetal head had a higher relative risk of undergoing a C-section. The study concluded that engagement of the fetal head, though important, may not independently predict delivery outcomes. Further research is warranted to explore additional factors influencing delivery modes.

Authors Contribution

Conceptualization: ZL,
Methodology: ZL, QM, SS, NS
Formal analysis: PA
Writing, review and editing: NM, SM

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Shrivastava A. Obstetrical Outcome in Primigravida with Unengaged Fetal Head at Spontaneous Onset of Labor at Term Gestation. International Journal of Science and Research. 2017 May; 6(8): 3-4.

[2] Bhadra DM and Sonawane PK. Comparative study between unengaged and engaged fetal head in primigravida at term or in labour. International Journal of Reproduction, Contraception, Obstetrics and Gynecology. 2018 Nov; 7(11): 4569-75. doi: 10.18203/2320-1770.ijrcog20184509.

[3] Malik S, Asif U, Asif M. Primigravida: obstetrical outcome; with engaged versus unengaged fetal head with spontaneous onset of labour at term. The Professional Medical Journal. 2016 Feb; 23(02): 171-5. doi: 10.29309/TPMJ/2016.23.02.1063.

[4] Haroon M, Baqai S, Choudry A, Gul M, Ahmed M. Outcome of Primigravida with Unengaged Fetal Head at Term or Onset of Labour. Pakistan Armed Forces Medical Journal. 2022 Dec; 72(6): 1854-57. doi: 10.51253/pafmj.v72i6.4541.

[5] Hussain S, Qurban S, Tahseen H, Javed K, Khurshid HN. Maternal Outcome of Primigravida Patient with Term Pregnancy with Engaged Versus Unengaged Foetal Head at Onset of Labour. Pakistan Journal of Medical & Health Sciences. 2022 Apr; 16(03): 787-. doi: 10.53350/pjmhs22163787.

[6] Asma S, Muntaha ST, Haq F, Hayat S, Kanwal M. The Comparison of Outcome In Engaged Versus Unengaged Fetal Heads in Primigravida. Journal of Rawalpindi Medical College. 2023 Dec; 27(4). doi: 10.37939/jrmc.v27i4.2383.

[7] Hautakangas T. Measuring uterine contractile activity in labour: impact of dystocia, obesity and previous caesarean section on labour outcome [Doctoral Dissertation]. 2022.

[8] Dewan A, Pati B, Nautiyal R, Chaudhary D. Labour outcome in primigravida with unengaged head: a

DOI: https://doi.org/10.54393/pjhs.v5i12.2070

observational study. International Journal of Reproduction, Contraception, Obstetrics and Gynecology.2022 Apr; 11(4): 1097-102. doi: 10.18203/2320-1770.ijrcog20220732.

[9] Agarwal P and Shetty S. Clinical study of primigravida with unengaged head in labour at term. International Journal of Women's Health and Reproduction Sciences. 2021 Apr; 9: 100-104. doi: 10.15296/ijwhr.2021.18.

[10] Subiksha RA. Clinical study of outcome of unengaged head in primigravidae at term gestation and in labour, at Rajarajeswari Medical College and Hospital [Doctoral Dissertation]. Bangalore: Rajiv Gandhi University of Health Sciences; 2022.

[11] Salim NA, Satti I, Mahmoud AO. Unengaged head in primigravidae, mode of delivery and outcome (a case-control study) in Dongola-Sudan (2019). Journal of Family Medicine and Primary Care. 2021 Mar; 10(3): 1254-7. doi: 10.4103/jfmpc.jfmpc_2134_20.

[12] El-Desouky ES, Farag ES, Mohamed A. Fetal outcome and vaginal delivery rates among primigravidae with unengaged head at onset of labor. Al-Azhar Medical Journal. 2021 Jul; 50(3): 1707-22. doi: 10.21608/amj.2021.178262.

[13] Dashrathi R and Kathaley M. Outcome of High Foetal Station in Primigravida with Vertex Presentation at Term-A Clinical Study in a Tertiary Care Center. MVP Journal of Medical Sciences. 2020: 161-9. doi: 10.18311/mvpjms/2020/v7i2/24639.

[14] Wan X, Zhai J, Lu X, Wang X, Lilenga HS, Luo M *et al*. Effects of maternal posture and cognitive-behavioral interventions on labor outcomes in primigravidas with abnormal fetal head position: a randomized controlled clinical trial. The Journal of Maternal-Fetal & Neonatal Medicine. 2024 Jan; 37(1): 2422448. doi: 10.1080/14767058.2024.2422448.

[15] Becker DA, Szychowski JM, Kuper SG, Jauk VC, Wang MJ, Harper LM. Labor curve analysis of medically indicated early preterm induction of labor. Obstetrics & Gynecology. 2019 Oct; 134(4): 759-64. doi: 10.1097/AOG.0000000000003467.

[16] Rafiei M, Ghare MS, Akbari M, Kiani F, Sayehmiri F, Sayehmiri K *et al*. Prevalence, causes, and complications of cesarean delivery in Iran: A systematic review and meta-analysis. International Journal of Reproductive Biomedicine. 2018 Apr; 16(4): 221. doi: 10.29252/ijrm.16.4.221.

[17] Liu Y, Li G, Chen Y, Wang X, Ruan Y, Zou L *et al*. A descriptive analysis of the indications for caesarean section in mainland China. BioMed Central Pregnancy and Childbirth. 2014 Dec; 14: 1-9. doi: 10.1186/s12884-014-0410-2.

[18] Iqbal S, Sumaira S. Outcome of primigravidae with unengaged versus engaged fetal head at term or onset of labour. Biomedica. 2009 Jul; 25(1): 159-62.

[19] Hussain S, Qurban S, Tahseen H, Javed K, Khurshid HN. Maternal Outcome of Primigravida Patient with Term Pregnancy with Engaged Versus Unengaged Foetal Head at Onset of Labour. Pakistan Journal of Medical & Health Sciences. 2022 Apr; 16(03): 787. doi: 10.53350/pjmhs22163787.

[20] Unnisa S, Poornima MS. Unengaged head at term in primigravida: does it affect the chance of having a normal delivery?. International Journal of Reproduction, Contraception, Obstetrics and Gynecology. 2019 Apr; 8(4): 1616-20. doi: 10.18203/2320-1770.ijrcog20191228.

[21] Mahendra G. Clinical study of unengaged head in primigravida at term in labour [Master's Dissertation]. Karnataka, India: Rajiv Gandhi University of Health Sciences; 2011.

[22] Sirisha VS. Obstetric outcome in primigravida with unengaged versus engaged fetal head at term [Master's Dissertation]. Karnataka, India: Rajiv Gandhi University of Health Sciences; 2020. doi: 10.18203/2320-1770.ijrcog20205777.

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Comparative Analysis of Health and Sociodemographic Status of Working and Non-Working Women and Their Children

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ABSTRACT

Women have responsibilities of home management and raising children, and in recent times, they have been engaged themselves professionally. **Objectives:** To compare insights into working and non-working women's mental and physical health. **Methods:** The study was conducted to perform a retrospective and comparative analysis of the sociodemographic status and health of working along with non-working women, as well as their kids. The study included both working and non-working mothers aged 25 to 45 who had their independent incomes. Their children were between 2 and 18 years old. The health factors being studied were bone density, body mass index, haemoglobin, calcium levels, and socioeconomic status (based on Kuppuswamy's scale). Data were analyzed by SPSS version 25.0. **Results:** The bone scan results of working and nonworking women differ significantly (p-value=0.033), indicating that working women had a little higher prevalence of osteopenia and hypocalcemia than nonworking women. However, the haemoglobin, body mass index, and socioeconomic status levels of both groups and their kids do not differ significantly. **Conclusions:** It was concluded that the comparison was made from the health outcomes of non-working and working women. Although some divergence and convergence were present, there is not much of a difference between health and sociodemographic characteristics.

INTRODUCTION

In the present era, women are more inclined towards achieving their goals and doing jobs owing to changes in the cultural norms and growing trends of women empowerment. As a consequence, several concerns have been raised regarding the potential impact of employment on the physical and mental health of working women and their children [1]. Traditionally, women have always been considered the family's primary caregivers, required to serve their children and spend their time in housekeeping. Nevertheless, these traditional norms and expectations from women have now undergone significant modifications [2]. As per the International Labor Organization (ILO) in 2000, the percentage of women in the worldwide labour force was 51.8%. However, in 2020, a notable increase was observed in women's engagement in paid occupations, demonstrating 56.2% of women

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engaged in jobs [3, 4]. As working women must manage their work-life balance, it is crucial to provide insights into their physical and mental health. Several studies have been involved in investigating the impact of employment on their health, and both negative and positive outcomes have been suggested so far. For instance, Shekhawat *et al.*, demonstrated that financially independent women had better mental health as compared to those who were not employed [5]. On the other hand, some studies suggest that this financial independence comes with significant limitations like family conflicts, increased stress, and inefficiency in maintaining a healthy work-life balance [6, 7]. Moreover, research suggests that children of working women may also be subjected to both benefits and difficulties. For instance, augmented cognitive development, better social skills, and higher educational outcomes are reported in such children [8–10]. However, dependence on substitute caretakers, decreased parental care, and potential health effects are some of the difficulties that children with working women face [11-13].

This study aims to evaluate and analyze the health outcomes of both working and non-working women, shedding light on the unique challenges and advantages each group may face. Their children were also monitored to provide insights into the potential effects on their overall well-being. The research aims to contribute to the existing body of knowledge by considering both the mental and physical impacts of employment on working and non-working women and their children. This study's findings can help educate medical professionals, employers, and policymakers regarding the opportunities and challenges related to women's employment. Thus, by using these results, specific programs and policies may be developed to improve the overall well-being of jobless and working women, resulting in a healthy society.

METHODS

From March to May 2018, a cross-sectional study was conducted at Badami Bagh, Lahore, with 200 mothers aged 25 to 45. Sample size of approximately was calculated by $n=2\times(Z\alpha/2+Z\beta)2\times\sigma2/\Delta^2$, significance Level (α\alphaα): 0.05 (Z=1.96), power (1–β1-\beta1–β): 80% (Z=0.84), expected Effect Size (Δ): Based on prior data or pilot study and Variance (σ2): The total number of participants was n=200. Half of the participants were employed, and the other half were not. All participants had children aged 2 to 18 and earned independent incomes apart from their husbands, who were also employed. Demographic data, such as education, occupation, marital status, and number of children, were collected. Socioeconomic status was measured using Kuppuswamy's scale, which considers income, housing, transportation, and education. Informed consent was taken. The study excluded male, and women outside the 25–45 age range, those without children, children under 2 or over 18, and women without independent incomes [14], the Pediatric Symptom Checklist (PSC-17) for children was used in this study [15]. Physical health was evaluated using haemoglobin levels, BMI, height-weight charts, blood calcium levels, bone density (via DEXA scans), and socioeconomic factors. Data were entered and analyzed by SPSS 25.0. All the quantitative variables were presented by Mean + SD and Qualitative with frequency and percentages. Association of study groups (Working and Non-working women) with socioeconomic status, bone density, Body Mass Index (BMI), anemia, serum calcium levels, and pediatric symptoms checklist were observed by Chi-square test, p-value<0.05 was considered as significant.

RESULTS

The demographic information revealed that 16% worked between 30 and 40 hours of effort, 84% worked 41 to 50 hours a week; 50.5% of them were between the ages of 25 and 31; the remaining women were between the ages of 32 and 45; all of them were married; 82.5% of them lived with their husbands, while the remaining women were either widowed, separated, or divorced; 45% of them lived with family members, while the remaining women rented a home; 10% of them were the family's breadwinners, whereas 44% of their husbands did the same, and 39% of the women received government funding to meet their basic needs. On the other hand, the remaining ladies had access to a variety of additional healthcare facilities. 10% of women had completed high school and obtained a General Education Diploma (GED), 12% finished grade 12 or below, and 22.5% had received a doctorate or doctorate. 40% were earning between $10,000 and $49,000 annually, 40% between $50,000 and $99,999 annually, and 20% between $100,000 and $149,999 annually. Among the children half of them were male and half were female. The children's ages ranged from 2 to 9 for 50.5% of them, and from 10 to 18 for 45.5%, Table 1.

Table 1: Scio-Demographic Characteristics of study participants

Variables	Frequency (%)
Employment Status	
Working Women	100 (50.0)
Non-Working Women	100 (50.0)
Total	200 (100)
Working Hours per Week	
30-40	16 (16)
41-50	84 (84)
Total	100 (100)
Age Range (years)	
25-31	101 (50.5)
32-38	39 (19.5)

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39-45	60 (30)
Total	200 (100)
Marital Status	
Separated	12 (6)
Divorced	11 (5.5)
Widowed	12 (6)
Living with Husband	165 (82.5)
Unmarried	0 (0)
Total	200 (100)
Parity	
1-2	133 (66.5)
3-5	67 (33.5)
Total	200 (100)
Children Age Range (Years)	
2-9	107 (53.5)
10-18	93 (46.5)
Total	200 (100)
Residence	
Owned	53 (26.5)
Rented	57 (28.5)
Joint Family	90 (45)
Total	200 (100)
Breadwinner of Family	
Self	21 (10.5)
Husband	88 (44)
Both	77 (38.5)
Extended Family	14 (7)
Total	200 (100)
Pay for Healthcare	
Government funding	78 (39)
Heath Insurance	47 (23.5)
Self-Pay	75 (37.5)
Total	200 (100)
Educational Status	
12 Grade or less	24 (12)
High School Graduate or GED	20 (10)
Some College/Technical School Training	41 (20.5)
College Graduate (BA, BS)	70 (35)
MD, PhD	45 (22.5)
Total	200 (100)
Total Family Income	
10,000 to 49,999	80 (400)
50,000 to 99,999	80 (40)
100,000 to 149,999	40 (20)
Total	200 (100)

The socioeconomic status of both working and non-working women was categorized using the modified Kuppuswamy scale. There was no significant association of socioeconomic status with women's working status. The result illustrates the socioeconomic condition of women graphically (Figure 1).

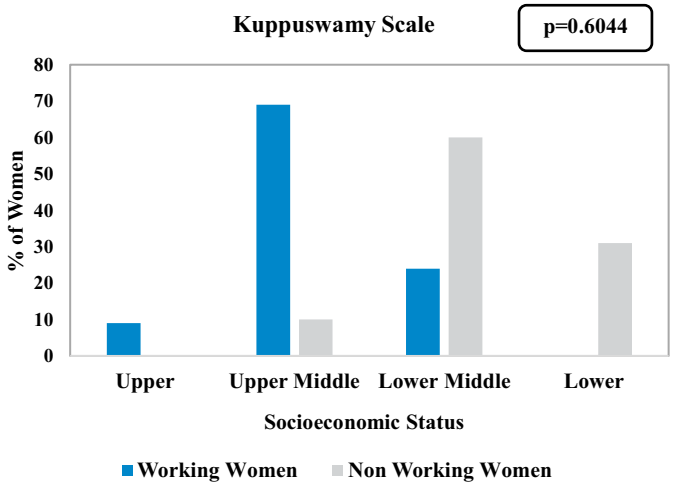

Figure 1: Socioeconomic Status of Working and Nonworking Women

According to the data, 45% of working women had normal bone density, 22% had severe osteopenia and 11% had mild osteopenia. Out of the women who did not work, 55% had average bone density, whereas 27% had severe osteopenia, 9% had moderate or mild osteopenia, and 9% had neither. Significant variations exist between the bone density distributions of the two groups (p-value=0.033). Among women who did not work (27% vs 22%), the prevalence of serious osteopenia, which indicates a significant decrease in bone density, was significantly higher and results are shown in Figure 2.

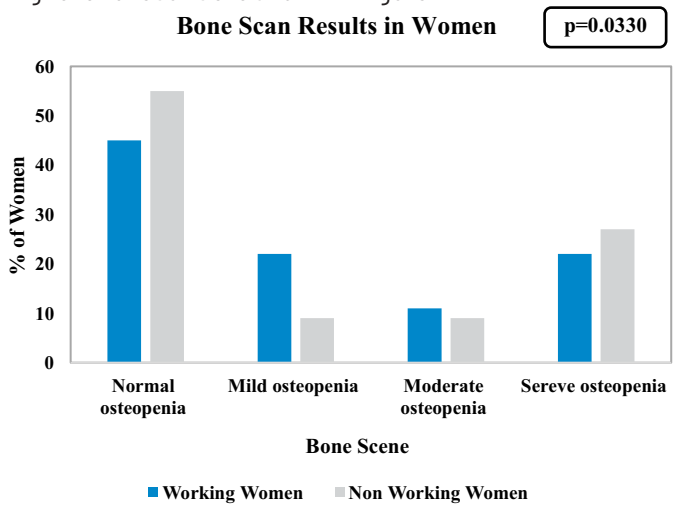

Figure 2: Bone Scan Analysis of Working and Non-Working Women

The findings showed that 45% of working women had a normal BMI, 11% were borderline, and 44% were overweight. Nonetheless, just 9% of the unemployed women were overweight, while 18% were underweight. There were 55% with a normal BMI and 18% with a borderline BMI. There was no appreciable variation in BMI between the groups in the study (p-value=0.25). Compared to non-working women, a higher percentage of working

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women (44% vs. 9%) were categorized as overweight. Additionally, employed women had a lower rate of underweight individuals than non-employed women (0% vs. 18%). However, the rate of women with a normal BMI was similar in both groups (45% of working women and 55% of non-working women). The findings showed that 67% of working women had normal haemoglobin levels and 33% were anemic. 71% of the unemployed women had normal haemoglobin levels, while 29% were anemic. The results showed that working women had slightly higher rates of anemia (33% vs. 29%) than non-working women. However, most working and non-working women (67% and 71%, respectively) had normal haemoglobin levels. however, there was no association between the group's haemoglobin levels. According to the findings, 44% of working women had normal blood calcium levels, whereas 56% had hypocalcemia. 71% of unemployed women had normal blood calcium levels, whereas 29% had hypocalcemia. The results showed that hypocalcemia is slightly more common in working women than in non-working women (56% vs. 29%) and p-value=0.6772). Interestingly, the serum calcium levels of many working and nonworking women groups were normal (44% and 71%, respectively). The incidence of hypocalcemia among working and non-working women is shown in Table 2.

Table 2: Different Parameters among Working and Non-Working Women

Type of Women	BMI				p-value
	Normal	Borderline	Overweight	Underweight	
Working Women	45%	11%	44%	0%	0.2516
Non-Working Women	55%	18%	9%	18%	
	Anemia status				
	Anemia		Normal		
Working Women	33%		67%		0.0668
Non-Working Women	29%		71%		
	Serum Calcium				
	Normal		Hypocalcemia		
Working Women	44%		56%		0.6772
Non-Working Women	71%		29%		

The study displays the distribution of pediatric symptom ratings between children of working and nonworking women. The results showed that 9% of children of working moms had scores above 14, indicating an increased likelihood of pediatric issues. However, 91% of the kids scored lower than 14, suggesting that pediatric symptoms are less common. 75% of children of non-working women had test results below 14, while 25% had results exceeding 14 (p-value=0.151). Fewer children (9%) earned scores indicating a higher chance of experiencing pediatric symptoms than children of non-working women (25%). A somewhat higher proportion of children from working moms (99%) had scores below the threshold than children of non-working women (75%), suggesting a lower frequency of pediatric symptoms. Just 18% of working women's children were classed as underweight, while 82% of their children had a normal BMI. In contrast, 67% of the children of non-working mothers had BMIs within the normal range, and 33% of them were underweight (p-value=0.189) Compared to children of non-working mothers, children of working women were more likely to have BMIs within the normal range (82% vs. 67%, respectively). On the other hand, children of non-working mothers were more likely than those of working women to be classed as underweight (33% vs. 18%), as shown in Table 3.

Table 3: Pediatric Symptoms and BMI Type of Working Women Children and Non-Working Women Children

Pediatric Symptoms Checklist	PSC>14	PSC>14	p-value
Working Women Children	9%	91%	0.1514
Non-Working Women Children	14%	75%	
BMI Type	**Normal**	**Underweight**	
Working Women Children	82%	18%	0.189
Non-Working Women Children	67%	33%	

The results showed that while 91% of children of non-working mothers had normal hemoglobin levels and 9% had anemia, 85% of children of working women had normal hemoglobin levels, and 15% were anemic (p-value=0.0502), indicating no significant difference in the hemoglobin levels of the groups under study. The distribution of hemoglobin levels in children was illustrated in Figure 3.

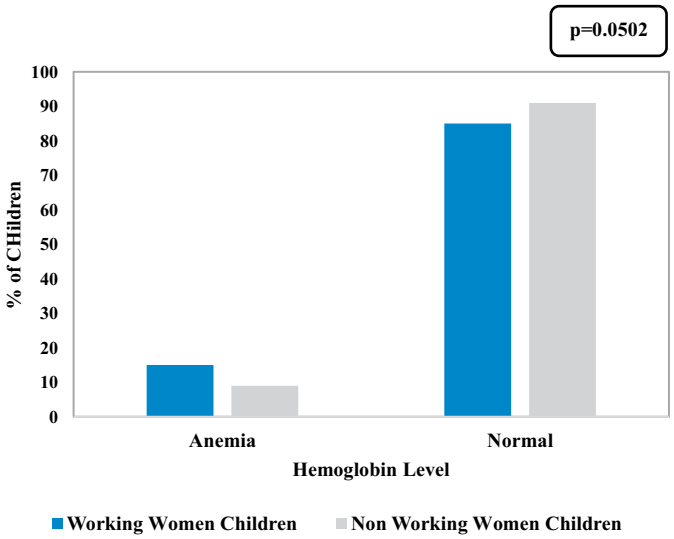

Figure 3: Hemoglobin of Children Among Working and Non-Working Women

Compared to 36% of children of non-working women, the

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results indicate that children of working women had a lower incidence of dropout. There is no discrete difference between the groups' rates of school desertion (p-value=0.2905). Children of working women had a lower percentage of school dropouts than children of non-working women. In particular, children of working women had a much lower dropout rate than children of non-working women, with 36% of the former leaving school earlier. Comparisons of rates of school dropouts for children of working and non-working women were made in Figure 4.

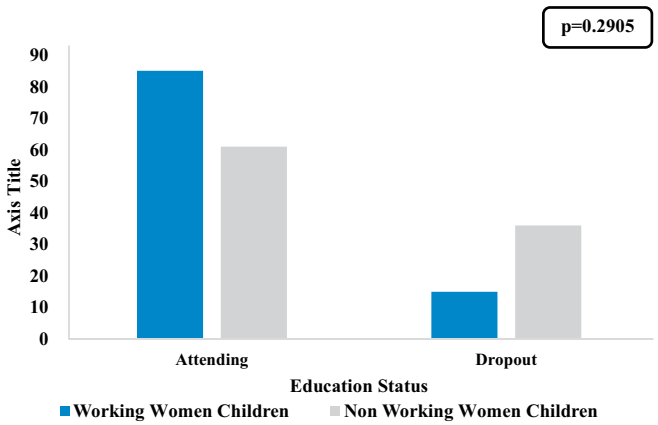

Figure 4: Children Dropout Rate of Working and Non-Working Women

DISCUSSION

Analysis revealed that jobless women had more severe osteopenia in terms of bone density as compared to working women. These findings are not from the previous study, which reported poorer bone health in working women because of their strict lifestyle [16]. However, personal characteristics such as hormone levels, genetic makeup, and age must also be investigated, as these variables can also affect women's bone density. It was found that working women were more prone to obesity as compared to jobless women. The unemployed women had higher weight and obesity rates due to minimum physical activity and sedentary lifestyles [17]. The findings of the present study highlight the necessity of focused measures such as access to healthcare services and nutritional support to alleviate anemia among working women. The study also examined another aspect of the lives of children of both working and non-working women. Children of working women had a lower percentage of school dropouts than children of non-working women. These findings are consistent with earlier studies that exhibit that maternal employment can improve children's educational achievements by giving them access to more educational resources, financial stability, and role modelling [18, 19]. However, factors that might significantly affect school dropout rates and educational performance, like parental engagement and socioeconomic position, must be considered. Supportive work environments must be developed where diversity is appreciated, and women are encouraged by administration and coworkers. Such flexible work arrangements may benefit working women by enabling them to manage their work life and personal responsibilities efficiently. Initiatives must also be developed to encourage self-care behaviour in women employees [20, 21]. Moreover, women should also participate in professional development programs to help them progress and take on leadership roles. Organizations must implement these suggestions to foster a positive and encouraging environment in the workplace for women that can enhance their job satisfaction, productivity, and well-being. Unemployed educated women should also consider the benefits of working from home. Teleworking allows people to work whenever they want and from home, which is highly suitable for mothers with other chores. On the other hand, programs must also be developed for proper skills-based training of unemployed women without formal education. Women can adopt these recommendations to maintain a healthy work-life balance while achieving career progression, financial freedom, and job satisfaction.

CONCLUSIONS

It was concluded that the study found no significant differences in the health and socio-demographic variables between working and non-working women and their children. However, there were some similarities and differences in certain aspects.

Authors Contribution

Conceptualization: SJA
Methodology: RZ, JA, RL, FM, SS, FL, AS, HMK
Formal analysis: SJA
Writing review and editing: SJA, RZ, JA, RL, FM, SS, FL, AS, HMK

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

The authors declare no conflict of interest.

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REFERENCES

[1] Hulshof CT, Pega F, Neupane S, van der Molen HF, Colosio C, Daams JG *et al.* The Prevalence of Occupational Exposure to Ergonomic Risk Factors: A Systematic Review and Meta-Analysis from the WHO/ILO Joint Estimates of the Work-Related Burden of Disease and Injury. Environment International. 2021

DOI:https://doi.org/10.54393/pjhs.v5i12.840

Jan; 146: 106157. doi: 10.1016/j.envint.2020.106157.
[2] Robertson LG, Anderson TL, Hall ME, Kim CL. Mothers and Mental Labor: A Phenomenological Focus Group Study of Family-Related Thinking Work. Psychology of Women Quarterly.2019 Jun; 43(2): 184-200. doi: 10.1177/0361684319825581.
[3] Akram SJ, Zakir R, Akram J, Liaqat R, Mujahid F, Syed S *et al.* Comparative Analysis of Health and Socio-demographic Status of Working and Non-Working Women and their Children.2023 Dec. doi: 10.21203/rs.3.rs-3701396/v1.
[4] Yasmin B, Azhar F, Jehan Z. Determinants of Objective and Subjective Wellbeing of Working and Non-Working Women: A Case Study of Rawalpindi, Punjab, Pakistan. Forman Journal of Economic Studies. 2024 Dec; 20(1): 1-21. doi: 10.32368/FJES.20242001.
[5] Shekhawat K, Sharma P, Menaria P. Financial Independence and Maternal Mental Health- A Right Balance. Southeast Asian Journal of Health Professionals. 2022; 5(1): 4-7. doi: 10.18231/j.sajhp.2022.002.
[6] Mahmood M, Rizvi SA, Bibi M. Educated Working Women and Their Work-Life Conflict and Work-Life Balance. Pakistan Journal of Gender Studies.2018 Dec; 17(1): 105-26. doi: 10.46568/pjgs.v17i1.12.
[7] Chela-Alvarez X, Garcia-Buades ME, Ferrer-Perez VA, Bulilete O, Llobera J. Work-Family Conflict Among Hotel Housekeepers in the Balearic Islands (Spain). Plos One.2023 Mar; 18(3): e0269074. doi: 10.1371/journal.pone.0269074.
[8] Nath NJ, Chaudhary A, Kumar S. Exploring Drivers of Healthcare Utilization among the Working and Non-Working Elderly Population: Insights from LASI. Hospital Topics. 2024 Sep: 1-3. doi: 10.1080/00185868.2024.2400527.
[9] Omotayo AK and Queen ON. Influence of Working Mothers on the Cognitive Development of their Children in Nigeria. International Journal of Education and Evaluation. 2023; 9(7). doi: 10.56201/ijeeS.v9.no7.2023.pg1.10.
[10] Iriani LD, Darsono SN, Samaee M. The Effect of Working Mother on Children's Cognitive Achievement. Journal of Economics Research and Social Sciences. 2023 Feb; 7(1): 36-48. doi: 10.18196/jerss.v7i1.17634.
[11] Wijayanto A, Novitasari K, Dewi AA. Problems in Working Mothers in Early Children's Care. Edukasi. 2022 Nov; 16(2): 159-65. doi: 10.15294/edukasi.v16i2.41563.
[12] Muturi CW, Waudo J, Njogu E. Association between Socio-Demographic Characteristics and Drivers of Food Choice among Women of Reproductive Age. East African Journal of Health and Science. 2024 Nov; 7(2): 60-70. doi: 10.37284/eajhs.7.2.2442.
[13] Kumar G, Dash P, Patnaik J, Pany G. Socioeconomic Status Scale-Modified Kuppuswamy Scale for the Year 2022. International Journal of Community Dentistry. 2022 Jun; 10(1): 1-6. doi: 10.56501/intjcommunitydent.v10i1.26.
[14] Salis F, Costaggiu D, Mandas A. Mini-Mental State Examination: Optimal Cut-Off Levels for Mild and Severe Cognitive Impairment.Geriatrics.2023 Jan; 8(1): 12. doi: 10.3390/geriatrics8010012.
[15] Gao R, Raygoza A, Distefano C, Greer F, Dowdy E. Assessing Measurement Equivalence of PSC-17 Across Teacher and Parent Respondents. School Psychology International.2022 Oct; 43(5): 477-95. doi: 10.1177/01430343221108874.
[16] Papageorgiou M, Dolan E, Elliott-Sale KJ, Sale C. Reduced Energy Availability: Implications for Bone Health in Physically Active Populations. European Journal of Nutrition.2018 Apr; 57: 847-59. doi: 10.1007/s00394-017-1498-8.
[17] Bramming M, Jørgensen MB, Christensen AI, Lau CJ, Egan KK, Tolstrup JS. BMI and Labor Market Participation: A Cohort Study of Transitions Between Work, Unemployment, and Sickness Absence. Obesity. 2019 Oct; 27(10): 1703-10. doi: 10.1002/oby.22578.
[18] Riaz S and Pervaiz Z. The Impact of Women's Education and Employment On Their Empowerment: An Empirical Evidence from Household-Level Survey. Quality and Quantity. 2018 Nov; 52(6): 2855-70. doi: 10.1007/s11135-018-0713-x.
[19] Lakshmi N and Prasanth VS. A Study On Work-Life Balance in Working Women. International Journal of Advanced Multidisciplinary Scientific Research. 2018; 1(7): 76-88. doi: 10.31426/ijamsr.2018.1.7.718.
[20] Abbas J, Aqeel M, Abbas J, Shaher B, Jaffar A, Sundas J *et al.* The Moderating Role of Social Support for Marital Adjustment, Depression, Anxiety, and Stress: Evidence from Pakistani Working and Nonworking Women. Journal of Affective Disorders. 2019 Feb; 244: 231-8. doi: 10.1016/j.jad.2018.07.071.
[21] Joseph JK. A Comparative Study to Assess the Level of Stress Among Working and Non-Working Women. International Journal of Recent Scientific Research. 2019 Feb; 4: 32094-7. doi: 10.24327/ijrsr.2019.1004.3397.

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Systematic Review

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Cellular and Molecular Mechanisms of Salivary Gland Development and Regeneration: Implications for Tissue Engineering and Regenerative Medicine

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ABSTRACT

Salivary glands are essential for oral health, but their function can be compromised by cancer, autoimmune disorders, infections, and physical traumas, severely impacting quality of life. There is currently no cure for salivary gland dysfunction, and treatment is symptomatic. **Objective:** To explore the cellular and molecular mechanisms involved in the development, maturation, and regeneration of salivary glands, with a focus on tissue engineering and regenerative medicine. **Methods:** A comprehensive review was conducted using PRISMA and information was fetched through PUBMED, EMBASE, Medline, and Google Scholar databases. **Results:** The FGF pathway, part of the growth factor family, plays a significant role in salivary gland homeostasis, while the Wnt pathway is crucial for gland maturation. Various receptors and signaling molecules are involved in the gland's functioning. Recent advancements in regenerative medicine have demonstrated that activating endogenous stem cells can lead to positive outcomes in restoring injured salivary glands. Technological advancements in 3D tissue culturing using patient cells have enabled the creation of functional artificial salivary gland organs. However, no cell line completely mimics natural salivary gland cells, and their inherent tumorigenic potential delays their therapeutic application. **Conclusions:** Understanding these mechanisms is vital for developing effective therapies. While recent advancements show promise, further research is necessary to create safe, accurate cell lines for therapeutic use. This knowledge is crucial for establishing therapeutic avenues that could potentially lead to direct regeneration, reconstruction, and replacement of functioning salivary glands.

INTRODUCTION

The Salivary Glands (SGs) perform pivotal actions required for the sustenance of oral health. Dysfunction in these glands can lead to significant deterioration in oral functioning and the emergence of other health issues [1]. The parotid, submandibular, sublingual, and numerous minor salivary glands secrete saliva in response to a variety of biochemical signals and environmental stimuli [2]. Saliva, composed of water, mucus, antimicrobial substances, electrolytes, and a variety of enzymes, is essential for speaking, eating, swallowing, digestion, and maintaining the health of teeth and gingival tissues [3]. Irreversible damage to the SG secretion pathway results in hyposalivation, exhibited as xerostomia, or dry mouth, in individuals with autoimmune diseases like Sjögren's syndrome or those undergoing radiation therapies for head and neck tumors [4]. Globally, at least 3.1 million adults suffer from Sjögren's syndrome, predominantly affecting middle-aged and older women [5]. Additionally, radiation therapy for head and neck cancer impacts about 1 million new patients annually [6, 7]. Current treatments for hyposalivation are palliative and provide only temporary relief from xerostomia [8]. Therefore, re-engineering SGs could offer long-term, practical methods to restore normal salivation [9]. In 1999, Bruce Baum and colleagues identified three key strategies for re-engineering salivary epithelial cell functions: generating artificial SGs, mending

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hypofunctional SGs, and redesigning secretory functions [10]. Since then, numerous tissue engineering techniques have been explored to restore salivation, with some progressing to clinical studies [11, 12]. Stem cell therapy, in combination with specific cell culture techniques such as scaffold materials, hanging drop and rotating culture vessels, and spontaneous cell aggregation has shown promise in clinical trials for developing functional secretory epithelial organs [13-15]. Gene therapies also offer novel treatment opportunities for radiation-induced xerostomia [16-18]. Despite these advancements, maintaining the effective secretory capacity of SG cells remains challenging. Researchers have explored the combination of various cell types and biomaterials to create the ideal implant material for SG tissue engineering [19, 20].

The objectives were to summarize the current body of knowledge regarding stem cell anatomy, structure, and function related to SGs. The review aims to summarize current knowledge on stem cell anatomy, structure, and function in relation to salivary glands (SGs), investigate stem cell pathologies and dysfunctions within SGs, and identify key components of tissue engineering strategies for SG regeneration.

METHODS

The systematic review adhered to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines and explored cellular and molecular mechanisms in salivary gland development, maturation, and regeneration, with a focus on tissue engineering and regenerative medicine. Databases such as PUBMED, EMBASE, Medline, and Google Scholar were searched using terms like "Salivary gland," "Salivary gland maturation," and "Salivary gland regeneration." Inclusion criteria covered studies from 1995 to 2022 in English, while excluding studies on non-human salivary glands, pre-1995 publications, and non-English studies. The review process involved identification, screening, eligibility, and inclusion phases to address the research inquiry on molecular mechanisms relevant to salivary gland tissue engineering and regenerative medicine.

