Higher Education
Commission of
Pakistan in "Y"
Category

Pakistan Medical
& Dental Council

College of Physicians
and Surgeons
Pakistan

Aims and Scope

The aim of the Pakistan Journal of Health Sciences (PJHS) is to provide an advanced forum for studies related to the areas of public health, applied medicine, study of microbes, molecular and cellular biology, basic mechanisms of biology, genetic studies, cancer biology, molecular medicine, pharmacology, virology, chemical biology, immunology, chemical biology, basic and clinical human physiology, pathology and population studies. PJHS is a scholarly, peer-reviewed, international, and open-access monthly journal that assures timely publication of manuscripts. In all cases, the key findings in multi-disciplinary articles must address some innovative or controversial practices related to health sciences. PJHS is committed to maintaining the highest standards of professional ethics, accuracy and quality in all matters related to the handling of manuscripts and reporting of scientific information. The journal welcomes empirical and applied research, viewpoint papers, conceptual and technical papers, case studies, meta-analysis studies, literature reviews, mini reviews and letters to editors, which take a scientific approach to the topics related to health sciences.

Types of Articles

- Research papers
- Short communications
- Review or mini-reviews
- Commentaries
- Perspectives and opinions
- Meta-analysis
- Case reports
- Case studies
- Case-control studies

Reviews on recent progress in health sciences are commissioned by the editors. The purpose of the Pakistan Journal of Health Sciences is to publish scientific and technical research papers to bring attention of international researchers, scientists, academicians, health care professionals towards recent advancements in health sciences. The articles are collected in the form of reviews, original studies and clinical studies. It may serve as a global platform for scientists in relevant fields to connect and mutually share ideas. This journal is open to all the research professionals whose work fall within our scope. Submissions are welcome and may be submitted here:

✉ editor@thejas.com.pk

Title

The title of the paper should provide a concise statement of the contents of the paper. A good title is very important and will attract readers and facilitate retrieval by online searches, thereby helping to maximize citations. The title should include topical keywords and allude to the interesting conclusions of the paper. A title that emphasizes the main conclusions, or poses a question, has more impact than one that just describes the nature of the study.

Running Head

Running head should be added in the header along with the page numbers.

Type of Article

Research Article/ Case Report/ Review Article/ Opinion/ Short Communication/ Mini Review/ Letter to Editor.

Running Title: A short version of the paper title.

Keywords: The major keywords used in the article have to be mentioned.

Authors

List here all author names Author[1], Author[2] and Author[3]

[1]Author department, University, Country

[2]Author department, University, Country

[3]Author department, University, Country

*Corresponding Author

Author Name, Affiliation, Department Name, University Name, Address, City, State, Country, E-mail.

ABSTRACT

Abstract should include a brief content of the article. It should be structured and not more than 250 words. It should include following sub headings: Objective, Methods, Results and Conclusions.

Abbreviations

If there are any abbreviations in the article they have to be mentioned.

INTRODUCTION

Provide a context or background for the study (i.e., the nature of the problem and its significance). State the specific purpose or research objective, or hypothesis tested the study or observation; the research objective is often more sharply focused when stated as a question. Both the main and secondary objectives should be made clear and any pre-specified subgroup analysis should be described. Give only strictly pertinent references and do not include data or conclusions from the work being reported.

METHODS

The methods section should include only information that was available at the time or plan of the protocol. All information gathered during the conduct of study should be included in the result section.

Study Design, Inclusion / Exclusion Criteria, Data collection Procedure and Statistical analysis.

RESULTS

Present your results in logical sequence in the text, tables and illustrations, giving the main or most important findings first.

Do not repeat in the text all the data in the tables or illustrations; emphasize or summarize only important observations. When data are summarized in the results section, give numeric results not only as derivatives (for example, percentages) but also as the absolute numbers from which the derivatives were calculated, and specify the statistical methods used to analyze them. Table font should be 10 and caption should be below table and figure.

Data should not be duplicated in both figures and tables. The maximum limit of tables and figures should not exceed more than 4. Mention the findings of the study in paragraph, while mentioning figure and table number in text in sequential order.

TABLE
Table should not be copy pasted or in picture form.

DISCUSSION
Discuss your findings by comparing your results with other literature.

REFERENCES
References should not be less than 20.
In text references should be in number style. For Example [1]
Follow the Pubmed Referencing style.
Provide the DOI link.

Example
Cook NR, Rosner BA, Hankinson SE, Colditz GA. Mammographic screening and risk factors for breast cancer. American Journal of Epidemiology. 2009 Dec;170(11):1422-32. doi: 10.1093/aje/kwp304.

If there are more than six authors, write *et al.* after the first six names.

CONCLUSION(S)
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
Provide the list of individuals who contributed in the work and grant details where applicable.

Plagiarism policy
Similarity index should be less than 19%, and less than 5% from individual sources.

Authorship Letter
Signed authorship letter by all authors including there current Department, University, City, Country, Email.

Declaration Form
Signed declaration form submit by corresponding author.

The submission of article should include: manuscript according to journal guidelines, authorship letter and declaration form. It should be submitted to the following email id: editor@thejas.com.pk

Editorial Team

Editor-in-Chief

Prof. Dr. Riffat Mehboob, Ph.D
National Heart, Lung and Blood Institute, National Institute of Health, Bethesda,
United States of America
Lahore Medical Research Center[LLP], Lahore, Pakistan
riffat.pathol@gmail.com

Editors

Prof. Miguel Munoz, Ph.D
Pediatrician in the Pediatric Intensive Care Unit of the Virgen del Rocio University Hospital, Seville, Spain
Researcher at the Institute of Biomedicine of Seville (IBIS), Spain
Leading Research of the Research Laboratory on Neuropeptides (IBIS) Seville, Spain

Dr. Asif Naveed, MBBS, FCPS
Associate Professor
University of Health Sciences, Lahore, Pakistan

Managing Editor

Khurram Mehboob
Lahore Medical Research Center[LLP],
Lahore, Pakistan

Production Editor

Zeeshan Mehboob
Lahore Medical Research Center[LLP],
Lahore, Pakistan

Biostatistician

Humaira Waseem
Fatima Jinnah Medical University, Lahore, Pakistan

Advisory Board

Dr. Asif Nadeem, Ph.D
Associate Professor
University of Veterinary and Animal Sciences,
Lahore, Pakistan

VOLUME 05 ISSUE 5

TABLE OF CONTENTS

VOLUME 05 ISSUE 5

TABLE OF CONTENTS

VOLUME 05 ISSUE 5

TABLE OF CONTENTS

VOLUME 05 ISSUE 5

Editorial

Next-Generation Sequencing (NGS) in Hematologic Diagnostics

Riffat Mehboob[1,2]

[1]National Heart, Lung and Blood Institute, National Institute of Health, Bethesda, United States of America
[2]Lahore Medical Research Center[LLP], Lahore, Pakistan
riffat.pathol@gmail.com

ARTICLE INFO

Next-Generation Sequencing (NGS) has played a vital role in field of medical diagnostics by providing insights into the genetic causes of various disorders. NGS enables the study of multiple genes linked to hematologic diseases simultaneously and is especially helpful in the diagnosis of complicated diseases such as lymphomas, leukemias and myelodysplastic syndromes [1]. NGS helps classify subtypes by detecting particular genetic changes, which is important for implementing the best treatment plans.

NGS integration into hematologic diagnostics improves patient care by using high-resolution data and increasing diagnosis accuracy. This is especially crucial for conditions where the clinical symptoms are similar. NGS-based genetic profiling aids in the prediction of patient outcomes and the course of disease, enabling more informed clinical decisions. Targeted therapy development is made possible by NGS, which also minimizes side effects and maximizes therapeutic efficacy. Despite its potential, the adoption of NGS faces several challenges including cost and accessibility, technical expertise and regulatory and ethical considerations.

These difficulties do, however, also provide opportunities: a broader use of NGS might greatly enhance diagnostic capacities and raise the standard of healthcare provided worldwide. International research projects that concentrate on the genetic components of hematologic illnesses can advance medical understanding worldwide and lead to novel therapeutic approaches. Global rates of morbidity and death can be decreased by better managing hematologic illnesses by early and precise diagnosis made possible by NGS.

Globally, next-generation sequencing has great potential to improve hematopoietic diagnosis and patient care. Unlocking this technology's full potential will require addressing its cost, accessibility, and technical expertise limitations. Integrating NGS into routine diagnostics could revolutionize the treatment of hematologic illnesses and improve patient outcomes and prospects globally as the world's healthcare infrastructure develops.

REFERENCES

[1] Thol F and Platzbecker U. Do next-generation sequencing results drive diagnostic and therapeutic decisions in MDS? Blood Advances. 2019 Nov; 3(21): 3449-53. doi: 10.1182/bloodadvances.2018022434.

[2] Tan DS, Tan DS, Tan IB, Yan B, Choo SP, Chng WJ *et al.* Recommendations to improve the clinical adoption of NGS-based cancer diagnostics in Singapore. Asia-Pacific Journal of Clinical Oncology. 2020 Aug; 16(4): 222-31. doi: 10.1111/ajco.13 339.

Review Article

Pakistan Society of Hepatology Guidelines on the Management of Hepatic Encephalopathy

Muhammad Usman Naeem[1*], Kashif Malik[2], Amna Fareed[1], Ramsha Kashif[1], Ali Haider[3], Daud Ghilzai[4] and Hafiza Sobia Ramzan[5]

[1]Sheikh Zayed Hospital, Lahore, Pakistan
[2]Department of Gastroenterology-Hepatology, Sheikh Zayed Hospital, Lahore, Pakistan
[3]Department of Gastroenterology, Chandka Medical College, Shaheed Mohtarma Benazir Bhutto Medical University, Larkana, Pakistan
[4]Department of Gastroenterology, Bolan Medical College, Quetta, Pakistan
[5]Department of Molecular Biology and Biotechnology, The University of Lahore, Lahore, Pakistan

ARTICLE INFO

ABSTRACT

Hepatic Encephalopathy (HE) is one of the major complications in patients with liver cirrhosis. Cirrhosis is a significant health burden worldwide, and due to the increasing population and aging, the burden has increased since 1990. The pathogenesis of HE has been explained by different hypotheses, like astrocyte dysfunction, the ammonia hypothesis, and the GABA hypothesis. Hyperammonemia is the most likely cause of MHE. The breakdown of amines, amino acids, and purines by bacteria in the gastrointestinal tract leads to the production of ammonia. Ammonia is converted to urea in the liver by the Krebs-Henseleit cycle. Guidelines are made to help physicians and gastroenterologists diagnose patients at an early stage of hepatic encephalopathy, and a prompt diagnosis can prevent overt hepatic encephalopathy. Since no previous national guidelines regarding PSE are available, the aim here is to create a unifying guideline regarding the treatment of both overt and covert encephalopathy in a cost-effective manner. The management plan given in these guidelines is flexible and can be changed with more authentic data. We recommended that these guidelines provide a valuable source of information regarding HE in the Pakistani population, its current diagnosis, and its treatment. There is a high cost of treatment for liver diseases, and according to the current available data, we must follow the guidelines of PSH.

INTRODUCTION

Hepatic Encephalopathy (HE) is one of the major complications in patients with liver cirrhosis. Cirrhosis puts out a significant health burden worldwide and due to the increasing population and aging, the burden has increased since 1990 [1]. The entire number of patients with chronic liver disease is estimated at 1.5 billion [2]. Amongst the Pakistani population, cirrhosis is the leading cause of mortality and the most common cause of hospital admission [3]. A study conducted in a tertiary care hospital in Rawalpindi revealed that the highest burden in health care centers, that is reaching an epidemic level, is cirrhosis [4]. Approximately 30% of patients dying of end-stage chronic liver disease have had at least one event of significant hepatic encephalopathy [5]. The most common reason for readmission in patients with decompensated chronic liver disease is HE [6]. Prevalence of clinically evident HE is approximately 30–45% in cirrhotic patients and 10–50% in patients with a Trans-jugular Intrahepatic Portosystemic Shunt (TIPS) [6]. Prevalence appeared to be between 30 to 84% of Minimal Hepatic Encephalopathy (MHE), increases in patients with advanced liver disease and in one study reported being 55 % [5-7]. A study conducted in tertiary care hospital revealed that 91 patients out of 150 had MHE [5]. However, due to the non-

availability of the central registry system, exact local prevalence of disease is difficult to find. Once hepatic encephalopathy is treated, most patients remain in MHE which affects the health-related quality of life. Such patients have increased frequency of falls and are prone to accidents [8-10]. Guidelines are made to help physicians and gastroenterologists to diagnose patients at an early stage of hepatic encephalopathy, as a prompt diagnosis can prevent overt hepatic encephalopathy. Since no previous national guidelines regarding PSE are available yet, the aim here is to create a unifying guideline regarding treatment of both overt and covert encephalopathy in a cost-effective manner. The management plan given in these guidelines is flexible and can be changed with more authentic data. These guidelines will be reviewed after a certain period when more data will be available. Consensus is drawn with Delphi panel. Guidelines have been based on international guidelines, literature and local data on the diagnosis and management of hepatic encephalopathy and include low-cost but internationally acceptable investigations and treatment options. For compilation of these guidelines, all recommendations were discussed and approved by panel of expert. Data was scrutinized and made simplified for primary and secondary health care level. Hepatic Encephalopathy (HE) is one of the complications of chronic liver disease. It is a syndrome that includes a wide range of neurobehavioral abnormalities observed in patients with liver disease after extrahepatic causes.

The guidelines under review were made in September 2022 and Pakistan Society of Hepatology approve these guidelines in September 2023.

The study was conducted to compare lipid peroxidation byproducts levels in patients of oral sub mucous fibrosis and control group.

CLASSIFICATION

Hepatic encephalopathy is graded according to: West Haven classification system, according to cause (type A: in patients with acute liver failure, type B: patients with portosystemic shunt, type C: patients with cirrhosis), according to timeline (episodic, recurrent, and persistent) and according to precipitating factors.

Minimal HE (MHE)

It is the mildest form of HE, is characterized by neurocognitive dysfunction and impairs health-related quality of life (HRQOL) despite nonappearance of appreciable clinical symptoms and signs of HE [7, 16, 17]. Patients with MHE have decreased decision making power, decreased attention and fine motor skills rendering them at a high risk of falls and difficulty in performing tasks requiring hand eye coordination such as operating motor vehicle [18, 19].

Pathogenesis of Hepatic Encephalopathy

The pathogenesis of HE has been explained by different hypotheses like astrocyte dysfunction, ammonia hypothesis and GABA hypothesis. Hyperammonemia is the most likely cause of MHE. Breakdown of amines, amino acids, and purines by bacteria in gastrointestinal tract leads to production of ammonia. Ammonia is converted to urea in liver by Krebs Henseleit cycle. Ammonia is also used in conversion of glutamate to glutamine-by-glutamine synthetase. In cirrhosis, due to the decreased number of functioning hepatocytes ammonia is not converted to urea. Secondly due to portosystemic shunt there is ammonia rich blood in systemic circulation without hepatic detoxification. Skeletal muscles contain glutamine synthetase which converts glutamate to glutamine, helping in ammonia metabolism. Muscle wasting in patients with chronic liver disease potentiates hyperammonemia. Kidneys have both glutaminase and glutamine synthetase so helps in ammonia production and metabolism respectively. Ammonia crosses the blood brain barrier and metabolizes in astrocytes by glutamine synthetase. Increased glutamine levels in astrocytes lead to shift of water into astrocytes resulting in edema, hence causing cerebral dysfunction.

Diagnosis of Overt Hepatic Encephalopathy

The diagnosis of Overt Hepatic Encephalopathy (OHE) is clinical and the West Haven Classification (WHC) system is considered the gold standard [13]. In stuporous and comatose patients with WHC 3 and 4, Glasgow Coma Scale (GCS) is widely used [11, 13]. Both the west haven classification system and the GCS can be applied to patients at all levels i.e., primary, secondary, and tertiary care to stage disease severity. Diagnostic modalities are broadly classified into four groups i.e. psychometric, neurophysiological, neuroimaging, and laboratory tests [16]. Two different testing modalities should be performed and at least one should be a Psychometric Hepatic Encephalopathy Test Score (PHES) and one should be selected from neurophysiological and computerized tests [7, 16]. The Psychometric tests include Psychometric Hepatic Encephalopathy Test Score (PHES), animal naming test, Continuous Reaction Test (CRT), Inhibitory Control Test (ICT), and Stroop Test. Neurophysiological tests include Critical Flicker Frequency (CFF), Electroencephalogram (EEG), evoked potential, neuroimaging modalities include CT, MRI, and PET scan and laboratory tests include serum ammonia level and IL-6 level. MHE can be diagnosed with PHES [7, 16]. PHES includes five paper-pencil tests i.e., Number Connection Test-A (NCT-A) Number Connection Test-B (NCT-B), Line Tracing Time (LTT), Digit Symbol Test (DST), and Serial-Dotting Test (SDOT).

PSH RECOMMENDATIONS

For Overt Hepatic Encephalopathy

All patients with overt HE should be evaluated by West Haven Criteria. For grade 3 and 4 hepatic encephalopathy, GCS should be used. Serum ammonia levels can be considered in doubtful cases to rule out the diagnosis. CT/MRI brain should be done when clinical suspicion of cerebral lesion, hemorrhage, focal neurological deficit or the patient is not responding after appropriate recommended treatment of 48 to 72 hours.

For Minimal Hepatic Encephalopathy:

All cirrhotic patients should be evaluated for minimal hepatic encephalopathy in each OPD visit. PHES should be done to make a diagnosis depending upon availability. Animal naming test is easy to perform at all levels, so can be done whenever there is suspicion of impairment of cognition.

TREATMENT

After excluding all other causes of altered sensorium [29-30], precipitating factors [13, 15] leading to encephalopathy should be corrected. Management options should focus on reducing hyperammonemia as it is the most common cause of hepatic encephalopathy.

Patients with grade 3, 4 encephalopathy with GCS less than 7 can be considered for intubation to reduce the risk of aspiration and managed in intensive care unit [21]. It is helpful for selected patients listed for liver transplant with grade 3 or 4 hepatic encephalopathy.

Treatment Options

Lactulose

Lactulose is non absorbable disaccharide which leads to acidification of lumen of gut which leads to impaired replication of ammonia producing bacteria. Lactulose is given as oral (30ml every 2 to 4 hours) or through nasogastric tube till passage of 2-3 loose stools. It can also be given as retention enema where indicated [24, 33]. In patients with cirrhosis, lactulose is given to prevent recurrence of overt hepatic encephalopathy [33-36]. In patients with minimal hepatic encephalopathy lactulose can be given to prevent overt HE [21, 27].

Lactitol

Lactilol is an osmotic laxative. For acute hepatic encephalopathy 45 to 90 ml per day in three divided doses along with meal is given.

Rifaximin

Rifaximin inhibits the ammonia producing bacteria in gut lumen. It is used in acute hepatic encephalopathy alone or with lactulose [38].

Dose is 10-15 mg/kg/day either cyclical (every month for 2 weeks) for 3 to 6 months or continuous maximum dose is 1100mg/day [39]. It should be given in patients with recurrent hepatic encephalopathy [40, 41]. It is recommended to add rifaximin to lactulose in patients with more than one episode of overt HE within 6 months of 1st episode [21, 42, 43].

L-Ornithine, L-Aspartate (LOLA)

20 to 30 grams of injectable LOLA is given in 4 hours for 3 to 7 days has proved beneficial in patients with HE for a minimum duration of 3 days [47, 49]. Injectable LOLA proves to be more beneficial than oral in patients with HE while, in MHE, oral administration has showed relative improvement in psychometric test [13, 16].

Branched Chain Amino Acids (BCAA)

BCAA taken orally have been found to improve hepatic encephalopathy [11, 50, 51]. However, there was no effect on the quality of life, nutritional status and mortality of patient [50, 51]. In various studies improvement in MHE and muscle mass has been noted [52, 53]. No beneficial effect has been noted with injectable use of BCAA [50, 53].

Probiotics

Probiotics help in reducing urease producing activity of gut bacteria by changing intestinal microflora [19]. Beneficial role in grade 1 and 2 of hepatic encephalopathy is better than grade 3 and 4 [55]. Analysis of 9 RCT revealed beneficial role of probiotics in MHE [13, 16, 56].

Neomycin

Neomycin is a glutaminase inhibitor which converts glutamine to glutamate and ammonia. It had been widely used in past but due to ototoxicity, nephrotoxicity and equivocal evidence, it is not used now a days [13, 57].

Metronidazole

Metronidazole reduces urease producing anerobic gram negative bacteria in the gut. Metronidazole can be used for a short period of time for hepatic encephalopathy in dosage of 200mg four times a day [51]. Adverse effects like metallic taste, nephrotoxicity and peripheral neuropathy has limited its long term use [13, 53]. It has same efficacy as rifaximin for short time in acute HE [56].

Zinc

Zinc is used as a cofactor in urea cycle enzymes. Zinc supplementation in HE has conflicting results in different studies so cannot be routinely recommended [21].

Liver Transplantation

Liver transplant should be considered in patients with recurrent or persistent HE not responding to all possible treatment options [21].

PSH RECOMMENDATIONS

Overt Hepatic Encephalopathy

The extrahepatic causes of altered sensorium/ acute confusion should be ruled out before establishing the diagnosis of hepatic encephalopathy. Precipitating factors leading to hepatic encephalopathy should be treated. Lactulose should be given in all patients either orally, through a nasogastric tube, or through enema if no

absolute contraindication with dose titration targeting 2-3 loose stools per day.

Secondary Prevention

Lactulose should be given with dose modification with the target of 2-3 bowel movements per day. Rifaximin 550 mg twice a day long term until LT, nutritional status improves, or liver function improves. Deficiency of multivitamins, macronutrients, micronutrients, and minerals should be clinically assessed and treated with supplements. Adequate protein intake should be encouraged. BCAA can be substituted to maintain adequate protein intake. BCAA, IV LOLA, and metronidazole will be used as alternative agents if the patient is nonresponsive to the above treatment.

Minimal Hepatic Encephalopathy

All cirrhotic patients should be assessed for minimal hepatic encephalopathy/covert hepatic encephalopathy. Lactulose can be given to prevent covert hepatic encephalopathy.

Liver Transplantation in Pakistan

Overt hepatic encephalopathy is an indication of liver transplant. All patients with one episode of overt hepatic encephalopathy should be assessed for liver transplant.

CONCLUSIONS

We recommended that these guidelines provide a valuable source of information regarding HE in Pakistani population, its current diagnosis and treatment.

Acknowledegment

Authors Contribution

Conceptualization: MUN, KM
Writing, review and editing: AF, RK, AH, DG, HSR

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

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

REFERENCES

[1] Sepanlou SG, Safiri S, Bisignano C, Ikuta KS, Merat S, Saberifiroozi M et al. The global, regional, and national burden of cirrhosis by cause in 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. The Lancet Gastroenterology and Hepatology. 2020 Mar; 5(3): 245-66. doi: 10.1016/S2468-1253(19)30349-8.

[2] Cheemerla S and Balakrishnan M. Global epidemiology of chronic liver disease. Clinical Liver Disease. 2021 May; 17(5): 365-70. doi: 10.1002/cld.1061.

[3] Iqbal M, Clement-Pervaiz MV, Ansari MJ, Pervaiz S, Sheikh S, Katpar S, et al. Proceedings of the 1st Liaquat University of Medical & Health Sciences (LUMHS) International Medical Research Conference. Eur J Med Res. 2017; 22:1-20.

[4] Shah SM, Mashia SA, Younus MF, Ghauri A, Ejaz R, Alshalabi H et al. Hepatic cirrhosis-disease burden. Journal of Rawalpindi Medical College Student Supplement. 2015; 19(1): 17-20.

[5] Yousaf S, Farhan S, Nadeem MA. Frequency of Minimal Hepatic Encephalopathy in Cirrhotic Patients with Normal Neurological Examination. Age (Years). 2016 Apr; 20(40): 22.

[6] Elwir S and Rahimi RS. Hepatic encephalopathy: an update on the pathophysiology and therapeutic options. Journal of Clinical and Translational Hepatology. 2017 Jun; 5(2): 142. doi: 10.14218/JCTH.2016.00069.

[7] Shiha G and Mousa N. Minimal hepatic encephalopathy: Silent tragedy. In: Georgios Tsoulfas, Luis Rodrigo editors. Liver Diseases Surgery. 2019. doi: 10.5772/intechopen.88231.

[8] Bibi M, Ali A, Sahar U, Sajid A, Kumar S, Palh ZA, Naqvi SH, Baloch SK. A CLINICAL MANIFESTATION OF HEPATITIS C AMONG THE POPULATION OF HYDERABAD, PAKISTAN. Pakistan Journal of Biotechnology. 2023 Jun 11;20(02):193-207.

[9] Khan RT, Hussain SZ, Shahzad S, Majid Z, Naeem MU, Harjani R, Lail G, Khalid MA, Laeeq SM, Luck NH. Frequency of Non-Alcoholic Fatty Liver Disease Among the Non-Obese Population Presenting to the Gastrointestinal Outpatient Clinic. J Liaquat Natl Hosp. 2024;1:117-21.

[10] Ali B, Salim A, Alam A, Zuberi BF, Ali Z, Azam Z, Kamani L, Farooqi JI, Salih M, Nawaz AA, Chaudhry AA. HEP-Net opinion on the management of ascites and its complications in the setting of decompensated cirrhosis in the resource constrained environment of Pakistan. Pakistan Journal of Medical Sciences. 2020 Jul;36(5):1117.

[11] Tamzaourte M, Rokhsi S, Berrag S, Adioui T. Minimal Hepatic Encephalopathy: Prevalence and Associated Factors. Asian Journal of Research and Reports in Hepatology. 2022 Jan 25;4(1):43-51.

[12] Ghosh J, Ghosh J. Current Management of Hepatic Encephalopathy: A Review Article. Journal for Research in Applied Sciences and Biotechnology. 2023 Sep 23;2(4):170-5.

[13] Dharel N and Bajaj JS. Definition and nomenclature of hepatic encephalopathy. Journal of Clinical and Experimental Hepatology. 2015 Mar; 5(1): S37-41. doi: 10.1016/j.jceh.2014.10.001.

[14] Rafiq Q, Zeeshan M, Mustafa G, Irfan M. Tracheobronchial aspiration affects the outcome of hospitalization among Hepatic Encephalopathy patients. Pakistan Journal of Medical Sciences. 2022 Mar;38(4Part-II):928.

[15] Pisarek, W.J.G.R.P.G., Minimal hepatic encephalopathy–diagnosis and treatment. 2021 Dec; 16(4): 311-317. doi: 10.5114/pg.2021.111389.

[16] Dhiman RK, Saraswat VA, Sharma BK, Sarin SK, Chawla YK, Butterworth R *et al.* Minimal hepatic encephalopathy: consensus statement of a working party of the Indian National Association for Study of the Liver. Journal of Gastroenterology and Hepatology. 2010 Jun; 25(6): 1029-41. doi: 10.1111/j.1440-1746.2010.06318.x.

[17] Pessidjo Djomatcho L, Kowo MP, Ndam AN, Njonnou SR, Kenfack GU, Andoulo FA et al. Normalisation of the psychometric encephalopathy score within the Cameroonian population. Baseboard Management Controller gastroenterology. 2021 Dec; 21: 1-7. doi: 10.1186/s12876-021-01858-7.

[18] Ridola L, Cardinale V, Riggio O. The burden of minimal hepatic encephalopathy: from diagnosis to therapeutic strategies. Annals of Gastroenterology. 2018 Mar; 31(2): 151. doi: 10.20524/aog.2018.0232.

[19] Gou LB, Zhang W, Guo DJ, Zhong WJ, Wu XJ, Zhou ZM. Aberrant brain structural network and altered topological organization in minimal hepatic encephalopathy. Diagnostic and Interventional Radiology. 2020 May;26(3):255.

[20] European Association for the Study of the Liver. EASL Clinical Practice Guidelines on the management of hepatic encephalopathy. Journal of Hepatology. 2022 Sep; 77(3): 807-824. doi: 10.1016/j.jhep.2022.06.001.

[21] Campagna F, Montagnese S, Ridola L, Senzolo M, Schiff S, De Rui M *et al.* The animal naming test: an easy tool for the assessment of hepatic encephalopathy. Hepatology. 2017 Jul; 66(1): 198-208. doi: 10.1002/hep.29146.

[22] Lauridsen MM, Mikkelsen S, Svensson T, Holm J, Klüver C, Gram J *et al.* The continuous reaction time test for minimal hepatic encephalopathy validated by a randomized controlled multi-modal intervention–a pilot study. PLOS One. 2017 Oct; 12(10): e0185412. doi: 10.1371/journal.pone.0185412.

[23] Thomas S, Fiebig JE, Kuhn EM, Mayer DS, Filbeck S, Schmitz W, Krischke M, Gropp R, Mueller TD. Design of glycoengineered IL-4 antagonists employing chemical and biosynthetic glycosylation. ACS Omega. 2023;8(28).

[24] Luo M, Ma P, Li L, Cao WK. Advances in psychometric tests for screening minimal hepatic encephalopathy: From paper-and-pencil to computer-aided assessment. The Turkish Journal of Gastroenterology. 2019 May; 30(5): 398. doi: 10.5152/tjg.2019.18226.

[25] Mehreen N, Aziz B, Taj MK, Saleem M, Taj G, Zafar U. Hepatic encephalopathy and its management. 2022 June; 20(6): 45-64. doi:10.12692/ijb/20.6.45-64.

[26] Edward Ukamaka C, Nwanjo Harrison U, Nwosu Dennis C. Studies on Acute Phase Inflamatory Proteins of Type 2 Diabetics in Owerri. 2019 Oct; 4(10): 324-332. doi: 10.36348/SJBR.2019.v04i10.002.

[27] Gairing SJ, Anders J, Kaps L, Nagel M, Michel M, Kremer WM *et al.* Evaluation of IL-6 for Stepwise Diagnosis of Minimal Hepatic Encephalopathy in Patients with Liver Cirrhosis. Hepatology Communications. 2022 May; 6(5): 1113-22. doi: 10.1002/hep4.1883.

[28] Akhtar AJ, Alamy ME, Yoshikawa TT. Extrahepatic conditions and hepatic encephalopathy in elderly patients. The American Journal of the Medical Sciences. 2002 Jul; 324(1): 1-4. doi: 10.1097/00000441-200207000-00001.

[29] Amodio P. Hepatic encephalopathy: Diagnosis and management. Liver International. 2018 Jun; 38(6): 966-75. doi: 10.1111/liv.13752.

[30] Weissenborn K. Challenges in diagnosing hepatic encephalopathy. Neurochemical Research. 2015 Feb; 40: 265-73. doi: 10.1007/s11064-014-1416-x.

[31] Díaz-Fontenla F, Castillo-Pradillo M, Díaz-Gómez A, Ibañez-Samaniego L, Gancedo P, Guzmán-de-Villoria JA *et al.* Refractory hepatic encephalopathy in a patient with hypothyroidism: Another element in ammonia metabolism. World Journal of Gastroenterology. 2017 Jul; 23(28): 5246. doi: 10.3748/wjg.v23.i28.5246.

[32] Wijdicks EF. Hepatic Encephalopathy. The New England Journal of Medicine. 2016 Oct; 375(17): 1660-1670. doi: 10.1056/NEJMra1600561.

[33] Gluud LL, Vilstrup H, Morgan MY. Non-absorbable disaccharides versus placebo/no intervention and lactulose versus lactitol for the prevention and treatment of hepatic encephalopathy in people with cirrhosis. Cochrane Database of Systematic Reviews. 2016; 5: CD003044. doi:10.1002/14651858 .CD003044.

[34] Butt NI, Butt UI, Kakar AA, Malik T, Siddiqui AM. Is lactulose plus rifaximin better than lactulose alone in the management of hepatic encephalopathy? Journal of College of Physicians and Surgeons Pakistan. 2018 Feb; 28(2): 115-7. doi: 10.29271/jcpsp. 2018.02.115.

[35] Acharya C and Bajaj JS. Current management of hepatic encephalopathy. Official Journal of the American College of Gastroenterology. 2018 Nov; 113(11): 1600-12. doi: 10.1038/s41395-018-0179-4.

[36] Sharma P, Sharma BC, Puri V, Sarin SK. An open-label randomized controlled trial of lactulose and probiotics in the treatment of minimal hepatic encephalopathy. European Journal of Gastroenterology and Hepatology. 2008 Jun; 20(6): 506-11. doi: 10.1097/MEG.0b013e3282f3e6f5.

[37] Cash WJ, McConville P, McDermott E, McCormick PA, Callender ME, McDougall NI. Current concepts in the assessment and treatment of hepatic encephalopathy. QJM: An International Journal of Medicine. 2010 Jan; 103(1): 9-16. doi: 10.1093/qjmed /hcp152.

[38] Iadevaia MD, Prete AD, Cesaro C, Gaeta L, Zulli C, Loguercio C. Rifaximin in the treatment of hepatic encephalopathy. Hepatic Medicine: Evidence and Research. 2011 Dec; 22(3): 109-17. doi: 10.2147/HMER. S11988.

[39] Flamm SL. Rifaximin treatment for reduction of risk of overt hepatic encephalopathy recurrence. Therapeutic Advances in Gastroenterology. 2011 May; 4(3): 199-206. doi: 10.1177/1756283X11401774.

[40] Bass NM, Mullen KD, Sanyal A, Poordad F, Neff G, Leevy CB *et al.* Rifaximin treatment in hepatic encephalopathy. New England Journal of Medicine. 2010 Mar; 362(12): 1071-81. doi: 10.1056/NEJMoa0 907893.

[41] Kimer N, Krag A, Møller S, Bendtsen F, Gluud LL. Systematic review with meta-analysis: the effects of rifaximin in hepatic encephalopathy. Alimentary Pharmacology and Therapeutics. 2014 Jul; 40(2): 123-32. doi: 10.1111/apt.12803.

[42] 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.

2021 Aug; 71(4): 1296-99. doi: 10.51253/pafmj.v71i4.24 81.

[43] Ali B, Zaidi YA, Alam A, Anjum HS. Efficacy of Rifaximin in prevention of recurrence of hepatic encephalopathy in patients with cirrhosis of liver. Journal of College of Physicians and Surgeons Pakistan. 2014 Apr; 24(4): 269-73.

[44] Mittal VV, Sharma BC, Sharma P, Sarin SK. A randomized controlled trial comparing lactulose, probiotics, and L-ornithine L-aspartate in treatment of minimal hepatic encephalopathy. European Journal of Gastroenterology and Hepatology. 2011 Aug; 23(8): 725-32. doi: 10.1097/MEG.0b013e32834 696f5.

[45] Sidhu SS, Sharma BC, Goyal O, Kishore H, Kaur N. L-ornithine L-aspartate in bouts of overt hepatic encephalopathy. Hepatology. 2018 Feb; 67(2): 700-10. doi: 10.1002/hep.29410.

[46] Jain A, Sharma BC, Mahajan B, Srivastava S, Kumar A, Sachdeva S *et al.* l-ornithine l-aspartate in acute treatment of severe hepatic encephalopathy: a double-blind randomized controlled trial. Hepatology. 2022 May; 75(5): 1194-203. doi: 10.1002/ hep.32255.

[47] Aidrus F, Razzaque S, Siddiqui A, Kumar A, Ghaur MI. Therapeutic efficacy of l-ornithine l-aspartate in patients with hepatic encephalopathy. Pakistan Journal of Neurological Sciences. 2015; 10(3): 37-41.

[48] Merli M, Berzigotti A, Zelber-Sagi S, Dasarathy S, Montagnese S, Genton L *et al.* EASL Clinical Practice Guidelines on nutrition in chronic liver disease. Journal of Hepatology. 2019 Jan; 70(1): 172-93. doi: 10.1016/j.jhep.2018.06.024.

[49] Gluud LL, Dam G, Les I, Marchesini G, Borre M, Aagaard NK *et al.* Branched-chain amino acids for people with hepatic encephalopathy. Cochrane Database of Systematic Reviews. 2017 May; 2015(9). doi: 10.1002/14651858.CD001939.pub3.

[50] Ferenci, P.J.G.r., Hepatic encephalopathy. Gastroenterol Report. 2017 May; 5(2): 138-147. doi: 10.1093/gastro/gox013.

[51] Chandio SH, Fatima T, Hassan B, Jabeen S, Mumtaz H, Owais M *et al.* Role of probiotics in decreasing ammonia levels. Can they be used as a treatment of hepatic encephalopathy? 2020 Aug; 9(10): 1328-1337. doi: 10.20959/wjpr202010-18629.

[52] Dalal R, McGee RG, Riordan SM, Webster AC. Probiotics for people with hepatic encephalopathy. Cochrane Database of Systematic Reviews. 2017 Feb; (2): CD008716. doi: 10.1002/14651858.CD008716.pub 3.

[53] Patidar KR and Bajaj JS. Antibiotics for the treatment of hepatic encephalopathy. Metabolic Brain Disease. 2013 Jun; 28: 307-12. doi: 10.1007/s11011-013-9383-5.

[54] Morgan MH, Read AE, Speller DC. Treatment of hepatic encephalopathy with metronidazole. Gut. 1982 Jan; 23(1): 1-7. doi: 10.1136/gut.23.1.1.

[55] Mekky MA, Riad AR, Gaber MA, Abdel-Malek MO, Swifee YM. Rifaximin versus metronidazole in management of acute episode of hepatic encephalopathy: An open labeled randomized clinical trial. Arab Journal of Gastroenterology. 2018 Jun; 19(2): 76-9. doi: 10.1016/j.ajg.2018.06.001.

[56] Rehman S, Fatima QU, Rehman S, Sami Z, Ali H, Saddiqa I. Comparison of current and emerging strategies for treating hepatic encephalopathy. The Professional Medical Journal. 2021 Nov; 28(12): 1705-10. doi: 10.29309/TPMJ/2021.28.12.6644.

Original Article

Effects of Rhythmic Stabilization and Mckenzie Techniques on Pain and Function in Patients with Non-Specific Chronic Low Back Pain

Arzoo Nawaz[1], Sana Hafeez[2], Usama Ahmad Khan[3] and Muhammad Usama[4]

[1]Riphah International Islamic University, Lahore, Pakistan
[2]University of Management and Technology, Lahore, Pakistan
[3]SMC Physio Care Centre, Gujranwala, Pakistan
[4]The University of Lahore, Lahore, Pakistan

A R T I C L E   I N F O

A B S T R A C T

Non-specific chronic low back pain affects 90% of people around the world, resulting in impairment. Their quality of life can be enhanced by exercising. However, due to the complexity of non-specific chronic low back pain (NSCLBP) the most effective type of exercise as a rehabilitation technique is unknown, and more research is required. **Objective:** To assess the effects of rhythmic stabilization and McKenzie techniques on pain and function in patients with NSCLBP. **Methods:** A total of 36 NSCLBP patients were randomly assigned to the McKenzie group and the rhythmic stabilization group. Over a four weeks' period, both groups received 12 sessions. Numeric pain rating scale (NPRS), modified oswestry low back pain (MODI), and bubble inclinometer were used to measure outcomes at baseline of 2nd, and 4th week. **Results:** Across the group, both rhythmic stabilization and McKenzie's results were significant. McKenzie had more significant results within the group than rhythmic stabilization (p<0.05). **Conclusion:** It was concluded that both rhythmic stabilization and McKenzie were helpful in improving pain, functional status, and mobility, with significant changes in NPRS, MODI score, and ranges. In CNSLBP patients, however, McKenzie's technique was demonstrated to be more effective in alleviating pain and impairment, as well as improving mobility, when compared to the technique of rhythmic stabilization.

INTRODUCTION

Low back pain that is not caused by a specific pathology like osteoporosis, fractures, infections, tumors, structural deformities, and inflammatory diseases such as ankylosing spondylitis, cauda equina syndrome, and radicular syndrome is defined as non-specific chronic low back pain (NSCLBP) by the European recommendations for the treatment of chronic nonspecific low back pain [1]. Around 18 % of the population suffers from low back pain on a global scale and approximately 39 % will be suffering not less than an episode of back pain at least once in their life [2]. The approximation is that between 5.0% and 10.0% of the population result in the onset of chronic low back pain, which is responsible for costly treatments, patient suffering, and sick leave additionally being one of the key reasons for people to pursue health care services [3]. In adults, the annual worldwide incidence of low back pain LBP is 15% and the point prevalence is 30% [4]. Lack of physical activities and a sedentary lifestyle, which can result in muscular weakness and power loss, is a predictor of low back pain that leads to recurrent LBP [5]. The cause of non-specific LBP is multifactorial [6]. Patients have become increasingly uncertain of the growing variety of therapy techniques usually given as a method for coping with their problems due to the self-limiting nature of CLBP [7]. In these circumstances, conservative treatment focused on physiotherapy is the safest treatment option for

patients [8]. There is also plenty of evidence that therapeutic exercise can assist individuals with chronic non-specific LBP with pain and disability [9]. Proprioceptive neuromuscular facilitation (PNF) exercises use proprioceptors to improve neuromuscular pathway responsiveness. PNF training may even excite the proprioceptors in the lower back muscles and joints, which may be beneficial in improving balance and sensorimotor modulation [10]. PNF exercises improve flexibility and break the pain-spasm cycle which results in improvement of lumbar range of motion. The topographic organisation of the muscles being treated is taken into account when performing PNF workout programmes [11]. Proprioceptive neuromuscular facilitation (PNF) exercises maximize improvements in flexibility. Prior research advocated the three most common PNF approaches for CLBP, rhythmic stabilization (RS), chop and lift (CL) [12]. The approach involves isometric muscular contractions of antagonistic patterns, which outcomes in antagonist co-contraction if the physiotherapist does not interfere with the isometric contraction. Mechanical Diagnosis and Therapy (MDT), also termed as McKenzie method, is a well-known classification system [13]. McKenzie's extension exercise program aiming at sustained posture or repeated movement in a precise direction, along with an educational approach and following instructions, could reduce the severity of pain in low back discomfort, both acute and sub-acute [14, 15]. Various studies have previously been carried out on the non-specific CLBP using PNF techniques, McKenzie, and core stability exercises, but there is a study gap regarding comparing rhythmic stabilization and McKenzie techniques in pain reduction, and functional status improvement, and lumbar ROM.

This study was conducted to provide an evidence-based approach to the impact of rhythmic stabilization and McKenzie approach on pain and function in individuals with chronic non-specific low back pain.

METHODS

This single-blinded, randomized clinical trial was initiated in October 2021 and ended in February 2022 at Department of Physiotherapy, Rasheed Hospital Lahore, Pakistan after receiving approval from the ethics committee of Riphah International University Lahore, Pakistan (Ref.No.REC/RCR and AHS/21/0121). This trial was registered with ClinicalTrials.gov NCT05207605. A sample size of 40 people was calculated, with a 10% attrition rate calculated by epitool. Sample size was used to detect a significant difference between two means. The mean of both groups were 24 and 22.67, with a variance of 2, confidence level of 0.95 and a power of 0.8. It was a 2 tailed analysis and sample size per group was 18 and for both groups was 36. Due to transportation issues, one

participant in the rhythmic stabilization group did not receive the intervention, and another dropped out of the study due to financial concerns. Two McKenzie group members dropped out due to personal reasons. The study had 36 participants who completed it and the results were analyzed. The consort flow diagram for the study is shown in figure 1.
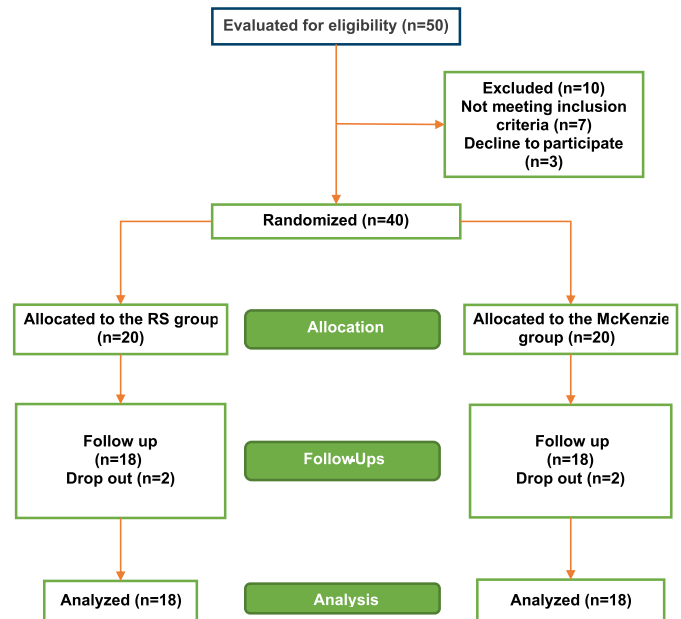
Figure 1: Consort Flow Diagram for Study Design

Subjects with NSCLBP suffering discomfort for at least three months were enrolled, with an age range of 18 to 45 years, at least with mild to moderate pain scoring 2-6 out of 10 on the pain scale. Patients agreement was obtained before therapy, and the treatment method was explained. Members were rejected if there is any set of experiences any feeling of pain below gluteal fold or pain radiating in legs, metabolic and neurologic condition, pathological conditions, past experience of any back or lower limb surgical procedure, pregnancy or any experience of other physiotherapy treatment in past few weeks. Participants were allocated into 2 groups (A and B) by non-probability consecutive random sampling. The outcome assessor diagnosed the patient's disorder before any intervention, observe and examined baseline values before treatment technique, post-treatment values after two weeks, and post-treatment values after 4 weeks of intervention. Initially, fifty people were considered for inclusion. Seven individuals were dropped from the study because they didn't match the eligibility requirements, and three others declined to take part. Participants who meet the inclusion criteria were registered. A complete physical history and assessment of demographic characteristics (age, height, weight, BMI, etc.) were collected. Three sessions of treatment per week with a total of twelve sessions were

given in four weeks. Patients were requested to maintain other normal activities and avoid performing any other treatment protocol during the study duration. Other than the selected treatment protocol, patients were not allowed to administer other techniques like steroids, tapings, other electrotherapy modalities, and other manual therapy techniques during the interventional trial. When the patient walked in for the initial visit, he or she was asked to fill out the NPRS and MODI questionnaire. As a standard course of treatment for non-specific chronic low back pain in both groups, a heat pack was applied for 15 minutes before the technique was given. Participants in Group A received rhythmic stabilization techniques. The patient was requested to maintain a sitting position and the physical therapist stands in front of the patient. The rhythmic stabilization techniques (RST) programme involved doing 10 seconds of alternating isometric trunk flexion-extension contractions against a resistance with no anticipated movement. In the presence of a similar physiotherapist, the patient completes three sets of fifteen repetitions at maximum resistance. Rest periods of 30 and 60 seconds were permitted after completing 15 repetitions of each pattern and in between sets. Each patient received the RS technique programme for a total of about 33 minutes. The McKenzie approach was taught to Group B participants. Group B patients were instructed to perform four extension and three flexion exercises. Group B four extension exercises were: First exercise include the patient lying in a face-down position for one to two minutes. Second, involves having the patient lie in an extension position with their face down. The patient was first encouraged to lie face down, then be asked to extend their trunk on their elbows and hold for five seconds before returning to the beginning position as a relaxation. Third, with an extension exercise in lying posture, the patient was asked to lie face-down for ten seconds, then conduct a trunk extension followed by elbow extension (push-up position), and then return to the original position for rest. Forth, include trunk extension in standing posture, in which the patient is asked to stand and then directed to conduct trunk extension for five seconds with hands on back and fingers pointing backward, followed by relaxation and return to standing position. Each extension exercise was performed twice for a total of ten repetitions. The flexion exercises in Group B were; First, in order to incorporate flexion in the lying position, the patient was directed to lie supine and do trunk flexion with both knees holding the chest, which she was to hold with both hands. Patients were taught to hold that position for a few seconds before returning to the starting position to relax. Second, the patient was instructed to perform the exercise by sitting on the edge of a chair and bending forward while gripping

either an ankle or the floor with both hands. After holding this position for five seconds, the start position was relaxed once more. Third, the patient was requested to stand and then advised to bend forward or perform trunk flexion as far as they could with their fingers down to their knees with flexion on standing. The patient was requested to hold the prior position for five seconds before returning to standing position as a relaxation exercise. All of the exercises in the flexion group were also repeated twice for a total of ten repetitions. After a three-minute rest period, each set is completed. The McKenzie therapy lasted between 20 and 40 minutes [16]. The primary outcome measures were NPRS and MODI scales, and lumbar range of motion was recorded using a bubble inclinometer at baseline, two weeks after treatment, and four weeks after treatment. SPSS for Windows Software, version 25.0 was used to analyze the data. $p < 0.05$ was used to calculate statistical significance. The Shapiro-Wilk test resulted in a value larger than 0.05, the data had been found to be distributed equally, and parametric tests were used to analyze it.

RESULTS

This study was completed with 36 NSCLBP patients, eighteen in each group. Table 1 shows demographic data of the patients, male: female ratio was 12:24. The mean age of Group A was 36.61 + 7.19 years while in Group B was 31.89 ± 6.81 years. While the patients had a minimum BMI of 17 and a maximum BMI of 26, their total mean was 21.30 ± 2.21 (table 1).

Table 1: Participant Demographic Data

Variables	Frequency (%)
Gender	
Male	12 (33)
Female	24 (66.7)
Age (Mean ± SD)	
Group A	36.61 ± 7.19
Group B	31.89 ± 6.81
BMI	
Mean ± SD	21.30 ± 2.21

Comparison of clinical variables within the groups using a level of significance less than 0.05 is shown in table 2. Both Groups had Significant Findings, However Group B Findings are more Significant than Group A (table 2).

Table 2: Comparison of Clinical Variables within the Groups

Variables		Group A Mean ± SD	Group B Mean ± SD	Rhythmic Stabilization	McKenzie	p-Value
NPRS	Baseline – Week 2	5.89 ± 0.47	5.72 ± 0.67	1.33	1.88	0.03
	Week 2 – Week 4	4.56 ± 0.78	3.83 ± 0.92	1.94	1.83	0.002
	Week 4 – Baseline	2.61± 0.78	2.00 ± 0.59	3.2	3.72	0,.001
NPRS	Baseline – Week 2	36.12 ± 5.28	34.33 ±5.89	7.56	6.05	0.04
	Week 2 – Week 4	28.61 ± 6.29	28.27 ±5.49	4.61	5.61	0.02
	Week 4 – Baseline	24.00 ± 8.25	22.67 ±5.37	11.67	12.68	0.01
NPRS	Baseline – Week 2	39.89 ± 3.63	39.94 ± 1.59	3.78	6.39	0.005
	Week 2 – Week 4	43.67 ± 3.53	46.33 ± 2.14	5.89	7.33	0.002
	Week 4 – Baseline	49.56 ± 2.75	53.67 ± 1.78	9.67	13.72	0.01
NPRS	Baseline – Week 2	11.61 ± 1.61	14.83 ± 1.29	3.05	2.61	0.003
	Week 2 – Week 4	14.67 ± 1.53	17.44 ± 1.54	3.16	3.38	0.001
	Week 4 – Baseline	17.83 ± 1.97	20.83 ± 1.38	6.22	6.00	0.04
NPRS	Baseline – Week 2	10.61 ± 1.14	12.94 ± 1.16	3.11	2.67	0.01
	Week 2 – Week 4	13.72 ± 1.44	15.61 ± 1.24	3.72	3.33	0.01
	Week 4 – Baseline	17.44 ± 2.09	18.94 ± 1.76	6.00	6.83	0.03
NPRS	Baseline – Week 2	11.38 ± 1.29	12.00 ± 1.13	2.22	2.33	0.01
	Week 2 – Week 4	13.61 ± 1.37	14.33 ± 1.02	3.61	3.56	0.01
	Week 4 – Baseline	17.22 ± 1.76	17.89 ± 1.07	5.89	5.83	0.001

Table 3 shows NPRS comparisons across the group (Mixed Model ANOVA). P-value was less than 0.05 showed significance. MODI comparison across the group (Mixed Model ANOVA). Mean (I–J) Difference between baseline MODI and Week 2 MODI across the group comparison was 6.80 and 5.11 between 2nd to 4th week and 11.9 between post-treatment and baseline (table 3).

Table 3: Comparison of Clinical Variables across the Groups

Variables		Mean Difference (I–J)	p-Value
NPRS	Baseline – Week 2	1.61	0.02
	Week 2 – Week 4	1.89	0.01
	Week 4 – Baseline	3.50	0.01
NPRS	Baseline – Week 2	6.80	0.01
	Week 2 – Week 4	5.11	0.002
	Week 4 – Baseline	11.9	0.03
NPRS	Baseline – Week 2	5.08	0.01
	Week 2 – Week 4	6.61	0.01
	Week 4 – Baseline	11.6	0.04
NPRS	Baseline – Week 2	2.89	0.02
	Week 2 – Week 4	3.52	0.01
	Week 4 – Baseline	6.41	0.03
NPRS	Baseline – Week 2	2.27	0.02
	Week 2 – Week 4	3.58	0.001
	Week 4 – Baseline	5.86	0.003

DISCUSSION

The current study investigated the impacts of the Rhythmic Stabilisation and McKenzie methods in combination with a hot pack on the degree of pain, functional status, and mobility among people with non-specific chronic low back pain. This study found that both therapy strategies, Rhythmic Stabilization and the McKenzie technique, were helpful in improving pain, functional status, and mobility, with significant differences in numerical pain rating scale (NPRS), modified Oswestry disability index (MODI), and range of motion (ROM). The McKenzie technique, as opposed to Rhythmic Stabilisation, had, however, shown to be more effective in lowering pain and disability in people with chronic nonspecific low back pain. Arcanjo et al., conducted a systematic review and concluded that pain and impairment are reduced with PNF training for persistent low back pain. This systematic review combed through five datasets. 16 studies met the criteria for inclusion of 722 patients. PNF was compared to a control group, core strengthening, and conventional physical therapy. PNF training decreased pain and impairment when compared to the control group. In terms of pain reduction and disability improvement, PNF training was found to be more beneficial than core strengthening [17]. Rhythmic stabilization was also found to be beneficial in terms of pain reduction, lumbar mobility, and disability. Areeudomwong et al., executed a randomized trial in 2019 to examine the effects of proprioceptive neuromuscular facilitation training and core stabilisation exercises on outcomes. This study concluded that four weeks of CSE and PNF training had advantages in both the short and long term for CLBP patients in regards to pain-related outcomes and deep trunk muscle activation [18]. In the current study, pain-related outcomes also improved after 4 weeks of rhythmic stabilization intervention. A randomized trial conducted to determine whether proprioceptive neuromuscular facilitation training can assist people with chronic low back pain manage their pain and improve their

balance. According to the findings of this study, a period of three weeks of proprioceptive neuromuscular facilitation training results in greater improvement in pain intensity, disability, and static balance ability in working-age individuals suffering from low back pain than general trunk exercises [19]. These results are consistent with a recent study that reported a significant reduction in pain and an improvement in MODI scores in the rhythmic stabilisation group. A study in 2018 was conducted to check the efficacy of MDT in comparison to placebo in people who had persistent LBP. At the end of the five weeks, the major outcomes were pain severity and functional status. The MDT group was found to be more effective in this investigation. However, according to a recent study, the McKenzie group was equally successful for long-term handicap when compared to the rhythmic stabilization approach. Yamin et al., in a randomized control experiment, McKenzie exercises were compared to general conditioning activities in order to determine which one was more effective for reducing back pain. The study's findings showed that Group B, which received McKenzie exercises, proved significantly higher than Group A, which received general conditioning exercises, with a value of 0.23 ± 0.43 compared to Group A value of 2.6 ± 1.1. In comparison to general conditioning activities, this study found that using the McKenzie approach to treat low back pain results in significant short-term pain relief [20]. In current study's results recommended that McKenzie treatment produces a significant reduction in pain over a period of four weeks; also it produces appreciable results in a reduction of disability and improving lumbar ranges.

CONCLUSIONS

Rhythmic stabilization and McKenzie were helpful in improving pain, functional status, and lumbar range of motion, with significant differences in NPRS, MODI score, and lumbar ranges. McKenzie, on the other hand, has been shown to be more helpful than rhythmic stabilization in lowering pain and increasing lumbar ranges in people with non-specific chronic low back pain.

Authors Contribution

Conceptualization: AN
Methodology: AN, UAK
Formal analysis: SH
Writing-review and editing: MU

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

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

REFERENCES

[1] Park HJ, Choi JY, Lee WM, Park SM. Prevalence of chronic low back pain and its associated factors in the general population of South Korea: a cross-sectional study using the National Health and Nutrition Examination Surveys. Journal of Orthopaedic Surgery and Research. 2023 Jan; 18(1): 29. doi: 10.1186/s13018-023-03509-x.

[2] Lozano R, Fullman N, Abate D, Abay SM, Abbafati C, Abbasi N et al. Measuring progress from 1990 to 2017 and projecting attainment to 2030 of the health-related Sustainable Development Goals for 195 countries and territories: a systematic analysis for the Global Burden of Disease Study 2017. The Lancet. 2018 Nov; 392(10159): 2091-138.

[3] Júnior MA, De Almeida MO, Santos RS, Civile VT, Costa LO. Effectiveness of kinesio taping in patients with chronic nonspecific low back pain: a systematic review with meta-analysis. Spine. 2019 Jan; 44(1): 68-78. doi: 10.1097/BRS.0000000000002756.

[4] Ganesan S, Acharya AS, Chauhan R, Acharya S. Prevalence and risk factors for low back pain in 1,355 young adults: a cross-sectional study. Asian Spine Journal. 2017 Aug; 11(4): 610. doi: 10.4184/asj.2017.11.4.610.

[5] Sipaviciene S and Kliziene I. Effect of different exercise programs on non-specific chronic low back pain and disability in people who perform sedentary work. Clinical Biomechanics. 2020 Mar; 73: 17-27. doi: 10.1016/j.clinbiomech.2019.12.028.

[6] Ramond-Roquin A, Bouton C, Bègue C, Petit A, Roquelaure Y, Huez JF. Psychosocial risk factors, interventions, and comorbidity in patients with non-specific low back pain in primary care: need for comprehensive and patient-centered care. Frontiers in Medicine. 2015 Oct; 2:73. doi: 10.3389/fmed.2015.00073.

[7] Chiarotto A, Maxwell LJ, Ostelo RW, Boers M, Tugwell P, Terwee CB. Measurement properties of visual analogue scale, numeric rating scale, and pain severity subscale of the brief pain inventory in patients with low back pain: a systematic review. The Journal of Pain. 2019 Mar; 20(3): 245-63. doi: 10.1016/j.jpain.2018.07.009.

[8] Czajka M, Truszczyńska-Baszak A, Kowalczyk M. The effectiveness of McKenzie Method in diagnosis and treatment of low back pain–a literature review. Advances in Rehabilitation. 2018; 32(1): 5-11. doi: 10.5114/areh.2018.76985.

[9] Maher C, Underwood M, Buchbinder R. Non-specific low back pain. The Lancet. 2017 Feb; 389(10070): 736-47. doi: 10.1016/S0140-6736(16)30970-9.

[10] Lam OT, Strenger DM, Chan-Fee M, Pham PT, Preuss RA, Robbins SM. Effectiveness of the McKenzie method of mechanical diagnosis and therapy for treating low back pain: literature review with meta-analysis. Journal of Orthopaedic & Sports Physical Therapy. 2018 Jun; 48(6): 476-90. doi: 10.2519/jospt.2018.7562.

[11] Anggiat L, Hon WH, Sokran SN, Mohammad NM. The changes of functional disability in non-specific low back pain among university population after proprioceptive neuromuscular facilitation and mckenzie method. International Journal of Medical and Exercise Science. 2020; 6(1): 656-67. doi: 10.36678/ijmaes.2020.v06i01.001.

[12] Malla S, Chahal A, Tiku RK, Kaul B. Effect of motor control exercise on Swiss ball and PNF technique on non-specific low back pain. International Journal of Medical Research and Health Sciences. 2018 Jan; 7(4): 114-24.

[13] Garcia AN, Costa LD, Hancock MJ, De Souza FS, de Oliveira Gomes GV, De Almeida MO et al. McKenzie Method of Mechanical Diagnosis and Therapy was slightly more effective than placebo for pain, but not for disability, in patients with chronic non-specific low back pain: a randomised placebo controlled trial with short and longer term follow-up. British Journal of Sports Medicine. 2018 May; 52(9): 594-600. doi: 10.1136/bjsports-2016-097327.

[14] Waqqar S, Shakil-ur-Rehman S, Ahmad S. McKenzie treatment versus mulligan sustained natural apophyseal glides for chronic mechanical low back pain. Pakistan Journal of Medical Sciences. 2016 Mar; 32(2): 476. d

[15] Bose GN and Gohill D. Effect of Mckenzie Therapy and Lumbar Strengthening Program in Lumbar Spine Derangement Syndrome 1. European Journal of Pharmaceutical and Medical Research. 2018; 5(3), 160-164.

[16] Panjaitan LA, Hon WH, Baait SN, Mawaddah N. Comparison between proprioceptive neuromuscular facilitation and mckenzie method in lumbar range of motion on non-specific low back pain. ACTIVE: Journal of Physical Education, Sport, Health and Recreation. 2020 Feb; 9(1): 63-71.

[17] Arcanjo FL, Martins JV, Mote P, Leporace G, de Oliveira DA, de Sousa CS et al. Proprioceptive neuromuscular facilitation training reduces pain and disability in individuals with chronic low back pain: A systematic review and meta-analysis. Complementary Therapies in Clinical Practice. 2022 Feb; 46: 101505. doi: 10.1016/j.ctcp.2021.101505.

[18] Areeudomwong P and Buttagat V. Comparison of core stabilisation exercise and proprioceptive neuromuscular facilitation training on pain-related and neuromuscular response outcomes for chronic low back pain: a randomised controlled trial. The Malaysian Journal of Medical Sciences. 2019 Nov; 26(6): 77. doi: 10.21315/mjms2019.26.6.8.

[19] Areeudomwong P and Buttagat V. Proprioceptive neuromuscular facilitation training improves pain-related and balance outcomes in working-age patients with chronic low back pain: a randomized controlled trial. Brazilian Journal of Physical Therapy. 2019 Sep; 23(5): 428-36. doi: 10.1016/j.bjpt.2018.10.005.

[20] Iizuka Y, Iizuka H, Mieda T, Tsunoda D, Sasaki T, Tajika T et al. Prevalence of chronic nonspecific low back pain and its associated factors among middle-aged and elderly people: an analysis based on data from a musculoskeletal examination in Japan. Asian Spine Journal. 2017 Dec; 11(6): 989. doi: 10.4184/asj.2017.11.6.989.

Original Article

Frequency of Fetomaternal Outcomes in Severe Preeclampsia

Aroosa Usman Khattak[1] and Saima Khattak[1*]

[1]Department of Obstetrics and Gynaecology, Medical Teaching Institution, Lady Reading Hospital, Peshawar, Pakistan

ARTICLE INFO

ABSTRACT

Preeclampsia, severe preeclampsia, and eclampsia are hypertension illnesses that occur during pregnancy. The severe spectrum that includes organ failure, unconsciousness, and, sadly, maternal, and fetal deaths, is known as preeclampsia and eclampsia. **Objective:** To investigate the prevalence of fetomaternal outcomes in severe preeclampsia. **Methods:** This descriptive cross-sectional study was conducted from February 1st to August 1st, 2021, a descriptive case series was carried out at the Obstetrics and Gynecology Department at Lady Reading Hospital (LRH), Peshawar. A total of 232 pregnant women with severe preeclampsia were included in the research. Several unfavorable fetomaternal outcomes, such as caesarean section, mortality, low birth weight, fetal death, poor Apgar score, preterm birth, and birth asphyxia, were recorded along their course till delivery. **Results:** The study encompassed women aged 18 to 40, with mean values of 28.14 ± 2.72 years for age, 1.24 ± 1.23 for parity, 36.37 ± 2.17 weeks for gestational age, and 25.86 ± 1.39 kg/m2 for BMI. Among the observed outcomes, cesarean section was noted in 56% of patients, mortality occurred in 8.6% cases, low birth weight in 17.2%, fetal death in 11.2%, low Apgar score in 19%, preterm birth in 8.6%, and birth asphyxia in 7.8%. **Conclusions:** The results highlight a significant rate of morbidity and death among mothers and perinatals linked to severe preeclampsia. Better prenatal care may be able to delay the onset of severe preeclampsia and eclampsia, which might significantly reduce the risk of negative outcomes.

INTRODUCTION

Preeclampsia, severe preeclampsia, and eclampsia are hypertension illnesses that occur during pregnancy and are major causes of maternal and neonatal death worldwide [1]. Clinical indicators of preeclampsia, such as high blood pressure and the presence of albumin in the urine, indicate the possibility of eclampsia and its development to severe forms, necessitating close observation and prompt action [2]. Severe preeclampsia is very difficult to treat, especially in low and middle income nations where there are often limited resources, medical staff, and systemic barriers that delay necessary therapies [3]. To lower the number of deaths linked to eclampsia, recent international programs have placed a strong emphasis on task shifting, which empowers frontline healthcare staff to recognize these situations and begin managing them [4]. The severe spectrum that includes organ failure, unconsciousness, and, sadly, maternal, and fetal deaths, is known as

preeclampsia and eclampsia [5]. The substantial impact that pregnancy-induced hypertension has on maternal and perinatal morbidity and death has been shown by several research conducted worldwide [6]. Research undertaken in many places, including the Mettu Karl Referral Hospital, has revealed alarming rates of perinatal death associated with severe cases of preeclampsia and eclampsia [7, 8]. Studies like Ajah LO et al., and Melese MF et al., which explain rates of cesarean sections, low birth weights, mortality, fetal deaths, and various neonatal complications associated with severe preeclampsia, demonstrate how important it is to investigate the frequency and seriousness of adverse outcomes in severe preeclampsia [9-11]. Although prior research has endeavored to examine the patterns and contributing variables associated with severe preeclampsia and eclampsia, dependence on secondary data necessitates the necessity of thorough

primary investigations [12]. The best treatment for severe preeclampsia and eclampsia is delivery due to the deterioration of the condition of the mother and fetus. One of the main pillars of management is proper obstetric care; premature fetal and placental delivery can hurt both mother and fetal outcomes. Preeclampsia related maternal and neonatal death and morbidity may only be avoided with access to high quality prenatal care early risk factor identification and diagnosis vigilant observation and prompt management. Healthcare professionals should provide these women needs extra consideration. When giving them preventative healthcare they may complete their outpatient follow up because they are aware of the incidence and clinical characteristics of preeclampsia.

This study used a large sample size of 232 individuals to investigate the prevalence of unfavorable fetomaternal outcomes in severe preeclampsia. The knowledge gained from this study will contribute to the body of knowledge and be used as a practical manual for healthcare professionals, providing high-risk preeclampsia patients in the general population with counseling options.

METHODS

The cross-sectional study was carried out from February 1st, 2021 to August 1st, 2021, at the Department of Obstetrics and Gynecology at LRH, Peshawar. Using the WHO sample size program, the sample size of 232 was calculated with a 95% confidence interval, a 4% margin of error, and a reported prevalence rate of Low Apgar score of 10.8%. Non-probability sequential sampling was the method used for sampling. Women between the ages of 18 and 40 who met the operational definition of severe preeclampsia and had ultrasound confirmation of a singleton pregnancy, a gestational age more than 30 weeks based on the Last Menstrual Period (LMP), and any parity. A history of anemia, diabetes, or hypertension before pregnancy was one of the exclusion criteria. After receiving approval from the Institutional Review Board (IRB) with Reference Number: 10/LR/MTI on dated 14-09-2021. The first stage was to collect basic demographic information such age, parity, gestational age, and BMI. Following this, until delivery, all adverse fetomaternal outcomes were recorded, as detailed in the specially created proforma. These outcomes included but were not limited to caesarean section, mortality, low birth weight, fetal death, low Apgar score, preterm birth, and birth asphyxia. Adverse result management followed departmental procedures. SPSS version 23.0 was used for statistical analysis. While categorical data like caesarean section, mortality, low birth weight, fetal death, poor Apgar score, preterm delivery, and birth asphyxia were computed for frequency and percentage, quantitative factors like age, parity, gestational age, and BMI were provided as Mean ± SD. Age, parity, gestational age, and BMI were used to stratify fetomaternal outcomes. Chi-square tests were used for post-stratification analysis, with $p < 0.05$ being regarded as statistically significant.