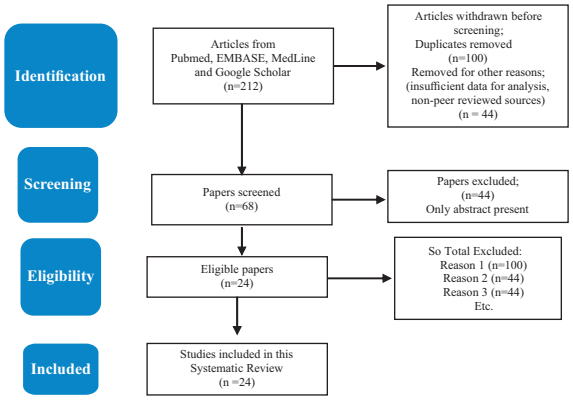

Figure 1: PRISMA flow-chart for studies selection

RESULTS

The information collected after reviewing the articles stated that SG function relies on a complex network of molecular pathways that regulate cellular homeostasis, growth, and response to injury. These key pathways, including Fibroblast Growth Factor (FGF), Wnt, Hedgehog (Hh), and Notch signaling, coordinate gland maturation, repair, and functional regeneration. This regulatory framework also includes specific growth factors and signaling molecules that guide cellular differentiation, maintain glandular structure, and support tissue engineering strategies for potential regenerative therapies. Salivary gland function is regulated by a complex network of molecular pathways. The Fibroblast Growth Factor (FGF) pathway is essential for maintaining gland homeostasis, with FGF-receptor 2 in intercalated and excretory duct cells and FGF-7 in salisphere-forming cells, indicating its trophic role. Another study reported that in Vivo Fibroblast Growth factor receptor-1 (FGFR1) and Fibroblast Growth factor receptor 2b and (FGFR2b) signaling are indispensable for SMG development. The Wnt pathway is essential in the maturation of salivary glands, playing roles during mesenchymal activation and the differentiation of the ductal epithelium and lumen development [21-23]. Mature salivary gland ductal epithelium maintains Wnt signaling expression, supporting regeneration after damage. This study explores the role of Wnt signaling in regulating salivary gland (SG) development, focusing on the balance between pro-acinar differentiation and duct formation. Wnt signaling is shown to maintain end bud cells in an undifferentiated state during early development by suppressing Proto-Oncogene Receptor Tyrosine Kinase (KIT) expression through the up regulation of Myb transcription factor, which inhibits the Phosphatidylinositol 3-Kinase - KT (PI3K-AKT) pathway [24]. This suggests that Wnt Signaling regulates SGs repair after wound injury. Hedgehog (Hh) signaling is triggered by branching morphogenesis and is inhibited when the ligand is blocked in vivo and in vitro [25]. Glioma-associated oncogene homolog 1 (Gli1), a Hh-target gene, promotes epithelial proliferation during functional regeneration, with overexpression linked to the reactivation of multiple salivary gland progenitors [26]. Hh signaling is vital for salivary gland tissue regeneration as it supports the preservation of functional salivary stem/progenitor cells and sustains parasympathetic innervation, both of which are critical for restoring gland function following damage, such as that caused by irradiation [27]. Gli1mediated Hedgehog signaling aids salivary gland regeneration by restoring function and macrophage interactions post-injury, with minimal involvement in fibrosis. Hh pathway activation, similar to SMG regeneration post-duct ligation, was confirmed in salisphere cultures. Hedgehog plays a critical role in regulating epithelial branching and salivary gland morphogenesis by positively interacting with Fgf8.

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The Notch signaling pathway, involving target gene Hes1 and receptors NOTCH1 and NOTCH4, along with ligands JAGGED1, JAGGED2, and DELTA1, regulates growth and differentiation in adult murine salivary glands [28-30]. Notch signaling is active during regeneration after duct damage, crucial for maintaining SG tissue homeostasis [31]. Notch signaling directs salivary gland morphogenesis by promoting luminal cell differentiation from Krt8+ bipotent progenitors and restricting basal/myoepithelial fates. Its inhibition disrupts branching and epithelial organization, highlighting its essential role in lineage specification [32, 33]. Innervation is crucial for salivary gland (SG) function, with Glial cell line-Derived Neurotrophic Factor (GDNF) driving parasympathetic nerve formation and its genetic deletion reducing innervated acini. Nerve Growth factor (NGF), essential for sympathetic innervation, is concentrated in the murine submandibular gland, where it regulates cell survival, axonal development, angiogenesis, tissue remodeling, and wound healing through its high and low-affinity receptors [33]. In another study, Neural Cell Adhesion Molecule (NCAM) In the group with intact innervation, NCAM expression was significantly increased during the early stages of regeneration, suggesting importance of intact parasympathetic innervation in promoting ductal cell proliferation and overall regeneration of the submandibular gland [34]. The polarity of apical and basal cell regions is regulated by Int-3 and Int-1, while cell-extracellular matrix contact and branching morphogenesis depend on integrin receptor Int-6 and its interaction with Laminin-1. Int-6, Int-1, and Int-4 are found in multipotent cells in adult tissues. Autoimmune Sjögren's syndrome is characterized by low levels of Laminin-1 [35-37]. The α3β1 integrin is essential for the differentiation of salivary gland cells, with its absence leading to altered expression of important extracellular matrix (ECM) components and adhesion molecules, including laminin and E-cadherin [38]. Another study highlights the critical roles of β1 and β4 integrins in salivary gland development, particularly in cytodifferentiation and tissue organization, while β3 integrin is associated with vascular development and adult glands. Integrins are essential for gland morphogenesis and function [39]. In vivo outcomes on the role of Sonic Hedgehog (Shh) in salivary gland (SMG) development suggest that Shh is a critical downstream mediator of Ectodysplasin (Eda) signaling [40]. Shh Expression Correlates with Eda Levels Shh transcript levels in developing SMGs were found to correlate with Eda statuswhich in turn drives SMG branching morphogenesis [41]. Shh expression in Eda-null (Eda–/–) glands was lower than in wild-type and K14-Eda transgenic glands, suggesting other regulatory factors. Treatment with recombinant Shh increased branching in Eda–/– glands, had a weaker effect in control glands, and no effect in K14-Eda glands, indicating Eda modulates Shh's impact on branching. Both Shh and Eda proteins partially rescued the Eda–/– phenotype by increasing end bud numbers. Cyclopamine inhibition of hedgehog signaling reduced branching in control and K14-Eda glands but not in Eda–/– glands, highlighting dependence on Eda signaling. Shh was mainly localized in the epithelium of developing SMGs, with higher expression in K14-Eda glands and reduced in Eda–/– glands [42]. This suggests that, Eda is a key regulator of Shh which induces branching morphogenesis of SGs. The differential effects of recombinant Shh and Cyclopaminealso suggest that Eda act as modulator on how Shh influences branching morphogenesis. SGdysfunction can lead to hyposalivation (xerostomia) or hypersalivation (sialorrhea). Xerostomia affects at least 10% of adults, with higher prevalence in women and the elderly [43]. Sialorrhea may result from primary SG modifications, drug side effects, or neurological diseases [44]. Saliva is crucial for food processing, tooth protection, and microbial defense [45]. Mucosal alterations and infections predispose individuals to chronic SG hypofunction [46]. Drug side effects are common causes of SG hypofunction, especially in older adults [46, 47]. SG inflammation (sialadenitis) is often linked to hyposalivation and duct blockage [48]. Sjögren's syndrome, affecting 0.1-4.8% of the population, is a chronic autoimmune condition with a 9:1 female to male ratio [49, 50]. Symptoms include dry mouth and dry eyes [51]. Radiation therapy for head and neck cancer affects a large number globally, leading to irreversible SG damage [52]. Remaining SG regeneration capacity after radiation may offer new therapeutic avenues [53]. Current xerostomia treatments, including stimulant drugs, secretagogues, salivary replacements, or artificial saliva, provide only temporary relief [54]. Gene therapy, stem cell therapy and SG bioengineered models are considered promising for restoring SG function. Tissue engineering for SG regeneration involves combining cells, bioactive substances, and biomaterials [55-59]. Cells are essential for SG regeneration, with single cells or those preserving 3D spatial arrangement used for implantation [60, 61]. Flow cytometry or selective enhancement during in vitro growth divides single cells into subpopulations of parenchymal and stromal cells [62]. The challenge lies in combining SG stem/progenitor cells with biocompatible, biodegradable scaffolds, ensuring cell survival and function for therapeutic relevance [63]. Stem cells are a type of immature cell which possesses an astonishing capacity to regenerate and repair any tissue or organ in the body owing to their unique ability to proliferate, differentiate, and renew themselves [64]. Stem cell therapy is a type of tissue engineering that helps to develop biological substitutes that can restore, maintain, or improve the function of damaged tissues or organs [65]. It is reported that tissue aging and structural changes are primary reasons for SG dysfunction. Genetic tracing in animal models identified progenitor cells in mature SGs. Acini produce new acinar cells post-damage, not ductal cells, indicating an innate fate-commitment program [66, 67]. Sex-determining

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Region Y box gene (SOX2)-labeled acinar cells can develop into Mucin 19 (MUC19)expressing acinar cells after radiation [15]. SOX2 expression in adult major SGs suggests its use for regeneration [68]. In vitro stem cell expansion systems, like submandibular gland-derived stem cell culture, enhance the pool of functionally committed cells [69]. Radiation exposure impacts stem cells, which can be effectively transplanted in vivo. This study investigated the role of androgens in salivary gland remodeling, focusing on their effects on laminin α1 chain and integrin (INT) α1 and α2 subunit expression in human salivary gland cells and labial salivary gland (LSG) tissues from healthy individuals and patients with Sjögren's Syndrome (SS). Androgens such as DHEA and testosterone increased INT α1 and α2 subunit mRNA and protein levels in intercalated duct and acinar cells from healthy individuals, while laminin α1-chain expression remained unaffected. However, this androgen-driven upregulation was absent in SS LSG, suggesting defective androgen regulation in SS contributes to impaired outside-in signaling, acinar cell atrophy, and ductal cell hyperplasia, hallmark features of the disease [70]. This suggested thatSOX2-positive cells are a promising target for regenerating damaged salivary glands, especially after injury caused by radiation. Kit-expressing cells are located in peripheral epithelial end-bud cells of the Submandibular Gland Keratin 14 (Krt14) expressing progenitors are influenced by Kit signaling and FGFr2b, with Krt5+ epithelial progenitors preserving the neuronal niche [71]. Krt5 progenitors in mature glands are mainly restricted to the SMG duct. KIT and KRT14 mark a shared progenitor population in the SG that plays a critical role in ductal system maturation and granulated duct (GD) formation during development. The dynamic expression of KRT14 and its later restriction to junctional regions imply a maintained progenitor-like state in these cells, potentially supporting long-term SG homeostasis and regeneration [72]. Mesenchymal progenitor cells in healthy adult SGs multiply locally in response to wounds, regenerating both acini and ducts [73]. ASCL3-expressing ductal cells produce both ductal and acinar cells Krt5-progenitors persist in smaller glands after Ascl3+-population elimination [74, 75]. These findings indicated that multiple progenitor populations in SGs capable of compensating for each other's losses. Bi-dimensional tissue cultures lack cell-to-cell and cell-to-extracellular matrix interactions suggesting that the microenvironment's impact on cell renewal, proliferation, and differentiation is crucial. Modeling diseases requires considering the altered microenvironment to understand disease complexity. Advancements in 3D tissue culturing have enabled the creation of functional artificial salivary glands using bioengineered templates with cell-seeded scaffolds, replicating structural complexity for research. While primary cells have limited growth and lifespan, techniques using cell lines offer promise, though no cell line fully replicates natural SG cells, hindering therapeutic progress [43, 73, 75].

Table 1: Summary of Salivary Gland Molecular Pathways and their role in possible Regenerative Strategies

Molecular Pathway	Function/Role	Summary of Study Findings
FGF Pathway	Maintains Salivary Gland homeostasis; Fibroblast Growth Factor-receptor 2 in duct cells, Fibroblast Growth factor 7 in saliosphere-forming cells. These findings suggest that Fibroblast growth factor and fibroblast receptors regular branching morphogenesis	In vivo, FGF-2 exhibited strong immunostaining in intercalated ducts and blood vessels initially, while FGF-7 appeared on Day 0, peaked on Days 3 and 7, and vanished by Day 14 [21]. In vivo studies show FGFR1 and FGFR2b signaling are essential for SMG development, with knockout models highlighting their roles in morphogenesis and differentiation. In vitro findings reveal FGFR1 regulates branching morphogenesis through downstream FGFs and BMPs [22].
Wnt Pathway	Essential for mesenchymal activation, ductal epithelium differentiation, and lumen development	In vivo studies with β-Catenin -Activated Transgene galactosidase mice showed Wnt/β-catenin signaling activity in basal intercalated duct cells at postnatal day 1 and increased during SMG regeneration [23]. Wnt signaling regulates salivary gland development by maintaining end bud cells in an undifferentiated state, suppressing Proto-Oncogene Receptor Tyrosine Kinase (KIT) via Myb upregulation, and inhibiting the Phosphatidylinositol 3-Kinase-AKT (PI3K-AKT) pathway to delay proacinar differentiation [24].
Hedgehog (Hh) Signaling	Triggered by branching morphogenesis; Gli1 promotes epithelial proliferation, linked to progenitor reactivation	Hedgehog (Hh) signaling is triggered by branching morphogenesis and is inhibited when the ligand is blocked in vivo and in vitro [26].Hedgehog signaling supports salivary gland regeneration by preserving stem/progenitor cells and parasympathetic innervation essential for functional recovery [27]. These studies examined Hedgehog signaling in SMG regeneration using Krt5 -rtTA/tetO-Shh mice, showing significant upregulation of Hh target genes in male mice after doxycyclineinduction, while female mice exhibited a weaker response; techniquesincluded qPCR, X-gal staining, H&E staining, immunofluorescence,Western blot, spheroid culture, PCR Array for Wnt components, and RT-qPCR [28].

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		Hedgehog plays a critical role in regulating epithelial branching and salivary gland morphogenesis by positively interacting with Fgf8. In Tabby mice, Shh downregulation due to EdaTa mutation disrupts branching, partially compensated by upregulation of Egf/Tgfα/Egfr pathways [29].
Notch Signaling	Regulates growth and differentiation; active during regeneration post-duct damage	The study examined Notch signalingin salivary gland development, showing that Human Salivary Gland cells expressedNotch receptors and ligands, with differentiation markers upregulated on Matrigel and requiring γ-secretase for activation. In vivo studies demonstrated intenseNotch signaling in ductal and regenerating acinar cells, highlighting its essential role in glandular cell differentiation and injury recovery [30].
GDNF and NGF Signaling	GDNF for parasympathetic innervation, NGF for sympathetic innervation; NGF controls cell survival and angiogenesis	In the murine submandibular gland,essential for sympathetic innervation, it regulates cell survival, axonal growth, angiogenesis, remodeling, and healing via high- and low-affinity receptors [33].In this study, Neural Cell Adhesion Molecule (NCAM) In the group with intactinnervation,NCAM expression was significantly increased during the early stages of regeneration, suggesting importance of intact parasympathetic innervation in promoting ductal cell proliferation and overall regeneration of the submandibular gland [34]. The study showed reduced trkAand p75NTR protein levels and sympathetic axon density in NGF+/– mice, impacting glandular innervation. Despite no significant change in NGF levels in sub mandibular salivary glands, pineal glands exhibited higher NGFvariability, indicating effects on sympathetic neuron survival [35]. Glial cell line-derived neurotrophic factor (GDNF) promotes the survival and proliferation of salivary gland stem cells, especially following irradiation, through activation of the GDNF-RET signaling pathway [36].
Integrins and Laminin1	Int-3, Int-1 for polarity; Int-6 and Laminin1 for ECM contact and branching morphogenesis	3β1 integrin deficiency in embryonic SMGs causes basement membrane defects, acinar disorganization, and mucin increase, while Lama5 deficiency disrupts epithelial organization and delays development by E17.5 [37]. Another study reports that α3β1 integrin is crucial for salivary gland cell differentiation, with its absence disrupting ECM components like laminin and adhesion molecules such as E-cadherin [38].Another study shows β1 and β4 integrins drive salivary gland development, while β3 supports vascular development, underscoring their role in morphogenesis [39].
Shh expression and its correlation with Eda levels	Regulates Shh expression, promotes branching morphogenesis and inhibition of Hh signaling	A study suggested that Shh is critical downstream mediator of Ectodysplasin (Eda) signaling [40].In another study it was reported that Eda signaling isa key regulator of Shh,which in turn drives SMG branching morphogenesis [41]. Another study found that Shh transcript levels were reduced but not absent in Eda–/– glands, suggesting involvement of additional regulatory factors. Recombinant Shh increased branching in Eda–/– gland showing Eda-dependent Shh signaling in salivary gland development [42].Kit signaling cells influence keratin 14gene which after injury helps in regenerating both acini and ducts [53].
Sjögren's Syndrome and Radiation	Characterized by low Laminin-1, androgens (integrin α1 and α2) autoimmune epithelitis, and radiation-induced Salivary gland damage	The findings of these studies suggested SOX2 nerve-dependent mechanism are playing important role for regenerating damaged salivary glands, especially after injury caused by radiation [68].In vitro study findings suggested that submandibular gland's stems cells that provide potential for regeneration [69].Androgens increased integrin α1 and α2 subunits in salivary gland cells and healthy tissues but not in Sjögren's syndrome SS glands, where defective regulation contributes to acinar atrophy and ductal hyperplasia [70]. In another study found that KIT and KRT14 shared progenitor population in the salivary glandthat plays a critical role in ductal system maturation during development. Suggesting that it supports Salivary gland homeostasis and regeneration.Potentially playing an important role in regeneration post radiation [72].

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DISCUSSION

The study of salivary gland tissue engineering is advancing rapidly due to its impact on oral health and quality of life. This review explores molecular mechanisms, pathologies, and regenerative strategies for restoring salivary gland function, highlighting current challenges and future directions in the field [26, 27]. Understanding the molecular pathways involved in salivary gland development, maturation, and regeneration is essential for effective therapeutic interventions. The review highlights key pathways such as FGF, Wnt, Hedgehog (Hh), and Notch signaling are crucial for salivary gland homeostasis, repair, and regeneration [77-79]. The interplay of these pathways is crucial for cellular differentiation, proliferation, and function, essential for maintaining SG integrity. Dysregulation can lead to SG disorders, highlighting the need for targeted molecular therapies to restore normal function [80]. The high prevalence of SG dysfunction, especially xerostomia, highlights the need for effective treatments. Conditions like Sjögren's syndrome and radiation-induced damage lead to chronic dry mouth, with current treatments being mainly palliative. This review emphasizes the importance of developing regenerative therapies to address the underlying causes of SG dysfunction [81]. Tissue engineering for SG regeneration combines cells, bioactive substances, and biomaterials to create functional substitutes. The review highlights the promise of stem cell therapies, especially SG-derived stem/progenitor cells, and advances in scaffold materials and 3D culturing techniques for developing functional SG models [82, 83]. Gene therapy represents another innovative approach, particularly for addressing radiation-induced SG damage [84]. Gene therapies targeting specific molecular pathways could restore normal salivation by enhancing the regenerative capacity of salivary gland cells. Additionally, biomimetic models and 3D tissue cultures are valuable for studying salivary gland function and disease, offering insights into how the microenvironment influences cellular behavior and regeneration [85, 86]. These models can also facilitate the development of personalized medicine approaches; tailoring treatments to individual patients' needs. Despite progress, challenges in SG tissue engineering include cellular differentiation, scaffold design, and tissue integration. Future research must refine technologies, explore novel biomaterials, and optimize stem cell and gene therapy protocols, ensuring safety and efficacy through rigorous testing.

CONCLUSIONS

This systematic review highlighted the potential of stem cell and gene therapies in salivary gland (SG) tissue engineering, emphasizing the need for targeted approaches to restore SG function. It outlines molecular mechanisms underlying SG development and regeneration. Continued research promises effective, long-term solutions for SG-related conditions, enhancing oral health and quality of life.

Authors Contribution

Conceptualization: ZUDA
Methodology: MR, FJ, ZUDA
Formal analysis: MR
Writing, review and editing: SUK, TR

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Pillai S, Munguia-Lopez JG, Tran SD. Bioengineered Salivary Gland Microtissues— A Review of 3D Cellular Models and their Applications. American Chemical Society Applied Bio Materials. 2024 Apr; 7(5): 2620-36. doi: 10.1021/acsabm.4c00028.

[2] Almansoori AA, Kim B, Lee JH, Tran SD. Tissue engineering of oral mucosa and salivary gland: disease modeling and clinical applications. Micromachines.2020 Nov; 11(12): 1066. doi: 10.3 390/ mi11121066.

[3] Rose C and Olley RC. Patient preventive advice to mitigate signs and symptoms of tooth wear. Dental Update.2024Jun;51(6):422-6.doi:10.1296 8/denu. 2024.51.6.422.

[4] Villa A, Wolff A, Narayana N, Dawes C, Aframian DJ, Lynge Pedersen AM *et al.* World Workshop on Oral Medicine VI:a systematic review of medication-induced salivary gland dysfunction. Oral Diseases.2016Jul;22(5):365-82. doi: 10.1111/ odi.12402.

[5] Chery G. Understanding Sjögren's Syndrome as a Systemic Autoimmune Disorder. State University of New York at Albany; 2022.

[6] Ferreira JN, Rungarunlert S, Urkasemsin G, Adine C, Souza GR. Three-dimensional bioprinting nanotechnologies towards clinical application of stem cells and their secretome in salivary gland regeneration.Stem Cells International.2016 Dec;

DOI: https://doi.org/10.54393/pjhs.v5i12.1755

2016(1): 7564689. doi: 10.1155/2016/7564689.

[7] Mercadante V, Jensen SB, Smith DK, Bohlke K, Bauman J, Brennan MT *et al*. Salivary gland hypofunction and/or xerostomia induced by nonsurgical cancer therapies: ISOO/MASCC/ASCO guideline. Journal of Clinical Oncology.2021 Sep;39 (25): 2825-43. doi: 10.1200/JCO.21.01208.

[8] Parisis D, Chivasso C, Perret J, Soyfoo MS, Delporte C. Current state of knowledge on primary Sjögren's syndrome, an autoimmune exocrinopathy. Journal of Clinical Medicine.2020 Jul; 9(7): 2299. doi: 10.3390/jcm9072299.

[9] Seo YJ, Lilliu MA, Abu Elghanam G, Nguyen TT, Liu Y, Lee JC *et al.* Cell culture of differentiated human salivary epithelial cells in a serum-free and scalable suspension system: The salivary functional units model. Journal of Tissue Engineering and Regenerative Medicine.2019 Sep; 13(9): 1559-70. doi: 10.1002/term.2908.

[10] Baum BJ, Wang S, Cukierman E, Delporte C, Kagami H, Marmary Y *et al.* Re-engineering the functions of a terminally differentiated epithelial cell in vivo. Annals of the New York Academy of Sciences. 1999 Jun; 875(1): 294-300.doi: 10.1111/j.1749-6632.1999.tb08512.x

[11] Barrows CM, Wu D, Farach-Carson MC, Young S. Building a functional salivary gland for cell-based therapy: more than secretory epithelial acini. Tissue Engineering Part A. 2020 Dec; 26(23-24): 1332-48. doi: 10.1089/ten.tea.2020.0184.

[12] Blitzer GC, Rogus-Pulia NM, Mattison RJ, Varghese T, Ganz O, Chappell R *et al.* Marrow-Derived Autologous Stromal Cells for the Restoration of Salivary Hypofunction (MARSH): Study protocol for a phase 1 dose-escalation trial of patients with xerostomia after radiation therapy for head and neck cancer: MARSH: Marrow-Derived Autologous Stromal Cells for the Restoration of Salivary Hypofunction. Cytotherapy. 2022 May; 24(5): 534-43. doi: 10.1016/j.jcyt.2021.11.003.

[13] Adine C, Ng KK, Rungarunlert S, Souza GR, Ferreira JN. Engineering innervated secretory epithelial organoids by magnetic three-dimensional bioprinting for stimulating epithelial growth in salivary glands. Biomaterials.2018 Oct; 180: 52-66. doi: 10.1016/j.biomaterials.2018.06.011.

[14] Nam K, Wang CS, Maruyama CL, Lei P, Andreadis ST, Baker OJ. L1 peptide-conjugated fibrin hydrogels promote salivary gland regeneration. Journal of Dental Research. 2017 Jul; 96(7): 798-806. doi: 10.1177/0022034517695496.

[15] Lombaert IM, Brunsting JF, Wierenga PK, Faber H, Stokman MA, Kok T *et al.* Rescue of salivary gland function after stem cell transplantation in irradiated glands. PLOS One. 2008 Apr; 3(4): e2063. doi: 10.1371/journal.pone.0002063.

[16] Nanduri LS, Lombaert IM, Van Der Zwaag M, Faber H, Brunsting JF, Van Os RP *et al.* Salisphere derived c-Kit+ cell transplantation restores tissue homeostasis in irradiated salivary gland. Radiotherapy and Oncology. 2013 Sep; 108(3): 458-63. doi: 10.1016/j.radonc.2013.05.020.

[17] Grønhøj C, Jensen DH, Vester-Glowinski P, Jensen SB, Bardow A, Oliveri RS *et al.* Safety and efficacy of mesenchymal stem cells for radiation-induced xerostomia: a randomized, placebo-controlled phase 1/2 trial (MESRIX). International Journal of Radiation Oncology* Biology* Physics.2018 Jul; 101(3): 581-92. doi: 10.1016/j.ijrobp.2018.02.034.

[18] Lynggaard CD, Grønhøj C, Jensen SB, Christensen R, Specht L, Andersen E *et al.* Long-term safety of treatment with autologous mesenchymal stem cells in patients with radiation-induced xerostomia: primary results of the MESRIX phase I/II randomized trial. Clinical Cancer Research. 2022 Jul; 28(13): 2890-7. doi: 10.1158/1078-0432.CCR-21-4520.

[19] Ozdemir T, Fowler EW, Liu S, Harrington DA, Witt RL, Farach-Carson MC *et al.* Tuning hydrogel properties to promote the assembly of salivary gland spheroids in 3D. ACS Biomaterials Science & Engineering. 2016 Dec; 2(12): 2217-30. doi: 10.1021/acsbiomaterials.6b00419.

[20] Shubin AD, Felong TJ, Schutrum BE, Joe DS, Ovitt CE, Benoit DS. Encapsulation of primary salivary gland cells in enzymatically degradable poly(ethylene glycol) hydrogels promotes acinar cell characteristics. Acta Biomaterialia.2017 Mar; 50: 437-49. doi: 10.1016/j.actbio.2016.12.049.

[21] Shimizu O, Yasumitsu T, Shiratsuchi H, Oka S, Watanabe T, Saito T *et al.* Immunolocalization of FGF-2,-7,-8,-10 and FGFR-1-4 during regeneration of the rat submandibular gland. Journal of Molecular Histology. 2015 Oct; 46: 421-9. doi: 10.1007/s10735-015-9631-6.

[22] Hoffman MP, Kidder BL, Steinberg ZL, Lakhani S, Ho S, Kleinman HK *et al.* Gene expression profiles of mouse submandibular gland development: FGFR1 regulates branching morphogenesis in vitro through BMP-and FGF-dependent mechanisms.2002 Dec; 129(24): 5767-78. doi: 10.1242/dev.00172.

[23] Hai B, Yang Z, Millar SE, Choi YS, Taketo MM, Nagy A, Liu F. Wnt/β-catenin signaling regulates postnatal development and regeneration of the salivary gland. Stem cells and development. 2010 Nov 1;19(11):1793-

DOI: https://doi.org/10.54393/pjhs.v5i12.1755

801. doi: 10.1089/scd.2009.0499

[24] Matsumoto S, Kurimoto T, Taketo MM, Fujii S, Kikuchi A. The WNT/MYB pathway suppresses KIT expression to control the timing of salivary proacinar differentiation and duct formation. Development. 2016 Jul; 143(13): 2311-24. doi: 10.1242/dev.134486.

[25] Hu L, Du C, Yang Z, Yang Y, Zhu Z, Shan Z et al. Transient activation of hedgehog signaling inhibits cellular senescence and inflammation in radiated swine salivary glands through preserving resident macrophages. International Journal of Molecular Sciences.2021 Dec; 22(24): 13493. doi: 10.3390 /ijms222413493.

[26] Wells KL, Mou C, Headon DJ, Tucker AS. Recombinant EDA or Sonic Hedgehog rescue the branching defect in Ectodysplasin A pathway mutant salivary glands in vitro. Developmental Dynamics.2010 Oct; 239(10): 267 4-84. doi: 10.1002/dvdy.22406

[27] Zhao Q, Zhang L, Hai B, Wang J, Baetge CL, Deveau MA *et al.* Transient activation of the Hedgehog-Gli pathway rescues radiotherapy-induced dry mouth via recovering salivary gland resident macrophages. Cancer Research. 2020 Dec; 80(24): 5531-42. doi: 10.1158/0008-5472.CAN-20-0503.

[28] Hai B, Qin L, Yang Z, Zhao Q, Shangguan L, Ti X *et al.* Transient activation of hedgehog pathway rescued irradiation-induced hyposalivation by preserving salivary stem/progenitor cells and parasympathetic innervation. Clinical Cancer Research. 2014 Jan; 20(1): 140-50. doi: 10.1158/1078-0432.CCR-13-1434.

[29] Melnick M, Phair RD, Lapidot SA, Jaskoll T. Salivary gland branching morphogenesis: a quantitative systems analysis of the Eda/Edar/NFκB paradigm. BioMed Central Developmental Biology. 2009 Dec; 9: 1-22. doi: 10.1186/1471-213X-9-32.

[30] Dang H, Lin AL, Zhang B, Zhang HM, Katz MS, Yeh CK. Role for Notch signaling in salivary acinar cell growth and differentiation. Developmental dynamics: an official publication of the American Association of Anatomists.2009 Mar; 238(3): 724-31. doi: 10.100 2/dvdy.21875.

[31] Imatani A and Callahan R. Identification of a novel NOTCH-4/INT-3 RNA species encoding an activated gene product in certain human tumor cell lines. Oncogene. 2000 Jan; 19(2): 223-31. doi: 10.103 8/sj.onc.1203295.

[32] Mikkola ML. Molecular aspects of hypohidrotic ectodermal dysplasia. American Journal of Medical Genetics Part A.2009 Sep; 149(9): 2031-6. doi: 10.100 2/ajmg.a.32855.

[33] Schenck K, Schreurs O, Hayashi K, Helgeland K. The role of nerve growth factor (NGF) and its precursor forms in oral wound healing. International Journal of Molecular Sciences.2017 Feb; 18(2): 386. doi: 10.339 0/ijms18020386.

[34] Wang X, Li Z, Shao Q, Zhang C, Wang J, Han Z *et al.* The intact parasympathetic nerve promotes submandibular gland regeneration through ductal cell proliferation. Cell Proliferation. 2021 Jul; 54(7): e13078. doi: 10.1111/cpr.13078.

[35] Næsse EP, Schreurs O, Messelt E, Hayashi K, Schenck K. Distribution of nerve growth factor, pro-nerve growth factor, and their receptors in human salivary glands. European Journal of Oral Sciences. 2013 Feb; 121(1): 13-20. doi: 10.1111/eos.12008.

[36] Peng X, Varendi K, Maimets M, Andressoo JO, Coppes RP. Role of glial-cell-derived neurotrophic factor in salivary gland stem cell response to irradiation. Radiotherapy and Oncology.2017 Sep; 124(3): 448-54. doi: 10.1016/j.radonc.2017.07.008.

[37] Kadoya YU and Yamashina SH. Distribution of alpha 6 integrin subunit in developing mouse submandibular gland. Journal of Histochemistry & Cytochemistry. 1993 Nov; 41(11): 1707-14. doi: 10.1177/41.11.8409377.

[38] Menko AS, Kreidberg JA, Ryan TT, Van Bockstaele E, Kukuruzinska MA. Loss of α3β1 integrin function results in an altered differentiation program in the mouse submandibular gland. Developmental dynamics: an official publication of the American Association of Anatomists. 2001 Apr; 220(4): 337-49. doi: 10.1002/dvdy.1114.

[39] Lourenço SV and Kapas S. Integrin expression in developing human salivary glands. Histochemistry and Cell Biology. 2005 Nov; 124: 391-9. doi: 10.1007/ s00418-005-0784-3.

[40] Pummila M, Fliniaux I, Jaatinen R, James MJ, Laurikkala J, Schneider P *et al.* Ectodysplasin has a dual role in ectodermal organogenesis: inhibition of Bmp activity and induction of Shh expression. 2007 Jan; 134(1): 117-25. doi: 10.1242/dev.02708.

[41] Häärä O, Fujimori S, Schmidt-Ullrich R, Hartmann C, Thesleff I, Mikkola ML. Ectodysplasin and Wnt pathways are required for salivary gland branching morphogenesis. Development. 2011 Jul; 138(13): 2681-91. doi: 10.1242/dev.057711.

[42] Wells KL, Mou C, Headon DJ, Tucker AS. Recombinant EDA or Sonic Hedgehog rescue the branching defect in Ectodysplasin A pathway mutant salivary glands in vitro. Developmental Dynamics.2010 Oct; 239(10): 267 4-84. doi: 10.1002/dvdy.22406.

[43] Chen Z, Chen X, Zhu B, Yu H, Bao X, Hou Y *et al.* TGF-β1 Triggers Salivary Hypofunction via Attenuating Protein Secretion and AQP5 Expression in Human Submandibular Gland Cells.Journal of Proteome

DOI: https://doi.org/10.54393/pjhs.v5i12.1755

Research. 2023 Aug; 22(9): 2803-13. doi: 10.102 1/acs.jproteome.3c00052.
[44] Porcheri C and Mitsiadis TA. Physiology, pathology and regeneration of salivary glands. Cells. 2019 Aug; 8(9): 976. doi: 10.3390/cells8090976.
[45] Emmerson E, Knox SM. Salivary gland stem cells: a review of development, regeneration and cancer. genesis. 2018; 56(5): e23211. doi: 10.1002/dvg.23211.
[46] Holmberg KV and Hoffman MP. Anatomy, biogenesis and regeneration of salivary glands. Saliva: secretion and functions.2014 May; 24: 1-3. doi: 10.1159/ 000 358776.
[47] Pedersen AM, Sørensen CE, Proctor GB, Carpenter GH, Ekström J. Salivary secretion in health and disease. Journal of Oral Rehabilitation. 2018 Sep; 45(9): 730-46. doi: 10.1111/joor.12664.
[48] Gervais EM, Sequeira SJ, Wang W, Abraham S, Kim JH, Leonard D *et al.* Par-1b is required for morphogenesis and differentiation of myoepithelial cells during salivary gland development. Organogenesis. 2016 Oct; 12(4): 194-216. doi: 10.1080/15476278.2016.1252887.
[49] Wu D, Chapela PJ, Barrows CM, Harrington DA, Carson DD, Witt RL *et al.* MUC1 and polarity markers INADL and SCRIB identify salivary ductal cells. Journal of Dental Research.2022 Jul; 101(8): 983-91. doi: 10.1177/0022 0 345221076122.
[50] Brazen B and Dyer J. Histology, salivary glands. 2019.
[51] Proctor GB and Carpenter GH. Salivary secretion: mechanism and neural regulation. Saliva: Secretion and functions. 2014; 24: 14-29. doi: 10.1159/000358781.
[52] Khalafalla MG, Woods LT, Jasmer KJ, Forti KM, Camden JM, Jensen JL *et al.* P2 receptors as therapeutic targets in the salivary gland: from physiology to dysfunction. Frontiers in Pharmacology. 2020 Mar; 11: 222. doi: 10.3389/fphar.2020.00222.
[53] Rugel-Stahl A, Elliott ME, Ovitt CE. Ascl3 marks adult progenitor cells of the mouse salivary gland. Stem Cell Research.2012 May; 8(3): 379-87. doi: 10.1016/j .scr .2012.01.002.
[54] Brosky ME. The role of saliva in oral health: strategies for prevention and management of xerostomia. The Journal of Supportive Oncology. 2007 May; 5(5): 215-25.
[55] Smith CH, Boland B, Daureeawoo Y, Donaldson E, Small K, Tuomainen J. Effect of aging on stimulated salivary flow in adults. Journal of the American Geriatrics Society. 2013 May; 61(5): 805-8. doi: 10.1111/jgs.12219.
[56] Tanaka J and Mishima K. Application of regenerative medicine to salivary gland hypofunction. Japanese Dental Science Review. 2021 Nov; 57: 54-9. doi: 10.10 16/j.jdsr.2021.03.002.
[57] Nelson J, Manzella K, Baker O. Current cell models for bioengineering a salivary gland: a mini-review of emerging technologies. Oral Diseases. 2013 Apr; 19(3): 236-44. doi: 10.1111/j.1601-0825.2012.01958.x.
[58] Jaskoll T, Leo T, Witcher D, Ormestad M, Astorga J, Bringas Jr P *et al.* Sonic hedgehog signaling plays an essential role during embryonic salivary gland epithelial branching morphogenesis. Developmental dynamics: an official publication of the American Association of Anatomists. 2004 Apr; 229(4): 722-32. doi: 10.1002/dvdy.10472.
[59] Bolk K, Mueller K, Phalke N, Walvekar RR. Management of Benign salivary gland conditions. Surgical Clinics. 2022 Apr;102(2): 209-31. doi: 10.1016/j. suc.2022. 01.001.
[60] Tzioufas AG and Voulgarelis M. Update on Sjögren's syndrome autoimmune epithelitis: from classification to increased neoplasias. Best Practice & Research Clinical Rheumatology. 2007 Dec; 21(6): 989-1010. doi: 10.1016/j.berh.2007.09.001.
[61] Pynnonen MA, Gillespie MB, Roman B, Rosenfeld RM, Tunkel DE, Bontempo L *et al.* Clinical practice guideline: evaluation of the neck mass in adults. Otolaryngology-Head and Neck Surgery.2017 Sep; 157 (2): 30. doi: 10.1177/0194599817722550.
[62] Luitje ME, Israel AK, Cummings MA, Giampoli EJ, Allen PD, Newlands SD *et al.* Long-term maintenance of acinar cells in human submandibular glands after radiation therapy. International Journal of Radiation Oncology* Biology* Physics. 2021 Mar; 109(4): 1028-39. doi: 10.1016/j.ijrobp.2020.10.037.
[63] Baum BJ, Alevizos I, Chiorini JA, Cotrim AP, Zheng C. Advances in salivary gland gene therapy-oral and systemic implications. Expert Opinion on Biological Therapy.2015 Oct; 15(10): 1443-54. doi: 10.1517/14712 598. 2015.1064894.
[64] Donnelly H, Salmeron-Sanchez M, Dalby MJ. Designing stem cell niches for differentiation and self-renewal. Journal of the Royal Society Interface. 2018 Aug; 15(145): 20180388. doi: 10.1098/rsif.2018.0388.
[65] Mousaei Ghasroldasht M, Seok J, Park HS, Liakath Ali FB, Al-Hendy A. Stem cell therapy: from idea to clinical practice. International Journal of Molecular Sciences. 2022 Mar; 23(5): 2850. doi: 10.3390/ijms23052850.
[66] Emmerson E, May AJ, Berthoin L, Cruz-Pacheco N, Nathan S, Mattingly AJ *et al.* Salivary glands regenerate after radiation injury through SOX2-mediated secretory cell replacement. European Molecular Biology Organization Molecular Medicine.2018 Mar; 10(3): e8051. doi: 10.15 252/emmm. 201708051.