RESULTS

The research examining fetomaternal outcomes in severe preeclampsia has enrolled individuals. The individuals' mean age was 28.1 ± 2.72 years, and their parity was 1.2 ± 1.2, meaning they had one or two prior pregnancies. The enrolment occurred approximately during the 36th week of pregnancy, based on the mean gestational age of 36.37 ± 2.17 weeks. The individuals' average BMI was 25.86 ± 1.39kg/m², which indicates that they are overweight. The average age, prior pregnancies, stage of pregnancy upon enrolment, and body mass index of the enrolled population are all highlighted in these figures, which offer a glimpse into their profile (Table 1).

Table 1: Demographic Characteristics of Study Participants

S.No	Demographics	Mean ± SD
1	Age (Years)	28.14 ± 2.72
2	Parity	1.24 ± 1.23
3	Gestational Age	36.37 ± 2.17
4	BMI (Kg/m²)	25.86 ± 1.39

The frequency of fetomaternal outcomes in patients with severe preeclampsia is shown in the table 2. Among the subjects, 130 (56%), required a cesarean section, whereas 102 (44%) cases, did not. 20 (8.6%) cases had mortality, 40 (17.2%) cases had low birth weight, 20 (11.2%) cases had fetal death, 40 (19%) cases had low Apgar scores, 20 (8.4%) cases had preterm births, and 18 (7.8%) cases had birth asphyxia. During the research period, the remaining subjects did not display any of these issues. This study provide insight into the incidence rates of various fetomaternal problems by summarizing the frequency of distinct unfavorable outcomes suffered by individuals with severe preeclampsia (Table 2).

Table 2: Fetomaternal Outcome Frequencies in Severe Preeclampsia Participants

Variables	Detail	N (%)
Cesarean Section	Yes	130 (56%)
	No	102 (44%)
Mortality	Yes	20 (8.6%)
	No	212 (91.4%)
Low Birth Weight	Yes	40 (17.2%)
	No	192 (82.8%)
Fetal Death	Yes	26 (11.2%)
	No	206 (88.8%)
Low Apgar Score	Yes	44 (19%)
	No	188 (81%)
Preterm Birth	Yes	20 (8.4%)
	No	212 (91.4%)
Birth Asphyxia	Yes	18 (7.8%)
	No	214 (92.2%)

Khattak AU _et al.,_

The relationship between fetomaternal outcomes in instances of severe preclampsia and demographic characteristics (age, parity, gestational age, and BMI) is displayed in the table. The demographic variables, as well as the incidence of Cesarean Section, Mortality, Low Birth Weight, Fetal Death, Low Apgar Score, Preterm Birth, and Birth Asphyxia, are used to split the table. Non-significant p-values (>0.05) in the statistical study show that there are no significant relationships between the demographic parameters (age, parity, gestational age, and BMI) and the majority of fetomaternal outcomes. A few exceptions exist, though: low birth weight has a significant link with BMI (p=0.013) and low Apgar score has a substantial correlation with age (p=0.046). Except for significant correlations between Low Birth Weight and BMI and Low Apgar Score and age, these data point to a limited relationship between demographic characteristics and the majority of fetomaternal outcomes in severe preclampsia (Table 3).

Table 3: Correlation Between Demographic Factors and Fetomaternal Outcomes in Severe Preeclampsia

Variables	Detail	Age (Years)			Parity			Gestational Age (Weeks)			BMI		
		18-30 N (%)	>30 N (%)	p-Value	0-2 N (%)	>2 N (%)	p-Value	30-39 N (%)	>39 N (%)	p-Value	≤25 N (%)	>25 N (%)	p-Value
Cesarean Section	Yes	105 (55.6)	25 (58.1)	0.758	101 (55.8)	29 (56.9)	0.893	112 (54.6)	18 (66.7)	0.236	58 (52.3)	72 (59.5)	0.266
	No	84 (44.4)	18 (41.9)		80 (44.2)	22 (43.1)		93 (45.4)	9 (33.3)		53 (47.7)	49 (40.5)	
Mortality	Yes	15 (7.9)	5 (11.6)	0.436	14 (7.7)	6 (11.8)	0.365	17 (8.3)	3 (11.1)	0.624	7 (6.3)	13 (10.7)	0.229
	No	174 (92.1)	38 (88.4)		167 (92.3)	45 (88.2)		188 (91.7)	24 (88.9)		104 (93.7)	108 (89.3)	
Low Birth Weight	Yes	35 (18.5)	5 (11.6)	0.280	35 (19.3)	5 (9.8)	0.111	36 (17.6)	4 (14.8)	0.723	12 (10.8)	28 (23.1)	0.013
	No	154 (81.5)	38 (88.4)		146 (80.7)	46 (90.2)		169 (82.4)	23 (85.2)		99 (89.2)	93 (76.9)	
Fetal Death	Yes	22 (11.6)	4 (9.3)	0.661	20 (11)	6 (11.8)	0.886	23 (11.2)	3 (11.1)	0.987	11 (9.9)	100 (90.1)	0.549
	No	167 (88.4)	39 (90.7)		161 (89)	45 (88.2)		182 (88.8)	24 (88.9)		15 (12.4)	106 (87.6)	
Low Apgar Score	Yes	35 (18.5)	9 (20.9)	0.716	34 (18.8)	10 (19.6)	0.895	42 (20.5)	2 (7.4)	0.103	27 (24.3)	17 (14)	0.046
	No	154 (81.5)	34 (79.1)		147 (81.2)	41 (80.4)		163 (79.5)	25 (92.6)		84 (75.7)	104 (86)	
Preterm Birth	Yes	17 (9)	3 (7)	0.670	16 (8.8)	4 (7.8)	0.823	20 (9.8)	0 (0)	0.090	10 (9)	10 (8.3)	0.840
	No	172 (91)	40 (93)		165 (91.2)	47 (92.2)		185 (90.2)	27 (100)		101 (91)	111 (91.7)	
Birth Asphyxia	Yes	14 (7.4)	4 (9.3)	0.675	14 (7.7)	4 (7.8)	0.980	14 (6.8)	4 (14.8)	0.145	11 (9.9)	7 (5.8)	0.241
	No	175 (92.6)	39 (90.7)		167 (92.3)	47 (92.2)		191 (93.2)	23 (85.2)		100 (90.1)	114 (94.2)	

DISCUSSION

Consistent with other studies conducted in other contexts, this investigation demonstrated a relationship between the incidence of severe preclampsia and eclampsia and poor maternal socioeconomic position. The social disadvantages that this group experiences may be the cause of this relationship, which may lead to a decrease in awareness and less-than-ideal health-seeking behaviour [13]. Remarkably, 83.1% of patients had no reservations, a sign of subpar prenatal care. This study found a substantial correlation between adolescent pregnancy and severe preeclampsia and eclampsia, which deviates from patterns seen in industrialized nations where older mothers are more prevalent [14]. This discrepancy might be attributed to greater rates of adolescent pregnancy and early marriage in this setting, which is consistent with Black communities experiencing higher rates of preeclampsia and eclampsia than Caucasians [15]. Furthermore, a robust correlation was seen between nulliparity and severe preeclampsia and eclampsia, particularly in line with previous studies [16]. These patients may have a higher risk of premature birth because of the hospital's intervention efforts, which frequently call for an early delivery following patient stabilization [17]. The greater incidence of cesarean sections among instances of severe

preeclampsia and eclampsia may be related to the need for an immediate response to prevent additional difficulties for the mother and fetus, particularly in cases with unfavourable cervical circumstances [18]. The frequency of cesarean births also matched those from other areas. Despite being lower than other studies conducted in Tanzania and India, the 17.2% reported low birth weight in this study showed a strong correlation with severe preeclampsia and eclampsia [19]. This correlation may have been caused by intervention-driven deliveries regardless of gestational age and a higher incidence of intrauterine growth restriction [20]. The incidence of antepartum eclampsia in this research was consistent with rates from Ethiopia, Enugu, and Ibadan, albeit being higher than in Lagos [21]. While it was lower than those from Enugu and Irrua, the maternal mortality rate was equivalent to figures from Tanzania, India, and Ibadan, Nigeria [21-23]. The reasons for maternal death were like those found in Sokoto, Lagos, and Ibadan. The greater number of cesarean sections and the related hazards may possibly be contributing factors to the high maternal death rate, in addition to preeclampsia and its sequelae [24]. The study's fetal mortality rates were greater than those reported in Ibadan but comparatively lower than those in Ethiopia and Kaduna [25, 26]. As previously seen in Bangladesh, there

may be an association between the high frequency of low birth weight among cases of severe preeclampsia and eclampsia and the prevalence of perinatal death [27, 28]. Compared to the control group, severe preeclampsia and eclampsia had a substantial correlation with maternal and perinatal death rates, which may be attributed to the complexities of the condition and the hospital's ability to handle them[29].

CONCLUSIONS

Adolescent, rural, and poor socioeconomic group women in this research were more likely to have preeclampsia with severe characteristics and eclampsia.

Authors Contribution

Conceptualization: AUK
Methodology: AUK, SK
Formal analysis: AUK, SK
Writing, review and editing: SK

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

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

REFERENCES

[1] Khan B, Yar RA, khan Khakwani A, Karim S, Ali HA, Khakwani A *et al.* Preeclampsia incidence and its maternal and neonatal outcomes with associated risk factors. Cureus. 2022 Nov; 14(11): e31143. doi: 10.7759/cureus.31143.

[2] Machano MM and Joho AA. Prevalence and risk factors associated with severe pre-eclampsia among postpartum women in Zanzibar: a cross-sectional study. BMC Public Health. 2020 Dec; 20: 1-0. doi: 10.1186/s12889-020-09384-z.

[3] Robbins T, Shennan A, Sandall J, Guangul TE, Demissew R, Abdella A *et al.* Understanding challenges as they impact on hospital-level care for pre-eclampsia in rural Ethiopia: a qualitative study. British Medical Journal Open. 2023 Apr; 13(4): e061500. doi: 10.1136/bmjopen-2022-061500.

[4] Srinidhi V, Karachiwala B, Iyer A, Reddy B, Mathrani V, Madhiwalla N *et al.* ASHA Kirana: when digital technology empowered front-line health workers. British Medical Journal Global Health. 2021 Sep; 6(5): e005039. doi: 10.1136/bmjgh-2021-005039.

[5] Phipps EA, Thadhani R, Benzing T, Karumanchi SA. Pre-eclampsia: pathogenesis, novel diagnostics and therapies. Nature Reviews Nephrology. 2019 May; 15(5): 275-89. doi: 10.1038/s41581-019-0119-6.

[6] 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): 831-40. doi: 10.4314/ejhs.v29i1.4.

[7] Melese MF, Badi MB, Aynalem GL. Perinatal outcomes of severe preeclampsia/eclampsia and associated factors among mothers admitted in Amhara Region referral hospitals, North West Ethiopia, 2018. BMC Research Notes. 2019 Dec; 12: 1-6. doi: 1186/s13104-019-4161-z.

[8] Tlaye KG, Endalfer ML, Kassaw MW, Gebremedhin MM, Aynalem YA. Preeclampsia management modalities and perinatal death: a retrospective study in Woldia general hospital. BMC Pregnancy and Childbirth. 2020 Dec; 20: 1-9. doi: 10.1186/s12884-020-02909-9.

[9] Belay AS and Wudad T. Prevalence and associated factors of pre-eclampsia among pregnant women attending anti-natal care at Mettu Karl referal hospital, Ethiopia: cross-sectional study. Clinical Hypertension. 2019 Dec; 25: 1-8. doi: 10.1186/s40885-019-0120-1.

[10] Getaneh Y, Fekadu E, Jemere AT, Mengistu Z, Tarekegn GE, Oumer M *et al.* Incidence and determinants of adverse outcomes among women who were managed for eclampsia in the University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia. BMC Pregnancy and Childbirth. 2021 Dec; 21: 1-2. doi: 10.1186/s12884-021-04199-1.

[11] Syoum FH, Abreha GF, Teklemichael DM, Chekole MK. Fetomaternal Outcomes and Associated Factors among Mothers with Hypertensive Disorders of Pregnancy in Suhul Hospital, Northwest Tigray, Ethiopia. Journal of Pregnancy. 2022 Nov; 2022. doi: 10.1155/2022/6917009.

[12] Kell DB and Kenny LC. A dormant microbial component in the development of preeclampsia. Frontiers in Medicine. 2016 Nov; 3: 60. doi: 10.3389/fmed.2016.00060.

[13] Zewude B, Siraw G, Engdawork K, Tadele G. Health seeking behavior of street connected children in Addis Ababa, Ethiopia. Frontiers in Sociology. 2023 Aug; 8: 1188746. doi: 10.3389/fsoc.2023.1188746.

[14] Grum T, Seifu A, Abay M, Angesom T, Tsegay L. Determinants of pre-eclampsia/Eclampsia among women attending delivery Services in Selected Public Hospitals of Addis Ababa, Ethiopia: a case control study. BMC Pregnancy and Childbirth. 2017 Dec; 17: 1-7. doi: 10.1186/s12884-017-1507-1.

[15] Savage AR and Hoho L. Knowledge of pre-eclampsia in women living in Makole Ward, Dodoma, Tanzania. African Health Sciences. 2016 Jul; 16(2): 412-9. doi: 10.4314/ahs.v16i2.9.

[16] Ngwenya S. Severe preeclampsia and eclampsia: incidence, complications, and perinatal outcomes at a low-resource setting, Mpilo Central Hospital, Bulawayo, Zimbabwe. International Journal of Women's Health. 2017 May: 9: 353-357. doi: 10.2147/IJWH.S131934.

[17] Schleußner E. The prevention, diagnosis and treatment of premature labor. Deutsches Ärzteblatt International. 2013 Mar; 110(13): 227. doi: 10.3238/arztebl.2013.0227.

[18] Irene K, Amubuomombe PP, Mogeni R, Andrew C, Mwangi A, Omenge OO et al. Maternal and perinatal outcomes in women with eclampsia by mode of delivery at Riley mother baby hospital: a longitudinal case-series study. BMC Pregnancy and Childbirth. 2021 Jun; 21(1): 439. doi: 10.1186/s12884-021-03875-6.

[19] Beltran AJ, Wu J, Laurent O. Associations of meteorology with adverse pregnancy outcomes: a systematic review of preeclampsia, preterm birth and birth weight. International Journal of Environmental Research and Public Health. 2014 Jan; 11(1): 91-172. doi: 10.3390/ijerph110100091.

[20] Sharma D, Shastri S, Sharma P. Intrauterine growth restriction: antenatal and postnatal aspects. Clinical medicine insights: Pediatrics. 2016 Jan; 10: CMPed-S40070. doi: 10.4137/CMPed.S40070.

[21] Ajah LO, Ozonu NC, Ezeonu PO, Lawani LO, Obuna JA, Onwe EO et al. The feto-maternal outcome of preeclampsia with severe features and eclampsia in Abakaliki, South-East Nigeria. Journal of clinical and diagnostic research: Journal of Clinical and Diagnostic Research. 2016 Sep; 10(9): QC18. doi: 10.7860/JCDR/2016/21078.8499.

[22] Oladapo OT, Adetoro OO, Ekele BA, Chama C, Etuk SJ, Aboyeji AP et al. When getting there is not enough: a nationwide cross-sectional study of 998 maternal deaths and 1451 near-misses in public tertiary hospitals in a low-income country. BJOG: An International Journal of Obstetrics & Gynaecology. 2016 May; 123(6): 928-38. doi: 10.1111/1471-0528.13450.

[23] Sharma V, Brown W, Kainuwa MA, Leight J, Nyqvist MB. High maternal mortality in Jigawa State, Northern Nigeria estimated using the sisterhood method. BMC Pregnancy and Childbirth. 2017 Dec; 17: 1-6. doi: 10.1186/s12884-017-1341-5.

[24] Sageer R, Kongnyuy E, Adebimpe WO, Omosehin O, Ogunsola EA, Sanni B et al. Causes and contributory factors of maternal mortality: evidence from maternal and perinatal death surveillance and response in Ogun state, Southwest Nigeria. BMC Pregnancy and Childbirth. 2019 Dec; 19: 1-8. doi: 10.1186/s12884-019-2202-1.

[25] Ugwa E, Ashimi A, Abubakar MY. Caesarean section and perinatal outcomes in a sub-urban tertiary hospital in North-West Nigeria. Nigerian Medical Journal. 2015 May; 56(3): 180-4. doi: 10.4103/0300-1652.160360.

[26] Falade-Fatila O and Adebayo AM. Male partners' involvement in pregnancy related care among married men in Ibadan, Nigeria. Reproductive Health. 2020 Dec; 17: 1-2. doi: 10.1186/s12978-020-0850-2.

[27] Mou AD, Barman Z, Hasan M, Miah R, Hafsa JM, Das Trisha A et al. Prevalence of preeclampsia and the associated risk factors among pregnant women in Bangladesh. Scientific Reports. 2021 Oct; 11(1): 21339. doi: 10.1038/s41598-021-00839-w.

[28] Sutan R, Aminuddin NA, Mahdy ZA. Prevalence, maternal characteristics, and birth outcomes of preeclampsia: A cross-sectional study in a single tertiary healthcare center in greater Kuala Lumpur Malaysia. Frontiers in Public Health. 2022 Oct; 10: 973271. doi: 10.3389/fpubh.2022.973271.

[29] Jeyabalan A. Epidemiology of preeclampsia: impact of obesity. Nutrition Reviews. 2013 Oct; 71(1): S18-25. doi: 10.1111/nure.12055.

Original Article

Pathological Pulmonary Manifestations in Chronic Kidney Disease Patients Undergoing Hemodialysis

Henna Khalid[1*], Mariam Riaz[1], Saba Shafiq[1], Sara Ali[1], Anwar Shahzad[2] and Raheela Bano[3]

[1]Department of Pathology, Women Medical and Dental Collage, Abbottabad, Pakistan
[2]Department of Community Medicine, Abbottabad International Medical College, Abbottabad, Pakistan
[3]Department of Pathology, Gomal Medical College, Dera Ismail Khan, Pakistan

ARTICLE INFO

ABSTRACT

Provenance of chronic kidney diseases is much more common in these days especially in patients suffering from secondary causes like diabetes mellitus and hypertension. **Objective:** To study the prevalence of pathological pulmonary manifestations in chronic kidney diseases patients. **Methods:** A descriptive cross-sectional study was done to examine the spectrum of pulmonary manifestations and any significant correlation with raised serum urea and creatinine level in patients on hemodialysis at various dialyzing units in Abbottabad for chronic kidney diseases. 200 patients with end-stage renal diseases were selected with convenience sampling for study with complaints of breathlessness, cough or chest discomfort. Evidence of pulmonary manifestations was gathered from histopathological and radiological reports records. **Results:** The most common findings in the acute phase of the patients were pneumonia 30% and 14% in males and females respectively. Pleural effusion was 20% prevalent in males while 6% in females. Empyema was 7% in males and 2% in females. Lung abscess and fibrosis was less common in patients suffering from chronic kidney disease. Spearmen rho results showed significant two tailed correlations between pulmonary manifestations and raised level of serum urea and creatinine levels. In most patients, co-morbidities such as diabetes mellitus and chronic hypertension, urolithiasis were evident as co-factors with significant raised urea and creatinine levels responsible for chronic kidney diseases. **Conclusions:** Pulmonary manifestations are common in patients on hemodialysis due to chronic kidney disease and strong correlation exists between raised serum urea and creatinine markers with pulmonary manifestations.

INTRODUCTION

Chronic renal failure commonly termed CKD is a pathological state in which glomerular structural derangements results in morphological and functional disruption of the whole kidney resulting in diminished GFR (Glomerular Filtration Rate) not less than or equal to 3 months. Globally estimated records suggest that about 10% population worldwide suffer from this fatal condition and deaths have been recorded in millions due to lack of inadequate treatment provided at time [1]. Pakistan has been ranked eight globally with a high rate of chronic kidney diseases, with almost 17 million people due to diagnosis at an advance stage, urolithiasis and secondary pathologies like diabetes mellitus and uncontrolled hypertension [2].

Initially it appears asymptomatic despite increased urea and creatinine concentration in serum. Symptoms usually appear at an advance in the form of decreased GFR and chronic anemia usually and untreated chronic kidney diseases results in kidney failure and renal dialysis become the mainstay of survival only [3]. Although hemodialysis improves the prognosis but it results in hemodynamic complications invading many systems of the body especially cardiovascular and respiratory system [4]. Organs in the thorax region are main targets of this fatal uremia, which can be diagnosed by histopathological and radiological techniques. Cardiovascular and pulmonary manifestations are more marked in complex format,

Khalid H et al.,

pulmonary manifestations most commonly encountered are pneumonia, pleural effusion, pleural infections, and fibrosis in later stages etc [5]. Pleural effusion and pulmonary edema account for the majority of pulmonary symptoms in hemodialysis patients with chronic kidney diseases. These conditions are diagnosed radiologically and confirmed by pathological examination using needle aspiration cytology [6]. These pathological manifestations are caused by excess fluid in the systemic vascular system, which leads to cardiac failure indirectly. In hemodialysis patients, uremia becomes the primary cause of pulmonary edema, which is typically caused by excess fluid volume with left ventricular failure. These manifestations can occur with or without superimposed bacterial infections [7]. The primary diagnostic and confirmatory tests are thorax imaging and fine needle aspiration cytology. These are readily available, reasonably priced, and non-invasive diagnostic procedures. These pathologies are usually detected on radiological examinations and confirmed on histopathological examination [8].

METHODS

It was cross sectional descriptive study on patients undergoing hemodialysis at various dialyzing units in Abbottabad. The study duration was 6 months starting from June 2023 and was conducted at the Pathology Department of Women Medical and Dental College Abbottabad. IRB approval was taken via letter no: WMC/PL/1018-2023, Dated: 10-05-2023. 200 patients with end-stage renal diseases were selected with convenience sampling for study with complaints of breathlessness, cough or chest discomfort. The sample size using Open Epi (https://www.openepi.com/SampleSize/SSPropor.htm) with an error margin of 5 % and a 95 % confidence interval. Evidence of pulmonary manifestations was gathered from histopathological and radiological reports records. Inclusion Criteria was patients suffering from chronic kidney diseases with pulmonary manifestations were included in the study. Exclusion Criteria was patients OF CKD with non-pulmonary manifestation and patients of CKD without pulmonary manifestation were not included in the study. The patient's spectrum of lung pathologies was recorded from histopathological reports and radiological findings. The data of histopathological and radiological reports was taken from medical records. SPSS version 24.0 was applied for statistical analysis. Descriptive statistics were applied for frequency measures and inferential statistics like spearmen rho correlations were applied for any significant correlation between raised urea and creatinine levels with co-morbidities and pulmonary manifestations in chronic kidney disease patients.

RESULTS

The results of the study consist of 200 patients on hemodialysis suffering from chronic kidney disease secondary to multiple causes. The table depicts that the majority of patients with CKD with pulmonary manifestations belonged to the age group range of 51-60 years. The results also showed that CKD was more common in the male population (55%). The majority of the population with CKD (52.5%) were of normal weight and only 2.5% of patients were obese. Recording BMI has been considered vital in this study due to its association with diseases like diabetes and hypertension. Body Mass Index (BMI) is a measure of weight versus height of individuals calculated by dividing the weight by height (m^2) and is characterized by different scales of measurement classified into 4 categories (Table 1).

Table 1: Frequency Distribution of CKD

Physiological/Biometric Index		N (%)
Age (Years)	30-40 Years	15 (7.5%)
	41-50 Years	45 (22.5%)
	51-60 Years	90 (45%)
	61-70 Years	40 (20%)
	>70 Years	10 (5%)
Gender	Male	110 (55%)
	Female	90 (45%)
BMI (Body Mass Index)	Under Weight	50 (25%)
	Normal Weight	105 (52.5%)
	Over weight	40 (20%)
	Obese Person	05 (2.5%)

The results shown in table 2 indicate the frequency/percentage of CKD with different physiological or biometric indices like age, gender, and BMI. Table 2 shows the frequency distribution of comorbid diseases seen in patients of CKD. Hypertension was the most common disease with diabetes as second most frequent co morbid disease seen in CKD patients on hemodialysis.

Table 2: Distribution of Comorbid Diseases among Patients

Co Morbid Diseases	N (%)
Hypertension	82 (41%)
Diabetes Mellitus	86 (43%)
Serum Lipids Level	62 (31%)
Urolithiasis	42 (21%)

Figure 1 demonstrates that pneumonia was the most common pulmonary manifestation and it was more common in males as compared to females. While non-specific findings were more marked in female individuals rather in males. Lung abscess prevalence was marked in males (72%) and females (28%), empyema (80%) and (20%) in males and females respectively. Pleural effusion (70%), and fibrosis (60%) were seen in males while in females it was 30% and 40 % respectively. Metastatic findings were

seen only in male individuals.
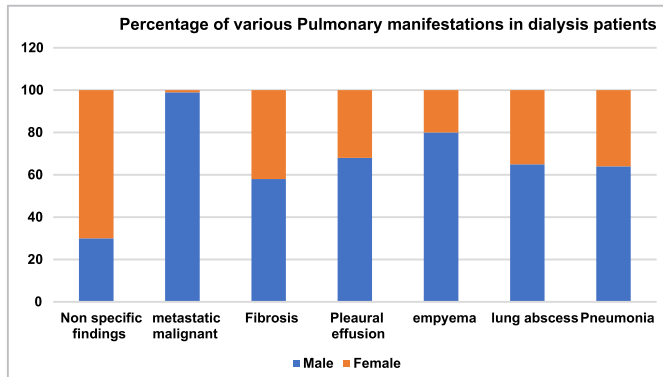
Figure 1: Frequency Distribution of Pulmonary Manifestations in Patients Suffering from Chronic Kidney Diseases on Hemodialysis

Table 3 shows the Spearman's rho Correlations results of the patients with pulmonary manifestations, co-morbidities suffering from chronic kidney disease. There is significant Sig. (2-tailed) correlation between raised levels of serum urea and creatinine of chronic kidney disease patients with severe pulmonary manifestations. Raised level serum urea and creatinine were also correlated with co-morbidities like high blood pressure and diabetes.

Table 3: Spearman's Rho Correlations Results of the Patients with Pulmonary Manifestations, Co-Morbidities Suffering from Chronic Kidney Disease.

Variables		Urea level mg/dl	Creatinine mg/dL	Pulmonary pathologies	Blood pressure	Blood sugar random
Urea Level mg/dl	Correlation Coefficient	10.00	0.50	0.46	0.46	10.00**
	Sig. (2-Tailed)	-	0.00	0.00	0.00	-
Creatinine mg/dL	Correlation Coefficient	0.59	-	0.21	0.21	0.59
	Sig. (2-Tailed)	0.00	-	0.01	0.01	0.00
Pulmonary Pathologies	Correlation Coefficient	0.46	0.21	10.00	10.00**	0.46
	Sig. (2-Tailed)	0.00	0.01	-	-	0.00
Blood Pressure	Correlation Coefficient	0.46	0.21	10.00**	10.00	0.46
	Sig. (2-Tailed)	0.00	0.01	-	-	0.00
Blood Sugar Random	Correlation Coefficient	10.00**	0.59	0.46	0.46	-
	Sig. (2-Tailed)	-	0.00	0.00	0.00	10.00

**. Correlation is significant at the 0.01 level (2-tailed).

DISCUSSION

Results of the study show that prevalence of pneumonia is much common in the patients on dialysis suffering from chronic kidney disease, study by Sise et al., found the similar results in which majority of patients suffering from chronic kidney disease on hemodialysis found pneumonia on histopathological examination, 61% whereas 39% do not [9]. Several co-morbidity factors contribute towards chronic kidney disease like diabetes mellitus, hypertension, urolithiasis and high serum lipids levels. Similar results have been found in studies conducted by Sorino et al., KN Mukhtar et al., and M Yigla et al., found that female patients suffer more with pulmonary manifestations than males, which is contradictory to our findings [10]. Various other studies also beckon our findings. Based on the study findings, 72% of females suffering from chronic kidney disease on hemodialysis have non-significant findings on histopathological examination while the non-significant percentage is lower in males in our study group which is the parallel study finding in a study done by Lee et al., the 43% of chronic kidney disease patients under hemodialysis have non-significant findings on hemodialysis [11]. CKD patients suffer with higher prevalence of pleural effusion than the general population due to fluid overload during the dialysis process and at a greater risk. Age, diabetes mellitus uncontrolled hypertension, deranged serum lipids, malnutrition, and urolithiasis. Study based results show that, 7 % suffer from empyema and 6% from lung fibrosis which is common in females than in males [12]. Study conducted by DJ Piersonet et al., and JA Herrero et al., show that 19 % of patients suffering from chronic kidney disease hemodialysis exhibit pulmonary fibrosis, whereas 81% do not, this assimilates with a study by Pradesya and Faesol in which findings on 69 subjects of chronic kidney disease on hemodialysis have histopathological findings and imaging techniques indicate similar results [13]. Study results, less than 1% of population showed malignant manifestation on histopathological findings counter confirmed by imaging techniques. Unilateral pleural effusion was 24% while 14% marked bilateral pleural effusion and 62% didn't indicate pleural effusion it is similar with the study conducted by Walter et al [14]. Study by Zhao et al., demonstrates that from 257 hemodialysis patients on long term only 50 patients suffered from pleural effusion, half of the patients suffered from unilateral and the rest half from bilateral pleural effusion [15]. Pleural effusion is recurrent in nature in CKD present with dyspnea, paroxysmal nocturnal dyspnea, and in some cases orthopnea. Pleural effusion is secondary to uremic pleuritis, overhydration, and bronchopulmonary bacterial infection. A study done by Nitin et al., found that transudative pleural effusion in CKD patients was commonly caused by cardiac failure whereas exudative effusions were due to tuberculosis [16]. There is a strong correlation between deranged pulmonary function tests and chronic kidney disease patients. This fact was supported by a study conducted by Anees et al., in which pulmonary functions were abnormal in almost half of the patients with CKD [17]. Many studies focused on the association of pulmonary hypertension with CKD patients

but in our research, we only assessed the pulmonary complications of our patients [18, 19]. Raised urea and creatinine always result in pulmonary edema and pulmonary effusion according to the study conducted by Borg et al. In our research, there is a significant two-tailed correlation with 0.00 which is found in one of the studies conducted by Zhou et al [20].

CONCLUSIONS

It can be concluded that patients on hemodialysis due to chronic kidney disease do have pulmonary manifestations especially pneumonia and pleural effusion and it is more common in males than females and in advanced ages particularly. There is a strong correlation between raised serum urea and creatinine markers with pulmonary manifestations in patients suffering from chronic kidney diseases especially having co-morbidities like hypertension and diabetes.

Authors Contribution

Conceptualization: HK
Methodology: HK, SA, AS
Formal analysis: MR, SS
Writing, review and editing: RB, AS, MR, SS

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

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

REFERENCES

[1]   Amin M, Fawzy A, Hamid MA, Elhendy A. Pulmonary hypertension in patients with chronic renal failure: role of parathyroid hormone and pulmonary artery calcifications. Chest. 2003 Dec; 124(6): 2093-7. doi: 10.1378/chest.124.6.2093.

[2]   Hasan AM, Alashkar AM, Esmael NF, Ibrahim AA. Assessment of pulmonary function in end stage renal disease patients on regular hemodialysis. The Egyptian Journal of Hospital Medicine. 2019 Jul; 76(1): 3319-23. doi: 10.21608/ejhm.2019.36895.

[3]   Babovic B, Djuranovic S, Mihaljevic O, Sakic K, Borovinic Bojovic J, Radoman Vujacic I et al. Dyspepsia in Montenegrin chronic kidney disease patients undergoing hemodialysis: endoscopic and histopathological features. International Urology and Nephrology. 2022 Aug; 54(8): 1891-7. doi: 10.1007/s11 255-021-03075-3.

[4]   Ferrey AJ, Choi G, Hanna RM, Chang Y, Tantisattamo E, Ivaturi K et al. A case of novel coronavirus disease 19 in a chronic hemodialysis patient presenting with gastroenteritis and developing severe pulmonary disease. American Journal of Nephrology. 2020 May; 51(5): 337-42. doi: 10.1159/000507417.

[5]   Gluhovschi G, Velciov S, Petrica LI, Gluhovschi CR. Aspects of renal-pulmonary pathogenic replationships in chronic kidney disease and chronic pulmonary diseases-a less-known connection. Romanian Journal of Internal Medicine. 2014 Apr; 52 (2): 68-77.

[6]   Kitamura M, Mochizuki Y, Miyata Y, Obata Y, Mitsunari K, Matsuo T et al. Pathological characteristics of periodontal disease in patients with chronic kidney disease and kidney transplantation. International Journal of Molecular Sciences. 2019 Jul; 20(14): 3413. doi: 10.3390/ijms20143413.

[7]   Pradhan RR and Sigdel MR. Prevalence, clinical presentation, and outcome of tuberculosis in patients with chronic kidney disease at a tertiary care hospital in Nepal. International Journal of Nephrology. 2020 Nov: 2020: 7401541. doi: 10.1155/2020/7401541.

[8]   Ren W, Pan H, Wang P, Lan L, Chen W, Wang Y et al. Clinical analysis of pulmonary infection in hemodialysis patients. Experimental and Therapeutic Medicine. 2014 Jun; 7(6): 1713-7. doi: 10.3892/etm.2014.1646.

[9]   Sise ME, Courtwright AM, Channick RN. Pulmonary hypertension in patients with chronic and end-stage kidney disease. Kidney International. 2013 Oct; 84(4): 682-92. doi: 10.1038/ki.2013.186.

[10]   Sorino C, Scichilone N, Pedone C, Negri S, Visca D, Spanevello A. When kidneys and lungs suffer together. Journal of Nephrology. 2019 Oct; 32: 699-707. doi: 10.1007/s40620-018-00563-1.

[11]   Utami SN, Uli HM, Septadina IS. Pathological Findings in Chest Radiographs of Chronic Kidney Disease Patients Undergoing Hemodialysis. Sriwijaya Journal of Medicine. 2021 Jan; 4(1): 38-45. doi: 10.32539/sjm.v 4i1.247.

[12]   Vikrant S. Clinical profile of tuberculosis in patients with chronic kidney disease: A report from an endemic Country. Saudi Journal of Kidney Diseases and Transplantation. 2019 Mar; 30(2): 470-7. doi: 10.41 03/1319-2442.256854.

[13]   Visconti L, Santoro D, Cernaro V, Buemi M, Lacquaniti A. Kidney-lung connections in acute and chronic diseases: current perspectives. Journal of Nephrology. 2016 Jun; 29: 341-8. doi: 10.1007/s40620 -016-0276-7.

[14]   Walther CP, Nambi V, Hanania NA, Navaneethan SD. Diagnosis and management of pulmonary

hypertension in patients with CKD. American Journal of Kidney Diseases. 2020 Jun; 75(6): 935-45. doi: 10.1053/j.ajkd.2019.12.005.

[15] Zhao LJ, Huang SM, Liang T, Tang H. Pulmonary hypertension and right ventricular dysfunction in hemodialysis patients. European Review for Medical and Pharmacological Sciences. 2014 Nov; 18(21): 3267-73.

[16] Nitin G, Patel R, Shet T, Patil A, Mahajan S. Study of Pleural Effusion in Chronic Kidney Disease. Journal of Medical Science And Clinical Research. 2019 May; 7(5): 10-8535. doi: 10.18535/jmscr/v7i5.62.

[17] Anees M, Akbar H, Ibrahim M, Saeed MS, Ismail M. Pulmonary functions and factors affecting them in patients with chronic kidney disease. Age (Years). 2020 Oct; 30(10): 1082-1085. doi: 10.29271/jcpsp.20 20.10.1082.

[18] Gaur J, Singh RK, Kulkarni C, Dube S. Assessment of pulmonary hypertension in chronic kidney disease patients using doppler echocardiography. Heart Views. 2023 Jan; 24(1): 24-8. doi: 10.4103/heartviews. heartviews_31_22.

[19] Mann A, Kampani G, Bansal S, Ranga S. Study of Pulmonary Arterial Hypertension in Patients of Chronic Kidney Disease Stage IV and V. Journal of the Association of Physicians of India. 2021 Oct; 69(10): 11-12.

[20] Zhou S, Liu X, Hu P, Liu H, Wang Y, Zhang L *et al*. Diverse CT findings of pulmonary infection in patients with kidney diseases under immunosuppressive therapy or on maintenance hemodialysis. Preprints. 2022 Aug; 1. doi: 10.20944/ preprints202208.0416.v1.

Original Article

Patient Satisfaction with Quality of Dentures at Teaching Hospital of Lahore

Khezran Qamar[1*], Syed Hammad Azeem Rizvi[1], Faiqua Yasser[2], Hira Aamir[3], Rana Ammar Ahmed[1], Maham Muzaffar[1] and Sajid Naeem[1]

[1]Department of Prosthodontics, Lahore Medical and Dental College, Lahore, Pakistan

[2]Department of Oral Pathology, Institute of Dentistry, Lahore Medical College, Combined Military Hospital, Lahore, Pakistan

[3]Department of Anatomy, Akhtar Saeed Medical and Dental College, Lahore, Pakistan

ARTICLE INFO

ABSTRACT

Complete dentures are fabricated to restore functional and esthetic needs of edentulous patients. Poor psychomotor abilities undermine their satisfaction level with well fabricated dentures and prosthodontic treatment becomes unsuccessful. **Objective:** To evaluate the patient's satisfaction level with newly inserted complete dentures fabricated by final year students and senior prosthodontists. **Methods:** The cross-sectional observational study population comprised of completely edentulous patients. The study conducted at Prosthodontic department of Lahore Medical and Dental College Lahore; from 8th June till 8th December 2023. A questionnaire was designed to assess parameters. Likert scale was used to answer; ranging from 1 to 5 where 1 is the poorest and 5 is the best value. Dentist, gender and previous experience were compared with patient satisfaction parameters. **Results:** Out of 62 complete denture patients; 72.6% had no denture wearing experience. 43.5% tooth loss was due to caries followed by periodontitis. Tooth loss in past 5 years' time was 61.3%. Denture aesthetics was rated as good 46.8%. Patient satisfaction parameters with age group and doctor group showed significant association. Correlation of patient satisfaction parameters with doctor group was statistically significant for mandibular denture speech, mandibular function and operator service p-value <0.05. **Conclusions:** Patient satisfaction with removable prosthesis determines the success of the prosthodontics intervention. Evaluation of patients' satisfaction level should be carried out routinely after the completion of the treatment as will help in the improvement of the work quality of a dental practitioner.

INTRODUCTION

Edentulism is a worldwide problem where patients lose all his teeth [1]. The rehabilitation of such patients is always challenging due to the involvement of functional and psychological factors that need to be restored through removable prosthesis [2]. The success of complete denture largely depends on two factors i.e. patients' acceptance to the new prosthesis and the denture quality. Certain patient related factors like age, gender, previous denture experience along with the operator related factors such as dentist expertise/experience and quality of newly fabricated dentures affect successful treatment [3]. Out of all the factors the dentist experience greatly affects the patient's satisfaction and acceptance of dentures [1, 3]. Dental literature has documented that 60 % patients accept their dentures after a week of insertion and 20% need at least 1 month for adaptation [1]. Few studies reported an inconclusive and insignificant correlation between patient satisfactions with dentures ad dentist experience [4]. According to few researchers besides providing high quality prosthesis by expert dentists patients satisfaction level with the provided prosthesis is low therefore it is difficult to assess the importance of experience in this field of dentistry [5]. At college of Dentistry Lahore Medical and Dental College Lahore supervised denture fabrication by final year BDS students is carried out every year. Each student is supposed to fabricate 2 dentures under the direct supervision of a qualified prosthodontist. Their clinical work involves

25

Qamar K et al.,

different steps of complete denture fabrication which they perform on their own. The concerned faculty member verifies weather the work has been done correctly and advices if any correction or retake needed. At the end of the rotation students are graded for their performance. For post operational complaints; a recall visit for every patient is planned after 1 week of denture insertion. The attributes of a well-constructed denture include excellent denture qualities like good retention, stability and support of both maxillary and mandibular dentures along with superior aesthetics and comfort [6, 7]. Besides having all the above mentioned qualities, the success of well fabricated complete denture is still assessed differently by prosthodontist and by the patients [8]. Some reports say that technically well fabricated dentures are not accepted by certain patients. Some excellent prosthesis treatments end up in failure due to patient related factors [9]. There is no documented method that can assess the successful denture treatment service. However, patient's satisfaction level could be as efficient way to check the clinical success of a denture [8]. Satisfaction results are also easily measurable and allow effective computation and direct patients opinion about prosthodontic treatment procedures [9].

The objective of the current study was to evaluate the patient's satisfaction level with newly inserted complete dentures fabricated by final year students and senior prosthodontists.

METHODS

This cross-sectional observational study population comprised of all the completely edentulous patients of both genders who reported to Prosthodontic Department of Lahore Medical and Dental College, Lahore from 8th June 2023 till 8th December 2023 in 6 months duration. The age ranged from 40 to 80 years. Non probability purposive sampling was used for sample selection. Sample size was calculated from a previous study done on factors affecting patient satisfaction with complete dentures [13]. The inclusion criteria were patients seeking new complete dentures for the first time or replacement of old complete dentures. Patient with last extraction of at least 3 months, without severe medical conditions e.g. neuromuscular disorder, mental condition and oral pathologies. All the patients who wore dentures for at least one month after denture construction and agreed to participate. Only those complete dentures made by final year dental students supervised by faculty, post graduates and senior faculty were included. Exclusion criteria included patients wearing complete dentures made elsewhere, patients wearing complete dentures for less than a month and those who refused to participate in the study. The selected patients after obtaining informed consent were comfortably seated in a dental chair. Questionnaire including 4 sections was

designed, i.e., personal information, assessment of denture with respect to aesthetics, speech, mastication and comfort. Likert scale was used to answer each section ranging from 1 to 5 where 1 is the poorest and 5 is the best value. Operator service was divided in to 2 groups, seniors with 5 years' minimum experience group 1 and students in group 2 under supervision of senior prosthodontists. Age was also divided in to 2 groups, less than 50 years and more than 50 years. Patients were given confidence and encouraged to give frank opinion about the newly inserted dentures. The questionnaire was explained and questions asked in their own mother tongue. Ethical clearance was obtained from Dental College Ethical Review Board. Patients' demographic information such as age, gender and prior denture use experience was registered. Dentist, gender and previous experience was compared with satisfaction. The data were entered and statistically analyzed using SPSS version 26.0. Descriptive statistics were computed. The Kruskal Wallis test was used to find out the association between patients' satisfaction with age groups and doctor groups. P-value <0.05 was kept as significant level. Pearson correlation between doctors' group and previous denture experience verses all parameters of patients' satisfaction was obtained; p- value <0.05 was the level of significance.

RESULTS

The studied sample included 62 complete denture patients where 29 (46.8%) were males and 33 (53.2%) were females, the age of the patients ranged from 40 to 77 years and mean age recorded was 60.40 ± 8.01 years. 18 (29.0%) patients were employed and 44 (71.0%) patients were unemployed. 17 (27.4%) had previous denture experience where majority patients had good denture experience 7 (11.3%) however poor denture experience was documented by 4 (6.5%) patients. 45 (72.6%) had no denture wearing experience. The main reason of tooth loss was caries 27 (43.5%) followed by periodontitis 24 (38.7%), trauma 7 (11.3%) and least frequent was patients with tooth loss due to other causes 4 (6.5%). Maximum patients lost teeth in past 5 years' time 38 (61.3%) and least number of patients lost their teeth for more than 10 years 6 (9.7%). Denture aesthetics was rated as good 29 (46.8%), very good 20 (32.3%), average 13 (21.0%), none has reported poor aesthetics 0 (0.00%). Maximum patients were satisfied with their dentures (Table 1).

Table 1: Frequency Distribution of Patient Satisfaction Levels with Denture Attributes (N=62)

Patient Satisfaction Level	Maxillary Denture Function N (%)	Maxillary Denture Speech N (%)	Mandibular Denture Function N (%)	Mandibular Denture Speech N (%)	Operator Service N (%)
Very Poor	2 (3.2%)	1 (1.6%)	6 (9.7%)	7 (11.3%)	0 (0.00)
Poor	2 (3.2%)	3 (4.8%)	4 (6.5%)	4 (6.5%)	2 (3.2%)
Acceptable	4 (6.5%)	4 (6.5%)	27 (43.5%)	40 (64.5%)	13 (21.0%)

Good	34 (58.8%)	31 (50.0%)	20 (32.3%)	3 (4.8%)	42 (67.7%)
Very Good	20 (32.3%)	23 (37.1%)	5 (8.1%)	8 (12.9%)	5 (8.1%)

Kruskal-Wallis test significance was calculated for patient satisfaction with age group and doctor group; statistically significant association of maxillary denture speech, mandibular denture function and speech and operator service within group of doctors was found p-value <0.05 (Table 2).

Table 2: Association of Denture Functions with Age and Group of Doctors (N=62)

Variables	Group of Doctors			Age Groups		
	Students (Mean Rank)	Seniors (Mean Rank)	p-value < 0.05	<50 years (Mean Rank)	>50 years (Mean Rank)	p-value < 0.05
Aesthetics	29.54	35.33	0.19	15.40	3.91	0.024
Maxillary Function	32.87	28.83	0.35	25.50	32.03	0.39
Maxillary Speech	28.38	37.60	0.04	24.00	32.16	0.28
Mandibular Function	24.07	46.00	0.00	28.70	31.75	0.70
Mandibular Speech	27.68	38.95	0.01	31.40	31.51	0.98
Operator Service	29.43	35.55	0.12	29.50	31.68	0.75

Correlation of patient satisfaction parameters with doctor group was statistically significant for mandibular denture speech p-value 0.06, mandibular function p-value 0.00 and operator service p-value 0.00. However statistically significant results were only found between denture wearing experience and mandibular denture speech p-value 0.01.

DISCUSSION

The current study was conducted on 62 completely edentulous patients who received removable complete dentures made by final year BDS students and senior prosthodontists. Level of patient satisfaction with newly inserted dentures was assessed. High satisfaction level was expressed by majority patients with respect to denture function, speech, aesthetics and operator's performance. These results are in concordance with the results of a study conducted by Waseem et al., in University of Gaza [10]. 92.1% patient satisfaction level was reported furthermore, upper denture was found superior to the lower one in all aspects of denture attributes. In contrast low satisfaction level was reported by Turker et al., in their research conducted on Turkish population [11]. Similarly, Al Essa et al., stated low satisfaction level with removable dentures in their respective study [12]. Yara et al., evaluated patient satisfaction with denture 8 weeks after denture insertion [13]. They stated that 6 to 8 weeks is a required time period to assess satisfaction level with newly installed dentures. The time potentially establish new masticatory muscle memory. The reason for high satisfaction level in the current study could be explained on the basis that the service cost of prosthodontic treatment was very low that

skewed patients level of satisfaction positively. Secondly, prosthodontic faculty mentored the denture fabrication process meticulously. Lastly the edentulous patients considered the loss of natural teeth as a result of aging process and they did not expect much from the complete dentures. All these factors eventually raised their satisfaction levels. Majority patients also rated operator performance good that created a good patient doctor repute. In our opinion all the mentioned factors positively affected the satisfaction levels. In the current study 50.0 % patients rated quality of maxillary denture speech as good whereas 64.5% found mandibular denture speech acceptable. Similarly, Bhatt et al., assessed phonetics in patients using removable prosthesis and reported complains of speech impairment during denture adaption period [14]. They further claimed that the patient's speech gradually improves with practice and persistent denture use. In the present study maximum patients reported good masticatory performance with maxillary denture 54.8%. Similarly, with respect to good speech majority patients reported maxillary denture to be better than mandibular. Only 1.6% patients reported bad phonetics. Likewise, Waseem et al., reported better satisfaction levels with maxillary dentures [10]. Congruent results were seen in other studies as well [15-18]. In contrast a smaller number of patients were happy with masticatory function in a study done by Vinaya et al., [19]. Motivation by patient can overcome this tissue dependent factor efficiently. The denture chewing ability with mandible denture was considered acceptable by majority patients; 43.5%. Yara et al., found dissatisfaction with mandibular dentures [13]. Their patients registered decrease retention, stability and mastication of mandibular denture. Many patients complained of food lodgment under dentures and rest could not function. We believe that better satisfaction results were attributed because of less tongue interference with maxillary denture. Furthermore, large denture bearing area and better seal due to post dam area are additional factors for better performance of maxillary dentures [20]. Whereas, in contrast mandible provides poor control of denture because of the factors like forces via tongue movement, increase ridge resorption and less denture bearing surfaces [18, 19, 21]. All mentioned factors result in poor denture retention and stability. Denture stability and retention improves and affected by impression taking skills of dentist. However, few studies compared psychological factors like good patient dentist relation and patient expectation with denture outcome are more important than technical, clinical and anatomical factors [22]. This was seen in results of current study where denture fabricated by seniors were more acceptable as compared to junior doctors. Maxillary and mandibular denture speech, function and operator service was all

27

significantly good in senior doctor group. However, contrasting results were found in a study stating fact that high expectation of patients from senior altered the satisfaction level negatively [13]   Yara et al., found that no correlation between dentist experience and patient satisfaction existed [13]. However, majority were happy with their prosthesis made by junior and claimed that was difficult to investigate the importance of experience in prosthodontics. Maximum patients had good previous denture experience. However, majority patients; 72.6% were getting their prosthesis for very first time. Patients who had good previous denture experience were highly satisfied. Similar results were obtained by Waseem et al., in their respective study and good adaptation was seen [10]. Mandibular denture speech was significantly good in patient with previous denture experience in our study. Similarly, 46.8% patients in the current study were satisfied with their denture aesthetics. Color of artificial dentition as well as denture bases are major contributing factors responsible for achieving acceptable aesthetics. Patient satisfaction level is directly related to denture aesthetics [19, 20]. Nausea speech difficulty, sense of having foreign body, increase salivary flow difficult chewing swallowing and frequent complaints of patients during denture adaptation [23]. When dentures do not match patients' expectation, they refuse to use. It is important to evaluate patient satisfaction in routine prosthodontic practice that will help in improvement of the quality of services provided.

CONCLUSIONS

Patient satisfaction with removable prosthesis determines the success of the prosthodontic intervention. Evaluation of patients' satisfaction level should be carried out routinely after the completion of the treatment as will help in the improvement of the work quality of a dental practitioner.

Authors Contribution

Conceptualization: MM
Methodology: SHAR, RAA, HA
Formal analysis: FY, SN
Writing, review and editing: KQ, SN

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

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

REFERENCES

[1]   Parel S. Removable and Fixed Fully Edentulous Treatment Options for the Aging Patient. Compendium of Continuing Education in Dentistry. 2018 Jul; 39(7): 448-53.

[2]   McCunniff M, Liu W, Dawson D, Marchini L. Patients' esthetic expectations and satisfaction with complete dentures. The Journal of Prosthetic Dentistry. 2017 Aug; 118(2): 159-65. doi: 10.1016/j.prosdent.2016.10.015.

[3]   Barazanchi A, Pande N, Park J, Hong CL. Patient satisfaction levels for complete dentures (F/F) delivered by undergraduate dental students. International Islamic University Malaysia Journal of Orofacial and Health Sciences. 2023 Feb; 4(1): 33-46. doi: 10.31436/ijohs.v4i1.202.

[4]   Iftikhar J, Saleem MN, Awais F, Naz A, Tuasene A, Saleem Z et al. Frequency and causes of fracture of acrylic resin complete dentures in edentulous patients. Pakistan Journal of Medical & Health Sciences. 2022 Aug; 16(07): 160. doi: 10.53350/pjmhs 22167160.

[5]   Dhaded S, Kumar SM, Kaur M, Hegde P. Effect of physical and psychological status on oral health quality of life of geriatric patients undergoing complete denture treatment. The Journal of Indian Prosthodontic Society. 2022 Jul; 22(3): 262-7. doi: 10.4103/jips.jips_162_22.

[6]   Choudhary S, Kumar A, Arora H. Effect of age, gender, and mental attitude on complete denture satisfaction in north Indian population. Journal of Contemporary Dentistry. 2019 Jan; 9(1): 8-12. doi: 10.5005/jp-journals-10031-1245.

[7]   Sghaireen MG and Al-Omiri MK. Relationship between impact of maxillary anterior fixed prosthodontic rehabilitation on daily living, satisfaction, and personality profiles. The Journal of Prosthetic Dentistry. 2016 Feb; 115(2): 170-6. doi: 10.1016/j.prosd ent.2015.07.009.

[8]   Wafa'a R, Swelem AA, Abdelnabi MH, Mofadhal A. Effect on patient satisfaction of mandibular denture tooth arrangement in the neutral zone. The Journal of Prosthetic Dentistry. 2019 Mar; 121(3): 440-6. doi: 10.1016/j.prosdent.2018.06.020.

[9]   Abu-Awwad M, Ereifej N, Al-Hattab M, Baker DA, Petridis H. Impact of adding palatal rugae to complete dentures on patient satisfaction and oral health-related quality of life: a randomized crossover clinical trial. The Journal of Prosthetic Dentistry. 2021 Nov; 126(5): 646-52. doi: 10.1016/j.prosdent.202 0.09.002.

[10] Mushtaha W, Harb HA, Elhout W, Seyam A. Patient Satisfaction with Complete Denture Prosthesis Made By Clinical Year Students at the Faculty of Dentistry, Al Azhar University-Gaza. International Journal of Academic Health and Medical Research (IJAHMR). 2020 Oct; 4(10):1-6.

[11] Turker SB, Sener ID, Özkan YK. Satisfaction of the complete denture wearers related to various factors. Archives of Gerontology and Geriatrics. 2009 Sep; 49(2): e126-9. doi: 10.1016/j.archger.2008.11.003.

[12] Al Essa HA. A study to evaluate the satisfaction level in conventional complete dentures patients after reducing the vertical dimension of occlusion. International Journal of Applied Dental Sciences. 2019 Sep; 5: 25-8.

[13] Oweis Y, Ereifej N, Al-Asmar A, Nedal A. Factors affecting patient satisfaction with complete dentures. International Journal of Dentistry. 2022 Apr; 2022. doi: 10.1155/2022/9565320.

[14] Bhat JT, Kumar N, Singh K, Tanvir H. Phonetics in prosthodontics: its clinical implications in designing of prosthesis. International Journal of Applied Dental Sciences. 2021 Mar; 7(2): 84-93. doi: 10.22271/oral.2021.v7.i2b.1193.

[15] Sharma A, Singh R, Sharma R, Dhanda A, Neha TV. Post insertion problems in complete denture: A review. IP Annals of Prosthodontics and Restorative Dentistry. 2020 Dec; 6: 189-93. doi: 10.18231/j.aprd.2020.040.

[16] De Lucena SC, Gomes SG, Da Silva WJ, Del Bel Cury AA. Patients' satisfaction and functional assessment of existing complete dentures: correlation with objective masticatory function. Journal of Oral Rehabilitation. 2011 Jun; 38(6): 440-6. doi: 10.1111/j.1365-2842.2010.02174.x.

[17] Limpuangthip N, Somkotra T, Arksornnukit M. Impacts of denture retention and stability on oral health-related quality of life, general health, and happiness in elderly Thais. Current Gerontology and Geriatrics Research. 2019 Jul; 2019. doi: 10.1155/2019/3830267.

[18] Kumari S, Khushboo B, Arvind A, Singh S, Ahsan A, Singh CK *et al.* Assessment of role of complete dentures in improving the chewing efficiency of edentulous patients. Journal of Pharmacy and Bioallied Sciences. 2022 Jul; 14(1): S792-5. doi: 10.4103/jpbs.jpbs_187_22.

[19] Bhat VS and Malli P. A survey to assess patient satisfaction after receiving complete denture prostheses in AB Shetty Memorial Institute of Dental Sciences. Journal of Health and Allied Sciences Nu. 2014 Jun; 4(02): 081-5. doi: 10.1055/s-0040-1703768.

[20] Mishra S, Krishna R, Mandokar RB, Agarwal S, Sharma A, Shaw M *et al.* A comparative clinical trial for evaluating the posterior palatal seal developed from the conventional method and a novel functional swallow method. The Journal of Indian Prosthodontic Society. 2022 Jan; 22(1): 21-8. doi: 10.4103/jips.jips_235_21.

[21] Kaur R, Kumar M, Jindal N, Badaka. Residual ridge resorption revisited. Dental Journal of Advance Studies. 2017 Aug; 05(02): 076-080.

[22] Seenivasan M, Banu F, Inbarajan A, Natarajan P, Natarajan S, Karthigeyan J *et al.* The consequence of complete dentures on quality of life of edentulous patients in the south-Indian population based on educational and socioeconomic grades. Cureus. 2020 Feb; 12(2): e6923. doi: 10.7759/cureus.6923.

[23] Hassan H, Rafique A, Andleeb S, Javaid M, Ahmad H, Khalid S. Post-insertion complaints associated with complete denture prosthesis in a tertiary care hospital. Rawal Medical Journal. 2023 Mar; 48(1): 200.

Original Article

Photographic Analysis of Facial Soft Tissue by Angular and Proportional Measurements in Adult Pakistani Population

Anum Aziz[1*], Qasim Khalid[2], Muhammad Fayyaz Nafees[3], Saadia Ata[4], Kashif Haroon[5] and Nida Habib[5]

[1]Department of Orthodontics, Avicenna Dental College, Lahore, Pakistan
[2]Department of Orthodontics, Combined Military Hospitals, Medical and Dental College, Institude of Dentistry, Lahore, Pakistan
[3]Department of Orthodontics, Rashid Latif Medical and Dental College, Lahore, Pakistan
[4]Department of Orthodontics, Akhtar Saeed Medical and Dental College, Lahore, Pakistan
[5]Department of Orthodontics, Azra Naheed College of Medicine and Dentistry, Lahore, Pakistan

ARTICLE INFO

ABSTRACT

An important requisite of orthodontic treatment is achieving well balanced, pleasant face. Precise diagnosis and treatment planning, on facial hard and soft tissue norms basis, is fundamental for that purpose. **Objective:** To use photogrammetry technique on standardized photographs, and determination of mean angular and proportional parameters defining characteristics of facial soft tissue, on an adult Pakistani population. **Methods:** A cross sectional study, on 78 subjects from OPD and students of FMH College of Medicine and Dentistry, were selected. Data were entered and SPSS 2.0 was used for analysis. Mean and standard deviations were used for the quantitate variables used in the study. To control confounders with respect to age and gender, stratification was done and independent t-test was used, taking statistically significant p-value at ≤ 0.05. **Results:** All parameters were statistically insignificant on the basis of gender and age. The average values of nasolabial angle, angle of facial convexity and facial height proportion were greater in males than in females. The mean values of mentolabial angle, lower face to total face height and facial index were found to be greater in females as compared to males. **Conclusions:** This study concluded that gender and age based average values for angular and proportional parameters should be used while planning cases for Pakistani population for orthodontic treatment.

INTRODUCTION

The word Orthodontic, derivated of Greek word 'orthos', means "to straighten" and 'dontos' meaning "teeth" [1-13]. This field of dentistry deals with the correction of anomalies of jaws and dentition. Malocclusions has high prevalence and its consequences are unsatisfactory, physically and socially [2-16]. This impairs the quality of an individual's life and alters appearance and functions [2-17]. The aim of an orthodontist is hence correction of skeletal and soft tissue disharmonies and in addition to that of teeth, during diagnosis treatment planning [3-11]. For the purpose of evaluating an orthodontic case thoroughly, photogrammetry is being used worldwide consistently [4-15]. Photogrammetry serves as an alternative to directly measuring patients in clinical settings, enabling the determination of distances and angles between facial landmarks through both 2D and 3D approaches [4-19]. Extracting measurements from photographs offers operators greater convenience, minimizes patient intrusion, and proves to be more time and cost-effective [4]. Apart from its various uses, its extensive usage in the field of orthodontics enables to develop the standard normal values for skeleton, soft tissue and dentition [4-12]. From researches done on different populations, the average values have been obtained. The measurement-

Aziz A et al.,

based assessment of facial soft tissue dimensions and contours is extensively utilized across diverse medical fields, including Orthodontics [4]. Facial appearance is dependent on many factors; sex, age and ethnicity, to name the few, hence, it is obvious to conclude that what is considered to be attractive as the norm for one culture, may not be so for another [4-11]. Therefore, it is impertinent that for different populations, different standards norms should exist.

The objective of this study was to create average angular and proportional photogrammetry norms of adult Pakistani population, further aiding diagnosis, planning treatment and favorable outcomes of esthetics and stability at commencement of treatment, due to limited local literature and the variability of these parameters amongst different populations.

METHODS

The research carried out was descriptive cross- sectional, and 78 subjects were piloted, calculated at 5% level of significance and 1% margin of error and by taking expected mean of facial index as 84.58 ± 4.48, using 95% confidence level, at 5% level of significance in Department of Orthodontics, Fatima Memorial Hospital College of Medicine and Dentistry Lahore. The duration of this research was 1.5 years, from January, 2020 till June, 2021. IRB department of FMH College of Medicine & Dentistry permitted this research concept in December, 2019 (IRB Letter: FMH-12-2019-IRB-698-M), demographic data were recorded and informed consent was taken from all participants. Non-probability consecutive sampling technique was used. Subjects reporting in dental OPD of FMH, should be a Pakistani descent, with age bracket of 15-35 years, with developed dentition and straight well balanced facial profile, having class I occlusion pattern, with minimal or no crowding of teeth, were included in the study, under inclusion criteria. The set-up for photographs comprised of a tripod, holding a camera (DSLR, Nikon D7200) with flash. Facial photos were taken from frontal and profile aspects with standard method of all subjects, in neutral head position. All photographs were printed and labelled, and calculations were drawn on them. Photographic variables were logged in a precisely made proforma. All the data collected was then entered and analyzed in SPSS version 20 computer program. Variables that were quantifiable; age, angle of facial convexity (G-Sn-Pg), nasolabial angle (NLA), facial height proportions (MFH ÷ LFH and LFH ÷ TFH), facial index (facial height ÷ width × 100) and Mento-Labial Angle (MLA) were exhibited as mean and standard deviation. Frequency and percentages were used for qualitative data i.e. gender. In reference to age and gender; stratification was done to control confounders and "t" test was applied. 0.05 or less was appointed for P-value to be significant statistically.

RESULTS

A 78 subjects with straight profile and class 1 skeletal pattern were part of the research. As evident from table 1, the median age; 24.48 ± 5.38 years was observed, of which 43 (55.1%) were women and 35 men (44.9%). In addition, statistically insignificant differences were present in all age brackets, across all variables table 1.

Table 1: Angular and Proportional Calculations from Age Groups Perspective

Variables		Age Groups (Years)				p-Value
		15-19	20-24	25-29	30-35	
(Mean ± SD)						-
Angular Variables	Nasolabial Angle	100.65 ± 8.86	102.35 ± 8.41	99.05 ± 10.36	99.18 ± 4.97	0.638
	Mentolabial Angle	127.52 ± 9.75	127.17 ± 10.50	127.33 ± 12.06	129.45 ± 13.40	0.899
	Angle of Facial Convexity	168.91 ± 5.91	167.83 ± 5.49	169.81 ± 4.25	172.64 ± 4.86	0.092
Proportional Variables	Lower Face-Total Face Height	53.91 ± 5.06	53.87 ± 2.26	53.90 ± 3.30	54.97 ± 6.23	0.909
	Facial Index	86.26 ± 5.01	87.96 ± 4.49	87.81 ± 4.67	88.55 ± 2.20	0.524
	Facial Height Proportion	1.18 ± 0.04	1.15 ± 0.13	1.15 ± 0.10	1.18 ± 0.10	0.449

Similarly, as seen from table 2, sexual dimorphism was found in all parameters, including NLA (nasolabial angle), MLA (mentolabial angle), and G-Sn-Pg (angle of facial convexity), LFH ÷ TFH (lower face height to total face height), facial height ÷ width × 100 (facial index), and MFH ÷ LFH (facial height proportion).

Table 2: Angular and Proportional Calculations from Gender Perspective

Variables		Gender		p-Value
		Males	Females	
		Mean ± SD		
Angular Variables	Nasolabial Angle	100.97 ± 8.05	100.14 ± 9.26	0.888
	Mentolabial Angle	125.94 ± 11.52	129.02 ± 10.43	0.178
	Angle of Facial Convexity	169.91 ± 5.41	168.91 ± 5.34	0416
Proportional Variables	Lower Face-Total Face Height	53.79 ± 3.96	54.26 ± 4.23	0.358
	Facial Index	86.77 ± 5.28	88.09 ± 3.63	0.133
	Facial Height Proportion	1.17 ± 0.08	1.16 ± 0.11	0.964

The NLA (nasolabial angle) and G-Sn-Pg (angle of facial convexity) showed higher values in mem as compared to women on average angular measurements Table- 2. However, MLA (mentolabial angle) was larger in females versus male's table- 2. Typically, lower face height to total face height (LFH ÷ TFH) and Facial index (height ÷ width × 100) calculations were found to be greater in female's. Facial height proportion on the other hand was smaller in females versus male's (Table 2).

DISCUSSION

Pandian KS et al., studied angular photogrammetric analysis of Indian adults and showed in their study, that NLA (Nasolabial Angle) and MLA (Mentolabial Angle) showed significant statistical differences, based on gender, and these angles exhibited significant diversity in maximum and minimum values in both genders. The NLA and MLA were more acute from statistical standpoint in females versus males [9]. Our study revealed in comparison, all angular measurements including NLA and MLA, to be statistically insignificant, on both gender and age basis. In 2019, Akter L et al., studied facial profile analysis of soft tissue of young Bangladeshi adults and proposed that average angular measurement for MLA were broader in women. The average estimates for NLA was higher in males. Statistically significant difference was displaced for mentolabial angle. Highest variability for MLA was evident [10]. Contrarily, the average angular and proportional values in our study for NLA were larger in males (100.97 ± 8.053 vs 100.14 ± 9.267). Whereas, MLA had higher values in women than in men (129.02 ± 10.43 vs 125.94 ± 11.52). Imtiaz A et al., in 2022, studied facial profile convexity and found gender dimorphism with higher average value of G-Sn-Pg (angle of facial convexity), i.e.; 23.22 ± 7.61 in women [20]. On the other hand, in our study G-Sn-Pg, was more acute in women (169.91 ± 5.41 vs 168.91 ± 5.34). In 2022, Rao SJ et al., researched soft tissue treatment goals for orthodontic patients- a photogrammetric analysis of facial profile for soft tissue norms and gender variations in young adults, Hyderabad [21]. They found significant sexual dimorphism in the angular measurements including (angle of facial convexity; women-173.2° ± 4.4°, men-169.6° ± 54.8°). In their study, NLA (Nasolabial, p-value=0.314), and MLA (Mentolabial, p-value=0.798) angles showed remarkable variability. In contrast our research yielded, all angular and proportional measurements to be statistically insignificant, on both gender and age basis. Kır İrem et al., in 2024, evaluated facial aesthetics in young-adult Turkish society and found Facial height ÷ width× 100 (facial index) and G-Sn-Pg (angle of facial convexity) to be showing a larger value in women from statistical point of view, whereas, height proportions were lower [22]. In our research, however, lower face height to total face height (LFH ÷ TFH)(males= 53.79 ± 3.96, female= 54.26 ± 4.23) and Facial index (height ÷ width × 100) were found to be greater in females (males= 86.77 ± 5.28, females= 88.09 ± 3.63). Facial height proportion (MFH ÷ LFH) on the other hand was smaller in females (males= 1.17± 0.08, females= 1.16 ± 0.11). As depicted by these variations in different researches, average values must always be applied for the specific demographic group. The results are anticipated to offer substantial objective databank, which will further help in diagnosing and for case planning for best pretreatment and postoperative results.

CONCLUSIONS

Angle of facial convexity, Nasolabial angle, Lower face to total facial height proportion, Mentolabial angle, Facial height proportion, and Facial index, displayed no sexual dimorphism. Age distribution did not yield significant differences across all parameters. The means of Facial height proportion, Nasolabial angle and Angle of facial convexity were found to be higher in men. The mean values of Facial Index, Mentolabial angle and Lower face to total face height, displayed higher estimates in women than in men.

Authors Contribution

Conceptualization: AZ
Methodology: MFN
Formal analysis: MFN, SA, KH
Writing, review and editing: QK, NH

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

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

REFERENCES

[1] Hassan AH and Amin HE. Association of orthodontic treatment needs and oral health-related quality of life in young adults. American Journal of Orthodontics and Dentofacial Orthopedics. 2010 Jan; 137(1): 42-7. doi: 10.1016/j.ajodo.2008.02.024.

[2] Morosini ID, Peron AP, Correia KR, Moresca R. Study of face pleasantness using facial analysis in standardized frontal photographs. Dental Press Journal of Orthodontics. 2012 Oct; 17(5): 24-34. doi: 10.1590/S2176-94512012000500005.

[3] Profit WR, Fields HW, Larson BE, Sarver DM. Contemporary Orthodontics 6th Edition. St Louis: Mosby Elsevier. 2018.

[4] Moshkelgosha V, Fathinejad S, Pakizeh Z, Shamsa M, Golkari A. Photographic facial soft tissue analysis by means of linear and angular measurements in an adolescent persian population. The Open Dentistry Journal. 2015 Jul; 9: 346. doi: 10.2174/1874210601509010346.

[5] Menéndez López-Mateos ML, Carreño-Carreño J, Palma JC, Alarcón JA, Menéndez López-Mateos C, Menéndez-Núñez M et al. Three-dimensional photographic analysis of the face in European adults

from southern Spain with normal occlusion: reference anthropometric measurements. BMC Oral Health. 2019 Dec; 19: 1–8. doi: 10.1186/s12903-019-0898-y.

[6] Navic P, Palee P, Prapayasatok S, Prasitwattanaseree S, Sinthubua A, Mahakkanukrauh P *et al.* The development and testing of Thai facial soft tissue thickness data in three-dimensional computerized forensic facial reconstruction. Medicine, Science and the Law. 2022 Apr; 62(2): 113–23. doi: 10.1177/00258024211057689.

[7] Lepi JM and Norman NH. Evolution of facial profile and soft tissue methods of orthodontic assessments: A narrative review. Journal of International Oral Health. 2022 May; 14(3): 215–21. doi: 10.4103/jioh.jioh_302_21.

[8] Ajami S, Javidi A, Salehi P, Malekpou B. Proportional and Angular Photogrammetric Analysis of the Soft Tissue Facial Frontal View of Young Adults in Shiraz, Iran. Journal of Dentomaxillofacial. 2017 Jul; 6(2): 22–9. doi: 10.17795/ijo.4981.

[9] Pandian KS, Krishnan S, Kumar SA. Angular photogrammetric analysis of the soft-tissue facial profile of Indian adults. Indian Journal of Dental Research. 2018 Mar; 29(2): 137–43. doi: 10.4103/ijdr.IJDR_496_16.

[10] Akter L and Hossain M. Angular photogrammetric soft tissue facial profile analysis of Bangladeshi young adults. APOS Trends in Orthodontics. 2017 Nov; 7(6): 279. doi: 10.4103/2321-1407.219434.

[11] Riaz A, Ashraf A, Ramzan S, Kadir S, Ashraf F, Iqbal N. Comparison of Angular Measurements in Cephalometric And Photographs. Journal of Allama Iqbal Medical College. 2023 Oct; 21(3): 174–178. doi: 10.59058/jaimc.v21i3.114.

[12] Mortada AA, Burhan AS, Hajeer MY, Nawaya FR, Sahtout GF, Hajeer MY *et al.* Do the Most Attractive Faces of Patients with Class II Division 1 Malocclusion Differ from Those with the Least Attractive Faces in Terms of Angular and Proportional Measurements Assessed on Frontal and Lateral Photographs? Cureus. 2023 Jan; 15(1): e33455. doi: 10.7759/cureus.33455.

[13] Guimarães A, Lacerda-Santos R, Braga E. Does the aesthetic perception of protrusion correction change if the face is evaluated from the frontal or profile perspectives? Research, Society and Development. 2023 Apr; 12(4): e20712441195-. doi: 10.33448/rsd-v12i4.41195.

[14] Pedersoli L, Dalessandri D, Tonni I, Bindi M, Isola G, Oliva B *et al.* Facial asymmetry detected with 3D methods in orthodontics: a systematic review. The Open Dentistry Journal. 2022 Apr; 16(2). doi: 10.2174/18742106-v16-e2111251.

[15] Bayome M, Park JH, Shoaib AM, Lee NK, Boettner V, Kook YA *et al.* Comparison of facial esthetic standards between Latin American and Asian populations using 3D stereophotogrammetric analysis. Journal of the World Federation of Orthodontists. 2020 Sep; 9(3): 129–36. doi: 10.1016/j.ejwf.2020.06.003.

[16] Shaadouh RI, Hajeer MY, Burhan AS, Ajaj MA, Jaber ST, Zakaria AS *et al.* Evaluation of the Impact of Orthodontic Treatment on Patients' Self-Esteem: A Systematic Review. Cureus. 2023 Oct; 15(10): e48064. doi: 10.7759/cureus.48064.

[17] Mandava P, Singaraju GS, Obili S, Nettam V, Vatturu S, Erugu S *et al.* Impact of self-esteem on the relationship between orthodontic treatment and the oral health-related quality of life in patients after orthodontic treatment-a systematic review. Medicine and Pharmacy Reports. 2021 Apr; 94(2): 158. doi: 10.15386/mpr-1843.

[18] Parveen M, Muralidhar NV, Kiran J, Raghunath N. Photogrammetry Versus Cephalometric Analysis in Orthodontic Diagnosis and Treatment Planning. 2022 May. doi: 10.21203/rs.3.rs-1571230/v1.

[19] Pojda D, Tomaka AA, Luchowski L, Tarnawski M. Integration and application of multimodal measurement techniques: relevance of photogrammetry to orthodontics. Sensors. 2021 Dec; 21(23): 8026. doi: 10.3390/s21238026.

[20] Imtiaz A and Qamar R. Facial Profile Convexity in Skeletal Class II Malocclusion: How Soft Tissue Angle of Facial Convexity (SA-FC) Correlate with Angle ANB in Skeletal Class II Subjects. Journal of the Pakistan Dental Association. 2022 Apr; 31(2). doi: 10.25301/JPDA.312.86.

[21] Rao SJ and Valapula S. Soft Tissue Treatment Goals for Orthodontic Patients-A Photogrammetric Analysis of Facial Profile for Soft Tissue Norms and Gender Variations in Young Adults, Hyderabad, India. Journal of Clinical & Diagnostic Research. 2022 May; 16(5): 10. doi: 10.7860/JCDR/2022/55518.16362.

[22] Kır, İrem & Cicek, Orhan & Özkalaycı, Nurhat. Evaluation of facial aesthetics in young-adult Turkish society. Acta Odontologica Turcica. 2024 Jan, 41(1): 25–34. doi: 10.17214/gaziaot.1242198.

Original Article

The Knowledge, Attitude and Practice of Nurses, Technicians and Sanitary Workers Regarding Biomedical Waste Management at Healthcare Establishments of Dera Ismail Khan, Pakistan

Samina Qadir[1*], Rahila Bano[2], Anil Iqbal[1], Muhammad Saddozai[3], Maira Gul[3], Muhammad Younis[3], Fatima Dastageer[3], Muhammad Mussab[3] and Maheen Noor[3]

[1]Department of Community Medicine, Gomal Medical College, Dera Ismail Khan, Pakistan
[2]Department of Pathology, Gomal Medical College, Dera Ismail Khan, Pakistan
[3]Gomal Medical College, Dera Ismail Khan, Pakistan

ARTICLE INFO

ABSTRACT

Risk waste generated in hospitals can cause some serious health and environment related problems, if not disposed properly. **Objective:** To assess the knowledge, attitude and practice of healthcare workers regarding Biomedical Waste (BMW) management and to find out any significant difference across different sociodemographic variables. **Methods:** This was a cross sectional study conducted from 20th February to 20th August 2023. Sampling technique was consecutive non probability with a sample size of 287. Research variables were knowledge, attitude and practice. T-test and One-way ANOVA test were used to show statistically significant difference between research variables across demographic variables at p-value of ≤ 0.05. **Results:** 287 health care workers participated in this study. Around 84% nurses, 78% technicians and 64% sanitary worker have good knowledge about BMW management. Remaining participants had fair knowledge and none of the health care workers in any category had poor knowledge about BMW. 83% of the total participants from all three categories of workers had a good attitude regarding BMW management whereas around 16.7% participants had a fair attitude while 0.3% had a poor attitude. However, only 1% had good practices while 62% had poor practice and the remaining 37% participants had fair practice. It was found there was a statistically significant association of the category of workers with knowledge. **Conclusions:** The healthcare workers have good knowledge and attitude regarding BMW disposal but the practice was either fair or poor.

INTRODUCTION

Biomedical Waste (BMW) means any waste which is generated during diagnosis, treatment and immunization of human beings or animals or in a research activity pertaining there to or in the production or testing of biologicals [1]. BMW is a collective term used for all waste generated in different healthcare establishments [2]. Waste management is various measures taken in generation, segregation, collection, storage, transportation to final disposal of BMW to ensure safety of exposed humans and environment [3]. BMW is classified into risk waste and non-risk waste. Approximately 75-90% waste generated from healthcare establishments is non risk waste and 10-25% waste is risk waste. Health care staff, visitors to health care establishments, support staff, scavengers, community in general and its environment all are at risk of getting exposure to sharps, infectious, corrosive, toxic, inflammable, genotoxic and radioactive waste [1]. Globally almost every country produces BMW at an average of 0.5 to 3 kg/bed/day [4]. In Pakistan the rate of BMW generation is approximately 0.5 to 2.0 kg/bed/day [5]. It is different composition of BMW which makes it an issue of serious concern [6]. There is also a huge risk of reuse of the syringes and IV tubes as a result of improper management. Those who either handle BMW at some stage

or exposed to this as a result of careless management, are prone to some serious infections like AIDS, hepatitis B and hepatitis C etc. [2]. Approximately 16 billion injections are administered per year worldwide and many of them are not disposed properly, creating a risk to reuse these syringes. In 2010, 33,800 new HIV cases, 1.7 million hepatitis B infections and 315,000 new hepatitis C cases were reported due to these reused syringes [7]. According to a joint WHO/UNICEF assessment, if an already used syringe is administered to a patient, it has 30% risk of developing hepatitis B, 1.8% risk of hepatitis C and 0.8% risk of developing HIV infections. According to a report, based on data collected from 24 different countries, approximately 58% have adequate systems for the safe disposal of BMW and the rest do not [8]. In most hospitals of Pakistan, there is a great rush of patients and a huge amount of BMW is generated which is not managed properly [5]. Good knowledge attitude and practice of health care workers towards BMW are a must requirement [3]. BMW is a serious concern especially in developing countries. A lot of work and research studies have been done on knowledge, attitude and practice of health care workers regarding BMW management both nationally and internationally but no research has been done regarding this in the city of Dera Ismail Khan. This knowledge gap is our rationale.

Our objectives were to assess the knowledge, attitude and practice of healthcare workers, to find out any statistically significant difference of knowledge, attitude and practice score across different sociodemographic variables.

M E T H O D S

It was a cross-sectional study design. Study setting was Community Medicine Department, Gomal Medical College Dera Ismail Khan. The duration of our research was from 20 February to 20 August, 2023. Ethical approval was obtained from the Ethical Review Committee (ERC) of the institute. Study population was staff working in healthcare establishments of D.I. Khan which includes nurses, technicians and sanitary workers. The sampling technique used in this research is non-probability consecutive sampling. The inclusion criteria for our research include the nurses, technicians and sanitary workers, working in healthcare establishments of D.I. Khan. The exclusion criteria were those who didn't give consent and those with a work experience of less than 6 months. According to the Raosoft et al., sample size calculator, keeping the confidence level of 95%, margin of error 5.75% and response rate of 50%, our sample size was 287. Ethical approval was granted by Ethical Review Committee (ERC) through Letter No: 183/GJMS/JC. Data collecting tool was a questionnaire having two portions, one for research variables and other for demographic variables. The research variables were knowledge, attitude and practice

of health care personnel regarding hospital waste disposal. These were assessed on 5 point Likert Scale by 20 items (10 items for knowledge, 3 items for attitude and 7 items for practice). Practice items were different for different category of workers depending on their role in waste management. Means of scores were calculated for research variables. Minimum mean score was 1 and maximum mean score was 5 for each research variable. Score of 1 to 2.4 was considered Poor. Score of > 2.4 to 4 was considered as Fair. Score > 4 to 5 was considered as Good. The demographic variables included category of workers with three attributes (nurses, technicians, sanitary workers). Age with two attributes (Greater than 40 years or less than 40 years), gender with two attributes (male or female). Years of experience with two attributes (6 months to 1 year or > 1 year). Descriptive analysis for quantitative continuous variables was done by calculating their mean and standard deviation. Demographic variables were discrete and were expressed in terms of frequency and percentages. Inferential analysis was done by assessing the statistically significant difference between research variables across demographic variables, we used an independent sample T-test for dichotomous variable except for the category of workers (multichotomous) where we used one-way ANOVA test. Data analysis was done using SPSS version 24.0.

R E S U L T S

In table 1, total of 287 Health Care Workers (HCW) from health care establishments of Dera Ismail Khan participated in this study. Out of 287, 152 (53%) were nursing staff, 79 (28%) were technicians and 56 (19%) were sanitary workers (n= 287). Demographic information showed that around 42% were male, female healthcare workers accounted for 58% of the total. With respect to working experience, the 91% of the health care workers had greater than 1 year of experience whereas only 9% had been working in a hospital setting for less than 1 year. 31% of the participants were older than 40 years whereas the remaining 69% were younger than 40 years.

Table 1: Demographic Characteristics of Participants

Variables		Nurses N (%)	Technicians N (%)	Sanitary Workers N (%)	Total N (%)
Age	> 40 Years	36 (38%)	26 (30%)	31 (32%)	93 (100%)
	< 40 Years	116 (60%)	53 (26%)	25 (14%)	194 (10%)
Gender	Male	14 (11%)	64 (52%)	45 (37%)	123 (100%)
	Female	138 (83%)	15 (10%)	11 (7%)	164 (100%)
Years of Experience	6 Months to 1 Year	11 (48%)	6 (24%)	7 (28%)	24 (100%)
	> 1 Year	141 (53%)	73 (27%)	49 (20%)	263 (100%)

Mean score of knowledge 4.45, 4.43, 4.19 and attitude 4.67, 4.63, 4.53 of nurses, technicians and sanitary workers respectively was good. But the practice score of nurses,

technicians and sanitary workers was 2.4, 2.4 and 2.26 respectively which was poor. Mean knowledge score was 4.41, 4.38 and attitude score 4.64, 4.61 by age of health care workers aged <40 years and >40years respectively, which was good. But the practice in both categories was again poor. The mean practice score of workers aged greater than 40 years was 2.38 whereas the practice of workers age less than 40 years was 2.39. Mean of KAP score with regard to gender followed the similar trend where knowledge and attitude had good mean scores relative to practice scores which was poor. Males had a score of 4.347 of knowledge, 4.575 of attitude and only 2.345 of practice. On the other hand, females had a score of 4.441 of knowledge, 4.681 of attitude and only a 2.378 of practice. Those who had experience of 6 months to 1 year, had a mean score 4.26 of knowledge, 4.52of attitude and only 2.22 of practice. On the other hand, those who worked for greater than 1 year had a score of 4.41 of knowledge, 4.64 of attitude and only a 2.31 of practice (table 2).

Table 2: Mean and Standard Deviation of KAP Score by Category of Sociodemographic Variables

Category	Number of Respondents	Knowledge (Mean ± SD)	Attitude (Mean ± SD)	Practice (Mean ± SD)
Workers				
Nurses	152	4.45 ± 0.39	4.67 ± 0.49	2.42 ± 0.58
Technicians	79	4.43 ± 0.38	4.63 ± 0.47	2.43 ± 0.81
Sanitary Workers	56	4.19 ± 0.46	4.53 ± 0.55	2.26 ± 0.53
Age				
< 40 Years	197	4.41 ± 0.41	4.64 ± 0.49	2.39 ± 0.65
> 40 Years	90	4.38 ± 0.43	4.61 ± 0.52	2.38 ± 0.63
Gender				
Male	120	4.34 ± 0.41	4.57 ± 0.50	2.34 ± 0.69
Female	167	4.44 ± 0.41	4.68 ± 0.50	2.37 ± 0.61
Years of Experience				
6 Months to 1 Year	25	4.26 ± 0.38	4.52 ± 0.69	2.22 ± 0.47
>1 Year	262	4.41 ± 0.41	4.64 ± 0.48	2.31 ± 0.65

In table 3, after applying one-way ANOVA test there was statistically significant difference of knowledge in different categories of workers with degree of freedom 2, F value of 8.802 and p value of 0.00 between groups. Results showed that there was no statistically significant difference between the category of workers and their attitude and practice as p value was 0.180 and 0.220 respectively. After applying the t-test, there was no statistically significant difference of knowledge, attitude and practice by age groups as the p value was greater than 0.05. Similarly, there was no statistically significant difference of knowledge, attitude and practice across gender as the p-value was greater than 0.05. Furthermore, there was no statistically significant difference of knowledge, attitude and practice by years of experience as the p value was 0.094, 0.224 and 0.160 respectively.

Table 3: Difference of KAP Score by Age Groups

Variables	T Test Value	p-Value
Category of Workers (Nurses, Technicians, Sanitary Workers)		
Knowledge	8.808	0.000
Attitude	1.724	0.180
Practice	1.520	0.220
Age Groups (< 40 years; > 40 years)		
Knowledge	0.514	0.607
Attitude	0.511	0.610
Practice	0.99	0.921
Gender (Male, Female)		
Knowledge	1.8862	0.060
Attitude	1.775	0.077
Practice	1.083	0.280
Years of Experience (6 Months to 1 Year; > 1 Year)		
Knowledge	–1.679	0.094
Attitude	–1.218	0.224
Practice	–1.409	0.160

In table 4, results findings showed that 84% nurses, around 78% technicians and around 64% sanitary workers had good knowledge about biomedical waste, its types, importance of its segregation and the health hazards resulting from its improper disposal. Remaining participants had fair knowledge and none of the health care worker in any category had poor knowledge. Furthermore, 83% percent of the total participants from all three categories had good attitude regarding BMW management whereas around 16.7% participants had fair attitude. While 0.3% showed poor attitude. However, majority of the participants 62% had poor practice with regards. To safe BMW management including segregation, vaccination, disinfection of waste, use protective equipment among other practices. Despite having adequate knowledge of BMW, only 1% of the health care workers were found to have good practice while 37% of them had fair practices.

Table 4: KAP Levels among Healthcare Professionals

Variables		Nurses N (%)	Technicians (%)	Sanitary Workers (%)
Knowledge	Good	84%	78%	64%
	Moderate	16%	22%	35%
	Poor	–	–	–
Attitude	Good	83%	83%	83%
	Moderate	16.7%	16.7%	16.7%
	Poor	0.3%	0.3%	0.3%
Practice	Good	1%	1%	1%
	Moderate	37%	37%	37%
	Poor	62%	62%	62%

As shown in figure 1, although the mean score of practice is less overall, the mean score of workers with regards to washing hands is relatively high that is 4.68. But the mean score of practices like segregation of waste, disinfection and training of workers on BMW management is relatively

poor with mean score of these being less than 2. But the mean score of use of personal protective measures and vaccination of workers is 3.07 and 2.81 respectively which falls between the practices mentioned above and was fair.
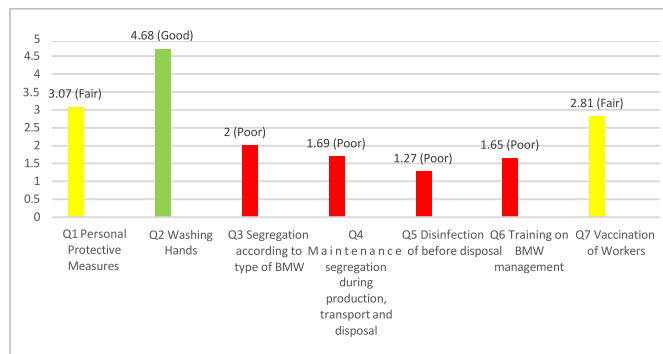
Figure 1: Mean Score of Individual Items of Practices of Health Care Workers

As per our operational definition of good, fair and poor, although the mean score of practice was less overall, the mean score of workers with regards to washing hands was relatively high that is 4.68. But the mean score of practices like segregation of waste, disinfection and training of workers on BMW management was relatively poor with mean score of these being less than 2. But the mean score of use of personal protective measures and vaccination of workers was 3.07 and 2.81 respectively which falls between the practices mentioned above was fair.

DISCUSSION

The study was conducted to assess the knowledge, attitude and practice of biomedical waste management in the health care establishments. It is vital to comprehend the significance of proper bio medical waste management in healthcare facilities since biochemical waste is found to have a hazardous impact on both the environment and human health. Not only are fundamental changes like adopting new regulations and choosing the most up-to-date safe management equipment is required, but a general understanding of proper waste disposals is also crucial. The study identifies certain inadequacies in knowledge, attitude and practice of healthcare workers. Despite majority of them having good or fair knowledge and attitude, our participants depicted poor practice. Overall, according to our study all 3 categories of workers only managed to acquire only 1% good practice which meant that only 3 people out of 287 followed proper protocols. Most of the participants showed good practice of washing hands with means scores 4.68. These results are similar to results of study conducted by Akkajit *et al.*, in which 95.6% of respondents claimed to wash hands after handling waste. Regarding wearing of personal protective equipment and vaccination mostly showed fair practice with a score of 3.07 and 2.81 respectively in our study. Again,

these results agree with results of Akkajit *et al.*, in which 93.6% respondents claimed to wear gloves for their protection [9]. But practices of our respondents regarding segregation, disinfection and training were astonishingly poor with the question with regards to disinfection of waste before disposal having the mean score as low as 1.27 and the question concerning training having score of 1.65. This all is very alarming for our district as improper segregation can lead to several health related hazards. Risk waste if mixed with non-risk waste produced in hospitals can convert all waste into hazardous waste both for humans and environment. A study conducted in large private and public sector hospitals in Rawalpindi and Islamabad regarding biomedical waste management reported that the practices were not up to the standards of WHO and Pakistan Biosafety rules 2005 [10]. Waste generated in health care establishments of low-income countries is not on the priority list of health-related issues of those countries [11]. Majority of our participants in our study, despite having good knowledge and attitude, depicted poor practice. This is in contrast with study done by Sekar M *et al.*, according to which health care workers had good co relation of knowledge with practice [12]. Poor practice may be attributed to lack of supplies or reckless attitude of workers. It was observed that most of the workers regardless of age and duration of experiences did not practice waste segregation, disinfection before disposal of biomedical waste. Furthermore, they hadn't received proper training regarding BMW safe disposal as well. A similar study at Alexandria Ambulatory Clinics revealed that none of the studied subjects received training in health-care waste management yet all of them were knowledgeable regarding the color coding used for segregation of waste [13]. Our study results also agree with study done by Soyam GC *et al.*, in which respondents had good knowledge and positive attitude towards safe waste disposal [14]. There was a statistically significant association of the category of workers with knowledge in our study and this finding agree with results of study done by Mehta TK *et al* [15]. A study done by Mariam Q *et al.*, also reported more than three fourth of respondents were having good knowledge of waste disposal steps [16]. The study of Harhay *et al.*, showed that six countries including China, India, Brazil, Pakistan, Bangladesh and Nigeria, were found to be facing unsafe BMW disposal issues [17]. Reasons for these issues are diverse from lack of interest from the hospital administration to poor practices of concerned people and economic issues in implementation of healthcare policy from the government. Although 20 years ago, WHO issued documents assessing in improving the waste management from hospitals but unfortunately did not trigger any change in Pakistan [18]. In a study done

by Mandal R *et al.*, 80.7% nursing staff showed the highest score of knowledge and these results are close to our findings with 84% of nurses showed good knowledge [19]. But in a study done by Deress T *et al.*, 45% of waste handlers had adequate knowledge, 78% had positive attitude and 80% had fair practice and practice score was higher as compared to our study in which 37% of HCW showed adequate practice [20].

CONCLUSIONS

This study concluded that although our participants had sufficient knowledge of safe biomedical waste disposal and a positive attitude towards it, but there were unsettling results regarding their practice. Only 38% of health care workers showed adequate practice (good and fair practice combined). It was revealed that there was a statistically significant association of the category of workers with knowledge.

Authors Contribution

Conceptualization: SQ, RB, AI
Methodology: SQ, RB, AI, MS
Formal analysis: SQ, AI, MG, MY, FD
Writing-review and editing: SQ, MS, MG, MY, FD, MM, MN

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

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Park K. Park's textbook of preventive and social medicine. Preventive Medicine in Obstet, Paediatrics and Geriatrics. 23rd Edition. Bhanot Publishers. 2005.

[2] Ilyas Ansaris. Public health and community medicine. 8th Edition. Karachi Pakistan: Time Publishers; 2016: 444.

[3] Uloma AA, Nkem Benjamin I, Kiss I. Knowledge, attitude and practice of healthcare workers towards medical waste management: a comparative study of two geographical areas. Journal of Waste Management and Disposal. 2022; 5: 101. doi: 10.18875/2641-8827.5.101.

[4] Saadoon NB, Kadum SA, Ali LH. Knowledge and Attitudes of Healthcare Workers regarding Medical Waste Management in Hospitals of Al-Najaf Province. Health Education and Health Promotion. 2022 Sep; 10(4): 649–56.

[5] Mahmood S, ud Din N, Mohsin J, Javed H. Practices regarding hospital waste management at public and private sector hospitals of Lahore. Annals of King Edward Medical University. 2011; 17(2): 113. doi: 10.21649/akemu.v17i2.283.

[6] Rao D, Dhakshaini MR, Kurthukoti A, Doddawad VG. Biomedical waste management: A study on assessment of knowledge, attitude and practices among health care professionals in a tertiary care teaching hospital. Biomedical and Pharmacology Journal. 2018 Sep; 11(3): 1737-43. doi: 10.13005/bpj/1543.

[7] Pepin J, Abou Chakra CN, Pepin E, Nault V, Valiquette L. Evolution of the global burden of viral infections from unsafe medical injections, 2000–2010. Public Library of Science One. 2014 Jun; 9(6): e99677. doi: 10.1371/journal.pone.0099677.

[8] Lineberger H, Cronk R, Kpodzro S, Salzberg A, Anderson DM. Does WASH FIT improve water, sanitation, and hygiene and related health impacts in healthcare facilities? A systematic review. medRxiv. 2024: 2024-04. doi: 10.1101/2024.04.05.24305396.

[9] Akkajit P, Romin H, Assawadithalerd M. Assessment of knowledge, attitude, and practice in respect of medical waste management among healthcare workers in clinics. Journal of Environmental and Public Health. 2020 Sep; 2020. doi: 10.1155/2020/8745472.

[10] Alam MM, Sujauddin M, Iqbal GM, Huda SM. Report: healthcare waste characterization in chittagong medical college hospital, Bangladesh. Waste Management and Research. 2008 Jun; 26(3): 291-6. doi: 10.1177/0734242X07087661

[11] Kumar R, Somrongthong R, Ahmed J, Almarabheh AJ. Correlates of knowledge, attitude and practices about health care waste management among hospital workers of Pakistan. Journal of Liaquat University of Medical and Health Sciences. 2018; 17(01): 1-7. doi: 10.22442/jlumhs.181710541.

[12] Sekar M, Swapna M, Easow JE. A study on knowledge, attitude and practice of biomedical waste management among health care workers in a Tertiary Care Hospital in Puducherry. Indian Journal of Microbiology Research. 2018; 5(1): 57-60. doi: 10.18231/2394-5478.2018.0011.

[13] Soliman SM, Mostafa MA, Ibrahim HZ. Medical waste management situation at alexandria ambulatory Clinics. IOSR Journal of Nursing and Health Science. 2016 Sep; 5(05): 1-9. doi: 10.9790/1959-0505050109.

[14] Soyam GC, Hiwarkar PA, Kawalkar UG, Soyam VC, Gupta VK. KAP study of bio-medical waste management among health care workers in Delhi. International Journal of Community Medicine and

Public Health. 2017 Aug; 4(9): 3332. doi: 10.18203/239 4-6040.ijcmph20173840.

[15] Mehta TK, Shah PD, Tiwari KD. A knowledge, attitude and practice study of biomedical waste management and bio-safety among healthcare workers in a tertiary care government hospital in western India. National Journal of Community Medicine. 2018 May; 9(05): 327-33.

[16] Mariam Q, Ahmed N, Abbasi MS, Nadeem R, Rizwan A, Vohra F *et al.* Safe practices of biomedical and dental waste management amongst practicing dental professionals amid the COVID-19 pandemic. Work. 2022 Jan; 71(4): 851-8. doi: 10.3233/WOR-211099.

[17] Harhay MO, Halpern SD, Harhay JS, Olliaro PL. Health care waste management: a neglected and growing public health problem worldwide. Tropical Medicine and International Health. 2009 Nov; 14(11): 1414-7. doi: 10.1111/j.1365-3156.2009.02386.x.

[18] Khalid S, Haq N, Sabiha ZU, Latif A, Khan MA, Iqbal J *et al.* Current practices of waste management in teaching hospitals and presence of incinerators in densely populated areas. BMC Public Health. 2021 Dec; 21: 1-0. doi: 10.1186/s12889-021-11389-1.

[19] Ramkrishna M and Satyanarayana P. Knowledge, Attitude and Practice (KAP) Study Regarding Bio-Medical Waste Management Am ong Staff in a Tertiary Care Hospital at Andhra Pradesh. Asian Journal of Management. 2018; 9(1): 267-71. doi: 10.5958/2321-5763.2018.00040.9.

[20] Deress T, Jemal M, Girma M, Adane K. Knowledge, attitude, and practice of waste handlers about medical waste management in Debre Markos town healthcare facilities, northwest Ethiopia. BMC research notes. 2019 Dec; 12: 1-7. doi: 10.1186/s13104-019-417.

Original Article

The Role of Lipid Peroxidation Products in the Development of Oral Sub Mucous Fibrosis- A Cross-Sectional Survey

Nooria Naeem[1], Chaman Nasrullah[1], Maria Shakeel[1*], Zobiah Hafiz[1], Sara Mukhtar[1] and Maimoona Nasreen[1,2]

[1]Department of Physiology, University College of Medicine and Dentistry, University of Lahore, Lahore, Pakistan
[2]Equator University of Science and Technology, Masaka, Uganda

ARTICLE INFO

ABSTRACT

Oral sub mucous fibrosis (OSMF) is a premalignant condition. Factors that cause OSMF are areca nut, nutritional deficiency and genetics. These factors produce free radicals which generate oxidative stress by damaging DNA, lipids and proteins. Levels of 4 hydroxynonenal (4HNE), 8-hydroxy-2-deoxy guanosine (8-OHdG), C reactive protein (CRP), and malondialdehyde (MDA) were raised due to oxidative DNA damage and lipid damage. **Objective:** To determine the levels of lipid peroxidation by-products such as MDA, 4HNE, 8-OHdG, and CRP in patients with OSMF. **Methods:** A cross-sectional comparative study was conducted at The University of Lahore from January 2020 to August 2021. Fifty OMSF cases and fifty healthy controls were recruited by using non-probability convenient sampling technique. Serum of participants was analyzed for lipid peroxidation byproducts by using ELISA kits. The results were analyzed by applying independent t-test in SPSS version 21.0. **Results:** The mean MDA levels in OSMF patients were (3.22 ± 1.265 nmol/ml) as compared to those of control group (1.26 ± 0.568 nmol/ml). Serum CRP levels were significantly raised (1.23 ± 0.124 mg/l) in patients of OSMF as compared to those of control group (1.04 ± 0.0324 mg/l). The levels of 4-HNE, 8-OHdG were recorded as significantly increased in OSMF (1.5 ± 0.965 pg/ml and 1.9 ± 0.265 pg/ml) as compared to the those of control group (0.72 ± 0.065 pg/ml and 0.09564 ± 0.00058 pg/ml). **Conclusions:** It was concluded that the levels of MDA, 4HNE, 8-OHdG, and CRP were increased significantly in patients with OSMF compared to healthy controls.

INTRODUCTION

Oral sub mucous fibrosis (OSMF) is a progressive and precancerous disease that involves the whole oral cavity and sometimes extends to different parts of neck [1, 2]. Patients with oral sub mucous fibrosis often present with discoloration of teeth and gums, limited mouth opening and burning sensation on taking spicy food. There are many factors which are associated with oral sub-mucosal fibrosis like excessive chewing of areca nut (Betel nut), nutritional deficiency and some genetic factors. There is a high tendency 7% to 30% of OSMF to be converted into malignant disorders such as oral squamous cell carcinoma [3]. One of the early clinical signs of OSMF is inflammation. Inflammation and decrease in vascularity ultimately lead to thick bands of fibrous tissue which are white in color called "fibrosis in diseased area". There are different stages of oral sub mucous fibrosis and severity increases as the stage increases. In last stage of OSMF, the mouth opening is limited which causes poor oral hygiene, difficulty in eating food and problems with speech. In stage-I, mouth opening is (>3cm), stage-II (2-3cm) and in stage-III (<2cm). Fibrosis involves lips (thick and rubber like appearance), cheeks which are puffed out, tongue (unable to move due to fibrosis), soft palate, uvula and gums. Fibrosis spreads to different parts of throat such as pharynx, esophagus, eustachian tube that blocks these regions [4]. Worldwide, oral cancer is 6th most common cancer. Its occurrence rate is high in India and Southeast Asia and also in some of the Western countries. OSMF is a precancerous condition

which is converted to oral squamous cell carcinoma [5]. The chewing habit of areca nut is the most common and potent endogenous factor leading to OSMF that ultimately transforms into cancerous lesion [6, 7]. More than 80% of cases are transformed into cancer [8]. Epithelium becomes hyperplasic with the use of Betel nut. There are two mechanisms running side by side in human cancerous cells, one is the formation of free radicals such as reactive oxygen species (ROS) which generate oxidative stress and other is antioxidant defense system. Presence of an unpaired electron on a fragmented molecule is known as free radical. Superoxide anions and hydroxyl radicals are the most frequently formed free radicals [9]. ROS changes the macromolecules such as carbohydrates, lipids and proteins. ROS are produced due to the formation of byproducts and intermediate molecules in normal cellular processes. There is oxidative damage to nucleic acids such as 8-hydroxydeoxyguanosine (8-OHdG) and proteins (Protein carbonyl) [10]. Lipid peroxidation produces ROS which damage cell products and its membrane. Malondialdehyde (MDA) is a poisonous aldehyde and is a potent marker of oxidative stress produced by lipid peroxidation. Free radical formation such as 8-OHdG is one of the most commonly used biomarker for oxidative stress conditions and cancerous diseases [11]. 8-OHdG was found in oral leukoplakia and lichen planus [12]. Areca nut contains some chemicals which increase the production of ROS and DNA adducts. 4-hydroxynonenal (4HNE) is also a byproduct of lipid peroxidation is activated and causes DNA mutation [10]. Several genes are responsible for OSMF. Cytochrome P450 subtype gene is decreased in OSMF [3]. There are also some undergoing immunological processes in OSMF patient such as increased expression of HLA-A10, HLA-B7, and HLA-DR3 and CD4 cells. This leads to an increase in Langerhans cell. These cells imbalance the immune regulation by increasing the number of CD4 in OSMF leading to atrophic changes in oral epithelium. These processes are activated either due to ingestion of areca nut or autoimmune responses as a result of tissue alteration [13]. There was limited data available on the role of lipid peroxidation by products (MDA, 4-HNE and 8-OHdG) in oral sub mucous fibrosis.

The study was conducted to compare lipid peroxidation byproducts levels in patients of oral sub mucous fibrosis and control group.

METHODS

This cross-sectional comparative study was conducted at the institute of Molecular Biology and Biotechnology, The University of Lahore, from January 2020 to August 2021 after obtaining approval from Institutional Review Board of The University of Lahore, IMBB/BBBC/24/324 and permission letter, RS-FAHS-24921/1. Sample size was

calculated using "Open Epi calculator" by keeping mean levels of MDA in OSMF group as 3.3nmol and in healthy control as 2.4nmol. Mean S.D was 0.45 and variance was 0.2025. Confidence interval was taken as 5. Power was taken as 80 [14]. The estimated sample size was 5 for each group but for better power of study was took 50 subjects in both control group and case group. Fifty dental patients (male or female above 18 years of age) visiting ULTH dental OPD from March 2020 to August 2020 having pain and burning sensation in mouth, limited mouth opening, oral ulcers, white and red patches in oral mucosa with or without depigmentation were recruited in the study after taking informed consent by using non-probability convenient sampling technique. Study participants with suspicious clinical signs of oral carcinoma were excluded. Healthy dental patients (male or female above 18 years) with no clinical features of OSMF were taken as controls. 5ml blood was taken from both cases and controls after clinical assessment. Blood was centrifuged at 4000 rpm for 10 min for serum separation. Serum was analyzed for 4HNE, 8-OHdG, 8-isoprostane and MDA by using Enzyme-linked immunosorbent assay (ELISA) (OxiSelect™) kits as per Manufacturers protocol. CRP levels were assessed by using Latex kit (Bioscien). The results were analyzed by applying independent t-test in SPSS version 21.0. Mean values and standard deviations for quantitative variables were calculated. Independent t-test was applied to determine the statistical significance of various parameters amongst two groups. Results were presented as mean ± SD. p value ≤ 0.005 was considered significant and p value ≤ 0.001 was considered highly significant.

RESULTS

A total of 50 participants were enrolled in each group, out of which 44 (88%) were males and 6 (12%) females in control group, whereas 46 (92%) males and 4 (8%) females were in OSMF group. The mean age of the OSMF participants was 34.6 years, with a standard deviation of 7 years. In the control group, the mean age was 33.4 years, with a standard deviation of 7 years (Table 1).

Table 1: Distribution and mean age and standard deviation of males and females in both groups (n=50)

Gender	Control (%)	Mean ± SD*	OSMF* (%)	Mean ± SD
Male	44 (88)	34.1 ± 8	46 (92%)	33.8 ± 7
Female	6 (12)	26.6 ± 0	4 (8%)	44.5 ± 4
Total	50 (100)	33.4 ±7	50 (100)	34.6 ± 7

*SD= Standard deviation **OSMF= Oral sub mucous fibrosis

The data assembled in table 2 shows that serum CRP levels were significantly raised in the OSMF patients (1.23 ± 0.124mg/l) as compared to those of control group (1.04 ± 0.0324mg/l). The levels of 4-HNE in OSMF were also significantly raised (1.5 ± 0.965pg/ml vs 2.6 ± 0.845pg/ml) as compared to the healthy group. Levels of 8-OHdG were also

significantly raised in OSMF patients (0.09564 ± 0.001pg/ml) as compared to those of control groups (1.9 ± 0.27pg/ml). The MDA levels were significantly raised in patients suffering from oral sub mucous fibrosis (3.22 ± 1.265nmol/ml) as compared to controls (1.26 ± 0.568nmol/ml).

Table 2: Lipid Peroxidation Products in Patients of Oral Sub Mucous Fibrosis

Variables	Control (n= 50)	OSMF* (n=50)	p-Value
4-HNE (pg/ml)	0.72 ± 065	1.5 ± 0.97	0.02
8-OHdG (pg/ml)	0.09 ± 0.001	1.9 ± 0.27	0.02
CRP (mg/l)	1.04 ± 0.03	1.2 ± 0.12	0.01
MDA (nmol/ml)	1.26 ± 95	3.22 ± 1.26	0.002

*OSMF= Oral sub mucous fibrosis

DISCUSSION

The levels of lipid peroxidation by-products that is MDA, 4HNE, 8 -OHdG, and CRP were raised in the patients having oral sub mucous fibrosis. In a scoping review conducted by Saso *et al.,* various articles were evaluated for the levels of different oxidative stress markers and antioxidants in patients with oral sub mucous fibrosis. All studies whether in vitro or human revealed that levels of oxidative stress markers increased as the disease progressed. Furthermore, the use of antioxidants decreased the levels of oxidative stress markers and improved the symptoms of patients. We checked the levels of lipid peroxidation byproducts in patients of OSMF, but did not administer any antioxidants to the patients. Future studies may be planned to see the baseline levels of antioxidants as well as the effects of administration of antioxidants on prognosis of OSMF [15]. In a study conducted by Shirzaiy *et al.,* 34 patients of OSMF of different grades were studied for association of ROS and OSMF. Plasma MDA levels were found to be significantly higher in OSMF patients. Vitamin E and beta carotenes levels were significantly reduced in these patients and oral administration of these 2 antioxidants increased their level and decreased the levels of MDA in plasma [9]. Our study had the same results regarding levels of stress markers. In a cross-sectional survey conducted by Sumithrarachchi *et al.,* 368 patients attending the dental clinic were assessed for the use of tobacco, areca nut and presence of oral lesions. This study revealed that more than 90% of tobacco users and areca nut had oral lesions. OSMF had a prevalence of 2.4%. This study highlighted the importance of awareness programs for the patients visiting dental clinics [16]. In this study, we took samples from the patients of OSMF consuming areca nut and assessed the levels of various oxidative biomarkers. Mobeen *et al.,* administered a herbal paste to 80 patients with OSMF for 3 months and assessed various subjective and objective symptoms of the patients like tongue protrusion, blanching, mouth opening, intolerance to spicy food and burning sensation. This study showed that Gutka was being used by most of the patients with OSMF. Use of herbal paste containing turmeric, tulsi and honey significantly improved various parameters like mouth opening, tongue protrusion, burning sensations, mucosal bands and oral blanching [17]. The limitation of our study is that it did not include the symptoms and various pathological parameters of OSMF or use of any antioxidant remedy. Singh *et al.,* studied the prevalence of various oral lesions among tobacco users. The most common lesions observed were pouch keratosis in chewers and leukoplakia amongst chronic smokers [18]. In our study, all the OSMF patients were consumers of areca nut. Levels of oxidative markers like MDA, 4HNE, 8-OHdG and CRP were raised in all the patients because areca nut causes oxidation in the oral mucosa. Yashveer *et al.,* demonstrated that patients of OSMF have lower levels of serum HDL, LDL, cholesterol, VLDL, TG probably because these lipids were utilized for the synthesis of new cell membranes. They proposed that serum lipid levels may be used for the diagnosis of OSMF [19]. However, we did not measure serum lipid levels. Pant *et al.,* demonstrated that areca nut induced TGF–β (transforming growth factor-beta) pathway to induce fibrosis in OSMF. TGF– β is an inflammatory biomarker. This finding would help in defining the treatment strategies for OSMF [20]. We determined the levels of oxidative biomarkers that might have similar mechanistic induction of fibrosis, but we did not measure inflammatory biomarkers. Rai *et al.,* studied various intermediate products of metabolism and products of oxidative stress in 20 patients of OSMF. They demonstrated how the metabolic pathways are switched to adapt to malignant changes in epithelial cells and how these pathways are reprogrammed to fulfill the nutritional demands of malignant cells [5]. Our study could also be extended to find out the biochemical mechanisms responsible for oxidative stress and metabolic reprogramming as a result of malignant changes.

CONCLUSIONS

This study showed that levels of MDA, 4HNE, 8-OHdG, and CRP were increased significantly in patients with oral sub mucous fibrosis as compared to healthy controls. Lipid peroxidation byproducts such as MDA, 4HNE, CRP and 8-OHdG are biomarkers of oxidative stress. Elevated levels of these byproducts in OSMF may help in the early detection of disease. These may serve as a tool to assess the severity of the disease and may be used as prognostic markers. These markers may guide the clinician for therapeutic interventions in the patient of OSMF to reduce the oxidative stress generated by these byproducts. Our study may improve patient outcome by designing a non-invasive diagnostic and prognostic tool for oral sub mucous fibrosis.

Authors Contribution

Conceptualization: NN
Methodology: NN, MS
Formal analysis: CN
Writing-review and editing: ZH, SM, MN

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

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Shih YH, Wang TH, Shieh TM, Tseng YH. Oral submucous fibrosis: a review on etiopathogenesis, diagnosis, and therapy. International Journal of Molecular Sciences. 2019 Jun; 20(12): 2940. doi: 10.3390/ijms20122940.

[2] Rao NR, Villa A, More CB, Jayasinghe RD, Kerr AR, Johnson NW. Oral submucous fibrosis: a contemporary narrative review with a proposed inter-professional approach for an early diagnosis and clinical management. Journal of Otolaryngology-Head & Neck Surgery. 2020 Jan; 49(1): 3. doi: 10.1186/s40463-020-0399-7.

[3] Peng Q, Li H, Chen J, Wang Y, Tang Z. Oral submucous fibrosis in Asian countries. Journal of Oral Pathology & Medicine. 2020 Apr; 49(4): 294-304. doi: 10.1111/jop.12924.

[4] Wollina U, Verma SB, Ali FM, Patil K. Oral submucous fibrosis: an update. Clinical, Cosmetic and Investigational Dermatology. 2015 Apr; 193-204. doi: 10.2147/CCID.S80576.

[5] Rai V, Bose S, Saha S, Chakraborty C. Evaluation of oxidative stress and the microenvironment in oral submucous fibrosis. Heliyon. 2019 Apr; 5(4). doi: 10.1016/j.heliyon.2019.e01502.

[6] Sharma M, Sarode SC, Sarode G, Radhakrishnan R. Areca nut-induced oral fibrosis–Reassessing the biology of oral submucous fibrosis. Journal of Oral Biosciences. 2024 Feb. doi: 10.1016/j.job.2024.02.005.

[7] Li L, Gu L, Yao Z, Wang Y, Tang Z, Wu X. Arecoline suppresses epithelial cell viability by upregulating tropomyosin-1 through the transforming growth factor-β/Smad pathway. Pharmaceutical Biology. 2020 Jan; 58(1): 1253-60. doi: 10.1080/13880209.2020.1851729

[8] Li W, Cheng B. Knockdown of LncRNA NEAT1 inhibits myofibroblast activity in oral submucous fibrosis through miR-760/TPM1 axis. Journal of Dental Sciences. 2022 Apr; 17(2): 707-17. doi: 10.1016/j.jds.2021.11.003.

[9] Shirzaiy M, Salehian MA, Dalirsani Z. Salivary antioxidants levels in patients with oral lichen planus. Indian Journal of Dermatology. 2022 Nov; 67(6): 651-6.

[10] Zhou Q, Ye F, Zhou Y. Oxidative stress-related biomarkers in oral squamous cell carcinoma patients: A systematic review and meta-analysis. Biomarkers in Medicine. 2023 Jun; 17(6): 337-47. doi: 10.2217/bmm-2022-0846.

[11] Kulasekaran C, Devi M, Dhivya K, Vijayalakshmi D, Sathishkumar M, Madhanmohan A. Immuno-histochemical detection of 8 hydroxyde-oxyguanosine: A biomarker of oxidative DNA damage in oral submucous fibrosis. Journal of Oral and Maxillofacial Pathology. 2020 Sep; 24(3): 53 6-41. doi: 10.4103/jomfp.JOMFP_42_20.

[12] Nandakumar A, Nataraj P, James A, Krishnan R, Mahesh KM. Estimation of salivary 8-hydroxydeoxyguanosine (8-OHdG) as a potential biomarker in assessing progression towards malignancy: a case-control study. Asian Pacific Journal of Cancer Prevention: APJCP. 2020 Aug; 21(8): 2325. doi: 10.31557/APJCP.2020.21.8.2325.

[13] Rani P, Singh RN, Sharma S, Shahi AK, Chandra S, Singh B. Prevalence of Oral Submucous Fibrosis, Its Correlation of Clinical Grading to Various Habit Factors among Patients of Bihar: A Cross Sectional Study. Journal of Pharmacy and Bioallied Sciences. 2023 Jul; 15(Suppl 1): S554-7. doi: 10.4103/jpbs.jpbs_467_22.

[14] Gupta S, Reddy MV, Harinath BC. Role of oxidative stress and antioxidants in aetiopathogenesis and management of oral submucous fibrosis. Indian journal of Clinical biochemistry. 2004 Jan; 19: 138-41. doi: 10.1007/BF02872409.

[15] Saso L, Reza A, Ng E, Nguyen K, Lin S, Zhang P *et al.* A comprehensive analysis of the role of oxidative stress in the pathogenesis and chemoprevention of oral submucous fibrosis. Antioxidants. 2022 Apr; 11(5): 868. doi: 10.3390/antiox11050868.

[16] Sumithrarachchi S, Athukorala I, Rumy F, Jayasinghe R. Prevalence of tobacco and areca-nut use among patients attending dental teaching hospital in the central province of Sri Lanka and its association with oral mucosal lesions; a cross sectional study. Journal of Oral Biology and Craniofacial Research. 2024 Jan; 14(1): 39-43. doi: 10.1016/j.jobcr.2023.11.006.

[17] Mobeen S, Ravindra SV, Sunitha JD, Prakash R, Satyanarayana D, Swayampakula H *et al.* A Novel Herbal Paste Formulation of Turmeric, Tulsi, and

Honey for the Treatment of Oral Submucous Fibrosis. Cureus. 2023 Oct; 15(10). doi: 10.7759/cureus.46608.

[18] Singh G, Preethi B, Chaitanya KK, Navyasree M, Kumar TG, Kaushik MS. Prevalence of Oral Mucosal Lesions among Tobacco Consumers: Cross-Sectional Study. Journal of Pharmacy and Bioallied Sciences. 2023 Jul; 15(Suppl 1): S562-5. doi: 10.4103/jpbs.jpbs_104_23.

[19] Yashveer JK and Pankaj D. Alteration of serum lipid in oral sub mucous fibrosis in central India. Indian Journal of Otolaryngology and Head & Neck Surgery. 2018 Sep; 70: 421-4. doi: 10.1007/s12070-018-1434-0.

[20] Pant I, Rao SG, Kondaiah P. Role of areca nut induced JNK/ATF2/Jun axis in the activation of TGF-β pathway in precancerous Oral Submucous Fibrosis. Scientific reports. 2016 Oct; 6(1): 34314. doi: 10.1038/srep34314.

Original Article

Seasonal and Time-Series Analysis of Alcohol Intoxication-Related Cases in Hyderabad, Pakistan

Aisha Rasheed[1], Naseem Akter[2], Rabail Altaf[3], Ishrat Bibi[1], Abdul Samad[1*], Muhammad Shafay[4] and Mohammad Akber Kazi[5]

[1]Department of Forensic Medicine and Toxicology, Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan

[2]Department of Anatomy, Sindh Medical College, Jinnah Sindh Medical University, Karachi, Pakistan

[3]Department of Forensic Medicine and Toxicology, Gambat Medical College, Pir Abdul Qadir Shah Jeelani Institute of Medical Sciences, Gambat, Pakistan

[4]Department of Forensic Medicine and Toxicology, Hazrat Bari Imam Sarkar Medical and Dental College, Islamabad, Pakistan

[5]Department of Forensic Medicine and Toxicology, Bilawal Medical College, Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan

ARTICLE INFO

ABSTRACT

Cases related to alcohol intoxication are important because they can help raise awareness about the dangers of excessive alcohol consumption and the need for responsible alcohol use. The present research studied the seasonal trend of alcohol intoxication-related cases in Hyderabad, Pakistan. **Objective:** To conduct seasonal and time series analysis of alcohol intoxication cases. **Methods:** Prospective study was conducted at Casualty Department, Liaquat University Hospital Hyderabad from January 2020 to December 2022. One hundred and eighty nine cases of alcohol intoxication-related cases were enrolled. Data was presented as frequency and averages of month-wise cases. Different plots i.e, seasonal index plot and time series plot were created to demonstrate the seasonal trend. **Results:** The largest number of cases were observed in April and December (n ≥ 25). The second most frequent cases occurred in months of June and November with 18 to 20 frequencies. The seasonal pattern was further illustrated by time-series analysis which showed that April and December had higher numbers of cases compared to other months. **Conclusions:** The study suggested a little decline in alcohol intoxication-related sufferer. These findings may highlight the importance to developed public awareness about the responsible use of alcohol.

INTRODUCTION

Medico-Legal Cases (MLCs) are those cases which affect legal matters related to medical issues or questions. These cases can be related to different aspects that may include claims for personal injury claims, for lawsuits related medical malpractice, about criminal cases, and regarding claims of workers' compensation [1]. Additionally, MLCs can have massive influence on all parties that may be affected in a case [2]. MLCs are appropriate predominant with attributing to alcohol intoxication since they are able to help ensuring appropriate medical care for the individuals who are harmed by alcohol-related incidents and ensuring legal representation for such individuals [3]. MLCs related to alcohol intoxication are also important in a view of help in raising alertness about the dangers of over consumption of alcohol and the need for responsible alcohol use. MLCs can also aid in promoting public health and safety by identifying individuals and organizations responsible for alcohol-related harms [4]. Plenteous research has underlined a strong link between season and mortality. The mortality rates can fluctuate with seasons

[5-7]. This changeability has been detected to occur in natural causes like cardiovascular deaths, which take peaks during hot weather and cold waves [8]. The seasonality has also been observed in unnatural causes for example drowning, hypothermia, and suicide. Drowning shows peaks in summer, hyperthermia exhibits increase in numbers during winters, whereas suicide shows various peaks depending on the region and the population [9-12]. Additionally, environmental and behavioural factors, such as weather and holidays, have been indicated as potential facilitators in seasonality pattern of disease [13]. The number and profiling of MLCs can demonstrate variation from region to region, probably because of the effect which is exerted by different cultures and seasonal variations [14]. Therefore, studying seasonal variations may assist in identifying the factors which may be involved in specific kinds of injuries or incidents, resulting to assessment in medicolegal departments. Considering alcohol intoxication in MLCs, the seasonal variation can be helpful in spotlighting the factors that can influence certain injuries, such as factors that might be common in some cultures and other social. This method studies the dynamic observations from time point 1 to time point t and helps determine the seasonal or periodic trend of particular events. This method also shows potential in forecasting the events in multiple fields, including medicine, such as forecasting disease prevalence [15]. Herein, the seasonal trend of alcohol-related MLCs was determined using three-year data from a leading tertiary care hospital in Hyderabad, Pakistan, by using a time series analysis method.

The objective of this study was to conduct seasonal and time series analysis of alcohol intoxication cases.

The objective of this study was to create average angular and proportional photogrammetry norms of adult Pakistani population, further aiding diagnosis, planning treatment and favorable outcomes of esthetics and stability at commencement of treatment, due to limited local literature and the variability of these parameters amongst different populations.

METHODS

The present study was conducted at the Casualty Department, Liaquat University Hospital and Hyderabad, Pakistan. The monthly data from January to December was collected for the years 2020 to 2022. Utilizing a non-probability sampling method, patients of all ages and age groups were selected. The approval of this study was obtained from Institutional Review Board (IRB) of Liaquat University Hospital, Hyderabad, Pakistan, (IRB letter number: LUMBHS/FM/77/19 dated 28 November 2019). The inclusion criteria were set to be the case of medico-legal nature, whereas non-medico-legal cases were not included in the present study. The data was collected in MS EXCEL sheets. The month-wise frequency of alcohol intoxication cases was recorded and their average and total was determined in MS EXCEL. Then, the month-wise occurrence of alcohol intoxication-related MLCs was transferred to Statgraphics Centurion XIX software. The months of the year were entered as sampling intervals. Subsequently, the built-in models for time-series analysis and seasonal decomposition models in Statgraphics Centurion XIX software were applied to obtain seasonal and time series pattern of alcohol intoxication-related cases at the casualty department of Liaquat University Hospital, Hyderabad, Pakistan [16]. Data were presented as monthly frequency distributions for the period of three years.

RESULTS

There were 92, 52, and 45 cases in 2020, 2021, 2022, respectively, with a total of 189 cases over the three-year period. The number of cases related to alcohol intoxication occurring in each month of three years is summarized in table 1.

Table 1: Month-Wise Frequency of Alcohol Intoxication for Three Consecutive Years

Month	Year			Total N (%)
	2020	2021	2022	
January	3	2	5	10 (5.29%)
February	7	3	6	16 (8.47%)
March	8	1	2	11 (5.82%)
April	19	4	3	26 (13.76%)
May	12	1	1	14 (7.41%)
June	10	2	8	20 (10.58%)
July	5	4	1	10 (5.29%)
August	7	3	1	11 (5.82%)
September	3	4	7	14 (7.41%)
October	2	10	2	14 (7.41%)
November	3	11	4	18 (9.52%)
December	13	7	5	25 (13.23%)
Total	92	52	45	189 (100%)

The data in figure 1 showed that the average number of total alcohol intoxication cases remained highest in the months of April and December (≥25). The second most frequencies of total alcohol intoxication cases were observed for the months of June and November with 18-20 occurrences. The least numbers of alcohol intoxication-related cases at study site were conducted during months of January and July, 10 total cases in each month. The month of April exhibited highest average cases (n=8.67), followed by December (n=8.33). The quarterly distribution of alcohol intoxication-related cases for the period of three years showed highest total for the second quarter i.e., April to June, with total 60 cases. The fourth quarter (October to December) also demonstrated similar frequency of alcohol

intoxication-related cases (n=57). The first and third quarters of three years data revealed approximately 40% less cases of alcohol intoxication-related cases than second and fourth quarters. A seasonal index plot for alcohol toxicity-related cases is given in Figure 1, which showed the seasonal pattern of alcohol intoxication-related medico-legal cases.
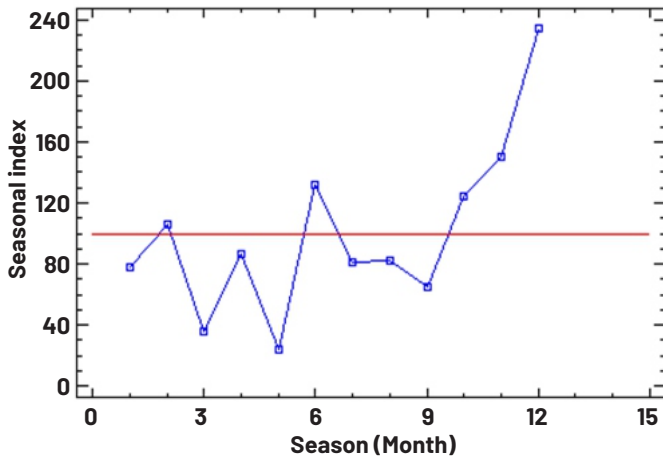
Figure 1: Seasonal Index Plot for Alcohol Toxicity Related Cases

The plot indicated that there is a clear seasonal pattern, with higher numbers of cases occurring in the months of April, June, November, and December. A smooth time series plot was constructed which provides a visual representation of the data over time. The plot suggests a slightly decreasing trend in the number of cases over the three-year period. Moreover, it indicates that in certain months of the year, a higher number of alcohol intoxication-related cases are presented in Liaquat University Hospital, Hyderabad, Pakistan. The graph indicated that the monthly frequency of alcohol intoxication-related cases is mostly centered on the average number of cases. However, the trend takes the peaks due to increased number of alcohol intoxication-related cases during the months of April and December
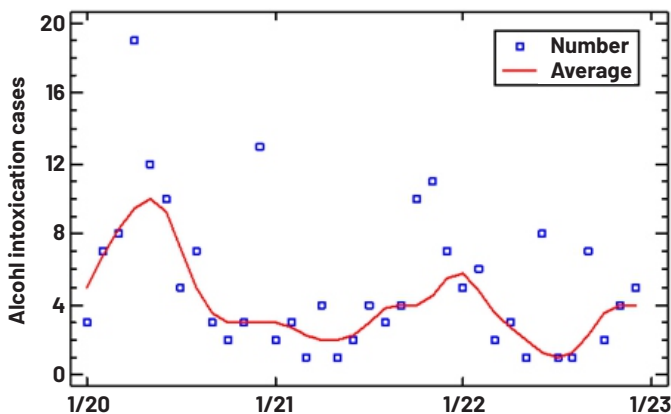
Figure 2: Smoothed Time Series Plot for Alcohol Toxicity-Related Cases

DISCUSSION

The present study found a seasonal trend in alcohol-related MLCs. Olson conducted a cross-sectional study via urine drug testing of adult patient specimens to determine the influence of season, gender, age, and geography on the detection of alcohol. This study found peaks of alcohol positivity in summer and low detection in winter [17]. However, the present study noted the highest numbers both in summer and winter; the first two highest numbers in April and December, and second two highest frequencies in July and November. The comparison between the present study and study by Olson *et al.*, study reported summer as peak season for alcoholism and the present study found both summer and winter as seasons for increased alcohol intoxication-related cases [17]. Another study determining the link between season and alcohol consumption in college student-athletes reported higher use of alcohol in out-of-sports-season athletes than their in-sports-season counterparts [18]. This can be compared to present study with reference to potential existence of seasonality and alcohol use, leading to alcohol intoxication. A time-series analysis of weekly alcohol sales in various counties of United States found that retail sales of various types of alcoholic beverages were temperature sensitive throughout the year [19]. This indicates that alcohol use increases during certain months of the year, comparing to the present study, the present study also reports a link between season and alcohol use, following the observation of higher number of alcohol intoxication-related cases in intense weathers. Seasonality in the death rates in England and Scotland was reported to be associated with alcohol intake, showing higher peaks in January every year [20]. This is similar to the present study's observation about increased alcohol toxicity cases in December (winter in Hyderabad region). The present study found an increasing trend in alcohol toxication-related MLCs both in warm and cold weather months. This is similar to a study form Unites States which found amplitude of alcohol-related hospitalizations with summer peak and winter trough [21]. The comparison between the two studies, study in United States and the present study, reveals a similarity of higher alcohol-intake related requirements of medical intervention in the months of summer or cold seasons which are usually characterized by higher heat or cold, respectively [21]. Overall, the observations in the present study are in line with the previous studies. However, the peaks observed in April in the present study differ from previously reported observations. This difference may appertain to local cultural events or social conditions exclusive to the region of the present study.

CONCLUSIONS

The seasonal trend of alcohol-related cases was studied using time series analysis. The data analysis showed that the average number of total alcohol intoxication cases was highest in April and December, with more than 25 cases in each month every year. This was followed closely by June and November, with 18-20 occurrences. Conversely, the months with the lowest number of alcohol intoxication cases were January and July, each with 10 cases. April had the highest average number of cases at 8.67, followed by December at 8.33. The study showed a potential seasonality of alcohol intoxication cases as the quarterly distribution was comparatively higher in the second quarters.

Authors Contribution

Conceptualization: AR, MAK
Methodology: AR, AS
Formal analysis: NA, MAK
Writing, review and editing: RA, MS, IB

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

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

REFERENCES

[1] Treglia M, Pallocci M, Passalacqua P, Sabatelli G, De Luca L, Zanovello C *et al.* Medico-legal aspects of hospital-acquired infections: 5-years of judgements of the civil court of Rome. InHealthcare. 2022 Jul; 10(7): 1336. doi: 10.3390/healthcare10071336.

[2] Patel PR. Strategies of Avoiding Medicolegal Problems. Annals of Indian Academy of Neurology. 2016 Oct; 19(1): 15-20. doi: 10.4103/0972-2327.192886.

[3] Fouché L, Bezuidenhout J, Liebenberg C, Adefuye AO. Medico-legal aspects regarding drunk driving: experience and competency in practice of community service doctors. South African Family Practice. 2018 Mar; 60(2): 63-9. doi: 10.4102/safp.v60i2.4869.

[4] Sontate KV, Rahim Kamaluddin M, Naina Mohamed I, Mohamed RM, Shaikh MF, Kamal H *et al.* Alcohol, aggression, and violence: From public health to neuroscience. Frontiers in Psychology. 2021 Dec; 12: 699726. doi: 10.3389/fpsyg.2021.699726.

[5] Wu Y, Li S, Zhao Q, Wen B, Gasparrini A, Tong S et al. Global, regional, and national burden of mortality associated with short-term temperature variability from 2000-19: a three-stage modelling study. The Lancet Planetary Health. 2022 May; 6(5): e410-21. doi: 10.1016/S2542-5196(22)00073-0.

[6] Guo Y, Gasparrini A, Armstrong B, Li S, Tawatsupa B, Tobias A *et al.* Global variation in the effects of ambient temperature on mortality: a systematic evaluation. Epidemiology. 2014 Nov; 25(6): 781-9. doi: 10.1097/EDE.0000000000000165.

[7] Ledberg A. A large decrease in the magnitude of seasonal fluctuations in mortality among elderly explains part of the increase in longevity in Sweden during 20th century. Biomedicine Central Public Health. 2020 Dec; 20: 1-0. doi: 10.1186/s12889-020-09749-4.

[8] Abrignani MG, Lombardo A, Braschi A, Renda N, Abrignani V. Climatic influences on cardiovascular diseases. World Journal of Cardiology. 2022 Mar; 14(3): 152. doi: 10.4330/wjc.v14.i3.152.

[9] Girela-López E, Beltran-Aroca CM, Dye A, Gill JR. Epidemiology and autopsy findings of 500 drowning deaths. Forensic Science International. 2022 Jan; 330: 111137. doi: 10.1016/j.forsciint.2021.111137.

[10] Brändström H, Eriksson A, Giesbrecht G, Ängquist KA, Haney M. Fatal hypothermia: an analysis from a sub-arctic region. International Journal of Circumpolar Health. 2012 Jan; 71(1): 18502. doi: 10.3402/ijch.v71i0.18502.

[11] Lasota D, Pawłowski W, Krajewski P, Staniszewska A, Goniewicz K, Goniewicz M *et al.* Seasonality of suicides among victims who are under the influence of alcohol. International Journal of Environmental Research and Public Health. 2019 Aug; 16(15): 2806. doi: 10.3390/ijerph16152806.

[12] Kaya A, Tasar PT, Meral O, Sahın S, Balkay M, Aktas EO *et al.* The characteristics of older people suicides by sex and age subgroups. Legal Medicine. 2020 Sep; 46: 101721. doi: 10.1016/j.legalmed.2020.101721.

[13] Madaniyazi L, Chung Y, Kim Y, Tobias A, Ng CF, Seposo X *et al.* Seasonality of mortality under a changing climate: a time-series analysis of mortality in Japan between 1972 and 2015. Environmental Health and Preventive Medicine. 2021 Dec; 26(1): 69. doi: 10.1186/s12199-021-00992-8.

[14] Qadir MA. Forensic Survey for Medico-Legal Cases: Real Figures from Liaquat University Hospital Hyderabad, Sindh. Alcoholism. 2020 Apr; 92: 2-53.

[15] Aydin S. Time series analysis and some applications in medical research. Journal of Mathematics and Statistics Studies. 2022 Oct; 3(2): 31-6. doi: 10.32996/jmss.2022.3.2.3.

[16] Rayalu GM. Utilizing the Box-Jenkins Time Series Model for Predicting Diarrheal Mortality in Kenya.

Turkish Journal of Computer and Mathematics Education (TURCOMAT). 2020 Dec; 11(3): 2465-73. doi: 10.61841/turcomat.v11i3.14247.

[17] Olson KL, Whitley P, Velasco J, LaRue L, Dawson E, Huskey A *et al*. Seasonal and regional influences on alcohol consumption: an analysis of near-real-time urine drug test results in those seeking health care. Drug and Alcohol Dependence. 2021 Oct; 227: 108908. doi: 10.1016/j.drugalcdep.2021.108908.

[18] Mastroleo NR, Barnett NP, Bowers KM. Association between sex, race/ethnicity, season, day of week, and alcohol use and related risks in college student athletes and nonathletes. Journal of American College Health. 2019 Jul; 67(5): 422-32. doi: 10.1080/07448481.2018.1484367.

[19] Hirche M, Haensch J, Lockshin L. Comparing the day temperature and holiday effects on retail sales of alcoholic beverages-a time-series analysis. International Journal of Wine Business Research. 2021 Jan; 33(3): 432-55. doi: 10.1108/IJWBR-07-2020-0035.

[20] Wyper GM, Mackay DF, Fraser C, Lewsey J, Robinson M, Beeston C *et al.* Evaluating the impact of alcohol minimum unit pricing on deaths and hospitalisations in Scotland: a controlled interrupted time series study. The Lancet. 2023 Apr; 401(10385): 1361-70. doi: 10.1016/S0140-6736(23)00497-X.

[21] Shmelev A, Sill AM, Horrigan T, Cunningham SC. Trends and seasonality in hospitalizations for acute alcohol-related and biliary pancreatitis in the USA. Hepatobiliary & Pancreatic Diseases International. 2021 Apr; 20(2): 173-81. doi: 10.1016/j.hbpd.2020.10.003.