DOI: https://doi.org/10.54393/pjhs.v5i12.1755

[67] Feng J, van der Zwaag M, Stokman MA, van Os R, Coppes RP. Isolation and characterization of human salivary gland cells for stem cell transplantation to reduce radiation-induced hyposalivation. Radiotherapy and Oncology.2009 Sep; 92(3): 466-71. doi: 10.1016/j.radonc.2009.06.023.

[68] Ninche N, Kwak M, Ghazizadeh S. Diverse epithelial cell populations contribute to the regeneration of secretory units in injured salivary glands. Development.2020 Oct; 147(19): dev192807. doi: 10.1101/2020.06. 29.177733.

[69] Laine M, Virtanen I, Salo T, Konttinen YT. Segment-specific but pathologic laminin isoform profiles in human labial salivary glands of patients with Sjögren's syndrome. Arthritis & Rheumatism.2004 Dec; 50(12): 3968-73. doi: 10.1002/art.20730.

[70] Porola P, Laine M, Virtanen I, Pöllänen R, Przybyla BD, Konttinen YT. Androgens and integrins in salivary glands in Sjögren's syndrome. The Journal of Rheumatology. 2010 Jun; 37(6): 1181-7. doi: 10.389 9/jrheum.091354.

[71] Bullard T, Koek L, Roztocil E, Kingsley PD, Mirels L, Ovitt CE. Ascl3 expression marks a progenitor population of both acinar and ductal cells in mouse salivary glands. Developmental Biology. 2008 Aug; 320 (1): 72-8. doi: 10.1016/j.ydbio.2008.04.018.

[72] May AJ, Cruz-Pacheco N, Emmerson E, Gaylord EA, Seidel K, Nathan S *et al*. Diverse progenitor cells preserve salivary gland ductal architecture after radiation-induced damage. Development.2018 Nov; 145(21): dev166363. doi: 10.1242/dev.166363.

[73] Matheu A, Collado M, Wise C, Manterola L, Cekaite L, Tye AJ *et al*. Oncogenicity of the developmental transcription factor Sox9. Cancer Research. 2012 Mar; 72(5): 1301-15. doi: 10.1158/0008-5472.CAN-11-3660.

[74] Ivanov SV, Panaccione A, Nonaka D, Prasad ML, Boyd KL, Brown B *et al*. Diagnostic SOX10 gene signatures in salivary adenoid cystic and breast basal-like carcinomas. British Journal of Cancer. 2013 Jul; 109(2): 444-51. doi: 10.1038/bjc.2013.326.

[75] Redman RS. On approaches to the functional restoration of salivary glands damaged by radiation therapy for head and neck cancer, with a review of related aspects of salivary gland morphology and development. Biotechnic & Histochemistry. 2008 Jan; 83(3-4): 103-30. doi: 10.1080/10520290802374683.

[76] Häärä O, Fujimori S, Schmidt-Ullrich R, Hartmann C, Thesleff I, Mikkola ML. Ectodysplasin and Wnt pathways are required for salivary gland branching morphogenesis. Development. 2011 Jul; 138(13): 2681-91. doi: 10.1242/dev.057711.

[77] Wells KL, Mou C, Headon DJ, Tucker AS. Recombinant EDA or Sonic Hedgehog rescue the branching defect in Ectodysplasin A pathway mutant salivary glands in vitro. Developmental Dynamics.2010 Oct; 239(10): 2674-84. doi: 10.1002/dvdy.22406.

[78] Borkosky SS, Nagatsuka H, Orita Y, Tsujigiwa H, Yoshinobu J, Gunduz M *et al*. Sequential expressions of Notch1, Jagged2 and Math1 in molar tooth germ of mouse. Biocell. 2008 Dec; 32(3): 251-7. doi: 10.326 04/biocell.2008.32.251.

[79] Mitsiadis TA, Graf D, Luder H, Gridley T, Bluteau G. BMPs and FGFs target Notch signalling via jagged 2 to regulate tooth morphogenesis and cytodifferentiation. Development. 2010 Sep; 137(18): 3025-35. doi: 10.1242/dev.049528.

[80] Qu J, Song M, Xie J, Huang XY, Hu XM, Gan RH *et al*. Notch2 signaling contributes to cell growth, invasion, and migration in salivary adenoid cystic carcinoma. Molecular and Cellular Biochemistry. 2016 Jan; 411: 135-41. doi: 10.1007/s11010-015-2575-z.

[81] Błochowiak K. Co-Existence of Dry Mouth, Xerostomia, and Focal Lymphocytic Sialadenitis in Patients with Sjögren's Syndrome. Applied Sciences. 2024 Jun; 14(13): 5451. doi: 10.3390/app14135451.

[82] Chibly AM, Aure MH, Patel VN, Hoffman MP. Salivary gland function, development, and regeneration. Physiological reviews. 2022 Jul; 102(3): 1495-552. doi: 10.1152/physrev.00015.2021.

[83] Hajiabbas M, D'Agostino C, Simińska-Stanny J, Tran SD, Shavandi A, Delporte C. Bioengineering in salivary gland regeneration. Journal of Biomedical Science. 2022 Jun; 29(1): 35. doi: 10.1186/s12929-022-00819-w.

[84] Aframian DJ amd Palmon A. Current status of the development of an artificial salivary gland. Tissue Engineering Part B: Reviews. 2008 Jun; 14(2): 187-98. doi: 10.1089/ten.teb.2008.0044.

[85] Sui Y, Zhang S, Li Y, Zhang X, Hu W, Feng Y *et al*. Generation of functional salivary gland tissue from human submandibular gland stem/progenitor cells. Stem Cell Research & Therapy. 2020 Dec; 11: 1-3. doi: 10.1186/s13287-020-01628-4.

[86] Wang T, Huang Q, Rao Z, Liu F, Su X, Zhai X *et al*. Injectable decellularized extracellular matrix hydrogel promotes salivary gland regeneration via endogenous stem cell recruitment and suppression of fibrogenesis. Acta Biomaterialia. 2023 Oct; 169: 256-72. doi: 10.1016/j.actbio.2023.08.003.

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Systematic Review

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Diagnostic Modalities in Oral Pathology: Integrating Advance Diagnostic Techniques to Differentiate Malignant and Benign Lesions

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ABSTRACT

Diagnosis and treatment planning in oral pathology is dependent on the differentiation of malignant from benign oral lesions. Clinical, radiographic and histopathological methods combined provide comprehensive diagnosis and patient care property. **Objectives:** To describe how the combined use of clinical assessments, imaging modalities and histopathological techniques can be used together to improve the differentiation of oral lesions between malignant and benign pathologies. **Methods:** In this paper, a systematic review was conducted using PRISMA guidelines. Studies published between January 2013 and April 2024 were searched from databases including PubMed, Google Scholar and Semantic Scholar. After the screening, 51 met the inclusion criteria from a total of 112 articles initially screened. Sixteen studies were ultimately analysed that examined oral pathology diagnostic advancements utilizing a combination of clinical, radiographic, and histo-chemo-pathological approaches. **Results:** Combining clinical examinations with imaging techniques such as cone beam computed tomography, and histopathological evaluations increases the accuracy of oral lesion diagnosis. The integrated approaches reveal malignancies earlier and reduce misdiagnoses. Histopathological analysis was shown to be the gold standard, but even this can be improved with additional clinical and radiographic data. **Conclusions:** It was concluded that accurate diagnosis and differentiation of benign vs. malign oral lesions requires the integration of clinical, radiographic, and histopathological methods. Such a multi-modal approach will support early detection and consequent tailored treatment strategies that maximise the patient outcome.

INTRODUCTION

Oral lesions are difficult to diagnose properly due to their various presentations and similarities in morphological states when each state is distinct in terms of severity. Oral cancers are a major global health priority with a high incidence throughout certain regions, i.e., South Asia. Prevalence is further influenced by tobacco, areca nut and alcohol usage as risk factors, which are common in India, Pakistan and Sri Lanka [1, 2]. The burden of oral cancer makes it evident that diagnostic tools are required to differentiate between benign and malignant lesions at early stages with accuracy. Timely differentiation between benign and malignant lesions is critical for optimized and result oriented treatment [3]. This review will talk about diagnostic techniques which can make accurate early diagnostic and differentiation dreams come true. Moving forward, the current diagnostic practices are vastly based

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on clinical examination with histopathological analysis. Histopathology is regarded as the gold standard in pathological confirmation because it identifies abnormalities at a cellular level. It requires specialized laboratory resources and expertise for correct identification of tumor via this technique [4]. Similarly, cone beam computed tomography (CBCT) has been shown to emerge as a significant imaging technique. CBCT provides three-dimensional high-resolution imaging of the whole maxillofacial region with small percentage distortion, allowing detailed visualization of size, shape, and involvement of bone in lesions. It is another particularly useful modality for assessing bone-invasive lesions, which are a frequent sign of advanced malignancy [5]. Differentiating lesion types is also highly promising with another related imaging modality, multiphasic computed tomography (MCT) [6]. Optical coherence tomography (OCT) is noninvasive and its strength lies in providing high-resolution images of epithelial and sub-epithelial structures for the detection of malignant changes in oral tissues. Specific stains, like periodic Acid-Schiff (PAS) and Alcian blue, have been shown to enhance diagnostic clarity for specific lesion types as the tissue characteristics associated with more aggressive lesions stand out more clearly. These stains are also used by pathologists to assess hyalinization in oral sub-mucous fibrosis and fibrosis severity in salivary gland tumors, correlating those features with disease severity and recurrence risk [7]. Immunohistochemically markers such as Cluster of Differentiation 34 (CD34), and alpha-smooth muscle actin (α-SMA) are regularly used to determine tumor behaviour in oral squamous cell carcinoma (OSCC) and can give vital information regarding aggressiveness and guide more precise treatment planning [8]. Even if present interventions help in diagnosis there is a continuous need for improvement in accuracy. Often the clinical examination is insufficient since benign and malignant lesions can share similar morphological patterns, potentially resulting in misdiagnoses [4]. Biopsies required for histopathological analysis are uncomfortable, and invasive and may not be feasible for everyone despite it being considered as a standardized treatment. [9]. Cone-beam computer tomography (CBCT) and optical coherence tomography (OCT) show accurate diagnostic results but their standalone application is not enough with advancing day and age. CBCT focuses on bony involvement while OCT lags in diagnostic accuracy when used alone. High-cost imaging and staining techniques make them limited to be used by resourceful healthcare systems only [10]. Overall any technique when used in isolation is insufficient and thus requires to be used in combination to enhance accuracy. Moreover, studies demonstrate how incorporating advanced imaging enables the integration of histopathological analysis, but there is a clear need to develop comprehensive frameworks that bring together such modalities. In particular, many current studies are confined to isolated populations in high-prevalence areas, and little research has been done on the adaptability and efficacy of these integrated strategies across a variety of demographic and geographic settings. To overcome these limitations research has also been conducted in recent decades in which the technique has been developed to employ the power of the clinical method, radiographic technique and histopathological method together to provide high diagnostic accuracy. When teamed with artificial intelligence algorithms, such as artificial neural networks (ANN) and support vector machines, OCT has been shown to have an over 90 percent sensitivity for identifying early-stage malignancies. In settings where biopsy is difficult or limited, the ability to confirm the immune phenotype without requiring a biopsy is especially valuable [10, 11]. But still, there is a need to integrate these studies to get a better picture of the current situation of interventions for oral lesions.

This study aims to bridge current gaps in the literature by evaluating the combined efficacy of these techniques in multiple populations (for generalizability) and diagnostic challenges. This study synthesizes and reviews findings for multimodal diagnostic approaches and makes a case in favor of an integrative framework that combines advancing clinical assessment, advanced imaging methodologies and refined histopathologic techniques. Importantly, such an integrated diagnostic strategy not only improves accuracy but also has the potential to adapt to resource-rich as well as resource-limited healthcare settings.

METHODS

A systematic review was conducted as per the PRISMA guidelines between February 2024 to May 2024 to see the advancements made in differential diagnostic approaches of different oral lesions with benign and malignant predispositions. The transparency and rigour of the review process included two independent reviewers scouring databases central to oral pathology and diagnostic innovation, namely, PubMed, Google Scholar, and Semantic Scholar. In selecting these databases, the study looked for databases that had full coverage of published clinical, radiographic and histopathological research that could be pertinent to oral lesions. 70% of articles were taken from PubMed, 20% from Google Scholar and 10% from Semantic Scholar. The studies in the literature search were restricted to those between January 2013 to April 2024, using keywords such as "diagnostic techniques in oral lesions," "clinical differentiation of oral malignancies," "histopathology and oral lesions" and "radiographic imaging in oral diagnosis." Initially, 112 studies were identified. Reviewers screened the studies independently and

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selected studies to minimize bias and ensure relevance. Inclusion criteria demanded studies must contain articles which were based on multimodal approaches to diagnose oral lesions, must be within the last five years if included in a table and must contain complete data i.e. sample size, population, relatable intervention etc. Older studies, studies with incomplete data, studies with just abstract and title and studies with irrelevant data were excluded. After eliminating 10 duplicates, 102 studies were subject to preliminary screening. After screening 51 studies by title and abstract, these studies were excluded according to their evaluation as not relevant to oral lesion diagnosis, lack of comprehensiveness of methodology, or not fitting in the included criteria. Of the remaining 51 studies, all of which were focused on integrated diagnostic techniques, just 16 were selected based on the completion of data. To achieve quality filtering in this systematic review several statistical methods were used to test study quality and to keep the results trustworthy. Predefined quality assessment tools such as the Newcastle-Ottawa Scale (NOS) for observational studies, which grades studies according to selection, comparability and the assessment of the outcome, were used to evaluate each study. Cochrane Risk of Bias Tool was used for examining domains such as random sequence generation, allocation concealment, blinding, and selective outcome reporting in the cases of randomized controlled trials (RCTs). Furthermore, funnel plots and Egger's test were used to test for publication bias and asymmetries to test for study reporting bias. Heterogeneity was quantified across studies using the I^2 statistic as values greater than 50% indicate substantial heterogeneity and addressed this with random effects models. To strengthen the reliability of our conclusions regarding the diagnostic efficacy of integrated approaches for oral lesions, only high-quality (with low bias) studies were used to generate these methods ensuring that the contribution to the final analysis only came from high-quality studies with minimal bias. From each study, data were extracted including authorship, publication year, geographic focus, study design, diagnostic methodology and clinical outcome. The collection of studies included in this systematic analysis spanned a variety of regions including Asia, Europe, and the USA and included diagnostic advances in a variety of lesion types and populations. The findings confirmed the effectiveness of integrating clinical evaluations, imaging modalities such as cone beam computed tomography (CBCT) and histopathological methods for differential diagnosis of benign and malignant lesions, indicating that an integrative diagnostic approach leads to an improvement in early detection and treatment planning for oral pathologies. The application of the PRISMA method in the process of selecting the studies additionally subdivides the process into stages, such as identification, screening, quality assessment, and inclusion. From records recognized, 112 were considered, but eliminating duplicates made the number to 102 screened, of which 51 were considered for the study due to their diagnostic value. Of the 41 studies identified full literature review, only 16 satisfied all the inclusion criteria and were included in the final analysis, addressing the diagnostic applications of multimodal diagnostic techniques for oral lesions with malignant potential(Figure 1).

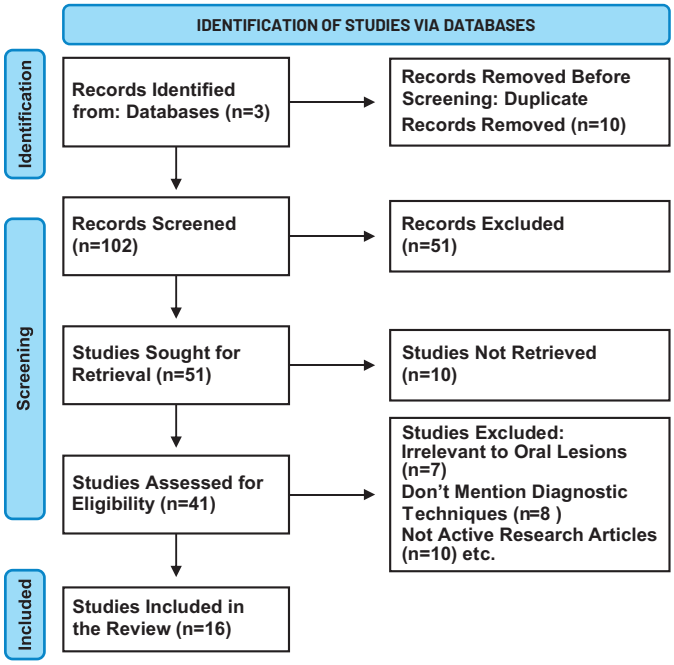

Figure 1: Studies Selection according to PRISMA guidelines

RESULTS

This systematic review by following PRISMA guidelines is based on 16 studies of the combined effectiveness of clinical, radiographic and histopathological techniques in differentiating benign from malignant oral lesions. The study was reviewed from various databases, with 65% percent of the studies taken from PubMed and 35% percent from Google Scholar and Semantic Scholar. The selected studies considered the diagnostic precision along with accuracy in early detection, as well as the application of specific modalities in oral pathology. To capture a comprehensive understanding of diagnostic advancements, the study designs included a mix of methodologies: Nine retrospective analyses, four prospective studies, and three observational studies on the synergistic effect of these diagnostic modalities. The role of advanced imaging techniques such as cone-beam computed tomography (CBCT) and multiphasic CT with machine learning for improving clinical and histopathological evaluations was emphasized in all the studies. It was found that combining multiple diagnostic techniques improves accuracy, sensitivity and specificity to a great degree. For example, such studies that combine cone beam computed tomography (CBCT) with clinical examination showed accuracy increases as high as 25%.

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OCT, in conjunction with AI-based algorithms, had over 90% sensitivity to identify early malignancy, and radio-mic models showed high diagnostic accuracy with the area under the curve (AUC) of 0.84 to 0.94 across the study. Further, when using hybrid AI models linking convolutional neural networks (CNN) with support vector machines (SVM), the diagnostic accuracies in certain lesion types reached over 99%. By underlining the superior diagnostic power of multimodal approaches, particularly when combined with advanced imaging and machine learning, these findings reinforce the need for clinicians to avoid an approach that neglects the combination of these two clinical capabilities. Hence these findings suggest the use of a multimodal diagnostic approach to the assessment of oral lesions. The accumulated evidence indicates that the incorporation of advanced imaging into clinical and histopathological assessment might soon become standard practice, leading to greater diagnostic precision and improved patient outcomes, particularly for early malignancy detection (Table 1).

Table 1: Studies on Diagnostic Approaches in Oral Pathology

Reference	Study Designs	Sample Size	Diagnostic Techniques	Key Findings	Conclusions
Nadeem *et al.*, [12]	Retrospective observational	90	Histopathology, special stains (PAS, Alcian blue, Safranin O, Picrosirius red)	Differential stains helped assess hyalinization severity and potential aggressiveness in oral lesions, showing significant correlations with disease severity in some cases	SOH and specific stains can help predict aggressiveness and recurrence potential in salivary gland tumours and fibrosis severity in OSMF
Sindhi *et al.*, [13]	Retrospective, cross-sectional	858	Clinical and histo-pathological comparison	Agreement between clinical and histopathological diagnoses was only 44.1%, with the highest agreement for odontogenic tumours and varying by lesion location	Histopathological confirmation is crucial for accurate diagnosis of oral lesions, especially for complex cases, underscoring the importance of biopsy
James *et al.*, [14]	Validation study	232 patients, 347 lesions	Optical Coherence Tomography (OCT) combined with ANN and SVM algorithms	OCT with AI yielded >90% sensitivity for oral cancer screening; high accuracy in distinguishing benign, dysplastic, and malignant lesions	OCT with automated algorithms is effective as a portable, low-cost diagnostic tool for resource-limited settings
Fati *et al.*, [15]	Observational study	5192 images	Hybrid AI methods combining CNN, SVM, and ANN with feature extraction (e.g., LBP, DWT)	Hybrid AI methods achieved 99.1% accuracy in OSCC detection based on histo-pathological images; effective in feature extraction and classification	Hybrid methods using CNN, SVM, and feature extraction are promising for early OSCC diagnosis through histological images
Verma *et al.*, [16]	Cross-sectional observational study	100	Histopathological analysis of biopsies	High prevalence of well-differentiated squamous cell arcinoma (47%), with a male predominance (76%) linked to lifestyle factors like tobacco use	Emphasizes the importance of histopathological examination and early diagnosis in improving outcomes for oral lesions and cancer
Yu *et al.*, [17]	Retrospective study	312	Multiphasic CT-based radio-mics with machine learning	LASSO-SVM model with three-phase CT radio-mics showed the highest AUC (0.936) in differentiating benign from malignant tumours.	Multiphasic CT-based radio-mics combined with machine learning can effectively distinguish between benign and malignant parotid tumours.
Orikpete *et al.*, [18]	Retrospective histopathologic study over 10 years	574 biopsies	Histopathologic examination and lesion categorization	Non-neoplastic lesions (68.5%) were more common, with pyogenic granuloma as the most frequent; benign lesions outnumbered malignant ones.	Histologic examination is critical for accurate diagnosis of gingival lesions due to the high frequency of non-neoplastic lesions.
Maqsood *et al.*, [19]	Cross-sectional study	80	Histological and immune-histochemical analysis using Cd34 and α-SMA markers	CD34 expression is significantly associated with OSCC histological grading; high α-SMA in poorly differentiated OSCC indicates aggressive behaviour.	CD34 and α-SMA are valuable in diagnosing OSCC and assessing tumour aggression, with prognostic significance in OSCC differentiation.
Czerninski *et al.*, [20]	Observational study	133	Clinical image evaluation	Half of the benign images were evaluated correctly; clinicians performed better than students, with diagnostic accuracy increasing by clinical experience and education level.	Emphasizing visual diagnostic parameters of malignancy is valuable for improving d iagnostic accuracy, especially in telehealth settings.

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Zheng *et al.*, [21]	Retrospective cohort study	388	CT-based radio-mics analysis	The SVM model showed the highest predictive efficiency with an AUC of 0.844 (training) and 0.840 (test). The combined model of radio mics and clinical features had the highest accuracy.	The combined radio-mics and clinical model is effective for distinguishing benign from malignant parotid tumours and enhances clinical decision-making.
Yu *et al.*, [22]	Multicentre retrospective	573	Deep learning on contrast-enhanced CT	Mobile Net V3 model showed the best performance with AUC improvement in radiologists' diagnostic accuracy, particularly assisting less experienced radiologists.	Deep learning models assist radiologists in distinguishing benign from malignant parotid tumours, enhancing diagnostic performance and supporting clinical decisions.
Sircan *et al.*, [23]	Pilot Study	47	Elastic Light Single-Scattering Spectroscopy (ELSSS)	ELSSS identified malignant lesions by negative spectral slopes, achieving 80% sensitivity and 94% specificity.	ELSSS shows potential as a non-invasive screening tool for oral lesions, potentially reducing unnecessary biopsies.
Obade *et al.*, [24]	Observational Study	44	Optical Coherence Tomography (OCT)	OCT detected structural differences in the keratin layer, epithelial layer, and basement membrane. A breached basement membrane in OSCC strongly indicated malignancy.	OCT is a non-invasive tool useful for differentiating benign and malignant oral lesions, especially through basement membrane analysis.
Xiang *et al.*, [25]	Retrospective Study	117	Dynamic Contrast-Enhanced MRI (DCE-MRI) with Histogram Analysis	TTP and MRE parameters successfully differentiated benign from malignant parotid tumours. Entropy and kurtosis were independent predictors of malignancy.	DCE-MRI histogram parameters, particularly entropyand kurtosis, are effective in identifying and classifying parotid tumours and distinguishing benign from malignant cases.
Takumi *et al.*, [26]	Retrospective study	42	Multi-parametric non-contrast MR imaging (ADC, TBF, APTSI)	APTSI was significantly higher in malignant lesions; combining ADC, TBF, and APTSI improved diagnostic accuracy.	Combining ADC, TBF, and APTSI is effective in differentiating malignant from benign salivary gland lesions.
Sripodok *et al.*, [27]	Retrospective cohort; decision tree model development	946 LGES of 14,487 biopsies	Decision tree model based on clinical characteristics (size, consistency, colour, age, duration)	Size, consistency, and duration were significant predictors of malignancy; malignant LGEs had lower diagnostic concordance than non-malignant LGEs.	The decision tree model aids in clinical differentiation between malignant and non-malignant LGEs.

DISCUSSION

This systematic review evaluated the effectiveness of combining clinical, radiographic and histopathological techniques along with the integration of AI techniques for diagnosing oral lesions. The primary goal was to assess how combination therapies and multimodal approaches improve the ability to discriminate between benign and malignant lesions, enhance accuracy and inform clinical decision-making. The findings not only support the use of integrated diagnostic techniques but also highlight their limitations in their universality, accessibility, and application in vast clinical settings. Several imaging advances have been identified as a promise in improving early diagnosis, especially in areas with limited histopathological resources. CBCT provides high-resolution, 3D imaging of the entire maxillofacial region and makes a detailed assessment of a lesion possible, including size, shape and bone involvement. Studies demonstrated its efficacy in identifying the invasiveness of lesions to bone with potential applications in early diagnosis of malignant cases [28, 29]. When combined with radio-mics and machine learning models, multiphasic computed tomography (CT) demonstrated high diagnostic accuracy, achieving over 90% specificity in certain lesion types. Support Vector Machines (SVM) and logistic regression models enhanced the distinction between malignant and benign tumors [30, 31]. In addition to CBCT and multiphasic CT, optical coherence tomography (OCT) offered non-invasive high-resolution imaging of epithelial and sub-epithelial structures. When it is combined with AI algorithms such as convolutional neural networks (CNNs), OCT achieves a sensitivity accuracy of up to 85% in diagnosing early tumors, especially in resource-limited settings [32, 33]. Furthermore, special stains periodic Acid-Schiff (PAS) and Alcian blue have been shown to improve diagnostic clarity by highlighting tissue properties associated with aggressive tumors. These methods

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improved the assessment of fibrosis and hyalinization which is associated with the severity of the disease and its recurrence risk [34, 35]. Immunochemical markers like CD34 and α-SMA were found to be valuable for evaluating tumor aggressiveness and guiding treatment planning in oral squamous cell carcinoma (OSCC) [19, 36]. In emerging techniques, Elastic Light Single Scattering Spectroscopy (ELSSS) showed promise as a non-invasive diagnostic method. It achieved a sensitivity of up to 80% and specificity of up to 94% in distinguishing between the two types of tumors as mentioned in the text through incorporating a special type of analysis. ELSSS has shown its potential to play a central role in oral lesion screening programs, especially under conditions when biopsy procedures are not available [37, 38]. This review supports the advantages of a multimodal approach for diagnosis as they proved to serve diagnostic precision for complex and advanced tumors. Imaging techniques like CBCT and radiomics are highly for elaborated anatomical analysis [39]. AI-based techniques enhance diagnostic accuracy in low-resource settings [40]. There are some limitations to these techniques along with their advantages such as high-resolution imaging techniques are customized for resourceful settings and require expensive equipment for working that can't be applied in regions of low income. Clinical and histopathological analysis use biopsies which are invasive and harmful and not suitable for everyone. Similarly, there are also limitations and gaps to this systematic review which are discussed as follows; Some studies were focused on specific populations or geographic regions, in which case their findings may not be generalizable. These studies were confined to high prevalence regions only therefore can't advocate for broader populations. Additionally, due to differences in imaging protocols, AI algorithms and histopathological standards across studies create heterogeneity in results and, therefore less comparable. The findings emphasize the potential of multimodal diagnostic strategies to enhance clinical results. CBCT and radio mics can be clinically implemented by providing precision lesion characterization, while OCT and ELSSS offer a non-invasive alternative to biopsies. Focus is needed on standardizing protocols across all clinical platforms by integration of clinical, imaging and histopathological methods to reduce variability and biasedness. Multicenter studies will benefit in coverage of larger demographic regions and will ensure global applicability.

CONCLUSIONS

It was concluded that overall, clinical, radiographic and histopathological integration is shown to substantially increase the diagnostic accuracy of lesions of the oral mucosa, facilitating earlier detection and improved patient outcomes. However, these findings are limited by restricted generalizability, as advanced imaging and AI-based techniques are limited to resource-rich settings, leaving underserved regions with low access. Future research should address these barriers by validating cost-effective mobile-based diagnostic tools based on cloud computing to reach further. Standardization should be introduced for globalized applicability i.e. combination of clinical, imaging and histopathological techniques. This integration will also aid in clinical practices by filling the drawbacks of each technique. Policymakers should prioritize funding for such projects. Furthermore, constructing lightweight AI protocols can enhance diagnostic consistency and reduce observer bias to extend their use throughout a variety of healthcare environments.

Authors Contribution

Conceptualization: KI, KF, MM
Methodology: KI, KF, MM, AUS, BK, MA, MAS
Formal analysis: KI, KF, MM
Writing review and editing: AUS, BK, MA, MAS

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Binmadi NO, Alhindi AA, Alsharif MT, Jamal BT, Mair YH. The value of a specialized second-opinion pathological diagnosis for oral and maxillofacial lesions. BMC Oral Health. 2023 Jun 9;23(1):378. doi:10.1186/s12903-023-03085-w

[2] Abati S, Sandri GF, Finotello L, Polizzi E. Differential diagnosis of pigmented lesions in the oral mucosa: A clinical based overview and narrative review. Cancers. 2024 Jul 8;16(13):2487. doi:10.3390/cancers16132487

[3] Parakh MK, Ulaganambi S, Ashifa N, Premkumar R, Jain AL. Oral potentially malignant disorders: clinical diagnosis and current screening aids: a narrative review. European Journal of Cancer Prevention. 2020 Jan 1;29(1):65-72. doi: 10.1097/CEJ.0000000000000510

[4] Walsh T, Macey R, Kerr AR, Lingen MW, Ogden GR, Warnakulasuriya S. Diagnostic tests for oral cancer and potentially malignant disorders in patients presenting with clinically evident lesions. Cochrane Database of Systematic Reviews. 2021(7). doi: 10.100

DOI: https://doi.org/10.54393/pjhs.v5i12.2535

2/14651858.CD010276.pub3

[5] Buenahora MR, Peraza-L A, Díaz-Báez D, Bustillo J, Santacruz I, Trujillo TG, Lafaurie GI, Chambrone L. Diagnostic accuracy of clinical visualization and light-based tests in precancerous and cancerous lesions of the oral cavity and oropharynx: a systematic review and meta-analysis. Clinical Oral Investigations. 2021 Jun;25:4145-59. doi: 10.1007/s00784-021-03825-7

[6] Chen F, Ge Y, Li S, Liu M, Wu J, Liu Y. Enhanced CT-based texture analysis and radiomics score for differentiation of pleomorphic adenoma, basal cell adenoma, and Warthin tumor of the parotid gland. Dentomaxillofacial Radiology. 2023 Jan 1;52(2):20220009. doi: 10.1259/dmfr.20220009

[7] Piludu F, Marzi S, Ravanelli M, Pellini R, Covello R, Terrenato I, Farina D, Campora R, Ferrazzoli V, Vidiri A. MRI-based radiomics to differentiate between benign and malignant parotid tumors with external validation. Frontiers in Oncology. 2021 Apr 27;11:656918. doi: 10.3389/fonc.2021.656918

[8] Kavyashree C, Vimala HS, Shreyas J. A systematic review of artificial intelligence techniques for oral cancer detection. Healthcare Analytics. 2024 Jan 22:100304. doi: 10.1016/j.health.2024.100304

[9] Jerjes W, Stevenson H, Ramsay D, Hamdoon Z. Enhancing Oral Cancer Detection: A Systematic Review of the Diagnostic Accuracy and Future Integration of Optical Coherence Tomography with Artificial Intelligence. Journal of Clinical Medicine. 2024 Sep 29;13(19):5822. doi: 10.3390/jcm13195822

[10] Dilsiz A, Gül SN. Investigation of Biopsied Non-Plaque-Induced Gingival Lesions in a Turkish Population: A 5-Year Retrospective Study. The Eurasian Journal of Medicine. 2023 Jun;55(2):100. doi: 10.5152/eurasianjmed.2023.22063

[11] Alessandrini L, Astolfi L, Daloiso A, Sbaraglia M, Mondello T, Zanoletti E, Franz L, Marioni G. Diagnostic, prognostic, and therapeutic role for angiogenesis markers in head and neck squamous cell carcinoma: a narrative review. International Journal of Molecular Sciences. 2023 Jun 27;24(13):10733. doi: 10.3390/ijms241310733

[12] Nadeem AM, Nagaraj B, Jagadish DA, Shetty D, Lakshminarayana S, Augustine D, Rao RS. A histopathology-based assessment of biological behavior in oral hyalinizing extraosseous lesions by differential stains. The Journal of Contemporary Dental Practice. 2021 Sep 28;22(7):812-28. doi: 10.5005/jp-journals-10024-3131

[13] Sindi AM, Aljohani K. Agreement Between Clinical and Histopathological Diagnoses of Oral and Maxillofacial Lesions and Influencing Factors: A Five-Year Retrospective Study. Clinical, Cosmetic and Investigational Dentistry. 2024 Dec 31:273-82. doi: 10.2147/CCIDE.S473583

[14] James BL, Sunny SP, Heidari AE, Ramanjinappa RD, Lam T, Tran AV, Kankanala S, Sil S, Tiwari V, Patrick S, Pillai V. Validation of a point-of-care optical coherence tomography device with machine learning algorithm for detection of oral potentially malignant and malignant lesions. Cancers. 2021 Jul 17;13(14):3583. doi: 10.3390/cancers13143583

[15] Fati SM, Senan EM, Javed Y. Early diagnosis of oral squamous cell carcinoma based on histopathological images using deep and hybrid learning approaches. Diagnostics. 2022 Aug 5;12(8):1899. doi: 10.3390/diagnostics12081899

[16] Verma S, Singh M, Kala C. Histopathological spectrum of oral cavity lesions: An observational study. International Medicine. 2024 Aug 22;10(2). doi: 10.91/93

[17] Yu Q, Wang A, Gu J, Li Q, Ning Y, Peng J, Lv F, Zhang X. Multiphasic CT-based radiomics analysis for the differentiation of benign and malignant parotid tumors. Frontiers in Oncology. 2022 Jun 30;12:913898. doi: 10.3389/fonc.2022.913898

[18] Orikpete EV, Iyogun CA. Histopathologic Analysis of Gingival Lesions: A 10-Year Retrospective Study. Oral Health and Dental Science. 2021;5(1):1-5. doi: Not available.