Original Article

Unraveling the Mind-Gut Connection: Investigating Anxiety and Depression in Functional Dyspepsia

Ammarah Saeed[1*], Bushra Rabbani[2], Adeel Ahmed[2], Muhammad Kamran[3], Syed Muhammad Zulfiqar Hyder Naqvi[4] and Jameel Ahmed[2]

[1]Department of Medicine, Fazaia Medical College, Islamabad, Pakistan
[2]Department of Medicine, Baqai Medical University, Karachi, Pakistan
[3]Department of Gastroenterology, Fazaia Ruth Pfao Medical College, Karachi, Pakistan
[4]Department of Community Medicine, Baqai Medical University, Karachi, Pakistan

ARTICLE INFO

ABSTRACT

Psychological association with functional dyspepsia underscores the importance of a holistic approach to its management, addressing both physical and psychological aspects of the condition. **Objective:** To determine the relationship of anxiety and depression with severity of dyspepsia. **Methods:** A prospective cross sectional study was carried out in the Endoscopy Unit, Department of Gastroenterology, Baqai Medical Institute. All patients fulfilling the Rome III criteria for functional dyspepsia with normal endoscopy findings were included in the study, Pregnant females, patients with known diabetes, chronic kidney disease, chronic liver disease and known psychiatric illness, history of peptic ulcer disease and use of NSAIDs, steroids or alternative medicine were excluded. Severity of dyspepsia was assessed by Short Form Leeds Dyspepsia Questionnaire (SF-LDQ). Whereas hospital anxiety and depression scale (HADS) was used to assess the psychological factors. **Results:** A total of 223 participants were included in the study. Out of 223 participants, majority 55.6% (124) had moderate dyspepsia, followed by severe dyspepsia 26.9% (60), mild dyspepsia 12.6% (28) and very mild dyspepsia 4.9% (11). Using Hospital Anxiety And Depression Scale (HAD-S), we found that out of 223 participants, 56.5% (126) had moderate to severe anxiety and depression while 29.1% (65) had mild anxiety and depression. **Conclusions:** It was concluded that functional dyspepsia is clearly associated with common psychological disorders like depression and anxiety. Early recognition and timely linkage to care in such cases can considerably improve the health-related quality of life and hence decrease the global burden of this common disorder.

INTRODUCTION

Functional dyspepsia (FD) is the most common gastrointestinal disorder prevalent in people coming to the outpatient department [1]. FD is defined as the presence of one or more dyspeptic symptoms that originate from the gastroduodenal region without any organic, metabolic or systemic disease likely to explain the symptom complex [2]. It has different subtypes with different aetiopathological factors. Two common varieties along with the third variety with overlapping features from both subtypes are identified. Amongst them is the postprandial distress syndrome (PDS) and epigastric pain syndrome (EPS) with a third type carrying features from both.

Functional dyspepsia is considered as a multifactorial disorder. Various factors are involved in its pathophysiology ranging from abnormal gastric motility to increased visceral hypersensitivity while several other factors like life style, *Helicobactor pylori* infection, dietary habits and psychological factors pitch in to make a person more vulnerable to these physiological abnormalities. It is also known that patients with functional dyspepsia have an abnormal response to stress and a gut brain disorder play a vital role in these individuals. Anxiety, depression and somatoform disorders are identified as the most prevalent form of psychological disorders among the patient with

functional dyspepsia. Psychological factors affect the symptom threshold and dyspepsia is the physiological manifestation of psychological distress [3, 4]. Functional dyspepsia is diagnosed via Rome III criteria which consist of a single symptom or more than one symptom of burning in epigastrium, pain in epigastrium, post prandial fullness or early satiety after meals without any evidence of structural disease that is likely to explain symptoms. These symptoms must be chronic occur at least weekly for at least 6 months. According to the criteria the global prevalence is around 8.4% [5, 6]. Although functional dyspepsia is not a life threatening condition, its bothersome symptoms lead the patients to frequent hospital visits, increased consumption of drugs and more absentees from workplace hence affecting their quality of life [7]. Psychological disorders are often overlooked, resulting in sub-optimal psychiatric and medical management [8]. Scientific work has been conducted worldwide to assess the psychological factors associated with functional dyspepsia, however there is very little literature from Pakistan. In Peshawar a hospital based study revealed that the functional dyspepsia was recorded in 89.9% of patients [9]. According to a study majority of patients with functional dyspepsia had underlying psychiatric disorders [10]. Every country has its own demographics and different cultural aspects affect the citizens differently.

The aim of this study was to assess the psychological factors affecting the patients of functional dyspepsia and their effect in a person's day to day life.

METHODS

A prospective cross sectional study carried out in the Endoscopy Unit of Gastroenterology Department of Fatima Hospital at Baqai Medical University, Gadap Town Sindh from December 2021 to April 2024 after the approval of ethics review board of Baqai Medical University on 17th Nov 2021, Ref: BMU-EC/05-2021. All patients coming to the endoscopy suit of gastroenterology department with dyspeptic symptoms who fulfilled the Rome III criteria for functional dyspepsia with no gross abnormality on esophagogastroduodenoscopy (EGD) were included in the study. Pregnant females, patients with known diabetes, chronic kidney disease, chronic liver disease and known psychiatric illness, history of peptic ulcer disease and use of NSAIDs, steroids or alternative medicine were excluded. All patients with a history of abdominal surgery, with the exception of appendectomy, cholecystectomy, or hysterectomy more than 1 year previously were also excluded from the study. Demographic data comprising of age, gender, ethnicity, marital status, education, occupation, employment status, and any addiction were collected after written informed consent. Severity of

dyspepsia was assessed by Short Form Leeds Dyspepsia Questionnaire (SF-LDQ). The SF LDQ has four questions along with one question asking about the most troublesome symptom. Each question has two stems regarding the severity and frequency of dyspepsia during the past two months. SF-LDQ is interpreted as score of 0 'no dyspepsia', score of 1-4 as 'very mid dyspepsia', score of 5-8 as 'mild dyspepsia', score of 9-15 as 'moderate dyspepsia' and score of >15 indicates 'very severe dyspepsia' (Annexure-I)[11]. Patients were assessed for psychological disorders, using the Hospital anxiety and depression scale (HAD) [12]. HADS measures symptoms of anxiety and depression on separate subscales each having seven items. Scoring for each item is on Likert scale ranging from 0-3. The maximum attainable score was 21 for each. A subscale was used to depict them as Normal (0-7), Borderline abnormal (8-10) and as a Case (11-21) for each anxiety and depression separately, with the highest score denoting high level of depression and anxiety (Annexure-II). Using online open epi calculator keeping the prevalence 75.3% with 95% confidence interval and 6% precision, the required sample size was calculated to be 199 participants [13, 14]. All the participants were included using non probability convenient sampling. Data entry and analysis was performed using SPSS version 21.0. Categorical variables were described using frequency and percentages whereas continuous variables were summarized using mean ± standard deviation. Chi-square was used to assess bivariate association between the study variables. The significance level was kept at 0.05.

RESULTS

A total of 223 participants were included in the study with a response rate of 98 %. The mean age of study participants was 35.2 + 9.5 years, 123 (55.2%) of them were females, 155 (69.5%) were married, 89 (39.9%) belonged to Pushtoon ethnicity, 125 (56.1%) had history of addiction, 116 (52%) were literate and 140 (62.8%) were unemployed (Table 1).

Table 1: Demographic Characteristics

Demographic Characteristics (n=223)	Frequency (%)
Age	
Mean ± SD	35.2 + 9.5
Up to 35 Years	129 (57.8)
35 Years or Above	94 (42.2)
Gender	
Male	100 (44.8)
Female	123 (55.2)
Marital Status	
Married	155 (69.5)
Unmarried	68 (30.5)
Employment Status	
Employed	83 (37.2)
Un employed	140 (62.8)

Education	
Literate	116 (52)
Illiterate	107 (48)
Addiction	
Yes	125 (56.1)
No	98 (43.9)
Ethnicity	
Pushtoon	89 (39.9)
Sindhi	68 (30.5)
Others	66 (29.6)

In this study, we categorized participants with dyspepsia on the basis of SF-LDQ score. Out of 223 participants, majority 55.6% (124) had moderate dyspepsia, followed by severe dyspepsia 26.9% (60), mild dyspepsia 12.6% (28) and very mild dyspepsia 4.9% (11) (figure 1).

Severity of Dyspepsia

■ Very Mild dyspepsia ■ Mild dyspepsia ■ Moderate dyspepsia ■ Severe dyspepsia
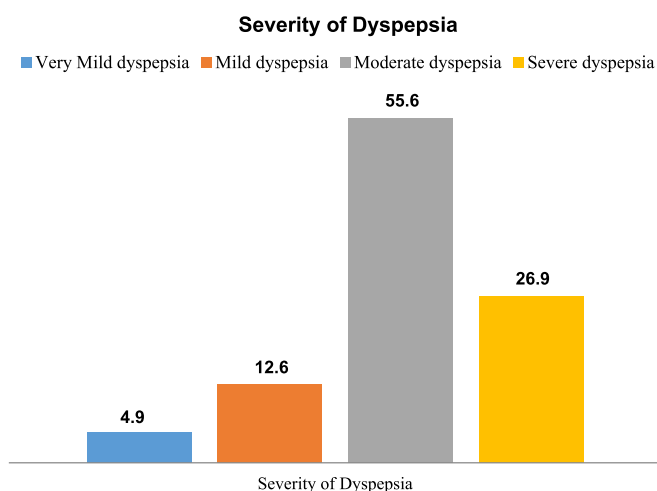
Figure 1: Severity of Dyspepsia

In this study, using HAD-S, we found that out of 223 participants, 56.5% (126) had moderate to severe anxiety and depression while 29.1% (65) had mild anxiety and depression (figure 2).

Anxiety and Depression

■ **Moderate to severe (11-21)** ■ **Mild (8-10)** ■ **None (0-7)**
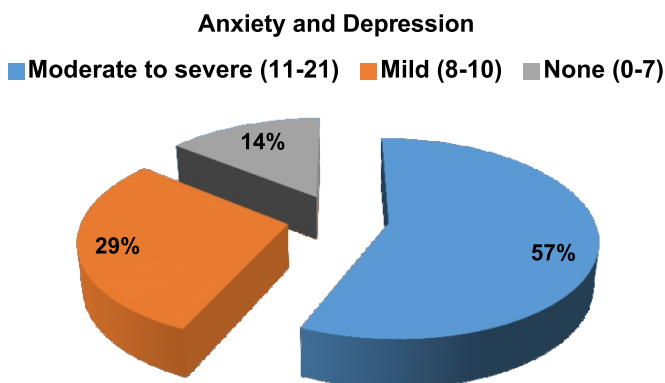
Figure 2: Anxiety and Depression

The study results further revealed that among participant characteristics, only dyspepsia was significantly associated with the presence of anxiety and depression (p=0.001) where (table 2).

Table 2: Association between Participant Characteristics and Presence of Anxiety and Depression

Participant Characteristics (n=223)		Anxiety and Depression				p-Value
		Count (%)				
		Total	None	Mild	Moderate to Severe	
Age	Up to 35 Years	129 (57.8)	22 (9.9)	36 (16.1)	71 (31.8)	0.399
	36 Years or Above	94 (42.2)	10 (4.5)	29 (13)	55 (24.7)	
Gender	Male	100 (44.8)	16 (7.2)	31 (13.9)	53 (23.8)	0.622
	Female	123 (55.2)	16 (7.2)	34 (15.2)	73 (32.7)	
Marital Status	Married	155 (69.5)	23 (10.3)	45 (20.2)	87 (39)	0.951
	Unmarried	68 (30.5)	9 (4)	20 (9)	39 (17.5)	
Education	Literate	116 (52)	14 (6.3)	32 (14.3)	61 (27.4)	0.870
	Illiterate	107 (48)	18 (8.1)	33 (14.8)	65 (29.1)	
Employment Status	Employed	83 (37.2)	13 (5.8)	28 (12.6)	42 (18.8)	0.381
	Unemployed	140 (62.8)	19 (8.5)	37 (16.6)	84 (37.7)	
Addiction	Yes	125 (56.1)	17 (7.6)	43 (19.3)	65 (29.1)	0.148
	No	98 (43.9)	15 (6.7)	22 (9.9)	61 (27.4)	
Ethnicity	Pushtoon	89 (39.9)	15 (6.7)	23 (10.3)	51 (22.9)	0.740
	Sindhi	68 (30.5)	7 (3.1)	21 (9.4)	40 (17.9)	
	Others	66 (29.6)	10 (4.5)	21 (9.4)	35 (15.7)	
Dyspepsia	Very Mild	11 (4.9)	3 (1.3)	6 (2.7)	2 (0.9)	0.001
	Mild	28 (12.6)	7 (3.1)	10 (4.5)	11 (4.9)	
	Moderate	124 (55.6)	20 (9)	37 (16.6)	67 (30)	
	Severe	60 (26.9)	2 (0.9)	12 (5.4)	46 (20.6)	

DISCUSSION

Functional dyspepsia (FD) is a commonly prevailing clinical condition, frequently requiring clinic visits [2]. Common symptoms of FD include epigastric pain and/ or burning, and early satiety. It has a fluctuating course, with patients being asymptomatic followed by periods of symptoms relapse. Being a non-fatal disorder, FD is not associated with increased mortality [2, 3]. However, as with most chronic illnesses, FD has a significant impact on the health related quality of life (HRQOL) of most individuals suffering from this condition, as shown in a meta-analysis [13]. Pathophysiology of FD is multi-factorial. Dysfunction of the intestinal barrier, gut motility alterations, visceral hypersensitivity and dysbiosis of gut microbiomes can lead to FD [16]. However, currently available evidence strongly suggests that alterations of the gut-brain axis a major contributory factor in the development of FD and other forms of functional gastrointestinal disorders (FGID) [17]. The psychosocial impact of FD is considerable. Robust data from Asian countries showed that patients suffering from FD were more likely to display physical, social and emotional dysfunction as opposed to their healthy counterparts [18]. We showed that majority of patients suffering from FD belonged to younger age group, which was < 35 years in our study (57.8%). Other studies done regionally also reported similar results [19, 20]. However, when we analyze international data, we notice relatively higher age group of patients presenting with FD [21, 22]. A

significant number of patients included in our study were not literate and were unemployed (48% and 62.8% respectively), reflecting the fact that our younger population suffers more from socio-economic challenges like unemployment, illiteracy etc. Majority of the patients in our study were females (55.2%), supporting the concept that women with FGID are more likely to have concomitant anxiety and depressive symptoms [23]. Another observation in our study was the dominance of those patients who had some form of addictions (56.1%), again strengthening the notion that population with addiction frequently suffer from underlying psychiatric disorder. Since the population of Gadap Town (where our study was conducted) is multi-ethnic, our sample size included patients of various ethnicities and backgrounds. However, the predominant ethnic group in our study was Pushtoon (39.9%) followed by Sindhi (30.5%). According to the SF-LDQ questionnaire, majority of patients in our study were having FD of moderate intensity. This was in contrast to a recent study from Saudi Arabia, which reported mild dyspepsia as the most common type according to the SF-LDQ questionnaire [11]. This variation can be explained by the difference in dietary patterns and other socio-economic factors between the Saudi and Pakistani population. Additionally, the level of literacy was also higher in patients in the Saudi Arabian study as compared to our recruited individuals, another aspect that seems to be a potentially protective feature against FD [24]. The Hospital Anxiety and Depression Scale (HAD-S) is a simple, reliable and easy to perform tool to measure the level of anxiety and depression, helping physicians to classify those patients who need specialized psychiatric care. This scale has not only been used successfully in Pakistani population, but has also been validated in regional languages of Pakistan [25, 26]. The association between FD and psychosocial dynamics has been studied in the past. Symptoms of FD are thought to be a cause of psychiatric illnesses as low-grade inflammation of the gut can elicit a cytokine response, which is believed to play an imperative part in kicking off psychological stress in patients with FD [27]. However, this association is far more complex. Many studies showed that where females are more likely to suffer from FD [28, 29]. Men suffered more from psychological distress [30]. In the present study, we found that a significantly high number of patients with FD had abnormal HAD-S (56.5%), which indicated moderate to severe anxiety and depression. This association was statistically significant when we compared mild, moderate and severe dyspepsia with the presence of any severity of anxiety and depression. Another study from Pakistan reported moderate to severe depression to be prevalent (49.5%) among a study population of 400 dyspeptic individuals, using the same scale [31, 32]. A similar study from Iran reported even higher prevalence (65%) of these psychosocial disorders among patients with FD. Comparable results were shown in a placebo-controlled trial of 107 patients suffering from FD [30]. Our study was a single center study and this was our major limitation. However, in our opinion, the multi-ethnic population of Gadap town and the prospective nature of this study makes our data generalizable and robust. Further prospective studies with bigger sample size are needed to consolidate the findings of this study, especially in an underprivileged population of a third world country like ours, which can help identify the gaps in the management of FGIDs.

CONCLUSIONS

Functional dyspepsia is clearly associated with common psychological disorders like depression and anxiety. Our data also revealed that majority of the study participants (56.5%) suffered from moderate to severe anxiety and depression, with dyspepsia being significantly associated with the presence of some form of anxiety and depression (p=0.001). Therefore, early recognition and timely linkage to care in such cases can considerably improve the health-related quality of life and hence decrease the global burden of this common disorder.

Authors Contribution

Conceptualization: AS, JA
Methodology: BR, AA, SMZHN, JM
Formal analysis: AS, BR, AA, MK, SMZHN,
Writing-review and editing: AS

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

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

REFERENCES

[1]   Von Wulffen M, Talley NJ, Hammer J, McMaster J, Rich G, Shah A *et al*. Overlap of irritable bowel syndrome and functional dyspepsia in the clinical setting: prevalence and risk factors. Digestive Diseases and Sciences. 2019 Feb; 64: 480-6. doi: 10.1007/s10620-018-5343-6.

[2]   Lacy B, DiBaise J, Pimentel M, Ford A. Essential medical disorders of the stomach and small intestine. Switzerland. Springer International Publishing. 2019. doi: 10.1007/978-3-030-01117-8.

[3]   Ford AC, Mahadeva S, Carbone MF, Lacy BE, Talley NJ. Functional dyspepsia. The Lancet. 2020 Nov; 396(10263): 1689-702. doi: 10.1016/S0140-6736(20)30469-4

[4] Mounsey A, Barzin A, Rietz A. Functional dyspepsia: evaluation and management. American Family Physician. 2020 Jan; 101(2): 84-8.

[5] Carbone F, Vanuytsel T, Tack J. Analysis of postprandial symptom patterns in subgroups of patients with Rome III or Rome IV functional dyspepsia. Clinical Gastroenterology and Hepatology. 2020 Apr; 18(4): 838-46. doi: 10.1016/j.cgh.2019.07.053.

[6] Lee K, Kwon CI, Yeniova AÖ, Koyanagi A, Jacob L, Smith L *et al.* Global prevalence of functional dyspepsia according to Rome criteria, 1990–2020: a systematic review and meta-analysis. Scientific Reports. 2024 Feb; 14(1): 4172. doi: 10.1038/s41598-024-54716-3.

[7] Goyal O, Goyal P, Kishore H, Kaur J, Kumar P, Sood A. Quality of life in Indian patients with functional dyspepsia: Translation and validation of the Hindi version of Short-Form Nepean Dyspepsia Index. Indian Journal of Gastroenterology. 2022 Aug; 41(4): 378-88. https://doi.org/10.1007/s12664-021-01233-0

[8] Kovács DB, Szekely A, Hubai AG, Palsson O. Prevalence, epidemiology and associated healthcare burden of Rome IV irritable bowel syndrome and functional dyspepsia in the adult population of Gibraltar. BMJ Open Gastroenterology. 2022 Aug; 9(1): e000979. doi: 10.1136/bmjgast-2022-000979.

[9] Qayyum W, Anwar MN, Iftikhar M, Khan MF, Jawad M, Saeed L. Endoscopic findings in patients with refractory dyspepsia at A Tertiary Care Hospital in Peshawar, KPK Province, Pakistan. The Professional Medical Journal. 2021 Apr; 28(04): 585-91. doi: 10.29309/TPMJ/2021.28.04.5824.

[10] Yao X, Yang Y, Zhang S, Shi Y, Zhang Q, Wang Y. The impact of overlapping functional dyspepsia, belching disorders and functional heartburn on anxiety, depression and quality of life of Chinese patients with irritable bowel syndrome. BMC Gastroenterology. 2020 Dec; 20: 1-8. doi: 10.1186/s12876-020-01357-1.

[11] Alwhaibi A, Alghadeer S, Bablghaith S, Wajid S, Alrabiah Z, Alhossan A *et al.* Prevalence and severity of dyspepsia in Saudi Arabia: A survey-based study. Saudi Pharmaceutical Journal. 2020 Sep; 28(9): 1062-7. doi: 10.1016/j.jsps.2020.07.006.

[12] Yue T, Li Q, Wang R, Liu Z, Guo M, Bai F *et al.* Comparison of Hospital Anxiety and Depression Scale (HADS) and Zung Self-Rating Anxiety/Depression Scale (SAS/SDS) in evaluating anxiety and depression in patients with psoriatic arthritis. Dermatology. 2020 Aug; 236(2): 170-8. doi: 10.1159/000498848.

[13] OpenEpi. Open Source Epidemiologic Statistics for Public Health. [Last cited: 22nd May 2024]. Available at: https://www.openepi.com/Menu/OE_Menu.htm.

[14] Hassan MK, Haq MU, Babar AN, Khattak AK. Frequency of Depression in Functional Dyspepsia Patients Presenting to a Tertiary Care Hospital. Journal of Postgraduate Medical Institute. 2016 Jul; 30(3).

[15] Rodrigues DM, Motomura DI, Tripp DA, Beyak MJ. Are psychological interventions effective in treating functional dyspepsia? A systematic review and meta-analysis. Journal of Gastroenterology and Hepatology. 2021 Aug; 36(8): 2047-57. doi: 10.1111/jgh.15566.

[16] Tziatzios G, Gkolfakis P, Papanikolaou IS, Mathur R, Pimentel M, Giamarellos-Bourboulis EJ, Triantafyllou K. Gut microbiota dysbiosis in functional dyspepsia. Microorganisms. 2020 May; 8(5): 691. doi: 10.3390/microorganisms8050691

[17] Wauters L, Li H, Talley NJ. Disruption of the Microbiota-Gut-Brain Axis in Functional Dyspepsia and Gastroparesis: Mechanisms and Clinical Implications. Frontiers in Neuroscience. 2022 Jul; 16: 941810. doi: 10.3389/fnins.2022.941810

[18] Egbo O, Omuemu C, Okeke E, Egbo OH, Mokogwu N. Health-related quality of life in patients with dyspepsia presenting at the University of Benin Teaching Hospital, Benin City, South-South Nigeria: a cross-sectional study. The Pan African Medical Journal. 2024 Mar; 47(107). doi: 10.11604/pamj.2024.47.107.36151.

[19] Yamamoto Y, Furukawa S, Watanabe J, Kato A, Kusumoto K, Miyake T *et al.* Association between eating behavior, frequency of meals, and functional dyspepsia in young Japanese population. Journal of Neurogastroenterology and Motility. 2022 Jul; 28(3): 418. doi: 10.5056/jnm21146.

[20] Bai P, Bano S, Kumar S, Sachdev P, Ali A, Dembra P, Bachani P, Shahid S, Jamil A, Rizwan A. Gastroesophageal reflux disease in the young population and its correlation with anxiety and depression. Cureus. 2021 May; 13(5). doi: 10.7759/cureus.15289.

[21] Carbone F, De Buysscher R, Van den Houte K, Schol J, Goelen N, Tack J. Relationship between gastric emptying rate and simultaneously assessed symptoms in functional dyspepsia. Clinical Gastroenterology and Hepatology. 2022 Mar; 20(3): e429-37. doi: 10.1016/j.cgh.2021.03.023

[22] Chuah KH, Cheong SY, Lim SZ, Mahadeva S. Functional dyspepsia leads to more healthcare utilization in secondary care compared with other

functional gastrointestinal disorders. Journal of Digestive Diseases. 2022 Feb; 23(2): 111-7. Doi: 10.1111/1751-2980.13082

[23] Shams N, Usmani F, Andaleeb H, Niaz F, Meraj L, Munir N. Association Of Functional Dyspepsia With Depression; Gut-Brain Axis And Mental Health. Journal of Rawalpindi Medical College. 2024 Mar; 28(1). doi: 10.37939/jrmc.v28i1.2427

[24] Nirwan JS, Hasan SS, Babar ZU, Conway BR, Ghori MU. Global prevalence and risk factors of gastro-oesophageal reflux disease (GORD): systematic review with meta-analysis. Scientific Reports. 2020 Apr; 10(1): 5814. doi: 10.1038/s41598-020-62795-1.

[25] Waqas A, Aedma KK, Tariq M, Meraj H, Naveed S. Validity and reliability of the Urdu version of the Hospital Anxiety and Depression Scale for assessing antenatal anxiety and depression in Pakistan. Asian Journal of Psychiatry. 2019 Oct; 45: 20-5. doi: 10.1016/j.ajp.2019.08.008.

[26] Irfan M, Sethi MR, Khan I, Awan NR, Naz F, Saleem U *et al.* Translation and validation in Pashto (1): Hospital anxiety and depression scale. Journal of Postgraduate Medical Institute. 2017 Dec; 31(4).

[27] Esterita T, Dewi S, Suryatenggara FG, Glenardi G. Association of functional dyspepsia with depression and anxiety: a systematic review. Journal of Gastrointestinal and Liver Diseases. 2021 Jun; 30(2): 259-66. doi: 10.15403/jgld-3325.

[28] Nam K, Kim N, Song HJ, Baik GH, Choi SC, Kim HJ *et al.* Gender difference in the overlap of irritable bowel syndrome and functional dyspepsia: a prospective nationwide multicenter study in Korea. Journal of Gastroenterology. 2021 Jun; 56: 537-46. doi: 1007/s00535-021-01775-2

[29] Abid S, Rehman H, Awan S, Artani A, Siddiqui I. Epidemiology of functional gastrointestinal disorders using ROME III adult questionnaire, a population based cross sectional study in Karachi—Pakistan. PLOS One. 2022 Jun; 17(6): e0268403. doi: 10.1371/journal.pone.0268403.

[30] Adibi P, Keshteli AH, Daghaghzadeh H, Roohafza H, Pournaghshband N, Afshar H. Association of anxiety, depression, and psychological distress in people with and without functional dyspepsia. Advanced Biomedical Research. 2016 Jan; 5(1): 195. doi: 10.4103/2277-9175.190936.

[31] Alam L, Naqvi M, Saeed F. Relation of Functional Dyspepsia with anxiety and depression and its impact on the quality of life of patients. Pakistan Armed Forces Medical Journal. 2019 Apr; 69(2): 230-35.

[32] Tabish MH, Nawab A, Javaid U, Rehman A, Naeem A, Javaid M. Prevalence of Anxiety and Depression in Patients of Functional Dyspepsia and their Association with Demographic Features. Age (years).;30(80):54-0.

Original Article

Frequency of Anemia among Patients of Rheumatoid Arthritis: Cross Sectional Study

Hira Aslam[1], Amna Shoukat[2], Hafiz Muhammad Matloob[3*], Yumna Athar[2], Syeda Azka Waqar[2] and Sadaf Inayat[2]

[1]Department of Medicine, Capital Development Authority Hospital, Islamabad, Pakistan
[2]Department of Hematology, Shaikh Zayed Hospital, Lahore, Pakistan
[3]Department of Hematology, Mohi-ud-Din Islamic Medical College, Mirpur, Pakistan

ARTICLE INFO

ABSTRACT

Anemia of inflammation is the common manifestation of chronic inflammatory diseases like rheumatoid arthritis. There is a lack of local data regarding this heath issue so we conducted this study order to assess the frequency of anemia among RA patients. Our results will help clinicians to manage anemia actively with chronic inflammatory disorders in our clinical setups. **Objective:** To evaluate the frequency of anemia of inflammation in rheumatoid arthritis patients. **Methods:** Both male and female patients having age 40-70 years with confirmed rheumatoid arthritis were enrolled. Patients with history of any previous blood loss or any co-morbidities like CLD, CRF and thalassemia were ruled out. Blood sample drawn from each patient was sent for laboratory measurement of hemoglobin levels thus indicating the presence or absence of anemia. **Results:** Mean age was 50.85 ± 9.07 years. Out of the 79 patients, 63 (79.75%) were female and 16 (20.25%) were females. Frequency of anemia in rheumatoid arthritis was found in 64 (81.01%) patients, whereas there was no anemia in 15 (18.99%) patients. **Conclusions:** It was concluded that anemia is a common disorder and its frequency is very high among patients of rheumatoid arthritis.

INTRODUCTION

Rheumatoid arthritis is an inflammatory autoimmune disease that involves many joints of body. According to an estimate this disease affects about 1% of the adult population globally [1]. Joints usually involve wrists, hand and elbows symmetrically. Patho-physiology of disease involved hyperplasia of synovial fibroblasts that cause bone and joint destruction [2]. As this is an autoimmune disease, cytokines and other mediators of inflammation play vital role in developing systemic manifestations of this disease [3]. Literature review revealed that globally, its annual incidence is approximately 3 cases per 10,000 populations with prevalence rate is approximately 1% [4]. Various factors increase its incidence like aging, smoking, alcohol abuse, trauma and medications. This disease is less prevalent among blacks due to different genetic makeup in comparison to other races [5]. However, family members of victim are at high risk of developing disease due to same genetics. Hence, genetic factors and immune system abnormalities contribute to disease propagation [2]. Sex hormones may play a role in RA, as evidenced by the disproportionate number of females with this disease, its amelioration during pregnancy, its recurrence in the early postpartum period, and its reduced incidence in women using oral contraceptives. Hyperprolactinemia may be a risk factor for RA [6]. Anemia of inflammation is the common manifestation of chronic inflammatory diseases like rheumatoid arthritis. Literature review revealed that anemia of inflammation and iron deficiency anemia in combination cause extreme breathlessness among RA patients. Main pathology that cause iron

deficiency anemia involved changes in iron metabolism with reduced formation of iron carrying protein like serum ferritin and storage protein serum hepcidin [7]. As a result, the pro-inflammatory cytokines, primarily interleukin-6 are released thus causing inflammation of involved joints [4]. Previous literature review has shown that most common extra-articular manifestation is low hemoglobin levels among patients of RA [8, 9]. As previous studies have shown controversy and variation in frequency of anemia in rheumatoid arthritis in different populations.

The objective of current study was to evaluate the frequency of anemia of inflammation in rheumatoid arthritis patients. Our results will provide local magnitude as well as help to design guidelines for early recognition and management of this condition.

METHODS

This cross-sectional study was conducted at medicine department CDA Hospital Islamabad for six months from 1st September 2017 to 31th March 2018 after approval of synopsis by research evaluation unit of CPSP vide Ref No. CPSP/REU/MED-2015-253-10187 dated 07.03.2019. Total of 79 patients of rheumatoid arthritis through non-probability, consecutive sampling having age 40-70 years and both genders were included. Sample size was determined by the formula n= Z^2 P(1-P)/d^2. Where z= 1.96, P= 28.8, and d= 10%. Patients with any previous blood loss, CLD, CRF and thalassemia were excluded [11]. Blood sample drawn from each patient was sent for laboratory measurement of hemoglobin levels thus indicating the presence or absence of anemia. Hemoglobin levels of 10.0 g/dL or lower indicate anemia [10]. All information was recorded in performa. SPSS version 20.0 analyzed the data. Mean ± SD was calculated for age and duration of RA. Frequency and percentage was calculated for quantitative variables like gender, socioeconomic status. Post-stratification Chi square was applied with p-value of < 0.05 taken as significant.

RESULTS

Baseline parameters like age and duration of disease was shown in table I. Mean duration of RA was 95.82 ± 77.42 months.

Table 1: Baseline Parameter among Enrolled Patients

Variables	Groups	Percentage (%)	Mean + SD
Age (Years)	40-55	72.15	50.85 ± 9.07
	56-70	27.85	
Duration of Disease (Months)	≤36	27.85	95.82 ± 77.42
	>36	72.15	

Out of the 79 patients, 63 (79.75%) were female and 16 (20.25%) were females (Figure 1).
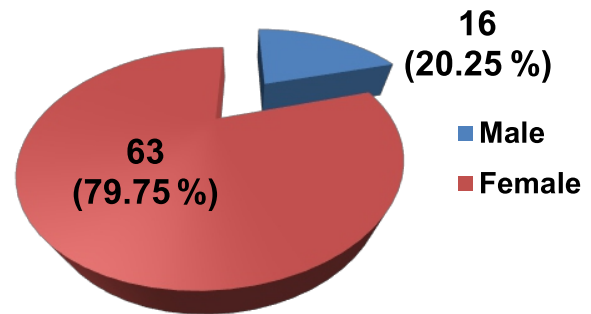
Figure 1: Gender Distribution of Patients

Frequency of anemia in rheumatoid arthritis was found in 64 (81.01%) patients as shown in figure 2.
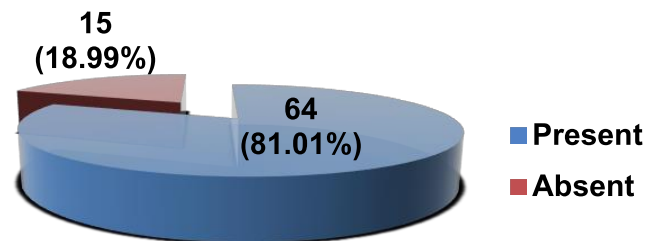
Figure 2: Distribution of Patients with Anemia (n=79)

Distribution of patients with other confounding variables was shown in table-2. Majority of the patients were employed (56.96%) but belong to low socioeconomic status having income less than 50k (92% roughly).

Table 2: Confounding Variables among Patients

Confounding Variables		Percentage (%)
Socioeconomic Status	≤10k	46.84
	20-50k	45.57
	>50k	7.59
Occupation	Employed	56.96
	Unemployed	2.53
	Laborer	40.51

Stratification of anemia with respect to age, duration of RA and education status was shown in table 3. Significant difference was seen among patients having anemia with respect to duration of disease with p-value of 0.04 as shown in table 3.

Table 3: Stratification of Anemia with Respect to Age, Duration of Rheumatoid Arthritis and Education Status

Age (Years)	Anemia (n)		p-Value
	Present	Absent	
40-55	46	11	0.910
56-70	18	04	
Education Status			
Uneducated	33	08	0.902
Educated	31	07	
Duration of Disease			
≤36	21	01	0.042*
>36	43	14	

*Statistically significant

DISCUSSION

Rheumatoid arthritis is an inflammatory autoimmune disease that involves many joints of body. According to an estimate this disease affects about 1% of the adult population globally [1]. Joints usually involve wrists, hand and elbows symmetrically. Patho-physiology of disease involved hyperplasia of synovial fibroblasts that cause bone and joint destruction [2]. As this is an autoimmune disease, cytokines and other mediators of inflammation play vital role in developing systemic manifestations of this disease [3, 12]. According to many previous studies, anemia prevalence among RA patients ranges from 30-70% among different populations [11, 13]. Our results showed that incidence of anemia among our enrolled patients was 81% thus our results were in line with many previous studies. Previous many studies showed that iron deficiency anemia was on top followed by anemia of chronic disease. Iron deficiency accounted more than 65% cases of anemia among RA patients in many different studies [13, 14]. This prevalence was high among developing countries of overall anemia of Asia like India, SriLanka, Pakistan and Bangladesh. This issue has with a negative impact on both RA symptoms and quality of life [11]. Anemia is associated with a negative impact on both RA symptoms and quality of life [15, 16]. Low erythropoietin levels and a diminished response to erythropoietin have also been shown to contribute to anemia in Rain addition to the role of reticulocyte hemoglobin in causing inflammatory disorders like RA. These observations have led to the use of erythropoietin, iron supplements resulting in improvement of the anemia in some patients [17, 18]. Our results showed that iron deficiency anemia was in majority of our patients. This may be due to low income and lack of awareness thus our results supported findings of previous studies. Present study determined the frequency of anemia in rheumatoid arthritis. Age range in my study was from 40 to 70 years with mean age of 50.85 ± 9.07 years. Majority of the patients 57 (72.15%) were between 40 to 55 years of age. Out of the 79 patients, 63 (79.75%) were female and 16 (20.25%) were females with male to male ratio of 1:3.9. Frequency of anemia in rheumatoid arthritis was found in 64 (81.01%) patients, whereas there was no anemia in 15 (18.99%) patients. In patients with Rheumatoid Arthritis (RA), the prevalence of anemia ranges from 30 to 70 percent [7]. One previous study demonstrated that duration of disease has significant impact of developing anemia. [19]. Results in present study showed significant p-value of 0.04 when duration of disease was stratified for anemia table-3. Thus our results supported above mentioned study. Anemia which is the commonest extra articular manifestation of RA has traditionally not been considered a major problem in RA patients by the vast majority of physicians. This is due to lack literature on its prevalence and effect on various clinical and functional outcomes, including morbidity, mortality, and quality of life [20, 21]. Thus more studies with bigger sample size, duration of study, genetic workup, inflammatory markers and multi-centered research is highly recommended to see its true magnitude of disease.

CONCLUSIONS

This study concluded that frequency of anemia in rheumatoid arthritis is very high (81.01%) patients, whereas there was no anemia in 15 (18.99%) and also reduced level of hemoglobin is associated with duration of disease. So, we recommend that early recognition and management of this condition should be done in rheumatoid arthritis patients in order to improve the quality of life of these particular patients.

Authors Contribution

Conceptualization: HA, AS
Methodology: SAW, SI
Formal analysis: HA, AS, HMM, YA
Writing, review and editing: HMM, YA

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

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

REFERENCES

[1]   Chen YF, Xu SQ, Xu YC, Li WJ, Chen KM, Cai J *et al.* Inflammatory anemia may be an indicator for predicting disease activity and structural damage in Chinese patients with rheumatoid arthritis. Clinical Rheumatology. 2020 Jun; 39: 1737-45.

[2]   Conforti A, Di Cola I, Pavlych V, Ruscitti P, Berardicurti O, Ursini F *et al.* Beyond the joints, the extra-articular manifestations in rheumatoid arthritis. Autoimmunity Reviews. 2021 Feb; 20(2): 102735. doi: 10.1016/j.autrev.2020.102735.

[3]   Khan S, Mohan K, Muzammil S, Alam MA, Khayyam KU. Current Prospects in Rheumatoid Arthritis: Pathophysiology, Genetics, and Treatments. Recent Advances in Anti-Infective Drug Discovery. 2023 Apr. doi: 10.2174/2772434418666230406083149.

[4]   Deane KD and Holers VM. Rheumatoid Arthritis Pathogenesis, Prediction, and Prevention: An Emerging Paradigm Shift. Arthritis & Rheumatology. 2021 Feb; 73(2):181-193.

[5]   Haville S and Deane KD. Pre-RA: Can early diagnosis lead to prevention? Best Practice & Research Clinical

Rheumatology. 2022 Mar; 36(1):101737. doi: 10.1016/j.berh.2021.101737

[6] Raine C and Giles I. What is the impact of sex hormones on the pathogenesis of rheumatoid arthritis? Frontiers in Medicine (Lausanne). 2022 Jul; 9: 909879. doi: 10.3389/fmed.2022.909879.

[7] Sun Z, Shao H, Liu H, Ma L. Anemia in elderly rheumatoid arthritis patients: a cohort study. Archives of Medical Science: AMS. 2024; 20(2): 457.

[8] Wilson A, Yu HT, Goodnough LT, Nissenson AR. Prevalence and outcomes of anemia in rheumatoid arthritis: a systematic review of the literature. The American Journal of Medicine. 2004 Apr; 116(7): 50-7. doi: 10.1016/j.amjmed.2003.12.012.

[9] Mitrović J, Hrkač S, Tečer J, Golob M, Ljilja Posavec A, Kolar Mitrović H et al. Pathogenesis of Extraarticular Manifestations in Rheumatoid Arthritis-A Comprehensive Review. Biomedicines. 2023 Apr; 11(5): 1262. doi: 10.3390/biomedicines11051262.

[10] Bari MA, Sutradhar SR, Sarker CN, Ahmed S, Miah AH, Alam MK et al. Assessment of anaemia in patients with rheumatoid arthritis. Mymensingh Medical Journal. 2013 Apr; 22(2): 248-54.

[11] Hajar TL, Rostom S, Hari A, Lahlou R, Bahiri R, Abouqal R et al. Prevalence of anemia and its association with parameters of rheumatoid arthritis patients: a study from the Moroccan quest-RA data. Journal of Palliative Care and Medicine. 2015; 5(221): 2. doi: 10.4172/2165-7386.1000221.

[12] Petrovská N, Prajzlerová K, Vencovský J, Šenolt L, Filková M. The pre-clinical phase of rheumatoid arthritis: from risk factors to prevention of arthritis. Autoimmunity Reviews. 2021 May; 20(5): 102797.

[13] Barton A and Worthington J. Genetic susceptibility to rheumatoid arthritis: an emerging picture. Arthritis Care and Research. 2009; 61(10): 1441-6. doi: 10.1002/art.24672.

[14] Chen Y, Xu W, Yang H, Shao M, Xu S, Deng J et al. Serum levels of hepcidin in rheumatoid arthritis and its correlation with disease activity and anemia: a meta-analysis. Immunological investigations. 2021 Feb; 50(2-3): 243-58.

[15] Möller B, Scherer A, Förger F, Villiger PM, Finckh A, Swiss Clinical Quality Management Program for Rheumatic Diseases. Anaemia may add information to standardised disease activity assessment to predict radiographic damage in rheumatoid arthritis: a prospective cohort study. Annals of the Rheumatic Diseases. 2014 Apr; 73(4): 691-6. doi: 10.1136/annrheumdis-2012-202709.

[16] Adamson JW. Iron deficiency and other hypoproliferative anemias. Harrison's Principles of Internal Medicine. 2008: 628-34.

[17] Boyd HK and Lappin TR. Erythropoietin deficiency in the anaemia of chronic disorders. European Journal of Haematology. 1991 Apr; 46(4): 198-201. doi: 10.1111/j.1600-0609.1991.tb00540.x.

[18] Singh BG, Duggal L, Jain N, Chaturvedi V, Patel J, Kotwal J. Evaluation of reticulocyte hemoglobin for assessment of anemia in rheumatological disorders. International Journal of Rheumatic Diseases. 2019 May; 22(5): 815-25.

[19] GBD 2021 Anaemia Collaborators. Prevalence, years lived with disability, and trends in anaemia burden by severity and cause, 1990–2021: findings from the Global Burden of Disease Study 2021. The Lancet Haematology. 2023 Sep; 10(9): e713-34.

[20] Pawłocik W, Wojtala L, Pawlak W, Szymańska J, Możdżyńska A, Musiał L et al. Juvenile idiopathic arthritis-classification and methods of treatment. Journal of Education, Health and Sport. 2023 Apr; 18(1): 76-88. doi: 10.12775/JEHS.2023.18.01.009.

[21] Maranini B, Bortoluzzi A, Silvagni E, Govoni M. Focus on sex and gender: what we need to know in the management of rheumatoid arthritis. Journal of Personalized Medicine. 2022 Mar; 12(3): 499.

Original Article

Evaluation of Risk Factors Associated with Severe Suicide Attempts among Individuals Presenting at the Emergency Department

Ijaz Aziz[1]*, Aftab Alam Tanoli[2], Faqirullah[3], Abdul Samad[4], Aisha Rasheed[4] and Nadia Aslam[4]

[1]Department of Forensic Medicine, Makran Medical College, Turbat, Pakistan
[2]Department of Forensic Medicine, Loralai Medical College, Loralai, Pakistan
[3]Department of Forensic Medicine and Toxicology, Northwest School of Medicine, Peshawar, Pakistan
[4]Department of Forensic Medicine and Toxicology, Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan

ARTICLE INFO

ABSTRACT

Severe suicide attempts represent critical incidents characterized by high lethality or medical acuity, posing significant risks of morbidity and mortality. **Objective:** To assess the risk factors linked to severe suicide attempts among those presenting in the Emergency Department. **Methods:** The cross-sectional study took place at the Department of Forensic Medicine, Makran Medical College, Turbat, Pakistan covering the period from 21 December 2023 to 21 March 2024. The study included 90 patients aged 18 years or older who were admitted to the ED with a documented suicide attempt. Variables related to demographic characteristics, clinical presentations, substance use history, and details of the suicide attempt. Collected data were processed and analyzed using IBM SPSS, version 27.0. **Results:** The majority of participants were female (56.7%), with a mean age of 31.01 ± 12.42 years. Major depressive disorder was the most prevalent (33.3%), followed by anxiety disorder (18.9%). Other conditions included abuse of narcotics (6.7%), schizophrenia (4.4%), and a history of previous suicide attempts (1.1%). The most frequently cited reasons were psychiatric illnesses (n=28, 31.1%) and family problems (n=26, 28.9%), followed by financial problems (13.3%) and romantic relationship issues (6.7%). In the study cases, suicide attempts mostly occurred between 6 am to 12 pm (38.9%) and 12 pm to 6 pm (34.4%). The majority of patients were hospitalized (61.1%). **Conclusions:** It was concluded that the urgent need for targeted suicide prevention initiatives, with major depressive disorder identified in 33.3% and drug poisoning as prevalent in 40.0% of suicide attempts.

INTRODUCTION

Suicide, a profoundly complex and tragic phenomenon, involves intentionally ending one's own life [1]. Suicide claims approximately 800,000 lives annually worldwide, with rates varying across regions and demographics. Globally, it ranks as the second most common cause of death among individuals aged 15-29 years [2, 3]. Unlike completed suicides, suicide attempts involve deliberate self-harm with non-fatal outcomes. While these attempts may not result in death, they carry significant physical, emotional, and societal ramifications [4, 5]. Suicide attempts are frequently preceded by overwhelming psychological distress, including but not limited to depression, anxiety, trauma, substance abuse, and psychotic disorders. Individuals experiencing intense emotional pain or hopelessness may perceive suicide as the only means of escape from their suffering [6]. Additionally, a history of earlier attempts of suicide is common prognosticators of future suicidal actions, underscoring the need for targeted intervention and support for at-risk individuals [7]. Contact with the emergency department (ED) provides a chance to proactively address and prevent suicide attempts and fatalities. In order to effectively prevent suicidal behaviour, it is imperative for EDs to implement strong interventions, thus establishing themselves as a vital component of the suicide prevention continuum [8]. Severe suicide

attempts, marked by either high lethality or acute medical urgency, require specific attention owing to their increased likelihood of unfavorable consequences [9]. In severe suicide attempts, prevalent risk factors include mental health disorders such as depression (60-70%), substance abuse (30-40% alcohol, 20-30% drugs), previous suicide attempts (20-40%), psychosocial stressors like relationship difficulties (40-50%), and access to means such as firearms (50-60%) [10]. Despite the critical importance of identifying and addressing risk factors associated with severe suicide attempts, limited research has focused specifically on this population within the ED setting.

This study sought to address this gap by systematically evaluating the risk factors associated with severe attempts of suicide in persons presenting at the ED. This study contributed novel insights into the risk factors for severe suicide attempts among Emergency Department patients, addressing a dearth of literature on this topic. This study aimed to fill a critical gap in research within the context of Pakistan, offering context-specific findings to inform targeted interventions and suicide prevention efforts in the region.

METHODS

A cross-sectional study took place at the Department of Forensic Medicine, Makran Medical College, Turbat, Pakistan covering the period from 21 December 2023 to 21 March 2024. This study adhered to the principles set forth in the Declaration of Helsinki and obtained approval from the Institutional Review Board (Reference number: MMC/ERC/115/2023, dated: 20th December 2023). Patient confidentiality was strictly maintained throughout the study, and all data were anonymized prior to analysis. The sample size calculation was done using WHO calculator (www.openepi.com) and 90 sample size was determined using a 95% confidence level, 5% margin of error, and assuming a prevalence of severe suicide attempts of 17.2% [11]. The study included 90 patients presenting at the Emergency Department (ED) following a suicide attempt aged 18 years or individuals of advanced age who were admitted to the Emergency Department (ED) with a documented suicide attempt. Patients with incomplete medical records and patients presenting with accidental injuries or self-harm without suicidal intent were excluded. Data were collected using a standardized data collection form after informed consent from the patients. Variables of interest included demographic characteristics, clinical presentations, psychiatric diagnoses, substance use history, psychosocial stressors, and details of the suicide attempt. The primary outcome measure was the severity of the suicide attempt, classified as severe or non-severe based on criteria such as lethality of method, medical acuity, and need for intensive medical intervention. The

data collected underwent processing and analysis using IBM SPSS, version 27.0. Categorical variables were depicted as frequency and percentage, while continuous variables were represented by mean and standard deviation (SD). Chi-square tests was conducted to explore the correlation between potential risk factors and severe suicide attempts.

RESULTS

The sociodemographic characteristics of 90 patients, who were admitted to the emergency department due to suicide attempts. The majority of participants were female 51 (56.7%), with a mean age of 31.01 ± 12.42 years. The age distribution revealed that 60% of participants fell within the age group of 21-40 years. Regarding marital status, 45.6% were single, 40.0% were married, and 14.4% were divorced. Educational status varied, with 24.4% having completed high school, 22.2% completing elementary school, and 10.0% attaining university education. Most participants resided in urban areas 64 (71.1%), and the majority identified as Muslim 83 (92.2%) (Table 1).

Table 1: Sociodemographic Characteristics of Study Participants (n = 90)

Parameters	n (%)
Gender	
Female	51 (56.7%)
Male	39 (43.3%)
Age Groups (Years)	
20 or Less	15 (16.7%)
21-40	54 (60.0%)
41-60	16 (17.8%)
More than 60	5 (5.6%)
Age (Years)	
Mean ± SD	31.01 ± 12.42
Marital Status	
Divorced	13 (14.4%)
Married	36 (40.0%)
Single	41 (45.6%)
Educational Status	
Illiterate	3 (3.3%)
Read and Write	4 (4.4%)
Elementary School	20 (22.2%)
Middle School	9 (10.0%)
High School	22 (24.4%)
University	9 (10.0%)
Unknown	23 (25.6%)
Region of District	
Rural	26 (28.9%)
Urban	64 (71.1%)
Religion	
Christian	6 (6.7%)
Hindu	1 (1.1%)
Muslim	83 (92.2%)

The prevalence of clinical psychiatric conditions among suicide attempters presenting at the emergency department. Major depressive disorder was the most prevalent (33.3%), followed by anxiety disorder (18.9%). Other conditions included abuse of narcotics (6.7%), schizophrenia (4.4%), and a history of previous suicide attempts (1.1%) (Table 2).

Table 2: Prevalence of Clinical Psychiatric Conditions among Suicide Attempters Presenting at Emergency Department

Clinical Psychiatric Data	n (%)
Abuse Of Narcotic	6 (6.7%)
Anxiety Disorder	17 (18.9%)
Bipolar Disorder	1 (1.1%)
History Of Suicide Attempt	1 (1.1%)
Major Depressive Disorder	30 (33.3%)
Schizophrenia	4 (4.4%)
Unknown	31 (34.4%)

Drug poisoning was found to be the most common suicide method with 36 (40.0%) followed by pesticide poisoning 21 (23.3%), cutting/stabbing objects 13 (14.4%), hanging 8 (8.9%), jump from high place (7.8%), firearm (2.2%) and corrosive intake (2.2%) (Table 3).

Table 3: Methods Employed in Suicide Attempts among Study Participants

Methods Of Suicidal Attempt	n (%)
Corrosive Substance Drinking	2 (2.2%)
Cutting/Stabbing Object	13 (14.4%)
Drug Poisoning	36 (40.0%)
Firearm	2 (2.2%)
Hanging	8 (8.9%)
Jump From High Place	7 (7.8%)
Narcotic Poisoning	1 (1.1%)
Pesticide Poisoning	21 (23.3%)

Drug poisoning was found to be the most common suicide method with 36 (40.0%) followed by pesticide poisoning 21 (23.3%), cutting/stabbing objects 13 (14.4%), hanging 8 (8.9%), jump from high place (7.8%), firearm (2.2%) and corrosive intake (2.2%) (Table 3).

Table 4: Motivating Factors Behind Suicide Attempts among Study Participants

Reasons For Suicidal Attempt	n (%)
Family Problems	26 (28.9%)
Financial Problems	12 (13.3%)
Psychiatric Illnesses	28 (31.1%)
Romantic Relationship Issue	6 (6.7%)
Unknown	18 (20.0%)
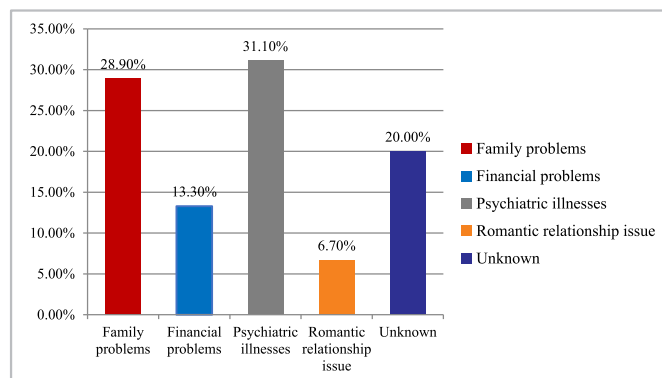
Figure 1: A Comparison between Males and Females was Conducted Based on the Reasons for Attempted Suicide

In the study cases, suicide attempts mostly occurred between 6 am to 12 pm (38.9%) and 12 pm to 6 pm (34.4%) (Table 5).

Table 5: The Temporal Distribution of the Time of Suicide Attempts was Examined

Time of Suicide Attempt	n (%)
6 am to Noon	35 (38.9%)
6 pm to Midnight	18 (20.0%)
Midnight to 6 am	6 (6.7%)
Noon to 6 pm	31 (34.4%)

Of the total cases, 13 (14.4%) resulted in death, while 22 (24.4%) were discharged from the emergency department. The majority, 55 (61.1%), were hospitalized (table 6).

Table 6: Clinical Outcomes of the Suicidal Attempters Presented to the Emergency Room

Clinical Outcome	n (%)
Death	13 (14.4%)
Discharged from Emergency	22 (24.4%)
Hospitalization	55 (61.1%)

DISCUSSION

Suicide entails intentionally ending one's own life, typically following a sequential progression of ideation, planning, and attempted execution [12]. This intricate phenomenon is characterized by its multifaceted nature, influenced by a myriad of contributing and facilitating factors. The interplay of neurobiological, familial, and environmental elements, alongside exposure to stressors within socio-cultural contexts, shapes the dynamics of suicidal behavior [13, 14]. Our study assessed the major risk factors associated with severe suicide attempts among individuals presenting to the ER. In terms of socio-demographic characteristics of the patients, mean age of the patients was (31.01 ± 12.42 years) with 60% of participants in the age group of 21-40 years. Around similar mean age (28.4 ± 11 years) were reported in India and a bit lower mean age (26.44 ± 8.1 years) was reported by Yaqoob et al., in Pakistan [15]. Naveed et al., reported age of the participants as 31.1% (10-20 years), 40.1% (21-30 years) and 14.8% (31-40 years).

These discrepancies may stem from regional variations or differences in healthcare circumstances of these studies [16]. In terms of gender distribution, the study included 51 females (56.7%) and 39 males (43.3%). This aligns with findings reported by Alvi et al., where females constituted 53% of the sample [17]. While other studies like Naveed et al., reported male dominance as 61.8% and Imran et al., reported male dominance as 51.5%. Regarding marital status, 45.6% were single, 40.0% were married, and 14.4% were divorced [16, 18]. Educational status varied, with 24.4% having completed high school, 22.2% completing elementary school, and 10.0% attaining university education. Most participants resided in urban areas (n=64, 71.1%), and the majority identified as Muslim (n=83, 92.2%). High prevalence among the single patients was reported by Khan et al., which were around 40% and high incidence among the school students was reported by Imran et al., which turned out to be 77.78% [18, 19]. Regarding the method of suicide, drug poisoning was found to be the most common suicide method (n=36, 40%), followed by pesticide poisoning (n=21, 23.3%), cutting/stabbing objects (n=13, 14.4%), hanging (n=8, 8.9%), jump from high place (7.8%), firearm (2.2%) and corrosive intake (2.2%). Similar methods of suicide were reported by Naveed et al., with poisoning (43.69%) followed by hanging (30.6%) and firearms (13.57%) of completed suicides. Yaqoob et al., documented a range of distinct self-harm methods, including medication overdose (35.9%), severing critical veins (26.4%), bodily cutting resulting in scars (19.5%), hanging (5.5%), burning (5%), jumping from elevated locations (3.2%), and firearm use (2.3%). The variations could be assumed considering the regional and cultural differences in the behaviors [15, 16]. The most frequently found reasons of suicide attempts were psychiatric illnesses (31.1%) and family problems (28.9%), followed by financial problems (13.3%) and romantic relationship issues (6.7%). Naveed et al., stated the reasons like domestic conflicts (70.7%), financial reasons/poverty (14.1%), failure in marriage (6.2%), mental illness (3.3%) etc. Concerning the clinical psychiatric conditions, major depressive disorder (MDD) was the most prevalent (33.3%), followed by anxiety disorders (18.9%), abuse of narcotics (6.7%), schizophrenia (4.4%), a history of previous suicide attempts (1.1%) along with (34.4%) cases occurring due to unknown causes. Khan et al., also stated high prevalence of depression (69%) in the cases [16, 19]. Regarding the time of the attempts, we found that most of the cases occurred during the day time (73.3%) which was contrary to what was found by Khan et al., were (60%) of the cases occurred during the late night period. Moreover, majority of patients were hospitalized (61.1%), around (24.4%) of the patients were discharged and the mortality rate in our study was (14.4%). (92%) of the cases were discharged (including the ones on demand) and mortality rates were 8% [14, 19].

Shekhani et al., and Wordefo et al., also find similar results regarding the prevalence of major depressive disorder and drug poisoning as primary factors in suicide attempts [20, 21]. The main strengths of our study were that it provided meaningful insights into the critical risk factors associated with severe suicide attempts in the community. We aimed at a multifaceted approach addressing the identified socio-demographic, clinical and circumstantial factors regarding suicides in our population.

CONCLUSIONS

This study underscores the urgent need for targeted suicide prevention initiatives, with major depressive disorder identified in 33.3% and drug poisoning as prevalent in 40.0% of suicide attempts. With a mortality rate of 14.4% observed, there is a critical imperative for comprehensive mental health support services for individuals presenting with suicidal behaviors in Emergency Department settings.

Authors Contribution

Conceptualization: AAT
Methodology: IA, AAT, AR, NA
Formal analysis: F, AS
Writing-review and editing: AS, AR, NA

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

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

REFERENCES

[1] Nurtanti S, Handayani S, Ratnasari NY, Husna PH, Susanto T. Characteristics, causality, and suicidal behavior: a qualitative study of family members with suicide history in Wonogiri, Indonesia. Frontiers of Nursing. 2020; 7(2): 169-78. doi: 10.2478/fon-2020-0016.

[2] Zohuri B and Zadeh S. Global suicide rate among youngsters increasing significantly. Online Journal of Neurology and Brain Disorders. 2020 Apr; 3(5): 300-10. doi: 10.32474/OJNBD.2020.03.000175.

[3] Mendagudli VG and Sarawad SS. Suicide prevention strategies: An overview. Asian Journal of Nursing Education and Research. 2021; 11(3): 447-8. doi: 10.52711/2349-2996.2021.00108.

[4] Cathelyn F, Van Dessel P, De Houwer J. Predicting nonsuicidal self-injury using a variant of the Implicit Association Test. Suicide and Life-Threatening Behavior. 2021 Dec; 51(6): 1259-71. doi: 10.1111/sltb.12808.

[5] Olayinka AR and Olukayode OJ. Demographic Variables as Predictors of Youths Susceptibility to Suicide in Kogi State, Nigeria. American Journal of Multidisciplinary Research and Innovation. 2022 Aug; 1(3): 98-104. doi: 10.54536/ajmri.v1i3.183.

[6] Tahir MN, Akbar AH, Naseer R, Khan QO, Khan F, Yaqub I. Suicide and attempted suicide trends in Mianwali, Pakistan: social perspective/Tendances des suicides et des tentatives de suicide à Mianwali (Pakistan)^ sup o^: perspective sociale. Eastern Mediterranean Health Journal. 2013 Mar; 19(3): S111.

[7] Obuobi-Donkor G, Nkire N, Agyapong VI. Prevalence of major depressive disorder and correlates of thoughts of death, suicidal behaviour, and death by suicide in the geriatric population—A general review of literature. Behavioral Sciences. 2021 Oct; 11(11): 142. doi: 10.3390/bs11110142.

[8] Da Silva AP, Henriques MR, Rothes IA, Zortea T, Santos JC, Cuijpers P, et al. Effects of psychosocial interventions among people cared for in emergency departments after a suicide attempt: a systematic review protocol. Systematic reviews. 2021;10(3):1-5. doi.org/10.1186/s13643-021-01609-5

[9] Alkhatib AJ and Alrakaf NA. An Inquiry into Suicide: Conceptualization, Etiology, and Prophylactic Measures. Kurdish Studies. 2023 Dec; 11(3): 750-8.

[10] Kwon M, Kim SA, Seo K. Factors Influencing Suicide Attempts of Adolescents with Suicidal Thoughts in South Korea: Using the 15th Korean Youth Risk Behavior Web-Based Survey (KYRBS). Iranian Journal of Public Health. 2022 Sep; 51(9): 1990. doi: 10.18502/ijph.v51i9.10553.

[11] Liu X, Huang Y, Liu Y. Prevalence, distribution, and associated factors of suicide attempts in young adolescents: School-based data from 40 low-income and middle-income countries. PLOS One. 2018 Dec; 13(12): e0207823. doi: 10.1371/journal.pone.0207823.

[12] Dávila Cervantes CA and Luna Contreras M. Suicide attempt in teenagers: Associated factors. Revista Chilena de Pediatría. 2019 Dec; 90(6): 606-16. doi: 10.32641/andespediatr.v90i6.1012.

[13] Turecki G and Brent DA. Suicide and suicidal behaviour. The Lancet. 2016 Mar; 387(10024):1227-39. doi: 10.1016/S0140-6736(15)00234-2.

[14] Miller IW, Camargo CA, Arias SA, Sullivan AF, Allen MH, Goldstein AB, et al. Suicide prevention in an emergency department population: the ED-SAFE study. JAMA Psychiatr. 2017;74(6):563-70. DOI:10.1001/jamapsychiatry.2017.0678

[15] Yaqoob N, Ahsan S, Shaikh S. Depression, Anxiety and Social Support as Predictors of Suicide Intent among Self-Harm Inpatients. Pakistan Armed Forces Medical Journal. 2023 May; 73(2): 557-60. doi: 10.512 53/pafmj.v73i2.7900.

[16] Naveed S, Tahir SM, Imran N, Rafiq B, Ayub M, Haider II et al. Sociodemographic characteristics and patterns of suicide in Pakistan: an analysis of current trends. Community Mental Health Journal. 2023 Aug; 59(6): 1064-70. doi: 10.1007/s10597-022-01086-7.

[17] Alvi T, Hussain S, Farjam A, Azhar M, Assad F, Yasein S. Attempted suicide and seriousness of intent. Journal of the College of Physicians and Surgeons Pakistan. 2017 Jan; 27(1): 55-6.

[18] Imran N, Naveed S, Rafiq B, Tahir SM, Ayub M, Haider II. Pattern of adolescent suicides in Pakistan: a content analysis of newspaper reports of two years. Pakistan Journal of Medical Sciences. 2023 Jan; 39(1): 6. doi: 10.12669/pjms.39.1.6851.

[19] Hayat Khan F, Aftab A, Arain T. Deliberate Self Harm! An Inquiry of a Potential Link with Depression. Pakistan Armed Forces Medical Journal. 2011 Jun; 61(2): 218-20.

[20] Shekhani SS, Perveen S, Hashmi DE, Akbar K, Bachani S, Khan MM. Suicide and deliberate self-harm in Pakistan: a scoping review. BMC Psychiatry. 2018 Dec; 18:1-5. doi: 10.1186/s12888-017-1586-6.

[21] Wordefo DK, Kassim FM, Birhanu E, Mamo G. Suicidal behaviors and associated factors among patients attending an emergency department: a facility-based cross-sectional study. BMC Psychiatry. 2023 Jun; 23(1): 462. doi: 10.1186/s12888-023-04949-9.

Original Article

Iron Deficiency Anemia in Patients with Chronic Renal Insufficiency at Tertiary Care Hospital in Northern Punjab

Muhammad Shuaib[1], Muhammad Imran[1], Hasan Akbar Khan[2*], Muhammad Ikram ul Haq[3], Hafiz Muhammad Zubair[4] and Muhammad Irfan[5]

[1]Department of General Medicine, Mohi-ud-Din Islamic Medical College, Mirpur, Pakistan
[2]Department of Biochemistry, Al-Aleem Medical College, Lahore, Pakistan
[3]Department of Medicine, Niazi Medical and Dental College, Sargodha, Pakistan
[4]Department of Medicine, KRL Hospital, Islamabad, Pakistan
[5]Department of Peads Medicine, Mohi-ud-Din Islamic Medical College, Mirpur, Pakistan

ARTICLE INFO

ABSTRACT

Anemia is a frequently encountered complication of chronic kidney disease (CKD) leading to worse outcomes in terms of quality of life and premature death. However, the current prevalence of iron deficiency anemia (IDA) in CKD is understudied in Pakistan. **Objective:** To assess the frequency of IDA in patients with CKD at Bewal International Hospital, Gujar Khan, Pakistan. **Methods:** A cross-sectional was executed at the Department of Nephrology, Bewal International Hospital, Pakistan from January 1, 2022, to June 30, 2022. The study comprised 97 patients aged >13 years of either gender having CKD (GFR <60 ml/min/1.73m^2) for at least 90 days. All patients were tested for serum creatinine, ferritin, and hemoglobin levels. IDA was considered if hemoglobin was ≤12 mg/dL in women and ≤13 mg/dL in men. **Results:** Among 97 patients, there were 57(58.7%) males and 40(41.3%) females. The mean age was 51.23 ± 12.99 years while the mean disease duration was 6.01 ± 1.610 years. 57(58.7%) patients had IDA. IDA was more frequent in women with CKD (67.5%), compared to men (52.64%). However, this association was statically insignificant (p>0.05). When data was stratified, a substantial association was found between IDA and the stage of CKD (p=0.007). There was no significant association between IDA and disease duration (p>0.05). **Conclusions:** It was concluded that anemia is common in CKD patients, with a high prevalence in females. Stage 3–5 CKD is significantly associated with developing iron deficiency anemia. Early identification and timely management can avoid unfavorable outcomes in these patients.

INTRODUCTION

Chronic renal insufficiency, commonly known as chronic kidney disease, is an irreversible condition characterized by gradual deterioration in kidney function with glomerular filtration rate (GFR) < 60 ml/min/1.73m2 for ≥ 3 months [1]. It is becoming a worldwide epidemic and is associated with poor outcomes. Global reports consider it as one of the major causes of mortality worldwide [1, 2]. In Pakistan, the overall prevalence of CKD was reported to be 21.2%, irrespective of the demographic factors [3, 4]. As kidneys function in regulating blood composition and volume, and removing metabolic waste products by urination [5], CKD leads to the development of various blood irregularities including iron deficiency anemia (IDA) [6]. IDA is a commonly encountered problem in CKD. Multiple factors are responsible for anemia in CKD such as erythropoietin insufficiency from decreased renal mass, elevated pro-inflammatory mediators affecting erythropoiesis, reduced red cell survival, increased blood loss, and iron and nutritional deficits [6]. It is linked with unfavorable outcomes such as sleep disorders, cognitive impairment, serious cardiovascular and neurovascular implications, progression of CKD, increased hospitalization, and

Shuaib M *et al.,*

increased mortality rates[7], causing a substantial burden on healthcare infrastructure due to amplified costs of disease management[8]. The prevalence of anemia in CKD varies across regions, ranging from 25.3% in the United States [8] to 85.33% in Ethiopia[7]. The prevalence snowballs further as the disease progresses [7]. However, little is known regarding the prevalence of IDA in patients presenting with CKD in Pakistan. Several studies reported its prevalence in dialysis patients [9] while only a few reported the prevalence of IDA in non-dialysis CKD patients, ranging between 38.83% to 77.9% [10, 11].

This study aimed to assess the more recent prevalence of IDA in CKD patients. This study will guide us to know the disease burden in the Northern Punjab region of Pakistan.

The aim of this study was to assess the psychological factors affecting the patients of functional dyspepsia and their effect in a person's day to day life.