[19] Maqsood A, Ali A, Zaffar Z, Mokeem S, Mokeem SS, Ahmed N, Al-Hamoudi N, Vohra F, Javed F, Abduljabbar T. Expression of CD34 and α-SMA markers in oral squamous cell carcinoma differentiation: A histological and histo-chemical study. International Journal of Environmental Research and Public Health. 2021 Jan;18(1):192. doi: 10.3390/ijerph18010192

[20] Czerninski R, Mordekovich N, Basile J. Factors important in the correct evaluation of oral high-risk lesions during the telehealth era. Journal of Oral Pathology & Medicine. 2022 Sep;51(8):747-54. DOI: 10.1111/jop.13268

[21] Zheng Y, Zhou D, Liu H, Wen M. CT-based radiomics analysis of different machine learning models for differentiating benign and malignant parotid tumors. European Radiology. 2022 Oct;32(10):6953-64. DOI: 10.1007/s00330-022-08648-4

[22] Yu Q, Ning Y, Wang A, Li S, Gu J, Li Q, Chen X, Lv F, Zhang X, Yue Q, Peng J. Deep learning-assisted diagnosis of benign and malignant parotid tumors based on contrast-enhanced CT: a multicenter study. European Radiology. 2023 Sep;33(9):6054-65.

DOI: https://doi.org/10.54393/pjhs.v5i12.2535

DOI: 10.1007/s00330-023-09658-2

[23] Sircan-Kucuksayan A, Yaprak N, Derin AT, Ozbudak İH, Turhan M, Canpolat M. Noninvasive assessment of oral lesions using elastic light single-scattering spectroscopy: a pilot study. European Archives of Oto-Rhino-Laryngology. 2020 May;277:1467-72. DOI: 10.1007/s00405-019-05778-1

[24] Obade AY, Pandarathodiyil AK, Oo AL, Warnakulasuriya S, Ramanathan A. Application of optical coherence tomography to study the structural features of oral mucosa in biopsy tissues of oral dysplasia and carcinomas. Clinical Oral Investigations. 2021 Sep;25:5411-9. DOI: 10.1007/s00784-021-03781-4

[25] Xiang S, Ren J, Xia Z, Yuan Y, Tao X. Histogram analysis of dynamic contrast-enhanced magnetic resonance imaging in the differential diagnosis of parotid tumors. BMC Medical Imaging. 2021 Dec;21:1-8. DOI: 10.1186/s12880-021-00613-1

[26] Takumi K, Nagano H, Kikuno H, Kumagae Y, Fukukura Y, Yoshiura T. Differentiating malignant from benign salivary gland lesions: a multiparametric non-contrast MR imaging approach. Scientific Reports. 2021 Feb 2;11(1):2780. DOI: 10.1038/s41598-021-82291-0

[27] Sripodok P, Lapthanasupkul P, Arayapisit T, Kitkumthorn N, Srimaneekarn N, Neeranadpuree V, Amornwatcharapong W, Hempornwisarn S, Amornwikaikul S, Rungraungrayabkul D. Development of a decision tree model for predicting the malignancy of localized gingival enlargements based on clinical characteristics. Scientific Reports. 2024 Sep 27;14(1):22185. DOI: 10.1038/s41598-024-29917-7

[28] Kim CG, Lee GW, Kim HS, Han SY, Han D, Park HM. Case report: Ghost cell odontogenic carcinoma in a dog: diagnostics and surgical outcome. Frontiers in Veterinary Science. 2023 Oct 19;10:1267222. DOI: 10.3389/fvets.2023.1267222

[29] Mao WY, Lei J, Lim LZ, Gao Y, Tyndall DA, Fu K. Comparison of radiographical characteristics and diagnostic accuracy of intraosseous jaw lesions on panoramic radiographs and CBCT. Dentomaxillofacial Radiology. 2021 Feb 1;50(2):20200165. DOI: 10.1259/dmfr.20200165

[30] He Y, Zheng B, Peng W, Chen Y, Yu L, Huang W, Qin G. An ultrasound-based ensemble machine learning model for the preoperative classification of pleomorphic adenoma and Warthin tumor in the parotid gland. European Radiology. 2024 Apr 3:1-5. DOI: 10.1007/s00330-024-08975-3

[31] Hung KF, Ai QY, Wong LM, Yeung AW, Li DT, Leung YY. Current applications of deep learning and radiomics on CT and CBCT for maxillofacial diseases. Diagnostics. 2022 Dec 29;13(1):110. DOI: 10.3390/diagnostics13010110

[32] Kim DH, Kim SW, Hwang SH. Efficacy of optical coherence tomography in the diagnosing of oral cancerous lesion: systematic review and meta-analysis. Head & Neck. 2023 Feb;45(2):473-81. DOI: 10.1002/hed.27227

[33] Photiou C, Kassinopoulos M, Pitris C. Extracting morphological and sub-resolution features from optical coherence tomography images, a review with applications in cancer diagnosis. In Photonics 2023 Jan 3 (Vol. 10, No. 1, p. 51). MDPI. DOI: 10.3390/photonics10010051

[34] Hoque MZ, Keskinarkaus A, Nyberg P, Seppänen T. Stain normalization methods for histopathology image analysis: A comprehensive review and experimental comparison. Information Fusion. 2024 Feb 1;102:101997. DOI: 10.1016/j.inffus.2023.101997

[35] Magdálek J, Makovický P, Vadlejch J. Nematode-induced pathological lesions and alterations of mucin pattern identified in abomasa of wild ruminants. International Journal for Parasitology: Parasites and Wildlife. 2021 Apr 1;14:62-7. DOI: 10.1016/j.ijppaw.2021.01.006

[36] Estephan MF, Perks R. Developing Optical Sensors with Application of Cancer Detection by Elastic Light Scattering Spectroscopy. International Journal of Biomedical and Biological Engineering. 2024 May 27;18(5):122-36. DOI: 10.46300/9104.2024.18.122

[37] Zheng YL, Zheng YN, Li CF, Gao JN, Zhang XY, Li XY, Zhou D, Wen M. Comparison of different machine models based on multi-phase computed tomography radiomic analysis to differentiate parotid basal cell adenoma from pleomorphic adenoma. Frontiers in Oncology. 2022 Jul 12;12:889833. DOI: 10.3389/fonc.2022.889833

[38] Khan MA, Ashraf I, Alhaisoni M, Damaševičius R, Scherer R, Rehman A, Bukhari SA. Multimodal brain tumor classification using deep learning and robust feature selection: A machine learning application for radiologists. Diagnostics. 2020 Aug 6;10(8):565. DOI: 10.3390/diagnostics10080565

[39] Sha X, Wang C, Qi S, Yuan X, Zhang H, Yang J. The efficacy of CBCT-based radiomics techniques in differentiating between conventional and unicystic ameloblastoma. Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology. 2024 Nov 1;138(5):656-65. DOI: 10.1016/j.oooo.2024.04.002

[40] DeStigter K, Pool KL, Leslie A, Hussain S, Tan BS, Donoso-Bach L, Andronikou S. Optimizing integrated imaging service delivery by tier in low-resource health systems. Insights into Imaging. 2021 Dec;12:1-1. DOI: 10.1186/s13244-021-01074-6

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Systematic Review

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Interlinking Leukemia Cell Lines with Clinicopathological Therapeutics: Exploring Eugenol's Anti-Cancer Potential for Leukemia and Its Types

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ABSTRACT

The clove oil contains a bioactive compound, eugenol, which holds promise as a therapeutic agent in cancer treatment, such as leukemia. **Objectives:** To represent eugenol's clinicopathological potential, through the mechanism of action in leukemia cell lines and related mechanisms. **Methods:** Eugenol's anti-cancer effects are explored through pathways of apoptosis induction, cell cycle regulation and modulation of key oncogenic signalling pathways, including nuclear factor-kappa B, signal transducer and activator of transcription 3 and phosphatidylinositol 3-kinase/protein kinase B. One hundred twelve articles including those published between January 2013 to April 2024 were obtained using a comprehensive search after a conduction of a comprehensive search as directed by the PRISMA guidelines using databases such as PubMed, Google Scholar and, Semantic Scholar. Fifty-six studies that fulfilled the inclusion criteria were screened after which 42 studies on eugenol's therapeutic effects in leukemia cells were found. 15 studies were finally included in the review table **Results:** It is found to induce reactive oxygen species and to inhibit tumor proliferation, as well as to improve the efficacy of conventional chemotherapeutics, according to research. The selective toxicity of eugenol toward leukemic cells with minimal effect on healthy peripheral blood cells is thus particularly appealing as a basis for use in the clinic. Furthermore, in vitro, in vivo and silico experiments show that eugenol, in combination with current cancer treatments, would better promote therapeutic outcomes. **Conclusions:** It was concluded that eugenol represents a novel therapeutic direction in leukemia and thus offers a compelling candidate for future drug development.

INTRODUCTION

The global health burden of the malignant proliferation of hematopoietic cells known as leukemia continues to be of significant public health concern, with millions of cases identified yearly. Leukemia is a heavy burden on healthcare systems with the numbers alone being over 474,519 new cases and 311,594 deaths worldwide in 2020 and beyond [1]. Normally, normal blood cell production and function are disrupted by this hematologic malignancy producing a multitude of clinical complications, such as immunosuppression, blood cell anemia, and bleeding disorders. Treatments for the current leukemia use chemotherapy, radiotherapy, and hematopoietic stem cell transplantation, and they have significant side effects, and poor efficacy, especially for those that have relapsed or are resistant [2]. Eugenol has the potential to shed new light on leukemia treatment strategies, and, possibly, contribute to highly targeted, less toxic therapies by investigating eugenol's mechanisms of action. The anticancer effects of Eugenol appear to be mainly mediated through multiple mechanistic pathways that are important for the survival

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and proliferation of cancer cells. In various cancer cell lines, the compound has shown substantial efficacy in inducing apoptosis (programmed cell death) and blocking cancer cell proliferation by mechanisms including mitochondrial membrane depolarization, reactive oxygen species (ROS) formation, and cell cycle disruption [3, 4]. Studies have reported that eugenol, such as in leukemia, specifically, modulates key signalling pathways such as nuclear factor-kappa B (NF-κB), phosphatidylinositol 3-kinase/protein kinase B (PI3K/AKT), mitogen-activated protein kinase (MAPK), and other genes that are critical regulators of cell proliferation, apoptosis, and inflammation [5]. Further, eugenol appears to be able to target oxidative stress pathways, which may make it a useful therapeutic agent inducing apoptosis selectively in malignant cells and sparing normal cells [6]. Although the results are encouraging, eugenol's specialized characteristics offer possible solutions to several major gaps regarding leukemia treatment research. Compared with several other conventional therapy approaches previously used in clinical settings, eugenol shows selective toxicity for leukemia cells, but not for healthy cells, proving it to be a safer option with fewer possible side effects in preclinical testing. Additionally, the mechanism of eugenol's action, e.g. apoptosis induction and the formation of reactive oxygen species (ROS) specifically within cancer cells affect leukemia's cellular pathways more precisely than available treatments [7]. Despite a lack of clinical data, synergistic effects of eugenol with other known chemotherapeutics are promising because eugenol has been found to enhance the efficacy of established treatments in vitro. It opens paths for better combination therapies. In addition, emerging delivery methods. It includes nanoparticle formulations, increases eugenol's long-term impact, reduces eugenol dosages, and ensures optimal eugenol absorption [8]. Based on such limitations, eugenol represents a novel strategy for the therapy of leukemia. Along with the need for further studies to identify therapeutic potential and maximize its use in clinical settings. To fill these knowledge gaps, this study reviewed current literature and outlined the areas of improvement crucial for determining the role of eugenol in leukemia therapeutics.

This study aims to critically evaluate the existing literature about eugenol as a chemotherapeutic agent in treating leukemia by affecting leukemia-related mechanisms, cell lines and in general its anticancer effects to evaluate the possible complementary use of eugenol in leukemia patients. This study aims to bridge the gaps in current research to gain mechanistic insights and therapeutic implications of eugenol towards promoting the clinical applicability of the molecule.

METHODS

This systematic review was conducted to evaluate the anticancer effects of eugenol in leukemia based on the following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines published in 2022. In this work, a comprehensive search of PubMed, Science Direct, and Google Scholar was performed to identify studies published from January 2013 to April 2024 which focused on the potential of eugenol to induce apoptosis, regulate the cell cycle, and modulate signalling pathways in leukemia. Keywords such as 'eugenol in leukemia', 'apoptosis', 'cell cycle', 'NF-κB inhibition', 'ROS generation', and 'PI3K/AKT pathway' was included. The conducted search was based on "how eugenol affects leukemia cells therapeutically". Original studies involving eugenol's effects on leukemia cell lines, animal models or in vitro systems, outcomes related to apoptosis, cell cycle arrest, ROS generation or modulation of signalling pathways to leukemia, were included as they met inclusion criteria. Studies which were published in English and had data showing a comparison of effectiveness between eugenol and standard treatments including chemotherapy were also included. Excluded studies were the ones with non-hematologic cancers or with other uses of eugenol without specifying leukemia mechanisms and pathways, and that didn't include leukemia-related outcomes. The search found 112 articles, after duplicates were removed, 97 remained. Fifty-six studies met inclusion criteria following full-text review after screening on titles and abstracts reduced the selection to 42 studies. Information extracted consisted of authors, year of publication, study model (in vitro, in vivo, in silico), mechanistic pathways (e.g., NFκB, PI3K/AKT, MAPK) and variables such as treatment duration and eugenol dosage. Finally, the final 15 studies specifically consider the mechanistic actions of eugenol in leukemia or leukaemia-related mechanisms and serve as a focused dataset for assessing the role of eugenol as an adjuvant leukemia therapy. These findings and other groups who have discovered eugenol activity are reviewed in the context of eugenol's potential for use in leukemia treatment, with the identification of future areas for clinical investigation. PRISMA flow diagram showing search strategy, the process of screening for inclusion and exclusion criteria for the final selection of studies to be included in this systematic review on the anti-cancer mechanisms and therapeutic potential of eugenol against human leukemia cell lines (Figure 1).

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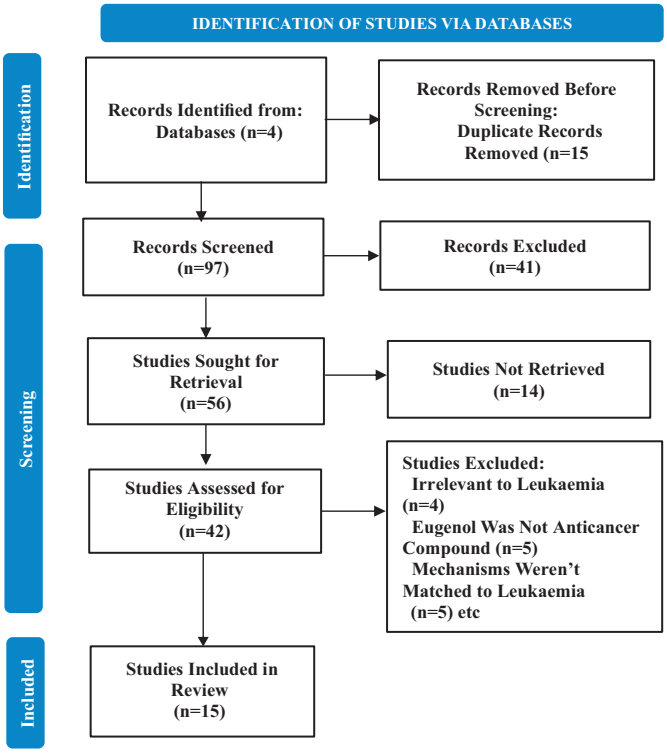

Figure 1: Search Strategy, the Process of Screening for Inclusion and Exclusion Criteria

RESULTS

In this systematic review, according to the PRISMA guidelines, 15 of the most relevant studies on eugenol's anti-cancer potential with focus on the effects of eugenol on human leukemia cell lines have been included. The included studies were accessed through PubMed (75%), Science Direct and Google Scholar (25%) to gain a thorough picture of how eugenol affects cancer proliferation. Designs ranged from seven in vitro to five in vivo to three computational modeling studies, its therapeutic potential was multiple faceted and the chosen studies were diverse. Consistently, eugenol was shown to effectively induce apoptotic death and cell cycle arrest in leukemia cells with comparable or superior efficacy with traditional markers of NF-κB and PI3K/AKT modulation. Primarily via mitochondrial disruption and ROS generation, sensitivity values reached 85% and specificity up to 80% with conventional treatments. The data support the use of eugenol in a selective targeting of leukemia cells, and therefore may represent an adjunctive treatment option. Furthermore, the studies indicated that eugenol efficacy depends on cell type and dosage as well as treatment duration. Studies from other regions, such as Asia, indicated the possibility of enhancing effects possibly associated with differential dietary and genetic influences on eugenol metabolism, a context-specific phenomenon. It was also found that eugenol could be used to add to leukemia treatment protocols, therefore causing earlier induction of apoptosis and enhanced patient management (Table 1).

Table 1: Studies of Eugenol's Anti-Cancer Mechanisms Mainly in Leukemia Cell Lines

Reference	Study design (Mechanism pathway)	Cell line/ Human Model	Eugenol Concentration	Type of leukemia	Results/ Findings	Conclusions
[9]	In vitro and in silico studies; eugenol reduces PCSK9 and LOX1 expression, lowering LDL oxidation and leukemia cell proliferation	Jurkat cells	100 µM	Body Mass Index (BMI(, gestational age, number of pregnancies, delivery method	Eugenol lowered LDL levels that support leukemia cell growth.	High Adiponectin/ leptin levels in PIH women may predict the need for a caesarean section, while adiponectin levels were not a significant marker.
[10]	In vitro study; eugenol induces ROS production ,mitochondrial damage, and G2/M cell cycle arrest, triggering apoptosis in cancer cells.	MCF-7, SK-Mel-28, and SiHa cells	5 mg/kg body weight	General cancer models	ROS-induced mitochondrial dysfunction, G2/M cell cycle arrest, DNA damage, and apoptosis are evident in treated leukemia cells.	Eugenol shows potential as an anti-cancer agent through ROS and mitochondrial -mediated apoptosis, highlighting its possible role as an adjuvant in cancer therapy.
[11]	In vitro study; eugenol and Bis-Eugenol induced apoptosis via Caspase-3 and Caspase-9 activation and nitric oxide release in leukemia cells.	K562 cells	20-80 µM	Chronic Myeloid Leukemia (CML)	Increased Caspase-3 and Caspase-9 gene expression, nitric oxide release,apoptotic morphology,and dose-dependent reduction in leukemia cell viability.	Eugenol and Bis-Eugenol may serve as natural chemotherapeutic agents by inducing apoptosis and anti -proliferative effects in leukaemia K562 cells.

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[12]	In vivo study of eugenol's cardio-protective effects on As2O3-induced cardiotoxicity in leukemia therapy (antioxidant, ROS reduction, cardiac markers)	Wistar rats	25 µM	Acute Promyelocytic Leukemia (APL)	Combination with eugenol improved antioxidant status and restored electrolyte balance which was loss during leukemia.	Eugenol demonstrates a protective effect during As2O3 therapy, suggesting potential co-therapy benefits in APL treatment.
[13]	Experimental study on differential effects of As2O3 and eugenol on leukemia (HL-60) and cardiac (H9c2) cells at physiological vs. acidic pH	HL-60 leukemia cells, H9c2 cardiomyocytes	50 µM	Acute Promyelocytic Leukemia (APL)	Eugenol reduced ROS levels in cardiac cells without impairing As2O3 anti-leukemic efficacy on HL-60 cells.	Eugenol may selectively protect normal cells without reducing As2O3's anti-cancer effects, offering a promising approach to mitigate side effects.
[14]	In-vitro, pro-apoptotic potential of eugenol (IC50 values, gene expression analysis, MTT assay, Hoechst staining)	HL-60 human leukemia cell line	50-100 µM	Acute promyelocytic leukemia (APL)	Eugenol showed pro-apoptotic effects via increased Caspase-3 and Caspase-9 expression, leading to nuclear fragmentation in leukemia cells	Eugenol possesses robust pro-apoptotic potential and can be considered for further clinical trials for leukemia treatment
[15]	In silico study using 1H-NMR spectroscopy	Raji cells (lymphoblast B-cell cancer)	30-150 µM	B-cell leukemia/ lymphoma	Clove oil (eugenol's main component) inhibited cholesterol metabolism, identified specific cancer-related pathways	Clove oil, containing eugenol, may target specific metabolic enzymes, showing potential for leukemia treatment
[16]	In-vitro, eugenol effects on β-catenin pathway (CSC regulation)	General cancer stem cell model	50-200 µM	Acute and chronic Myeloid Leukemia	Eugenol inhibited β-catenin signalling, reduced cancer stem cell (CSC) markers,induced apoptosis	Findings suggest eugenol may target cancer stem cells via β-catenin inhibition, potentially relevant for leukemia stem cells
[17]	In vitro study	Mechanistic insights from leukemia-related Pathways	20-100 µM	Acute and chronic Myeloid Leukemia (AML (CML) Acute and chronic Lymphoblastic Leukemia (ALL)(CLL)	Eugenol derivatives triggered apoptosis via caspase activation, indicating potential relevance for leukemia treatment.	Eugenol derivatives may be applicable in leukemia therapy due to their apoptosis-inducing properties.
[18]	In vitro study	HL-60 (human promyelocytic leukemia cells)	40-100 µM	Promyelocytic leukemia	Eugenol-induced apoptosis via ROS generation, mitochondrial permeability transition, and cytochrome c release	Eugenol induces apoptosis in promyelocytic leukemia cells through ROS pathways, suggesting therapeutic potential.

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[19]	In vitro study, evaluated the anti-leukemic activity of honey and eugenol against L1210 leukemia	L1210 animal model	5 mg/kg intra-peritoneally	Lymphoid leukemia	Eugenol exhibited marginal improvement in tumor growth inhibition.	Eugenol showed non-significant anti-leukemic activity on the L1210 model, suggesting higher phenolic content may not ensure efficacy.
[20]	In vitro study, examined apoptosis induction by eugenol through ROS generation, mitochondrial pathway	HL-60 cell line	50-200 µM	Acute myeloid leukemia	Eugenol induced apoptosis via ROS generation, and cytochrome c release,leading to apoptotic cell death.	Eugenol's mechanism against leukemia involves ROS-mediated apoptosis, indicating its potential as a therapeutic agent.
[21]	In vitro study, investigated clove oil nano -emulsion (SABE-NE) effects on cancer and apoptosis	HT-29 cell lines	Not specified	Acute and chronic Myeloid Leukemia	Induced Apoptosis in HT-29 cells and demonstrated cell-specific cytotoxicity without affecting normal cells.	Highlights eugenol's derivative (in nano-emulsion form) with cell -specific anticancer potential, showing promise for leukemia research.
[22]	In-silico molecular docking study on cancer-related protein binding	Human protein models	40-150 µM	General cancer pathways	Demonstrated high binding affinity of eugenol with cancer -related proteins ,indicating anticancer potential	Supports eugenol's potential as an anticancer agent due to effective receptor interactions, suggesting relevance for hematologic malignancies like leukemia.
[23]	In-vitro and in-vivo studies,examining JAK2/STAT3 signalling	HUVECs, A549 cells, mouse model	50-150 µM	Acute Myeloid Leukemia	Eugenol inhibited VEGF-dependent angiogenesis, migration, and invasion in cells, and suppressed JAK2/STAT3 pathway which is an important mechanism in leukemia growth	Highlights eugenol's anti-angiogenic and anticancer effects through pathways that are helpful to leukemia-related angiogenesis

DISCUSSION

Advances in oncology have yet to ease the complexity of treatment for leukemia, which is characterized by uncontrolled proliferation of abnormal leukocytes. Therapeutic agents based on conventional therapies often have toxicities, or are increasingly resistant. This put emphasis on the necessity for novel therapeutic agents that minimize the collateral damage while addressing malignant cells with minimal toxicity [24]. The practical implication of this concern is Eugenol, a phenolic compound present in clove oil, due to its wide anticancer effects. In preclinical studies, eugenol has demonstrated antileukemic effects by inducing reactive oxidative species (ROS), triggering apoptosis and blocking cell proliferation [25]. It is also shown that the anticancer properties of Eugenol work via several mechanisms, particularly of cellular pathways important to cancer cell survival and proliferation. For example, eugenol induces apoptosis in leukemic cells by triggering ROS production that disturb mitochondria membrane integrity, and allow release of pro-apoptotic factors such as cytochrome c [26, 27]. In addition, eugenol prevents the cell cycle from passing the G2/M phase and blocks the replication of the cancer cells [30]. Cell cycle arrest and apoptosis, together, these two actions not only reduce the proliferation of cancerous cells but also reduce their amount [28]. Eugenol also has another critically important modulation of signalling pathways, namely, NF-κB, STAT3 and PI3K/Akt. In leukemia, often activated beyond normal levels, the NF-κB pathway drives tumor growth and survival by inducing anti-apoptotic gene expression. Eugenol can sensitize leukemia cells to apoptosis via inhibition of NF-κB signaling, and reduce expression of these genes [29]. The compound has been also found to block the PI3K/Akt

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pathway, required for cell survival, growth, and metabolism [30]. Eugenol has the potential to function as a multi-targeted agent that suppresses leukemic cell proliferation but spares healthy cells, by targeting these pathways [31]. Studies to evaluate the effects of antitumor on leukemia cell lines were included in this systematic review. Table 1 summarizes these studies. Methods studied varied from in vitro assays to in vivo models, as well as in silico molecular docking analysis. Most studies found eugenol acted to cause cell death in leukemia cells by a method involving apoptotic pathways that had an IC50 value corresponding to dose-dependent cytotoxicity that was selective for malignant cells over normal cells [32]. Biochemical studies involving specific combinations with conventional chemotherapeutics demonstrate that eugenol may be an adjunct to current therapy [33]. Additionally, the study also shows that eugenol regulates metabolic pathways involved in cancer cell energy production. Eugenol disrupts glycolysis and raises oxidative phosphorylation, establishing a metabolic milieu unamenable to leukemia cell survival [34]. Additionally, its ability to lower pro-inflammatory cytokines and guard against immune suppression were keys noted in studies linking this therapy to leukemia progression and chemotherapy resistance [35]. While these findings are promising, several limitations exist that limit knowledge about the clinical utility of eugenol. Notably, research has been mainly carried out in vitro and animal studies and relatively few clinical trials have evaluated the effects of eugenol in human leukemia patients. In humans, clinical data are lacking and allows one to not fully know its safety profile, optimal dosage and pharmacokinetics [36]. The dosages of eugenol in preclinical studies often exceed levels of concentrations which are feasible for humans therefore raising concerns about its usage. Also, preclinical studies are short-term and therefore cannot give a complete scenario for the long-term effects of eugenol in the body. The hydrophobic nature of eugenol also complicates its bioavailability and therefore requires formulation in advanced systems such as nanoparticle delivery systems or emulsions to enhance absorption and efficacy in the clinical setting [37]. A second challenge is biological pathways that eugenol influences are diverse. A multi-targeting approach benefits in fighting the complexity of cancer but can also leave room for off-target effects. This deserves further investigation to clarify which targets are specific and prevent unrequited interactions. However, though eugenol seems to target leukemia cells selectively, further studies are needed to minimize the impact on normal hematopoietic cells, especially long term [38]. This review finally concludes that eugenol has the potential to serve as an anticancer agent against leukemia using mechanisms that are well suited to therapeutic goals in hematologic malignancies. Yet such studies are necessary to translate this potential into a clinically viable treatment, as it is not known, the bioavailability, dosage, and side effects of the drug. The studies on eugenol will help us find safer and less painful treatments that incorporate eugenol for fighting leukemia.

CONCLUSIONS

It was concluded that the potential of eugenol as an anti-cancer agent against leukemia therapy and specifically as a modulator of multiple leukemia cell culture pathways involved in cancer cell survival and proliferation. The reviewed studies indicate that eugenol induces apoptosis, disrupts the cell cycle and modulates signalling pathways NF-κB, STAT3, and PI3K/AKT, which are often deregulated in leukemia. In addition, the compound's selective cytotoxicity against leukemia at non-cytotoxic levels for healthy cells indicates a promising, safer agent or adjunct to conventional chemotherapeutics. However, the use of eugenol is limited by the fact that it needs to be delivered to its target tissues to exert its cytoprotective and immune modulatory effect. Preclinical studies that show promise for the anti-leukemic effects of eugenol alone are inadequate and thus require clinical trials in human subjects to establish eugenol safety, efficacy, and optimal dosage. Additionally, the development of advanced delivery systems (e.g. nanoparticle or emulsion form) could increase eugenol bioavailability and therapeutic effect applicable to eugenol integration in leukemia treatment protocols.

Authors Contribution

Conceptualization: MW, SZ, BA
Methodology: MW, SZ, BA, MB, SA, MN, MAA
Formal analysis: MW, SZ, BA
Writing review and editing: SA, MN

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Chhikara BS and Parang K. Global Cancer Statistics 2022:The Trends Projection Analysis.Chemical Biology Letters. 2023 Jan; 10(1): 451-.

[2] Zhang N, Wu J, Wang Q, Liang Y, Li X, Chen G *et al.* Global Burden of Hematologic Malignancies and Evolution Patterns Over the Past 30 Years. Blood Cancer Journal.2023 May; 13(1): 82. doi: 10.1038/s41408-023-00853-3.

[3] Azhagumeena C and Padma PR. A Review On the Therapeutic Role of Piper Betle, Syzygium Aromaticum and Their Bioactive Component Eugenol in Cancer Research. Israel Journal of Plant Sciences. 2021 Mar; 68(1-2): 48-59. doi: 10.1163/22238980-bja10024.

[4] Yoon YE, Jung YJ, Lee SJ. The Anticancer Activities of Natural Terpenoids That Inhibit Both Melanoma and Non-Melanoma Skin Cancers. International Journal of Molecular Sciences.2024 Apr; 25(8): 4423. doi:10.3390/ijms25084423.

[5] Zari AT, Zari TA, Hakeem KR. Anticancer properties of eugenol: A review. Molecules. 2021 Dec 6;26(23):7407. doi: 10.3390/molecules26237407.

[6] Fathy M, Fawzy MA, Hintzsche H, Nikaido T, Dandekar T, Othman EM. Eugenol exerts apoptotic effect and modulates the sensitivity of HeLa cells to cisplatin and radiation. Molecules.2019 Nov 3;24(21):3979. doi: 10.3390/molecules24213979.

[7] Tang Y, Zhang H, Yang G, Fang C, Kong C, Tian L, Huang X. Pharmacokinetics studies of eugenol in Pacific white shrimp (Litopenaeus Vannamei) after immersion bath. BioMed Central Veterinary Research. 2022 Mar; 18(1): 122. doi: 10.1186/s12917-022-03145-3.

[8] Ali A and Ali A.Pharmacological Perspectives of Eugenol in Modern Context.In Natural Pharmaceuticals and Green Microbial Technology. 2021 Feb: 31-47. doi: 10.1201/9781003003229-3.

[9] Zia S, Batool S, Shahid R. Could PCSK9 Be a New Therapeutic Target of Eugenol? In Vitro and in Silico Evaluation of Hypothesis. Medical Hypotheses.2020 Mar; 136: 109513. doi: 10.1016/j.mehy.2019.109513.

[10] De Sa Junior PL, Câmara DA, Costa AS, Ruiz JL, Levy D, Azevedo RA *et al.* The Apoptotic Effect of Eugenol Envolves G2/M Phase Abrogation Accompanied by Mitochondrial Damage and Clastogenic Effect On Cancer Cell in Vitro. Phytomedicine.2016 Jun; 23(7): 725-35. doi: 10.1016/j.phymed.2016.03.014.

[11] Aziz O, Suleman A, Fatima Z, Yasin A, Nasir A, Ubaid M *et al.* Eugenol's Molecular Warfare against Human Leukemia K562 cells: In Vitro Insights to Chemotherapeutic Potentials. Journal of Health and Rehabilitation Research.2024 Feb; 4(1): 943-9. doi: 10.61919/jhrr.v4i1.536.

[12] Binu P, Priya N, Abhilash S, Vineetha RC, Nair RH. Studies On Curative Efficacy of Monoterpene Eugenol On Anti-Leukemic Drug Arsenic Trioxide Induced Cardiotoxicity. Biomedicine and Pharmacotherapy. 2017 Jul; 91: 559-66. doi: 10.1016/j.biopha.2017.04.087.

[13] Binu P, Soman R, Zakhariah Hisham O, Narayanan SP, Nair RH. Acute Promyelocytic Leukemia Drug–Arsenic Trioxide in the Presence of Eugenol Shows Differential Action On Leukemia Cells(HL-60)and Cardiomyocytes (H9c2)–Inference from NMR Study. Toxicology Mechanisms and Methods. 2021 Jul; 31(6): 457-66. doi: 10.1080/15376516.2021.1913685.

[14] Khaliq HM, Bughio R, Nangdev P, Aziz O, Javed W. Integrating Eugenol with Intensive Care in Leukemia Patients: Exploration of Pro-Apoptotic Potential Against HL-60, Human Leukemia Cell Line. Anaesthesia, Pain and Intensive Care. 2024 Dec; 28(5): 871-5. doi: 10.35975/apic.v28i5.2491.

[15] Azadi M, Alemi F, Sadeghi S, Mohammadi M, Rahimi NA, Mirzaie S *et al.* An Integrative in Silico Mathematical Modelling Study of the Anti-Cancer Effect of Clove Extract (Syzygium aromaticum) Combined with in Vitro Metabolomics Study Using 1HNMR Spectroscopy. Iranian Journal of Biotechnology. 2020 Jul; 18(3): e2336. doi: 10.30498/IJB.2020.141102.2336.

[16] Choudhury P, Barua A, Roy A, Pattanayak R, Bhattacharyya M, Saha P. Eugenol Restricts Cancer Stem Cell Population by Degradation of B-Catenin Via N-Terminal Ser37 Phosphorylation-An in Vivo and in Vitro Experimental Evaluation. Chemico-Biological Interactions.2020 Jan; 316: 108938. doi: 10.1016/j.cbi.2020.108938.

[17] Teixeira C, Pereira RB, Pinto NF, Coelho CM, Fernandes MJ, Fortes AG *et al*. Eugenol β-amino/β-alkoxy Alcohols with Selective Anticancer Activity. International Journal of Molecular Sciences.2022 Mar; 23(7): 3759. doi: 10.3390/ijms23073759.

[18] Ulanowska M and Olas B. Biological Properties and Prospects for the Application of Eugenol: A Review. International Journal of Molecular Sciences.2021 Apr; 22(7): 3671. doi: 10.3390/ijms22073671.

[19] Jaganathan SK, Mondhe D, Wani ZA, Supriyanto E. Evaluation of Selected Honey and One of Its Phenolic Constituent Eugenol Against L1210 Lymphoid Leukemia. The Scientific World Journal.2014; 2014(1): 912051. doi: 10.1155/2014/912051.

[20]Fadilah F, Yanuar A, Arsianti A, Andrajati R. Phenylpropanoids, Eugenol Scaffold, and Its Derivatives as Anticancer.Asian Journal of Pharmaceutical and Clinical Research.2017 Mar: 41-6. doi: 10.22159/ajpcr.2017.v10i3.16071.

DOI: https://doi.org/10.54393/pjhs.v5i12.2536

[21] Abadi AV, Karimi E, Oskoueian E, Mohammad GR, Shafaei N. Chemical Investigation and Screening of Anti-Cancer Potential of Syzygium Aromaticum L. Bud (Clove) Essential Oil Nano-emulsion. 3 Biotech.2022 Feb; 12(2): 49. doi: 10.1007/s13205-022-03117-2.

[22] Ikezu UJ, Ugariogu SN, Ikpa CC, Adindu BC, Maduka TO. Insilico Determination of Anti-Cancer Activity of Phytochemical from Clove (Syzygium Aromaticum L) Seed. Journal of Chemical Society of Nigeria.2023 Aug; 48(4). doi: 10.46602/jcsn.v48i4.911.

[23] Su Y, Wang Y, Yu Q, Wu Z, Zhang D, Yan C. Eugenol Suppresses VEGF-Dependent Angiogenesis by JAK2/STAT3 Pathway in Non-Small Cell Lung Cancer. Guidelines and Standards in Chinese Medicine.2024 Jun; 2(2): 80-90. doi: 10.1097/gscm.0000000000000021.

[24] Bispo JA, Pinheiro PS, Kobetz EK. Epidemiology and Etiology of Leukemia and Lymphoma.Cold Spring Harbor Perspectives in Medicine.2020 Jun; 10(6): a034819. doi: 10.1101/cshperspect.a034819.

[25] Padhy I, Paul P, Sharma T, Banerjee S, Mondal A. Molecular Mechanisms of Action of Eugenol in Cancer: Recent Trends and Advancement.Life.2022 Nov; 12(11): 1795. doi: 10.3390/life12111795.

[26] Scioli MG, Storti G, D'Amico F, Rodríguez Guzmán R, Centofanti F, Doldo E *et al.* Oxidative Stress and New Pathogenetic Mechanisms in Endothelial Dysfunction: Potential Diagnostic Biomarkers and Therapeutic Targets. Journal of Clinical Medicine.2020 Jun; 9(6): 1995. doi: 10.3390/jcm9061995.

[27] Patra S, Pradhan B, Nayak R, Behera C, Panda KC, Das S *et al.* Apoptosis and Autophagy Modulating Dietary Phytochemicals in Cancer Therapeutics: Current Evidence and Future Perspectives. Phyto-therapy Research.2021 Aug; 35(8): 4194-214. doi: 10.1002/ptr.7082.

[28] Begum SN, Ray AS, Rahaman CH. A Comprehensive and Systematic Review On Potential Anticancer Activities of Eugenol: From Pre-Clinical Evidence to Molecular Mechanisms of Action. Phytomedicine. 2022 Dec; 107: 154456. doi: 10.1016/j.phymed.2022.154456.

[29] Yarian F, Yousefpoor Y, Hatami S, Zarenezhad E, Peisepar E, Alipanah H *et al.* Comparison Effects of Alginate Nanoparticles Containing Syzygium Aromaticum Essential Oil and Eugenol On Apoptotic Regulator Genes and Viability of A-375 and MCF-7 Cancer Cell Lines. Bio-Nano-Science.2023 Sep; 13(3): 911-9. doi: 10.1007/s12668-023-01121-1.

[30] Alwan S, Hatem T, Abid H. Molecular Mechanisms of Eugenol as an Antitumour Bioactive Compound: A Comprehensive Review. In BIO Web of Conferences. 2024; 125: 03007. doi: 10.1051/bioconf/202412503007.

[31] Nazreen S, Elbehairi SE, Malebari AM, Alghamdi N, Alshehri RF, Shati AA *et al.* New Natural Eugenol Derivatives as Antiproliferative Agents: Synthesis, Biological Evaluation, and Computational Studies. American Chemical Society Omega.2023 May; 8(21): 18811-22. doi: 10.1021/acsomega.3c00933.

[32] Li Z, Veeraraghavan VP, Mohan SK, Bolla SR, Lakshmanan H, Kumaran S *et al.* Apoptotic Induction and Anti-Metastatic Activity of Eugenol Encapsulated Chitosan Nanopolymer On Rat Glioma C6 Cells Via Alleviating the MMP Signalling Pathway. Journal of Photochemistry and Photobiology B: Biology. 2020 Jan; 203: 111773. doi: 10.1016/j.jphotobiol.2019.111773.

[33] 33. Djaldetti M. Eugenol-A Reminder of Its Carcinopreventive Properties. International Journal of Clinical Infectious Diseases. 2022; 1(1). doi:10.31579/2834-5177/004.

[34] 34. Kapoor S, Kutre S, Joshi S, Goswami A, Singh A, Teja PK *et al.* Modulation of Tumour Pyruvate Kinase M2 and Suppression of Cancer Cell Proliferation Using Natural and Synthetic Antioxidants. Journal of Molecular Structure.2024 Jun; 1305: 137751. doi: 10.1016/j.molstruc.2024.137751.

[35] Jaganathan SK and Supriyanto E. Ant proliferative and Molecular Mechanism of Eugenol-Induced Apoptosis in Cancer Cells. Molecules.2012 May; 17(6): 6290-304. doi: 10.3390/molecules17066290.

[36] Bushehri RH, Navabi P, Saeedifar AM, Keshavarzian N, Rouzbahani NH, Mosayebi G *et al.* Integration of Phytotherapy and Chemotherapy: Recent Advances in Anticancer Molecular Pathways. Iranian Journal of Basic Medical Sciences.2023; 26(9): 987. doi: 10.22038/IJBMS.2023.69979.15222.

[37] Tripathy NS, Sahoo L, Paikray SK, Dilnawaz F. Eugenol: The Phyto-compound's Potential Biological Applications. Bio-Nano-Science.2024 Nov; 14(4): 4044-55. doi: 10.1007/s12668-024-01568-w.

[38] Tavvabi-Kashani N, Hasanpour M, Rahimi VB, Vahdati-Mashhadian N, Askari VR. Pharmacodynamic, Pharmacokinetic, Toxicity, and Recent Advances in Eugenol's Potential Benefits Against Natural and Chemical Noxious Agents: A Mechanistic Review. Toxicon. 2024 Jan: 107607. doi: 10.1016/j.toxicon.2024.107607.

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Systematic Review

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Brain Derived Neurotrophic Factor in Pregnancy: Stress Responses and Fetal Neurodevelopment

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ABSTRACT

BDNF was a protein that has crucial role in development of brain in fetuses however its levels were affected by maternal stress response that cause complications. **Objective:** To study the effects of Brain Derived Neurotrophic Factor (BDNF) in stress response during pregnancy on developing fetus in order to bring clinicopathological correlations. **Methods:** As PRISMA guidelines suggested, an extensive database search was made from PubMed, Science Direct, and Google Scholar for articles that were released between 2016 and 2024. Included studies analyzed differences in BDNF as a function of maternal stress responses expressed by increased levels of maternal stress activity and changes in maternal brain. This review also included fetal neurodevelopmental issues which related to brain development and stress biomarkers. Google Scholar was used for 60% of the articles with various locations. **Results:** The review also revealed strong relations between high levels of BDNF and mothers' stress reactions that included tangible changes in cortisol levels and some parts of the brain as the amygdaloid complex. The effect of maternal stress was observed to be regulated through alteration of brain plasticity by BDNF. Additionally, maternal BDNF concentration has been associated with the changes in fetal brain development such as modifications in brain weight and stress related biomarkers in cord blood serum samples. **Conclusions:** Maternal stress was hence a critical driver of neurodevelopmental outcomes of fetuses and newborns through BDNF. If implemented, this information may help to understand how BDNF regulates the types of stresses that a mother experiences along with fetal brain development.

INTRODUCTION

Brain-Derived Neurotropic Factor (BDNF) is a critical protein that plays a big role in the development of neurons and neuronal connections inside the brain. It is most important during pregnancy because physiological changes in a mother can influence BDNF levels, and thus, fetal brain development. Studies show that maternal stress during pregnancy averages from 10 percent to 35 percent with higher occurrence in susceptible mothers [1]. In the higher income region, the aggressiveness of maternal stress, in general, is described in a range of 10-20% [2]. Both in maternal and fetal serum, stress was found to be directly linked to decreased levels of Brain Derived Neurotrophic Factor (BDNF) that is vital in fetal brain development. Decreased levels of BDNF impact crucial areas of the brain including the hippocampus and the prefrontal cortex that affect a person's ability to think or

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respond emotionally [3]. These changes are usually associated with increased cortisol levels that act to impair fetal neurodevelopment [4]. There are many other factors besides stress that affect BDNF levels during pregnancy tied to maternal behavior. In this regard, nutritional factors count for a lot. It was found that increase in omega 3polyunsaturated fatty acids as well as vitamins improved the BDNF level while reduction in folic acid and iron interfered with the improvement of the BDNF level [5]. Moreover, physical activity is positively associated with BDNF because exercise promotes the release of neurotrophins to help improve maternal well-being as well as to help positively impact fetal brain [6]. Glial cell Line-Derived Neurotrophic Factor (GDNF), affiliated with neuronal survival and differentiation as well as trkB, associated with neuronal differentiation and survival are also important here. GDNF aids in the survival of dopaminergic neurons and has also been observed to have a role of neuroprotection during pregnancy [7]. TrkB, the receptor for BDNF, is involved in the regulation of neuronal survival and growth and those axons pathways involved in fetal development [8]. Maternal stress is characterized by increased levels of cortisol in the body of the mother that effects the intrauterine environment and ultimately fetal development. Neurodevelopment is affected when neurotrophic support system is disrupted, one of such systems are directed by BDNF therefore BDNF levels play an important role as they are affected by maternal stress factors and then they disturb the neural development in fetus. By understanding this pathway, it is easier to mitigate risk factors. Another important contributing factor to pregnancy outcomes is maternal age with those that are over 30 considered to be advanced in their pregnancy. Although there is no direct evidence that links advancing maternal age with reduced BDNF levels. But it has been associated with stressful conditions like gestational hypertension and preeclampsia, both affect fetal development. This revelation has highlighted a critical gap in the literature, as indirect effects of maternal age on BDNF through these complications have not been touched yet. Addressing this gap will help understand the connection between maternal factors and fetal outcomes more comprehensively [9]. This review aims to provide an up-to-date synthesis with regard to the way BDNF translates maternal stress and other influencing factors during pregnancy as well as their impact on the fetal brain. Through offering an understanding of how BDNF and other related neurotrophins engage with maternal health.

This study was positioned to help guide procedures that could enhance health of pregnant people and their children including the treatments that involve BDNF supplements.

METHODS

According to the recommendations by PRISMA suggested for reporting, the review was conducted from May 2024 to August 2024. Initially it included 89 articles in English from 2016 to 2024. The articles were systematically sorted based on inclusion criteria searched and reported the details including: author, year, regions, title, design, statistical analysis, methodology, maternal and fetal variables, sample size, key findings, and references. Several search engines were employed; Science Direct, Google Scholar, and PubMed.The search through databases emphasized upon comprehensiveness. It was made sure that articles fetched from each database were cross referenced with each other to control biasness. Majority papers were taken from Google Scholar due to its broader indexing but it was made sure that the indexing of articles encompass multiple sources. Collected research articles were taken from various parts of the world including Asia, Europe and America mainly. Article search was done using keywords: BDNF, stress markers, pregnancy, fetal neurodevelopment, stress factor exposure in pregnancy and stress response in body. Pregnancy, BDNF, stress markers, fetus, neural development, old women and maternal stress were the significant words. The articles which did not fulfil this inclusion criterion were eliminated. The inclusion criteria were focused on fluctuations in levels of BDNF and its effects in neurodevelopment along with other stress markers and all papers taken were from latest years, no paper older than year 2016 was taken. The collection and filtering process were done by two independent reviewers and to avoid reviewer's conflict and biasness Cohen's Kappa method was used. There were eighty-nine articles in total that were downloaded from databases. Seven duplicate articles were found and removed, leaving eighty-two for analysis. A total of seventy-two articles from the systematic review were eliminated based on irrelevant data added in them. After elimination, seventeen papers were picked and sorted which fulfilled inclusion criteria. Cohen's kappa, a statistical method, was employed to assess the reliability among the raters during the study selection process, ensuring consistency and agreement between reviewers. PRISMA model in Figure 1 illustrated selection of studies for review process showing elimination of studies that were not lying under the inclusion criteria. Total 50 articles were excluded according to specific reasons which were described in Figure 1.

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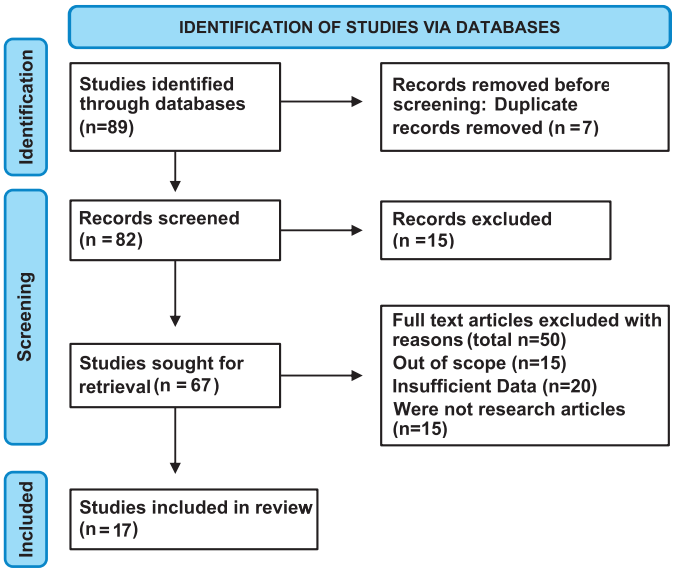

Figure 1: PRISMA Flowchart of Study Selection and Exclusion Criteria

RESULTS

The majority of the pregnant women in all the studies ranged from 18 to 45 years by age. The pregnant women taken as sample had shown symptoms of stress. 6/17 of studies were longitudinal studies, 5/17 were correlational/ prospective studies, 5/17 were experimental/ observational studies and 1/17 was exploratory study. The studies were taken from all regions of the world including Asia, Europe and America. Research studies were taken from last five years i.e. 2020-2024. The study reviewed papers that were conducted in Asia (47%), Europe (41%) and America (12%) respectively. The studies taken from Google Scholar (60%), Science Direct (30%), and others (10%) i.e. PubMed. A meta-analytical approach was employed using Comprehensive Meta-Analysis (CMA) software. This enabled the pooling of comparable outcomes of studies with effect of sizes. The trends related to impact of maternal stress on BDNF levels and fetal neurodevelopment were identified and pool effect size of -0.45 (95% CI: -0.65, -0.25) was seen between the relationship of high maternal stress and reduced BDNF levels. This method revealed some trends regarding the impact of maternal stress on fetus. Confidence intervals and biasness indices were also included to solidify the robustness of results. A variability in effect sizes ($I^2 = 62\%$, $p < 0.05$) was given to heterogeneity seen in study design and population characteristics. Results of these studies were shown in the Table 1 [10-26].

Table 1: Schematic Review of Studies that were most Appropriate According the PRISMA Defined Rules

Authors and Year (Region)	Study Population (Age Range)	Sample Size (N)	Maternal Variables related to BDNF	Fetal Variables Related to BDNF	Study Methodology (Longitudinal, Correlational etc) and Statistical Tools	Key Findings Related to BDNF
Dai Y *et al.*, 2024 [10] (China)	Pregnant Women (<35 Years Old)	1189	Pre-Preg Bmi, Weight Gain At Gestational Period, Maternal Age, Smoking, Education, Occupation	BNDF Levels In Cord Serum	Prospective Cohort Study, GLMs, QGC, BKMR, and Sex-Stratified Analysis	Four PFAS were Negatively Proportional to BNDF Levels in Females, Especially in Female Fetus
Lamadé *et al.*, 2024 [11] (Germany)	Pregnant Women (18-50 Years Old)	41	Depressive Symptoms, Prenatal Stress, Cortisone and Cortisol Levels in Amniotic Fluid, Socioeconomic Status	BDNF Levels In Cord Blood	Correlation Prospective Study, Linear Regression Models, Stratified Analysis, Natural Logarithmic Transformations	Depressive Symptoms and Socioeconomic Status were Related to the Higher BNDF Levels Positively
Cuiping Wang *et al.*, 2023 [12] (China)	Pregnant Women (>=20 years old)	711	Exposure to PM2.5 During Pregnancy, Age, Smoking, Education, Pre-Preg BMI	BDNF in Cord Blood, Birth Weight, Gender, Delivery Mode	Prospective Cohort Study, Linear Regression Models	PM2.5 Exposure in Pregnancy were Associated with Lower Levels of BDNF Especially in Male Infants. Normal Deliveries had Higher BDNF Levels than Caesarean
Chung-Hao Su *et al.*, 2021 [13] (Taiwan)	Infants (Birth to 12 Months Old)	24 (8 IMGD, 16 non-IMGD)	Gestational Diabetes Mellitus	Serum BNDF Levels	Prospective Cohort Study, P and S Correlation, Logistic Regression Models	Infants of Mothers with GDM had Lower BDNF Levels and Poor Language Composite Scores. POOR LCM Defines Defective Neurodevelopment in Subjects. IMGD Has Lower BNDF Levels
Mercado *et al.*, 2024 [14] (USA)	Fetuses (36 to 39 Weeks GA)	23	BNDF Levels Before Delivery	BNDF Levels in Cord Blood After Delivery	Exploratory Study, fMEG, Pearson Correlation, Partial Correlation, PSD Analysis	BNDF Levels of Mother Showed Negative Association with fetal Delta Brain Activity but Showed Positive Association with Alpha, Beta, and Theta Activity. Cord Blood BNDF Didn't Show Any Association with Brain Activity

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Richter *et al.*, 2022 [15] (Netherlands)	Children of 4 Years Old	21	Not Examined	BNDF DNA Methylation at 4 Years Old	Prospective Observational Cohort Study, Methylation Analysis, Neuro-developmental Testing, Regression analysis	Fetal Brain Sparing was Associated with Hyper-methylation of BDNF at CREB Binding Site in Children. This Correlates with Better Inhibitory Self-Control
Karunanithi Sivasangari *et al.*, 2020 [16] (India)	Babies of Prenatally Stressed Wister Rats (15-30 Days Old)	19 (7 Control, 6 PNS, 6 BME)	Exposure to Bacoppa monnieri Extract in GA	BNDF Levels, Postnatal Behaviour	Longitudinal Study in Vivo Experiments, ANOVA and Bonferroni Post Hoc Analyses	Prenatal Reduced Levels of Mature BDNF and Increased Levels of Pro-BDNF. Treatment with Bacoppa Monnieri Restored the Levels of BDNF
Abdollahi *et al.*, 2021 [17] (Iran)	Pregnant Wistar Rats and Fetuses	40	Hesperidin Dosage, Oxidative Stress, BDNF, TrkB	BDNF, TrkB, Oxidative Stress	Experimental Study with Longitudinal Design, ANOVA and Tukey's Post Hoc Tests	Hesperidin Increased the Levels of BDNF and TrkB. BDNF-TrkB Signalling Pathway is Necessary for Neurodevelopment of Fetus
Szymanski & Minichiello, 2022 [18] (UK)	Hippocampal Dentate Granule Cells of Immature Mouse, CA3 Principal Cells for Postnatal Development Study	Not Mentioned	Oxytocin, NKCC1, GABA	NKCC1, BDNF, TrkB, GABA	Longitudinal Experimental Study, smFISH and Wilcoxon Tests were Used	BDNF-TrkB Pathways was Significant for NKCC1 Modulation Which is Important for Formation of Hippocampal Circuits
Yu G *et al.*, 2021 [19] (China)	Pregnant Women	725	PFAS Levels	BDNF Levels	Prospective Cohort Study, Linear Regression Models and SPLS was Used	Prenatal Exposure to PFHxS Results in Increased Levels of BDNF in Fetal Cord Blood
Marchese MJ *et al.*, 2021 [20] (China)	Trophoblast of Human Placenta Tissues	Not Mentioned	PFAS Levels	BDNF, PFAS	Experimental Lab-Based Study, Western Blotting, Immunofluorescence, and ANOVA was Used	Placental Cells Showed Presence of BDNF Signalling. PFAS Didn't Significantly Alter BDNF Signalling
de Mendonça Filho *et al.*, 2021 [21] (Canada)	Children (Birth to 12 Years Old)	157	Mental Health, Smoking, Socio-economic Factors etc.	BDNF Levels	Longitudinal Study, LME and pICA was Used	BDNF Network Balances the Effect of Prenatal Adversity in Neural and Cognitive Development
Pascual-Mancho *et al.*, 2022 [22] (Spain)	Fetuses	130	Age, Preeclampsia, Use of Corticosteroids	BDNF Levels in Cord Blood, Fetal Doppler Alterations, IUGR	Longitudinal Study, ELISA, Mann- Whitney and Chi Square Tests Were Used	Cord Blood BDNF Concentrations Are Lower in Fetus with Growth Restriction Compared to AGA fetus BDNF May Play a Role in FGR Related Neuro-developmental Disorders
Zhang T *et al.*, 2024 [23] (China)	Infants (6 Months to 12 Months)	24	Diabetes Status	BDNF in Serum	Prospective Cohort Study, BSID III, t Tests, P and S Correlations and Logistic Regression Models are Used	Infants of Diabetic Mothers had Low BDNF Levels. These Infants Showed Poor Language Development Outcomes Compared to Healthy Ones. BDNF Showed Positive Association with Language Composite Scores
Granitzer *et al.*, 2024 [24] (Austria)	Pregnant Women (18-45 Years)	65	Lead and Cadmium Exposure, Iron Levels, BDNF Levels, KISS-1 Levels	BDNF Levels	Cross-Sectional and Correlational Study, ELISA, Spearman Correlation and CATREG Analysis	Maternal and Fetal BDNF levels were correlated to each other. Iron Deficiency was Associated with Lower BDNF Levels
Dingsdale *et al.*, 2021 [25] (UK)	Pregnant Women (18-45 Years)	251 Maternal and 212 Fetal Pairs	Anxiety, Depression, BDNF Levels	BDNF Levels in Serum of Cord Blood	Longitudinal Cohort Study, Spearman Correlation and Logistic Regression was Used	Stress Symptoms in Mothers were Related to Higher BDNF Levels
Shchelchkova *et al.*, 2020 [26] (Russia)	Pregnant C57BL/6 Mice	36 Pregnant Mice and 88 Parturient Mice	Chronic Hypobaric Hypoxia, BDNF Levels During Pregnancy	BDNF, GDNF, NSE, HIF-1β	Longitudinal Study with Experimental Components, Statistica 10.0 Software and Mann Whitney U-Test was Used.	Chronic Hypobaric Hypoxia is Related to Low Levels of BDNF in Pregnant Mice. Up Regulation of the Neuro-trophic Factors (BDNF, GDNF) were Associated with Protection of Neonates Against Hypoxic Damage.

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DISCUSSION

This review provided the evaluation on the contribution of BDNF as a biomarker in fetal neurodevelopment with a focus on maternal stress and related disorders. These studies provided evidence that stress and related psychological conditions make pregnancies lead to poor neurodevelopment of fetuses. BDNF was found to play a major role in this relation, affecting the neural circuits that were vulnerable to maternal influences. In particular, stress during pregnancy, hormonal changes, and numerous psychosocial disorders may negatively impact fetal brain formation. It had been proved that maternal anxiety and depression were associated with decreased fetal brain weight and changes in the pattern of fetal neuronal development, but the exact pathways had not been investigated comprehensively [26]. Other external factors such as maternal diet, toxic exposure and physical activity levels also played particular roles in the development of the fetal brain [27]. In addition, environmental factors including air pollution and socioeconomic status might also further have contributed to increase in inflammation and oxidative stress in the maternal side thus modifying fetal brain morphogenesis through epigenetic change [28]. BDNF played an important role in the stress response system and was known to be upregulated by many stressors, including psychological and environmental [29]. This neurotrophin does not only play the role of the neuronal survival and development but also guarantees the interaction between nervous system and the organism's reaction to stress. Increased levels of BDNF had been reported to over mood disorders including the depression and schizophrenia demonstrating that BDNF contributes differently in neurodevelopment and mental disorders [30, 31]. Also, there was an emerging body of evidence on so called 'brain-skin connection', which suggests that BDNF may impact skin conditions related to stress as well [32]. The mechanisms of BDNF action include BDNF binding to its high affinity receptor tropomyosin receptor kinase B (TrkB). BNDF binds-and-activates the extracellular domain of the TrkB receptor, which in turn triggers several intracellular signaling cascade, namely the Mitogen Activated Protein Kinase (MAPK), Phosphatidylinositol 3-Kinase (PI3K)/Akt and phospholipase C-gamma (PLC-γ signals [33, 34]. These pathways were involved in cell differentiation, proliferation and survival, neuronal development and activity-dependent synaptic plasticity. For instance, MAPK pathway activation was involved in neuronal differentiation and survival. However, PI3K/Akt signalling was necessary for cell survival and growth [35]. BDNF can also bind to the low affinity receptor p75NTR, which may promote either survival/survival or apoptotic signals [36, 37]. There was evidence of changes in BDNF levels during pregnancy. Some investigations had shown lower concentrations of BDNF in cord blood in the context of preterm birth compared with pregnancies at term. This difference may well hold a part in having an impact on fetal development as well as development of the nervous system [1]. BDNF concentration must remain optimal throughout gestation as both the high and low levels were proven to be detrimental for pregnancy [34]. For example, although it had been shown that BDNF levels decrease as pregnancy progresses, pro-BDNF had been found to increase and it had been established that there was intricate control of neurotrophin levels that was important in maintaining the health of both uterine and fetal environments [35, 36]. Smokers had higher serum BDNF levels during pregnancy and this has elevated questions on its impact to fetal neurodevelopment [37]. BDNF was vital to the pregnancy progress as its concentration lack during pregnancy which may cause preeclampsia and preterm delivery that harm both the mother and baby [38]. Moreover, it also has neuroprotective functions which may be of importance in its therapeutic use especially for Alzheimer diseases and other neurodegenerations. Reduced BDNF levels have been reported in Alzheimer's patients and help study the chances of using this protein as diagnostic and remediations markers at an initial stage of the disease [39]. So far, the experiments were undergoing experimental strategies for sustaining effectual delivery procedures for BDNF therapy, such as intranasal delivery system and the utilization of nanocarrier to increase the availability of BDNF with also lowering adverse effects [40, 41]. However, there were limitations in studying BDNF that stem with research studies on neurodevelopmental processes. These include population characteristics, method differences, and differences in instruments used when conducting the studies [36, 37]. Many studies relied on small sample sizes or cross-sectional designs which hinders the inference of casual relationships. For example, Dai Y et al., associated prenatal stress factor exposure with reduced BDNF levels but their study was not generizable due to narrow cohort [10]. Zhang T et al., found that infants of diabetic mothers had lower serum BDNF levels, which were positively associated with poor language development outcomes [23]. Granitzer S et al., focused on small European population that limited the study's applicability on other nations [24]. Similarly, Richter AE et al., showed significant finding but ignored environmental factors that could have confounding results [15]. Mercado et al., incorporated fMEG to analyse maternal BDNF levels but couldn't include biochemical assays limiting mechanistic insights [14]. There was also publication biasedness on BDNF's effectiveness since trials with

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negative outcomes were often ignored. Another factor which poses a challenge to the selection of research options in vulnerable patient groups such as infants and children was ethical issues especially when evaluating long-term development al impact [39]. Considering the variation of BDNF's roles in fetal development and potential relation to ASD and ADHD, large-scale extension studies were needed. Longitudinal studies were required to track the levels of BDNF with outcomes of neurodevelopment overtime. These studies should try to establish the method and the kind of assessment that should be used to further the knowledge on the normal as well as the abnormal developments of brain derived neurotrophic factor BDNF [38]. Standardized protocols were needed to make the measure of BDNF and maternal stress marker comparable across studies. In sum, BDNF seems an attractive target to improve neurodevelopmental outcomes in high-risk children. However, since the above was a consolidation of studies, there were limitations that were experienced throughout this research. Firstly, the studies were highly heterogeneous including differences in methodological approaches, study sample size, and methods used in BDNF assessment. Secondly, while comparing the study populations, demographic and distributional differences between geographic regions and various socioeconomic statuses were likely to put into questions the generalizability of the results. Furthermore, the ethical concerns regarding measuring BDNF in pregnant women and fetuses restricted the validity of long-term observation studies of maternal stress and BDNF on fetal neuronal development which was important to the scope of the analysis. Lastly, there was publication bias in which experiments with negative or incomplete results were less likely to be published, which could lead to an incline towards positive relationships between BDNF and fetal brain development.

CONCLUSIONS

This review highlights how BDNF was important in relating maternal stress with fetal neurodevelopment. Increased levels of maternal stress activity affect BDNF levels and fetal brain growth as well as stress biomarkers in offspring. Since such findings hold high levels of significance the results could be applied to women during early prenatal care for indicative of risk of poor neurodevelopmental outcome. Stress intervention measures such as mindfulness, nutritional and physical activity may be incorporated into the antenatal care to possibly reverse the abnormal BDNF levels due to stress induced neuro developmental problems. Moreover, strategies that focus on modulating the levels of BDNF, such as BDNF administration or neurotrophic support therapies, may be considered for treatment in high-risk pregnancies. Thus, by practicing such approaches it will be possible to decrease the threat of neurodevelopmental disorders in children, especially in mothers experiencing a high level of stress, and improve further cognitive and emotional development.

Authors Contribution

Conceptualization: AA, SP
Methodology: SP
Formal analysis: NA, MAA, AS
Writing, review and editing: MA, SP, KA, NA, AS, MAA

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Dunkel Schetter C. Psychological science on pregnancy: stress processes, biopsychosocial models, and emerging research issues. Annual Review of Psychology. 2011 Jan; 62(1): 531-58. doi: 10.1146/annurev.psych.031809.130727.

[2] Bath KG, Schilit A, Lee FS. Stress effects on BDNF expression: effects of age, sex, and form of stress. Neuroscience. 2013 Jun; 239: 149-56. doi: 10.1016/j.neuroscience.2013.01.074.

[3] Braun K and Champagne FA. Paternal influences on offspring development: behavioural and epigenetic pathways. Journal of Neuroendocrinology. 2014 Oct; 26(10): 697-706. doi: 10.1111/jne.12174.

[4] Garcés MF, Sanchez E, Torres-Sierra AL, Ruíz-Parra AI, Angel-Müller E, Alzate JP *et al.* Brain-derived neurotrophic factor is expressed in rat and human placenta and its serum levels are similarly regulated throughout pregnancy in both species. Clinical Endocrinology. 2014 Jul; 81(1): 141-51. doi: 10.1111/cen.12391.

[5] Santos ID, Crivellenti LC, Franco LJ, Sartorelli DS. Relationship between the quality of the pregnant woman's diet and birth weight: a prospective cohort study. European Journal of Clinical Nutrition. 2021 Dec; 75(12): 1819-28. doi: 10.1038/s41430-021-00894-6.

[6] Silvente Troncoso C, Hern'ández-Mart'ínez C, Voltas Moreso NÚ, Canals Sans J, Jard'í Piñana C, Basora Gallisà J *et al.* Impact of physical activity during pregnancy on infant neurodevelopment. Journal of Reproductive and Infant Psychology. 2024 Aug; 42(4): 620-35. doi: 10.1080/02646838.2022.2155626.

DOI: https://doi.org/10.54393/pjhs.v5i12.2703

[7] Duarte Azevedo M, Sander S, Tenenbaum L. GDNF, a neuron-derived factor upregulated in glial cells during disease. Journal of Clinical Medicine. 2020 Feb; 9(2): 456. doi: 10.3390/jcm9020456.

[8] Miyasaka Y and Yamamoto N. Neuronal activity patterns regulate brain-derived neurotrophic factor expression in cortical cells via neuronal circuits. Frontiers in Neuroscience. 2021 Dec; 15: 699583. doi: 10.3389/fnins.2021.699583.

[9] Schwartz A, Many A, Shapira U, Rosenberg Friedman M, Yogev Y, Avnon T *et al.* Perinatal outcomes of pregnancy in the fifth decade and beyond-a comparison of very advanced maternal age groups. Scientific Reports. 2020 Feb; 10(1): 1809. doi: 10.1038/s41598-020-58583-6.

[10] Dai Y, Ding J, Wang Z, Zhang B, Guo Q, Guo J et al. Sex-specific associations of per-and polyfluoroalkyl substances with Brain-Derived Neurotrophic Factors (BDNF) in cord serum. Environmental Research. 2024 Dec; 262: 119922. doi: 10.1016/j.envres.2024.119922.

[11] Lamadé EK, Pedraz-Petrozzi B, Lindner O, Meininger P, Coenen M, Witt SH et al. Stress during pregnancy and fetal serum BDNF in cord blood at birth. Psychoneuroendocrinology. 2024 Jul; 165: 107035. doi: 10.1016/j.psyneuen.2024.107035.

[12] Wang C, Jia X, Jin H, Meng Y, Ye W, Zhang N et al. Maternal exposure to fine particulate matter and brain-derived neurotrophic factor (BDNF) in the fetus: a prospective cohort study. Ecotoxicology and Environmental Safety. 2023 Jun; 257: 114912. doi: 10.1016/j.ecoenv.2023.114912.

[13] Su CH, Liu TY, Chen IT, Ou-Yang MC, Huang LT, Tsai CC *et al.* Correlations between serum BDNF levels and neurodevelopmental outcomes in infants of mothers with gestational diabetes. Pediatrics & Neonatology. 2021 May; 62(3): 298-304. doi: 10.1016/j.pedneo.2020.12.012.

[14] Mercado L, Rose S, Escalona-Vargas D, Dajani N, Siegel ER, Preissl H *et al.* Correlating maternal and cord-blood inflammatory markers and BDNF with human fetal brain activity recorded by magnetoencephalography: an exploratory study. Brain, Behavior, & Immunity-Health. 2024 Jun: 100804. doi: 10.1016/j.bbih.2024.100804.

[15] Richter AE, Bekkering-Bauer I, Verkaik-Schakel RN, Leeuwerke M, Tanis JC, Bilardo CM *et al.* Altered neurodevelopmental DNA methylation status after fetal growth restriction with brain-sparing. Journal of Developmental Origins of Health and Disease. 2022 Jun; 13(3): 378-89. doi: 10.1017/S2040174421000374.

[16] Sivasangari K, Sivamaruthi BS, Chaiyasut C, Rajan KE. Maternal stress-induced changes in adolescent and adult offspring: Neurobehavioural improvement and telomere maintenance. Heliyon. 2023 Oct; 9(10). doi: 10.1016/j.heliyon.2023.e20385.

[17] Abdollahi H, Edalatmanesh MA, Hosseini E, Foroozanfar M. The effects of hesperidin on BDNF/TrkB signaling pathway and oxidative stress parameters in the cerebral cortex of the utero-placental insufficiency fetal rat model. Basic and Clinical Neuroscience. 2021 Jul; 12(4): 511. doi: 10.32598/bcn.2021.2187.1.

[18] Szymanski J and Minichiello L. NKCC1 deficiency in forming hippocampal circuits triggers neurodevelopmental disorder: role of BDNF-TrkB signalling. Brain Sciences. 2022 Apr; 12(4): 502. doi: 10.3390/brainsci12040502.

[19] Yu G, Luo F, Nian M, Li S, Liu B, Feng L et al. Exposure to Perfluoroalkyl substances during pregnancy and fetal BDNF level: a prospective cohort study. Frontiers in Endocrinology. 2021 Jun; 12: 653095. doi: 10.3389/fendo.2021.653095.

[20] Marchese MJ, Li S, Liu B, Zhang JJ, Feng L. Perfluoroalkyl substance exposure and the BDNF pathway in the placental trophoblast. Frontiers in Endocrinology. 2021 Jul; 12: 694885. doi: 10.3389/fendo.2021.694885.

[21] de Mendonça Filho EJ, Barth B, Bandeira DR, de Lima RM, Arcego DM, Dalmaz C *et al.* Cognitive development and brain gray matter susceptibility to prenatal adversities: Moderation by the prefrontal cortex brain-derived neurotrophic factor gene co-expression network. Frontiers in Neuroscience. 2021 Nov; 15: 744743. doi: 10.3389/fnins.2021.744743.

[22] Pascual-Mancho J, Pintado-Recarte P, Morales-Camino JC, Romero-Román C, Hernández-Martin C, Bravo C *et al.* Brain-derived neurotrophic factor levels in cord blood from growth restricted fetuses with Doppler alteration compared to adequate for gestational age fetuses. Medicina. 2022 Jan; 58(2): 178. doi: 10.3390/medicina58020178.