METHODS

A cross-sectional study was executed at the Department of Nephrology, Bewal International Hospital, Gujar Khan, Pakistan from January 1, 2022, to June 30, 2022. A sample size of 97 was calculated using the WHO sample size calculator with a 95% confidence level, a 5% margin of error, and a 6.8% prevalence of mild anemia among adult male patients [12]. The study was approved by the hospital Ethical committee i.e. Ref No: /1/06/2021/S1 ERB dated, June 1, 2021. Data were collected using a convenient sampling technique. Patients aged >13 years of either gender having CKD (GFR <60 ml/min/1.73m^2) for at least 90 days were included in the study. Patients who underwent dialysis or renal transplant, having CKD Stage I or II, malignancy, any hematological condition, acute or chronic infection, and recent history of blood transfusion or severe bleeding episode from any orifice of the body were excluded. After obtaining informed consent from patients, a total of 97 patients meeting the inclusion criteria were taken from the Department of Nephrology, Bewal International Hospital, Gujar Khan. Socio-demographic profiles such as weight, gender, and age were noted. All patients were tested for serum creatinine, ferritin, and hemoglobin levels. Cockroft-Gault formula was used for GFR estimation [13], and patients having GFR <60 ml/min/1.73m^2 for ≥90 days were considered as having CKD [14]. Staging of CKD was done and explained as Stage III with GFR 30-59 mL/min/1.73m^2, stage IV with GFR 15-29 mL/min/1.73m^2, and stage V with GFR <15 mL/min/ 1.73m^2 [7]. IDA was considered if hemoglobin was ≤12 mg/dL in women and ≤13 mg/dL in men [7]. All tests were performed at the Laboratory of Bewal International Hospital Gujar Khan. All information was collected on a pre-structured questionnaire. Data analysis was performed using SPSS Version 24.0. The quantitative data such as age, weight, and duration of disease were executed as mean and standard deviation. The categorical data such as gender, presence of IDA, and CKD stage were shown as frequency and percentage. Stratification of data was performed to control the confounding variables such as gender, stage of CKD, and duration of disease. The chi-square test was implemented after stratification to assess the significance and a p-value ≤0.05 was regarded as significant.

RESULTS

The study included 97 patients. Demographic details are explained in table 1. The mean age was 51.23 ± 12.99 years. There were 57(58.7%) males and 40 (41.3%) females. The mean weight was 57.58 ± 15.78 kg and the mean duration of the disease was 6.01 ± 1.610 months. 7(7.22%) patients had stage 3 CKD, 23 (23.71%) had stage 4, and 67 (69.07%) had stage 5 CKD (Table 1).

Table 1: Baseline Details of Study Participants (n=97)

Characteristics		n (%)
Age* (Years)		51.23 ± 12.99
Gender	Male	57 (58.4)
	Female	40 (41.3)
Weight* (Kg)		57.58 ± 15.78
Duration of Disease* (Months)		6.01 ± 1.610
Stage Of CKD	3	7 (7.22)
	4	23 (23.71)
	5	67 (69.07)

n = number of patients; % = percentage of patients; * = mean ± standard deviation was given; CKD = chronic kidney disease; kg = kilograms.

57(58.7%) patients had iron deficiency anemia, as illustrated (Figure 1)

Iron Deficiency Anemia
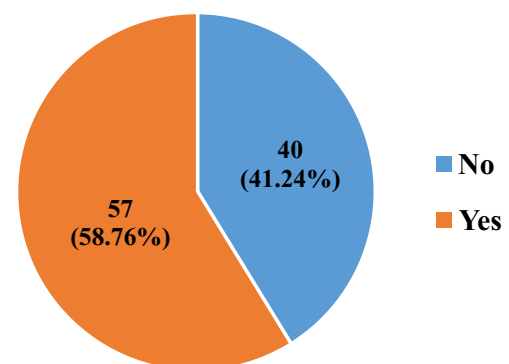
Figure 1 : Frequency of Iron Deficiency Anemia in CKD patients

When data were stratified, a significant association was found between IDA and the stage of CKD (p=0.007). IDA was more frequent in women with CKD (67.5%) compared to men (52.64%). However, this association was statistically insignificant. No significant difference was observed in IDA concerning gender and duration of disease (Table 2).

Table 2: Frequency of IDA in CKD to Gender, Stage of CKD, and Duration of Disease

Parameters		Iron Deficiency Anemia		p-value*
		Yes	No	
Gender	Male	30 (30.93%)	27 (27.83%)	0.143
	Female	27 (27.83%)	13 (13.40%)	
Stage of CKD	3	4 (4.12%)	3 (3.09%)	0.007*
	4	19 (19.59%)	4 (4.12%)	
	5	63 (64.95%)	4 (4.12%)	
Duration of Disease (Months)	3-5	18 (18.56%)	20 (20.62%)	0.187
	6-8	35 (36.08%)	18 (18.56%)	
	9-11	4 (4.12%)	2 (2.06%)	

CKD = chronic kidney disease; IDA = iron deficiency anemia; *= Chi-square test was used and p≤0.05 was taken as significant

DISCUSSION

Anemia is a commonly encountered complication in CKD and is associated with several adverse events. Assessing the prevalence of anemia in these patients helps in identifying the burden of disease, slowing the progression of CKD, and preventing these adverse outcomes [7]. Therefore, this study assessed the more recent prevalence of IDA in CKD patients. The current study reported that a total of 57(58.7%) CKD patients had IDA. This result is comparable to the findings of the studies conducted in Ethiopia (53.5%) [15], Oman (29.3%) [16], Malaysia (47.9-76.9%)[17-19], Ecuador(80.22%) [20], Japan(0–95%)[21], and Pakistan (38.83– 80.5%) [11, 22-24]. A meta-analysis was conducted to determine the pooled prevalence of anemia and revealed that it was 59.15% in CKD patients [25]. However, an American study reported a lower prevalence of anemia (15.4%) in CKD patients [26]. Similarly, two other studies conducted in England and the United States also documented a lower prevalence of 22.2% and 23.0%, respectively [27, 28], contrary to the results of the current study. The results of the present study disclosed a significant association between the stage of CKD and the occurrence of anemia (p =0.007). 94.02% of stage 5 patients had IDA, compared to 57.14% of stage 3 patients. Findings of a study conducted by Bishaw *et al*, in Ethiopia, [7] showed that there was a significant association between grades of anemia and grades of CKD and concluded that anemia severity differed according to the stage of chronic kidney disease (CKD), with a larger percentage of severe anemia in stage 5 (11.33%) compared to stage 3, 5 (3.33%), and stage 4, 2 (1.33%). A similar conclusion was laid down in a research study conducted by Stauffer *et al.,* where they concluded that anemia prevalence rose with CKD stages, rising from 8.4% at stage 1 to 53.4% at stage 5 [26]. Another study conducted in Peshawar by Khan et. al. came to a comparable outcome where 10.06% of stage I, 15.72% of stage II, 22.01% of stage

III, 23.27% of stage IV, and 28.93% of Stage V CKD patients had anemia [23]. Comparable results were also highlighted in another study done in Malaysia by Javed *et al.,* who concluded that a positive relationship exists between the severity of iron deficiency anemia and stages of CKD; i.e., the higher the grade of CKD, the higher the severity of IDA [17]. The limitations of the current study need to be recognized, including the cross-sectional study design and convenience sampling technique. Another limitation is the unavailability of research related to the prevalence of CKD in local settings. The findings of the current study are of a single center of the Nephrology Outdoor Department of Bewal International Hospital. Detailed researches including a larger sample size are required to generalize the results. In summary, the prevalence of anemia seems to be increasing in the Pakistani population with CKD and the prevalence increases with the advancement of stage of CKD.

CONCLUSIONS

Anemia is common in CKD patients, with a high prevalence in females. Having stage 3–5 CKD is significantly associated with developing iron deficiency anemia. Early identification and timely management can avoid unfavorable outcomes in these patients.

Authors Contribution

Conceptualization: MS, HAK
Methodology: MS, HAK
Formal analysis: MS, HAK, MI[1], MIUH, MZ, MI[2]
Writing-review and editing: MS, HAK, MI, MIUH

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

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

REFERENCES

[1] Kovesdy CP. Epidemiology of chronic kidney disease: an update 2022. Kidney international Supplements. 2022 Apr; 12(1): 7–11. doi: 10.1016/j.kisu.2021.11.003.

[2] Liyanage T, Toyama T, Hockham C, Ninomiya T, Perkovic V, Woodward M *et al.* Prevalence of chronic kidney disease in Asia: a systematic review and analysis. BMJ Global Health. 2022 Jan; 7(1): e007525. doi: 10.1136/bmjgh–2021–007525.

[3] Hasan M, Sutradhar I, Gupta RD, Sarker M. Prevalence of chronic kidney disease in South Asia: a systematic review. BMC Nephrology. 2018 Dec; 19: 1–2. doi: 10.1186/s12882-018-1072-5.

[4] Imtiaz S and Alam A. Epidemiology and demography of Chronic Kidney Disease in Pakistan-A review of Pakistani literature. Pakistan Journal of Kidney Diseases. 2023 Mar; 7(1): 2-7. doi: 10.53778/pjkd71209.

[5] Ahmed J, Azhar S, ul Haq N, Hussain S, Stájer A, Urbán E *et al*. Awareness of chronic kidney disease, medication, and laboratory investigation among nephrology and urology patients of Quetta, Pakistan. International Journal of Environmental Research and Public Health. 2022; 19(9): 5015. doi: 10.3390/ijerph19095015.

[6] Hain D, Bednarski D, Cahill M, Dix A, Foote B, Haras MS *et al*. Iron Deficiency Anemia in CKD: A Narrative Review for the Kidney Care Team. Kidney Medicine. 2023 May: 100677. doi: 10.1016/j.xkme.2023.100677.

[7] Bishaw F, Woldemariam MB, Mekonen G, Birhanu B, Abebe A. Prevalence of anemia and its predictors among patients with chronic kidney disease admitted to a teaching hospital in Ethiopia: A hospital-based cross-sectional study. Medicine. 2023 Feb; 102(6): e31797. doi: 10.1097/MD.0000000000031797.

[8] Kovesdy CP, Davis JR, Duling I, Little DJ. Prevalence of anaemia in adults with chronic kidney disease in a representative sample of the United States population: analysis of the 1999–2018 National Health and Nutrition Examination Survey. Clinical Kidney Journal. 2023 Feb; 16(2): 303-11. doi: 10.1093/ckj/sfac240.

[9] Khan MZ, Khan S, Khan A, Khan MA, Khattak MB. Frequency of Iron Deficiency Anemia in Chronic Kidney Disease Patients on Hemodialysis. National Editorial Advisory Board. 2018 Nov; 29(11).

[10] Kamil F, Dhrolia M, Hamid A, Qureshi R, Nasir K, Ahmad A. Frequency of iron deficiency anaemia in chronic kidney disease patients 3 not on dialysis 4. Journal of the Pakistan Medical Association. 2022 Jul; 72(7): 1396-400. doi: 10.47391/JPMA.4507.

[11] Khan M, Mahmood SN, Fatima N. Frequency of Iron Deficiency Anemia in Non-Dialysis Chronic Kidney Patients. Pakistan Journal of Kidney Diseases. 2022 Sep; 6(3): 17-22. doi: 10.53778/pjkd63191.

[12] Adamu AL, Crampin A, Kayuni N, Amberbir A, Koole O, Phiri A *et al*. Prevalence and risk factors for anemia severity and type in Malawian men and women: urban and rural differences. Population Health Metrics. 2017 Dec; 15: 1-5. doi: 10.1186/s12963-017-0128-2.

[13] Rostoker G, Andrivet P, Pham I, Griuncelli M, Adnot S. A modified Cockcroft-Gault formula taking into account the body surface area gives a more accurate estimation of the glomerular filtration rate. Journal of Nephrology. 2007 Sep; 20(5): 576-85.

[14] Chen TK, Knicely DH, Grams ME. Chronic kidney disease diagnosis and management: a review. JAMA. 2019 Oct; 322(13): 1294-304. doi: 10.1001/jama.2019.14745.

[15] Alemu B, Techane T, Dinegde NG, Tsige Y. Prevalence of anemia and its associated factors among chronic kidney disease patients attending selected public hospitals of Addis Ababa, Ethiopia: Institutional-based cross-sectional study. International Journal of Nephrology and Renovascular Disease. 2021 Mar: 67-75. doi: 10.2147/IJNRD.S296995.

[16] Alsalmani AA, Alalawi NM, Alsumri H, Aljabri MK, Alharami G, Alweshahi R *et al*. Prevalence of anemia in primary care patients with Type 2 diabetes mellitus and chronic kidney disease in Oman. Journal of Family and Community Medicine. 2023 Jan; 30(1): 18-22. doi: 10.4103/jfcm.jfcm_226_22.

[17] Pakianathan R, Kassab YW, Wen LS, Khan SU, Iqbal MZ. Prevalence of anemia and its management among chronic kidney disease patients in Malaysia. Latin American Journal of Pharmacy. 2021; 40(3): 599-608.

[18] LEONG LC. POS-237 Prevalence and risk factors of anemia among non-dialysis chronic kidney disease patients: a single-centre, cross-sectional study from Malaysia. Kidney International Reports. 2022 Feb; 7(2): S104. doi: 10.1016/j.ekir.2022.01.256.

[19] Salman M, Khan AH, Adnan AS, Sulaiman SA, Hussain K, Shehzadi N *et al*. Prevalence and management of anemia in pre-dialysis Malaysian patients: A hospital-based study. Revista da Associação Médica Brasileira. 2016; 62: 742-7. doi: 10.1590/1806-9282.62.08.742.

[20] Garrido D, Fontalvo N, Espinoza I, Arias L, Valarezo S, Almeida D *et al*. Description of iron deficiency in patients with end-stage chronic kidney disease on hemodialysis, Quito, Ecuador. Revista Colombiana de Nefrología. 2019 Dec; 6(2): 95-102. doi: 10.22265/acnef.6.2.342.

[21] Akizawa T, Okumura H, Alexandre AF, Fukushima A, Kiyabu G, Dorey J. Burden of anemia in chronic kidney disease patients in Japan: a literature review. Therapeutic Apheresis and Dialysis. 2018 Oct; 22(5): 444-56. doi: 10.1111/1744-9987.12712.

[22] Ali I, Khan MNA, Ali A, Hussain MZ, Khan MS, Ahmed SN (2022) Anaemia in Chronic Kidney Disease. Pakistan Armed Forces Medical Journal 72:1306–09.

[23] Khan AM, Afridi MA, Ali G, Idrees M, Waqas M. Prevalence of anemia in chronic kidney disease patients in lady reading hospital, Peshawar. Khyber Journal of Medical Sciences. 2018 Sep; 11(3): 439-42.

[24] Rajput R, Ahmad N, Khan A, Wahid A, Atif M. Prevalence, Risk Factors and Management of

Anaemia in Non-Dialysis Chronic Kidney Disease Patients: Findings from A Single Centre Study in Pakistan. Specialty Journal of Medical Research and Health Science. 2020; 5(1): 8-15.

[25] Taderegew MM, Wondie A, Terefe TF, Tarekegn TT, GebreEyesus FA, Mengist ST *et al*. Anemia and its predictors among chronic kidney disease patients in Sub-Saharan African countries: A systematic review and meta-analysis. PLOS One. 2023 Feb; 18(2): e0280817. doi: 10.1371/journal.pone.0280817.

[26] Stauffer ME and Fan T. Prevalence of anemia in chronic kidney disease in the United States. PLOS One. 2014 Jan; 9(1): e84943. doi: 10.1371/journal.pone.0084943.

[27] Dmitrieva O, de Lusignan S, Macdougall IC, Gallagher H, Tomson C, Harris K *et al*. Association of anaemia in primary care patients with chronic kidney disease: cross sectional study of quality improvement in chronic kidney disease (QICKD) trial data. BMC Nephrology. 2013 Dec; 14: 1-9. doi: 10.1186/1471-2369-14-24.

[28] Lamerato L, James G, van Haalen H, Hedman K, Sloand JA, Tang A *et al*. Epidemiology and outcomes in patients with anemia of CKD not on dialysis from a large US healthcare system database: a retrospective observational study. BMC Nephrology. 2022 Apr; 23(1): 166. doi: 10.1186/s12882-022-02778-8.

Original Article

Tracing the Connection of Iron and Copper in Chronic Telogen Effluvium

Shayan Zufishan[1*], Sara Rafique[2], Faiza Nasir[2], Erum Amir[1], Shazia Nazar[3] and Asma Bandhani[4]

[1]Karachi Medical and Dental College, Karachi, Pakistan
[2]Jinnah Medical and Dental College, Karachi, Pakistan
[3]Dow University of Health Sciences, Karachi, Pakistan
[4]Medicare Cardiac and General Hospital, Karachi, Pakistan

ARTICLE INFO

ABSTRACT

Chronic Telogen Effluvium (CTE) is a common non- scarring, diffuse type of hair loss, affecting a significant proportion of population. The purpose of the current study is to assess the relationship between CTE and trace metal levels, specifically copper and iron. **Objective:** To collect hair and serum samples from both control group and patients with CTE and to analyze the association between hair copper and iron content and serum copper and iron levels in both groups. **Methods:** The Dow University Hospital (DUHS) in Karachi, Sindh, Pakistan, served as the site of this case control research. The duration of study was one year. The study population encompassed hundred individuals, categorized into 50 cases with CTE and 50 healthy controls. Using non probability sampling technique (convenient sampling), the sample size was determined. Diagnostic criteria a positive hair pull test. Hair and serum samples were collected from both groups for trace metal analysis. Analysis was carried out using ab Atomic Absorption Spectrophotometer (Perkin Elmer Analyst 800, located in Waltham, MA, USA). Data analysis was carried out using SPSS® software for Windows® version 16.0. **Results:** Results showed that hair samples from patients had considerably lower iron levels than those from controls ($p<0.001$), while there was no significant difference in copper levels ($p=0.713$). Additionally, the CTE group showed noticeably greater copper levels ($p<0.001$) and significantly lower serum iron levels ($p<0.001$). **Conclusions:** The study identified a positive association between iron deficiency and hair loss.

INTRODUCTION

Alopecia is a common concern among men and women and is often a cause of distress [1]. Among the myriad factors contributing to occurrence of alopecia, Telogen Effluvium (TE) has emerged as a common cause [1]. It is a non-scarring form of alopecia, characterized by simultaneous diffuse shedding of a considerable amount of hair in telogen phase [1]. Alterations in the hair follicle cycle, particularly prolonged or reduced anagen and telogen phases as well as synchronous hair follicle cycling resulting in fallout of hair shafts in telogen, can be attributed to telogen effluvium [2]. It occurs as a response to metabolic or physiological stresses [1]. No racial inclination for this condition has been observed. However, the rate of occurrence among females is greater than males [3]. Acute

Telogen Effluvium (ATE) and Chronic Telogen Effluvium (CTE) are the two subtypes of TE that are distinguished by the duration of the illness. Where majority of cases of ATE resolve within a span of 6 months, in some cases the hair loss continues longer beyond this duration. Under these circumstances the condition is defined as CTE [1]. CTE typically exhibits an intermittent pattern, characterized by alternative episodes of spontaneous remissions and relapses [1]. Usually, conditions like severe iron deficiency anemia, idiopathic thyroid disorders, acrodermatitis, malnutrition etc. are linked with CTE [3]. Hair growth and structure can both be impacted by nutritional deficiencies [1]. Among these Copper and iron are significant contributors to metalloenzymatic processes including

cellular processes and hair follicle cycle [1]. Where copper is found to be an important player in proliferation and differentiation of a specialized type of fibroblasts (dermal papilla cell), which are involved in growth of hair follicles, Iron levels have also been found to be an essential factor affecting hair loss [1].

The rationale is systemic illnesses and CTE are strongly correlated with metals deficiency like iron and copper. Because of the poor nutritional state, it is vital to research the role of metals. In order to compare the Copper and iron contents of hair samples from patients with Chronic Telogen Effluvium (CTE) and controls with their corresponding serum copper and iron levels. The aim of the study was to explore the relationship between these two parameters.

METHODS

From April 2017 to May 2018, the case-control study was carried out at DUHS following Institutional Ethical Review Board Approval (IRB-842/DUHS/Approval/2017/57). Open Source Epidemiologic Statistics for Public Health was used to calculate the sample size with 80% power and a 95% Confidence Interval (CI) using non-probability sampling (convenient sampling) technique [1]. 50 subjects with CTE who attended the dermatology outpatient clinic, DUHS, were enrolled as cases. The diagnostic criteria for CTE were positive hair pull test. About sixty hairs were pulled gently using middle finger and thumb from all four quadrants including bi temporal. Falling of ≥10 strands was deemed indicative of a positive pull test, 50 healthy controls were sourced from the students and faculty of DUHS [1]. CTE individuals between the ages of 18 and 35 met the inclusion criteria for cases. Inclusion criteria for control group were a negative hair pull test. Exclusion criteria encompassed individuals who had undergone scalp surgery, those with systemic disorders, receiving medications for systemic disorders, currently undergoing copper and/or iron treatment or experiencing any hormonal abnormality. For trace element analysis in hair, hair samples were obtained from the nape of neck, with the help of stainless-steel scissors [1]. The samples measuring about 3-4 cm in length and 0.5-1 g in weight were then washed with ultra-pure water. Subsequently the washed sample was treated with methanol and afterwards, subjected to an ultrasonic bath. Following this the hair samples were dried and preserved in a desiccator until analysis. These samples then underwent microwave assisted digestion for analysis. Additionally, a venous blood sample of 3 ml was taken from both groups' determination of Trace metal levels in serum. The blood samples were centrifuged and stored for further analysis. An Atomic Absorption Spectrophotometer (AAS) equipped with hollow cathode lamps was used to measure the quantities of iron and copper in serum and hair samples. Flame mode was used for the analysis. The Perkin Elmer Analyst 800, based in Waltham, MA, USA, was the instrument used. The Statistical Package for Social Sciences (SPSS®) software for Windows® version 16.0 was used to analysed the data. The mean was calculated using descriptive analysis, and the mean values were compared using an independent sample t-test. P = 0.001 was maintained as the significance level.

RESULTS

The study sample comprised of 100 individuals, categorized into, age and sex matched, case and control group. With a mean age of 27.46 ± 4.98 years, 50 (50%) of the 100 participants were cases, and 50 (50%) were controls, with a mean age of 28.34 ± 4.92 years (p-value 0.502) (Table 1).

Table 1: Mean Age of the Controls and Cases

Study Variables	Controls (n=50) (Mean ± SD)	Cases (n=50) (Mean ± SD)	p-Value
Age (Years)	28.34 ± 4.92	27.46 ± 4.98	0.502

SD=Standard Deviation

56% of the subjects in the cases were men, and 44% were women (Figure 1A).
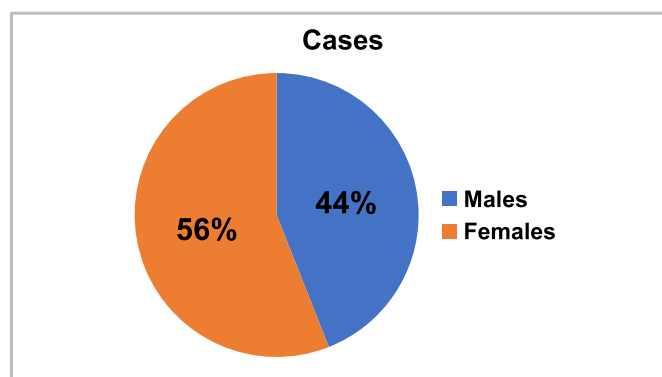
Figure 1: Gender Distribution of Cases

Among controls 48% of the subjects were male and 52% of the subjects were female. The p value was found to be 0.423 (Figure 1B).
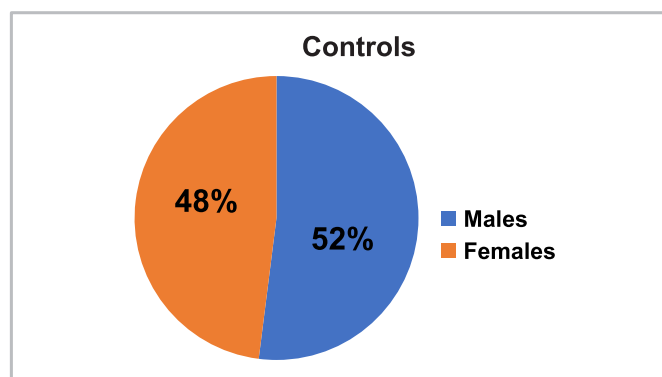
Figure 1B: Gender Distribution of Controls

Trace metal analysis of the hair samples revealed significantly lower iron levels (p<0.001) in cases as compared to controls. However, copper levels in hair samples did not exhibit a significant difference (p=0.713) (Table 2).

Table 2: Comparison of Iron and Copper Levels in Hair between CTE Cases and Control Samples

Biochemical Parameters	Controls (n=50) (Mean ± SD)	Cases (n=50) (Mean ± SD)	p–Value
Copper (μg/g)	27.36 ± 2.51	26.90 ± 8.47	0.713
Iron (μg/g)	32.34 ± 10.88	24.56 ± 10.27	<0.001*

The Mann–Whitney U test and Independent T-test were used to assess the statistical differences between controls and cases. The data were reported as mean and standard deviation; *(p<0.05) is regarded a significant difference, and ** (p<0.01) is deemed highly significant. Moreover, CTE group exhibited significantly lower serum iron levels (p<0.001), whereas coper levels were significantly higher in this group (Table 3). The Mann–Whitney U test and Independent T-test were used to assess the statistical differences between controls and cases. The data were reported as mean and standard deviation; *(p<0.05) is regarded a significant difference, and **(p<0.01) is considered highly significant.

Table 3: Comparison of Serum Levels of Copper and Iron between CTE Cases and Control Samples

Biochemical Parameters	Controls (n=50) (Mean ± SD)	Cases (n=50) (Mean ± SD)	p–Value
Copper (μg/dl)	110.30 ± 6.40	120.36 ± 18.79	0.001*
Iron (μg/dl)	134.96 ± 9.86	122.14 ± 10.98	<0.001*

DISCUSSION

Considering, that hair is the foremost defining feature of human appearance, hair loss or alopecia have a profound effect on an individual's quality of life and influences a person's psychological as well as emotional state [1-14]. A kind of noncicatricial hair loss known as TE is characterized by a noticeable daily increase in hair loss [13]. Iron deficiency is one of the most prevalent forms of malnutrition worldwide and is a contributing factor to TE [1]. The purpose of this case-control study was to compare the levels of iron and copper in serum and hair samples from CTE patients and normal controls. Copper ion levels may be involved in hair loss. Dermofibroblasts are involved in formation of Vascular Endothelial Growth Factor (VGEF) which in turn facilities formation of new capillaries. These dermofibroblasts are stimulated by copper ions, which is possibly why the hair follicle receives an appropriate blood supply [1-2]. Compared to previous research where blood levels of copper were shown to be much lower in cases, the current study's mean serum levels of copper were significantly higher in cases than in controls [1-4]. However other studies have reported that serum copper levels did not show any significant differences in patients with alopecia, indicating that hair loss might not be affected by serum copper levels [1-2]. Additionally, this study reported

significantly lower serum iron levels in the control group. These results were consistent with the findings of previous studies [1-10]. Additionally, another study further supported the role of low iron stores in the body by highlighting the strong negative correlation between decreased ferritin levels and hair fall in patients of TE [1]. These findings can be explained by the fact that iron is essential for the oxygen and electron transfer that occurs in hair cells. Iron also functions as a cofactor for the ribonucleotide reductase enzyme, which is an enzyme involved in DNA synthesis. Due to these functions presence of iron is essential for proliferation of hair follicles and deficiency would therefore disrupt the process [20]. Hair's structure, particularly the presence of sulphur rich keratin, makes it more likely to bind metal cations [21]. This affinity for metal binding and its slow growth makes hair a potential long term indicator of metal ion levels. While there was no discernible change in the quantities of copper ions, the CTE group's hair samples had much lower iron levels in the current investigation [22]. These conclusions run counter to those of an earlier study [4]. The evidence supporting the potential involvement of these metals in the aetiology of CTE is provided by the variations in the levels of these trace elements between the case and control groups.

CONCLUSIONS

Based upon the findings of current investigation, a positive association was found between occurrence of CTE and low levels of iron in serum as well as hair samples of the affected individuals.

Authors Contribution

Conceptualization: SN
Methodology: SZ, AB
Formal analysis: SZ
Writing, review and editing: FN, EA, SR

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

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

REFERENCES

[1]   Alizadeh N, Rafiei R, Darjani A, Eftekhari H, Nejad KG, Rafiei E, Vishkaei MS. Chronic telogen effluvium in women: role of micronutrients, a case-control study in north of Iran. Journal of the Egyptian Women's Dermatologic Society. 2021 Sep; 18(3): 205-9. doi: 10.4103/jewd.jewd_34_21.

[2]   Asghar F, Shamim N, Farooque U, Sheikh H, Aqeel R. Telogen effluvium: a review of the literature. Cureus.

2020 May; 12(5). doi: 10.7759/cureus.8320.

[3] Grover C and Khurana A. Telogen effluvium. Indian Journal of Dermatology, Venereology and Leprology. 2013 Sep; 79: 591. doi: 10.4103/0378-6323.116731.

[4] Nazik H and Bengu AS. Evaluation of the levels of trace elements in the blood and hair of female patients with chronic telogen effluvium. Trace Element Electrolytes. 2019 Jan; 36: 126-30. doi: 10.54 14/TEX01561.

[5] Ozuguz P, Dogruk Kacar S, Ekiz O. Evaluation of zinc, vitamin B12, folic acid and iron levels and thyroid functions in patients with chronic telogen effluvium. Journal of Dermatology Research and Therapy. 2015 Sep; 1(1): 8. doi.org/10.23937/2469-5750/1510008.

[6] Rebora A. Intermittent chronic telogen effluvium. Skin Appendage Disorders. 2017 Mar; 3(1): 36-8. doi: 10.1159/000455882.

[7] Guo EL and Katta R. Diet and hair loss: effects of nutrient deficiency and supplement use. Dermatology Practical and Conceptual. 2017 Jan; 7(1): 1. doi: 10.5826/dpc.0701a01.

[8] Cheung EJ, Sink JR, JC El. Vitamin and Mineral Deficiencies in Patients with Telogen Effluvium: A Retrospective Cross-Sectional Study. Journal of Drugs in Dermatology. 2016 Oct; 15(10): 1235-7.

[9] Pyo HK, Yoo HG, Won CH, Lee SH, Kang YJ, Eun HC *et al.* The effect of tripeptide-copper complex on human hair growth in vitro. Archives of Pharmacal Research. 2007 Jul; 30: 834-9. doi: 10.1007/Bf029788 33.

[10] QS A, TB H, MF K. Correlation Of Duration Of Hair Loss With Trace Element Level In Hair Loss Patients. Journal of Dhaka Medical College. 2020 Jan; 29(1). doi: 10.3329/jdmc.v29i1.51167.

[11] Ateeq A, Majid S, Memon NA, Hayat N, Somroo AQ, Fattah A. Suprachoroidal injection of triamcinolone acetonide for management of resistant diabetic macular oedema. Journal of the Pakistan Medical Association. 2023 Feb; 73: 239-44. doi: 10.47391/JP MA.2239.

[12] Shrivastava SB. Diffuse hair loss in an adult female: approach to diagnosis and management. Indian Journal of Dermatology, Venereology and Leprology. 2009 Jan; 75(1): 20-28. doi: 10.4103/0378-6323.45215.

[13] Meghrazi K, Sabet MS, Kheradmand F, Akhgar M. A Research on the Level of Zinc and Copper in the Hair of Students with Lower IQ. Zahedan Journal of Research in Medical Sciences. 2017 Dec; 19(12). doi: 10.5812/zjrms.11332.

[14] De Sousa Viana GF, de Carvalho CF, Nunes LS, Rodrigues JL, Ribeiro NS, de Almeida DA *et al.* Noninvasive biomarkers of manganese exposure and neuropsychological effects in environmentally exposed adults in Brazil. Toxicology Letters. 2014 Dec; 231(2): 169-78. doi: 10.1016/j.toxlet.2014.06.018.

[15] Almohanna HM, Ahmed AA, Tsatalis JP, Tosti A. The role of vitamins and minerals in hair loss: a review. Dermatology and Therapy. 2019 Mar; 9(1): 51-70. doi: 10.1007/s13555-018-0278-6.

[16] Roem NR, Tabri F, Waspodo NN, Patellongi I, Bukhari A, La Nafie N. Hair's Zinc Level on Androgenic Alopecia. American Journal of Clinical and Experimental Medicine. 2016 Aug; 4(5): 129-33. doi: 10.11648/j.ajcem.20160405.13.

[17] Rahman F and Akhter QS. Serum zinc and copper levels in alopecia. Journal of Bangladesh Society of Physiologist. 2019 Jun; 14(1): 21-5. doi: 10.3329/jbsp.v 14i1.41997.

[18] Ozturk P, Kurutas E, Ataseven A, Dokur N, Gumusalan Y, Gorur A *et al.* BMI and levels of zinc, copper in hair, serum and urine of Turkish male patients with androgenetic alopecia. Journal of Trace Elements in Medicine and Biology. 2014 Jul; 28(3): 266-70. doi: 10.1016/j.jtemb.2014.03.003.

[19] Kil MS, Kim CW, Kim SS. Analysis of serum zinc and copper concentrations in hair loss. Annals of Dermatology. 2013 Nov; 25(4): 405-9. doi: 10.5021/ad. 2013.25.4.405.

[20] Kang X, Zhang J, Guan M, Ding Y, Ma Y, Li T *et al.* Association between Iron Deficiency and Telogen Effluvium: a Systematic Review and Meta-Analysis. 2022 Apr. doi:10.21203/rs.3.rs-1519227/v1.

[21] Abdulqader MN, Fathi HB, Mahmood BT, Abdullah OY. Correlation between Serum Ferritin and Haemoglobin Level in Females with Hair Fall Count in Females with Chronic Telogen Effluvium. Annals of the College of Medicine, Mosul. 2023 Feb; 45(1): 1-6. doi: 10.33899/mmed.2023.137418.1178.

[22] Trost LB, Bergfeld WF, Calogeras E. The diagnosis and treatment of iron deficiency and its potential relationship to hair loss. Journal of the American Academy of Dermatology. 2006 May; 54(5): 824-44. doi: 10.1016/j.jaad.2005.11.1104.

Original Article

Comparative Sero-Analysis between Copper Levels and the Risk of Acute Myocardial Infarction in District Nowshera

Shabir Ahmed Orakzai[1], Munaza Khattak[2], Pervez Muhammad[3], Aurangzeb Khan[1], Farhan Abbas Baloch[4] and Haroon-Ur-Rasheed[5*]

[1]Department of Pathology, Swat Medical College, Swat, Pakistan
[2]Department of Physiology, Warsak Road Peshawar, Peshawar, Pakistan
[3]Department of Pathology, Jinnah Medical College, Peshawar, Pakistan
[4]Department of Pathology, College of Medicine, Qassim University Kingdom of Saudi Arabia, Buraydah, Saudi Arabia
[5]Department of Pathology, Saidu Medical College Swat, Saidu, Pakistan

ARTICLE INFO

ABSTRACT

There is an increasing evidence pointing to a possible correlation between AMI and copper levels. Serum copper levels serve as a valuable biomarker for assessing the body's copper status. **Objective:** To find the changes in serum copper level in patients with Acute Myocardial Infarction (AMI). **Methods:** This observational study was conducted in District Headquarter Hospital, Nowshera in duration of two years. A total of 240 patients were recruited in this study. Upon admission, demographic information, medical history, and clinical characteristics were collected. Blood samples were obtained for measurement of serum copper levels using established laboratory methods. All data were analyzed through SPSS version 29.0. **Results:** Among total, 65% males and 35% females and the prevalence of cardiovascular risk factors was notable, with 70% of patients having hypertension, 40% with diabetes mellitus, 60% with dyslipidemia, and 45% identified as smokers. Baseline serum copper levels averaged 110 ± 5.2 μg/dL, within 24 hours of admission, the peak serum copper level significantly increased to 125 ± 18.6 μg/dL. Subsequently, levels decreased gradually over the following days, with mean values of 120 ± 17.1 μg/dL on Day 2, 115 ± 16.4 μg/dL on Day 3, 112 ± 15.9 μg/dL on Day 4, and returning to baseline levels by Day 5, 110 ± 15.2 μg/dL. **Conclusions:** Serum copper levels exhibit significant changes during the acute phase of AMI, with a peak observed within 24 hours of admission. While patients with anterior infractions showed higher peak copper levels, no significant associations were found between copper levels and traditional cardiovascular risk factors or inflammatory markers.

INTRODUCTION

Reduced coronary blood flow can lead to cardiac ischemia and insufficient oxygen supply to the heart, which can cause Acute Myocardial Infarction (AMI) [1]. Numerous causes contribute to reduced coronary blood flow. Usually, atherosclerotic plaques burst and induce thrombosis, which causes a sudden drop in coronary blood flow [2]. Acute Myocardial Infarction (AMI), also referred to as heart attack, continues to be one of the world's major causes of mortality and morbidity. A deep understanding of the underlying mechanism of the disease is necessary for enhancing an effective therapy, prompt identification and risk assessment for this life threatening illness. In the last few years, an increased interest is seen in the function of trace elements like copper [3]. Copper being an antioxidant element, is important for energy metabolism, formation of connective tissue formation and neurotransmitter. Its involvement in copper dysregulation, oxidative stress, inflammation and endothelial dysfunction has been implicated in several cardiovascular diseases including AMI [3]. The biochemical processes in the heart muscle that are vital to cardiac metabolism and function entail copper, an important micronutrient for human health and development. One of study found that dietary copper supplementation replenished heart copper, increased

VEGF, promoted angiogenesis, and reversed mouse hypertrophic cardiomyopathy [4]. Although there is an increasing evidence pointing to a possible correlation between AMI and copper levels, the specifics of this correlation are yet not clear. Regarding variations in serum copper levels in patients with AMI, researches has given contradictory results; some have suggested high levels as a sign of oxidative stress, while others have suggested low levels as a result of acute myocardial damage [5]. Since Cardiovascular Disease (CVD) is the leading cause of morbidity and mortality globally, it is a serious threat to global public health. Despite current understanding, estimates suggest that by 2030, approximately 45% of adult Americans would have a (CVD). Globally, the top two causes of death and disability among individuals over 50 are ischemic heart disease and stroke [6]. While the known function of traditional risk factors in the pathophysiology of cardiovascular disease is well understood, new risk factors must be investigated in order to understand evolving mechanisms. Though findings are not consistent, there has been an increase in interest recently in the connection between CVD and metals like copper. Elevated exposure to certain metal compounds has fueled this interest, particularly regarding copper, which despite its vital role in cell metabolism, can also instigate oxidative stress through reactive oxygen species formation [7]. Serum copper levels serve as a valuable biomarker for assessing the body's copper status. The association between the Coronary Artery Disease (CAD) and trace elements shows two crucial aspects; one the protective role played to drinking water hardness due to the minerals including Chromium (Cr), magnesium (Mg), selenium (Si), and zinc (Zn) [8]. While the other minerals such as lead (Pb), manganese (Mn), and cadmium (Cd) are target to cause harmful to drinking water. Secondly, the involvement of serum level alteration of these trace elements following the ischemic heart disease and acute myocardial infarction [9]. The alteration has been dissimilar; for instance, stress inducing act such as marathon running have been found decrease significantly the level of serum Mg and Zn but not seen any change in Serum Cu level. Moreover, the previous experiments showed the association of coronary artery ligation in other animals like dogs have revealed marked decrease in level of serum Zn, while the level of Ca and Mg remained stable and unchanged [10].

The aim of this study was to investigate assessing baseline serum copper levels in patients treated for Acute Myocardial Infarction (AMI). Through an analysis of these baseline values, we looked at possible clinical consequences. Increased copper levels might be used as a biomarker to guide therapies and lifestyle changes related to cardiovascular risk assessment.

METHODS

This prospective observational study was conducted in District Headquarter Hospital, Nowshera, Khyber Pakhtunkhwa in duration of two years November 2021 to November 2023. The study included 240 patients, estimated using WHO software for sample size estimation. The sample size was based on a 20.8% percentage of AMI, a 95% confidence interval, and a 5% margin of error. The sample approach used was non-probability consecutive sampling. Patients aged ≥18 years, diagnosis of AMI based on clinical symptoms, electrocardiographic changes, and elevated cardiac biomarkers (troponin, CK-MB) were included in the study. While history of prior myocardial infarction or coronary revascularization, active malignancy, chronic inflammatory diseases, or other conditions affecting copper metabolism, and pregnancy or lactation were excluded from the study. The study was approved by Institution Review Board (IRB) on dated: 14-10-2021 with Reference No: ERB/DHQ/21/04. Upon admission, demographic information, medical history, and clinical characteristics of eligible patients were collected using standardized case report forms. Blood samples were obtained for measurement of serum copper levels using established laboratory methods. Serial blood samples were collected at predefined intervals during hospitalization and at follow-up visits for assessment of dynamic changes in copper levels over time. Patients underwent comprehensive clinical evaluation, including assessment of cardiovascular risk factors (hypertension, diabetes, dyslipidemia, smoking), comorbidities, and medication history. Cardiac imaging studies were performed as clinically indicated to evaluate myocardial function and coronary artery anatomy. Data were analyzed using SPSS version 29.0. Descriptive statistics were used to calculate and summarize the demographic and other clinical features of the studied participants/patients. Changes in serum copper levels over time were analyzed. Pearson correlation coefficient were used for p-value determination between serum copper levels and inflammatory markers. All data presented in the tables. P-value less than <0.05 were considered significant.

RESULTS

Data were collected from 240 patients. Mean age was 62.5 ± 8.3 years. There were 65% males and 35% females and the prevalence of cardiovascular risk factors was notable, with 70% of patients having hypertension, 40% with diabetes mellitus, 60% with dyslipidemia, and 45% identified as smokers. Baseline serum copper levels averaged 110 ± 15.2 µg/, indicating a varied range of copper concentrations within the study population (Table 1).

Table 1: Demographic Data of Patients

Variables	Values
Total Patients	240
Mean Age (Years) (Mean ± SD)	62.5 ± 8.3
Gender (%)	
Male	65%
Female	35%
Cardiovascular Risk Factors (%)	
Hypertension	70%
Diabetes Mellitus	40%
Dyslipidemia	60%
Smoking	45%
Baseline Serum Copper (µg/dL) (Mean ± SD)	110 ± 15.2

During the acute phase of Acute Myocardial Infarction (AMI), dynamic changes were observed in serum copper levels. At baseline, the mean serum copper level was 110 µg/dL with a standard deviation of 15.2. Within 24 hours of admission, the peak serum copper level significantly increased to 125 µg/dL (± 18.6). Subsequently, levels decreased gradually over the following days, with mean values of 120 µg/dL (± 17.1) on Day 2, 115 µg/dL (± 16.4) on Day 3, 112 µg/dL (± 15.9) on Day 4, and returning to baseline levels by Day 5 (110 µg/dL ± 15.2) (Table 2).

Table 2: Changes in Serum Copper Levels

Time Points	Serum Copper (µg/dL) (Mean ± SD)
Baseline	110 ± 15.2
Peak (within 24 hours)	125 ± 18.6
Day 2	120 ± 17.1
Day 3	115 ± 16.4
Day 4	112 ± 15.9
Day 5	110 ± 15.2

Peak troponin levels exhibited a strong positive correlation with serum copper levels ($r = 0.45$, $p < 0.001$), indicating a potential link between copper metabolism and myocardial damage. Similarly, peak CK-MB levels demonstrated a significant positive correlation with serum copper levels ($r = 0.38$, $p < 0.001$), further supporting the notion of copper's involvement in AMI pathogenesis. However, no significant correlations were found between serum copper levels and inflammatory markers, including CRP levels ($r = 0.12$, $p = 0.15$) and interleukin-6 levels ($r = 0.08$, $p = 0.32$) through Pearson correlation coefficient (Table 3).

Table 3: Association of Biomarkers in AMI Patients with serum coper levels

Variables	Serum coper Correlation Coefficient (r)	p-Value
Peak Troponin Levels	0.45	<0.001
Peak CK-MB Levels	0.38	<0.001
CRP Levels	0.12	0.15
Interleukin-6 Levels	0.08	0.32

Heart failure was the most common complication, occurring in 20% of patients, followed by arrhythmias in 15% and cardiogenic shock in 8%. Additionally, a subset of patients experienced other complications, collectively accounting for 5% of cases (Table 4).

Table 4: In-Hospital Complications in AMI Patients

Complications	Percentage of Patients (%)
Heart Failure	20
Arrhythmias	15
Cardiogenic Shock	8
Others	5

DISCUSSION

Our study reveals dynamic changes in serum copper levels during the acute phase of AMI, with a mean peak level of 125 µg/dL observed within 24 hours of admission, followed by a gradual decline to baseline levels over subsequent days. This study suggests strong association between alterations in the copper metabolism and AMI, possibly reflecting the release of copper from damaged myocardial tissue or changes in copper-binding proteins in response to oxidative stress and inflammation [10]. Interestingly, subgroup analysis demonstrates that patients with anterior myocardial infarction exhibit higher peak copper levels compared to those with inferior or lateral infarctions [11]. The most notable change observed in this study was the lower level of serum copper leads towards the acute myocardial infarction, particularly noteworthy among the trace divalent cations evaluated. Notably, this reduction did not reach statistical significance in females, likely due to their limited representation in the sample [12]. Nonetheless, we propose that such a reduction in serum copper levels could serve as a potential diagnostic marker for acute myocardial infarction [13]. While it is imperative to rule out causes of hypocupremia including the advance syndrome of malabsorption and the Wilson's disease, these conditions are either clinically apparent or rare occurrences [14]. The copper level in serum are increasing without treatment 125 ± 18.6 µg/dL observed in 1st 24 hours in Acute Myocardial Infarction (AMI) patients in our study but according to Omar M. Hameed in 2023 The level of Cu was observed to be significantly ($P<0.05$) higher in the serum of control people (118.50 ± 12.04 µg/dL) but according to S Begum et al 2023 control and case group respectively the copper was 105.44 ± 24.15µg/dL and 146.49 ± 23.52µg/dL [10, 15]. Asian persons had higher serum Cu levels than healthy controls SMD = 2.191, 95% CI = [1.401, 2.981] Z = 5.43, $p < 0.001$) whereas Caucasian individuals did not have higher serum Cu levels than MI SMD = 0.411, 95% CI = [−0.030, 0.851] Z = 1.83, $p = 0.068$). Increased serum Cu levels and MI are strongly correlated [16]. Serum Cu levels were significantly lower in the acute coronary syndrome group compared to the control group ($p<0.001$). Ayşegül Bayır et al., in 2013, reported that there was a significant

difference in serum Cu levels between patients with ACS and healthy control persons [17]. Increased risk factors for myocardial infarction total stroke and cardiovascular mortality have been associated with elevated levels of S-Cu. It indicates that hybrid research has changed the degree of association between S-Cu and the risk of ischemic stroke and cardiovascular mortality [18]. There is a strong association between serum trace element concentrations and certain coronary risk factors [19]. It was discovered that serum Cu and MT levels had considerably risen. The blood Zn and Cu levels in the subgroup of individuals who died were considerably lower [20]. The prevalence of cardiovascular risk factors was 65% in male and 35% females in our study is compare with Andersen et al., which reported that 47.9% females and 52.1% males with cardiovascular risk [21] but according to Wang et al., 2020 the higher prevalence in female then the male which is n=15,490 (39.4%) male and n= 23,769 (60.5%) females patient which Acute Myocardial Infarction (AMI) large population Cohort study conducted by China [22]. Taghavi *et al.,* 2020 shows that highest number of cardiac patients was male (65%) and female were 35% with the mean serum copper was 189.28 ± 58.3 [23]. Our study finding shows 8% of Acute Myocardial Infarction (AMI) patients have Cardiogenic shock is compared with Bertaina M *et al.,* in 2023 the 80% of Cardiogenic shock in Acute Myocardial Infarction (AMI) patents and 15% of of Acute Myocardial Infarction (AMI) patients were Arrhythmias [24] but according to Al Khatib *et al.,* in 2023. However it was also reported that during the peri-infarction phase, arrhythmias occur in around 75% of individuals with Acute Myocardial Infarction (AMI) [25]. Heart failure, which affects 20% of patients after an Acute Myocardial Infarction (AMI), is the most prevalent consequence, followed by arrhythmias in 15% of cases and cardiogenic shock in 8% of cases when compared across studies. In addition, 5% of cases were caused by various problems combined [26, 27]. A different study found that in-hospital mortality was 59.5% and that mechanical complications, including cardiac arrest, cardiac septal dissection, and Mitral Regurgitation (MR), were seen in 3.5 out of every thousand cases with AMI [28]. In addition, patients with Cardiogenic Shock linked to Heart Failure (HF-CS) had a reduced in-hospital mortality rate, a lower age, and a lower number of cardiac arrests in contrast to patients with cardiogenic shock due to AMI [29]. When considering several forms of cardiogenic shock in the setting of an acute myocardial infarction, these results highlight the differences in their clinical presentations and results.

CONCLUSIONS

This study concludes that during the acute phase of AMI, a significant change in serum copper levels are seen,

peaking within 24 hours of admission. Although patients with anterior infarcts had high copper levels, no meaningful associations were seen between levels of copper and inflammatory markers or cardiovascular risk factors.

Authors Contribution

Conceptualization: SAO
Methodology: SAO, PM
Formal analysis: PM, AK
Writing, review and editing: MK, FAB, HUR

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

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

REFERENCES

[1] Pagliaro BR, Cannata F, Stefanini GG, Bolognese L. Myocardial ischemia and coronary disease in heart failure. Heart Failure Reviews. 2020 Jan; 25(1): 53-65. doi: 10.1007/s10741-019-09831-z.

[2] Katari V, Kanajam LS, Kokkiligadda S, Sharon T, Kantamaneni P. A review on causes of myocardial infarction and its management. World Journal of Pharmaceutical Research. 2023 Mar; 12(6): 511-29. doi: 10.20959/wjpr20236-27881.

[3] Singh MM, Singh R, Khare A, Gupta MC, Patney NL, Jain VK *et al.* Serum copper in myocardial infarction-diagnostic and prognostic significance. Angiology. 1985 Aug; 36(8): 504-10. doi: 10.1177/000331978503600805.

[4] Bagheri B, Akbari N, Tabiban S, Habibi V, Mokhberi V. Serum level of copper in patients with coronary artery disease. Nigerian Medical Journal. 2015 Jan; 56(1): 39-42. doi: 10.4103/0300-1652.149169.

[5] Li X, Ling J, Hu Q, Fang C, Mei K, Wu Y *et al.* Association of serum copper (Cu) with cardiovascular mortality and all-cause mortality in a general population: a prospective cohort study. BMC Public Health. 2023 Nov; 23(1): 2138. doi: 10.1186/s12889-023-17018-3.

[6] Mirończuk A, Kapica-Topczewska K, Socha K, Soroczyńska J, Jamiołkowski J, Kułakowska A *et al.* Selenium, Copper, Zinc Concentrations and Cu/Zn, Cu/Se Molar Ratios in the serum of patients with acute ischemic stroke in Northeastern Poland-a new insight into stroke pathophysiology. Nutrients. 2021 Jun; 13(7): 2139. doi: 10.3390/nu13072139.

[7] Mandal R, Kaur S, Gupta VK, Joshi A. Heavy metals controlling cardiovascular diseases risk factors in myocardial infarction patients in critically

environmentally heavy metal-polluted steel industrial town Mandi-Gobindgarh (India). Environmental Geochemistry and Health. 2022 Oct; 44(10): 3215-38. doi: 10.1007/s10653-021-01068-w.

[8] Uddin SN, Rahaman MZ, Thammi TJ, Islam MR, Masud MI, Uddin MG *et al.* Low serum concentration of zinc, selenium, calcium, potassium and high serum concentration of iron, sodium are associated with myocardial infarction. Aging and Health Research. 2022 Mar; 2(1): 100063. doi: 10.1016/j.ahr.2022.100063.

[9] Wen H, Niu X, Hu L, Sun N, Zhao R, Wang Q *et al.* Dietary copper intake and risk of myocardial infarction in US adults: A propensity score-matched analysis. Frontiers in Cardiovascular Medicine. 2022 Nov; 9: 942000. doi: 10.3389/fcvm.2022.942000.

[10] Hameed OM. Estimation of some Trace Elements in the Sera of People with Myocardial Infarction Disease. InE3S Web of Conferences. 2023; 391: 01124. doi: 10.1051/e3sconf/202339101124.

[11] Hussein Challoob M and Mohammed MT. Evaluation of Some Trace Elements and Serum Electrolytes in Patients with Acute Myocardial Infraction. Egyptian Journal of Chemistry. 2023 May; 66(5): 93-7. doi: 10.21608/EJCHEM.2022.141245.6172.

[12] Nowicki GJ, Ślusarska B, Prystupa A, Blicharska E, Adamczuk A, Czernecki T *et al.* Assessment of Concentrations of Heavy Metals (Cu, Zn, Mn, Co, and Fe) in Postmyocardial Infarction Patients and Patients Free from Cardiovascular Event and Their Relationship with the Occurrence of Myocardial Infarction. 2021 Jan; 2021: 9546358. doi: 10.1155/2021/9546358.

[13] Yang S, Li Y, Zhou L, Wang X, Liu L, Wu M. Copper homeostasis and cuproptosis in atherosclerosis: metabolism, mechanisms and potential therapeutic strategies. Cell Death Discovery. 2024 Jan; 10(1): 25. doi: 10.1038/s41420-023-01796-1.

[14] Tarantino G, Porcu C, Arciello M, Andreozzi P, Balsano C. Prediction of carotid intima-media thickness in obese patients with low prevalence of comorbidities by serum copper bioavailability. Journal of Gastroenterology and Hepatology. 2018 Aug; 33(8): 1511-7. doi: 10.1111/jgh.14104.

[15] Begum S, Sultana I, Faysal MR, Alam S, Tasnim J, Akter T *et al.* Study of Changes in Serum Copper Level in Patients with Acute Myocardial Infarction. Mymensingh Medical Journal. 2023 Jan; 32(1): 39-43.

[16] Meng JB, Hu MH, Zhang M, Hu GP, Zhang W, Hu SJ. The correlation between whole blood copper (Cu), zinc (Zn) levels and Cu/Zn ratio and sepsis-induced left ventricular systolic dysfunction (SILVSD) in patients with septic shock: a single-center prospective observational study. International Journal of General Medicine. 2021 Oct; 27: 7219-34. doi: 10.2147/IJGM.S335348.

[17] Bayır A, Kara H, Kıyıcı A, Öztürk B, Akyürek F. Levels of selenium, zinc, copper, and cardiac troponin I in serum of patients with acute coronary syndrome. Biological Trace Element Research. 2013 Sep; 154: 352-6. doi: 10.1007/s12011-013-9754-0.

[18] Chen A, Li G, Liu Y. Association between copper levels and myocardial infarction: a meta-analysis. Inhalation Toxicology. 2015 Apr; 27(5): 237-46. doi: 10.3109/08958378.2015.1030480.

[19] Munoz-Bravo C, Soler-Iborte E, Lozano-Lorca M, Kouiti M, González-Palacios Torres C, Barrios-Rodriguez R *et al.* Serum copper levels and risk of major adverse cardiovascular events: a systematic review and meta-analysis. Frontiers in Cardiovascular Medicine. 2023 Jun; 10: 1217748. doi: 10.3389/fcvm.2023.1217748.

[20] Ghayour-Mobarhan M, Shapouri-Moghaddam A, Azimi-Nezhad M, Esmaeili H, Parizadeh SM, Safarian M *et al.* The relationship between established coronary risk factors and serum copper and zinc concentrations in a large Persian cohort. Journal of Trace Elements in Medicine and Biology. 2009 Jul; 23(3): 167-75. doi: 10.1016/j.jtemb.2009.03.006.

[21] Andersen KK, Andersen ZJ, Olsen TS. Age-and gender-specific prevalence of cardiovascular risk factors in 40 102 patients with first-ever ischemic stroke: A Nationwide Danish Study. Stroke. 2010 Dec; 41(12): 2768-74. doi: 10.1161/STROKEAHA.110.595785.

[22] Wang Y, Li Y, Liu X, Zhang H, Abdulai T, Tu R *et al.* Prevalence and influencing factors of coronary heart disease and stroke in Chinese rural adults: the Henan rural cohort study. Frontiers in Public Health. 2020 Jan; 7: 411. doi: 10.3389/fpubh.2019.00411.

[23] Taghavi S, Naderi N, Amin A, Mobini S, Safavirad A, *et al.* Serum Copper Level in Patients with Heart Failure and Its Related Factors. Multidiscip Cardio Annal. 2021;12(1):e108015.

[24] Bertaina M, Morici N, Frea S, Garatti L, Briani M, Sorini C *et al.* Differences between cardiogenic shock related to acute decompensated heart failure and acute myocardial infarction. ESC Heart Failure. 2023 Dec; 10(6): 3472-82. doi: 10.1002/ehf2.14510.

[25] Al Khatib M, Kteifan A, Shamiyeh M. A Study of Cardiac Arrhythmias in Patients with Myocardial Infarction (STEMI) During The First 48 Hours in The Intensive Care Unit and Its Relationship with Age, Sex, Site of Infarction And Other Risk Factors. Annals of Medicine and Surgery. 2023 Sep; 85(10): 4824-4829. doi: 10.1097/MS9.0000000000001264.

[26] Varshney AS, Berg D, Palazzolo MG, Bohula EA, Katz JN, Van Diepen S *et al.* End-Organ Dysfunction Differs in Patients With Heart Failure-Related vs. Acute Myocardial Infarction-Related Cardiogenic Shock. Circulation. 2022 Nov; 146(1): A11098-. doi: 10.1161/circ.146.suppl_1.11098.

[27] Sinha SS, Rosner CM, Tehrani BN, Maini A, Truesdell AG, Lee SB *et al.* Cardiogenic shock from heart failure versus acute myocardial infarction: clinical characteristics, hospital course, and 1-year outcomes. Circulation: Heart Failure. 2022 Jun; 15(6): e009279. doi: 10.1161/Circheartfailure.121.009279.

[28] Sawano S, Sakakura K, Taniguchi Y, Yamamoto K, Tsukui T, Seguchi M *et al.* Outcomes of patients with acute myocardial infarction who recovered from severe in-hospital complications. The American Journal of Cardiology. 2020 Nov; 135: 24-31. doi: 10.10 16/j.amjcard.2020.08.031.

[29] Sanmartín-Fernández M, Raposeiras-Roubín S, Anguita-Sánchez M, Marín F, García-Márquez M, Fernández-Pérez C *et al.* In-hospital outcomes of mechanical complications in acute myocardial infarction: Analysis from a nationwide Spanish database. Cardiology Journal. 2021; 28(4): 589-97. doi: 10.5603/CJ.a2020.0181.

PAKISTAN JOURNAL OF HEALTH SCIENCES

Original Article

Assessment of Workplace Difficulties Faced by Nurses Working in Public Sector Hospitals of Lahore

Naveeda Aslam[1*], Madiha Mukhtar[1] and Sarfaraz Masih[1]

[1]Lahore School of Nursing, University of Lahore, Lahore, Pakistan

ARTICLE INFO

*Corresponding Author:

Naveeda Aslam
Lahore School of Nursing, University of Lahore, Lahore, Pakistan
nida.asslam@gmail.com

ABSTRACT

Nursing is recognized as a stressful profession, with adverse effects on both personal health and professional performance. However, there is a scarcity of data on stress prevalence among nurses in developing countries like Pakistan. **Objective:** To assess stress prevalence and contributing factors among nurses in government hospitals, informing interventions to improve their work environment and well-being. **Methods:** This descriptive cross-sectional survey collected data from Mayo Hospital, Lady Atchison Hospital, and Said Mitha Hospital in Lahore. A structured questionnaire assessed demographic information and perceptions across four domains: Occupational Stress, Job Satisfaction, Workplace Violence, and Workplace Harassment. Likert scale items were analyzed using SPSS version 26.0, with logistic regression examining factors associated with job satisfaction. **Results:** Findings reveal significant concerns regarding occupational stress, job satisfaction, workplace violence, and harassment among nurses. While nurses express satisfaction with certain aspects of their job, including opportunities to utilize their abilities and relations between management and staff, concerns arise regarding workload, recognition, pay rates, and workplace violence and harassment. Logistic regression analysis indicates that age, educational qualifications, marital status, experience duration, and department insignificantly influence job satisfaction among nurses in public sector hospitals. **Conclusions:** These findings emphasize the urgent need to address the challenges faced by nurses to enhance their well-being and maintain a positive work environment conducive to high-quality patient care.

INTRODUCTION

Medical professionals experience considerable stress as a consequence of the challenging nature of their job, which often leads to negative effects on physical as well as mental wellness. Stress, which is defined as experiencing tension, worry, and excessive workload, may arise from a range of internal and environmental reasons. Healthcare personnel often experience occupational stress, particularly stress connected to their employment, which originates mostly from their workplace [1, 2]. In addition, the occupational environment of the healthcare institutions is fueled with stress and burnout and high turnover [3]. The magnitude of stress, bulling, or even violence among Nurses varies from country to country ranged from 24.7% to 88.9% and even, the extent worse from one working department to another department; emergency, geriatric and psychiatry facilities are among the leading departments Colleagues, supervisors/directors, physicians, patients and patients relatives are the primary perpetrators who inflict WPV on health professionals, which ultimately impact the Nurses health and safety and their service [4, 5]. Further, Patients can be challenging, angry and scared, and nurses may respond with increasing anger and irritation that may cause distress [6]. A study "found that 30% of the nursing assistants indicated that they previously experienced physical injuries from aggression by residents [7]. Nursing staff occasionally works long shifts and do not get enough rest. Consequently, it's a highly stressful profession, and also requires interaction with patients, who are also under stress due to their conditions. Patients can be challenging, angry and scared, and nurses may respond with increasing

anger and irritation that may cause distress [6]. The difficulty such as stress, bulling, or even violence inflicted injury could be physical, psychological or concurrent type that encompasses verbal abuse, bullying/mobbing, sexual harassment, racial harassment and from simple physical injury to possible homicide, that results physical, mental, spiritual, moral or social mal development. on the other hand a study conducted on health care staff working in an hospital in the United Kingdom showed that among all medical professionals nurses are under highest pressure [8]. An Indian study reported 87.3% prevalence rate of stress among the nurses [9]. The violence might be expressed in not only in a single incident but in repeated incidents also and in various forms, which cumulatively endangers the victim's wellbeing and their work performance. The healthcare workers might encounter the incident at work or from work or to work, which includes work related circumstances [10]. Previous research indicates that there is a higher incidence of violence against unmarried nurses in Pakistan and other developing regions[11, 12].

This study was aimed to assess stress prevalence and contributing factors among nurses in government hospitals, informing interventions to improve their work environment and well-being.

METHODS

This research used data obtained from a descriptive cross-sectional survey carried out at Mayo Hospital, Lady Atchison Hospital, and Said Mitha Hospital, located in Lahore. The measuring methodology performed in this research was the use of a structured questionnaire consisting of two primary components. The first component, designed to collect demographic data. The second component of the survey questionnaire aimed to evaluate nurses' attitudes as well as experiences in four specific areas: Workplace Harassment, Job Satisfaction, Occupational Stress, and Workplace Violence. This part was comprised of 43 Likert scale items. The survey lasted for a period of 4 months from January 2024 to 30, April 2024 after receiving clearance from Research Ethics Committee (REC) for the study description on January 1st, 2024, Ref No: REC-UOL-638-01-2024. The method of simple random sampling was used to select the participants.

Sample size of 303 nurses is estimated by using 95% confidence level, 8% absolute precision with expended % of Workplace difficulties faced by Nurses working in Public Sector Hospitals of Lahore As 73.1% [11].

$Z^2_{1-\alpha/2=}$ Confidence Level 95% = 1.96
p = Prevalence 73%
q = 1-p
d = absolute precision 8%
n = 303

$$n = \frac{Z^2_{1-\alpha/2} \cdot p.q}{d^2}$$

SPSS version 26.0 was used for data analysis. All the demographic variables were presented as frequency and percentages. The responses of the items of questionnaire were also summarized using frequency and percentages. Subsequently, the data were tabulated, and the distribution of responses across age categories and categories of marital status were analyzed using chi-square. To calculate the mean satisfaction score for each item, item no. 5,8,19 to 43 were reverse coded. Healthcare staff members were categorized into two groups based on their job satisfaction: satisfied and dissatisfied. The overall perception of job satisfaction for each respondent was determined by averaging their scores across 43 items related to job satisfaction. Individuals with a mean score exceeding 3 were classified into the satisfied group (coded as 1), while those with mean scores equal to or below 3 were categorized into the dissatisfied group (coded as 0). Binary logistic regression was employed to assess the factors significantly linked with the two levels of job satisfaction. The statistical significance of these findings was assessed using a p-value, with a threshold set at 0.05

RESULTS

A total of 303 only female nurses participated in the survey. The demographic profile of the study participants was diverse. The majority (55.8%) were aged between 22-30 years, followed by 27.4% in the 31-40 years age group. In terms of educational background, 43.8% held a diploma in general nursing, 29.4% had completed Post RN BSN, and 26.7% attained a Generic BSN qualification. Marital status indicated that 64.5% were married, 34.1% unmarried, and only 0.33% reported being divorced or separated. Experience levels varied, with 32.3% having 1-5 years of experience, 29.5% with 6-10 years, 15.1% with 11-15 years, and 23.4% with over 15 years. Distribution across departments showed 29.0% in medical, 10.8% in surgical, 26.1% in emergency, 6.2% in psychiatric, and 27.3% in pediatrics, reflecting the diverse participant profile (Table 1).

Table 1: Demographic Characteristics of the Respondents

Variable	n (%)
Age (n = 303)	
22-30 years	169 (55.8%)
31-40 years	83 (27.4%)
41-50 years	27 (8.9%)
>50 years	24 (7.9%)
Educational Status (n = 303)	
Diploma in general nursing	133 (43.8%)
Post RN BSN	89 (29.4%)
Generic BSN	81 (26.7%)

Marital Status (n = 303)	
Married	196 (64.5%)
Unmarried	106 (34.1%)
Divorced/ separation	1 (0.33%
Experience (n = 303)	
1-5 years	97 (32.3%)
6-10 years	89 (29.5%
11-15 years	46 (15.1%)
More than 15	71 (23.4%)
Department (n = 303)	
Surgical	33 (10.8%)
Medical	88 (29.1%)
Emergency	79 (26.1%)
Psychiatric	19 (6.2%)
Pediatrics	84 (27.7%)

The questionnaire data reveals various insights into occupational stress, job satisfaction, workplace violence, and harassment experienced by nurses. When it comes to occupational stress, approximately 34.6% of respondents agreed or strongly agreed that they have to handle a significant workload in their job. However, only about 37.7% felt that most of their suggestions were taken into consideration, and roughly 31.7% believed that higher authorities adequately care for their self-respect. Moreover, around 49.5% expressed dissatisfaction with the monotonous nature of their assignments, and about 29.7% reported having to undertake tasks unwillingly due to group or political pressure. Additionally, concerns regarding official interference in their working methods or jurisdiction were voiced by approximately 49% of respondents. Regarding job satisfaction, around 39.3% perceived the physical working conditions positively, while a similar percentage, approximately 48.2%, expressed dissatisfaction with the level of freedom to choose their working methods. Recognition for good work was acknowledged by about 37.7% of respondents, while similar, around 39%, felt secure in their job. Concerns about workplace violence were significant, with 42% expressing concerns about its increase over the last twelve months, and nearly 42% finding it worrying. The workplace violence affects nurses' ability to provide effective care, motivation to work, and potential for errors indicating adverse effects. Regarding workplace harassment, a substantial number of nurses reported experiencing various forms of mistreatment, including unwanted sexual advances, ridicule, verbal abuse, and threats of physical abuse. Instances of being deprived of responsibility or work tasks and social exclusion were also distressingly common. Moreover, approximately 32.4% reported experiencing unwanted sexual attention, while around 30.4% noted receiving hints or signals from others to quit their job. The study findings indicate that nurses generally expressed satisfaction with certain aspects of their job, as reflected

by mean satisfaction scores exceeding 3. These aspects include opportunities to use their abilities, relations between management and staff, and physical conditions in the workplace. However, where mean satisfaction scores were below (Table 2).