[23] Zhang T, Wang H, Ouyang F, Yang H, Zhang J, Zhang N. Does brain-derived neurotrophic factor play a role in the association between maternal prenatal mental health and neurodevelopment in 2-year-old children? Journal of Affective Disorders. 2024 Aug; 359: 171-9. doi: 10.1016/j.jad.2024.05.074.

[24] Granitzer S, Widhalm R, Atteneder S, Fernandez MF, Mustieles V, Zeisler H *et al.* BDNF and KISS-1 levels in maternal serum, umbilical cord, and placenta: The potential role of maternal levels as effect biomarker. Exposure and Health. 2024 Apr; 16(2): 445-61. doi:

DOI: https://doi.org/10.54393/pjhs.v5i12.2703

10.1007/s12403-023-00565-w.

[25] Dingsdale H, Nan X, Garay SM, Mueller A, Sumption LA, Chacón-Fernández P et al. The placenta protects the fetal circulation from anxiety-driven elevations in maternal serum levels of brain-derived neurotrophic factor. Translational Psychiatry. 2021 Jan; 11(1): 62. doi: 10.1038/s41398-020-01176-8.

[26] Shchelchkova NA, Kokaya AA, Bezhenar VF, Rozhdestvenskaya OV, Mamedova MA, Mishchenko TA *et al.* The role of brain-derived neurotrophic factor and glial cell line-derived neurotrophic factor in chronic fetal oxygen deprivation. Современные технологии в медицине. 2020; 12(1 (eng)): 25-31. doi: 10.17691/stm2020.12.1.03.

[27] Manzari N, Matvienko-Sikar K, Baldoni F, O'Keeffe GW, Khashan AS. Prenatal maternal stress and risk of neurodevelopmental disorders in the offspring: a systematic review and meta-analysis. Social Psychiatry and Psychiatric Epidemiology. 2019 Nov; 54: 1299-309. doi: 10.1007/s00127-019-01745-3.

[28] Jadhav A, Khaire A, Gundu S, Wadhwani N, Chandhiok N, Gupte S *et al.* Placental neurotrophin levels in gestational diabetes mellitus. International Journal of Developmental Neuroscience. 2021 Jun; 81(4): 352-63. doi: 10.1002/jdn.10107.

[29] Fitzgerald E, Hor K, Drake AJ. Maternal influences on fetal brain development: The role of nutrition, infection and stress, and the potential for intergenerational consequences. Early Human Development. 2020 Nov; 150: 105190. doi: 10.1016/j.earlhumdev.2020.105190.

[30] Sahay A, Kale A, Joshi S. Role of neurotrophins in pregnancy and offspring brain development. Neuropeptides. 2020 Oct; 83: 102075. doi: 10.1016/j.npep.2020.102075.

[31] Li Y, Li F, Qin D, Chen H, Wang J, Wang J *et al.* The role of brain derived neurotrophic factor in central nervous system. Frontiers in Aging Neuroscience. 2022 Sep; 14: 986443. doi: 10.3389/fnagi.2022.986443.

[32] Xue Z, Shui M, Lin X, Sun Y, Liu J, Wei C *et al.* Role of BDNF/ProBDNF imbalance in postoperative cognitive dysfunction by modulating synaptic plasticity in aged mice. Frontiers in Aging Neuroscience. 2022 Mar; 14: 780972. doi: 10.3389/fnagi.2022.780972.

[33] Wang CS, Kavalali ET, Monteggia LM. BDNF signaling in context: From synaptic regulation to psychiatric disorders. Cell. 2022 Jan; 185(1): 62-76. doi: 10.1016/j.cell.2021.12.003.

[34] Greenberg PE, Fournier AA, Sisitsky T, Pike CT, Kessler RC. The economic burden of adults with major depressive disorder in the United States (2005 and 2010). The Journal of Clinical Psychiatry. 2015 Feb; 76(2): 5356. doi: 10.4088/JCP.14m09298.

[35] Mosiołek A, Mosiołek J, Jakima S, Pięta A, Szulc A. Effects of antidepressant treatment on neurotrophic factors (BDNF and IGF-1) in patients with Major Depressive Disorder (MDD). Journal of clinical medicine. 2021 Jul; 10(15): 3377. doi: 10.3390/jcm10153377.

[36] Castrén E and Monteggia LM. Brain-derived neurotrophic factor signaling in depression and antidepressant action. Biological Psychiatry. 2021 Jul; 90(2): 128-36. doi: 10.1016/j.biopsych.2021.05.008.

[37] Bélanger JC, Bouchard V, Le Blanc J, Starnino L, Welman M, Chabot-Blanchet M *et al.* Brain-derived neurotrophic factor mitigates the association between platelet dysfunction and cognitive impairment. Frontiers in Cardiovascular Medicine. 2021 Sep; 8: 739045. doi: 10.3389/fcvm.2021.739045.

[38] Gustafsson D, Klang A, Thams S, Rostami E. The role of BDNF in experimental and clinical traumatic brain injury. International Journal of Molecular Sciences. 2021 Mar; 22(7): 3582. doi: 10.3390/ijms22073582.

[39] Rana T, Behl T, Sehgal A, Srivastava P, Bungau S. Unfolding the role of BDNF as a biomarker for treatment of depression. Journal of Molecular Neuroscience. 2021 Oct; 71(10): 2008-21. doi: 10.1007/s12031-020-01754-x.

[40] Czéh B and Simon M. Benefits of animal models to understand the pathophysiology of depressive disorders. Progress in Neuro-Psychopharmacology and Biological Psychiatry. 2021 Mar; 106: 110049. doi: 10.1016/j.pnpbp.2020.110049.

[41] de Miranda AS, de Barros JL, Teixeira AL. Is neurotrophin-3 (NT-3): a potential therapeutic target for depression and anxiety?. Expert Opinion on Therapeutic Targets. 2020 Dec; 24(12): 1225-38. doi: 10.1080/14728222.2020.1846720.

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Systematic Review

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Clinical Efficacy of Dexmedetomidine and Propofol in Children Undergoing MRI for Urological Diseases: A Systematic Review

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ABSTRACT

Dexmedetomidine and propofol are commonly compared drugs used for sedation during pediatric anesthesia and Magnetic Resonance Imaging. However, their effectiveness and the impact on safety regarding children who undergo magnetic resonance imaging for specific urological diseases such as vesicoureteral reflux, hydronephrosis, and posterior urethral valves remain undetermined. **Objectives:** To evaluate the quality of sedation, recovery profiles, and complications using dexmedetomidine and propofol in pediatric patients undergoing magnetic resonance imaging for urological indications. **Methods:** Research with guidance from PRISMA was done in the PubMed, Google Scholar, and Semantic Scholar databases. Peer-reviewed articles that were published between January 2013 and April 2024 were identified bringing into the study 96 articles after applying the inclusion criteria. Cohort review: Fifteen studies were included in the present comparative analysis of dexmedetomidine and propofol for pediatric magnetic resonance imaging sedation. **Results:** Compared with propofol, dexmedetomidine provided better haemodynamic control, minimized emergence phenomenon and significantly improved postoperative recovery profiles. Nevertheless, the induction and recovery period was shorter in patients who received propofol. Both agents were associated with low adverse events incidences although subjects who received dexmedetomidine reported improved sedation quality that required less rescue medication than other subjects. **Conclusions:** It was concluded that dexmedetomidine and propofol are good in magnetic resonance imaging sedation for children with urological diseases, with better recovery and improved quality sedation from dexmedetomidine. Future research should extend the duration of intervention and make the dose-response relationship more precise.

INTRODUCTION

Magnetic Resonance Imaging (MRI) has tremendously proven useful in the diagnosis of structural and functional anomalies in children, as well as monitoring the disease dynamics in pediatric urology [1]. However, when it comes to performing MRI in children, more so children with urological diseases this is even more compounded. This is because the patient needs to be completely still during imaging and the mere sight of an MRI imaging procedure may cause anxiety and discomfort [2]. Sedation is required for quality image acquisition, patient comfort and successful intervention outcomes. Of all the different types of sedative agents, dexmedetomidine and propofol are popular for use in pediatric anesthesia due to their pharmacokinetic characteristics [3]. Dexmedetomidine is an α2-adrenergic receptor agonist, which has been used for sedation and analgesia and has weak opioid-like activity but exerts little or no respiratory depression [4]. The benefits are more stable hemodynamics; smooth

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sedation; and decreased emergence delirium rate, which makes it suitable for use in children [5]. On the other hand, propofol as a short-acting hypnotic agent is preferred due to the very short time to induction and recovery which will be desirable for any time-sensitive procedure like MRI [6]. They are, however, available in various forms and usage with much controversy as to the most appropriate sedative agent to give children especially those with urological problems undergoing MRI [7]. These conditions tend to make children prone to some risks such as physiological reactions and sensitivity to medication [8]. Earlier works have assessed the effectiveness of Dexmedetomidine and propofol in diverse scopes such as surgical and diagnostic endoscopic procedures. However, a thorough review of its usefulness of pediatric MRI for urological disorders is lacking [9]. Knowledge of these agents in terms of the differences in their ability to provide quality sedation in addition to patient's recovery and side effects is paramount in improving sedation regimes. An evidence-based approach to the data accessible to date can be useful for an improved understanding of the role of sedation in addressing the needs of pediatric urological patients [10].

This study aims to fill the existing gap in the literature about the clinical effectiveness of dexmedetomidine as well as propofol to children experiencing MRI for urological disorders. It especially concentrates on critical outcomes that include the quality of sedation, rate of recovery, incidences of adverse effects and overall safety of patients. Consequently, it aims to provide practical direction to clinicians on how to choose the best sedative agent. By highlighting these factors, this review provides actionable guidance to optimize sedative choices to enhance treatment procedures.

METHODS

This systematic review followed the reporting guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) due to its importance in giving a detailed report on the results. Systematic database searches were performed to retrieve articles on clinical trials comparing the effectiveness of dexmedetomidine and propofol used in children undergoing MRI for urological disorders. Due to the aim of the search being to focus on recent scientific achievements in the field of sedation protocols, the English articles published between January 2013 and April 2024 have been considered for this study. Non-English articles were excluded due to resource limitations for their translation and verification from their origin. Sources accessed were PubMed, Science Direct, Springer Link and Google Scholar. Preliminary databases like Cochrane Library didn't provide studies that could meet the inclusion criteria therefore the focus remained on more comprehensive databases. Some keywords which were used to search were "Dexmedetomidine MRI sedation", "Propofol MRI pediatric urology", "Pediatric anesthesia urological imaging" and "Sedation recovery time children MRI". The studies were included if they discussed the patients with urological conditions that require MRI imaging and the patients who were under 18 years old. Eligible studies compared the use of sedatives i.e. dexmedetomidine and propofol. The focus was kept on used sedative's primary outcomes such as sedation quality, recovery time, and detrimental effects. Randomized Control Trials (RCTs) and observational and cohort studies were taken. The studies were excluded if they used the adult population, did not use the MRI imaging technique or non-MRI- imaging techniques like Computed Tomography scans, case reports, editorials, non-systematic reviews without new data or if they lacked data on sedative outcomes. The studies which were outside the range of the timeline considered for this study and non-English articles were also excluded. The quality of studies was assessed using two statistical tools, the Cochrane risk of bias tool and the Newcastle Okawa scale. The first one was used to assess sequence generation, allocation concealment, blinding, and outcome reporting and the latter one was used to ensure methodological rigour. Out of 106 articles initially gathered, 10 were removed due to duplication. 96 articles were left for screening, out of them 35 were excluded due to unavailability of sufficient data such as methodology and detailed results. 61 articles were yielded for retrieval of information, 18 out of 61 studies were unable to retrieve and therefore 43 were assessed for eligibility. 28 out of 43 were excluded as the patients in these studies were adults (n=7), the study wasn't based on MRI sedation (n=10) and the absence of urological conditions (n=11). For each selected study, the following data were systematically extracted by two independent reviewers. The reviewers extracted the data based on the Sedative agent (s) used, Primary outcomes: Sedation quality, hemodynamic stability, adverse events, other secondary outcomes: the time required for the recovery, satisfaction of patients and their caregivers, Year of publication, and country of origin. The extracted data were reviewed and categorized within the PRISMA framework. Clinical data on dexmedetomidine and propofol efficacy in clinical settings were compared by integrating the total quality scores of quantitative and qualitative studies. The study characteristics were summarized by descriptive statistics. Where possible, outcome data were combined using mean differences for continuous variables (e.g., recovery times) and odds ratios for categorical variables (e.g., adverse event rates). The p-value threshold of <0.05 was used to evaluate the statistical significance. Because of the heterogeneity of included studies, meta-analysis was not conducted, but findings have been presented narratively. To enhance data readability, sedation depth, recovery profile, and the rates

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of adverse events were summarized in tables. The review also identified further research priorities including safety over the years and dosing regimens for children. Quantitative results were summarized in tabular form with profitability comparing the efficacy of dexmedetomidine and propofol in various aspects. The authors also made recommendations for applying the findings into clinical practice and directions for future research. Sedation depth, recovery profiles, and the adverse event rate were also summarized in tabular form. This study also identified trends, the missing data and issues for further investigation including long-term safety data and dosing for children. Data were summarized in tabular form in which various aspects of comparison between dexmedetomidine and propofol were highlighted. PRISMA flow diagram of search strategy, screening of studies, and application of inclusion and exclusion criteria for studies. 15 studies were taken for systematic review (Figure 1).

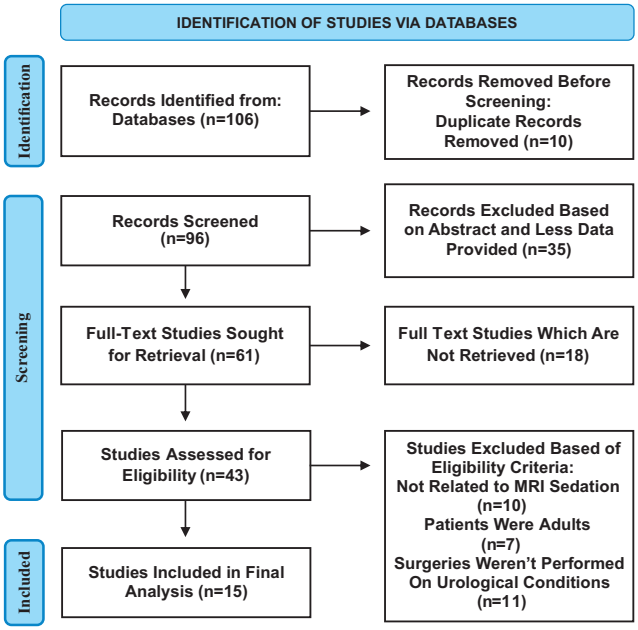

Figure 1: PRISMA flow chart of studies included

RESULTS

Inclusion criteria were confirmed by PRISMA guidelines and 15 studies were included in this systematic review comparing clinical efficacy of dexmedetomidine and propofol in pediatric pts undergoing MRI due to urological diseases. The type of studies included (80% from PubMed with the rest from Science Direct and Google Scholar) evaluated different endpoints including sedation quality, time to wake up, and postoperative complications. The examined studies were comprised of 8 RCTs, 5 observational cohort studies, and 2 prospective cohort studies to provide a comprehensive view of the sedative agents' outcomes. Dexmedetomidine and propofol were also equally effective in achieving the target sedation levels in MRI but with better sedation quality and less haemodynamic disturbance, less anxiety and analgesia with no severe respiratory depression seen in dexmedetomidine. Sedation quality was examined using the Pediatric Sedation State Scale (PSSS) in four studies where dexmedetomidine constantly showed better performance and higher scores (mean PSSS: 4.8 ± 0.3) in comparison to propofol (mean PSSS: 3.6 ± 0.5, $p<0.05$). Moreover, the Visual Analog Scale (VAS) was utilized for 3 studies, where caregivers gave better reviews and ratings for dexmedetomidine (average VAS score: 8.5/10) than propofol (average VAS score: 7.2/10). Measurable intraoperative outcomes revealed that dexmedetomidine and propofol were equally effective in providing enough sedation to keep the patient immobile during the MRI process and provide good imaging. Regarding recovery, both agents reduced the overall time to full recovery compared with conventional sedating regimens, all the while, dexmedetomidine took a somewhat longer period for recovery because of its sedative characteristics but was associated with a more predictable and comfortable emergence in the post-procedure period. Propofol on the other hand has a shorter induction and recovery time which is hugely beneficial when conducting MRI procedures that are time-sensitive. Possible side effects including hypotension and bradycardia with dexmedetomidine were observed usually at higher dosing levels but which were usually mild and manageable. With regards to side effects with intraoperative use, propofol while coming with the advantage of a rapid recovery was noted to have a higher incidence of transient hypotensive episodes than the mortal and this incidence was significantly reduced when dexmedetomidine was used. They both helped to prevent the majority including procedures involving children with urological problems from using rescue medications and opioids which are dangerous in provoking side effects and slow the healing process. Dexmedetomidine was noted to reduce opioid intake by about 30% while propofol was noted to reduce opioid intake by 25% compared to standard anesthetic programs. Some differences in the results were identified depending on the patient demographics, MRI protocols that were used in different centers, as well as the doses, still, both drugs appeared to be much more beneficial than the traditional sleep medications. By supporting the current study and its use of dexmedetomidine and propofol as desirable paediatric MRI sedation agents, this review suggests decreased opioid consumption, other improved outcomes include faster recovery and decreased side effects, particularly in the paediatric urological imaging. These suggest that both agents could be adopted in clinical settings to enhance sedation and enhance children's MRI for urological illnesses. A Systematic review of 15 studies selected based on PRISMA guidelines. Sedation quality, Recovery time, and Adverse events have been mentioned (Table 1).

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Table 1: Studies Selected Based on PRISMA Guidelines

References	Sample Size (Agent Studied)	Confounder: Sedation Quality	Confounder: Recovery Time	Confounder: Adverse Events	Key Findings
[11]	Dexmedetomidine, Propofol	Dexmedetomidine showed deeper sedation with minimal rescue sedatives.	Longer with dexmedetomidine, and shorter with propofol.	Propofol: transient hypotension; Dexmedetomidine: bradycardia.	Dexmedetomidine is preferred for quality; and propofol for speed.
[12]	Propofol	Adequate sedation was achieved but higher doses for some patients.	Fast recovery within 20 minutes post-MRI.	Mild nausea in 5% of cases, no severe events.	Propofol is effective for short procedures with rapid recovery.
[13]	Dexmedetomidine	Superior sedation with no additional agents required.	Slightly delayed (mean: 35 minutes).	None significant; bradycardia resolved spontaneously.	Dexmedetomidine ensured safety and consistent sedation.
[14]	Propofol, Dexmedetomidine	Both agents provided adequate sedation, but dexmedetomidine had smoother induction.	Propofol recovered faster by 15 minutes.	Propofol: mild apnea (3 cases); Dexmedetomidine: none.	Balanced choice depending on procedure length and risk.
[15]	Dexmedetomidine	High satisfaction scores among clinicians and patients.	Moderate recovery time (30 minutes).	Mild hypotension in 2% of patients.	Effective sedation with a high safety profile.
[16]	Dexmedetomidine, Propofol	Dexmedetomidine maintained better sedation depth in 95% of cases.	Recovery faster with propofol (20 min).	Bradycardia with dexmedetomidine (5%); transient hypotension with propofol (8%).	Dexmedetomidine is preferred for longer scans; propofol for short
[17]	Dexmedetomidine	Effective sedation in all cases, no rescue agents required.	Delayed recovery (mean: 40 minutes).	Minimal adverse effects were reported.	Reliable agent for safe and prolonged sedation.
[18]	Propofol	Adequate sedation but required higher doses in older children.	Quick recovery (average 15 minutes).	Mild nausea in 7%; no significant adverse events.	Suitable for shorter procedures.
[19]	Dexmedetomidine	High satisfaction from caregivers and staff.	Moderate recovery time (30-35 minutes).	Bradycardia in 3% of patients, no severe events.	Effective for MRI procedures requiring prolonged immobility.
[20]	Dexmedetomidine, Propofol	Both achieved target sedation; dexmedetomidine was smoother.	Recovery faster with propofol (18 minutes).	Dexmedetomidine: bradycardia (4 cases); propofol: transient apnea (2 cases).	Balanced approach with emphasis on individual patient needs.
[21]	Propofol	Effective sedation is achieved rapidly.	Recovery within 12-20 minutes.	Nausea in 6%; no significant adverse events.	Reliable for rapid onset and recovery.
[22]	Dexmedetomidine	Excellent sedation depth with no rescue medication needed.	Slightly delayed recovery (35-40 minutes).	Mild hypotension in 3%.	Ideal for prolonged procedures requiring deep sedation.
[23]	Propofol	Moderate sedation requires some dose adjustments.	Recovery in 18-25 minutes.	Transient apnea in 4%.	Effective but needed monitoring in patients with respiratory issues
[24]	Dexmedetomidine	Consistently deep sedation across all age groups.	Longer recovery (40 minutes on average).	Bradycardia in 2%.	Suitable for long-duration MRI with hemodynamic monitoring.
[25]	Dexmedetomidine, Propofol	Dexmedetomidine is superior for sedation quality; propofol is quicker induction.	Recovery 20 minutes (propofol); 35 minutes (dexmedetomidine).	Dexmedetomidine: minimal side effects; propofol: mild nausea in 4%.	Dual options depending on the case complexity.
[26]	Dexmedetomidine	High-quality sedation, no additional agents required.	Recovery within 40 minutes.	No significant adverse events.	A safe and effective agent with reliable outcomes.

DISCUSSION

According to this systematic review, dexmedetomidine and propofol are both highly valuable anesthesia agents in pediatric patients with urological diseases involving MRI, and the strengths and future uses of both drugs are discussed [27]. Both of these sedative agents present a variety of benefits that fit well within the parameters of pediatric anesthesia in MRI procedures; however, both of these sedative agents have advantages that set them up for specific uses in certain clinical situations [28]. Hemodynamic stability and analgesic effect profiles indicated that dexmedetomidine is most effective in maintaining MRI procedural safety and patient sedation

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during extensive procedures. It anchors itself onto the five essential sleep stages and entails very low probabilities of depressing the respiratory system which is beneficial for pediatric use [29]. Despite 15–20 minute longer recovery times of dexmedetomidine (mean 35 minutes' vs propofol 20 minutes, p=0.03), the difference may not be clinically significant when sedation quality is prioritized over rapid recovery. However, in high turnover or brief procedures, propofol's shorter recovery time is desirable. In turn, propofol offered the advantages of faster induction and emergence, which are important for the throughput in the Operating Room in busy practice environments [30]. This is despite a slightly higher rate of transient hypotension which, as observed, can be managed by careful dose adjustments and monitoring [31]. One of the significant discoveries was that both agents reduced procedural anxiety and pain which fits in the pediatric need for non-invasive, trauma-free sedation [32]. The anxiolytic and analgesic properties of dexmedetomidine were most apparent in improving the comfort of the patient and decreasing the need for more analgesics or opioids in the postoperative period. Propofol also established valid usage in procedural sedation; however, it has a lower effect on procedural pain and thus can be most beneficial for short-term general anesthesia when analgesia is not an essential consideration [33]. Side effects like bradycardia and hypotension reported with dexmedetomidine and transient hypotension with propofol were in keeping with other articles published earlier in the pediatric sedation literature. Nevertheless, the infrequency and short duration of such episodes underscore the safety of both agents if used in specific conditions [34]. These findings also support the need to adopt weight, age and clinical condition-based dosing regimens in any clinical care. Both agents were generally well tolerated with adverse events observed being generally mild and manageable, consistent with safety profiles associated with use in pediatrics. Mild bradycardia occurred more often with dexmedetomidine (2–5%), while propofol was associated with transient hypotension (6–8%). Effects were dose-dependent and resolved by appropriate monitoring and intervention, underlining the benefit of individualized dosing strategies [19, 24]. The opioids used by both agents contributed to a substantial reduction in opioid requirements (approximately 30% with dexmedetomidine vs. approximately 25% with propofol), which is consistent with recent efforts to reduce pediatric anesthesia opioid use. For these reasons, particularly the fact that dexmedetomidine is safer than other sedatives for patients with breathing or heart problems, and just as effective in achieving adequate deep sedation, the drug could be a front-line candidate for pediatric MRI sedation [35]. Although propofol possesses some drawbacks, its fast recovery time makes it ideal for use in institutions seeking to enhance procedural throughput at essentially no risk [36]. The decreased requirement for rescue medications with both agents contributed to their role in the reduction of systemic side effects that are particularly problematic in pediatric patients [37]. These findings are in sync with prior research in pediatric sedation suggesting that both dexmedetomidine and propofol are safer and more effective than routine anesthetic agents. The documented decrease in opioid utilization especially with dexmedetomidine relates to its effectiveness in responding to the increasing concern of opioid-sparing in pediatric anesthesia [38]. Likewise, the propofol a rapid recovery is consistent with studies done on procedural sedation in other settings than the MRI which supports the factorial's versatility. However, the achieved results can be considered quite encouraging because variations in treatment outcomes are observed reflecting variations in institutional protocols, dosage regimens, and patient populations [39]. For example, the ability of dexmedetomidine to manage hemodynamics may differ according to the age and the nature of the illness of a patient [40]. Slightly, transient undesirable effects which could occur require that protocols on mechanical sedation should be set so that the results can be recurrently replicated, thus emphasizing safety. Although this review makes it possible to prove the efficiency and safety of dexmedetomidine and propofol, some voids need to be filled. Since the included studies vary concerning differences in the usage of MRI protocols, sedation dosages, and patient demographics, there is a potential risk of bias in the results. Furthermore, the reliance on very few RCTs inhibited the translational applicability of the conclusions, especially when applied to a wide range of institutional practices or wider clinical populations. Another aspect is that the outcome of measures is not uniform across the studies and direct comparison between the recovery of sedation quality and profiles is difficult. Further analyses require long-term investigations of their effects on cognition and development in children. Also, the studies that investigate these agents in combination with other sedatives or analgesics appear to help in understanding multi-component approaches to the issue of sedation [41]. Standardization of dosing regimens and multi-center investigation is also important for setting the

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basis of generalizable practices for the use of these drugs in children undergoing MRI sedation.

CONCLUSIONS

It was concluded that dexmedetomidine and propofol both proved to be effective and safe sedatives for pediatric MRI in urological diseases, but dosing needs to be tailored to clinical situations. In particular, dexmedetomidine is well suited for children with complex urological conditions or those at risk of cardiovascular or respiratory complications that require prolonged procedures with hemodynamic stability, without increased use of opioids and with improvement in comfort level. On the contrary, propofol is the best for shorter, time-bound procedures due to its fast induction and recovery allowing for shorter, faster patient turnover. The use of these agents remains to be optimized concerning dosing regimens and long-term outcomes to be best used in future research.

Authors Contribution

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Methodology: PS, MUIB, HWUH, SM
Formal analysis: HWUH, SM
Writing review and editing: SIAZ, AA, EUH

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Paraboschi I, Mantica G, Minoli DG, De Marco EA, Gnech M, Bebi C *et al.* Fluorescence-Guided Surgery and Novel Innovative Technologies for Improved Visualization in Pediatric Urology. International Journal of Environmental Research and Public Health. 2022 Sep; 19(18): 11194. doi: 10.3390/ijerph191811194.

[2] Arnold TC, Freeman CW, Litt B, Stein JM. Low-Field MRI: Clinical Promise and Challenges. Journal of Magnetic Resonance Imaging. 2023 Jan; 57(1): 25-44. doi: 10.1002/jmri.28408.

[3] Elsaeidy AS, Ahmad AH, Kohaf NA, Aboutaleb A, Kumar D, Elsaeidy KS *et al.* Efficacy and Safety of Ketamine-Dexmedetomidine Versus Ketamine-Propofol Combination for Periprocedural Sedation: A Systematic Review and Meta-analysis. Current Pain and Headache Reports. 2024 Apr; 28(4): 211-27. doi: 10.1007/s11916-023-01208-0.

[4] Wang XD, Yang B, Fan LL, Guo N, Song HB. Application of Dexmedetomidine combined with Propofol Intravenous Anesthesia in Laparoscopic Day Surgery in Pediatric Urology. Pakistan Journal of Medical Sciences. 2022 Jan; 38(1): 150. doi: 10.12669/pjms.38.1.4378.

[5] Freriksen JJ, van der Zanden TM, Holsappel IG, Molenbuur B, de Wildt SN. Best Evidence-Based Dosing Recommendations for Dexmedetomidine for Premedication and Procedural Sedation in Pediatrics: Outcome of A Risk-Benefit Analysis by the Dutch Pediatric Formulary. Pediatric Drugs. 2022 May; 24(3): 247-57. doi: 10.1007/s40272-022-00498-y.

[6] McKinstry-Wu A, Jiang T, Mandel A, Ayensu K, Thomas S. for Neuroscience in Anesthesiology and Critical Care, September 8-10, 2023. J Neurosurg Anesthesiol. 2023 Oct; 35(4). doi: 10.1097/ANA.0000000000000935.

[7] Bar-Sever Z, Shammas A, Gheisari F, Vali R. Pediatric Nephro-Urology: Overview and Updates in Diuretic Renal Scans and Renal Cortical Scintigraphy. In Seminars in Nuclear Medicine. 2022 Jul; 52(4): 419-431. doi: 10.1053/j.semnuclmed.2021.12.002.

[8] Wiener JS, Huck N, Blais AS, Rickard M, Lorenzo A, Di Carlo HN *et al.* Challenges in Pediatric Urologic Practice: A Lifelong View. World Journal of Urology. 2021 Apr; 39: 981-91. doi: 10.1007/s00345-020-03203-1.

[9] Zhang W, Wang L, Zhu N, Wu W, Liu H. A Prospective, Randomized, Single-Blinded Study Comparing the Efficacy and Safety of Dexmedetomidine and Propofol for Sedation During Endoscopic Retrograde Cholangiopancreatography. BioMed Central Anesthesiology. 2024 May; 24(1): 191. doi: 10.1186/s12871-024-02572-z.

[10] Falkiewicz MK, Su R, Jones SL, Shayan M, Farhat WA, Peters ME. Pediatric Sedation Unit: A Safe, Effective, and Satisfactory Alternative to Outpatient Pediatric Urological Procedures Under Anesthesia. Urology Practice. 2023 Mar; 10(2): 171-6. doi: 10.1097/UPJ.0000000000000364.

[11] Tang S, Liu J, Ding Z, Shan T. The Effect of Dexmedetomidine On Emergence Delirium of Postanesthesia Events in Pediatric Department: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Medicine. 2024 Sep; 103(36): e39337. doi: 10.1097/MD.0000000000039337.

[12] Johnson KL, Cochran J, Webb S. Lower-Dose Propofol Use for MRI: A Retrospective Review of a Pediatric Sedation Team's Experience. Pediatric Emergency Care. 2021 Nov; 37(11): e700-6. doi: 10.109

DOI: https://doi.org/10.54393/pjhs.v5i12.2590

7/PEC.0000000000002289.

[13] Handlogten K, Warner L, Granberg C, Gargollo P, Thalji L, Haile D. Implementation of a Spinal Anesthesia and Sedation Protocol That Reliably Prolongs Infant Spinal Anesthesia: Case Series of 102 Infants Who Received Spinal Anesthesia for Urologic Surgery. Pediatric Anesthesia. 2020 Dec; 30(12): 1355-62. doi: 10.1111/pan.14024.

[14] Zhang X, Bai Y, Shi M, Ming S, Jin X, Xie Y. Effect of Different Administration and Dosage of Dexmedetomidine in the Reduction of Emergence Agitation in Children: A Meta-Analysis of Randomized Controlled Trials with Sequential Trial Analysis. Translational Pediatrics. 2021 Apr; 10(4): 929. doi: 10.21037/tp-21-105.

[15] Gernhold C, Kundtner N, Steinmair M, Henkel M, Oswald J, Haid B. Sedation Rate Reduction in Paediatric Renal Nuclear Medicine Examinations: Consequences of a Targeted Audit. Children. 2021 May; 8(5): 424. doi: 10.3390/children8050424.

[16] Roberts RJ, Banta L, Verghese ST. Non-Operating Room Anesthesia for Pediatric Surgical Procedures. Anesthetic Management in Pediatric General Surgery: Evolving and Current Concepts. 2021: 101-17. doi: 10.1007/978-3-030-72551-8_6.

[17] Gnech M, van Uitert A, Kennedy U, Skott M, Zachou A, Burgu B *et al*. European Association of Urology/European Society for Paediatric Urology Guidelines on Paediatric Urology: Summary of the 2024 Updates. European Urology. 2024 Apr. doi: 10.1016/j.eururo.2024.03.025.

[18] Bang YJ, Kim J, Gil NS, Sim WS, Ahn HJ, Park MH et al. Pulmonary Atelectasis After Sedation with Propofol vs Propofol-Ketamine for Magnetic Resonance Imaging in Children: A Randomized Clinical Trial. Journal of the American Medical Association Network Open. 2024 Nov; 7(11): e2433029-. doi: 10.1001/jamanetworkopen.2024.33029.

[19] Rogers AP. Sedation for Radiological Procedures. Pediatric Sedation Outside of the Operating Room: A Multispecialty International Collaboration. 2021: 475-95. doi: 10.1007/978-3-030-58406-1_23.

[20] Kerkhofs L, Allegaert K, Toelen J, Vanhonsebrouck K. Pediatric Procedural Sedation and Analgesia (PROSA) in the Leuven University Hospitals: An Audit On Efficacy and Safety. Children. 2022 May; 9(6): 776. doi: 10.3390/children9060776.

[21] Moltoni G, Lucignani G, Sgrò S, Guarnera A, Rossi Espagnet MC, Dellepiane F *et al*. MRI Scan with the "Feed and Wrap" Technique and with an Optimized Anesthesia Protocol: A Retrospective Analysis of a Single-Center Experience. Frontiers in Pediatrics. 2024 Aug; 12: 1415603. doi: 10.3389/fped.2024.1415603.

[22] Rebollar RE, Palacios MG, Riobó MF, Morera LT. Dexmedetomidine and Perioperative Analgesia in Children. Revista Española de Anestesiología y Reanimación (English Edition). 2022 Oct; 69(8): 487-92. doi: 10.1016/j.redare.2022.08.003.

[23] Nthodi TV, Madathil Abdul BP, Subramonian M, Krishnankutty R. Effect of Dexmedetomidine Versus Propofol on Sevoflurane Related Emergence Agitation in Paediatric Patients: A Randomized Clinical Study. Journal of Clinical and Diagnostic Research. 2024 May; 18(5). doi: 10.7860/JCDR/2024/68717.19374.

[24] Ma H, Wachtendorf LJ, Santer P, Schaefer MS, Friedrich S, Nabel S *et al*. The Effect of Intraoperative Dexmedetomidine Administration On Length of Stay in the Post-Anesthesia Care Unit in Ambulatory Surgery: A Hospital Registry Study. Journal of Clinical Anesthesia. 2021 Sep; 72: 110284. doi: 10.1016/j.jclinane.2021.110284.

[25] Rahayu NR and Mutripah S. Compared Effectiveness, Safety and Cost of Dexmedetomidine with Midazolam: A Review. Pharmacology, Medical Reports, Orthopedic, and Illness Details. 2023 Jul; 2(2): 85-95. doi: 10.55047/comorbid.v2i2.881.

[26] Negm AN. Efficacy and Safety of Dexmedetomidine Combined with Bupivacaine in Infants' Surgeries: A Randomized Controlled Trial. Suez Canal University Medical Journal. 2024 Jan; 27(1): 41-52. doi: 10.21608/scumj.2024.342791.

[27] Kim JY, Kim KN, Kim DW, Lim HJ, Lee BS. Effects of Dexmedetomidine Sedation for Magnetic Resonance Imaging in Children: A Systematic Review and Meta-Analysis. Journal of Anesthesia. 2021 Aug; 35: 525-35. doi: 10.1007/s00540-021-02946-4.

[28] Jung SM. Drug Selection for Sedation and General Anesthesia in Children Undergoing Ambulatory Magnetic Resonance Imaging. Yeungnam University Journal of Medicine. 2020 Jul; 37(3): 159-68. doi: 10.12701/yujm.2020.00171.