Table 2: Mean Satisfaction Scores for Various Aspects of Job Satisfaction, Occupational Stress, Workplace Violence, and Workplace Harassment

Variable	Mean ± SD
Occupational Stress	
I have to do lot of work at job	2.83 ± 1.25
Most of my suggestion are heeded and implemented here	2.87 ± 1.35
Higher authorities do care of myself respect	2.68 ± 1.25
My assignments are of monotonous nature	2.68 ± 1.25
I have to do some work unwillingly owning to certain group or political pressure	3.31 ± 1.25
Official do not interfere with jurisdiction or my working methodp or political pressure	2.75 ± 1.28
My decision and instruction concerning distribution among employees are properly followed	2.91 ± 1.37
The available information related to my job role and its outcomes are vague and insufficient	3.13 ± 1.38
Job Satisfaction	
The physical conditions in which you work is good	2.89 ± 1.39
Freedom to choose your own working methods	2.82 ± 1.33
The recognition you get for good work	2.85 ± 1.41
The amount of responsibility you are given	2.86 ± 1.30
The rate of pay for nurses is good	2.93 ± 1.41
The opportunity to use your abilities	3.01 ± 1.43
Relations between management and staff	3.09 ± 1.46
Future chance of promotion	2.72 ± 1.30
Security of employment	2.89 ± 1.39
Your job Security	2.89 ± 1.39
Workplace Violence	
Workplace violence has increased over the last twelve months	3.03 ± 1.42
Workplace violence is worrying for me	3.07 ± 1.33
Reduce ability to offer effective care to patients	3.07 ± 1.32
Reduce motivation to work	2.90 ± 1.43
Increase potential to make errors	3.02 ± 1.40
Negatively impacts relationship with staff	2.99 ± 1.40
Negative psychosocial effect	2.96 ± 1.40
Repeated disturbing memories or thoughts of attack	2.97 ± 1.40
Repeated thinking or thoughts of attack	3.06 ± 1.36
Being super alert or watchful and on guard	3.05 ± 1.31
Workplace Harassment	
Someone withholding necessary information so that your work gets complicated	3.11 ± 1.33
Unwanted sexual advances	3.17 ± 1.32
Ridicule or insulting teasing	3.09 ± 1.33
Ordered to do work below your level of competence	3.06 ± 1.36
Being deprived of responsibility or work tasks	3.31 ± 1.22
Gossip or rumors about you	3.27 ± 1.26
Social exclusion from co-workers or work group activities	3.34 ± 1.22
Repeated offensive remarks about you or your private life	3.28 ± 1.20
Verbal abuse	3.26 ± 1.35

Unwanted sexual attention	3.21 ± 1.33
Hint or signals from others that you should quit your job	3.37 ± 1.30
Physical abuse or threats of physical abuse	3.37 ± 1.32
Repeated reminders about your blunders	3.34 ± 1.25
Silence or hostility as a response to your questions or attempts at conversations	3.46 ± 1.25
Devaluing of your work and efforts	3.34 ± 1.28

Note: Item no. 5, 8, 19-43 are reverse coded.

The logistic regression analysis examined factors associated with job satisfaction among nurses in public sector hospitals of Lahore. Age, educational status, marital status, experience, and department were compared between "Dissatisfied" and "Satisfied" groups. Results showed no significant differences in job satisfaction across age groups, educational statuses, marital statuses, experience levels, or departments (p > 0.05 for all comparisons). Although nurses with Post RN BSN and Generic BSN qualifications had higher odds of satisfaction compared to those with a Diploma in general nursing, the difference was not statistically significant. Similarly, nurses in the Pediatrics department showed higher odds of satisfaction, but this result did not reach statistical significance. Overall, age, educational status, marital status, experience, and department were not significant predictors of job satisfaction among nurses in this study (Table 3).

Table 3: Factors Influencing Job Satisfaction among Nurses

Factors	Dis-satisfied (n = 135)	Satisfied (n = 168)	B	P value	OR	95% CI for OR Lower	95% CI for OR Upper
Age (n = 303)							
22-30 years (ref)	78 (57.8%)	91 (54.2%)	-	0.706	-	-	-
31- 40 years	38 (28.1%)	45 (26.8%)	-0.657	0.297	0.519	0.151	1.781
41- 50 years	10 (7.4%)	17 (10.1%)	-0.391	0.552	0.676	0.186	2.456
>50 years	9 (6.7%)	15 (8.9%)	-0.440	0.567	0.644	0.143	2.903
Educational Status							
Diploma in general nursing (ref)	78 (57.8%)	91 (54.2%)	-	0.706	-	-	-
Post RN BSN	38 (28.1%)	45 (26.8%)	-0.657	0.297	0.519	0.151	1.781
Generic BSN	10 (7.4%)	17 (10.1%)	-0.391	0.552	0.676	0.186	2.456
Marital Status (ref: married)							
Unmarried/ divorced	43 (35.2%)	48 (32.0%)	0.168	0.674	1.183	0.540	2.594
Experience							
1-5 years (ref)	45 (33.8%)	50 (31.1%)	-	0.518	-	-	-
6-10 years	40 (30.1%)	47 (29.2%)	0.629	0.334	1.875	0.524	6.711
11-15 years	22 (16.5%)	22 (13.7%)	-0.193	0.669	0.824	0.339	2.001
More than 15	26 (19.5%)	42 (26.1%)	-0.181	0.730	0.835	0.299	2.333

Department							
Surgical (ref)	11 (11.2%)	8 (5.9%)	-	0.427	-	-	-
Medical	30 (30.6%)	44 (32.4%)	-1.031	0.086	0.357	0.110	1.156
Emergency	31 (31.6%)	35 (25.7%)	-0.155	0.685	0.856	0.404	1.815
Psychiatric	1 (1%)	5 (3.7%)	-0.424	0.273	0.654	0.307	1.396
Pediatrics	25 (25.5%)	44 (32.4%)	0.439	0.721	1.551	0.140	17.234
Constant	-	-	0.077	0.929	1.080	-	-

DISCUSSION

The proportion of working women within Pakistan had a progressive growth from thirteen percent in 2000 to 22 percent in the year 2011 [13]. Nevertheless, despite the advancements made, women often encounter restrictions that confine them to traditionally feminine professions like nursing and teaching. Consequently, they typically have little employment benefits and insufficient safeguards in the workplace. Studies indicate that workplace violence (WPV) targeting nurses has substantial adverse effects, affecting their physical as well as emotional well-being, their responsibilities in patient care, hospital collaboration, including overall security of patients [14]. A study conducted recently on the difficulties encountered by nurses has uncovered concerning revelations. According to a research, 42 percent of nurses see an exacerbation of violence in the workplace in the last year. Approximately 28.1% of the participants reported encountering physical aggression, while 32.6% experienced verbal abuse, and 34.7 percent faced various other types of violence [11]. According to local research, nurses often work in dangerous and aggressive environments, experiencing as much as 80% of incidents involving patient aggression as well as verbal abuse [15]. Patients, relatives, and colleagues are the main culprits responsible for workplace violence towards nurses. Crucially, female nurse practitioners who encounter violence in hospital environments may also be subjected to abuse at home, since individuals who commit acts of violence at work are more prone to engaging in domestic abuse [16, 17]. This highlights the pressing need to tackle incidents of violent behavior at work towards nurses in Pakistan. The present research results on occupational stress amongst nurses, when compared to previous studies, demonstrate similar patterns and difficulties encountered by nursing professionals. The data suggests that a substantial percentage of nurses (about 35%) have a sense of burden due to the demands of their task. This finding is consistent with prior research that has identified workload as a primary source of stress amongst nurses [18]. Furthermore, the failure to put into effect the recommendations made by nurses and the perception of

83

inadequate concern from higher authorities align with the results of previous research studies, underscoring the need of resolving these problems in order to avoid dissatisfaction as well as disconnection among nursing professionals [19]. Regarding job satisfaction, nurses often express worries about insufficient recognition, wages, and advancement chances, which consistently emerge as challenges in many surveys. However, they also acknowledge positive features such as decent working conditions and opportunity to maximize their expertise [19]. These characteristics have a substantial influence on the overall work satisfaction as well as motivation of nurses, highlighting the necessity for interventions to tackle these problems and improve job satisfaction in nursing field. The data also revealed concerns regarding violence in the workplace, as nurses express concern about its frequency and influence on their capacity to deliver efficient care, as well as a possibility for errors. This aligns with extensive research indicating the adverse effects of violence in the workplace on nursing staff's overall well-being as well as the outcomes of patient care [20].

CONCLUSIONS

In conclusion, this study sheds light on the prevalence of stress among nurses in government hospitals in Pakistan, highlighting the need for targeted interventions to alleviate their burden. Despite some positive indicators of job satisfaction, concerns regarding occupational stress, workplace violence, and harassment persist. Future research and policy initiatives should focus on implementing effective strategies to create supportive work environments in Pakistan.

Authors Contribution

Conceptualization: AS, JA
Methodology: BR, AA, SMZHN, JM
Formal analysis: AS, BR, AA, MK, SMZHN,
Writing-review and editing: AS

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

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

REFERENCES

[1]   Cohen J and Venter WDF. The integration of occupational-and household-based chronic stress among South African women employed as public hospital nurses. PloS One. 2020; 15(5): e0231693. doi:10.1371/journal.pone.0231693.

[2]   Novaes Neto EM, Xavier AS, Araújo TM. Factors associated with occupational stress among nursing professionals in health services of medium complexity. Revista Brasileira de Enfermagem. 2020 Jun 1; 73: e20180913. doi:10.1590/0034-7167-2018-0913

[3]   Legesse H. Workplace violence and its associated factors among nurses working in government hospitals of Harari regional state and Dire Dawa City Administration, Eastern Ethiopia [Doctoral dissertation]. Ethiopia: Haramaya university; 2021.

[4]   Phillips JP. Workplace violence against health care workers in the United States. New England Journal of Medicine. 2016 Apr; 374(17): 1661-9. doi:10.1056/NEJMra1501998.

[5]   Alkorashy HAE and Al Moalad FB. Workplace violence against nursing staff in a Saudi university hospital. International Nursing Review. 2016 Jun; 63(2): 226-32. doi:10.1111/inr.12242.

[6]   Lebni JY, Toghroli R, Abbas J, Kianipour N, NeJhaddadgar N, Salahshoor MR, *et al.* Nurses' work-related quality of life and its influencing demographic factors at a public hospital in Western Iran: a cross-sectional study. International Quarterly of Community Health Education. 2021 Oct; 42(1): 37-45. doi:10.1177/0272684X20972838.

[7]   Botngård A, Eide AH, Mosqueda L, Malmedal W. Resident-to-resident aggression in Norwegian nursing homes: a cross-sectional exploratory study. BMC Geriatrics. 2020 Dec; 20(1): 1-10. doi:10.1186/s12877-020-01623-7.

[8]   Hunter B, Fenwick J, Sidebotham M, Henley J. Midwives in the United Kingdom: Levels of burnout, depression, anxiety and stress and associated predictors. Midwifery. 2019 Dec 1; 79: 102526. doi:10.1016/j.midw.2019.08.008

[9]   Sharma P, Srivastava K, Landge J, Vyas S. Impact of imparting emotional intelligence skills training program to enhance emotional intelligence and work stress among staff nurses of tertiary care hospital of North Gujarat. Medical Journal of Dr DY Patil University. 2023 May; 16(3): 348-52.

[10]   Boyle MJ, Wallis J. Working towards a definition for workplace violence actions in the health sector. Safety in Health. 2016 Dec; 2: 1-6. doi:10.1186/s40886-016-0015-8

[11]   Jafree SR. Workplace violence against women nurses working in two public sector hospitals of Lahore, Pakistan. Nursing Outlook. 2017; 65(4): 420-7. doi:10.1016/j.outlook.2017.01.008.

[12]   Boafo IM, Hancock P, Gringart E. Sources, incidence and effects of non-physical workplace violence against nurses in Ghana. Nursing Open. 2016 Apr; 3(2):

99–109. doi:10.1002/nop2.43

[13] Begum Sadaquat M, Sheikh QT. Employment situation of women in Pakistan. International Journal of Social Economics. 2011 Jan; 38(2): 98-113. doi:10.1108/03068291111091981

[14] Roche M, Diers D, Duffield C, Catling-Paull C. Violence toward nurses, the work environment, and patient outcomes. Journal of Nursing Scholarship. 2010 Mar; 42(1): 13-22. doi:10.1111/j.1547-5069.2009.01321.x.

[15] Ferri P, Stifani S, Accoto A, Bonetti L, Rubbi I, Di Lorenzo R. Violence against nurses in the triage area: a mixed-methods study. Journal of Emergency Nursing. 2020 May; 46(3): 384-97. doi:10.1016/j.jen.20 20.02.013

[16] Najafi F, Fallahi-Khoshknab M, Ahmadi F, Dalvandi A, Rahgozar M. Antecedents and consequences of workplace violence against nurses: A qualitative study. Journal of Clinical Nursing. 2018 Jan; 27(1-2): e116-28. doi:10.1111/jocn.13884

[17] Alshammari KF, McGarry J, Higginbottom GM. Nurse education and understanding related to domestic violence and abuse against women: An integrative review of the literature. Nursing Open. 2018 Jul; 5(3): 237-53. doi:10.1002/nop2.133

[18] Okuhara M, Sato K, Kodama Y. The nurses' occupational stress components and outcomes, findings from an integrative review. Nursing Open. 2021 Sep; 8(5): 2153-74. doi:10.1002/nop2.780

[19] Werke EB, Weret ZS. Occupational stress and associated factors among nurses working at public hospitals of Addis Ababa, Ethiopia, 2022; A hospital based cross-sectional study. Frontiers in Public Health. 2023 Apr; 11: 1147086. doi:10.3389/fpubh.20 23.1147086

[20] Liu J, Zheng J, Liu K, Liu X, Wu Y, Wang J, You L. Workplace violence against nurses, job satisfaction, burnout, and patient safety in Chinese hospitals. Nursing Outlook. 2019 Sep; 67(5): 558-66. doi:10.1016/ j.outlook.2019.04.006

Original Article

Zinc Deficiency in Type II Diabetes Mellitus

Muhammad Faisal Javaid[1*], Saima Rasheed[2], Rafiq Ahmad Siddiqui[3], Bilal Habib[4], Erum Rashid Chaudhry[2] and Anam Abdul Rasheed[5]

[1]Department of Biochemistry, Niazi Medical and Dental College, Sargodha, Pakistan
[2]Department of Biochemistry, Watim Medical and Dental College, Rawalpindi, Pakistan
[3]Department of Biochemistry, Services Institute of Medical Sciences, Lahore, Pakistan
[4]Department of Physiology, Rai Medical College, Sargodha, Pakistan
[5]Department of Physiology, Niazi Medical and Dental College, Sargodha, Pakistan

ARTICLE INFO

ABSTRACT

Zinc (Zn) is an essential trace element for various biochemical, physiological and immunological functions in the human body. Zn deficiency affects up to 25% of the population in poor countries and up to 15% in industrialized countries. Diabetes Mellitus (DM) refers to impaired glucose metabolism, which leads to a constellation of disorders and is marked by poor immunity in the diseased subject. Zn deficiency has an inverse relationship with glycemic control. **Objective:** To assess the serum Zn level in diabetic patients in comparison with healthy subjects. **Method:** A cross sectional study was conducted at Department of Biochemistry, Niazi Welfare Foundation Teaching Hospital, Sargodha, Pakistan from 1st June, 2023 to 31st December, 2023. Data were collected after institutional review board (IRB) approval (NM&DC-IRB-53; Dated 1st Dec, 2022) and informed consent was taken from all the participants. A total of 150 participants were equally divided into two groups based on glycemic control. Serum Zn levels of all participants were estimated via atomic absorption spectrophotometry. Descriptive statistic was used to calculate mean and standard deviation on SPSS version 23.0. **Results:** The mean value of serum Zn level was significantly lower (8.83 ± 1.64 µmol/L) in diabetic subjects as compared to healthy participants (18.63 ± 6.13 µmol/L). **Conclusions:** Deficiency of serum Zn level has a negative relationship with the body's glycemic control.

INTRODUCTION

Diabetes mellitus (DM) refers to a spectrum of disorders characterized by hyperglycemia [1]. Multiple factors play a role in its etiogenesis, including defects in insulin secretion, insulin action, or both, and disorderly metabolism of carbohydrates, fat and protein. It has two subtypes, Type 1 DM and Type II DM, depending on the absence of insulin secretion in cases of autoimmune destruction of pancreatic beta cells or its reduced secretion with resistant insulin receptors [2]. The diagnostic criteria for confirmation of disease is fasting plasma glucose ≥ 7.0 mmol/L or 2-hour post-load plasma glucose ≥ 11.1 mmol/L or Hba1c ≥ 48 mmol/mol [1]. The international diabetes federation (IDF) estimated the presence of 463 million cases of DM in 2019, which is expected to reach 700 million in 2045 [3]. It is a disease of urbanization, predominant among residents of urban (10.8%) regions than rural (7.2%) inhabitants, and in developed (10.4%) than underdeveloped countries (4.0%) [4]. Due to diverse pathogenic pathways, DM affects the human body in various harmful ways. One such phenomenon is the defective homeostasis of trace elements in the body. Trace elements include chromium (Cr), copper (Cu), iron (Fe), manganese (Mn), mercury (Hg), nickel (Ni), lead (Pb), selenium (Se), and zinc (Zn) etc. They are an integral part of a healthy life. These trace elements are crucial for many physiological and biochemical

processes in the body, including several enzymatic reactions [5]. Zn is the 2nd most abundant element in the human body, responsible for several biochemical reactions including bone metabolism, numerous hormone regulations, as well as cellular immune functions [6]. One of its major functions is the metabolism of carbohydrates in the human body. Zinc is stored with the insulin, in the beta cells of the pancreas and stimulates the phosphorylation of insulin receptor beta subunit [7]. Moreover, it facilitates the entry of glucose into the cells with the help of an enzyme insulin-responsive aminopeptidase (IRAP), being abundant in muscles and adipose tissues [8]. There is another enzyme glycogen synthase kinase 3β which produces insulin resistance at the level of the cell membrane and it is directly affected by the protective effect of Zn [9]. The approximate quantity of Zn in an adult's body is 1.4 - 2.3 gm, whereas 85% is concentrated in bone and muscles [10]. It is richly available in the earth's crust and resultantly gains access to the human body via drinking water and various plant-based diets [11]. Zn deficiency in human beings was identified in 1963 and the United States National Academy of Sciences established a recommended dietary allowance (RDA) for Zn (11mg) in 1964 [12]. The World Health Organization (WHO) estimation for Zn deficient population is nearly 2 billion subjects, living in the developing world. The phytates present in the cereal-protein diet of the people living in poor countries impede the absorption of Zn. The clinical manifestation depends on the severity of its deficiency, thus they vary from impaired taste and smell, reduced immunity exhibited as recurrent respiratory infections, gastrointestinal upset, skin changes, impaired glucose tolerance, progression of DM [13]. The lack of data on predictors and indicators of Zn deficiency has hindered accurate estimation of its prevalence. DM is widely spreading in our impoverished country.

The aim of this study was to find out the evidence of Zn deficiency in controls vs. diabetic subjects. It is an easily modifiable risk factor of DM, participates as a causative agent and speeds up the disease progression as well. Zn-supplemented diets may reverse the fatal outcomes of DM to fair control status.

M E T H O D S

This cross sectional study was conducted from 1st June, 2023 to 31st December, 2023 in the Department of Biochemistry at Niazi Welfare Foundation Teaching Hospital, Sargodha, Pakistan. A sample size of 150 was calculated on the basis of prevalence of type II diabetes at 95% confidence interval and 5% margin of error. The prevalence was determined to be 11.77 % in a prior study conducted in Pakistan [14]. Inclusion criteria of the study were a) Age group of 25- 65 year (type II diabetes is dominant in this age group) [15] b) willing to participate in

the study c) absence of any medical illness that can affect glycemic control such as hepatitis, cirrhosis, kidney or heart disease. Patients with a debilitating illness or any endocrine disability were excluded from the study. Data were collected after approval (NM&DC-IRB-53; Dated 1st Dec, 2022) from institutional review board and an informed consent was taken from all the participants. The study utilized non-probability convenient sampling technique. All participants were divided into two groups: "Group A" consisted of controls with a glycemic level below 7 mg/dl, and "Group B" consisted of cases with glycemic levels of 7 mg/dl or higher. Each group had 75 individuals. The age and sex of the participants were documented, and blood samples were collected using aseptic techniques in vacuum containers to measure HbA1C and serum zinc levels. HbA1c was measured by using Immunoturbidimetric method (Hitachi 917). Serum Zn levels were estimated via atomic absorption spectrophotometry (Hitachi Z-2000) [16]. Descriptive statistics were used to calculate the frequency and percentages. The mean and standard deviation was calculated for age and serum Zn level. Statistical analysis was done using SPSS version 23.0.

R E S U L T S

Group A with fair glycemic control showed 49 (65.3%) males and 26 (34.6%) females with mean age (Years) of 51.42 ± 8.62. Group B with poor glycemic control, included 34 (45%) male and 41 (55%) females having mean age (Years) of 53.22 ± 6.88 as depicted (Table 1).

Table 1: Frequency of Sex distribution in Group A vs. Group B (n=150)

Gender Distribution	Group A (n=75)	Group B (n=75)
Male	49 (65.3%)	34 (45%)
Female	26 (34.6%)	41 (55%)
Mean Age	51.42 ± 8.62	53.22 ± 6.88

The estimated mean value of serum Zn was higher in Group A (18.63 ± 6.13 µmol/L) as compared to Group B (8.83 ± 1.64 µmol/L) illustrated (Figure 1).
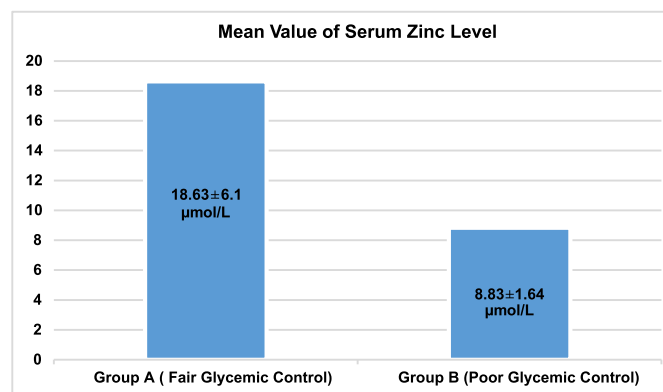
Figure 1: Mean Serum Zinc Value; Group A vs. Group B

DISCUSSION

Zinc is crucial for β-cell function, insulin action, and glucose homeostasis, thus influencing the pathogenesis of diabetes mellitus. Moreover, zinc deficiency may contribute to the development of diabetic complications [7, 8]. Zinc deficiency in type 2 diabetes can lead to complications such as impaired glucose metabolism, increased oxidative stress, and immune dysfunction, resulting in poor glycemic control, higher infection risk, and delayed wound healing. It also exacerbates inflammation and contributes to cardiovascular issues and diabetic neuropathy [10]. Glycemic control has an inverse relationship with serum zinc level. Zn is responsible for controlling cytokine-induced immune destruction processes, thus autoimmune destruction of insulin-secreting islet cells is seen in cases of Zn-deficient type 1 DM [17]. Genetic polymorphism is seen in the zinc transporter 8 genes and in metallothionein (MT)-encoding genes related to type 2 DM. Moreover, higher urinary excretion of Zn is seen in cases of DM, which consequently contributes to its deficiency [8, 9]. The study found higher proportion of female patients with poor glycemic control. This suggests that women with diabetes may face additional challenges in managing their blood sugar levels effectively. This finding is supported by a previous study reporting poorer glycemic control among females as compared to males, owing to late presentation, different lifestyles and hormonal changes [18]. The messenger RNA ratio of the Zn transporter i.e. ZnT1 (zinc export) to Zip1 (zinc import) was lower in diabetic females as compared to healthy controls; it indicating the suboptimal zinc homeostasis in them [17]. Our results revealed that diabetic patients have significantly lower serum zinc level than control group. There was a statistically significant negative correlation between zinc serum level and HbA1C in diabetics. Consistent with our findings, another study demonstrated that serum zinc concentration was lower in diabetics compared to controls and identified a negative correlation between serum zinc and glycated protein [19]. Similarly, another study documented that serum zinc was significantly lower in diabetics than healthy controls [20]. In our study, the mean value of serum Zn level in healthy control subjects was 18.63 ± 6.13 µmol/L. Similarly, a study determined serum Zn level 17.91 ± 2.86 µmol/L in control group [11]. In present study, serum Zn level were deficient in diabetic group i.e. 8.83 ± 1.64 µmol/L. Compared to a study conducted by Farooq *et al.,* found the mean Zn level as 9.3 ± 1.6 µmol/L in the diabetic group, the deficient group's result almost matches our findings [21]. A systematic review and meta-analysis encompassing 25 studies explored the effects of zinc supplementation on clinical and biochemical parameters in patients with diabetes, demonstrated significant benefits. The analysis revealed that zinc supplementation positively impacts glycemic control, helping to regulate blood sugar levels more effectively. This finding underscores the potential role of zinc in diabetes management, highlighting its importance in improving clinical outcomes and biochemical markers associated with the disease. The comprehensive nature of this review, including a diverse range of studies, strengthens the evidence, supporting the use of zinc as a beneficial supplement for individuals with diabetes [22]. Serum zinc (Zn) deficiency is recognized as a modifiable risk factor for diabetes mellitus (DM). Given its modifiable nature, addressing zinc deficiency represents a practical and effective strategy in the broader effort to combat diabetes and its associated complications. This study provided the data of a limited population, more studies are needed to be carried out to conclude the role of Zn and other trace elements in diabetic patients and find out their part in the disease progression and its complications.

CONCLUSIONS

Diabetic patients significantly suffer from the deficiency of serum Zn level. There is a need for preventive measures which should be promptly implemented for early supplementation of Zn in identifiable risky groups.

Authors Contribution

Conceptualization: MFJ
Methodology: MFJ, ERC
Formal analysis: SR, BH, AAR
Writing-review and editing: RAS, AAR

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

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Feldman H, Sayed NA, Freeman R, McCoy RG, Moverley JA, Oser SM *et al.* Standards of medical care in diabetes—2022 abridged for primary care providers. Clinical Diabetes. 2022; 40(1): 10-38. doi: 10.2337/cd22-as01.

[2] Nederstigt C, Uitbeijerse BS, Janssen LG, Corssmit EP, de Koning EJ, Dekkers OM. Associated auto-immune disease in type 1 diabetes patients: a systematic review and meta-analysis. European journal of endocrinology. 2019 Feb; 180(2): 135-44. doi: 10.1530/EJE-18-0515.

[3] Lovic D, Piperidou A, Zografou I, Grassos H, Pittaras A, Manolis A. The growing epidemic of diabetes mellitus. Current Vascular Pharmacology. 2020 Mar; 18(2): 104-9. doi: 10.2174/1570161117666190405165911.

[4] Aung WP, Htet AS, Bjertness E, Stigum H, Chongsuvivatwong V, Kjøllesdal MK. Urban–rural differences in the prevalence of diabetes mellitus among 25–74 year-old adults of the Yangon Region, Myanmar: Two cross-sectional studies. BMJ Open. 2018 Mar; 8(3): e020406. doi: 10.1136/bmjopen-2017-020406.

[5] Duan M, Li T, Liu B, Yin S, Zang J, Lv C *et al.* Zinc nutrition and dietary zinc supplements. Critical Reviews in Food Science and Nutrition. 2023 Apr; 63(9): 1277-92. doi: 10.1080/10408398.2021.1963664.

[6] Baltaci AK, Mogulkoc R, Baltaci SB. The role of zinc in the endocrine system. Pakistan Journal of Pharmaceutical Sciences. 2019 Jan; 32(1).

[7] Descamps D, Evnouchidou I, Caillens V, Drajac C, Riffault S, Van Endert P *et al.* The role of insulin regulated aminopeptidase in endocytic trafficking and receptor signaling in immune cells. Frontiers in Molecular Biosciences. 2020 Oct; 7: 583556. doi: 10.3389/fmolb.2020.583556.

[8] Oruc A, Oruc KY, Yanar K, Mengi M, Caglar A, Kurt BO *et al.* The Role of Glycogen Synthase Kinase-3β in the Zinc-Mediated Neuroprotective Effect of Metformin in Rats with Glutamate Neurotoxicity. Biological Trace Element Research. 2024 Jan; 202(1): 233-45. doi: 10.1007/s12011-023-03667-3.

[9] Gondal AH, Zafar A, Zainab D, Toor MD, Sohail S, Ameen S *et al.* A detailed review study of zinc involvement in animal, plant and human nutrition. Indian Journal of Pure and Applied Biosciences. 2021 Apr; 9(2): 262-71. doi: 10.18782/2582-2845.8652.

[10] Grüngreiff K, Gottstein T, Reinhold D. Zinc deficiency—an independent risk factor in the pathogenesis of haemorrhagic stroke?. Nutrients. 2020 Nov; 12(11): 3548. doi: 10.3390/nu12113548.

[11] Feng J, Wang H, Jing Z, Wang Y, Wang W, Jiang Y *et al.* Relationships of the trace elements zinc and magnesium with diabetic nephropathy-associated renal functional damage in patients with type 2 diabetes mellitus. Frontiers in Medicine. 2021 Mar; 8: 626909. doi: 10.3389/fmed.2021.626909.

[12] Heinz-taheny KM, Rudmann DG, Mahler BW. Haschek and Rousseaux's Handbook of Toxicologic Pathology. 4th ed. Academic Press; 2023.

[13] Mashhadi MA, Bakhshipour A, Zakeri Z, Ansari-Moghadam A. Reference range for zinc level in young healthy population in southeast of Iran. Health Scope. 2017 Feb; 6(1). doi: 10.17795/jhealthscope-18181.

[14] Meo SA, Zia I, Bukhari IA, Arain SA. Type 2 diabetes mellitus in Pakistan: Current prevalence and future forecast. JPMA. The Journal of the Pakistan Medical Association. 2016 Dec; 66(12): 1637-42.

[15] Daradkeh G, Zerie M, Othman M, Chandra P, Jaiosi A, Mahmood L *et al.* Zinc status among type (2) diabetes mellitus in the State of Qatar. Frontiers in Public Health. 2014 Mar; 3(1): 4-10. doi: 10.5963/PHF0301002.

[16] Matsunaga T, Tsujimoto M, Kawashima T, Tsujimoto Y, Fujiwara M, Ookubo A *et al.* Analysis of arsenic in gray and white mineral trioxide aggregates by using atomic absorption spectrometry. Journal of Endodontics. 2010 Dec; 36(12): 1988-90. doi: 10.1016/j.joen.2010.08.045.

[17] Hussain W, Mumtaz A, Yasmeen F, Khan SQ, Butt T. Reference range of zinc in adult population (20-29 years) of Lahore, Pakistan. Pakistan Journal of Medical Sciences. 2014 May; 30(3): 545. doi: 10.12669/pjms.303.4027.

[18] Yokokawa H, Fukuda H, Saita M, Miyagami T, Takahashi Y, Hisaoka T *et al.* Serum zinc concentrations and characteristics of zinc deficiency/marginal deficiency among Japanese subjects. Journal of General and Family Medicine. 2020 Nov; 21(6): 248-55. doi: 10.1002/jgf2.377.

[19] Romero CD, Sanchez PH, Blanco FL, Rodríguez ER, Majem LS. Serum copper and zinc concentrations in a representative sample of the Canarian population. Journal of Trace Elements in Medicine and Biology. 2002 Jan; 16(2): 75-81. doi: 10.1016/S0946-672X(02)80032-3.

[20] Safarzad M, Jazi MS, Kiaei M, Asadi J. Lower serum zinc level is associated with higher fasting insulin in type 2 diabetes mellitus (T2DM) and relates with disturbed glucagon suppression response in male patients. Primary Care Diabetes. 2023 Oct; 17(5): 493-8. doi: 10.1016/j.pcd.2023.05.008.

[21] Farooq DM, Alamri AF, Alwhahabi BK, Metwally AM, Kareem KA. The status of zinc in type 2 diabetic patients and its association with glycemic control. Journal of Family and Community Medicine. 2020 Jan; 27(1): 29-36. doi: 10.4103/jfcm.JFCM_113_19.

[22] Jayawardena R, Ranasinghe P, Galappatthy P, Malkanthi RL, Constantine GR, Katulanda P. Effects of zinc supplementation on diabetes mellitus: a systematic review and meta-analysis. Diabetology and Metabolic Syndrome. 2012 Dec; 4: 1-2. doi: 10.1186/1758-5996-4-13.

89

Original Article

Comparison of Misoprostol and Manual Vacuum Aspirator for Managing Early Pregnancy Miscarriage

Hina Pirzada[1], Nosheena Shabbir[1], Saima Saeed[1], Amina Anwar[1], Uzma Khawaja[1] and Hina Sarwar[2]

[1]Department of Gynecology, Combined Military Hospitals, Muzaffarabad, Pakistan
[2]Department of Gynecology, District Head Quarter Hospital Jhelum Valley, Jhelum, Pakistan

ARTICLE INFO

ABSTRACT

Manual vacuum aspiration is a safe and effective technology for the treatment of incomplete miscarriage but it is not widely available and affordable in rural areas particularly in low-resource countries. **Objective:** To compare efficacy, safety and acceptability of misoprostol and manual vacuum aspirator in management of early pregnancy miscarriage **Methods:** Prospective quasi experimental study Department of gynecology and obstetrics, Sheikh Khalifa Bin Zayed Al Nahyan (CMH).Muzaffar Abad. Study duration was 6 months. A sample of 90 women was calculated using WHO calculator. Patients were approached through non probability consecutive sampling. After following inclusion and exclusion criteria, Patients were randomly divide into two groups; Group A was given misoprostol while group B was patients underwent manual vacuum aspiration. Data were analyzed with SPSS version 25.0. Chi-square and fissure exact test was applied. **Results:** Total 90 patients were included in study. Mean age of patients was 35.4 ± 3.2SD. Treatment failure/incomplete uterine evacuation was significantly lower in manual vacuum aspiration group as compared to misoprostol group (45.6% vs 36.7%, p=0.05). Misoprostol showed less adverse events (p=0.03) and high satisfaction rate (p=0.00) as compared to manual vacuum aspirator. **Conclusions**: Manual vacuum aspirator is more effective in complete uterine evacuation as compared to misoprostol. However, misoprostol is found as more safe with limited side effects and highly acceptable drug as compared to manual vacuum aspirator. It is recommended to use misoprostol as a better choice for management of early pregnancy loss in resource limited areas.

INTRODUCTION

Miscarriage is a common complication of early pregnancy of first trimester. European society of Human Reproduction and Embryology (ESHRE) in 2005 revised early pregnancy events terminologies [1]. Pregnancy loss without ultrasound verification but positive human chorionic gonadotropin (before 6 weeks of gestation) is referred as biochemical loss. Pregnancy loss after confirmation of intrauterine pregnancy with ultrasound or histological evidence is termed as clinical miscarriage. Clinical miscarriage is divided into two main categories; early clinical pregnancy loss and late clinical pregnancy loss (before 12 weeks of gestation and 12-21 weeks of gestation respectively) [2]. It is estimated that approximately 46 million induced abortions take place annually worldwide. A significant number of these procedures are carried out unlawfully in unsafe conditions, leading to roughly 78,000 annual fatalities across the globe. The primary causes of these deaths are septicemia and hemorrhaging [3]. Literature reported that incidence of early pregnancy loss varies from 20-24 years women to 40-44 years (10% to 51% respectively) [4]. Over the years Maternal Mortality Ratio (MMR) worldwide has decreased by 38% from 2000 to 2017 [5]. Early pregnancy loss (before an embryo developed) is physiological phenomenon associated with chromosomal abnormalities. Several clinical studies reported vaginal bleeding as serious sign of early miscarriage while nausea and vomiting was reported a protective sign against pregnancy loss. Several drugs are used for early pregnancy loss management. Misoprostol is most common one. Misoprostol is an effective

prostaglandin E1 analogue [6]. Success rate of misoprostol in managing early pregnancy loss depend upon on its dose and route of administration. It can be administrated orally, vaginally or sublingually with dose ranging from 100-800 micrograms. National institute for health and care excellence recommended single dose of 800 micrograms of misoprostol (orally or vaginally) [7]. Manual vacuum aspirator is cheap and safe method for early pregnancy loss without use of anesthesia. World Health The treatment of first-trimester missed miscarriages has been a topic of debate and discussion in the medical community. Patients have a variety of options, including expectant care, medicinal treatment, or surgical intervention [8]. Ibiyemi *et al.,* reported manual vacuum aspirator is associated with high evacuation rate as compared to misoprostol while both methods showed high acceptability and satisfaction [9]. Khaniya *et al.,* reported that misoprostol and manual vacuum aspirator both are effective in 1st trimester incomplete miscarriages[10].

Data available on comparison of two methods did not provide evidence of treatment choice in resource limited areas. Present study will contribute knowledge in choice of treatment. Present study was planned to compare efficacy, safety and acceptability of misoprostol and manual vacuum aspirator in management of early pregnancy miscarriage.

METHODS

A prospective study Quasi Experimental Interventional pre and Post Design was conducted at department of gynecology and obstetrics, Sheikh Khalifa Bin Zayed Al Nahyan, CMH, Muzaffar Abad. Study duration was 6 months (18th September 2019-March 2020). A sample size of 90 women was calculated with P1=99%, P2=93% [9]. 95% confidence interval, 80% power of study using WHO calculator (45 patients in each group). Non Probability consecutive sampling was used for participant's selection in study. All participating women signed consent forms. Research approval was taken from ethical committee of respective institute. Inclusion criteria were based upon age 20-42 years and ultrasound based diagnosis of incomplete miscarriage (defined as patients with present history of vaginal bleeding, history of passing tissue or positive pregnancy urinary test with transvaginal ultrasound showing evidence of substantial debris) of ≤13 weeks of gestation (gestational age was determined from last period date in each patient). Exclusion criteria was based upon uterine scar, excessive bleeding, induced or septic miscarriage, hemodynamically unstable, patients with hemoglobin level <8gm%, patients with other metabolic disorders and patients who had allergy to E1 prostaglandin. Patients were randomly divided into two categories using

random number table (computer generated). Group A patients were given 50 ml water with 600µg of misoprostol (orally). However patients in group B were give 60µg intramuscular administration of pentazocine, ergometrine (0.5mg) and undergone manual vacuum aspiration by resident doctors. Patients were observed for 6 hours after intervention for any side effect. They were followed 1 week after discharge from hospital. Patients were undergone transvaginal ultrasound after 1 week. Efficacy of treatment was measurement in terms of treatment failure. Treatment failure was defined as ultrasound findings of diameter >1.5 (anteroposterior), persistent vaginal bleeding and incomplete uterine evacuation. Safety was measured in terms of adverse effects while acceptability was measured in terms of satisfaction using Satisfaction with Life Scale (SWLS). The Satisfaction with Life Scale (SWLS) is a widely used instrument designed to measure an individual's global cognitive judgments of their life satisfaction. It consists of five statements that respondents rate on a scale from 1 (strongly disagree) to 7 (strongly agree), resulting in a total score that can range from 5 to 35. The SWLS has been demonstrated to possess favorable psychometric properties. High internal consistency means that the items on the scale are highly correlated with one another, indicating that they reliably measure the same underlying concept of life satisfaction. This is often quantified using Cronbach's alpha, which for the SWLS typically exceeds 0.80, suggesting excellent consistency. High temporal reliability, or test-retest reliability, refers to the stability of scores over time; in other words, individuals tend to receive similar scores when they retake the scale after a period, reflecting its reliability [11]. The study was approved by the ethical committee of H.H. Sheikh Khalifa Bin Zayed Al Nahyan Hospital / CMH, Muzaffar Abad, Azad Kashmir (Ref No. Ethical Committee / DME-391 dated: 18th-Sep-2019). Data were analyzed using SPSS version 25.0. Numerical data were presented in terms of mean ad standard deviation. Categorical and nominal data were presented in terms of percentage ad frequency. Post stratification chi-square and fissure exact test was applied to avoid selection bias. P value ≤ 0.05 was considered significant in our study results.

RESULTS

Total 90 patients were included in study. Mean age of patients was 35.4 ± 3.2 S.D. There were 51(56.7%) women in 20-30 years' age group and 39 (43.3%) in 31-42 years' age group. Among all, 56 (62.2%) women were house wife while 34 (37.8%) were working women. Marital status was single in 8 (8.9%) and married in 82 (91.1%) women. Estimated gestation age was ≤6 weeks in 41 (45.6%) and 7-13 weeks in 49 (54.4%). Parity was zero in 42 (46.7%) while ≤ 1 in 48 (53.3%). Treatment failure was significantly lower in manual vacuum aspiration group as compared to

misoprostol group (45.6% vs 36.7%, p=0.05). Misoprostol group showed low adverse events rash, pyrexia, uterine perforation and diarrhea as compared to MVA group (0% vs 5.6%, 2.2% vs 4.4%, 0% vs 3.3%, 3.3% vs 3.3%, pain 0% vs 1.1% respectively, p=0.03) as shown in table 1.

Table 1: Comparison of Treatment Failure and Adverse Events in Misoprostol and Manual Vacuum Aspiration Group

Variables	Interventional Groups		Total	p-Value
	Misoprostol Group N (%)	Manual Vacuum Group N (%)		
Treatment Failure/Incomplete Uterine Evacuation				
No	33 (36.7%)	33 (36.7%)	74 (82.2%)	0.05
Yes	12 (13.3%)	12 (13.3%)	16 (17.8%)	
Adverse Events				
No	40 (44.4%)	29 (32.2%)	70 (77.8%)	
Rash	0 (0%)	5 (5.6%)	5 (5.6%)	
Pyrexia	2 (2.2%)	4 (4.4%)	6 (6.7%)	
Uterine Perforation	0 (0%)	3 (3.3%)	3 (3.3%)	0.03
Diarrhea	3 (3.3%)	3 (3.3%)	6 (6.7%)	
Pain	0 (0%)	1 (1.1)	1 (1.1%)	
Total	45 (50%)	45 (50%)	90 (100%)	

Misoprostol group patients shows more satisfaction scores as compared to manual vacuum aspirator (extremely satisfied 6.7% vs 0%, satisfied 11.1% vs 13.3%, slightly satisfied 8.9% vs 4.4%, neutral 6.7% vs 4.4%, slightly dissatisfied 11.1% vs 6.7%, dissatisfied 2.2% vs 11.1% and extremely unsatisfied 3.3% vs 10% respectively, p=0.00) as shown in table 2. Treatment failure showed significant association with elder age group (0.02) and low level of education (p=0.03) while in significant association with education (p=0.564) and parity (p=0.231). Safety/adverse events and satisfaction showed in significant association with age, education, occupation and parity (p>0.05) explained in table 2.

Table 2: Comparisons of Satisfaction in Misoprostol and Manual Vacuum Aspirator Using Satisfaction with Life Scale

Satisfaction	Interventional Groups		Total N (%)	p-Value
	Misoprostol Group N (%)	Manual Vacuum Group N (%)		
31-35 Scores= Extremely Satisfied	6 (6.7%)	0 (0%)	6 (6.7%)	
26-30 Scores= Satisfied	10 (11.1%)	12 (13.3%)	22 (24.4%)	
21-25 Scores= Slightly satisfied	8 (8.9%)	4 (4.4%)	12 (13.3%)	
20 Scores= Neutral	6 (6.7%)	4 (4.4%)	10 (11.1%)	
15-19 Scores= Slightly Dissatisfied	10 (11.1%)	6 (6.7%)	16 (17.8%)	0.008
10-14 Scores= Dissatisfied	2 (2.2%)	10 (11.1%)	12 (13.3%)	
5-9=Extremely Unsatisfied	3 (3.3%)	9 (10%)	12 (13.3%)	
Total	45 (50%)	45 (50%)	90 (100%)	

DISCUSSION

Spontaneous and unsafe miscarriages are leading cause of maternal emergency worldwide. [12]. Misoprostol is cheap, safe, heat-stable, easy to store, and requires no surgical skills to administer, making it attractive for use [13]. In preset study, manual vacuum aspiration group patients showed better efficacy in terms of less treatment failure as compared to misoprostol group women (p=0.05). Shwekerela *et al.*, reported that success rate was high in both MVA and misoprostol group, however, misoprostol was found to be more effective in treating incomplete miscarriages with <12 weeks of uterine size [14]. Niinimaki *et al.*, reported that medical (misoprostol) and surgical (MVA) treatment both are effective for evacuation of debris. However, surgical treatment showed more evacuation as compared to medical option [15]. Another similar study reported that complete uterine evacuation rate was high in MVA group as compared to misoprostol (p<0.001). [9]. Weeks *et al.*, reported a slight difference in success rate of both treatments for 8-10 weeks of gestation. Moreover, they concluded that efficacy of each treatment is dependent upon provider skills of performing MVA and misoprostol quality [16]. In our study, misoprostol showed less adverse events diarrhea and pyrexia while manual vacuum aspirator showed slightly high adverse events (diarrhea, pyrexia, rash, pain and uterine perforation) (p=0.03). Kim *et al.*, reported that misoprostol is associated with pyrexia, chills and nausea as compared to MVA [17]. Elati *et al.*, reported that most common side effect of misoprostol is pyrexia on central thermoregulatory center [18]. Bique *et al.*, reported that manual vacuum aspirator is reported as more painful procedure as compared to misoprostol [19]. In our study, patients were found more satisfied with misoprostol as compared to MVA (p=0.00) using Satisfaction with Life Scale (SWLS). Dao *et al.*, reported high satisfaction with both misoprostol and MVA due to high tolerability. Several participants in their study were willing to grecommend both treatments to their family and friend to consider it as a better approach [20]. However, Dabash *et al.*, found majority of patients satisfied with misoprostol due to less pain and discomfort as compared to MVA [21].

CONCLUSIONS

Manual vacuum aspirator is more effective in complete uterine evacuation as compared to misoprostol. However, misoprostol is found as more safe with limited side effects and highly acceptable drug as compared to manual vacuum aspirator. It is recommended to use misoprostol as a better choice for management of early pregnancy loss in resource limited areas.

Authors Contribution

Conceptualization: HP
Methodology: SS, AA
Formal analysis: NS, UK
Writing, review and editing: HS, HP, SS, AA, NS, UK

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

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

REFERENCES

[1] Farquharson RG, Jauniaux E, Exalto N. Updated and revised nomenclature for description of early pregnancy events. Human Reproduction. 2005 Nov; 20(11): 3008-11. doi: 10.1093/humrep/dei167.

[2] Soltanghoraee H, Mohazzab A, Soltani A, Ansaripour S, Tavakoli M, Rafati M *et al.* Histological Evaluation of Products of Conception, Who Benefits from It?. Fetal and Pediatric Pathology. 2023 Jan; 42(1): 30-43. doi: 10.1080/15513815.2022.2053916.

[3] Nwafor JI, Agwu UM, Egbuji CC, Ekwedigwe KC. Misoprostol versus manual vacuum aspiration for treatment of first-trimester incomplete miscarriage in a low-resource setting: A randomized controlled trial. Nigerian Journal of Clinical Practice. 2020 May 18; 23(5): 638-46. doi: 10.4103/njcp.njcp_379_19.

[4] Kanmaz AG, İnan AH, Beyan E, Budak A. The effects of threatened abortions on pregnancy outcomes. Ginekologia Polska. 2019 Mar; 90(4): 195-200. doi: 10.5603/GP.a2019.0035.

[5] Baranovskaya EI. Maternal mortality in modern world. Obstetrics, Gynecology and Reproduction. 2022 Jul; 16(3): 296-305. doi: 10.17749/2313-7347/ob.gyn.rep.2022.279.

[6] Kyejo W, Moshi B, Kapesi V, Ntiyakunze G, Gidion D, Kaguta M. Cervical vasovagal shock: A rare complication of incomplete abortion case report. International Journal of Surgery Case Reports. 2022 Aug; 97: 107455. doi: 10.1016/j.ijscr.2022.107455.

[7] Chu JJ, Devall AJ, Beeson LE, Hardy P, Cheed V, Sun Y *et al.* Mifepristone and misoprostol versus misoprostol alone for the management of missed miscarriage (MifeMiso): a randomised, double-blind, placebo-controlled trial. The Lancet. 2020 Sep; 396(10253): 770-8. doi: 10.1016/S0140-6736(20)31788-8.

[8] Ehrnstén L, Altman D, Ljungblad A, Kopp Kallner H. Efficacy of mifepristone and misoprostol for medical treatment of missed miscarriage in clinical practice—a cohort study. Acta Obstetricia et Gynecologica Scandinavica. 2020 Apr; 99(4): 488-93. doi: 10.1111/aogs.13780

[9] Ibiyemi KF, Munir'deen AI, Adesina KT. Randomised trial of oral misoprostol versus manual vacuum aspiration for the treatment of incomplete abortion at a Nigerian Tertiary Hospital. Sultan Qaboos University Medical Journal. 2019 Feb; 19(1): e38. doi: 10.18295/squmj.2019.19.01.008.

[10] Khaniya B and Yadav R. Comparison of use of misoprostol versus manual vacuum aspiration in the treatment of incomplete abortion. Nepalese Medical Journal. 2019 Dec; 2(2): 239-42. doi: 10.3126/nmj.v2i2.25855.

[11] Diener ED, Emmons RA, Larsen RJ, Griffin S. The satisfaction with life scale. Journal of Personality Assessment. 1985 Feb; 49(1): 71-5. doi: 10.1207/s15327752jpa4901_13.

[12] Musarandega R, Nyakura M, Machekano R, Pattinson R, Munjanja SP. Causes of maternal mortality in Sub-Saharan Africa: a systematic review of studies published from 2015 to 2020. Journal of Global Health. 2021 Oct; 11: 04048. doi: 10.7189/jogh.11.04048.

[13] Ani VC, Enebe JT, Dim CC, Dim NR, Ozumba BC. Sublingual misoprostol versus manual vacuum aspiration for treatment of incomplete abortion in Nigeria: a randomized control study. Pan African Medical Journal. 2022 Feb; 41(90). doi: 10.11604/pamj.2022.41.90.29364.

[14] Shwekerela B, Kalumuna R, Kipingili R, Mashaka N, Westheimer E, Clark W *et al.* Misoprostol for treatment of incomplete abortion at the regional hospital level: results from Tanzania. BJOG: An International Journal of Obstetrics and Gynaecology. 2007 Nov; 114(11): 1363-7. doi: 10.1111/j.1471-0528.2007.01469.x.

[15] Niinimäki M, Jouppila P, Martikainen H, Talvensaari-Mattila A. A randomized study comparing efficacy and patient satisfaction in medical or surgical treatment of miscarriage. Fertility and Sterility. 2006 Aug; 86(2): 367-72. doi: 10.1016/j.fertnstert.2005.12.072.

[16] Weeks A, Alia G, Blum J, Winikoff B, Ekwaru P, Durocher J *et al.* A randomized trial of misoprostol compared with manual vacuum aspiration for incomplete abortion. Obstetrics and Gynecology. 2005 Sep; 106(3): 540-7. doi: 10.1097/01.AOG.0000173799.82687.dc.

[17] Musik T, Grimm J, Juhasz-Böss I, Bäz E. Treatment options after a diagnosis of early miscarriage: expectant, medical, and surgical. Deutsches

Ärzteblatt International. 2021 Nov; 118(46): 789. doi: 10.3238/arztebl.m2021.0346.

[18] Elati A and Weeks A. Risk of fever after misoprostol for the prevention of postpartum hemorrhage: a meta-analysis. Obstetrics and Gynecology. 2012 Nov; 120(5): 1140-8. doi: 10.1097/AOG.0b013e3182707341.

[19] Bique C, Usta M, Debora BE, Chong E, Westheimer E, Winikoff B. Comparison of misoprostol and manual vacuum aspiration for the treatment of incomplete abortion. International Journal of Gynecology and Obstetrics. 2007 Sep; 98(3): 222-6. doi; 10.1016/j.ijgo.2007.05.003.

[20] Dao B, Blum J, Thieba B, Raghavan S, Ouedraego M, Lankoande J *et al.* Is misoprostol a safe, effective and acceptable alternative to manual vacuum aspiration for postabortion care? Results from a randomised trial in Burkina Faso, West Africa. BJOG: An International Journal of Obstetrics and Gynaecology. 2007 Nov; 114(11): 1368-75. doi: 10.1111/j.1471-0528.2007.01468.x.

[21] Dabash R, Ramadan MC, Darwish E, Hassanein N, Blum J, Winikoff B. A randomized controlled trial of 400-µg sublingual misoprostol versus manual vacuum aspiration for the treatment of incomplete abortion in two Egyptian hospitals. International Journal of Gynecology and Obstetrics. 2010 Nov; 111(2): 131-5. doi: 10.1016/j.ijgo.2010.06.021.

Original Article

Comparing the efficacy of Chlorhexidine Mouthwash and Natural Honey in Reducing Plaque and Improving Gingival Health. A Randomized Controlled Trial

Muhammad Abid[1*], Muhammad Ilyas Baig[2], Ambreen Khurshid[3], Ajet Kumar[4], Sidra Farooq[5] and Zafar Iqbal[6]

[1]Department of Periodontology, Liaquat College of Medicine and Dentistry, Karachi, Pakistan

[2]Alkhidmat Hospital, Shah Faisal Colony, Karachi, Pakistan

[3]Department of Oral Biology, Shifa College of Dentistry, Islamabad, Pakistan

[4]Department of Pharmacology, Ghulam Muhammad Mahar Medical College, Sukkur, Pakistan

[5]Department of Community Medicine, Heavy Industries Taxila Education City Institute of Medical Sciences, Taxila, Pakistan

[6]Department of Community and Preventive Dentistry, Bhitai Dental and Medical College, Mirpurkhas, Pakistan

ARTICLE INFO

ABSTRACT

Plaque control is essential for maintaining gingival health, if left untreated can lead to conditions like gingivitis and progress to periodontitis. Natural honey has been historically utilized for its antibacterial properties, while Chlorhexidine (CHX) is used as synthetic antimicrobial agent in oral care. **Objective:** The objective was to assess and compare the effectiveness of natural honey-based mouthwash and chlorhexidine in preventing dental plaque formation and improving gingival health. **Methods:** An open-label, randomized controlled trial was conducted with 60 participants aged 18 to 25. The study compared the effects of natural honey and chlorhexidine mouthwashes on dental plaque levels, employing the Silness and Loe index for plaque assessment. Participants were randomly assigned to either Group A (Chlorhexidine Mouthwash) or Group B (Natural Honey Mouthwash). Both groups followed a prescribed oral hygiene regimen, and plaque levels were measured at baseline and after two weeks. **Results:** Demographic characteristics of both groups were documented, including age, gender distribution, and level of education. Plaque and gingival indices were measured at baseline and after 21 days. Both groups showed a significant decrease in plaque and gingival indices after 21 days (p=<0.001). The honey mouthwash demonstrated a more pronounced reduction in the plaque (p=<0.001) and ginigival index (p=0.001) on Day 21, with a notable and statistically significant difference between the two groups. **Conclusions:** The study concludes that both natural honey and chlorhexidine mouthwashes effectively reduce plaque and improve gingival health. However, honey mouthwash exhibits superior efficacy, suggesting it as a promising alternative for oral hygiene maintenance.

INTRODUCTION

Maintaining a healthy periodontium necessitates effective removal of supragingival plaque, as dental plaque, a bacterial biofilm on tooth surfaces, significantly contributes to gingival inflammation, often resulting in conditions such as gingivitis [1]. Although gingivitis is a preventable and reversible condition frequently encountered in dental practice, untreated cases may progress to periodontitis, potentially leading to tooth loss. Therefore, controlling dental plaque through proper oral hygiene practices is imperative [2]. The utilization of mechanical tools for supragingival plaque control, such as toothbrushes, floss, wood sticks, and interdental brushes, is common. Though, there is a belief that the requisite level of motivation and skill needed for effective use of these oral hygiene products exceeds the abilities of the majority of patients. Consequently, to counteract potential shortcomings in regular self-performed oral hygiene, a chemical approach to plaque control in the form of mouthwashes is considered more desirable [3]. In routine oral care, various interventions are employed to reduce plaque accumulation and improve gingival health. While Chlorhexidine (CHX) mouthwash, a widely accepted conventional antimicrobial agent, is recognized as the "gold standard" antiplaque agent, its efficacy is moderated

by adverse effects such as tooth staining and taste disturbance [4]. Despite being used successfully for over three decades by dental professionals and pharmaceutical companies, chlorhexidine is not a "Magic Bullet." Recent attention has turned to natural honey for its potential antimicrobial and wound-healing properties [5]. Honey, a sweet liquid substance produced by bees, has served as both a nutrient and medicinal remedy since ancient times [6]. Its extended shelf life, attributable to high osmotic pressure and inherent antibacterial properties, enables long-term preservation. Demonstrating expansive antimicrobial activity, honey effectively impedes the growth of diverse bacteria, fungi, protozoa, and viruses. The gradual dilution of unprocessed honey leads to the production of hydrogen peroxide, further enhancing its antimicrobial capabilities[7].

The main aim of this study was to evaluate the effectiveness of a natural honey-based preparation in comparison to a commercially available chlorhexidine mouthwash in preventing the formation of dental plaque. This comparison is motivated by the accessibility, cost-effectiveness, and organic nature of honey. The study was aimed to contribute valuable data specific to our community, with the anticipation that positive results could introduce a new, potentially more accessible method of oral hygiene maintenance, one that may come with fewer side effects.

METHODS

An open-label, randomized controlled trial (https://clinicaltrials.gov/study/NCT05258955) was conducted to evaluate the impact of natural honey and chlorhexidine mouthwashes on dental plaque levels in young adults. Sixty new patients, aged 18 to 25, with complaints of dental stains and bleeding gums, were enrolled at the Department of Periodontology of Dar-ul-Sehat hospital in Karachi. Participants were involved between June 2020 and December 2020. Participants aged 18-25 with 28 retained teeth (excluding wisdom teeth) and recommended to use the modified bass method were included. Exclusions applied to those with medical conditions affecting the oral cavity (e.g., diabetes, Sjögren's syndrome, Crohn's disease), multiple extractions, overhang restorations, dental appliances, periodontal pockets over 3mm, recent antibiotic use, poor hygiene compliance, and harmful oral habits such as tobacco or betel nut use. Randomization was achieved through the opaque sealed envelope method. Each patient chose an envelope containing the group assignment to ensure confidentiality. The envelopes, prepared and sealed by personnel other than the principal investigator, were signed on the back to prevent tampering. The research protocol, permitted by the ethical review board of Liaquat College of Medicine and Dentistry (Reference Number:

EC/11/20), on 5th February 2020. All participants provided written informed consent before enrollment. The sample size was estimated using Openepi sample size calculator for mean difference after inserting mean and SD of honey and chlorhexidine group at 15th day 2.85 ± 0.44 and 2.40 ± 0.51. The minimum sample size was 27 in each group. By adding 10 % drop out rate sample size was taken as 30 in each group. Participants were divided into two groups: Group A received Chlorhexidine Mouthwash, and Group B received Natural Honey Mouthwash. The sample size of 60 (30 in each group) was calculated using open epi based on mean and SD values. Plaque levels were assessed using the Silness and Loe index, measuring deposits on specific teeth in both upper and lower arches. Baseline scores were calculated before scaling and polishing. Market available chlorhexidine gluconate (0.12 %) mouthwash and natural Sidr Honey were used. Mouthwash solutions were dispensed in coded bottles, and participants were instructed to swish 10 ml of their assigned solution twice daily for at least 60 seconds. Participants were guided to use a modified bass method for oral hygiene and abstain from using any other mouthwash during the study period. After two weeks, participants were summoned for a follow-up, and plaque levels were assessed using a periodontal probe and tablets that reveal plaque. The data were analyzed using SPSS 21.0, considering mean, standard deviation, frequency, and percentage. Statistical tests included the Paired t test before and after the intervention and Independent Samples t-Test between two groups, with significance set at p < 0.05.

RESULTS

A total of 60 patients sought consultation at the Outpatient Department (OPD) at the Department of Periodontology of Dar-ul-Sehat Hospital in Karachi. The study participants were divided into two groups: Group A, receiving treatment with Chlorhexidine, and Group B, receiving treatment with Honey. Demographic characteristics of Group A and Group B. Group A, with a mean age of 23.53 ± 2.60, comprises 66.7% males and 33.3% females. In Group B, there are 73.33% males and 26.67% females, with a mean age of 24.0 ± 3.76. Age is presented as mean ± SD. Gender and level of education is presented as frequency and percentages as mentioned in table 1.

Table 1: Demographic Characteristics of Group A (Chlorhexidine) and Group B (Honey)

Demographic Characteristic	Group A	Group B
Age (Mean ± SD)	23.53 ± 2.60	24.0 ± 3.76
Gender N (%)		
Male	20 (66.7%)	22 (73.33%)
Female	10 (33.3%)	08 (26.67%)
Level of Education N (%)		
Matriculation	7 (23%)	9 (30%)

Abid M *et al*.,

Intermediate	9 (30%)	8 (26.6%)
Undergraduate	10 (33.3%)	6 (20%)
Graduate	4 (13.3%)	7 (23.3%)
Total (n)	30	30

Table 2 presents the comparison of measurements for Plaque Index and Gingival Index between Group A and Group B on Day 0 and Day 21. In the Plaque Index, both groups showed a decrease from Day 0 (A: 1.93 ± 0.20, B: 1.89 ± 0.18) to Day 21 (A: 1.04 ± 0.18, B: 0.85 ± 0.14), with highly significant p-values (<0.001). Similarly, for the Gingival Index, there was a reduction from Day 0 (A: 1.74 ± 0.19, B: 1.71 ± 0.16) to Day 21 (A: 0.91 ± 0.13, B: 0.79 ± 0.15), with significant p-values (p = 0.001 for Group A and <0.001 for Group B). These findings indicate a notable improvement in oral health parameters over the 21-day period. On Day 0, there was no significant difference in the Plaque Index and Gingival Index between Group A and Group B. However, by Day 21, a notable and significant difference emerged in both Plaque (p=<0.001) and Gingival Indices (p=0.001) between the two groups. Group B, treated with honey, exhibited more promising results compared to Group A, which received chlorhexidine. Values are Mean ± Standard Deviation (Std. Dev.). [b] Independent Samples t-Test, p-values <0.05 indicate highly significant differences, No significant differences at baseline (Day 0) between group A and B. Significant differences between group A and B at Day 21. [a] Paired t test was used, p-values <0.05 indicates significant reductions from Day 0 to Day 21 in each group.

Table 2: Comparison of Plaque and Gingival Indices in Group A and Group B at Day 0 and Day 21

Group	Day 0 (Mean ± SD)	Day 21 (Mean ± SD)	p-Value (Group A, B)	p-Value (Day 0)	p-Value (Day 21)
Plaque Index					
A	1.93 ± 0.20	1.04 ± 0.18	<0.001[b]	0.54[a]	<0.001[a]
B	1.89 ± 0.18	0.85 ± 0.14	<0.001[b]		
Gingival Index					
A	1.74 ± 0.19	0.91 ± 0.13	<0.001[b]	0.53[a]	0.001[a]
B	1.71 ± 0.16	0.79 ± 0.15	<0.001[b]		

[a]Paired t test was used, p-values <0.05
[b]Independent Samples t-Test, p-values <0.05

DISCUSSION

Honey, recognized for its role as a natural sweetener with a rich nutritional profile, contains 70% sugar, traditionally considered a cariogenic agent. Research findings have demonstrated the effectiveness of honey in combating a diverse array of clinically resistant multibacteria, leading to its emergence as a viable alternative to industrial pharmaceutical products [8-10]. Also, numerous studies have demonstrated that honey possesses antibacterial properties that can counteract its potential to contribute to tooth decay [8-11]. Honey exhibits broad-spectrum inhibition of various bacterial species in vitro. Its antimicrobial activity arises from several factors, including high osmotic pressure, unique physical properties, and enzymatic glucose oxidation reactions [12,13]. The initial stage in the development of dental plaque involves the adhesion of *S. mutans* bacteria to tooth surfaces, a well-documented phenomenon [14]. In an experiment, Badet and colleagues demonstrated that a 10% concentration of honey could influence the formation of an *S. mutans* biofilm [15]. In the present study, the effects of a 10% honey solution and a 0.12% chlorhexidine gluconate mouth rinse on dental plaque levels revealed that both interventions, when used twice daily, demonstrated clinical effectiveness in preventing plaque and managing gingival bleeding. However, at day 30, the effectiveness of the honey mouth rinse, showed significant difference in the clinical efficacy in reducing both plaque and the gingival index when compared to chlorhexidine. Similarly, in a study by Jain A *et al.*, a significant effect was observed between honey and chlorhexidine mouthwash on their impact on plaque [16]. However, in a study conducted by Nayak PA *et al.*, analyzing the effects of Manuka honey and chlorhexidine mouthwash, no important difference was found between the two groups [17]. Similarly, a study conducted in India among children mentioned that Manuka Honey demonstrated effectiveness comparable to chlorhexidine in reducing gingivitis and *Streptococcus mutans* count, suggesting its potential as an antimicrobial agent for oral health improvement and caries risk reduction [18]. However, in Karnataka, a study compared three types of mouthwash. The 0.2% Chlorhexidine mouthwash was found to be the most effective in reducing plaque and gingival scores. However, both 40% Mauka Honey and 20% Raw Honey mouthwashes also showed significant reductions in plaque and gingivitis from day 0 to day 22 [19]. In a study conducted by Aparna *et al.*, both in vitro and clinical assessments were utilized to examine the antimicrobial activity of a 0.2% chlorhexidine mouthwash and a mouthwash containing honey. The in vitro results indicated that the honey mouthwash successfully suppressed the growth of *Streptococcus mutans*, although 0.2% chlorhexidine exhibited superior efficacy. A comparative investigation between chlorhexidine and honey demonstrated significant reductions in plaque formation for both formulations (p < 0.001). Despite chlorhexidine showing greater effectiveness than the honey-containing mouthwash, there was no statistically noteworthy change between them [20]. The change between our research and the prior one may be attributed to the variability in the biological activity of honey. This variation is influenced by factors such as the chemical composition, which is contingent on the botanical origin (type of honey), geographical source, meteorological conditions, and additionally, the concentration employed in diverse studies [21,22].

CONCLUSIONS

In conclusion, this randomized controlled trial comparing the efficacy of natural honey-based mouthwash and chlorhexidine in preventing dental plaque formation demonstrated that both interventions effectively reduced plaque and improved gingival health. The honey mouthwash, with its potential antimicrobial properties, showed notable clinical effectiveness, surpassing chlorhexidine. These findings suggest that honey may offer a promising and accessible alternative for oral hygiene maintenance, presenting fewer side effects compared to conventional chlorhexidine mouthwash.

Authors Contribution

Conceptualization: MA
Methodology: MA
Formal analysis: MIB, AK
Writing, review and editing: AK, SF

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

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

REFERENCES

[1] Lazar V, Ditu LM, Curutiu C, Gheorghe I, Holban A, Popa M *et al.* Impact of dental plaque biofilms in periodontal disease: Management and future therapy. In: Arjunan P, Editor. Periodontitis: A Useful Reference. London: InTech Open; 2017. 11-42. doi: 10.5772/intechopen.69959.

[2] Mann J, Bernstein Y, Findler M. Periodontal disease and its prevention, by traditional and new avenues. Experimental and Therapeutic Medicine. 2020 Feb; 19(2): 1504-6. doi: 10.3892/etm.2019.8381.

[3] Ng E and Lim LP. An overview of different interdental cleaning aids and their effectiveness. Dentistry Journal. 2019 Jun; 7(2): 56. doi: 10.3390/dj7020056.

[4] Takenaka S, Sotozono M, Ohkura N, Noiri Y. Evidence on the use of mouthwash for the control of supragingival biofilm and its potential adverse effects. Antibiotics. 2022 May; 11(6): 727. doi: 10.3390/antibiotics11060727.

[5] Hall TJ, Villapún VM, Addison O, Webber MA, Lowther M, Louth SE *et al.* A call for action to the biomaterial community to tackle antimicrobial resistance. Biomaterials Science. 2020 Aug; 8(18): 4951-74. doi: 10.1039/D0BM01160F.

[6] Alkhaled A, Alsabek L, Al-assaf M, Badr F. Effect of chlorhexidine, honey and propolis on Streptococcus mutans counts: In vitro study. Dentistry. 2021 Nov; 9(1): 107-17. doi: 10.5195/d3000.2021.166.

[7] Majtan J, Bucekova M, Kafantaris I, Szweda P, Hammer K, Mossialos D. Honey antibacterial activity: A neglected aspect of honey quality assurance as functional food. Trends in Food Science and Technology. 2021 Dec; 118: 870-86. doi: 10.1016/j.tifs.2021.11.012.