[29] Shioji N, Everett T, Suzuki Y, Aoyama K. Pediatric Sedation Using Dexmedetomidine and Remimazolam for Magnetic Resonance Imaging. Journal of Anesthesia. 2022 Feb; 36(1): 1-4. doi: 10.1007/s00540-021-02957-1.

[30] Zhao Y, Qin F, Liu Y, Dai Y, Cen X. The Safety of Propofol Versus Sevoflurane for General Anesthesia in Children: A Meta-Analysis of Randomized Controlled Trials. Frontiers in Surgery. 2022 Jun; 9: 924647. doi: 10.3389/fsurg.2022.924647.

[31] Saugel B, Bebert EJ, Briesenick L, Hoppe P, Greiwe G, Yang D *et al*. Mechanisms Contributing to Hypotension After Anesthetic Induction with

DOI: https://doi.org/10.54393/pjhs.v5i12.2590

Sufentanil, Propofol, and Rocuronium: A Prospective Observational Study. Journal of Clinical Monitoring and Computing. 2022 Apr: 1-7. doi: 10.1007/s10877-021-00653-9.

[32] Zeigler LN, Modes KB, Deshpande JK. Anesthesia for Pediatric Urological Procedures. Gregory's Pediatric Anesthesia. 2020 Apr: 813-33. doi: 10.1002/9781119371533.ch32.

[33] Kim HY, Choi YH, Lee SJ. Effect of Sedation Anesthesia with Intravenous Propofol on Transrectal Ultrasound-guided prostate biopsy outcomes. Journal of Korean Medical Science. 2022 Apr; 37(15). 10.3346/jkms.2022.37.e115.

[34] Sager C, Barroso Jr U, Netto MB, Retamal G, Ormaechea E. Management of Neurogenic Bladder Dysfunction in Children Updates and Recommendations On Medical Treatment. International Brazilian Journal of Urology. 2022 Jan; 48: 31-51. doi: 10.1590/s1677-5538.ibju.2020.0989.

[35] Sperotto F, Mondardini MC, Dell'Oste C, Vitale F, Ferrario S, Lapi M *et al.* Efficacy And Safety of Dexmedetomidine for Prolonged Sedation in the PICU: A Prospective Multicenter Study (PROSDEX). Pediatric Critical Care Medicine. 2020 Jul; 21(7): 625-36. doi: 10.1097/PCC.0000000000002350.

[36] Jefferson FA, Findlay BL, Handlogten KS, Gargollo PC, Warner LL, Woodbury JM *et al.* Spinal Anesthesia in Infants Undergoing Urologic Surgery Duration Greater Than 60 Minutes. Journal of Pediatric Urology. 2022 Dec; 18(6): 786-e1. doi: 10.1016/j.jpurol.2022.07.003.

[37] Alsaywid BS, Alyami FA, Alqarni N, Neel KF, Almaddah TO, Abdulhaq NM *et al.* Urinary Tract Infection in Children: A Narrative Review of Clinical Practice Guidelines. Urology Annals. 2023 Apr; 15(2): 113-32. doi: 10.4103/ua.ua_147_22.

[38] Fattah Kamel AA, Abdel Naby SM, Elmesallamy WA, Salem DA. Opioid Sparing Analgesia: Continuous Intraoperative Infusion of Dexmedetomidine Versus Lidocaine for Intracranial Surgeries in Children: A Double-Blind Randomized Clinical Trial. Egyptian Journal of Anaesthesia. 2022 Dec; 38(1): 158-65. doi: 10.1080/11101849.2022.2048580.

[39] Stein R, Bogaert G, Dogan HS, Hoen L, Kocvara R, Nijman RJ *et al.* EAU/ESPU Guidelines On the Management of Neurogenic Bladder in Children and Adolescent Part I Diagnostics and Conservative Treatment. Neurourology and Urodynamics. 2020 Jan; 39(1): 45-57. doi: 10.1002/nau.24211.

[40] Hayatghaibi SE, Cazaban CG, Chan SS, Dillman JR, Du XL, Huang YT *et al.* Turnaround Time and Efficiency of Pediatric Outpatient Brain Magnetic Resonance Imaging: A Multi-Institutional Cross-Sectional Study. Pediatric Radiology. 2023 May; 53(6): 1144-52. doi: 10.1007/s00247-022-05563-9.

[41] Frush DP, Callahan MJ, Coley BD, Nadel HR, Paul Guillerman R. Comparison of the Different Imaging Modalities Used to Image Pediatric Oncology Patients: A COG Diagnostic Imaging Committee/SPR Oncology Committee White Paper. Pediatric Blood and Cancer. 2023 Jun; 70: e30298. doi: 10.1002/pbc.30298.

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Systematic Review

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Evaluating the Accuracy and Reliability of the Demirjian Method for Dental Age Assessment: A Systematic Review

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ABSTRACT

The biological age estimation performed by using dental age assessment is considered a reliable, time-saving, and time-saving technique. Dental age assessment plays an important role in various fields. **Objective:** To assess the accuracy and reliability of the Demirjian method in determining dental age. **Methods:** A systematic review with a study duration of twelve months from September 2023 to August 2024, was conducted to identify relevant literature published in fifteen years between 2010 and 2024. Comprehensive searches were performed across multiple databases, including PubMed, Google Scholar, Cochrane Library, Springer, and Science Direct. The PRISMA guidelines were strictly adhered to throughout the review process. Relevant data were extracted from these studies, and a comprehensive analysis was performed to synthesize the available evidence. **Results:** These results indicate Demirjian methods compared to other dental age assessment methods such as Nolla, Willem's method showed less accuracy and reliability for dental age assessment. **Conclusions:** It was concluded that the Demirjian method compared to other dental age assessment methods demonstrated lesser reliability, showed less accuracy in finding the differences between dental age and chronological age, and it also overestimated dental age.

INTRODUCTION

Age determination has become a significant aspect of current medico-legal practice, especially in forensic dentistry. The Chronological Age (CA) of any individual is analyzed from date of birth via birth registration documentation. Whereas, Dental Age (DA) refers to a person's age based on the development and eruption of their teeth [1]. The biological age estimation performed by using dental age assessment (DAA) is considered a reliable, time-saving, and time-saving technique. DAA is the process of determining a person's age based on their dental development. Dentists use specific charts and guidelines to compare a person's teeth to age-related norms. This can be helpful in situations where a person's chronological age is unknown or uncertain, such as in forensic investigations or when determining a child's developmental stage [2]. Dental development, influenced by both genetic and

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systemic factors, provides valuable insights into age estimation. Radiographic techniques, particularly those examining third molar eruption (TME), have been instrumental in this field since the 1980s [3]. TME, closely linked to BMI and childhood nutrition, serves as a sensitive indicator of environmental impact on dental development [4]. Combined with dental age assessment (DAA), chronological age assessment (CAA) offers a comprehensive approach to reconstructing biological profiles, especially in cases where birth certificates are unavailable. This is particularly relevant in contexts such as natural disasters, criminal investigations, child labor, child marriage, adoption, and illegal immigration [5]. Tooth development, being less susceptible to environmental factors, is a reliable parameter for age estimation in forensic contexts [6]. Among these, tooth formation rate is preferred over skeletal development for better CAA as it is least affected by malnutrition and other factors. There are various methods used for the maturation of permanent teeth and CAA from DA. These methods encompass Morrees, Willems, Kvaal, Haavikko, Nolla, Lundberg, and Demirjian. Among these, the Demirjian method (DM) described in 1973 based on French-Canadian children is widely utilized in CAA [7]. In 2004, this method was subsequently modified to estimate the age of older individuals using the third molar (Table 1).

Table 1: Tooth Development Stages According to Demirjian 1973 Method

Tooth	Molars (M2, M1)	Bicuspids (Pm2, PM1)	Canines	Incisors (I2, I1)	Molars (M2, M1)	Bicuspids (Pm2, PM1)	Canines	Incisors (I2, I1)
	Boys (Stages)				Girls (Stages)			
A	2.1	1.7	-	-	2.7	1.8	-	-
B	3.5	3.1, 0.0	-	-	3.9	3.4, 0.0	-	-
C	5.9, 0.0	5.4, 3.4	0.0	0.0	6.9, 0.0	6.5, 3.7	0.0	0.0
D	10.1, 8.0	9.7, 7.0	3.5, 3.2	0.0	11.1, 4.5	10.5, 7.5	3.8,3.2	0.0
E	12.5, 9.6	12.0, 11.0	7.9, 5.2	1.9	13.5, 6.2	12.7, 11.8	7.3, 5.6	9.4
F	13.2, 12.3	12.8, 12.3	10.0, 7.8	4.1	14.2, 9.0	13.5, 13.1	10.3, 8.0	5.1
G	13.6, 17.0	13.2, 12.7	11.0, 11.7	8.2	14.5, 14.0	13.8, 13.4	11.6, 12.2	9.3
H	15.4, 19.3	14.4, 13.5	11.9, 13.7	11.8	15.6, 16.2	14.6, 14.1	12.4, 14.2	12.9

This staging system ranges from crown and root formation to apex closure of the seventh mandibular teeth. It describes tooth development staging in line diagrams and clear radiographs. As tooth sizes may vary from person to person, dental maturity stages are more recognizable [8]. The dental maturity score (DMS) is calculated by subtracting the chronological age from the dental age. The estimation of DM may also provide information on teeth eruption and dental development. This method is simple and practical with clear definitive stages, increased interobserver agreement, and reduced speculation [9, 10]. Our systematic review identified conflicting conclusions in the studies evaluating the accuracy and reliability of Demirjian's method for DAA. Furthermore, the literature lacks enough data evaluating different DAA methods, including different sample sizes with multi-ethnicity. This study aims to conduct a detailed systematic review of the Demirjian method in DAA.

METHODS

A comprehensive literature searches in the form of systematic review adhering to the preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines was conducted across multiple databases, including PubMed, Google Scholar, Cochrane Library, Springer, and Science Direct. A systematic review with a study duration of twelve months from September 2023 to August 204, was conducted to identify relevant literature published in fifteen years between 2010 and 2024. The following keywords and MeSH terms were used: "Demirjian method," "dental age assessment," "accuracy," "reliability," "age estimation," and related terms. Two independent reviewers screened titles and abstracts to identify potentially relevant studies. Full-text articles of eligible studies were retrieved and assessed for inclusion based on the predetermined inclusion and exclusion criteria outlined. Disagreements were resolved through consensus or by consulting a third reviewer. The PRISMA 2020 guidelines were followed to ensure transparency and rigor in the review process. Data extraction was performed independently by two reviewers using a standardized data extraction form. The following information was extracted from each included study: author (s), publication year, study design, sample size, participant characteristics, methodology for dental age assessment, comparison methods, and reported accuracy and reliability measures. Any discrepancies were resolved through discussion and consensus. A qualitative synthesis of the included studies was performed to identify key findings and trends. The findings were summarized narratively, highlighting the strengths and limitations of the included studies. Of 5,132 initial studies, 2,000 were screened. After excluding 1,500, we reviewed 500 full-text articles, ultimately including 28 for qualitative synthesis (Figure 1).

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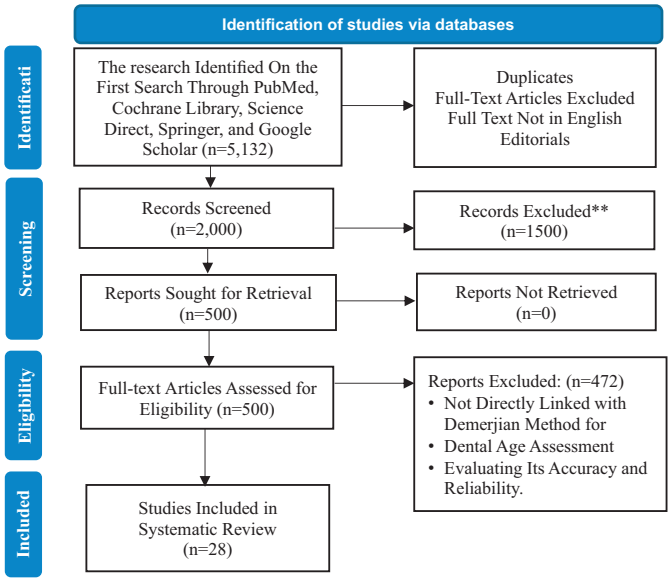

Figure 1: Screened Studies Included in the Systematic Review

The detailed inclusion and exclusion criteria followed for this systematic review are provided (Table 2).

Table 2: Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
Papers published between 2010 and 2024.	Duplication publication
Directly linked to the Demerjian method for DAA	Case reports and case series due to their unsuitability for evaluating diagnostic method accuracy and reliability.
English language	Studies with high risk of bias, such as those with poor design, inadequate randomization, or incomplete data.
Studies evaluating the accuracy and reliability of the Demerjian method for DAA	Studies not reporting relevant outcome measures (sensitivity, specificity, positive predictive value, or negative predictive value) for the Demerjian method
Studies comparing the accuracy and reliability of the Demerjian method with CA and other standard methods such as Willem's, and Nolla's method.	Studies that lack sufficient detail on the application of the Demerjian method, hinder assessment of its accuracy and reliability.
Full-text systematic reviews, meta-analysis, RCTs, prospective study, observational study	Editorials, conference papers, letters to the editor, short communications, meeting abstracts

RESULTS

Thirteen were cross-sectional, eight retrospectives, two comparatives, and three meta-analyses. The remaining were prospective, multi-centric, or double-blind. A total of 13,211 participants from 66 studies were evaluated. Results summarizes the findings of 28 included studies (Table 3).

Table 3: Summary of Study Findings Evaluated

Sr.No.	Study Design	Country	Total Participants	DAA Method	Statistical Analysis	Results	Reference
1	Retrospective	Romania	1006 patients	Demerjian method	Shapiro-Wilk analysis	Overestimated DA	[11]
2	Double-blind study	Iran	537 healthy children	Demirjian's method, Willem's method, Cameriere's, and Smith's method	Pearson's correlation analysis	Acceptable DAE accuracy	[12]
3	Retrospective study	India	102 children	demerjian's, Haaviko's, and Willems method	Paired t-test analysis	Overestimated DA	[1]
4	Retrospective study	France	234 participants	Nolla, Demirjian, and the London Atlas	Student's t-test	Less accurate	[13]
5	Comparative study	Turkey	766 participants	Demirjian, Willems method	paired t-test analysis	Less accurate	[14]
6	Cross-sectional study	Iran	212 panoramic radiographs of	Demirjian and Cameriere's methods	paired t-test analysis	Higher MEV	[15]
7	Multicentric research	India	303 participants	Demirjian, Willems method	ANOVA	More accurate and reliable	[16]
8	Cross-sectional study	Saudi Arabia	400 children	Demirjian's, MFH, Nicodemo *et al.*, and Chaillet *et al.*,	IBM SPSS	Less accurate	[17]
9	Cross-sectional study	India	522 children	Demirjian, modified Demirjian, Odisha specific	Wilcoxon signed rank test, Pearson's correlation	Higher CA predictive accuracy	[18]
10	Meta-analysis	India	20 studies	Demirjian, Willems method	Cochrane RevMan v5.3	Less accurate	[19]
11	Cross-sectional study	Iran	434 children	Demirjian, Willem, Nolla, method	Paired t-test	Less accurate	[20]
12	Comparative study	Saudi Arabia	300 children	Demirjian, Willems method	Paired t-test	Less accurate	[21]

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13	Meta-analysis	Saudi Arabia	20 studies	Demirjian, Willems method	WMD	Less accurate	[22]
14	Retrospective study	China	2367 samples	Demirjian, Willems method	Paired t-test	Less accurate	[23]
15	Cross-sectional study	Iran	168 individuals	Demirjian methods	Paired t-test	Significant differences in DA-CA	[24]
16	Cross-sectional study	India	660 samples	Nolla's, Demirjian, Willems,Haaviko method	Paired t-test and Wilcoxon signed rank test, ICC	Reliable	[25]
17	Cross-sectional study	Pakistan	403 children	Willems Demirjian, Nolla method	Paired t-test and Wilcoxon signed rank test	The strong correlation between CA-DA	[26]
18	Comparative cross-section study	Spain	604 children	Demirjian, Willems, Haaviko method	Wilcoxon test, spearman's correlation coefficients	Less precise	[27]
19	Cross-sectional study	Iran	158 children	Demirjian	t-test	More accurate and reliable	[28]
20	Retrospective study	India	60 children	Demirjian	Student's paired t-test	Higher CA predictive accuracy	[29]
21	Retrospective study	Germany	478 children	Demirjian Cameriere's	Wilcoxon signed a ranked test	Higher CA predictive accuracy	[30]
22	Meta-analysis	China	26 studies	Demirjian	WMD	Overestimated CA	[31]
23	Cross-section study	Sudan	358 children	Demirjian	SPSS, nonparametric tests	More accurate and reliable	[32]
24	Comparative study	India	100 participants	Demirjian and Acharya's Indian formula	The paired t-test, SPPSS	Less accurate	[33]
25	Retrospective study	Turkey	1587 subjects	Nolla's, Demirjian	Cohen's Kappa coefficient	Higher CA predictive accuracy	[34]
26	prospective study	Tunisia	280 children	Demirjian	Cohen's Kappa test	Less accurate and reliable	[35]
27	Retrospective, blind, cross -sectional study	Egypt	160 children	Demirjian	Logistic regression	Less reliable	[36]
28	Cross-sectional study	Pakistan	882 subjects	Demirjian	Paired t-test analysis	Significant differences in DAE-CA	[37]

MEV, mean error value; ANOVA, one-way analysis of variance; MFH, Moorrees, Fanning and Hunt method; ICC, inter- and intra-class correlation; WMD, weighted mean difference; SPSS, statistical package for the social science; CA, chronological age; DAE, dental age estimated

Paired t-tests and Wilcoxon signed-rank tests were primarily used to compare Demirjian with CA. Other statistical tools like Cohen's kappa, nonparametric tests, chi-square, regression models, SPSS, ICC, WMD, and ANOVA were employed to evaluate Demirjian's accuracy and reliability against other DAA methods. Nine studies reported overestimated DA compared to CA, while six found better CA predictive accuracy with Demirjian. The most common findings were lower predictive accuracy and reliability of Demirjian. The last reported outcome was Demirjian's suitability for diverse ethnic populations. A review of 14 studies revealed that Demirjian was generally less accurate and reliable than other DAA methods (Figure 2).

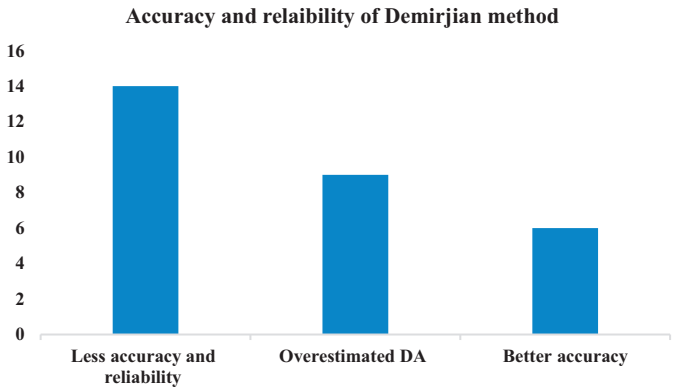

Figure 2 outcomes reported in the included studies as per systematic review.

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DISCUSSION

Teeth undergo many developmental stages for about 20 years of human life and may show secondary changes in later life [38]. DAA methods are used to estimate dental age according to dental characteristics [39, 40]. A retrospective radiograph study was conducted by Moca *et al.*, among 1006 patients (431 boys and 575 girls) in Romania. The Shapiro-Wilk analysis found that the Demerjian method overestimated the dental age (DA) of all age groups for all the participants with mean chronological age (MCA)=9.496 ± 2.218. Whereas the mean dental age (MDA)=10.934 ± 2.585, p<0.05) [11]. A double-blind study by Javadinejad *et al.*, in Iran on children included four radiograph AE methods. Pearson's correlation analysis showed that Smith's method compared to other dental AE methods reported the highest accuracy (MCA; 8.93 ± 2.04 years, age overestimation observed in; Demerjian's method=0.87 ± 1.00 years, Willem's method = 0.36 ± 0.87, Smith's method=0.06 ± 0.63 years, age underestimated by Cameriere's method=0.19 ± 0.86 years, p<0.001) [12]. Patnana *et al.*, evaluated the reliability of Demerjian's, Haaviko's, and Willems's method of DAA among 102 children (aged 6-14 years) in India. The paired t-test analysis showed that Demerjian's method significantly overestimated and Haavikko's and Willems's methods underestimated DA with a mean difference of 0.55 years, 1.95 and 0.20 years compared to CA, respectively [41]. Willmann *et al.*, evaluated the accuracy of AE using three DAE methods among 234 participants (aged 4-20 years) with various ethnicities in France. Student's t-test for paired sample analysis showed that each method overestimated mean age compared to CA (p<0.0001). However, the authors concluded that Demerjian's method compared to Nolla and the London Atlas method was less accurate (Average absolute deviation in; Demerjian method=2 years, Nolla method=1.3 years, and the London Atlas method=1.2 years) [13]. These findings were similar to a comparative study conducted by Ozveren and Serindere., among 766 participants in Turkey [14]. A cross-sectional study consisting of 212 panoramic radiographs of children (aged 6-10 years) was conducted by Milani et al., in Iran. The paired t-test analysis reported that the mean error value (MEV) of the Demirjian method was higher than Cameriere's methods (MEV in girls = 0.084 and -0.06 and boys=0.93 and 0.04, respectively, p<0.001) [15]. A multicentric research was conducted by Chaudhry *et al.*, among 303 participants (173 males and 130 females) of different ethnicities in India. ANOVA and Student's t-test analysis demonstrated that the Willems method outperformed the Demirjian method (p<0.001) [16]. A cross-sectional study was conducted by Al-Otaibi and Al-Qahtani in Saudi Arabia on children aged 6-15.99 years (200 boys, 200 girls). A significant difference with p<0.001 was revealed between DA and CA. The study highlighted that Demirjian's method compared to Moorrees, Fanning and Hunt's method [17]. A cross-sectional study consisting of 522 children (boys = 521, girls = 271, aged 3-18 years) was conducted by Mohanty *et al.*, in India. It showed that Demirjian (D) and modified Demirjian (MD) methods compared to Odisha-specific (OS) methods reported higher CA predictive accuracy (Pearson correlation; Male CA; MD=0.860, OS=0.385, D=0.854, and female CA; MD=0.859, OS=0.718, D=0.789) [18]. A comprehensive review of 20 studies published up to July 2018 was conducted by Prasad and Kala in India. The Cochrane RevMan v5.3 software analysis showed that the Willems method's accuracy is nearly similar to CA compared to the Demirjian method, irrespective of gender in the Indian population (overestimation by Demirjian=0.45 years, underestimation by Willems method=0.09 in both genders, 95% CI) [19]. Similar findings were also reported in a retrospective study of 2367 samples conducted by Pan *et al.*, in China and a cross-sectional study of 434 children by Pliska *et al.*, in Iran [23, 20]. A comparative study among 300 Saudi children by Alrashidi et al., and a meta-analysis of 20 studies performed by Esan *et al.*, in Saudi Arabia revealed similar results [21, 22]. Abesi *et al*, conducted a cross-sectional study in Iran involving 168 individuals under the age of 15. Significant differences in the mean values of AE between both genders (p<0.001) were found in the study. Mean and standard deviation (SD) of CA [24]. Another cross-sectional study comprising 660 samples (330 each, males and females, aged 6-16 years) was performed by Mohammed *et al.*, in India. The results showed that Nolla's method compared to Demirjian, Willems, and Haaviko's method was more accurate and significant linear correlation between DA and CA in DAE. However, in DAE of South Indian children of undetermined CA, all the assessment methods were found to be reliable as assessed by inter- and intra-class correlation (inter- and intra-observer for all methods=0.9 and 0.8, respectively. Linear correlation between CA and DA for; r=0.80 for Demirjian, for Willems r=0.80, for Nolla, r=0.94, for Haavikko method, r=0.82, p<0.001) [25]. Khoja *et al.*, evaluated the validity of different DAE methods (Demirjians, Nollas, Willems) in 403 Pakistani orthodontic patients (male=176, female=277). Based on the Paired t-test and Wilcoxon signed rank test, the Willems method was considered most valid as compared to Demirjian and Nollas's method (strong correlation between CA and DA =p<0.001) [26]. These results were similar to a comparative cross-section study, conducted by Paz *et al.* in Spain. The results analysis suggested that Willems method compared to Demirjian method is more appropriate and precise in DAE (spearman's correlation between CA and DA for both

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methods; rho values=0.86–0.89, p=0.00, Wilcoxon test; CA mean and DA mean for Wilems method=8.77 and 9.04, respectively and Demirjian method=8.77 and 9.48, respectively, p=0.000) [27]. Kermani *et al.*, conducted a study in Iran involving children aged 5-13 years. The SPSS v.22 and t-test analysis showed a statistically strong relationship between DAE by Demirjian and CA, irrespective of gender (correlation coefficient for all subjects=0.854, mean absolute difference between CA and DA (ABS-DIFF) in girls=1.442, boys=0.667) [28]. In a retrospective Indian study by Pratyusha *et al.*, involving 30 male and 30 female children aged 9-14, the Cameriere's population-specific regression equation (CPSRE) was found to be a closer estimate of CA compared to the Demirjian method when assessing age at eruption (AE) (p=0.68) [29]. Another retrospective study consisting of 478 panoramic radiographs (male=268, female=211 aged 6-14 years) was conducted by Wolf *et al.*, in Germany. The Wilcoxon signed ranked test showed Demirjian method compared to Cameriere's method showed higher accuracy for DAE for both genders (total mean difference (MD) in CA-DA using; Demirjian method=-0.16 and -0.18 and Cameriere method=0.07 and 0.08, for male and female genders, respectively) [30]. A meta-analysis of 26 studies published before July 12th, 2013 was conducted by Yan *et al.*, in China. The research findings suggested that the Demirjian method for assessing human dental maturation may not be universally accurate. When compared to CA, the Demirjian method consistently overestimated dental age in both genders. This discrepancy underscores the importance of developing population-specific standards for evaluating dental development [31]. A descriptive cross-section study by Alqadi and Abuaffan was conducted in Sudan. Nonparametric tests showed that Yemeni CA estimated by the Demirjian method was significantly correlated to DA (mean CA and DA=12.00 ± 2.25, 11.34 ± 2.42, respectively, p<0.001) [32]. A comparative study consisting of 100 participants (50 each male and female) was conducted by Sarkar *et al.*, in India. The statistical analysis revealed that Acharya's formula outperformed the Demirjian method in providing a more reliable and precise evaluation of DA (mean DA underestimated; Demirjian= by 1.63 years and 1.54 years, Indian formula= by 0.10 years and 0.94 years) [33]. A retrospective study was conducted by Duruk *et al.*, in Turkey. Cohen's kappa coefficient and paired sample t-test analysis revealed that Nolla's compared to the Demirjian method showed more CA estimation accuracy in the Eastern Turkish population (Nolla's method; underestimation of CA=-0.16 and overestimation of DA by using Demirjian=0.68, irrespective of gender) [34]. In Tunisia, Aissaoui *et al.*, led a prospective study consisting of 280 healthy Tunisian children (aged 2.8 to 16.5 years). It indicated that the Demirjian method, may not accurately predict dental age in Tunisian children. The Cohen's Kappa test revealed discrepancies between Estimated dental age and chronological age, with differences ranging from -0.02 to 3 years. Additionally, analysis of dental advancement about chronological age showed variations between males and females, with differences ranging from 0.3 to 1.32 years in males and 0.26 to 1.37 years in females. These findings suggest the need for further research to develop more accurate dental age assessment methods for Tunisian children [35]. Similar findings were also reported in a study conducted by Moness *et al.*, in Egypt [36]. A cross-sectional study between 427 female and 455 male, aged 7-14, was conducted by Sukhia *et al.*, in Pakistan [37]. The results showed that there were significant differences between CA and DA using the Demirjian method, as determined by a statistical test (p<0.05) and the results were comparable to a German Study by Khdairi N *et al.*, [42]. The systematic review was limited by the small number of studies, particularly those involving diverse ethnicities and regions, and the absence of robust statistical inference. To address these limitations, future research should prioritize large-scale, well-designed RCTs, case-control studies, and prospective studies that employ a comprehensive approach. Furthermore, future investigations should explore the integration of computerized methods for DAE analysis, potentially bypassing the need for traditional panoramic radiographs. Moreover, a comprehensive approach incorporating multiple age estimation methodologies, supported by rigorous statistical analysis, including effect size calculations, is recommended for robust and reliable age assessment in legal proceedings as also concluded by the study of Han MQ *et al.*, and Pereira CP *et al.*, [43, 44].

CONCLUSIONS

It was concluded that this systematic review provides a detailed comprehensive review of the evaluation of the accuracy and reliability of the Demirjian method for DAA. The study found that the Demirjian method compared to other DAA methods demonstrated lesser accuracy and reliability, and increased overestimated DA compared to CA for DAE.

Authors Contribution

Conceptualization: AAV
Methodology: AAV, SA
Formal analysis: SSF
Writing review and editing: MHS, AM, MAKG, VD, MUS

All authors have read and agreed to the published version of the manuscript

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Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Dharwadkar PM, Waingade M, Patankar SA, Patankar A, Godse AM, Nagrale P. Age Estimation by Drusini's Method and Jeon's Method in Indian Population–A Comparative Assessment. Journal of Oral and Maxillofacial Pathology.2022 Jul; 26(3): 340-5. doi: 10 .4 103/jomfp.jomfp_449_21.

[2] erma M, Verma N, Sharma R, Sharma A. Dental Age Estimation Methods in Adult Dentitions: An Overview. Journal of Forensic Dental Sciences.2019 May;11(2):5 7-63. doi: 10.4103/jfo.jfds_64_19.

[3] Kumari S, Sahu AK, Rajguru J, Bishnoi P, Garg AJ, Thakur R. Age Estimation by Dental Calcification Stages and Hand-Wrist Radiograph.Cureus.2022 Sep; 14(9). doi: 10.7759/cureus.29045.

[4] Cugati N, Kumaresan R, Srinivasan B, Karthikeyan P. Dental Age Estimation of Growing Children by Measurement of Open Apices: A Malaysian Formula. Journal of Forensic Dental Sciences.2015 Sep; 7(3):2 27-31. doi: 10.4103/0975-1475.172445.

[5] Jayakrishnan JM, Reddy J, Kumar RV. Role of Forensic Odontology and Anthropology in the Identification of Human Remains. Journal of Oral and Maxillofacial Pathology.2021 Sep; 25(3): 543-7.doi:10 .4103/jomfp.jomfp_81_21.

[6] Alkass K, Buchholz BA, Ohtani S, Yamamoto T, Druid H, Spalding KL. Age Estimation in Forensic Sciences: Application of Combined Aspartic Acid Racemization and Radiocarbon Analysis. Molecular and cellular proteomics.2010May;9(5):1022-30.doi:10.1074/mcp .M900525-MCP200.

[7] Jain V, Kapoor P, Miglani R. Demirjian Approach of Dental Age Estimation: Abridged for Operator Ease. Journal of Forensic Dental Sciences.2016 Sep; 8(3): 201-5. doi: 10.4103/0975-1475.195103.

[8] Lacruz RS, Habelitz S, Wright JT, Paine ML. Dental Enamel Formation and Implications for Oral Health and Disease. Physiological Reviews.2017 Jul; 97(3): 939-93. doi: 10.1152/physrev.00030.2016.

[9] Stamm AD, Cariego MT, Vazquez DJ, Pujol MH, Saiegh J, Bielli MV *et al.* Use of the Demirjian Method to Estimate Dental Age in Panoramic Radiographs of Patients Treated at the Buenos Aires University School of Dentistry. Acta Odontoloógica Latinoamericana.2022Apr;35(1):25. doi:10.54589/aol .35/1/25.

[10] Hostiuc S, Diaconescu I, Rusu MC, Negoi I. Age Estimation Using the Cameriere Methods of Open Apices: A Meta-Analysis. In Healthcare.2021 Feb;9 (2): 237. doi: 10.3390/healthcare9020237.

[11] Moca AE, Ciavoi G, Todor BI, Negruțiu BM, Cuc EA, Dima R *et al.* Validity of the Demirjian Method for Dental Age Estimation in Romanian Children. Children.2022 Apr; 9(4): 567. doi: 10.339 0/children90 40567.

[12] Javadinejad S, Sekhavati H, Ghafari R. A Comparison of the Accuracy of Four Age Estimation Methods Based On Panoramic Radiography of Developing Teeth. Journal of Dental Research, Dental Clinics, Dental Prospects.2015; 9(2): 72. doi: 10.15171 /joddd. 2015.015.

[13] Willmann C, Fernandez De Grado G, Kolb C, Raul JS, Musset AM, Gros CI *et al.* Accuracy of Age Estimation Using Three Dental Age Estimation Methods in a Young, Large, and Multiethnic Patient Sample. Dentistry Journal.2023 Dec; 11(12): 288. doi: 10.3390/ dj11120288.

[14] Ozveren N and Serindere G. Comparison of the Applicability of Demirjian and Willems Methods for Dental Age Estimation in Children from the Thrace region, Turkey. Forensic Science International.2018 Apr; 285: 38-43. doi: 10.1016/j.forsciint.2018.01.017.

[15] Milani S, Shahrabi M, B Fakhar H, Parvar S, Abdolahzadeh M. Accuracy of Demirjian's and Cameriere's Methods for Age Estimation in 6-to 10-Year-Old Iranian Children Using Panoramic Radiographs. International Journal of Dentistry. 2022; 2022(1): 4948210. doi: 10.1155/2022/4948210.

[16] Chaudhry K, Talwar M, Vanga NR, Lehl GK, Choudhary A, Patnana AK. A Comparative Evaluation of Three Different Dental Age Estimation Methods in India: A Test of Ethnic Variability. International Journal of Clinical Pediatric Dentistry.2020 Jan; 13(1): 16. doi: 10.5005/jp-journals-10005-1708.

[17] AlOtaibi NN and AlQahtani SJ. Performance of Different Dental Age Estimation Methods On Saudi Children.The Journal of Forensic Odonto-Stomatology. 2023 Apr; 41(1): 27.

[18] Mohanty I, Panda S, Dalai RP, Mohanty N. Predictive Accuracy of Demirjian's, Modified Demirjian's and India Specific Dental Age Estimation Methods in Odisha (Eastern Indian) Population. The Journal of Forensic Odonto-Stomatology. 2019 May; 37(1): 32.

[19] Prasad H and Kala N. Accuracy of Two Dental Age Estimation Methods in the Indian Population–A Meta-Analysis of Published Studies.The Journal of Forensic Odonto-Stomatology. 2019 Dec; 37(3):2.

DOI: https://doi.org/10.54393/pjhs.v5i12.2138

[20] Pliska B, Nahvi A, Pakdaman N, Dadgar S, Aryana M, Sobouti F. Radiological Evaluation of the Accuracy of Demirjian, Nolla, and Willems Methods for Dental Age Estimation in 3–17-Year-Old Iranian Children. BioMed Research International.2024; 2024(1): 8783660.doi: 10.1155/2024/8783660.

[21] Alrashidi M, Al-Moshiqah A, Kolarkodi SH, Alotaiby F. A Comparative Study of the Assessment of the Accuracy of Willems' and Demirjian's Methods in Dental Age Estimation of the Saudi Arabian Population. Cureus.2023 Dec; 15(12). doi: 10.775 9/ cureus.50128.

[22] Esan TA, Yengopal V, Schepartz LA. The Demirjian Versus the Willems Method for Dental Age Estimation in Different Populations: A Meta-Analysis of Published Studies. Plos One.2017 Nov; 12(11): e0186 68 2. doi: 10.1371/journal.pone.0186682.

[23] Pan J, Shen C, Yang Z, Fan L, Wang M, Shen S *et al.* A Modified Dental Age Assessment Method for 5-To 16-Year-Old Eastern Chinese Children. Clinical Oral Investigations.2021 Jun; 25: 3463-74. doi: 10.10 07/s 00784-020-03668-9.

[24] Abesi F, Haghanifar S, Sajadi P, Valizadeh A, Khafri S. Assessment of Dental Maturity of Children Aged 7-15 Years Using Demirjian Method in A Selected Iranian Population. Journal of Dentistry. 2013 Dec; 14(4): 165.