[8] Deglovic J, Majtanova N, Majtan J. Antibacterial and antibiofilm effect of honey in the prevention of dental caries: A recent perspective. Foods. 2022 Sep; 11(17): 2670. doi: 10.3390/foods11172670.

[9] Almasaudi S. The antibacterial activities of honey. Saudi Journal of Biological Sciences. 2021 Apr; 28(4): 2188-96. doi: 10.1016/j.sjbs.2020.10.017.

[10] Cilia G, Fratini F, Marchi M, Sagona S, Turchi B, Adamchuk L *et al.* Antibacterial activity of honey samples from Ukraine. Veterinary Sciences. 2020 Dec; 7(4): 181. doi: 10.3390/vetsci7040181.

[11] Kanaga Priyaa V. Comparative Evaluation of Antibacterial Efficacy of Manuka Honey, Indian Honey and Sodium Hypochlorite against Enterococcus Faecalis Biofilm: An Invitro study [Doctoral Dissertation]. Adhiparasakthi Dental College and Hospital, Melmaruvathur; 2020.

[12] Ahuja A and Ahuja V. Apitherapy-A sweet approach to dental diseases-Part I: Honey. Journal of Advanced Dental Research I. 2010 Oct; 1(1): 81-6. doi: 10.1177/2229411220110201.

[13] Cooper RA and Jenkins L. A comparison between medical grade honey and table honeys in relation to antimicrobial efficacy. Wounds. 2009 Feb; 21(2): 29-36.

[14] Cai JN and Kim D. Biofilm ecology associated with dental caries: understanding of microbial interactions in oral communities leads to development of therapeutic strategies targeting cariogenic biofilms. Advances in Applied Microbiology. 2023 Mar; 122: 27-75. doi: 10.1016/bs.aambs.2023.02.001.

[15] Badet C and Quero F. The in vitro effect of manuka honeys on growth and adherence of oral bacteria. Anaerobe. 2011 Feb; 17(1): 19-22. doi: 10.1016/j.anaerobe.2010.12.007.

[16] Jain A, Bhaskar DJ, Gupta D, Agali C, Gupta V, Gupta RK *et al.* Comparative evaluation of honey, chlorhexidine gluconate (0.2%) and combination of xylitol and chlorhexidine mouthwash (0.2%) on the clinical level of dental plaque: A 30 days randomized control trial. Perspectives in Clinical Research. 2015 Jan; 6(1): 53-7. doi: 10.4103/2229-3485.148819.

[17] Nayak PA, Nayak UA, Mythili R. Effect of Manuka honey, chlorhexidine gluconate and xylitol on the

clinical levels of dental plaque. Contemporary Clinical Dentistry. 2010 Oct; 1(4): 214-7. doi: 10.4103/0976-23 7X.76386.

[18] Sruthi KS, Yashoda R, Puranik PM. Effectiveness of manuka honey and chlorhexidine mouthwash on gingivitis and Streptococcus Mutans count among children: A randomized controlled trial. Journal of Indian Association of Public Health Dentistry. 2021 Oct; 19(4): 259-63. doi: 10.4103/jiaphd.jiaphd_225_20.

[19] Singhal R, Siddibhavi M, Sankeshwari R, Patil P, Jalihal S, Ankola A. Effectiveness of three mouthwashes-Manuka honey, Raw honey, and Chlorhexidine on plaque and gingival scores of 12-15-year-old school children: A randomized controlled field trial. Journal of Indian Society of Periodontology. 2018 Jan; 22(1): 34-9. doi: 10.4103/jis p.jisp_356_17.

[20] Aparna S, Srirangarajan S, Malgi V, Setlur KP, Shashidhar R, Setty S et al. A Comparative evaluation of the antibacterial efficacy of honey in vitro and antiplaque efficacy in a 4-day plaque regrowth model in vivo: preliminary results. Journal of Periodontology. 2012 Sep; 83(9): 1116-21. doi: 10.1902/jop.2012.110461.

[21] Pătruică S, Alexa E, Obiștioiu D, Cocan I, Radulov I, Berbecea A, Lazăr RN, Simiz E, Vicar NM, Hulea A, Moraru D. Chemical composition, antioxidant and antimicrobial activity of some types of honey from Banat region, Romania. Molecules. 2022 Jun; 27(13): 4179.

[22] Bang KW, Lewis G, Villas-Boas SG. Leptospermum scoparium (Mānuka) and Cryptomeria japonica (Sugi) leaf essential oil seasonal chemical variation and their effect on antimicrobial activity. Preprints. 2020 Aug; 1: 2020080623. doi: 10.20944/preprints202008. 0623.v1.

Original Article

Nurses Knowledge of Post Needle Stick Injury Prophylaxis at a Public Sector Hospital Karachi

Rasheed Ahmed Khan[1] , Mahboob Ali1, Jehangir Khan[1*], Aziz Ur Rehman Yousaf Zai[1], Ghulam Rasool[1], Feona Umair[1], Sana Jilani[1], Bhagwati Herchand[1] and Abida Faizi[1]

[1]Horizon School of Nursing and Health Sciences, Karachi, Pakistan

ARTICLE INFO

*Corresponding Author:
Jehangir Khan
Horizon School of Nursing and Health Sciences, Karachi, Pakistan
jehangirkhan4182@gmail.com

ABSTRACT

Post Needle Stick Injury Prophylaxis (PNSIP) is a stepwise medical management to prevent nurses from blood borne pathogens such as hepatitis B, hepatitis C, and AIDS after Needle Stick Injuries (NSI). **Objective:** To assess the knowledge of nurses regarding PNSIP at a public sector hospital in Karachi, Pakistan. **Methods:** A descriptive cross-sectional study was conducted at a public sector hospital, Karachi, Pakistan, among 109 staff nurses. Sample size was calculated with the help of openepi.com, data were collected through conveniences sampling technique from september to december 2023, by an adopted questionnaire which was distributed in the wards in hard copy among nurses. Data were entered and analysed in Statistical Package for Social Sciences software (version-26). **Results:** The result revealed that majority of the participants 58.7% were male and were in 25-30 years age group, 53.2% were diploma holders and 46.8% were graduate, half of them had less than 5 years of service in the hospital and 39.4% had 5-9 years of service, majority of them 33.9% had worked in emergeny ward, 33% in critical area and 15.6% in operation room. 26.6% of the participants did not know about the antiretroviral drugs used in PNSIP. Knowledge results revealed that nurses have a good knowledge level 78% regarding PNSIP. **Conclusions:** Results showed that although nurses have a good knowledge level regarding PNSIP, however, there is still some percentage of nurses who need education to enhance their knowledge regarding PNSIP.

INTRODUCTION

Needle Stick Injury (NSI) is a risk faced by nurses that can expose them to infectious diseases, such as hepatitis B, hepatitis C, and AIDS [1]. Due to the only possible way to prevent these infections only being the PNSIP protocols post-NSI prophylaxis protocol, ensuring a sequence of steps starting from wound cleaning with soup water, followed by source patient rapid screening for infection, risk assessment of infection transmission, and finally selecting the appropriate antibiotics and antivirals [2]. Many studies have proven that nurses do not possess the required competence concerning PNSIP, although in developed countries, the presence of PNSIP and infection control unambiguously reduce the rate of infection transmission within health workers [3]. The CDC study indicates the 0.3% rate of HIV infection transmission after NSI; however, in developing countries, the risk remains higher due to the inadequate availability of PNSIP [4]. To illustrate, the Cameroonian study exemplifies that 34% of nurses had a favorable attitude toward PNSIP protocols and that 6.6% of nurses had sufficient understanding about PNSIP [5]. According to a survey conducted in the United Kingdom, 36% of nurses had formal training in PNSIP, while 59% of nurses were aware of it [6]. Similarly, a study done in 2021 in Pakistan revealed that 30% of the nurses had knowledge of PNSIP and 40% had access to PNSIP [7]. A study conducted in Karachi found that only 26.6% of nurses had adequate knowledge regarding PNSIP [8]. Similarly, according to a study done in Nishtar Hospital, Multan,

78.4% of nurses had acceptable knowledge of NSI, but nearly 31% of nurses had satisfactory knowledge of PNSIP [9]. Likewise, another study conducted in 2022 determined that 44.8% of the nurses had good knowledge of PNSIP [10]. Similarly, a study done at Sindh Government Children Hospital, Lahore, to assess the knowledge of nurses regarding prevention from NSI showed that 58% of the nurses had poor knowledge of NSI and only 32% had obtained education on PNSIP [11]. In a neighboring country, India, research found that only 53% of nursing students were aware of PNSIP and its importance, and only 7.1% of them had ever gotten training on PNSIP [12]. Another study found that nursing students had inadequate knowledge of PNSIP, and 76.7% of nursing students were not aware of the perfect steps taken after NSI [13]. Similarly, another study of developing country suggested that only 9% of nursing students had knowledge of NSI and 85% did not [14]. It is vital to make sure that HCW have knowledge of PNSIP and are skilled in its right use to correctly lessen the chance of transmission of infection. There may be a need for advanced infrastructure and awareness to address the problems of NSI and PNSIP among nurses.

Therefore, the aim of this study was to evaluate the knowledge of nurses regarding PNSIP at a public sector hospital in Karachi.

METHODS

A cross-sectional study design was used from September to December 2023 at a public sector hospital in Karachi, among 109 staff nurses, through convenient sampling techniques, all nurses whose clinical experience was more than 1-year were included in the study and those who were on leave and were unwilling to participate in the study were excluded. Sample size was calculated with the help of openepi.com. Data were collected via an adopted questionnaire taken from a study conducted in 2020, which consisted of two sections. Section I has 5 questions regarding demographics and Section II has 11 questions regarding knowledge of PNSIP [15]. All 11 items were assigned one mark each, nurses who obtained more than 75% score considered as having good level of knowledge, 50-74% moderate and belove 50% having low level of knowledge regarding PNSIP. The questionnaire and consent forms were distributed in the wards in hard copy, and the benefits of the study were explained to the participants. Permission for data collection was obtained from the institution with reference number HSNHS/2023/369 dated 13 September 2023, and informed consent was also obtained from staff nurses after they were told about the objective and purpose of the study, their rights to leave at any time they wanted, were persuaded, and were also assured of their confidentiality and anonymity. Data were entered and analyzed using SPSS

software version 26.0, frequency and percentages were used for results.

RESULTS

Table 1 showed that 58.7% were male and 41.3% were female; the majority of the nurses, 45.9%, were in the age range of 25–30 years; 33.9% were in the age range of 20–25 years; and the remaining 20.2% were above the age range of 30 years. Moreover, 46.8% were degree holders and 53.2% were diploma holders. Half of the respondents (50.5%) had less than 5 years of service in the hospital, 39.4% had 5–9 years, and only 10.1% had more than 10 years of service. The study also found that the majority of the nurses (33.9%) worked in the emergency ward, followed by 33% in critical care, 13.8% in surgical wards, and 15.6% in the operation room.

Table 1: Sociodemographic Characteristics of the Nurses (n=109)

S. No.	Variables	Factors	N (%)
1.	Sex	Male	64 (58.7%)
		Female	45 (41.3%)
2.	Age (in Years)	20 –25	37 (33.9%)
		25-30	50 (45.9%)
		≥ 30	22 (20.2%)
3.	Education Level	Degree	51 (46.8%)
		Diploma	58 (53.2%)
4.	Length of Service in Hospital	<5 Years	55 (50.5%)
		5-9 Years	43 (39.4%)
		More than 10 Years	11 (10.1%)
5.	Place of Work	Emergency Ward	37 (33.9%)
		Surgical Ward	15 (13.8%)
		Operation Room	17 (15.6%)
		Critical Area (ICU,PICU, NICU)	36 (33.0%)
		Other	4 (3.7%)

Table 2 showed that most of the respondents (95.4%) had heard of PNSIP; 22% of them declared that they had gained knowledge of PNSIP from their colleagues or seniors; 17.4% from college; and 15% from books and journals. 79.8% stated that they have attended training or seminars on PNSIP. 56% of the nurses said that a needle stick is an indication of PNSIP. A total of 29.4% of the participants reported that promoting active bleeding from the wound is a first aid measure after the NSI. However, 68% of them reported that washing the wound with soap and water is a first aid protocol after NSI. 78% of the participants were aware that the protocol should be started within one hour of exposure, but 22.1% were not. Moreover, 60.6% said that prophalyxis should be considered 24 hours after injury, 20.2% mentioned 48 hours, and 19.3% said that PNSIP should be considered for 72 hours. Similarly, the table also showed that the majority of the participants (56%) reported that PNSIP should be continued for 2 weeks, whereas 36.7% said 4 weeks and 7.3% said 8 weeks. 61.5% of nurses

said that PNSIP is 80% effective, 21.1% said it is 100% effective, and 11.9% said it is 60–70% effective. Moreover, 29.4% of the nurses were aware that Zidovudine is used as an anti-retroviral drug, 25.7% of Tenofovir, and 18.3% of Lamivudine. In the end, 92.7% of the respondents reported that they knew the hospital's policy relating to PNSIP for HIV, HBV, and HCV, while 7.3 did not know about any policy.

Table 2: Knowledge of Nurses Regarding Post-NSI Prophylaxis (n=109)

S. No.	Variables	Factors	N (%)
1.	Have You Ever Heard About PNSIP	Yes	104 (95.4%)
		No	5 (4.6%)
2.	Source Of Information	College	19 (17.4%)
		Colleagues/Seniors	24 (22.0%)
		Internet/Media	19 (17.4%)
		Books/Journals	16 (14.7%)
		Seminar/Training	28 (25.7%)
		Can't Remember	3 (2.8%)
3.	Have You Got Training On PNSIP	Yes	87 (79.8%)
		No	22 (19.3%)
4.	For what Reason PNSIP Is Used	NSI	61 (56.0%)
		Seeing of Blood/ Fluids on Body	41 (37.6%)
		Sex	2 (1.8%)
		I Don't know	5 (4.6%)
5.	First Aid Action Taken After NSI	Activate Bleeding From The Wound	32 (29.4%)
		Soap Water	75 (68.8%)
		Don't Know	2 (1.8%)
6.	Should PNSIP Be Started In 1 Hour After Injury ?	Yes	85 (78.0%)
		No	24 (22.1%)
7.	PNSIP Should Be Continued For How Long Time?	24 Hours	66 (60.6%)
		48 Hours	22 (20.2%)
		72 Hours	21 (19.3%)
8.	Duration For PNSIP	2 Weeks	61 (56.0%)
		4 Weeks	40 (36.7%)
		8 Weeks	8 (7.3%)
9.	Effectiveness Of PNSIP	100%	23 (21.1%)
		80%	67 (61.5%)
		60-70 %	13 (11.9%)
		50%	5 (4.6%)
		<50%	1 (0.9%)
10.	Which Anti-Retroviral Drugs Are Used In PNSIP?	Tenofovir	28 (25.7%)
		Zidovudine	32 (29.4%)
		Lamivudine	20 (18.3%)
		Don't Know	29 (26.6%)
11.	Do You Know Hospital Policy For NSI	Yes	101 (92.7%)
		No	8 (7.3%)

Table 3 showed knowledge level of nurses regarding PNSIP, 77.9% had good level of knowledge, 15.5% average and 6.4% had poor level of knowledge regarding Post-NSI Prophylaxis.

Table 3: Nurses Knowledge Level of Post-NSI Prophylaxis(n=109)

Knowledge Level	N (%)
Good (> 75%)	85 (77.98%)
Moderate (50-74)	17 (15.59%)
Low Level (<50%)	7 (6.43%)

DISCUSSION

Nurses performing clinical duties in the hospitals should know about how to save themselves against blood borne pathogens like hepatitis B and C and HIV as they are prone to NSI, therefore, they should know the PNSIP protocols. In a nationwide survey conducted in 2016 on 1000 nurses from different healthcare settings in Pakistan, it was found that 55% of the nurses were aware of PNSIP treatment, which is lower than the percentage found in the present study, with 77.9% of the nurses being aware of PNSIP [16]. In another study conducted in 2018 on nurses working in a tertiary hospital in Karachi, it was found that 58% of the nurses were aware of PNSIP treatment, which is also lower than the present study [17]. Similar to our study's finding that training and college education are the main sources of information for nurses regarding PNSIP, a study conducted in 2021 in Lahore also found that 90% of the nurses acquired knowledge about PNSIP through in-service training and education programs [18]. In terms of knowledge about indications for PNSIP, our study found that 80% of the nurses correctly identified NSI as an indication for PNSIP, which is similar to the findings of a study conducted in 2018 on nurses working in tertiary hospitals in Karachi, which reported that 79% of the nurses correctly identified NSI as an indication for PNSIP [19]. In addition, three out of five antiretroviral drugs that the present research respondents identified is used for post-NSI prophylaxis. According to the current study, there are Tenofovir, Zidovudine, and Lamivudine. In 2018 in Karachi, a study found that all three substances, including Tenofovir, Zidovudine, and Lamivudine, were identified as antivirals as prophylactic. 60% of the nurses in this research claimed that PNSIP should be continued two weeks and at least for 24 hours after exposure to NSI. The aforementioned estimates match with the results of a study conducted in Quetta in 2014, where 64 % of nurses recognized the duration for PNSIP [20]. Likewise, a study conducted in Saudi Arabia showed that 80% of healthcare workers had knowledge of PNSIP, whereas, a study done in Ethioia found that 76.4% of healthcare workers had knowledge of PNSIP [21-22]. Similarly, a study conducted in India showed that 87% of healthcare workers had knowledge of PNSIP. All these results are higher as compared to the present study [23]. In contrast to the above, a study conducted in Ethiopia showed that 46% of HCW had knowledge of PNSIP, which is lower as compared to the present study [24].

102

PJHS VOL. 5 Issue. 5 May 2024

Another result from a meta-analysis in 2022, showed that 98% of HCW had knowledge of PNSIP, which is very high as compared with the present study [25]. The present study results contrasts to a study conducted in Bhutan, in 2020, which showed that majority (80.1%) of the participants had poor knowledge regarding Post Exposure Prophalaxis (PEP) for HIV and half (51.1%) of them had heard about PEP, but only 1.4% attended a formal training program on PEP for HIV [26].

CONCLUSIONS

The study showed that nurses at a public sector hospital in Karachi have a good level of knowledge (78%) regarding Post-NSI prophylaxis; however, there is still some percentage of nurses who need education to enhance their knowledge regarding Post-NSI prophylaxis and to protect them from the deadly viruses.

Authors Contribution

Conceptualization: RAK
Methodology: JK, SJ
Formal analysis: AURYZ, BH
Writing, review and editing: MA, GR, FU, AF

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

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Asanati K, Bhagani S, Boffito M, Cresswell F, Delpech V, Ellis J *et al*. UK Guideline for the use of HIV Post-Exposure Prophylaxis 2021. British Association for Sexual Health and HIV. 2023.

[2] Makhado L and Davhana-Maselesele M. Knowledge and uptake of occupational post-exposure prophylaxis amongst nurses caring for people living with HIV. Curationis. 2016 Jan; 39(1): 1-6. doi: 10.4102/curationis.v39i1.1593.

[3] Angadi N, Davalgi S, Vanitha SS. Needlestick injuries and awareness towards post exposure prophylaxis for HIV among private general practitioners of Davangere city. International Journal of Community Medicine and Public Health. 2016 Jan; 3(1): 335-9. doi: 10.18203/2394-6040.ijcmph20151587.

[4] Patel TC, Bagle TR, Maurya M, Sharma V. Knowledge, attitude and practice of needle stick injury and post exposure prophylaxis in undergraduate medical students. International Journal of Basic and Clinical Pharmacology. 2018 Jul; 7(7): 1297. doi: 10.18203/2319 -2003.ijbcp20182672.

[5] Aminde LN, Takah NF, Dzudie A, Bonko NM, Awungafac G, Teno D *et al*. Occupational Post-Exposure Prophylaxis (PEP) against human immunodeficiency virus (HIV) infection in a health district in Cameroon: Assessment of the Knowledge and Practices of Nurses. PLOS One. 2015 Apr; 10(4): e0124416. doi: 10.1371/journal.pone.0124416.

[6] Cresswell F, Asanati K, Bhagani S, Boffito M, Delpech V, Ellis J *et al*. UK guideline for the use of HIV post-exposure prophylaxis 2021. HIV Medicine. 2022 May; 23(5): 494-545. doi: 10.1111/hiv.13208.

[7] Fatima A, Alam S, Iftekhar H, Tewari RK, Andrabi SM, Faraz AA. Knowledge, practice, and awareness of dental undergraduate and postgraduate students toward postexposure prophylaxis and needlestick injuries: A descriptive cross-sectional institutional dental hospital study. Journal of Oral Research and Review. 2021 Jul; 13(2): 106-14. doi: 10.4103/jorr.jorr_4_20.

[8] Hanif F, Khurshid U, Khan HS, Mirza MZ. Needle Stick And Sharp Related Injuries-Ethical Considerations, Prevention, And Management. Journal of Bahria University Medical and Dental College. 2018; 8(4): 278-80. doi: 10.51985/JBUMDC2018071.

[9] Irshad R, Ateeb M, Bibi A, Asif M, Jabbar S. Assessment of Knowledge and practice about needle stick injury among nurses at nishtar hospital in Multan; A hospital based cross-sectional study. International Journal of Natural Medicine and Health Sciences. 2023 Mar; 2(2): 27-34.

[10] Nawafleh HA, El Abozead S, Al Momani MM, Aaraj H. Investigating needle stick injuries: Incidence, knowledge and perception among South Jordanian nursing students. Journal of Nursing Education Practice. 2017 Nov; 8(4): 59-69. doi: 10.5430/jnep.v8n4p59.

[11] Zarnigar Re, Sagir T, Zia T, Latif W, Laique T. Knowledge of Nurses Regarding Prevention From Needle Stick Injuries in Tertiary Care Hopital Lahore Pakistan. Hospital. 2021 May; 2021. doi: 10.53350/pjmhs211551389.

[12] Singh RK, Kumar M, Rawat CM, Rawat V. Awareness and practice of Post-Exposure Prophylaxis (PEP) of HIV among health-care workers in tertiary care hospital of Haldwani, Nainital, Uttarakhand, India. International Journal of Medical Science and Public Health. 2015 Jul; 4(7): 977. doi: 10.5455/ijmsph.2015.12022015207.

[13] Prasuna J, Sharma R, Bhatt A, Arazoo A, Painuly D, Butola H *et al*. Occurrence and knowledge about needle stick injury in nursing students. Journal of Ayub Medical College Abbottabad. 2015 Jun; 27(2):

430-3.

[14] Janjua SS, Hanan A, Sarwar H, Afzal M, Ali A. Awareness in Nursing Students Regarding Prevention of Needle Stick Injuries: Prevention of Needle Stick Injuries. Journal of Nursing and Midwifery Sciences. 2022 Jun: 20-4. doi: 10.54393/nrs.v2i01.30.

[15] Ajibola S, Akinbami A, Elikwu C, Odesanya M, Uche E. Knowledge, attitude and practices of HIV post exposure prophylaxis amongst health workers in Lagos University Teaching Hospital. Pan African Medical Journal. 2014 Oct; 19(1). doi: 10.11604/pamj.2014.19.172.4718.

[16] Khalid H, Siddique MK, Khalid H, Aftab A, Anwar H, Iftikhar K. Needle Stick Injuries: Knowledge, Attitude, Practice And Prevention Among Dental Practitioners And Students Of Islamic International Dental Hospital Islamabad. The Professional Medical Journal. 2018 Feb; 25(02): 218-25. doi: 10.29309/TPMJ/18.4246.

[17] Kaleem F, Saleem H, Shah MU, Ali U, Aftab I, Farwa U. Comparison of Awareness of Post-exposure Prophylaxis Protocol Following Needle Stick Injuries Against HBV, HCV and HIV among Different Groups of Health Care Workers: A Multicenter Experience. Infectious Diseases Journal of Pakistan. 2019; 28(1): 15-9.

[18] Cheeme S, Cheema U, Cheema U. Occupational Exposure to Sharp Instrument Injuries Among Registered Nurses in Public and Private Hospitals of Lahore Pakistan: Exposure to Sharp Instrument Injuries Among Nurses. Journal of Nursing and Midwifery Sciences. 2021 Dec 31: 02-6. doi: 10.54393/nrs.v1i02.13.

[19] Sharif F, Khan A, Samad MA, Hamid A, Aijaz A, Asad I *et al.* Knowledge, attitude, and practices regarding infection control measures among medical students. The Journal of the Pakistan Medical Association. 2018 Jul; 68(7): 1065-9.

[20] Pervaiz M, Gilbert R, Ali N. The prevalence and underreporting of needlestick injuries among dental healthcare workers in Pakistan: A systematic review. International Journal of Dentistry. 2018 Feb; 2018. doi: 10.1155/2018/9609038.

[21] Ibrahim NK, Omran DM, Noman GA, Babeer GA, Bandah ST, Milaat WA. Universal precautions needed for preventing blood-borne infections: Knowledge, attitude, and practices of health care workers at King Abdulaziz University Hospital, Jeddah, Saudi Arabia. Kuwait Medical Journal. 2019 Sep; 51(3): 294-301.

[22] Tsega D, Gintamo B, Mekuria ZN, Demissie NG, Gizaw Z. Occupational exposure to HIV and utilization of post-exposure prophylaxis among healthcare workers at St. Peter's specialized hospital in Addis Ababa, Ethiopia. Scientific Reports. 2023 Apr; 13(1): 7021. doi: 10.1038/s41598-023-34250-4.

[23] Vardhini H, Selvaraj N, Meenakshi R. Assessment on knowledge and practice of postexposure prophylaxis of human immuno-deficiency virus among staff nurses and paramedical workers at a tertiary care hospital in South India. Journal of Education and Health Promotion. 2020 Jan; 9: 279. doi: 10.4103/jehp.jehp_234_20.

[24] Eticha EM and Gemeda AB. Knowledge, attitude, and practice of postexposure prophylaxis against HIV infection among Healthcare Workers in Hiwot Fana specialized University Hospital, Eastern Ethiopia. AIDS Research and Treatment. 2019 Feb; 2019. doi: 10.1155/2019/7947086.

[25] Ou YS, Wu HC, Guo YL, Shiao JS. Comparing risk changes of needlestick injuries between countries adopted and not adopted the needlestick safety and prevention act: A meta-analysis. Infection Control and Hospital Epidemiology. 2022 Sep; 43(9): 1221-7. doi: 10.1017/ice.2021.372.

[26] Tshering K, Wangchuk K, Letho Z. Assessment of knowledge, attitude and practice of post exposure prophylaxis for HIV among nurses at Jigme Dorji Wanghuck National Referral Hospital, Bhutan. PLOS One. 2020 Aug; 15(8): e0238069. doi: 10.1371/journal.pone.0238069.

Original Article

Pattern of Diseases Presenting in ENT Outpatient Department in a Postgraduate Teaching Hospital in S.I.T.E. Area Karachi

Tahir Hussain Khan[1], Ashfaq Hussain Rana[2], Muhammad Jamil Memon[3], Danishur Rahim[4], Mukhtar Ibrahim[5] and Tariq Zia Siddiqui[6]

[1]Department of Ear, Nose and Throat, Kulsum Bai Valika Social Security SITE Hospital, Karachi, Pakistan
[2]Department of Ear, Nose and Throat, Shahida Islam Medical Complex, Lodhran, Pakistan
[3]Department of Ear, Nose and Throat, Ziauddin Hospital, Karachi, Pakistan
[4]Department of Ear, Nose and Throat, Dow University of Health Sciences, Karachi, Pakistan
[5]Department of Ear, Nose and Throat, Indus Medical College and Hospital, Tando Muhammad Khan, Pakistan
[6]Department of Ear, Nose and Throat, Hamdard University Hospital, Karachi, Pakistan

ARTICLE INFO

ABSTRACT

Ear, Nose and Throat (ENT) diseases are one of the public health problems and affect a huge number of the patient around the globe. **Objective:** To determine the pattern of ENT disorders or diseases in those patients who were attended outpatient department of ORL in a postgraduate teaching hospital of Karachi. **Methods:** Patients presenting at ENT OPD were selected randomly for the study. Data about ENT problems and information were collected through well structured questionnaire. After data collection, it was entered and analyzes by using software SPSS-23. Variables were age, sex, residence, socioeconomic status and different ENT diseases including wax, otitis media, allergic rhinitis, pharyngitis, tonsillitis, Deviated Nasal Septum (DNS) etc. **Results:** Male patients were 585 (46.8%) while female patients were 665 (53.2%) out of 1250 patients. Most of the patients were from industrial areas 775 (62%) and 475 (38%) were from city areas. 355 (28%) were suffering from wax followed by acute otitis media 300 (24%), acute tonsillitis and deviated nasal septum each in 225 (18%), otitis externa 150 (12%) and acute pharyngitis 145 (11%). In our study, a huge number of 72% of cases had ear disorders. 43.2% of patients had nasal issues, while 45.2% were related to laryngopharyngeal issues. **Conclusions:** Majority of the patients attending outpatient ENT department were related to ear wax followed by acute otitis media, acute tonsillitis, DNS, otitis externa, acute pharyngitis and many patients have multiple diseases.

INTRODUCTION

Ear, Nose and throat related diseases are on rise due to multiple individual and environmental factors. The distribution of ENT disorders also varies considerably among communities based on age and demographic [1]. They might be acquired or congenital. Infectious, inflammatory, neurological, vascular, and trauma-related disorders are examples of acquired illnesses. Complications included are disorders of phonation, breathing, speaking, taste, olfaction and swallowing. Hearing, breathing, phonation, swallowing. ENT diseases may be source of morbidity and produces heavy burden on health management system [2]. There are many Ear infections seen in ENT OPD i.e. Otitis externa, chronic suppurative otitis media, and conductive deafness. Diseases of ENT are not limited to ear nose and throat but also affect the quality of life which require much expensive treatment [3]. Otitis media has a stronger horizontal orientation in children than in adults, making it the most prevalent condition in younger patients. According to reports, the most frequent reason for decrease hearing in children in underdeveloped nations is Chronic Suppurative Otitis Media (CSOM). According to surveys on the

prevalence of CSOM, 65–330 million people worldwide are affected by the condition, with 60% of those affected by major defects. CSOM define as chronic or persistent ear discharge (otorrhea) through perforated tympanic membrane over 2-6 week's duration [4]. Sometimes chronic suppurative otitis media may have life threatening [5]. Nasal diseases that manifest as ENT OPD include nasal polyps, rhinitis, epistaxis, diseases of the nasal vestibule, tumors, and abnormalities of the nose. Nasal illnesses can be caused by infections, trauma, and nose surgery. Meningitis, cavernous sinus thrombosis, and septal abscess are complications that arise from nasal disorders. In children diagnosis of paranasal sinuses infection is difficult and require thorough knowledge about unique anatomy of Peripheral Nervous System (PNS) [6]. Prevalence of rhinosinusitis was 16% in US adult population [7]. Epistaxis is a prevalent nasal condition that affects a huge number of the patients in developing countries. While the majority of its instances are mild and treatable, some can be fatal. Anatomical abnormalities, tumors, and trauma are common local causes. Its systemic causes include hypertension and cardiovascular disorders. Epistaxis is very common emergency encountered by general physician. Up to 60% of general population experience epistaxis and 6% require medical attention [8]. First aid procedures are usually sufficient to treat epistemic episodes, although in certain cases, further treatments may be required. Sore throat, tonsillitis, pharyngitis, and malignancies are the most prevalent throat conditions in the outpatient department. Allergies are among the other common causes of throat illness, although viral infections are the main culprit [6-8]. Acute glomerular nephritis, peritonsillar abscess development, and acute rheumatic fever are complications of throat illnesses. Laryngeal carcinoma is the second most prevalent malignancy of the respiratory tract. Cigarette smoking, drinking alcohol, and maybe having Helicobacter pylori and Human Papillomavirus 16 are risk factors for this kind of cancer [9]. Obese children have more potential to suffer ENT diseases as compare to normal children or lean child [10]. Due to cross-infections, school-age children are more vulnerable to ENT illnesses. This persistent issue causes both physical and emotional discomfort in addition to impeding academic achievement and developmental progress [11]. Usually discovered in children under 10 years old, foreign things in the ear can be either accidental or iatrogenic. A Peshawar research found that the frequency of frequent ENT conditions presenting in Outpatient Departments (OPD) include chronic tonsillitis (37%), CSOM (14%), and rhinitis caused by a deviated nasal septum (67%). Commonest ENT disease was enlarged adenoids and tonsils in pediatric age group (23.1%), rhinitis (18.4%), CSOM

(15.9%) and in adult commonest disease was rhinosinusitis (21.9%)[12].

The objective of our study was to find frequency of ENT disorders or diseases in those patients who attended the outpatient department of ORL in a postgraduate teaching hospital of Karachi.

METHODS

This was a cross sectional study conducted at Kulsumbai Valika Social Security Postgraduate Teaching Hospital SITE Karachi, Pakistan. Permission was obtained by Institutional Review Board (IRB) with Reference Number: 2855 dated: 02-04-2024. The duration of the study was seventeen months from June 2022 to December 2023. Overall a data of 1250 patients was collected from the outdoor patient department of the ENT of our hospital. Non probability convenient sampling technique was used to collect data. Patients who visited ENT outdoor for seeking healthcare were included in this study. The patients were excluded who was in emergency or who refused to give consent for inclusion in the study. Properly data were collected and used a predesigned questionnaire or proforma. The variables included in this study were age of the patient, sex, socioeconomic status, residence (industrial area/city area) and disease for which patient came for health care such as Acute otitis media, Acute sinusitis, Acute pharyngitis, Acute tonsillitis, Ear wax (Bilateral), Allergic rhinitis, Chronic pharyngitis, Chronic Suppurative Otitis Media (CSOM), Chronic tonsillitis, Deviated nasal septum, Epistaxis, and Otitis externa. The data were entered and analyzed by using statistical software i.e. SPSS version 25.0. Mean and standard deviation were calculated for quantitative variables like age, while frequencies and percentages were calculated for categorical variables like gender, socioeconomic status and diseases frequency. Ethical approval was taken from Ethical Committee of the Hospital.

RESULTS

The data on demographic and pattern of ENT diseases, of 1250 study subjects was collected. The mean age was 31 ± 19 years, and mean duration of the diseases was 7 ± 12 days. Out of total 1250 patients, 665 (53.2%) were males and 585 (46.8%) were females. Most of the patients were from industrial areas 775 (62%) and 475 (38%) were city areas.

Table 1 shows that majority of the patients were poor i.e. 955 (76.4%), status of 295 (23.6%) patients were middle class and zero patient was from upper socioeconomic class. Overall it was noted that that out of 1250 patients, 715 (57.2%) were laborer, 535 (42.8%) were dependents of secured workers i.e. wives, sons, daughters and parents (Table 1).

Table 1: Socioeconomic Status and Residence Wise Distribution of the Patients

| Variables	Number of Patients N (%)
Patients Belong to Poor Family	955 (76.4%)
Belong to Middle Class	295 (23.6%)
Reside in SITE Industrial Area	775 (62%)
Reside in City Area	475 (38%)
Laborer	715 (57.2%)
Dependents	535 (42.8%)

Table 2 shows that 355 (28%) were having from ear wax, followed by acute otitis media 300 (24%), acute tonsillitis and deviated nasal septum each in 225 (18%), otitis externa 150 (12%) and acute pharyngitis in 145 (11%) out of 1250 patients. It was noted that many patients have multiple diseases. In our study, a huge number of 72% of cases had ear disorders. 43.2% of complaints are related to nasal issues, while 45.2% were related to laryngopharyngeal issues.

Table 2: Pattern of Diseases Presenting in ENT Outdoor of a Teaching Hospital

Diseases	N (%)
Ear Wax	355 (28.4%)
Acute Otitis Media	300 (24%)
Acute Pharyngitis	145 (11.6%)
Sinusitis	175 (14%)
Deviated Nasal Septum	225 (18%)
Acute Tonsillitis	225 (18%)
Otitis Externa	150 (12%)
Allergic Rhinitis	125 (10%)
Chronic Pharyngitis	120 (9.6%)
Chronic Suppurative Otitis Media	95 (7.6%)
Chronic Tonsillitis	75 (6%)
Epistaxis	16 (1.28%)
Nasal Polyp	20 (1.6%)
Others	75 (6%)

Note: Multiple Diseases in Same Patients

Figure 1 shows gender`s distribution 665 were male and 585 were female and socioeconomic status of the patients, 955 patients were poor and 295 were middle class. This figure also shows residence of patients more patients were resided in industrial area and numbers of labors were more as compared to their dependents.
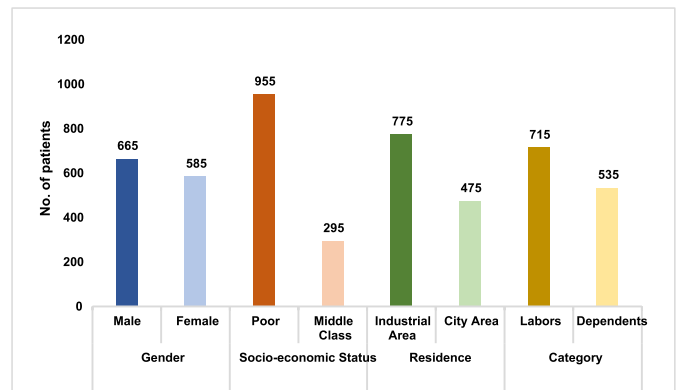
Figure 1: Showing Gender/Socioeconomic Status/Residence/Workers and their Dependents.

Figure 2 shows male and female distribution in the study, in this study male patients were 665 (53%) out of 1250 and female patients were 585 (47%).
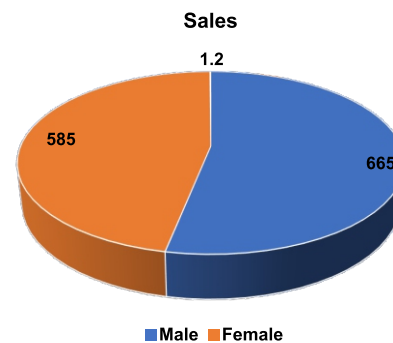
Figure 2: Male and Female Distribution

It was noted that among 1250 patients, 1090 (87.2%) patients had duration of their illness less than 1 year, 70 (5.6%) had between 1 to 5 years of age and 90 (7.2%) had more than 5 years of duration of illness. Regarding health seeking out of 1250, majority of patients have taken treatment due to free of cost treatment.

DISCUSSION

This study was carried out to find the frequency of different ENT disorders or diseases in those patients who were attended outpatient department of ENT in a postgraduate teaching hospital situated at industrial area of Karachi, Pakistan. The age and group-specific patterns of ENT illness differ considerably among communities. A research study published on allergic rhinosinusitis and related co-morbidities was conducted on all consecutive patients visiting the Otolaryngology clinic in Oman [13]. In a study it was reported that ENT involvement of diseases was 71.9%. In that research, 48% of patients had allergic rhinosinusitis [14]. Our study found that 125 (10%) individuals out of 1250 cases had allergic rhinitis. As sample size in our study was adequate so the results are comparable with that study. A previous research using a proforma questionnaire on 15718 primary school students examined the prevalence of avoidable ear diseases in students in primary school (ages

5 to 12). The most prevalent ENT disease was noted in these small kids were wax in their ear. 7.93% had chronic otitis media, 4.79% had otitis media with effusion, and 3.66% had otitis media with nodule. Children with acute otitis media were identified in 0.65% of cases, and 0.34% had foreign bodies discovered. Our study shows that among 1250 patients, 28% had ear wax, 7% had chronic otitis media, and 24% had acute otitis media. The difference may be attributed to the age groups and sample size selected from outpatient department in our study as compared to population based in previous study. Patient occupational classes in our study indicated that a greater number of patients belonged to lower occupational classes than to upper classes. Various links between asthma and allergic rhinitis have been reported in the last twenty years, pointing great concern in medical community [15]. Nasal blockage is the major symptom of sinus nasal pathology due to inflammation of lining epithelium of nasal cavity [12-14]. The same findings are reported in other studies. A prospective research of 32800 patients conducted at the ORL department of Khaybar Medical College Peshawar, Pakistan, between month of April 2011, May 2012 revealed that 47% of patients had ear problems, 36% had nasal complaints, and 17% had laryngopharyngeal symptoms. In our study, a huge number of 72% of cases had ear disorders. 43.2% of complaints are related to nasal issues, while 45.2% were related to laryngopharyngeal issues. This difference may be due to large sample size in that study and possibility of seasonal variation. In a Pakistani tertiary care hospital in Peshawar, a prospective research was carried out. The majority of ENT conditions that were identified in those babies included tonsillitis (25.33%), pharyngitis (30%), otitis media (29.53%), and nasal obstruction (53%). According to this study, youngsters are more likely to suffer from ENT disorders [16]. In current study, 355 (28%) were suffering from ear wax, followed by acute otitis media 300 (24%), acute tonsillitis and deviated nasal septum each in 225 (18%), otitis externa 150 (12% and acute pharyngitis in 145 (11%). The age group differences are the reason for the various results. In a study ear disease were found in 198 (46%) out of 430 patients [17]. In another study it was reported that ear wax was the most common in children 37 (35.9%), Otitis media with effusion in 7 patients and hearing loss was 13 (12.6%) [18]. According to a study on the prevalence of ENT disorders in children conducted in India, joint families, low socioeconomic position, and overcrowding may be to blame for the high prevalence of ENT diseases. In a study 583 patients were reported for FB in nose, mean age was 12.9 years, 56.7% were male while 43.22% were female [19]. In a study 230 patients were enrolled, 95% of them had ENT diseases. Nasal Obstruction was 59%, Loss of smell (Anosmia) was 57%, Hearing loss (Deafness) was 23% and Laryngeal involvement was15% [20]. In our study nasal obstruction was 53% i.e. little bit corelating.

CONCLUSIONS

This study showed that majority of the patients attending ENT outpatient department of our teaching hospital were related to ear with most common diseases were ear wax followed by acute otitis media, acute tonsillitis and deviated nasal septum, otitis externa, and other ENT diseases included acute pharyngitis. It was noted that many patients have multiple diseases. Most of the patients were from poor socioeconomic status.

Authors Contribution

Conceptualization: THK
Methodology: AHR, MI
Formal analysis: MJM, DR, MI
Writing-review and editing: THK, TZS

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

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

REFERENCES

[1]   Kumar S, Aslami AN, Rai T, Alwa B. Effect of living environment on ear, nose and throat diseases: a cross sectional survey in rural areas of Rohtas district in Bihar. International Journal of Otorhinolaryngology and Head and Neck Surgery. 2018 May; 4(3): 625. doi: 10.18203/issn.2454-5929.ijohns20181442.

[2]   Alhazmi WA, Almutairi AN, Al-Muqbil AA, Al-Ali AI, Alhasson MA. Pattern of ear, nose, and throat disease seen by otolaryngologists at Qassim University outpatient clinics, Saudi Arabia. International Journal of Medicine in Developing Countries. 2021 Jul; 5(7): 1430-. doi: 10.24911/IJMDC.51-1623238530.

[3]   Dey BK, Datta A, Rhaman MM, Sayeed MA. Pattern of ear nose and throat diaseses in a tertiary hospital of Dhaka city. Prevalence. 2018 Jan; 35: 0-18. doi: 10.3329/imcjms.v12i1.35173.

[4]   Rosario DC, Mendez MD. Chronic Suppurative Otitis. 2020 Mar; 3.

[5]   Bhatia R, Chauhan A, Kaur K, Rana M, Pradhan P, Singh M *et al.* Prevalence of ear infections in children (0 to 15 years) of India: a systematic review and meta-analysis. International Archives of Public Health and Community Medicine. 2022; 6(2): 080. doi: 10.23937/2643-4512/1710080.

[6]   Orman G, Kralik SF, Desai N, Meoded A, Vallejo JG, Huisman TA *et al.* Imaging of paranasal sinus infections in children: a review. Journal of

Neuroimaging. 2020 Sep; 30(5): 572-86. doi: 10.1111/jon.12737.

[7]   Alkholaiwi F, Alharbi MM, Aldayel AY, Shadid AM, Almutairi FE, Dahmash AB *et al.* Public perception in the management and prevention of common ear, nose, and throat diseases in Saudi Arabia. Journal of Nature and Science of Medicine. 2020 Apr; 3(2): 126-35. doi: 10.4103/JNSM.JNSM_50_19.

[8]   Ling HW. Which Are the Energy Imbalances Behind Children with Chronic Nosebleed. Journal of Clinical Pediatrics and Mother Health. 2022 Dec; 2(1). doi: 10.3 1579/jcpmh.2022/017.

[9]   Klug TE, Greve T, Hentze M. Complications of peritonsillar abscess. Annals of Clinical Microbiology and Antimicrobials. 2020 Dec; 19: 1-7. doi: 10.1186/s12 941-020-00375-x.

[10] Krajewska J, Krajewski W, Zatoński T. The association between ENT diseases and obesity in pediatric population: a systemic review of current knowledge. Ear, Nose and Throat Journal. 2019 Jun; 98(5): E32-43. doi: 10.1177/0145561319840819.

[11] Marengo R, Ortega Martell JA, Esposito S. Paediatric recurrent ear, nose and throat infections and complications: can we do more?. Infectious Diseases and Therapy. 2020 Jun; 9: 275-90. doi: 10.1007/s40121 -020-00289-3.

[12] Onotai LO, Osuji AE, Mbalaso OC, Nwankwo BE. Evaluation of Common Ear, Nose and Throat Diseases in Rivers State, Nigeria. Annals of Clinical Otolaryngology. 2020 Jun; 5(1). 2020; 1043.

[13] Nappi E, Paoletti G, Malvezzi L, Ferri S, Racca F, Messina MR *et al.* Comorbid allergic rhinitis and asthma: important clinical considerations. Expert Review of Clinical Immunology. 2022 Jul; 18(7): 747-58. doi: 10.1080/1744666X.2022.2089654.

[14] Felicetti M, Cazzador D, Padoan R, Pendolino AL, Faccioli C, Nardello E *et al.* Ear, nose and throat involvement in granulomatosis with polyangiitis: how it presents and how it determines disease severity and long-term outcomes. Clinical Rheumatology. 2018 Apr; 37: 1075-83. doi: 10.1007/s10067-018-4019-0.

[15] Riaz N, Ajmal M, Khan MS. Frequency of otitis media with effusion among children aged 1-5 years presenting to immunization center of tertiary care hospitals, Rawalpindi. World Journal of Otorhinolaryngology-Head and Neck Surgery. 2022 Dec; 8(04): 315-20. doi: 10.1016/j.wjorl.2021.03.002.

[16] Shekhar H, Khokhar A, Motwani G, Daral S. Prevalence of ear morbidities among school children in delhi, india: a cross-sectional study. International Journal of Adolescent Medicine and Health. 2022 Oct; 34(5): 289-95. doi: 10.1515/ijamh-2020-0088.

[17] Takwoingi YM, Fufore MB, Umar A, Musa GE, Thimnu WA, Abdullahi I *et al.* A Comparative Study of Ear Diseases in School Children from Lower versus Higher Socioeconomic Status. International Journal of Otolaryngology and Head & Neck Surgery. 2021 Mar; 10(2): 107-18. doi: 10.4236/ijohns.2021.102012.

[18] Alam M, Muhammad T, Usman M, Ahmad S. Effectiveness of Septoplasty in Releiving Nasal Obstruction in Patients with Deviated Nasal Septum. Journal of Saidu Medical College, Swat. 2022 Jun; 12(2): 71-4. doi: 10.52206/jsmc.2022.12.2.663.

[19] Khan TA, Mahboob HM, Tahir I, Nasir M, Ali A, Abbas I *et al.* Foreign Bodies Presentation at Otorhino-laryngology Emergencies in A Tertiary Care Hospital. Annals of King Edward Medical University. 2018 Sep; 24(S): 893-6.

[20] Kühn D, Hospowsky C, Both M, Hey M, Laudien M. Manifestation of granulomatosis with polyangiitis in head and neck. Clinical and Experimental Rheumatology. 2018 Jan; 36(111): S78-84.

Original Article

Evaluation of Mean Apical Sealing Ability of Bio Ceramic and AH Plus (Dentsply Sirona) Sealer in Single Rooted Teeth: An *In Vitro* Study

Jazib Memon[1*], Kanza Iqbal[2], Mariam Raza Mallick[3], Mohsin Ali Dehraj[4], Ahsan Ali[5] and Kelash Kumar[6]

[1]Department of Operative Dentistry and Endodontics, Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan
[2]Department of Operative Dentistry and Endodontics, Institute of Dentistry, Combined Military Hospital Lahore Medical College, Lahore, Pakistan
[3]Department of Operative Dentistry and Endodontics, Pakistan Institute of Medical Sciences, Islamabad, Pakistan
[4]Department of Operative Dentistry and Endodontics, Muhammad Dental College, Mirpurkhas, Pakistan
[5]Department of Operative Dentistry, Rehman College of Dentistry, Peshawar, Pakistan
[6]Department of Operative Dentistry and Endodontics, Baqai Dental College, Karachi, Pakistan

ARTICLE INFO

ABSTRACT

A good seal is essential to prevent bacteria from re-entering the canal. Sealers can significantly impact the success of the treatment. Understanding which sealant works better can help dentists improve the outcome of root canal treatments. **Objective:** To compare mean apical sealing ability of bioceramic sealer and AH plus sealer in single rooted tooth. **Methods:** Extracted single-rooted teeth were divided into two groups and sealed with either bioceramic or AH plus sealer. After soaking in dye solution, the depth of dye penetration was measured to assess leakage. **Results:** Bioceramic sealer showed significantly better apical sealing ability (mean 5.43 mm) compared to AH plus (mean 8.55 mm), suggesting it may be a more effective choice for preventing future problems after root canal treatment. **Conclusions:** The study concluded that bioceramic sealer is superior to AH plus in sealing the tips of single-rooted teeth. This finding can help dentists choose the most effective sealant for their patients, potentially reducing the chance of treatment failure.

INTRODUCTION

Root canal therapy aims to disinfect the inner chamber of the tooth (the root canal) and eliminate infected tissue. This creates a sterile environment essential for obturation, a process that seals the canal in three dimensions. A proper seal is crucial to prevent reinfection by isolating the tip of the root (apex), the surrounding gum tissue (periodontal space), and the entire canal. Unfortunately, inadequate sealing is a major cause of root canal failure. This can happen due to various factors like patient movement during treatment, improper isolation of the tooth, insufficient cleaning, or failing to create a watertight seal at the end [1]. Recent advancements offer improved techniques for achieving a tight seal. One approach involves using rotary instruments made of Nickel-Titanium (NiTi) alongside specially designed gutta-percha cones. This combination, when used with a special sealing material, can create a complete and impermeable three-dimensional seal. However, sealants themselves can

Memon J *et al.,*

sometimes be a problem. They might allow tiny leaks (microleakage) at the junction between the sealant, the dentin (tooth layer), or the core material placed on top. These leaks can provide entry points for bacteria, potentially leading to failure [2, 3]. Therefore, the success of a root canal heavily relies on the chosen sealant. An ideal root canal sealant should be biologically compatible, inert (not reactive), and strongly adhere to the canal walls after hardening. Additionally, it should provide excellent sealing properties once set. Despite ongoing research, no current sealant perfectly meets all these requirements. Several types are available, each with its own unique chemistry. Popular choices include calcium hydroxide, zinc oxide eugenol, and resin-based sealants [4, 5]. In recent years, AH plus (Dentsply Sirona) has become a favorite sealant due to its epoxy resin base. However, it has limitations. AH plus repels water (hydrophobic), which can be a disadvantage in the naturally moist environment of the mouth. Moreover, it shrinks as it hardens, potentially compromising the seal and causing microleakage [6, 7]. Bioceramics are a recent innovation in dentistry. These materials are composed of elements like zirconium oxide, calcium silicates and calcium phosphate, along with fillers and thickening agents. Despite their newness, bioceramics have gained popularity due to their high quality and user-friendliness. They come pre-mixed in syringes for injection, making them easier to use compared to traditional sealants. [8]. Previously, there was limited research comparing the effectiveness of bioceramic sealers with AH plus in sealing the tips of teeth (apical third). To address this gap, we investigated the efficacy of these sealers using a special microscope.

Our study aimed to compare how well bioceramic sealers and AH plus sealed the apices of single-rooted teeth. By understanding the differences between these sealers, dentists can choose the most suitable option for their patient's specific needs. This can significantly reduce the risk of apical microleakage and ultimately, root canal failure. This approach not only benefits patients by minimizing discomfort but also saves them time and money in the long run.

METHODS

An *in vitro* experimental study to assess the mean apical sealing ability of (insert material being tested) was conducted at the Department of Operative Dentistry, Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan. The study took place between October 2020 and April 2021 and received approval from the College of Physicians and Surgeons of Pakistan vide Ref No. CPSP/REU/DSG-2017-166-2145. To evaluate sealing effectiveness, researchers measured the depth of dye penetration in millimeters. Extracted teeth were filled with the test material, then soaked in a 1% methylene blue dye solution for 72 hours. A deeper dye penetration indicates a less effective seal [9]. Nonprobability consecutive sampling was used, with a sample size of 32 in each group. The sample size was calculated using OpenEpi, based on the mean dye penetration of bioceramic sealer 5.37 ± 1.42 and AH plus (Dentsply Sirona) 8.04 ± 2.02, with a 99% confidence interval [10]. Single-rooted teeth meeting the inclusion criteria of being permanent, single-rooted, single-canal teeth with a well-developed root, close apex, and straight roots were selected for the study. These teeth were extracted from the Department of Oral and Maxillofacial Surgery, Institute of Dentistry, Liaquat University of Medical and Health Sciences, Jamshoro. Teeth with prior endodontic therapy, root caries, root resorption, fractures, or cracks, as well as those with curved roots, were excluded. After extraction, the teeth were preserved in normal saline following a 2-hour soak in a 2.5% sodium hypochlorite solution. The teeth were then decoronated 12 mm from the apex to make the canals accessible. Finishing and shaping were performed using rotary protaper files, with irrigation using a 2.5% sodium hypochlorite solution. Sterile paper tips were inserted once the canals were dry. After fulfilling the inclusion criteria, teeth were divided into two groups. In group A, the canals were obturated using an endosequence bioceramic sealer, while in group B, AH plus (Dentsply Sirona) sealer. The coronal opening was then sealed with glass ionomer cement, and varnish was applied to the teeth's surfaces 2 millimeters before the apex. The teeth were immersed in a 1% methylene blue dye solution for three days, followed by thorough rinsing with water. The teeth were then sliced in half lengthwise using diamond discs, and dye penetration was measured using a stereomicroscope (Figure 2 and 3). These results were used to record all data in a proforma. SPSS 20.0 was used to analyze the data. Mean apical sealing ability was assessed by dye penetration depth and the means and standard deviations for both sets of sealers were calculated (in mm). The data on teeth were presented as a frequency and percentage distribution. Using a T-test, the mean apical sealing ability of the two groups was compared. P-value ≤ 0.05 was considered as significant.

RESULTS

The tooth in the study consists of equal distribution of Maxillary Central Incisor (18%), Maxillary Lateral Incisor (7%), Maxillary Canine (8%), Mandibular Central Incisors (15%), Mandibular Lateral Incisor (12%), Mandibular Canine (4%), Mandibular 1st premolar (32%) and mandibular 2nd premolar (4%) as shown in figure 1.
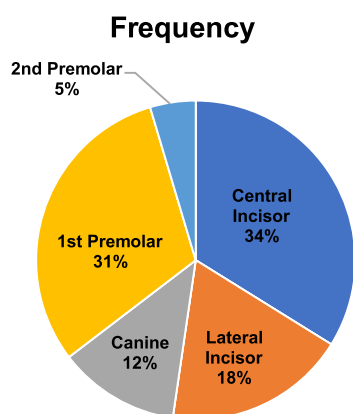
Frequency

Figure 1: Distribution of Various Tooth Types According to Frequency

The mean apical sealing ability of bioceramic sealer was 5.43 ± 0.43, and the mean apical sealing ability of AH plus (Dentsply Sirona) sealer was 8.55 ± 0.25 in single-rooted plants. P-value was 0.01 as shown in table 1.

Table 1: Mean Dye Penetration Depth in Both Groups

Groups	Bioceramic Sealer Treatment (Group A) Mean ± S.D	AH Sealer Treatment (Group B) Mean ± S.D	P-Value
Depth of Dye Penetration (mm)	5.43 ± 0.43	8.55 ± 0.25	0.01

Confocal laser microscopy shown the interfacial gaps and sealant depth at apical area. The comparison between bioceramic sealers and AH plus is visually represented, highlighting the differences in sealant profiles and gap formation as shown in figure 2.
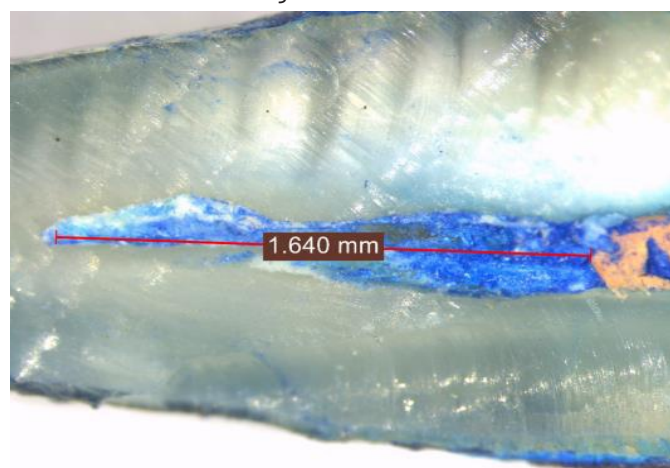
Figure 2: Dye Penetration in AH Plus Sealer Showing Leakage Depth

Utilizing confocal laser microscopy, the study illustrates interfacial gaps and sealant depth at the apical area, visually contrasting bioceramic sealers with AH plus, emphasizing differences in sealant profiles and gap formation as shown in figure 3.
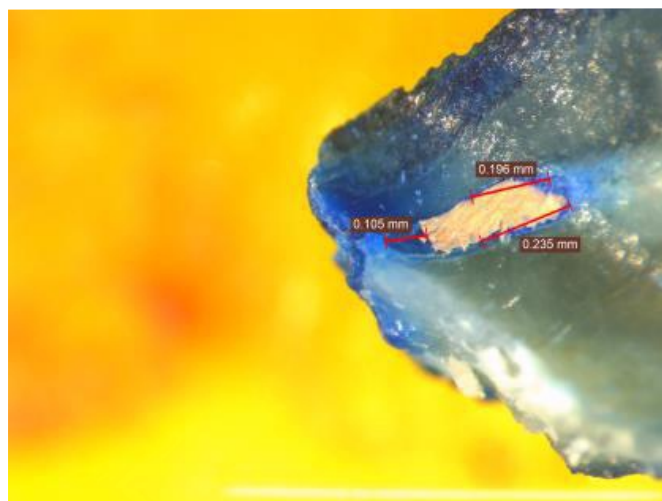
Figure 3: Dye Penetration Depth Showing Bioceramic Sealer

DISCUSSION

Root canal therapy is successful if the root canal system is properly debrided, pathogenic organisms are eradicated, and the canal area is sealed to prevent the flow of fluid. Utilizing an endodontic sealer in conjunction with a core material, a fluid-tight seal is created. If the sealer and core materials combine to produce a single mass that chemically adheres to the dentine, leakage can be reduced. Since it is biocompatible, readily accessible, radiopaque and easy to apply, the use of AH plus (Dentsply Sirona) sealant to fill root canals has gained in popularity [11, 12]. AH plus (Dentsply Sirona) is an adamantine-containing epoxy-bis-phenol resin that attaches to the root canal wall. AH plus (Dentsply Sirona) root canal sealant is a two-component paste/paste formulation. Since the epoxy resin in AH plus (Dentsply Sirona) sealer makes it adhere more securely to the dentin in your teeth's roots, you will experience fewer leaks. Due to its creep capacity and long setting time, AH plus (Dentsply Sirona) enhances the mechanical contact between the sealer and the root dentin, helping it to penetrate further into the micro defects [13]. As demonstrated by Pawar *et al.*, experiment's insufficient bonding between the sealant and the gutta-percha site allows for leakage at this contact [10]. AH plus (Dentsply Sirona) has a quicker setting time and contains resin, both of which lead to untimely root canal debonding. Mineral Trioxide Aggregate (MTA) is a promising biomaterial for root end fillings, pulpotomies, apexifications and perforation repairs, according to the dental community [8, 14, 15]. MTA, a bioactive material, can develop a surface coating of hydroxyapatite or carbonated apatite when exposed to a phosphate-containing solution for two months. This interfacial layer forms a chemical interaction between the MTA and the dentinal walls. Sealing ability and limited adjustability are two of MTA's greatest strengths. Its retention properties increased from 24 to 72 hours while

being 50% smaller than standard MTA and less than 1 micron in size. The two most important roles of a root canal filling material are sealing off the channel and preventing the entry of microorganisms. It aids in microbial control if any bacteria remain in the canal walls or tubules and creates an impermeable seal between the core filling material and canal wall [16, 17]. The results of the study show that there was an equal distribution of various types of teeth used in the study, including maxillary central incisor, maxillary lateral incisor, maxillary canine, mandibular central incisors, mandibular lateral incisor, mandibular canine, mandibular first premolar, and mandibular second premolar. The mean apical sealing ability of the bioceramic sealer was found to be 5.43 ± 0.43, while the mean apical sealing ability of the AH plus (Dentsply Sirona) sealer was 8.55 ± 0.25 in single-rooted teeth. The P-value of the study was found to be 0.01, which suggests a statistically significant difference between the mean apical sealing ability of the two sealants. These results indicate that the AH plus (Dentsply Sirona) sealer was more effective in sealing the apices of the teeth compared to the bioceramic sealer. Based on these results, dentists can consider the use of the AH plus (Dentsply Sirona) sealer for root canal therapy as it is more effective in sealing the apices of the teeth. This can reduce the risk of apical microleakage and endodontic treatment failure, thereby providing patients with more comfortable and cost-effective treatment options. Pawar *et al.,* did a study which is like findings in our study with bioceramics showing less leakage than AH plus (Dentsply Sirona) sealer [10]. In his study he utilized 75 extracted human permanent teeth with a single root. The root canals were instrumented, and the teeth were decorated. The specimens (n = 25) were obturated using a process involving continuous wave condensation and then randomly divided into three groups. Group A utilized the Endosequence BC, Group B utilized the AH plus (Dentsply Sirona) sealer, and Group C utilized the Resilon-Epiphany system. Microleakage was determined using the dye penetration method. At 2, 4, and 6 mm from the pointed end, horizontal lines were produced by slicing the teeth lengthwise through the middle. Under a stereomicroscope, authors measured the dye's penetration depth (30X magnification). Group B demonstrated greater vertical and horizontal dye penetration than groups A and C, showing that the root canal was more effectively sealed with the new BC sealer and Epiphany sealer than with the AH plus (Dentsply Sirona) sealer. However, another study comparing the effectiveness of the sealants AH plus (Dentsply Sirona), pulp canal sealer EWT, Sealapex, and MTA Fillapex for filling and dentinal penetration revealed no statistically significant differences [18]. Forty single-rooted teeth were treated with chemical-mechanical preparation and root-canal filling in this investigation. Using confocal laser scanning microscopy and stereomicroscopy, slices of the root obtained 2, 4, and 6 millimeters from the tip were examined. Apart from the MTA Fillapex, which failed at 4 and 6 mm from the root apex, each of the four sealers were found to be equivalent in terms of the filling material's capacity to adapt to the root canal walls. Except for the pulp canal sealer EWT, all of the sealants were shown to have comparable penetration into the dentinal tubules. Compared to MTA Fillapex and AH plus (Dentsply Sirona), the EWT pulp canal sealer performed poorly at 4 and 6 mm. In contrast to our findings, another study comparing bioceramic sealers with AH plus (Dentsply Sirona) sealer based on their interfacial adaptability and sealer thickness to root dentin found that the bioceramics permitted greater leakage [19]. In this study, 0.1% fluorescent Rhodamine B dye was added to sealants, and 60 extracted single-root premolars were randomly assigned to one of four groups. Calculated was the ratio of canal area to sealer area. Using a confocal laser microscope, the ratio of the gap-containing region to the canal's circumference was measured. The thickness of the sealant was greatest at the middle and apical levels and decreased toward the coronal levels. Compared to EndoSequence BC, the profiles of MTA Fillapex and AH plus (Dentsply Sirona) were substantially slimmer. Bioceramic sealants produced more gaps than AH plus (Dentsply Sirona), but there were no noticeable differences between the other kinds. The coronal level displayed the fewest interfacial gaps as compared to the apical and intermediate levels. In another trial, both with and without the butterfly effect, the depth and quality of root canal sealer and ProRoot MTA penetration into the buccolingual and mesial regions of roots were evaluated [20]. Where dentinal tubule density is extremely great, the butterfly effect can be observed in a few roots. Then, 120 teeth were randomly assigned to one of five obturation groups: ProRoot MTA alone, gutta-percha with AH With, EndoREZ, Kerr Pulp Canal Sealer, MTA Fillapex, or MTA Fillapex plus a sealer (each containing 10 butterfly and 10 non-butterfly roots). The authors examined penetration and adaptability with confocal laser scanning and scanning electron microscopy. The bucco-lingual penetration of butterfly teeth, on average, was greater than their mesio-distal penetration. The butterfly effect augments positive therapeutic effects.

CONCLUSIONS

In conclusion, the results of this study suggest that bioceramic sealer is a more effective sealing material compared to AH plus (Dentsply Sirona) sealer in sealing the apices of single-rooted teeth. This information can be useful for dentists in choosing the best sealant for their

patients, which can reduce the risk of apical microleakage and endodontic treatment failure.

Authors Contribution

Conceptualization: JM
Methodology: JM, MAD
Formal analysis: KK
Writing, review and editing: KI, MRM, AA

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

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1]   Tabassum S and Khan FR. Failure of endodontic treatment: The usual suspects. European Journal of Dentistry. 2016 Jan; 10(01): 144-7. doi: 10.4103/1305-7456.175682.

[2]   Seema T, Ahammed H, Parul S, Cheranjeevi J. Comparative evaluation of dentin removal and taper of root canal preparation of hand K file, ProTaper rotary file, and Kedo S rotary file in primary molars using cone-beam computed tomography. International Journal of Clinical Pediatric Dentistry. 2020 Jul; 13(4): 332. doi: 10.5005/jp-journals-10005-1787.

[3]   Ahluwalia Y, Sharma U, Kumar N, Malik A, Singh A, Narayan A. Adaptation of single-cone gutta-percha in curved canals prepared and obturated with protaper and heroshaper systems by using cone beam computed tomography. Journal of International Society of Preventive and Community Dentistry. 2019 Mar; 9(2): 185-93. doi: 10.4103/jispcd.JISPCD_398_18.

[4]   Vishwanath V and Rao HM. Gutta-percha in endodontics-A comprehensive review of material science. Journal of Conservative Dentistry and Endodontics. 2019 May; 22(3): 216-22. doi: 10.4103/JCD.JCD_420_18.

[5]   Li GH, Niu LN, Zhang W, Olsen M, De-Deus G, Eid AA *et al.* Ability of new obturation materials to improve the seal of the root canal system: a review. Acta Biomaterialia. 2014 Mar; 10(3): 1050-63. doi: 10.1016/j.actbio.2013.11.015.

[6]   Sultana M, Musani MA, Ahmed IM. An in-vitro comparative study for assessment of apical sealing ability of Epiphany/AH Plus sealer with Resilon/gutta-percha root canal filling materials. Journal of International Society of Preventive and Community Dentistry. 2016 Jul; 6(4): 321-6. doi: 10.4103/2231-0762.186806.

[7]   Kikly A, Jaâfoura S, Kammoun D, Sahtout S. Sealing ability of endodontic cements: An *in vitro* study. International Journal of Dentistry. 2020 Feb; 2020(1): 5862598. doi: 10.1155/2020/5862598.

[8]   Kwak SW, Koo J, Song M, Jang IH, Gambarini G, Kim HC. Physicochemical properties and biocompatibility of various bioceramic root canal sealers: *in vitro* study. Journal of Endodontics. 2023 Jul; 49(7): 871-9. doi: 10.1016/j.joen.2023.05.013.