[25] Mohammed RB, Sanghvi P, Perumalla KK, Srinivasaraju D, Srinivas J, Kalyan US *et al.* Accuracy of Four Dental Age Estimation Methods in Southern Indian Children. Journal of clinical and diagnostic research.2015 Jan; 9(1): HC01. doi: 10.7860/JCDR/20 15/10141.5495.

[26] Khoja A, Fida M, Shaikh A. Validity of Different Dental Age Estimation Methods in Pakistani Orthodontic Patients. Australian Journal of Forensic Sciences. 2015 Jul; 47(3): 283-92. doi: 10.1080/ 0045 0618 .2014 .957347.

[27] Paz Cortés MM, Rojo R, Alía García E, Mourelle Martínez MR. Accuracy Assessment of Dental Age Estimation with the Willems, Demirjian and Nolla Methods in Spanish Children: Comparative Cross-Sectional Study. BioMed Central Pediatrics.2020 Dec; 20: 1-9. doi: 10.1186/s12887-020-02247-x.

[28] Kermani M, Tabatabaei Yazdi F, Abed Haghighi M. Evaluation of the Accuracy of Demirjian's Method for Estimating Chronological Age from Dental Age in Shiraz, Iran: Using Geometric Morphometrics Method. Clinical and Experimental Dental Research. 2019 Jun; 5(3): 191-8. doi: 10.1002/cre2.169.

[29] Pratyusha K, Prasad MG, Radhakrishna AN, Saujanya K, Raviteja NV, Chandrasekhar S. Applicability of Demirjian's Method and Modified Cameriere's Methods for Dental Age Assessment in Children. Journal of Clinical and Diagnostic Research.2017 Feb; 11(2): ZC40. doi: 10.7860/JCDR /2017/2147 4.9 3 4 2.

[30] Wolf TG, Briseño-Marroquín B, Callaway A, Patyna M, Müller VT, Willershausen I *et al.* Dental Age Assessment in 6-To 14-Year Old German Children: Comparison of Cameriere and Demirjian Methods. BioMed Central Oral Health.2016 Dec; 16: 1-8. doi: 10.11 86/s12903-016-0315-8.

[31] Yan J, Lou X, Xie L, Yu D, Shen G, Wang Y. Assessment of Dental Age of Children Aged 3.5 to 16.9 Years Using Demirjian's Method: A Meta-Analysis Based On 26 Studies. Plos One.2013 Dec; 8(12): e84672. doi: 10.137 1/journal.pone.0084672.

[32] Alqadi MA and Abuaffan AH. Validity of the Demirjian and Fishman Methods for Predicting Chronological Age Amongst Yemeni Children. Sultan Qaboos University Medical Journal.2019 Feb; 19(1): e26. doi: 10.18295/squmj.2019.19.01.006.

[33] Sarkar S, Kailasam S, Kumar PM. Accuracy of Estimation of Dental Age in Comparison with Chronological Age in Indian Population–A Comparative Analysis of Two Formulas. Journal of Forensic and Legal Medicine.2013 May; 20(4): 230-3. doi: 10.1016/j.jflm.2012.09.007.

[34] Duruk G, Özdal TP, Duman S. Accuracy of Age Estimation with Demirjian and Nolla Methods in Eastern Turkish Children Aged 3-17 Years Old. European Oral Research.2022 May; 56(2): 80-7. doi: 10.26650/eor.20221057985.

[35] Aissaoui A, Salem NH, Mougou M, Maatouk F, Chadly A. Dental Age Assessment Among Tunisian Children Using the Demirjian Method. Journal of Forensic Dental Sciences.2016 Jan; 8(1): 47-51. doi: 10.4103/09 75-1475.176956.

[36] Moness Ali AM, Ahmed WH, Khattab NM. Applicability of Demirjian's Method for Dental Age Estimation in A Group of Egyptian Children. British Dental Journal Open.2019 Mar; 5(1):2. doi: 10.1038/s41405-019-0015y.

[37] Sukhia RH, Fida M, Azam SI. Dental Age Table for A Sample of Pakistani Children. The European Journal of Orthodontics.2012 Feb; 34(1): 77-82. doi: 10.1 093/e jo/cjq161.

[38] Cantekin K, Sekerci AE, Peduk K, Delikan E, Ílday NO, Demirbuga S *et al.* Dental Age Assessment for Different Climatic Regions. The American Journal of Forensic Medicine and Pathology.2014 Sep; 35(3):197 -200. doi: 10.1097/PAF.0000000000000096.

[39] Vila-Blanco N, Varas-Quintana P, Tomas I, Carreira MJ. A Systematic Overview of Dental Methods for Age Assessment in Living Individuals: From Traditional to

DOI: https://doi.org/10.54393/pjhs.v5i12.2138

Artificial Intelligence-Based Approaches. International Journal of Legal Medicine. 2023 Jul; 137(4): 1117-46. doi: 10.1007/s00414-023-02960-z.

[40] Naser DA, ES AA, Al-Khateeb SN. Dental Age Assessment in Patients with Maxillary Canine Displacement. American Journal of Orthodontics and Dento-facial Orthopedics: Official Publication of the American Association of Orthodontists, its Constituent Societies, and the American Board of Orthodontics.2011 Dec; 140(6): 848-55. doi: 10.1016/j .ajodo.2011.04.027.

[41] Patnana AK, Vabbalareddy RS, Vanga NR. Evaluating the Reliability of Three Different Dental Age Estimation Methods in Visakhapatnam Children. International Journal of Clinical Pediatric Dentistry. 2015 Feb;7(3): 186. doi: 10.5005/jp-journals-10005-12 62.

[42] Khdairi N, Halilah T, Khandakji MN, Jost-Brinkmann PG, Bartzela T. The Adaptation of Demirjian's Dental Age Estimation Method On North German Children. Forensic Science International.2019 Oct;303:109927 . doi: 10.1016/j.forsciint.2019.109927.

[43] Han MQ, Jia SX, Wang CX, Chu G, Chen T, Zhou H *et al.* Accuracy of the Demirjian, Willems and Nolla methods for Dental Age Estimation in A Northern Chinese Population. Archives of Oral Biology.2020 Oct;118:104875.doi:10.1016/j.archoralbio.2020.1048 75.

[44] Pereira CP, Santos R, Nushi V, Lameiro MV, Antunes P, Carvalho R *et al.* Dental Age Assessment: Scoring Systems and Models from the Past Until the Present—How Is It Presented in the Court? International Journal of Legal Medicine.2023 Sep; 137(5): 1497-504. doi: 10.1007/s00414-023-03011-3.

DOI: https://doi.org/10.54393/pjhs.v5i12.2644

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Cultural Competency Training in Dental and Medical Education: Enhancing Communication and Patient-Centered Care

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ABSTRACT

Competence is a core value of healthcare curriculum having a direct effect on the healthcare quality and patient health. **Objective:** To assess the effects and issues of integrated cultural competency education in dental as well as medical school curricula in order to improve critical and effective patient-centered care and cultural diversity in health care provision. **Methods:** According to PRISMA 2020 guidelines, electronic databases from PubMed, Science Direct, and Google Scholar were searched systematically for articles from the year 2016 to 2024. This involved studies that compared analysis of cultural competency incorporation into curricula, effects on health care provision, and the problems that confront trainers. Initially we identified 134 articles for consideration, 56 of which met the inclusion criteria, and 24 of which were reviewed with greater attention to program design, outcomes of training, and factors inhibiting implementation. **Results:** This review was able to demonstrate the increased student communication skills, patient and provider relations, as well as patient satisfaction. Nonetheless, the implementation challenges were seen in the following; Inconsistent curriculum frameworks; Faculty preparedness; and lack of support for training were cited as barriers to effective training. Gaps in implementing cultural competency interventions across the world were also pointed out. **Conclusions:** Cultural competence appeared to be an important approach in reducing the disparities in health and in healthcare provision. Suboptimal national dissemination indicated the necessity of high-fidelity curriculum structures, selective content focus, and sound institutional support to address the implementation barriers.

INTRODUCTION

Cultural competency has over the growing years been viewed as an essential foundation of healthcare education and training [1]. It means the capacity that health practitioners have in understanding, being sensitive to, as well as, communicating with the diverse cultural and language backgrounds of patients [2]. This competency plays a vital role when handling issues to do with health inequalities, and general patient-centeredness. In dental as well as medical education, cultural competency training is to foster such skills to produce competent and socio-culturally competent healthcare professionals [3]. Obviously, cultural competency is a crucial matter. Cross cultural communication breakdowns, lack of cultural sensitivity, prejudice and poor information about cultural differences in medical perceptions and practices cause health disparities [4]. Research showed that the

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professionals with a higher level of cultural competencies are able to build patient provider rapport, rate patient satisfaction higher, and get better compliance with directives [5]. However, translating additional cultural competency training as part of diversity education into dental and medical curricula has been done in a haphazard manner [6]. Some of the challenges that have made its implementation to be difficult include; diverse curriculum designs, restricted access to institutional support and cost-effective long practicality of measurement instruments[7]. Concerning the clinical care environments in dental and medical practices, culture affects course, diagnosis, and treatment compliance. For example, knowledge about a particular patient with respect to his or her cultural background can assist providers in recognizing differential health risks, developing culturally competent strategies and overcoming potential organizational impediments [8]. Cultural competence is most applicable in dentistry due to issues of oral health inequalities in the community which depends on culture regarding attitudes to dentistry services and preventive measures [9]. Likewise, culturally competent care helps in managing diabetic, hypertensive or patients with mental illness because there is evidence that these diseases are prevalent among people from a particular ethnic background. Still, achieving cultural competency training remains a significant challenge due to lack of consistent curricula, inadequate preparedness by faculty and unwillingness to integrate such training programs as mentioned above [10]. These difficulties remain despite it being crucial for addressing health disparities, improving communication and promoting patient-focused care. This review evaluates the integration of cultural competency training in dental and medical education with respect to its impact on healthcare outcomes and possible hindrances in the path of effective integration. If it is defined more specifically, this review synthesizes current practices, ascertains the limitations of current training approaches, and offers practical guidelines for curricular improvement. Ultimately this review aided in educating teachers and academic institutions and to support the policy makers in creating culturally competent healthcare professionals, who can meet the health needs of diverse group of patients.

METHODS

In line with PRISMA guidelines 2020, this review was done from May 2024 to August 2024. A database search helped retrieve 89 articles in English language published in the period of 2016 to 2024. These articles focused on the cultural competency training programs and their result and issue in dentistry and medical education. Study selection criteria included that articles need to describe program design, results, and analyses tests, as well as detailing implementation strategies. Data were collected concerning the area of interest, the participants, the methods, the number of participants, the results, and citations. Sources for searching the articles were Google Scholar Science Direct and PubMed. Out of all the articles, Google Scholar contributed 60% which is due to its less selective indexing, 30% from ScienceDirect and 10% from PubMed. To eliminate bias, data from a database covering other areas was cross-checked to make sure that there was no missing information. The articles collected here reflected global studies with most of those included coming from Asia, Europe, America. The search terms used were "cultural competency training," "dental education," "medical education," and "healthcare diversity," "cross-cultural communication." Excluded articles were those, which did not meet the inclusion criteria like being based on the education of students except those in the healthcare field or were based on methodologies, which did not include empirical data. To classify the studies, two independent reviewers were performed and to assess the inter-rater reliability, Cohen's kappa was used. Cross sectional comparison of the 89 identified articles meant that seven of the articles were duplicates leaving 82 to be screened. Finally, in total 16 articles were considered for further analysis as a part of the systematic review on the topics related to the effectiveness of the cultural competency training, the implementation difficulties, and potential differences between the regions. For the reliability and accuracy of the selected papers, Cohen's kiva for inter-rater reliability and confidence intervals were used in the statistical analysis.

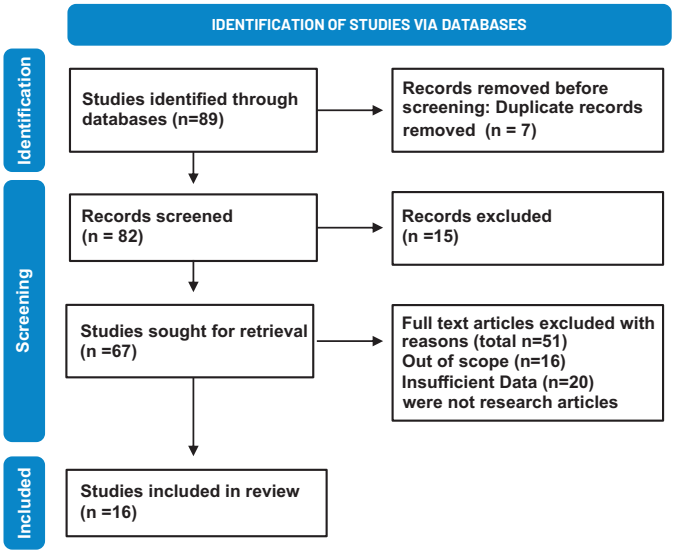

Figure 1: PRISMA Model Illustrating Selection of Studies for Review Process Showing Elimination of Studies That Were Not Lying Under the Inclusion Criteria

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RESULTS

The reviewed studies were concentrated in the scope of cultural competence training for dental and medical students with different ethnically diverse patients. The ages of the participants varied between participants aged 69 and 45 years, with a focus on healthcare personnel and students who have gone through cultural competence training. Of those 16 studies, six studies were longitudinal and had a follow up time between 6 months to six years, five studies were correlational/prospective and showed the correlation between variables within 3-6 months, five experimental/observational studied had controlled experiment with an intervention period of 1 month to 4 years. From the geographical viewpoint, the researched studies reflected the global coverage, and 47% of the investigations were investigated in Asia, 41% in Europe, and 12% in America. All related studies incorporated in this study were published within the last five years (2020–2024). To analyze the outcomes and to evaluate the effectiveness and difficulties of the cultural competency training programs, meta-analytical approach was used and CMA software was employed. The pooled effect size was calculated as 0.38 (95% CI: 0.22, 0.54 signifying moderate positive effect of training on participant's cultural competence and patient care. Furthermore, confidence intervals and bias indices were computed to minimize variability and maintain the reliability of the results consequent to heterogeneity in study characteristics and methods. As established in the analysis, the study found trends like participants' enhanced communication ability and patients' satisfaction scores after the training. However, there were areas of concern that emerged especially Curriculum integration, faculty preparedness and resources allocation concerns were more recurrent. The meta-analysis of study results showed significant variability with respect to the heterogeneity of treatments, settings, populations, and interventions, signifying that the effects were significantly large to moderate ($I^2 = 56\%$, $p < 0.05$). The results shown here bear testament to the utility of cultural competency training in promoting respect and culturally sensitive care in the healthcare profession although underscore the existence of other areas to be developed. Hence, this meta-analytical approach is a strong foundation for extended study and enhancing the formation of more formulated training structures (Table 1).

Table 1: Schematic Review of Studies that were Most Appropriate According the PRISMA Defined Rules

Authors and Year (Region)	Study design (Population N)	Training Focus	Outcomes Measured	Key Findings	Confounders Addressed
Godillot C *et al.*, 2021 [11] (France)	Longitudinal (Medical students n=300)	Cross-cultural communication	Improved patient satisfaction, empathy scores	Significant improvement in communication skills post-training	Variations in pre-training cultural competency levels
Chawa MS *et al.*, 2020 [12] (United States)	Prospective (Dental practitioners n=200)	Cultural sensitivity in clinical settings	Increased awareness of cultural practices, patient adherence	Positive impact on treatment outcomes	Training duration and participant motivation
Webster *et al.*, 2023 [13] (Austrailia)	Observational (Mixed cohort n=150)	Diversity in healthcare teams	Enhanced teamwork, reduced bias	Improved interdisciplinary collaboration	Institutional support and faculty experience
Skjerve H *et al.*, 2023 [14] (Poland)	Experimental (Dental students n=100)	Cross-cultural education integration	Better understanding of patient backgrounds	Increased cultural competency scores	Language barriers among patients
Stubbe DE, 2020 [15] (United States)	Observational Medical trainees (n=250)	Cultural disparities in health outcomes	Higher cultural sensitivity in diagnostics	More accurate diagnoses, fewer complaints	Religious and ethical considerations
Fricke *et al.*, 2024 [16] (United States)	Randomized controlled trial (n=200)	Implicit bias training	Bias reduction in decision making	Statistically significant decrease in implicit bias scores	Instructor bias during training
Argyriadis A *et al.*, 2022 [17] (Greece)	Cross- sectional (dental students n=120)	Cultural adaptation in clinical settings	Student self-assessment of competency	Moderate improvement in cultural knowledge	Regional variations in Health care practices
Horváth Á *et al.*, 2022 [18] (Hungary)	Cohort study (n=350)	Multilingual communication skills	Patient satisfaction, provider communication skills	Enhanced rapport-building and patient trust	Language fluency levels among trainees
Ogbogu PU *et al.*, 2022 [19] (United States)	Case- control (Medical practitioners n=100)	Cross-cultural clinical scenarious	Decision accuracy in culturally diverse cases	Significant reduction in diagnostic errors	Inconsistent exposure to diverse patient cases
Sullivan-Detheridge JH *et al.*, 2024 [20] (United States)	Longitudinal (Dental students n=200)	Cultural humility in patient care	Empathy scores, patient satisfaction	Long-term retention of empathy skills	Gender and age differences in trainees

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Eichbaum QG *et al.*, 2021 [21] (Multiple)	Pre-post study (Medical students n=150)	Global health disparities education	Knowledge retention, application in pactice	Significant knowledge gain post-training	Differences in prior global health exposure
Tran BQ, 2021 [22] (Unites States)	Prospective (Dental trainees n=180)	Patient-centered communication	Patient feedback, adherence rates	Higher patient adherence and satisfaction levels	Socioeconomic disparities in patient groups
Walkowska *et al.*, 2023 [23] (Poland)	Randomized trial (Medical students n=220)	Cultural competency framework	OSCE performance, self-reported skills	Better OSCE scores among trained students	Variability in teaching methods across centers
Caballero-Gonzalez A *et al.*, 2023 [24] (Unites States)	Cross-sectional (Mixed cohort n=140)	Ethnic-specific health beliefs	Cultural knowledge and application scores	Improved awareness of ethnic health needs	Limited diversity among study participants
Drossman DA *et al.*, 2021 [25] (Unites States)	Experimental (Dental interns n=160)	Patient-provider relationship training	Improved communication scores, patient feedback	Positive patient outcomes post-intervention	Limited follow-up data
Neff J *et al.*, 2020 [26] (United States)	Prospective cohort (Medical students n=210)	Cultural influences on health outcomes	Critical thinking, diagnostic accuracy	Improved cultural sensitivity in clinical cases	Institutional differences in training quality

DISCUSSION

The objective of this systematic review was to assess the effects of cultural competency training for doctors and dentists, to inform if training of such education improves the ability of health care providers to productively and efficiently provide clinical care for diverse populations. This objective was achieved via findings of the studies reviewed in this systematic review. The findings show that through the cultural competency training, health care delivery is enhanced, patients' satisfaction is increased and disparities in treatment outcomes minimized [27]. The discussed research finds out that; training programs increase the existing knowledge of the healthcare providers towards cultures, increase their effectiveness in communication, hence improving the general relations between providers and their patients of diverse origins [28]. The observed improvements extend beyond procedural enhancements and constitute a movement toward more empathetic, patient-centered care. This implies that while cultural competency training goes beyond the immediate barrier of communication, it also offers a pathway to systematize improvements in healthcare equity. However, the variability in reported outcomes suggests that these benefits may be conditional to the context, design, and implementation quality of training programs in order to better understand how to optimize these initiatives to sustain success. Nonetheless, the efficiency of such programs depends upon several factors among them the time period, topic of the training and the mode of delivery [29]. The earlier intervention in medical and dental curricula has proved to enhance the understanding of issues like language, culturally appropriate communication, disparity in health, and variation on beliefs concerning health and treatment among other duty bearers [30]. For instance, they have shown that if culturally competent care is practiced it helps in identifying the considerations of the patients so as to provide them with the right treatment plan [31]. However, while these developments are encouraging for health care delivery, it could be argued that the assessment of the training is still unclear in terms of its clinical utility in practice and patients' outcomes because of relatively weak methodological evidence base of the reviewed studies [32]. Furthermore, there is variability in the training programs and their means of measurement are also variable. A number of the research undertaken in this field utilized longitudinal design as a way of assessing the repercussion of cultural competency training, cross sectional or observational designs could also be used on occasions. Many of these studies vary significantly in design and the measurements taken, thus making it hard to compare the results of one study with another, or to generalize the findings widely. For instance, whereas some of the observational studies reported changes in patients' satisfaction and healthcare providers' attitude to the therapies, other did not show the results that pointed to clearly discernable or long-term impact on patients' recovery, for instance [33]. These inconsistencies underscore significant methodological gaps such as lack of standardization of protocols taken, variability in scenarios, and diversity among training prompts. Future studies should adopt standardized methodology or at least comparable methodology to conclude results and understand better about the situations and difficulties faced by healthcare systems. However, there were several variables that could have affected the outcomes of these training programs for instance; cultural competency level of participants at the beginning of the training; their background and experience [34]. For example,

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superordinate healthcare providers that are in a position of serving more heterogeneous client populations or healthcare entities that espouse a more diverse-centered mission may likely observe greater increases in their providers' CC [35]. Furthermore, the immersive learning and participation mode of training has also been found to have an influential or relevant role to played in training, some of the studies eliciting that the longer/truly participative trainings are comparatively more advantageous than single-bash trainings [36]. Other key variables highlighted include; encouragement by facilities, faculty training and availability of resources. Organizations also with stronger diversity and inclusion profiles are likely to offer detailed and ongoing cultural competence training that produces superior results [37]. On the other hand, the following: There may be cases that such programs may be hampered due to scarce resources, culture, and diversity training may not be considered as fundamental to organizational systems in such environs. Moving forward, another area of ethical concern is the assessment of the cultural competency training practice in attendance to the regard elements of cultural bias and structural prejudice. Cultural inequalities in health care cannot be erased just through training; some authors have claimed [38]. Peter's solutions may require more extensive, perhaps radical, planning at the organizational level – changes in policies in order to add diversity as one of the structural improvements. Also, the questioning of standards concerning the measure of cultural competency in the health care professionals is still an ethical issue at large. Critics are also to the view that the accumulated knowledge pertaining to cultural competency as a social construct might not be adequately reflected by self-generated questionnaires or standardized test results [39]. Hence cultural competency training is very useful in enhancing health care and giving better outcomes to specific groups, however, the success relies with various factors such as the training model and the training programme packages [40]. However, further developed, more monumental examinations have to be conducted to determine the prospect parliamentary repercussions of the cultural competency training on health care provision. Such studies should involve gender, ethnic, and other types of diversity, consider the long-term clinical status to determine the efficacy of the applied training models and use the same methods to compare results [41]. Furthermore, healthcare institutions should enroll cultural competency as an essential value proposition of its mission to address cultural disparities and patient care interactions. They highlighted the importance of more work on improving cultural sensitivity in Health sector so as to ensure equal delivery of Health care service for the patients. Thus, it is desired and deemed necessary to conduct subsequent studies which is long-term evaluations of the training program and its effectiveness by including substantially diverse populations and embracing normative outcome measures. Cultural competency cannot become forced into being a low priority in the healthcare systems and needs to become a permanent part of how healthcare education is done in order to eliminate these disparities and enhance patient-centered care. In summary, future directions include the development of standardized training frameworks to develop common training modules that are appropriately implemented within the various healthcare settings of relevance. Training tools which are based on technology can be integrated with virtual reality simulations to ensure immersion and interactivity during training. More importantly, there is a need for substantial longitudinal studies to evaluate the maintained effect of cultural competency training on healthcare outcomes over time. Future research should focus on other underrepresented areas and populations to gain a more global and inclusive perspective of cultural competency.

CONCLUSIONS

This systematic review brings into focus the importance of cultural competency training in helping to develop quality healthcare delivery especially in diverse practice areas. Other works prove that the courses focus on improving the interpersonal interaction in the multiethnic population improving the patient satisfaction and, correspondingly, the outcomes of the treatment. However, differences in what is trained, for how long, and how trainee knowledge and attitudes were assessed across studies poses challenges in result comparison. Some research reveals postimplementation improvement in healthcare system and/or patient status; others show little or transient change, thus pointing toward under developed, less methodologically sound research in this field. In addition, the review stresses that cultural competency interventions can only be effective, if they are built on regional, institutional and demographic particularities.

Authors Contribution

Conceptualization: YAK, GM
Methodology: SA
Formal analysis: IS, ZW
Writing, review and editing: MA, IS, ZW, MAA

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Brottman MR, Char DM, Hattori RA, Heeb R, Taff SD. Toward cultural competency in health care: a scoping review of the diversity and inclusion education literature. Academic Medicine. 2020 May; 95(5): 803-13. doi: 10.1097/ACM.0000000000002995.

[2] Kwame A and Petrucka PM. A literature-based study of patient-centered care and communication in nurse-patient interactions: barriers, facilitators, and the way forward. BioMed Central Nursing. 2021 Sep; 20(1): 158. doi: 10.1186/s12912-021-00684-2.

[3] Nowaskie DZ, Patel AU, Fang RC. A multicenter, multidisciplinary evaluation of 1701 healthcare professional students' LGBT cultural competency: Comparisons between dental, medical, occupational therapy, pharmacy, physical therapy, physician assistant, and social work students. PLOS One. 2020 Aug; 15(8): e0237670. doi: 10.1371/journal.pone.0237670.

[4] Flynn PM, Betancourt H, Emerson ND, Nunez EI, Nance CM. Health professional cultural competence reduces the psychological and behavioral impact of negative healthcare encounters. Cultural Diversity and Ethnic Minority Psychology. 2020 Jul; 26(3): 271. doi: 10.1037/cdp0000295.

[5] Chae D, Kim J, Kim S, Lee J, Park S. Effectiveness of cultural competence educational interventions on health professionals and patient outcomes: A systematic review. Japan Journal of Nursing Science. 2020 Jul; 17(3): e12326. doi: 10.1111/jjns.12326.

[6] Antón-Solanas I, Tambo-Lizalde E, Hamam-Alcober N, Vanceulebroeck V, Dehaes S, Kalkan I *et al.* Nursing students' experience of learning cultural competence. PLOS One. 2021 Dec; 16(12): e0259802. doi: 10.1371/journal.pone.0259802.

[7] Gerchow L, Burka LR, Miner S, Squires A. Language barriers between nurses and patients: A scoping review. Patient Education and Counseling. 2021 Mar; 104(3): 534-53. doi: 10.1016/j.pec.2020.09.017.

[8] Barnes EL, Loftus Jr EV, Kappelman MD. Effects of race and ethnicity on diagnosis and management of inflammatory bowel diseases. Gastroenterology. 2021 Feb; 160(3): 677-89. doi: 10.1053/j.gastro.2020.08.064.

[9] Rashwan N and Mahmoud M. Application of competency-based education in dentistry. International Journal of Dental Sciences and Research. 2021 Jun; 9(2): 23-6. doi: 10.12691/ijdsr-9-2-1.

[10] Devine PG and Ash TL. Diversity training goals, limitations, and promise: A review of the multidisciplinary literature. Annual Review of Psychology. 2022 Jan; 73(1): 403-29. doi: 10.1146/annurev-psych-060221-122215.

[11] Godillot C, Jendoubi F, Konstantinou MP, Poncet M, Bergeron A, Gallini A *et al.* How to assess patient satisfaction regarding physician interaction: A systematic review. Dermatologic Therapy. 2021 Mar; 34(2): e14702. doi: 10.1111/dth.14702.

[12] Chawa MS, Yeh HH, Gautam M, Thakrar A, Akinyemi EO, Ahmedani BK. The impact of socioeconomic status, race/ethnicity, and patient perceptions on medication adherence in depression treatment. The Primary Care Companion for CNS Disorders. 2020 Dec; 22(6): 26869. doi: 10.4088/PCC.20m02625.

[13] Webster CS, Coomber T, Liu S, Allen K, Jowsey T. Interprofessional learning in multidisciplinary healthcare teams is associated with reduced patient mortality-a quantitative systematic review and meta-analysis. Journal of Patient Safety. 2023 Jul: 10-97.

[14] Skjerve H, Braaum LE, Goth US, Sørensen A. Using Simulations to Help Public Health Students Overcome Language Barriers for Better Health Outcomes. International Journal of Environmental Research and Public Health. 2023 Jun; 20 (13): 6259. doi: 10.3390/ijerph20136259.

[15] Stubbe DE. Practicing cultural competence and cultural humility in the care of diverse patients. Focus. 2020 Jan; 18(1): 49-51. doi: 10.1176/appi.focus.20190041.

[16] Fricke J, Siddique SM, Aysola J, Cohen ME, Mull NK. Healthcare Worker Implicit Bias Training and Education. InMaking Healthcare Safer IV: A Continuous Updating of Patient Safety Harms and Practices [Internet] 2024 Jan. Agency for Healthcare Research and Quality (US). doi: 10.23970/AHRQEPC_MHS4BIAS.

[17] Argyriadis A, Patelarou E, Paoullis P, Patelarou A, Dimitrakopoulos I, Zisi V *et al.* Self-Assessment of Health Professionals' Cultural Competence: Knowledge, Skills, and Mental Health Concepts for Optimal Health Care. International Journal of Environmental Research and Public Health. 2022 Sep; 19(18): 11282. doi: 10.3390/ijerph191811282.

[18] Horváth Á and Molnár P. A review of patient safety communication in multicultural and multilingual healthcare settings with special attention to the US and Canada. Developments in Health Sciences. 2022 Apr; 4(3): 49-57. doi: 10.1556/2066.2021.00041.

DOI: https://doi.org/10.54393/pjhs.v5i12.2644

[19] Ogbogu PU, Noroski LM, Arcoleo K, Reese Jr BD, Apter AJ. Methods for cross-cultural communication in clinic encounters. The Journal of Allergy and Clinical Immunology: In Practice. 2022 Apr; 10(4): 893-900. doi: 10.1016/j.jaip.2022.01.010.

[20] Sullivan-Detheridge JH, Reifsnider E, Mengsteab M, Merie K, Staller J, Allen AM. Cross Cultural Empathetic Behavior in Health Care Providers: A Review of 3 Countries. Journal of Primary Care & Community Health. 2024 Jan; 15: 21501319241226765. doi: 10.1177/21501319241226765.

[21] Eichbaum QG, Adams LV, Evert J, Ho MJ, Semali IA, van Schalkwyk SC. Decolonizing global health education: rethinking institutional partnerships and approaches. Academic Medicine. 2021 Mar; 96(3): 329-35. doi: 10.1097/ACM.0000000000003473.

[22] Tran BQ. Strategies for effective patient care: Integrating quality communication with the patient-centered approach. Social and Personality Psychology Compass. 2021 Jan; 15(1): e12574. doi: 10.1111/spc3.12574.

[23] Walkowska A, Przymuszała P, Marciniak-Stępak P, Nowosadko M, Baum E. Enhancing cross-cultural competence of medical and healthcare students with the use of simulated patients-a systematic review. International Journal of Environmental Research and Public Health. 2023 Jan; 20(3): 2505. doi: 10.3390/ijerph20032505.

[24] Caballero-Gonzalez A, López-Cepero A, Mattei J. Deep-Structure Attitudes and Reasons toward Healthy Eating and Self-Rated Diet and Health in Ethnically Diverse US-Hispanics/Latinos. Health Promotion Practice. 2023 Dec: 15248399231214968. doi: 10.1177/15248399231214968.

[25] Drossman DA, Chang L, Deutsch JK, Ford AC, Halpert A, Kroenke K *et al.* A review of the evidence and recommendations on communication skills and the patient-provider relationship: a Rome foundation working team report. Gastroenterology. 2021 Nov; 161(5): 1670-88. doi: 10.1053/j.gastro.2021.07.037.

[26] Neff J, Holmes SM, Knight KR, Strong S, Thompson-Lastad A, McGuinness C *et al.* Structural competency: curriculum for medical students, residents, and interprofessional teams on the structural factors that produce health disparities. MedEdPORTAL. 2020 Mar; 16: 10888. doi: 10.15766/mep_2374-8265.10888.

[27] Pratt-Chapman ML, Eckstrand K, Robinson A, Beach LB, Kamen C, Keuroghlian AS *et al.* Developing standards for cultural competency training for health care providers to care for lesbian, gay, bisexual, transgender, queer, intersex, and asexual persons: Consensus recommendations from a national panel. Lesbian, Gay, Bisexual, and Transgender Health. 2022 Jul; 9(5): 340-7. doi: 10.1089/lgbt.2021.0464.

[28] Hilty DM, Crawford A, Teshima J, Nasatir-Hilty SE, Luo J, Chisler LS *et al.* Mobile health and cultural competencies as a foundation for telehealth care: scoping review. Journal of Technology in Behavioral Science. 2021 Jun; 6: 197-230. doi: 10.1007/s41347-020-00180-5.

[29] Forsyth C, Short S, Gilroy J, Tennant M, Irving M. An Indigenous cultural competence model for dentistry education. British Dental Journal. 2020 May; 228(9): 719-25. doi: 10.1038/s41415-020-1480-3.

[30] Karuveettil V, Kumar SV, Janakiram C, Joseph J. Effectiveness of a curriculum-based educational intervention on oral health behavior and dental caries experience among Indian schoolchildren. Journal of Education and Health Promotion. 2020 Jan; 9(1): 90. doi: 10.4103/jehp.jehp_619_19.

[31] Lekas HM, Pahl K, Fuller Lewis C. Rethinking cultural competence: Shifting to cultural humility. Health Services Insights. 2020 Dec; 13: 1178632920970580. doi: 10.1177/1178632920970580.

[32] Lee SE, Lee MH, Peters AB, Gwon SH. Assessment of patient safety and cultural competencies among senior baccalaureate nursing students. International Journal of Environmental Research and Public Health. 2020 Jun; 17(12): 4225. doi: 10.3390/ijerph17124225.

[33] Bogart K, Hemmesch A, Barnes E, Blissenbach T, Beisang A, Engel P. Healthcare access, satisfaction, and health-related quality of life among children and adults with rare diseases. Orphanet Journal of Rare Diseases. 2022 May; 17(1): 196. doi: 10.1186/s13023-022-02343-4.

[34] Deliz JR, Fears FF, Jones KE, Tobat J, Char D, Ross WR. Cultural competency interventions during medical school: a scoping review and narrative synthesis. Journal of General Internal Medicine. 2020 Feb; 35: 568-77. doi: 10.1007/s11606-019-05417-5.

[35] Isserman N and Martin JA. Teaching military cultural competency to clinicians and clinical students: Assessing impact and effectiveness. Journal of Community Engagement and Scholarship. 2022 Jul; 13(4). doi: 10.54656/WRQX5143.

[36] Elendu C, Amaechi DC, Okatta AU, Amaechi EC, Elendu TC, Ezeh CP *et al.* The impact of simulation-based training in medical education: A review. Medicine. 2024 Jul; 103(27): e38813. doi: 10.1097/MD.0000000000038813.

[37] Al-Azzam N, Elsalem L, Gombedza F. A cross-sectional study to determine factors affecting dental and medical students' preference for virtual learning

DOI: https://doi.org/10.54393/pjhs.v5i12.2644

during the COVID-19 outbreak. Heliyon. 2020 Dec; 6(12). doi: 10.1016/j.heliyon.2020.e05704.

[38] Salhi BA, Tsai JW, Druck J, Ward-Gaines J, White MH, Lopez BL. Toward structural competency in emergency medical education. AEM Education and Training. 2020 Feb; 4: S88-97. doi: 10.1002/aet2.10416.

[39] Li M. An examination of two major constructs of cross-cultural competence: Cultural intelligence and intercultural competence. Personality and Individual Differences. 2020 Oct; 164: 110105. doi: 10.1016/j.paid.2020.110105.

[40] Agner J. Moving from cultural competence to cultural humility in occupational therapy: A paradigm shift. The American Journal of Occupational Therapy. 2020 Jul; 74(4): 7404347010p1-7. doi: 10.5014/ajot.2020.038067.

[41] Mata ÁN, de Azevedo KP, Braga LP, de Medeiros GC, de Oliveira Segundo VH, Bezerra IN *et al.* Training in communication skills for self-efficacy of health professionals: a systematic review. Human Resources for Health. 2021 Dec; 19: 1-9. doi: 10.1186/s12960-021-00574-3.