[9]   Ozbay G, Kitiki B, Peker S, Kargul B. Apical sealing ability of a novel material: analysis by fluid filtration technique. Acta Stomatologica Croatica: International Journal of Oral Sciences and Dental Medicine. 2014 Jul; 48(2): 132-9. doi: 10.15644/asc48/2.132.

[10]   Pawar SS, Pujar MA, Makandar SD. Evaluation of the apical sealing ability of bioceramic sealer, AH plus & epiphany: An: *in vitro*: study. Journal of Conservative Dentistry and Endodontics. 2014 Nov; 17(6): 579-82. doi: 10.4103/0972-0707.144609.

[11]   Wolch I. A new approach to the basic principles of endodontics. International Dental Journal. 1975 Sep; 25(3): 179-84.

[12]   Siotia J, Acharya SR, Gupta SK. Efficacy of ProTaper retreatment system in root canals obturated with gutta-percha using two different sealers and GuttaFlow. International Journal of Dentistry. 2011 Oct; 2011(1): 676128. doi: 10.1155/2011/676128.

[13]   Nunes VH, Silva RG, Alfredo E, Sousa-Neto MD, Silva-Sousa YT. Adhesion of Epiphany and AH Plus sealers to human root dentin treated with different solutions. Brazilian Dental Journal. 2008; 19: 46-50. doi: 10.1590/S0103-64402008000100008.

[14]   Aggarwal V, Singla M, Rizvi A, Miglani S. Comparative evaluation of local infiltration of articaine, articaine plus ketorolac, and dexamethasone on anesthetic efficacy of inferior alveolar nerve block with lidocaine in patients with irreversible pulpitis. Journal of Endodontics. 2011 Apr; 37(4): 445-9. doi: 10.1016/j.joen.2011.01.016.

[15]   Asgary S, Kamrani FA, Taheri S. Evaluation of antimicrobial effect of MTA, calcium hydroxide, and CEM cement. Iranian Endodontic Journal. 2007 Oct; 2(3): 105–109.

[16]   Roberts HW, Toth JM, Berzins DW, Charlton DG. Mineral trioxide aggregate material use in endodontic treatment: a review of the literature. Dental Materials. 2008 Feb; 24(2): 149-64. doi: 10.1016/j.dental.2007.04.007.

[17]   Cervino G, Laino L, D'Amico C, Russo D, Nucci L, Amoroso G *et al.* Mineral trioxide aggregate applications in endodontics: A review. European

Journal of Dentistry. 2020 Oct; 14(04): 683-91. doi: 10.1055/s-0040-1713073.

[18] Silva RV, Silveira FF, Horta MC, Duarte MA, Cavenago BC, Morais IG *et al.* Filling effectiveness and dentinal penetration of endodontic sealers: a stereo and confocal laser scanning microscopy study. Brazilian Dental Journal. 2015 Oct; 26: 541-6. doi: 10.1590/0103-6440201300138.

[19] Al-Haddad A, Kasim NH, Ab Aziz ZA. Interfacial adaptation and thickness of bioceramic-based root canal sealers. Dental Materials Journal. 2015 Jul; 34(4): 516-21. doi: 10.4012/dmj.2015-049.

[20] Russell A, Friedlander L, Chandler N. Sealer penetration and adaptation in root canals with the butterfly effect. Australian Endodontic Journal. 2018 Dec; 44(3): 225-34. doi: 10.1111/aej.12238.

Original Article

Evaluation of Dyslipidaemia in Patients with Chronic Viral Hepatitis in a Lower Socio-Economic Country

Rakhshinda Jabeen[1*], Aziz Ur Rehman[2], Ahsan Mobin[1], Hussain Haroon[1], Imtiaz Manzoor[3] and Muhammad Ubaid[1]

[1]Department of Medicine, Dow University of Health Sciences, Karachi, Pakistan
[2]Department of Medicine, Dr.Ruth K M Pfau Civil Hospital, Karachi, Pakistan
[3]Department of Medicine and Allied Health Sciences, Chiniot General Hospital, Karachi, Pakistan

ARTICLE INFO

ABSTRACT

Patients having chronic viral hepatitis do have disturbances in their serum lipid profiles, still the monitoring of dyslipidemia is not a routine part of management in low socio economic countries. **Objective:** To investigate the status of lipid profile among patients with chronic hepatitis and compare them with non-infected individuals. **Methods:** A cross-sectional study was done in a Tertiary Care Hospital of Karachi, from 5th September 2022 to 31st May 2023. Patients with chronic hepatitis B and C, diagnosed within two years with a body mass index (BMI) of 25-29.9 kg/m2 were included. Their comparison was done with non-infected individuals of the same BMI. All patients were evaluated with different parameters of lipid profile along with haemoglobin, alanine aminotransferase, albumin and international normalized ratio. **Results:** Among 521 participants of the study, the grouping was almost equal. The age range was 12-75 years, with an increased number of females in each group. In comparing the different statuses of lipid profile, each parameter including cholesterol, triglycerides, high-density lipoprotein, low-density lipoprotein, all were significantly much less in patients with chronic viral hepatitis as compared to controls with a p-value of 0.000 in all. **Conclusions:** It was concluded that Dyslipidaemia is not common among chronic viral hepatitis patients' despite being overweight, particularly among patients with child's class A.

INTRODUCTION

Dyslipidaemia is a common illness among the general population and one of the main risk factors in the development of cardiovascular illness. Aggressive treatment of dyslipidaemia leads to a reduction in mortality and morbidity of cardiovascular illness [1]. The liver metabolises various lipid-lowering agents, in addition to being the primary source of cholesterol and other lipids. Thus, it is always questionable to start these medications in patients with liver disease. Both chronic viral hepatitis, Hepatitis B and C, chronically infect 240 million and 170 million people respectively worldwide [2, 3]. Like every other reason leading to chronic liver disease, chronic viral hepatitis is associated with the development of end-stage liver disease, cirrhosis, hepatocellular carcinoma and may need liver transplantation if not treatable by medications [4, 5]. Hepatitis C virus (HCV) replication infects hepatocytes via interlinking with circulating lipoproteins. Both acute and chronic HCV leads to a decrease in serum low density lipids (LDL) and total cholesterol levels [5]. There are several mechanisms of hepatitis C replication which affects lipid metabolism. Interaction of the virus with lipoproteins with the help of LDL receptors may infect hepatocytes. Further interacts with host cytosolic lipid droplets inside the hepatocytes causing HCV core protein formation and used synthesis pathway of cholesterol for replication. Despite having decreased LDL risk of

cardiovascular disease among HCV-infected patients remains higher when matched with control subjects. It may also get increased after spontaneous or treatment-induced clearance of HCV[6]. Hepatitis B viral infection like HCV also interferes with the metabolism of lipids, especially cholesterol. The binding of hepatitis B virus (HBV) with polypeptide leads to impairment of bile acid uptake, leading to increased bile acid synthesis and thus conversion to cholesterol [7]. Liver damage is due to the immune response exerted by the virus into the hepatocytes. Alteration of plasma lipid levels is a consequence of pro-inflammatory cytokines exhibited by chronic hepatitis B infection. Although not much work has been done in the association of lipid levels in HBV. Few data showed decreased triglyceride and high-density lipoprotein among HBV-infected individuals when compared to matched control subjects [8]. The focus of the study is to determine the variables of lipid levels among patients with chronic viral hepatitis and compare them with the control group. Similarly, a study previously done in Hyderabad, Pakistan among patients with HCV with dyslipidaemia also showed a higher incidence of dyslipidaemia among these patients [9], while comparing another study in the same province showed contradictory results, despite among patients with metabolic syndrome with HCV[10]. There is a paucity of research on Hepatitis B; however, a study done previously showed a decrease in the levels of all parameters of the lipid profile[11].

The aim of this study was to evaluate the status of dyslipidaemia among patients with chronic viral hepatitis and compare them with patients without chronic viral hepatitis.

METHODS

A cross sectional study was conducted at the outpatient Department of Dr. Ruth K M Pfau Civil Hospital Karachi, Karachi, Pakistan. The total time required to collect the specified number of patients was 9 months between 5th September 2022 to 31st May 2023. Patients were only inducted after taking proper consent and approval from the ethical review board (ERC-001/CGH/MO/2022; Dated: 5th Sep, 2022). Calculated using Rao software keeping anticipated 299 patients in view of a study done in Mexico [12]. Confidence of 95% and absolute precision of 5% gave the total sample of 169. The study was conducted on 169 patients in each group. All patients with chronic viral hepatitis, hepatitis B and C, diagnosed within two years, with child's class A, were included in the study, and they were compared with the same age group without chronic liver disease. Patients of both gender between the age group 12-80 were included. Patients with a body mass index of 25.0 – 29.9 kg/m2. Patients with other causes of chronic liver disease were excluded on the basis of history. Patients

with child's Class B and C were excluded. Patients with HIV, and other chronic illness were excluded. The sampling technique used for data collection were non-probability purposive sampling. Approximately 5-10 mL of blood was drawn from each patient using a sterile needle and syringe. The blood was then transferred into appropriate collection tubes: EDTA tubes for complete blood count (CBC) and serum separator tubes for biochemical analyses (ALT, albumin, INR, and lipid profile). All patients were subjected to laboratory tests including haemoglobin, alanine aminotransferase (ALT), platelets, albumin, international normalized ratio (INR), and lipid profile including cholesterol, HDL, LDL and triglycerides(TG). Figure 1 shows the summary of storage and processing of collected samples (figure 1). Data were analysed using the statistical package for the social sciences (SPSS) version 23.0. Frequencies and percentages have been computed for categorical responses and Chi-square test and T-test to measure the associations between quantitative variables. A p-value of less than 0.05 was taken as being statistically significant. Blood was drawn from each patient using a sterile needle and syringe, then stored in EDTA and serum separator tubes under controlled temperatures, processed with aseptic techniques, properly labelled, and handled in compliance with the Declaration of Helsinki and other ethical guidelines to ensure sample integrity, patient confidentiality, and accurate results.
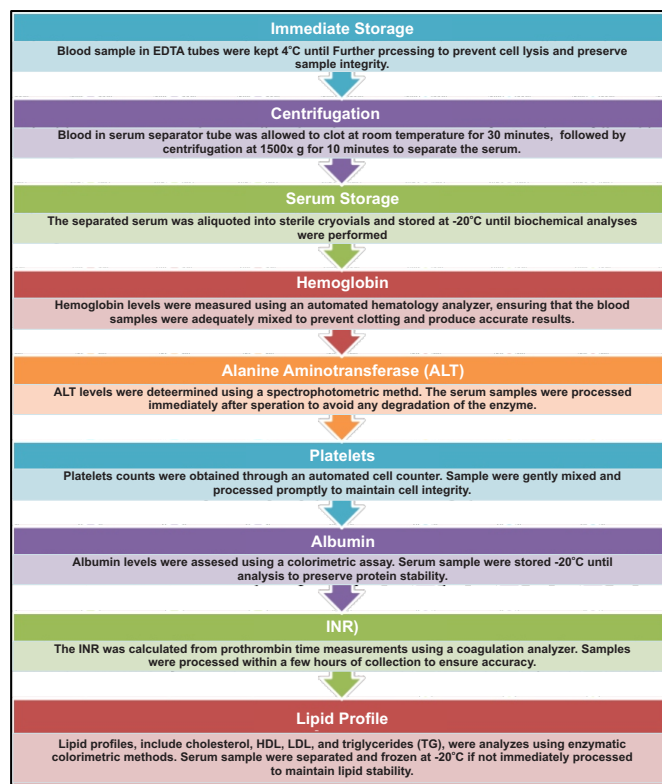

Figure 1: Flowchart showing the Storage and Processing

RESULTS

Among 521 patients incurred in the study, the division among the three groups was almost equal. Regarding demographic features among three groups of the study population, there was a higher number of females in each group. In the control group, out of 171 patients, 102 (59.64%) were females. While in patients with hepatitis B and C; 193 (55.14%) were females. The age range was almost equal when comparing the three groups. The age range was 12-75 years with a mean age of 40.93 ± 11.89 years (Table 1).

Table 1: Age Range among Study Groups

Groups	Male	Female	Age Range
HBV	86	91	40.91 ± 12.99
HCV	71	101	44.81 ± 12.30
Control	69	102	37.03 ± 8.61
Total	226	295	-

Among the laboratory measurements studied were haemoglobin levels, which were lower in non-infected people than in those with chronic viral hepatitis. INR and albumin were normal in all groups even though platelets were somewhat increased in non-infected people (Table 2).

Table 2: Laboratory Assessment among Study Population

Parameters	Control n=171	HBV n=177	HCV n=173	Pearson Correlation Coefficient	p-value
Haemoglobin	11.94 ± 2.14	13.37 ± 10.46	13.05 ± 8.27	-0.047	0.010
Platelets	272.80 ± 80.52	246.77 ± 94.04	214.55 ± 92.57	0.113	0.010
Albumin	1.27 ± 0.448	4.83 ± 4.80	3.95 ± 0.57	-0.159	0.000
INR	1.01 ± 0.626	0.97 ± 0.12	1.04 ± 0.22	0.055	0.213
ALT	40.83 ± 20.87	34.89 ± 13.75	69.67 ± 99.08	0.044	0.321

While comparing parameters of lipid profile, cholesterol and triglycerides were much lower in patients with viral hepatitis with p-value of 0.000 in both categories. While comparing HDL and LDL, the same pattern is observed. (Table 3)

Table 3: Lipid Profile of the Study Population

Parameters	Control n=171	HBV n=177	HCV n=173	Pearson Correlation Coefficient	p-value
Cholesterol	209.71 ± 90.57	148.48 ± 41.85	150.40 ± 85.09	0.310	0.000
Triglycerides	173.48 ± 59.08	133.29 ± 62.17	119.54 ± 65.12	0.246	0.000
HDL	33.69 ± 8.73	40.66 ± 32.60	39.09 ± 9.66	0.691	0.000
LDL	121.15 ± 34.86	92.11 ± 32.37	82.60 ± 33.76	-0.638	0.000

DISCUSSION

Viral hepatitis including hepatitis B and C is the major cause of chronic liver disease leading to cirrhosis of the liver around the world, but especially in lower socioeconomic countries including Pakistan. The prevalence of hepatitis B among blood donors is 0.84, while among healthy subjects it was 6.9%. The same distribution was seen among hepatitis C carriers among blood donors and affected healthy adults [13]. Among the commonest two, hepatitis B

is considered a metabolic virus affecting various metabolic pathways. Regarding extra-hepatic manifestations in hepatitis B polyarteritis nodosa, genotynon-Hodgkin's lymphoma, non-rheumatoidal arthritis, cryoglobulinemic vasculitis, glomerulonephritis, and dyslipidemia [14]. There are various extra-hepatic complications associated with hepatitis C as well including essential mixed cryoglibulinemia, porphyria cutanea tarda, type II diabetes mellitus, sicca syndrome, thyroid disorders, lichen planus, peripheral neuropathy and dyslipidemia [15]. The work on association with Hepatitis C with dyslipidaemia is more extensive than hepatitis B although the results are almost equal. Alteration in lipid levels may be deleterious to health when increased levels of cholesterol and triglycerides lead to atherosclerosis, pancreatitis and aortic dissection, [16] low levels may lead to hopelessness, confusion, and agitation [17]. Studies have shown that diseases of the liver are often associated with impaired liver metabolism because the liver is the main determinant of lipid metabolism and serum lipoprotein synthesis [18]. In most patients with hepatitis C, lower total cholesterol, as well as LDL are commonly seen as compared to patients with hepatitis B in whom there is a low level of TG and HDL is more commonly seen [19]. In current study, mean cholesterol level in patients with hepatitis C and B were 148.48 ± 41.85, respectively which is much lower than in control group which is 209.71 ± 90.5. In comparing the other study done in Ghana, [20] opposite results were in patients with hepatitis B in whom cholesterol was higher in control subjects. While the same pattern was seen among patients with hepatitis C as well [21]. In the present study both the triglyceride and LDL are lower as compared to control subjects in both viral hepatitis. The same pattern was seen in a study done in Iraq [22]. The observation is further endorsed by a study done in Pakistan which also showed low TC, TG and LDL in both hepatitis B and C, as compared to non-infected patients [11]. In view of various genotypes of hepatitis C, the commonest seen in our study was genotype 3, which is also more prevalent in other studies done in Pakistan [23]. Although we couldn't find a significant difference among different parameters of lipid profile in them. Although this is contradictory to one of the studies done previously in which there were much higher levels of cholesterol and LDL were seen in genotypes 1 and 3, while comparing different genotypes [24]. While comparing patients with hepatitis B with hepatitis C, the same pattern of decreased cholesterol and triglycerides was seen which is contrasting with non-infected individuals. Studies done before had the same pattern of observation as our study. As we further evaluated the rest of the parameters of dyslipidaemias including HDL and LDL, we also couldn't find much difference while comparing the previous studies, with decreased levels, as compared to normal subjects.

There is a lack of evidence of treatment of dyslipidaemias among patients with viral hepatitis. Both viruses are associated with cardiovascular complications, although more pronounced with chronic hepatitis C infection [21]. Patients are prone to develop myocardial infraction when matched with controls. Furthermore, LDL and cholesterol both might increase even after clearance of the virus. Decreased HDL and triglycerides in patients with chronic hepatitis may lead to cardiovascular complications. Thus it should be monitored vigilantly among chronic viral infections. It is advisable to follow guidelines to treat dyslipidaemias, and statins are safe and should be used as first-line therapy among both infections [25, 26].

C O N C L U S I O N S

Less evidence of dyslipidaemias among patients with chronic viral hepatitis with child's class A, despite being overweight. Although this study does not show high levels of parameter sit is imperative to advise monitoring it vigilantly as hepatitis C has an increased risk of cardiovascular illness, as compared to hepatitis B.

Authors Contribution

Conceptualization: RJ
Methodology: AUR, HH, MU
Formal analysis: RJ, AUR, HH, MU
Writing-review and editing: AM, IM

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

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

R E F E R E N C E S

[1]   Speliotes EK, Balakrishnan M, Friedman LS, Corey KE. Treatment of dyslipidemia in common liver diseases. Clinical Gastroenterology and Hepatology. 2018 Aug; 16(8): 1189-96. doi: 10.1016/j.cgh.2018.04.023.

[2]   Torre P, Aglitti A, Masarone M, Persico M. Viral hepatitis: Milestones, unresolved issues, and future goals. World Journal of Gastroenterology. 2021 Jul; 27(28): 4603. doi: 10.3748/wjg.v27.i28.4603.

[3]   Amponsah-Dacosta E. Hepatitis B virus infection and hepatocellular carcinoma in sub-Saharan Africa: Implications for elimination of viral hepatitis by 2030?. World Journal of Gastroenterology. 2021 Sep; 27(36): 6025. doi: 10.3748/wjg.v27.i36.6025

[4]   Thrift AP, El-Serag HB, Kanwal F. Global epidemiology and burden of HCV infection and HCV-related disease. Nature Reviews Gastroenterology & Hepatology. 2017 Feb; 14(2): 122-32. doi: 10.1038/nrgastro.2016.176.

[5]   Corey KE, Mendez-Navarro J, Barlow LL, Patwardhan V, Zheng H, Kim AY *et al.* Acute hepatitis C infection lowers serum lipid levels. Journal of Viral Hepatitis. 2011 Jul; 18(7): e366-71. doi: 10.1111/j.1365-2893.2011.01434.x.

[6]   Badawi A, Di Giuseppe G, Arora P. Cardiovascular disease risk in patients with hepatitis C infection: results from two general population health surveys in Canada and the United States (2007-2017). PLOS One. 2018 Dec; 13(12): e0208839. doi: 10.1371/journal.pone.0208839.

[7]   Oehler N, Volz T, Bhadra OD, Kah J, Allweiss L, Giersch K *et al.* Binding of hepatitis B virus to its cellular receptor alters the expression profile of genes of bile acid metabolism. Hepatology. 2014 Nov; 60(5): 1483-93. doi: 10.1002/hep.27159.

[8]   Hsu CS, Liu CH, Wang CC, Tseng TC, Liu CJ, Chen CL *et al.* Impact of hepatitis B virus infection on metabolic profiles and modifying factors. Journal of Viral Hepatitis. 2012 Feb; 19(2): e48-57. doi: 10.1111/j.1365-2893.2011.01535.x.

[9]   Bozdar K, Kumar P, Bajwa MA. Dyslipidemias in Hepatitis C Virus Infection at Isra University Hospital Hyderabad. Annals of PIMS-Shaheed Zulfiqar Ali Bhutto Medical University. 2020 Jan; 16(4): 209-13.

[10]   Qasim SF, Jami A, Imran P, Mushtaque R, Khan RN. Frequency of Metabolic Syndrome in Chronic Hepatitis C Patients: Findings from a Lower Middle Income Country. Cureus. 2020 Dec; 12(12). doi: 10.7759/cureus.11975.

[11]   Jabeen S, Rasheed A, Jabeen N, Naz SA, Raza A. Prevalence and association of HBV and HCV infection with cardiovascular disease risk factors in a peri-urban population. Journal of Pakistan Medical Association. 2020 Jan; 70(1): 58-63. doi: 10.5455/JPMA.1542.

[12]   Gonzalez-Aldaco K, Roman S, Torres-Valadez R, Ojeda-Granados C, Torres-Reyes LA, Panduro A. Hepatitis C virus clearance and less liver damage in patients with high cholesterol, low-density lipoprotein cholesterol and APOE ε4 allele. World Journal of Gastroenterology. 2019 Oct; 25(38): 5826. doi: 10.3748/wjg.v25.i38.5826.

[13]   Ghazanfer S and Osman H. Frequency of TTIs in apparently healthy blood donors in Sialkot District, a small district of Punjab-Pakistan with big reservoir of TTIs. Journal of Haematology and Stem Cell Research. 2021 Feb; 1(1): 29-33.

[14]   Amarapurkar DN and Amarapurkar AD. Extrahepatic manifestations of viral hepatitis. Annals of

Hepatology. 2002; 1(4): 192-5. doi: 10.1016/S1665-2681(19)32165-9.

[15] Jukić LV and Kralj D. Extrahepatic Manifestations of Hepatitis C Virus Infection. Update on Hepatitis C. 2017 Oct; 111. doi: 10.5772/intechopen.70728. doi: 10.5772/intechopen.70728.

[16] Nonogaki K, Fuller GM, Fuentes NL, Moser AH, Staprans IL, Grunfeld CA *et al.* Interleukin-6 stimulates hepatic triglyceride secretion in rats. Endocrinology. 1995 May; 136(5): 2143-9. doi: 10.1210/endo.136.5.7720663.

[17] Thomas RB. An Energy-Restricted, Low Glycemic Index Diet with Omega-3 Fatty Acid and Vitamin D3 Supplementation in Adults with Metabolic Syndrome. [Master's Thesis]. Guelph Ontario, Canada: University of Guelph; 2012.

[18] Kwarteng JK. Changes in serum lipids and other biochemical indices associated with liver damage in chronic Hepatitis B infection. [Master's Thesis]. Kumasi, Ghana: Kwame Nkrumah University of Science and Technology; 2013.

[19] Su TC, Lee YT, Cheng TJ, Chien HP, Wang JD. Chronic hepatitis B virus infection and dyslipidemia. Journal of the Formosan Medical Association. 2004 Apr; 103 (4): 286-91.

[20] Quaye O, Amuzu BG, Adadey SM, Tagoe EA. Effect of hepatitis B virus (HBV) infection on lipid profile in Ghanaian patients. Virology: Research and Treatment. 2019 Feb; 10: 1178122X19827606. doi: 10.1177/1178122X19827606.

[21] Butt AA, Yan P, Chew KW, Currier J, Corey K, Chung RT *et al.* Risk of acute myocardial infarction among hepatitis C virus (HCV)-positive and HCV-negative men at various lipid levels: results from ERCHIVES. Clinical Infectious Diseases. 2017 Aug; 65(4): 557-65. doi: 10.1093/cid/cix359.

[22] Aldabbagh L, Hmood AR, Aldahalemi AK, Almuhana S, Almussawi AS. Dyslipidemia in patients with hepatitis C virus infection. Annals of Tropical Medicine and Health. 2020; 23: 23-941. doi: 10.36295/ASRO.2020.23941.

[23] Mehmood S, Raza H, Abid F, Saeed N, Rehman HM, Javed S *et al.* National prevalence rate of hepatitis B and C in Pakistan and its risk factors. Journal of Public Health. 2020 Dec; 28: 751-64. doi: 10.1007/s10389-019-01081-5.

[24] Rojas Á, Del Campo JA, Maraver M, Aparcero R, García-Valdecasas M, Diago M *et al.* Hepatitis C virus infection alters lipid metabolism depending on IL 28B polymorphism and viral genotype and modulates gene expression in vivo and in vitro. Journal of Viral Hepatitis. 2014 Jan; 21(1): 19-24. doi: 10.1111/jvh.12209.

[25] Pascual-Oliver A, Casas-Deza D, Yagüe-Caballero C, Arbones-Mainar JM, Bernal-Monterde V. Lipid Profile and Cardiovascular Risk Modification after Hepatitis C Virus Eradication. Pathogens. 2024 Mar 25; 13(4): 278. doi: 10.3390/pathogens13040278

[26] Gebhardt A and Fichtenbaum CJ. Current pharmacotherapy for the treatment of dyslipidemia associated with HIV infection. Expert Opinion on Pharmacotherapy. 2019 Oct; 20(14): 1719-1729. doi: 10.1080/14656566.2019.16/36033.

Original Article

Seasonal and Time-Series Analysis of Road Traffic Accidents

Muhammad Shafay[1], Hafiza Naima Anwar[2], Ishrat Bibi[3], Abdul Samad[3], Naseem Akter[4], Aisha Rasheed[3*] and Mohammad Akber Kazi[5]

[1]Department of Forensic Medicine and Toxicology, Hazrat Bari Imam Sarkar Medical and Dental College, Islamabad, Pakistan
[2]Department of Forensic Medicine and Toxicology, Shahida Islam Medical Complex, Lodhran, Pakistan
[3]Department of Forensic Medicine and Toxicology, Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan
[4]Department of Anatomy, Sindh Medical College, Jinnah Sindh Medical University, Karachi, Pakistan
[5]Department of Forensic Medicine and Toxicology, Bilawal Medical College, Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan

ARTICLE INFO

ABSTRACT

Road Traffic Accidents (RTAs) contribute a significant and escalating rate in harm, hospitalization, and mortality. This study assesses the seasonal trend and time series analysis of RTAs cases brought to casualty department of Liaquat University Hospital, Hyderabad, Pakistan. **Objective:** To conduct seasonal and time series analysis of RTA cases at Casualty Department of Liaquat University Hospital Hyderabad. **Methods:** Nine hundred and sixty-six road traffic accidents-related cases were examined through prospective study at casualty department, Liaquat University Hospital, Hyderabad, Pakistan from January 2020 to December 2022. The seasonal trend was demonstrated by drawing seasonal index plot and time series plot. **Results:** The largest occurrences of RTA-related cases were reported in the month of December, having 103 total cases with a mean of 34.33 ± 18.92. July had the second highest frequency of RTAs-related cases, with a total of 94 cases having a mean of 31 ± 5.43 cases. The second-highest number of cases was observed in July and November with approximately equal mean number of RTAs. The time series analysis demonstrated an increasing trend of RTAs-related cases in the last three months of the year. **Conclusions:** The number of cases connected to RTAs increased during seasons of extreme weather, such as the summer and winter, and it also showed an increasing tendency in the last quarter of 2022.

INTRODUCTION

Cases involving inquiries or concerns about medicine are known as Medico-Legal Cases (MLCs). Personal injury claims, criminal proceedings, medical malpractice lawsuits, and workers' compensation claims are some of the many possible settings in which such instances might emerge [1]. Furthermore, MLCs might result in substantial repercussions for everyone concerned [2]. Road Traffic Accidents (RTAs) pose unique challenges for MLCs due to the high prevalence of RTA-related injuries requiring medical attention, the high prevalence of RTA-related severe injuries leading to long-term disabilities, and the fact that RTAs are among the top causes of death [3]. There have been a lot of papers and studies dealing with the topic of road accidents since they have become a worldwide problem [3, 4]. However, the rate of fatalities caused by RTAs differs across industrialised and developing nations. Developing countries have an exceptionally high rate of RTAs. Governments also announce victim compensation in Road Traffic Accidents (RTAs) based on the medico-legal evaluation report [3]. Since mortality and seasonality is a hot topic in epidemiological research, many studies have examined the complex relationship between the seasons and various causes of death [5-7]. Seasonal variations in mortality rates have been seen across several populations

and regions, indicating that various factors such as climate, ecosystems, social norms, and personal actions play a role [8]. Conversely, heat-related mortality rates may rise throughout the summer in regions that are already very hot and do not have adequate cooling facilities. Mortality rates can vary throughout the year due to a number of factors, including changes in the amount of outdoor activities, air pollution, allergen exposure, and the transfer of infectious diseases [9]. Much like mortality rates, MLCs can fluctuate in type and frequency from one area to another, perhaps influenced by cultural norms and seasonal shifts [10]. Seasonal changes can aid in medico-legal evaluations by revealing contributing elements to particular injury or occurrence types. In order to decrease the occurrence of accidents, it is helpful to understand the seasonal trends of RTAs. This will allow us to identify risk factors and create focused interventions. By estimating and comparing different risk and severity of accidents, the accident patterns of different populations, vehicles, and geographic groups in each season can also be revealed [11]. To determine seasonal variation, time series analysis is utilized as a simple method. This method studies the dynamic observations from time point 1 to time point t and helps determine the seasonal or periodic trend of particular events. Time series analysis is also used for forecasting events in various fields, including medicine, such as predicting disease prevalence [12]. Herein, the seasonal trend of RTA-related MLCs was determined using three-year data from a leading tertiary care hospital in Hyderabad, Pakistan, employing a time series analysis method.

The objective of this study was to conduct seasonal and time series analysis of RTA cases at Casualty Department of Liaquat University Hospital Hyderabad.

METHODS

This study was carried out at Casualty Department, Liaquat University Hospital, Hyderabad, Pakistan from January 2020 to December 2022. IRB approval was acquired for conducting this study (IRB approval number: LUMHS/FM/78/19 dated: 28 December 2019). The design of present study is prospective study. Non probability consecutive sampling technique was used. Nine hundred and sixty-six road traffic accidents related cases were examined. The seasonal trend was demonstrated by drawing seasonal index plot and time series plot. The monthly data of RTA-related cases were acquired from the casualty department. The inclusion criteria involved cases related to RTA-related injuries. The exclusion criteria were the cases identified as not related to RTA-caused injuries. All cases eligible as per inclusion criteria were included. The data were collected and analyzed using MS EXCEL and Stat graphics Centurion XIX software. The data were presented

as frequencies and their mean ± SD. The seasonal trend and time series analysis were presented using data plots.

RESULTS

Four hundred and eighty-nine RTAs-related cases were assessed in 2020, 283 cases in 2021, and 194 cases in 2022. The data showed that the highest number of RTA-related cases occurred in March, July, November, and December, with mean values of greater than 30 cases and a total number of more than 90 cases. The largest occurrence of RTA-related cases was reported in the month of December, having 103 total cases with a mean of 34.33 ± 18.92 (Table 1).

Table 1: Month-Wise Frequency of RTA for Three Consecutive Years

Month	Year (Cases)			Mean ± SD	Total N (%)
	2020	2021	2022		
January	31	23	16	23.33 ± 6.12	70 (7.24%)
February	36	15	8	19.66 ± 11.89	59 (6.1%)
March	39	30	22	30.33 ± 6.94	91 (9.42%)
April	50	13	18	27 ± 16.39	81 (8.38%)
May	40	17	26	27.66 ± 9.46	83 (8.59%)
June	42	20	15	25.66 ± 11.72	77 (7.97%)
July	39	28	27	31.33 ± 5.43	94 (9.73%)
August	40	8	8	18.66 ± 15.08	56 (5.79%)
September	44	22	8	24.66 ± 14.81	74 (7.66%)
October	34	38	15	29 ± 10.03	87 (9%)
November	33	46	12	30.33 ± 14.0	91 (9.42%)
December	61	23	19	34.33 ± 18.92	103 (10.66%)

The seasonal index and time series plots of RTA-related cases are presented in Figure 1 and Figure 2, respectively. The seasonal index plot shows a variation of RTAs in certain months of the year. The index reveals higher than average RTAs in the last three months of the year, indicating the influence of the winter season (Figure 1).
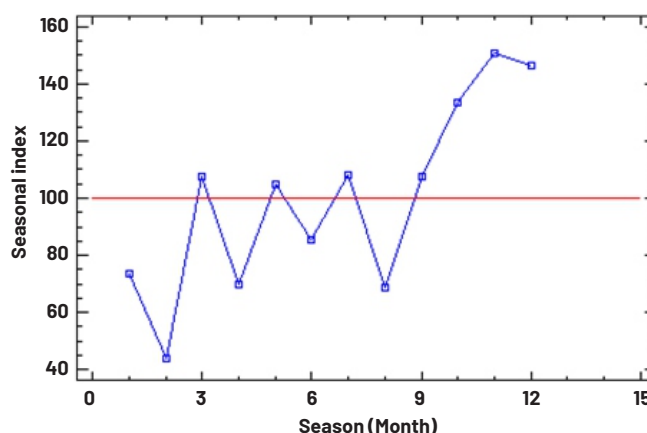
Figure 1: Seasonal Index Plot for RTA-Related MLCs

The RTAs are scattered across the average throughout the year, with most of the months taking place above the average. The seasonal index and time series plots of RTA-related cases appear in agreement with the data in table 1,

showing an increasing trend in November and December with a slight downward trend in year-wise total numbers of RTAs-related cases (Figure 2).
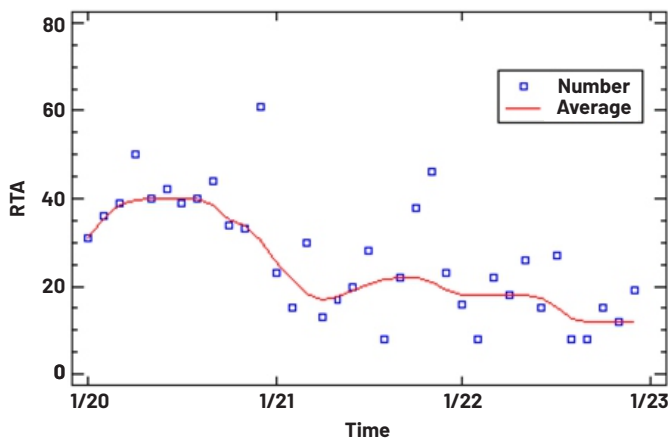
Figure 2: Smoothed Time Series Plot for RTA-Related Cases

DISCUSSION

Medico-legal assessment assists the process of law enforcement by determining the causes and probable factors of injuries to individuals and population groups. Knowledge of seasonal factors associated with MLCs can be useful to improve the provision of medico-legal representation and medical care to victims of road accidents [12]. The timing and seasonal patterns of road accidents are considered as useful factors to significantly decrease the number of accidents [3]. The present study found a seasonal trend in RTAs-related MLCs with an upward trend in November and December, which comprises the winter season in most areas of the country. The findings are approximately similar to the study from Rawalpindi, Pakistan, by Malik *et al.*, which showed a slightly elevated number of RTAs from the months of October to January and from May to August [13]. A study from Faisalabad reported the highest number of road traffic accidents in the months of March and April [14]. This is consistent with the present study in terms of higher number of RTAs occurring in March but differs regarding most frequent RTAs-related MLCs in the months of November and December. A month-wise distribution of RTA victims brought to the Civil Hospital of Karachi showed a higher frequency of RTA-related deaths in December, in line with the present study [15]. A study of RTAs over 53 months reported the highest number of road accidents in the dry season, followed by the rainy season [16]. This could explain the results of the present study showing the highest number of RTAs in November-December and July as the weather in Sindh province of Pakistan is characterized by cold and dry winter, whereas summer is mostly hot and rainy. A study conducted in Pakistan investigated the impact of environmental conditions on road accidents and stressed the need to exercise caution while driving in extreme weather [17]. Road accidents may occur more likely during intense heat, severe cold, rainfall, and fog, regardless of whether it is in urban or rural areas [17]. Various factors can influence RTAs, including poor infrastructure, vehicle conditions, distracted drivers, speeding, harsh environmental conditions, and noncompliance with road safety rules [18-20]. The present study suggested a slight decline in trend of RTAs-related MLCs in the Hyderabad region. However, this may not reflect any improvement with time in the factors associated with RTAs. Further exploration with increased data size and inclusion of data from other big hospitals of the region is suggested. Additionally, the data of the present study indicated that certain months of the year observe more than the average number of RTAs, implying the need to enhance the road safety, such as improving the infrastructure, street lighting, pedestrian crossings, road signage, and education and training about road safety. A recent study from Pakistan reported that most of RTAs occur at intersections of roads [21]. Such hotspots can be identified and managed specially to prevent surge in RTAs during months with harsh weather conditions leading to peaks in RTAs. Holidays, festivals, and celebratory events may see a higher prevalence of drunk driving incidents, contributing to seasonal spikes in RTAs [22, 23]. Therefore, public education campaigns and strict laws might be implemented to minimize seasonal peaks in RTAs. Additionally, the roads in Pakistan are considered among worst in the world [21]. The biological mechanisms and potential pathophysiological reasons of this link with seasonality are continually being filled in by researchers. This will influence research-based programs to enhance public health and reduce seasonal health inequalities.

CONCLUSIONS

Seasons of harsh weather, including the summer and winter, saw a rise in the number of cases associated with RTAs; this pattern continued in the last quarter of 2022.

Authors Contribution

Conceptualization: MS
Methodology: MS, AS
Formal analysis: MS, MAK
Writing, review and editing: HNA, IB, NK, AR

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

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

REFERENCES

[1] Treglia M, Pallocci M, Passalacqua P, Sabatelli G, De Luca L, Zanovello C *et al.* Medico-legal aspects of hospital-acquired infections: 5-years of judgements of the civil court of Rome. InHealthcare. 2022 Jul; 10(7): 1336. doi: 10.3390/healthcare10071336.

[2] Bevinahalli N, Raveesh, Ragavendra B. Nayak, Shivakumar F. Kumbar. Preventing medico-legal issues in clinical practice. Annals of Indian Academy of Neurology. 2016 Oct; 19(1): S15–S20. doi: 10.4103/09 72-2327.192886.

[3] Azmi AA and Ram S. Accident victim characteristics and identification of key parameters for compensation in Indian context. Urban, Planning and Transport Research. 2023 Dec; 11(1): 2235418. doi: 10.1080/21650020.2023.2235418.

[4] Popa Ş, Ciongradi CI, Sârbu I, Bîcă O, Popa IP, Bulgaru-Iliescu D. Traffic accidents in children and adolescents: a complex orthopedic and medico-legal approach. Children. 2023 Aug; 10(9): 1446. doi: 10.3390/children10091446.

[5] Wu Y, Li S, Zhao Q, Wen B, Gasparrini A, Tong S *et al.* Global, regional, and national burden of mortality associated with short-term temperature variability from 2000-19: a three-stage modelling study. The Lancet Planetary Health. 2022 May; 6(5): e410-21. doi: 10.1016/S2542-5196(22)00073-0.

[6] Madaniyazi L, Armstrong B, Chung Y, Ng CF, Seposo X, Kim Y *et al.* Seasonal variation in mortality and the role of temperature: a multi-country multi-city study. International Journal of Epidemiology. 2022 Feb; 51(1): 122-33. doi: 10.1289/isee.2021.P-667.

[7] Ledberg A. A large decrease in the magnitude of seasonal fluctuations in mortality among elderly explains part of the increase in longevity in Sweden during 20th century. Baseboard Management Controller Public Health. 2020 Dec; 20: 1-0. doi: 10.11 86/s12889-020-09749-4.

[8] Oura P. Seasonal variation in medico-legal autopsies in Finland-a nationwide analysis of the period 2016-2021. International Journal of Legal Medicine. 2024 Jan; 138(1): 277-80. doi: 10.1007/s00414-022-02880-4.

[9] Girela-López E, Beltran-Aroca CM, Dye A, Gill JR. Epidemiology and autopsy findings of 500 drowning deaths. Forensic Science International. 2022 Jan; 330: 111137. doi: 10.1016/j.forsciint.2021.111137.

[10] Qadir MA. Forensic Survey for Medico-Legal Cases: Real Figures from Liaquat University Hospital Hyderabad, Sindh. Alcoholism. 2020 Jun; 14(2): 607-609.

[11] Bardal KG and Jørgensen F. Valuing the risk and social costs of road traffic accidents-Seasonal variation and the significance of delay costs. Transport Policy. 2017 Jul; 57: 10-9. doi: 10.1016/j.tranpol.2017.03.015.

[12] Aydin S. Time series analysis and some applications in medical research. Journal of Mathematics and Statistics Studies. 2022 Oct; 3(2): 31-6. doi: 10.32996/jmss.2022.3.2.3.

[13] Malik R, Atif I, Rashid F, Abbas M. An analysis of 3105 medico legal cases at tertiary care hospital, Rawalpindi. Pakistan Journal of Medical Sciences. 2017 Jul; 33(4): 926. doi: 10.12669/pjms.334.11696.

[14] Saleem S, Haider A, Khan J, Saleem T. Study of fatal road traffic accidents: based on medico-legal autopsies. Gomal Journal of Medical Sciences. 2015 Mar; 13(1): 19-22.

[15] Baloch FA. Autopsy Based Study of Road Traffic Accidents Deaths Brought to Civil Hospital Karachi during 2016. Head and Neck. 2019 Sep; 13(3): 604.

[16] Moussa CZ, Victor EK, Zana K, Laurel TM, Mathurin D, Koffi B. Current data on road traffic fatalities in Bouake epidemiological and medico-legal aspects. Health. 2023 Mar; 9(2): 44-8. doi: 10.11648/j.cajph.20 230902.11.

[17] Touahmia M. Identification of risk factors influencing road traffic accidents. Engineering, Technology & Applied Science Research. 2018 Feb; 8(1): 2417-21. doi: 10.48084/etasr.1615.

[18] Hammad HM, Ashraf M, Abbas F, Bakhat HF, Qaisrani SA, Mubeen M *et al.* Environmental factors affecting the frequency of road traffic accidents: a case study of sub-urban area of Pakistan. Environmental Science and Pollution Research. 2019 Apr; 26: 11674-85. doi: 10.1007/s11356-019-04752-8.

[19] Naheed K, Nadeem S, Iqbal M, Qasim AP, Sadia S, Siddiqui BA. Medicolegal Autopsies;: Audit Of Medicolegal Autopsies In Faisalabad City. The Professional Medical Journal. 2019 May; 26(05): 696-701. doi: 10.29309/TPMJ/2019.26.05.425.

[20] Hussain T, Shu LiYu SL, Sosorburam T, Adji AS, Khan AH, Raja AF. Road traffic accidents; an observational and analytical study exploring the hidden truths in Pakistan and South East-Asian countries. Healthline. 2011 June; 2(1). doi: 10.3126/ajms.v1i2.2947.

[21] Mohsin M and Nazeer MA. Road Traffic Accidents (RTAs) in Bahawalpur City, Pakistan: A Comparative Injury Analysis. Pakistan Journal of Scientific and Industrial Research Series A: Physical Sciences. 2024 Feb; 67(1): 57-64.

[22] Hirche M, Haensch J, Lockshin L. Comparing the day temperature and holiday effects on retail sales of alcoholic beverages-a time-series analysis. International Journal of Wine Business Research. 2021 Jan; 33(3): 432-55. doi: 10.1108/IJWBR-07-2020-0035.

[23] Porpiglia NM, Tagliaro F, Micciolo R, Canal L, Musile G, Bortolotti F. New evidence of high association between carbohydrate deficient transferrin (CDT) and alcohol-related road traffic accidents. A retrospective study on 929 injured drivers. Forensic Science International. 2022 Nov; 340: 111438. doi: 10.1016/j.forsciint.2022.111438.

Original Article

Risk Factors and Prevalence of Hepatitis B and C in Badin City, Pakistan

Yasir Akbar Jamali[1*], Rukia Farzana[2], Jawad Ahmad Khan[3], Amjad Ali Mughal[4], Hira Saeed[5] and Sadia Kazi[6]

[1]Department of Physiology, University of Sindh, Jamshoro, Pakistan
[2]Khairpur Medical College, Khairpur, Pakistan
[3]Department of Pharmacy, Shah Abdul Latif University, Khairpur, Pakistan
[4]Institute of Microbiology, Shah Abdul Latif University, Khairpur, Pakistan
[5]Department of Physiology, Suleman Roshan Medical College, Tando Adam, Pakistan
[6]Department of Pharmacology, Isra University, Hyderabad, Pakistan

ARTICLE INFO

*Corresponding Author:
Yasir Akbar Jamali
Department of Physiology, University of Sindh, Jamshoro, Pakistan
yasirakbar021@gmail.com

ABSTRACT

Hepatitis is a global health concern, and its ever increasing prevalence in Pakistan has highlighted the need to study its epidemiology and develop preventative strategies. **Objective:** To determine the frequency and identify the risk factors associated with hepatitis virus infections B and C among the population of Badin city. **Methods:** Seven hundred sixty-seven people were tested for Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) using immunochromatographic methods. Additional testing was performed on blood samples from individuals who tested positive for hepatitis, and quantitative Polymerase Chain Reaction (PCR) was used to determine the viral load. **Results:** A total of 767 individuals had hepatitis. Among these, the research found that HCV was more common than HBV. However, men were more affected than women. Data on the exposure to risk factors for hepatitis B and C among the patients in our study are presented in Table 2 Of the 767 respondents, 473 (61.7%) were shaved from a barber/beauty parlour. Approximately 358 (46.7%) patients with hepatitis reused syringes. Drug addiction was observed in 66 (8.6%) patients. A history of blood transfusion was observed in 73 patients (9.5 %). Obstetrical procedures, ear pricks, and nose piercings were reported in 195 (68.1%), 245 (85.7%) and 240 (83.9%) female patients with hepatitis, respectively. **Conclusions:** Barbers, blood transfusions, and intravenous drug use are the most common risk factors for the spread of HBV and HCV are barbers, blood transfusions, and Intravenous Drug Use (IDUs), although newer variables, including piercings of the nose and ears and IDPs, also contribute.

INTRODUCTION

Liver diseases caused by hepatitis B and C viruses are a major financial and medical burden worldwide; however, they are particularly severe in underdeveloped nations such as Pakistan [1]. Approximately 296 million people have chronic HBV, and 1.4 million people die each year. More than two billion people are exposed to the virus [2]. It is the sixth most common killer in the world, with East Asia and sub-Saharan Africa having the highest rates [3, 4]. With a carrier incidence of 3-5%, Pakistan is home to an estimated 7-9 million HBV carriers. Zahoor *et al.,* found that by 2030, 3.25 percent of Pakistani patients tested positive for HBV, and 6.36 percent tested positive for HCV [5].

Having a mother infected with HCV, having intercourse with a man, using intravenous drugs, being hospitalised, dental treatment, using contaminated surgical equipment, being circumcised by a barber, blood transfusions, thalassaemia, and haemophilia are the main risk factors of HCV infection in Pakistan [6]. The primary risk factors for herpes simplex virus (HBV) infection include being born into an infected family, having the virus cut out of the body by a barber or other unsanitary means, reusing syringes, undergoing surgery with contaminated instruments, receiving blood transfusions, therapeutic injections, use of non-sterile invasive medical devices, hospitalisation, and sexual

contact [6, 7]. Following Egypt, the prevalence of HCV infection is highest in Pakistan [8]. A viral infection has been detected in one out of every 20 people in the nation [9, 10]. Exposures that occur in the course of medical treatment are believed to be the primary vector for the spread of HCV in Pakistan [9]. Factors contributing to the spread of this iatrogenic infection include insufficient screening of blood products and transfusions with tainted blood, inadequate cleaning of medical equipment, and reuse of both syringes and needles for therapeutic injections [9]. Additionally, it is believed that community-level exposures such as barbering, tattooing, and piercing play a significant role [11, 12]. A major factor in the spread of the herpes simplex virus (HCV) is the increasing prevalence of intravenous drug use in Pakistan [13]. According to a recent meta-analysis, injecting drug users (PWID) in Pakistan had a seroprevalence of 54% [14].

METHODS

From 1st January 2024 until 31st March 2024 researchers at the Civil Hospital in Badin collected the data. From individuals clinically suspected of having Hepatitis B or C, 845 blood samples were obtained. Patients were interviewed to gather personal details such as their medical history, sex, age, and pregnancy status. Following the manufacturer's instructions, the patients were tested for Hepatitis B surface Ag (HBs-Ag) and Anti-HCV antibodies using ELISA Kits (The Bio-kit ELISA system, BEST 2000). The data were analysed using the statistical program SPSS 26.0. We used the chi-square test to determine whether the link was statistically significant between two or more variables. To assess the relationship between the outcome and each independent variable, we used simple logistic regression analysis. We determined the Odds Ratios (OR) and 95% Confidence Intervals (CI) for each risk factor. Participants ranged from outpatients to inpatients at a Civil Hospital in Badin, Pakistan. Hepatitis B or C was confirmed by ICT/ELISA, and the participants had to be at least 18 years old to participate. Anyone not currently enrolled at the Civil Hospital Badin was automatically disqualified. This study was approved by the ethical review board of Shah Abdul Latif University in Khairpur (Dated 28-12-2023, Ref. No# IRB-C689). Patients at Civil Hospital Badin completed a questionnaire over the course of three months (1 January 2024–31 March 2024). Interviews were conducted in person using a standardised questionnaire after verbal agreement. Only multiple-choice questions were included in this survey. After translation into the respondent's native language, it was retranslated into English with the necessary adjustments already made.

RESULTS

Overall, 767 subjects tested positive for hepatitis C and C viral infections. Of, these 481 (62.7%) were male and 286 (37.3%) were female. 345 (44.9%) patients had hepatitis B and 422 (55%) patients had Hepatitis C. Majority 412 (53.7%) had primary school education. A total of 418 patients (54.5%) were married. The highest frequency of 640 (83.4%) hepatitis-positive patients belonged to the low-income class, and 115 (15%) of hepatitis-positive employees belonged to the middle-income class. Only 12 (1.5%) patients with hepatitis belonged to the high-income class table 1.

Table 1: Demographic Characteristics of the Study Population

Variables	Total N (%)	Male N (%)	Female N (%)	p-Value
	Total = 767	481 (62.7%)	286 (37.3%)	
Age				
18 – 30	145 (18.9%)	103 (21.4%)	42 (14.7%)	
31 – 45	158 (20.6%)	61 (12.7%)	97 (33.9%)	0.005
45 >	464 (60.5%)	317 (65.9%)	147 (51.4%)	
Hepatitis B	345 (44.9%)	231 (48%)	114 (39.9%)	0.027
Hepatitis C	422 (55%)	250 (52%)	172 (60.1%)	
Marital Status				
Single	339 (52.0%)	290 (60.3%)	49 (17.1%)	
Married	418 (54.5%)	191 (39.7%)	227 (79.4%)	0.000
Divorced/Separated/Widow	10 (1.3%)	0	10 (3.5%)	
Education				
Primary School	412 (53.7%)	270 (56.1%)	142 (49.7%)	
Secondary School	138 (18%)	78 (16.2%)	60 (21%)	
Intermediate	40 (5.2%)	63 (13.1%)	27 (9.4%)	0.000
Bachelor	40 (5.2%)	33 (6.9%)	7 (2.4%)	
Illiterate	87 (11.3%)	37 (7.7%)	50 (17.5%)	
Socio-Economic Status				
Lower Class	640 (83.4%)	431 (89.6%)	209 (73.1%)	
Middle Class	115 (15%)	41 (8.5%)	74 (25%)	0.000
Upper Class	12 (1.5%)	9 (1.9%)	3 (1.0%)	

Data on the exposure to risk factors for hepatitis B and C among the patients in our study are presented in Table 2. Of the 767 respondents, 473 (61.7%) were shaved from the barber/beauty parlour, and 315 (65.4%) male hepatitis patients were significantly higher than 158 (55.2%) female patients (p = 0.004777). Approximately 358 (46.7%) hepatitis patients reused syringes, although a significantly higher number of 190 (39.5%) male patients than 168 (58.7%) female hepatitis patients. Drug addiction was seen in 66 (8.6%) patients; among them, 56 (11.6%) were significantly higher than 10 (3.5%) female patients. A history of blood transfusion was found in 73 (9.5%) patients with hepatitis, with no gender significance Table 2. A total of 151 (19.7%) respondents reported sharing various items (Tooth-Brush, Hukkah, Miswak, Blades, Vax, and towel). Obstetrical procedures, ear pricks, and nose piercings were reported in 195 (68.1%), 245 (85.7%), and 240 (83.9%)

female patients with hepatitis, respectively. Almost 74 (25.9%) of the 114 (14.9 %) female patients were significantly higher than 40 (8.3 %) male patients with a history of family hepatitis (p <0.00001). On the other hand, patients asked about Knowledge about the spread of hepatitis and 283 (36.9%) of patients responded with no gender difference. The use of tattooing was also observed in 34 respondents (4.4 %). A total of 108 (14.1%) patients were vaccinated against hepatitis B virus infection. A dental treatment history was reported in 48 patients (6.3%) (Table 2).

Table 2: Risk Factors of the Study Population According to Sex

Variables	Total N (%)	Male N (%)	Female N (%)	p-Value
	Total = 767	481 (62.7%)	286 (37.3%)	
Blood Transfusion				
Yes	73 (9.5%)	45 (9.4%)	28 (9.8%)	0.842
No	694 (90.5%)	436 (90.6%)	258 (90.2%)	
Surgery				
Yes	224 (29.2%)	24 (5%)	200 (69.9%)	0.000
No	543 (70.8%)	457 (95%)	86 (30.1%)	
History of Hepatitis				
Yes	114 (14.9%)	40 (8.3%)	74 (25.9%)	0.000
No	653 (85.1%)	441 (91.7%)	212 (74.1%)	
Ever Admitted to a Hospital				
Yes	237 (30.9%)	113 (23.5%)	124 (43.4%)	0.000
No	530 (69.1%)	368 (76.5%)	162 (56.6%)	
Obstetrical Procedure				
Yes	195 (25.4%)	0	195 (68.1%)	0.000
No	537 (70.0%)	481 (100%)	56 (19.6%)	
Ear Prick				
Yes	248 (32.3%)	3 (0.6%)	245 (85.7%)	0.000
No	519 (67.7%)	478 (99.4%)	41 (14.3%)	
Nose Piercing				
Yes	245 (31.9%)	5 (1%)	240 (83.9%)	0.005
No	522 (68.1%)	476 (99%)	46 (16.1%)	
Dental Treatment				
Yes	48 (6.3%)	30 (6.2%)	18 (6.3%)	0.974
No	719 (93.7%)	451 (93.8%)	268 (93.7%)	
Use of Syringes				
Yes	731 (95.3%)	460 (95.6%)	271 (94.8%)	0.577
No	36 (4.7%)	21 (4.4%)	15 (5.2%)	
Drug Addiction				
Yes	66 (8.6%)	56 (11.6%)	10 (3.5%)	0.000
No	701 (91.4%)	425 (88.4%)	276 (95.5%)	
Sharing of Various Items (Tooth Brush, Hukaah, Miswak, Blades, Wax Towel)				
Yes	151 (19.7%)	95 (19.8%)	56 (19.6%)	0.954
No	616 (80.3%)	386 (80.2%)	230 (80.4%)	
Use of Reuse Syringes				
Yes	358 (46.7%)	190 (39.5%)	168 (58.7%)	0.000
No	349 (45.5%)	231 (48.0%)	118 (41.3%)	
Shave from Barber/Beauty Parlor				
Yes	473 (61.7%)	315 (65.4%)	158 (55.2%)	0.005
No	294 (38.3%)	166 (34.5%)	128 (44.8%)	

Hepatitis B Vaccination				
Yes	108 (14.1%)	75 (15.6%)	33 (11.5%)	0.118
No	659 (85.9%)	406 (84.4%)	253 (88.5%)	
Family History of Hepatitis				
Yes	157 (20.5%)	45 (9.4%)	112 (39.2%)	0.000
No	610 (79.5%)	436 (90.6%)	174 (60.8%)	
Knowledge about Spread of Hepatitis				
Yes	283 (36.9%)	170 (35.3%)	113 (46.5%)	0.247
No	484 (63.1%)	311 (64.6%)	173 (60.4%)	
Ever had Tattooing				
Yes	34 (4.4%)	25 (5.2%)	9 (3.1%)	0.182
No	733 (95.6%)	456 (94.8%)	277 (96.9%)	

DISCUSSION

Various environmental and behavioural risk factors contribute to the development of hepatitis, a highly infectious viral illness [15]. The purpose of this research was to track the incidence of hepatitis and its correlations with potential risk factors among people living in Badin City. Among the individuals surveyed, 55% had HCV, and 44.9% had HBV. Compared to HBV, which was shown to be 8.4% more prevalent in Punjab, Pakistan, another study found that HCV was 42.7% more prevalent [16]. In the Taiwanese population, 9.9% of HBV cases have been reported compared to four percent of HCV cases [17]. In the current study, 473 (61.7%) patients with hepatitis were shaved from a barber/beauty parlour. Various studies have determined the specific prevalence rates associated with barbers. Ali *et al.,* in 2023 and Naqvi *et al.,* in 2019 reported frequencies of 21.4% and 59.2%, respectively, while Noreen *et al.,* in 2022 observed a rate of for HBV 22.3% and HCV 31% for HCV among barbers [18-20]. Blades and razors that have not been sterilised may spread the illness if they come into contact with blood borne viruses. Research from around Pakistan has shown that barbers are a major vector for the spread of viral hepatitis [21, 22]. Approximately 358 (46.7%) patients with hepatitis reused syringes in our study. A study conducted in hospitals, clinics, and healthcare personnel in poor nations showed that they are more likely to reuse used medical needles, particularly among low-income families and people. Recycling trash and medical waste is a common activity among children from low-income households, putting them at increased risk of infection [23]. A nationwide poll conducted from 2007 to 2008 anticipated that 86% of women would inject themselves using an unopened packet for their previous injection [24]. Therapeutic injection is the second option [21, 25]. In the present study, drug addiction was observed in 66 patients (8.6 %). Intravenous drug use has been identified as a significant risk factor for the spread of viral infections through human contact in Pakistan, as reported by Irshad *et al.,* in 2021, with HBV and HCV rates of 19 (10%) [26]. Additionally, Noreen *et al.,* in 2022 highlighted this risk

Jamali YA *et al.*,

factor in 17.8% of cases, and Bibi *et al.*, in 2013 found it to be a concern for pregnant women 2.46% [20, 27]. A history of blood transfusion was observed in 73 (9.5%) patients with hepatitis. The main ways in which bloodborne infections may spread are through blood donations and transfusions. The association of this factor with HCV infection has been extensively documented in the literature. Various studies have confirmed this finding, including Ali *et al.*, in 2016, with a prevalence of 2.15%; Akhtar *et al.*, in 2016, 8.9%, and Rana *et al.*, in 2020, 43.3%, and Saleem *et al.*, in 2020, 1.8% [18, 28-30]. In our study, ear prick and nose piercing were reported in 245 (85.7%) and 240 (83.9%) women, respectively. The spread of bloodborne diseases is related to anything that might inadvertently cause blood injuries or leakage. Historically, more Pakistani women have pierced their ears and nose, putting them at a greater risk of infection [31, 32]. The equipment used to pierce the ears and nose is not usually sterilised. According to one study, hepatitis C was found in 17.8% of patients with pierced ears or nose [18]. A dental treatment history was reported in 48 patients (6.3%). Needless to say, there is a much higher risk of blood contamination and needlestick accidents during dental procedures since the majority of dental professionals do not utilise sterile devices, which contributes to the spread of the disease [33]. In our study, 481 (62.7%) male patients had more than 286 (37.3%) females. It is more common in men than in women, according to the research [34]. Noreen *et al.*, conducted a study on low socioeconomic communities and found a higher prevalence of hepatitis C in male 5%) than in female 3%) [20]. Pakistani men are more likely to spend time outdoors, have an array of sexual partners, sometimes engage in gay behavior, and be subjected to communal barbering and circumcision practices, according to the study. In the present study, 108 (14.1%) patients were vaccinated against hepatitis B virus infection. As they participate in mass vaccination campaigns that entail injections, vaccine providers may potentially increase the risk of infection. Viral infections may sometimes be transmitted from infected to uninfected individuals during vaccination via contaminated blood [32]. Tattooing was also observed in 34 respondents (4.4%). Since tattooing is less common in Pakistan than in Europe and Africa, there is an unknown risk factor associated with it. Very few studies have been published on HCV infection in Pakistan. A previous study conducted by Noreen *et al.*, in 2022 reported a significant association, whereas another study conducted by Alibrahim *et al.*, in 2018 observed that 1.5 of patients reported tattooing [20, 32]. A total of 151 (19.7%) respondents reported sharing various items (Tooth-Brush, Hukkah, Miswak, Blades, Vax, and towel). Interactions, which are inevitable in a family setting but may sometimes

be harmful, are inevitable. The virus can also be transmitted through contact with an infected household, as shown in studies of HCV by Shafiq *et al.*, in 2015 and Bibi *et al.*, in 2013 and Akhtar *et al.*, in 2015 [7, 27, 34]. In this study, 640 (83.4%) hepatitis-positive patients belonged to the low-income class and 115 (15%) were hepatitis-positive employees from the middle-income class. Only 12 (1.5%) patients with hepatitis belonged to the high-income class. A study conducted in Isfahan, Iran, by Ataei *et al.*, in 2019 found a 75.3% low-income rate of hepatitis [35]. Not only does a country's population vary greatly depending on its socioeconomic conditions, but the same is also true for other nations. Others who are well off may afford private healthcare providers and pristine facilities, while others with less means must make do with public health services that are underfunded. Only one study identified a statistically significant correlation between socioeconomic level and viral transmission, as opposed to other studies that cited it as a significant issue among low-income individuals and manufacturing workers [28, 36]. In our study, On the other hand patients asked about Knowledge about spread of hepatitis and 283 (36.9%) of patients response. Mansour-Ghanaei *et al.*, determined the low level of knowledge toward HBV among medical students in Iran and suggested more training for students [37]. In healthcare professional research, medical students' awareness was found to be lower than that of other study groups, with excellent knowledge 15.59 ± 3.69 and an analysis of variance (ANOVA) score of 11.57 ± 2.16, out of a total possible score of 22 [38].

CONCLUSIONS

The most common forms of hepatitis in underdeveloped nations are types B and C. The most common vectors for the spread of HIV are barbers, blood transfusions, and Intravenous Drug Use (IDUs), although newer variables, including piercings of the nose and ears and IDPs, also contribute. Many investigations have failed to identify virus-related risk variables because it is difficult to trace the history of the virus in patients.

Authors Contribution

Conceptualization: YAJ, SK
Methodology: RF, AAM
Formal analysis: JAK
Writing, review and editing: HS

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

Conflicts of Interest

Source of Funding

REFERENCES

[1] Kulkarni AV and Duvvuru NR. Management of hepatitis B and C in special population. World Journal of Gastroenterology. 2021 Oct; 27(40): 6861. doi: 10.3748/wjg.v27.i40.6861.

[2] Al-Busafi SA and Alwassief A. Global Perspectives on the Hepatitis B Vaccination: Challenges, Achievements, and the Road to Elimination by 2030. Vaccines. 2024 Mar; 12(3): 288. doi: 10.3390/vaccines12030288.

[3] Anwar F, Khan M, Salman M, Ahmad S, Ullah F, Khan J *et al.* Seroprevalence of hepatitis B virus in human population of district Buner Khyber Pakhtunkhwa Pakistan. Clinical Epidemiology and Global Health. 2021 Apr; 10: 100688. doi: 10.1016/j.cegh.2020.100688.

[4] Dekker SE, Green EW, Ahn J. Treatment and prevention of acute hepatitis B virus. Clinics In Liver Disease. 2021 Nov; 25(4): 711-24. doi: 10.1016/j.cld.2021.06.002.

[5] Zahoor S, Khan A, Asif S, Tabraiz SA, Mustafa H, Ansar S *et al.* Past and future perspectives for hepatitis B and C in Pakistan. Cureus. 2021 Aug; 13(8): e17521. doi: 10.7759/cureus.17521.

[6] Seerat I, Mushtaq H, Rafiq M, Nadir A. Frequency and associated risk factors of hepatitis B virus and hepatitis C virus infections in children at a hepatitis prevention and treatment clinic in Lahore, Pakistan. Cureus. 2020 May; 12(5). doi: 10.7759/cureus.7926.

[7] Shafiq M, Nadeem M, Sattar Z, Khan SM, Faheem SM, Ahsan I *et al.* Identification of risk factors for hepatitis B and C in Peshawar, Pakistan. HIV/AIDS-Research and Palliative Care. 2015 Aug: 223-31. doi: 10.2147/HIV.S67429.

[8] Abbas Z and Abbas M. The cost of eliminating hepatitis C in Pakistan. The Lancet Global Health. 2020 Mar; 8(3): e323-4. doi: 10.1016/S2214-109X(20)30036-X.

[9] Al Kanaani Z, Mahmud S, Kouyoumjian SP, Abu-Raddad LJ. The epidemiology of hepatitis C virus in Pakistan: systematic review and meta-analyses. Royal Society Open Science. 2018 Apr; 5(4): 180257. doi: 10.1098/rsos.180257.

[10] Mansoor M, De Glanville WA, Alam R, Aslam K, Ahmed M, Isaakidis P *et al.* Prevalence and risk factors for hepatitis C virus infection in an informal settlement in Karachi, Pakistan. PLOS Global Public Health. 2023 Sep; 3(9): e0002076. doi: 10.1371/journal.pgph.0002076.

[11] Qureshi H, Bile KM, Jooma R, Alam SE, Afrid HU. Prevalence of hepatitis B and C viral infections in Pakistan: findings of a national survey appealing for effective prevention and control measures. EMHJ-Eastern Mediterranean Health Journal. 2010; 16: 15-23. doi: 10.26719/2010.16.

[12] Trickey A, May MT, Davies C, Qureshi H, Hamid S, Mahmood H *et al.* Importance and contribution of community, social, and healthcare risk factors for hepatitis C infection in Pakistan. The American Journal of Tropical Medicine and Hygiene. 2017 Dec; 97(6): 1920. doi: 10.4269/ajtmh.17-0019.

[13] Ghazal P. Rising trend of substance abuse in Pakistan: a study of sociodemographic profiles of patients admitted to rehabilitation centres. Public Health. 2019 Feb; 167: 34-7. doi: 10.1016/j.puhe.2018.10.020.

[14] Shayan SJ, Nazari R, Kiwanuka F. Prevalence of HIV and HCV among injecting drug users in three selected WHO-EMRO countries: a meta-analysis. Harm Reduction Journal. 2021 May; 18(1): 59. doi: 10.1186/s12954-021-00505-4.

[15] Mokhtari M, Basirkazeruni H, Rostami M. The correlation between different risk factors of hepatitis C and different genotypes. Advanced Biomedical Research. 2017 Jan; 6(1): 45. doi: 10.4103/2277-9175.204588.

[16] Khan A, Afzal S, Yaqoob A, Fatima R, Ul Haq M, Junaid K *et al.* Epidemiology of viral hepatitis B and C in Punjab, Pakistan: a multicenter cross-sectional study, 2017-18. F1000Research. 2019 Dec; 8: 2065. doi: 10.12688/f1000research.20174.1.

[17] Huang WC, Lin YC, Chen PJ, Hsu NT, Tu CL, Chang TS *et al.* Community-based screening for hepatitis B and C infectivity using two quantitative antigens to identify endemic townships. Viruses. 2022 Feb; 14(2): 304. doi: 10.3390/v14020304.

[18] Ali F, Tahir M, Ali W, Habib M, Zeeshan M, Ullah H. Hepatitis B and C: Prevalence and Evaluation of its Associated Risk Factors in General Population of Okara District. The Journal of Microbiology and Molecular Genetics. 2023 Dec; 4(3): 95-105. doi: 10.52700/jmmg.v4i3.125.

[19] Naqvi IH, Talib A, Baloch G, Mahmood K, Qadari Z. Hepatitis B and C: frequency, modes of transmission and risk factors along with some unorthodox routes of spread. Pakistan Journal of Public Health. 2019 Sep; 9(3): 161-5. doi: 10.32413/pjph.v9i3.273.

[20] Noreen A, Adnan F, Alam N, Syed Z, Aftab A, Shamim F *et al.* Prevalence and Associated Risk Factors

Analysis of Hepatitis B & C Infections in the Low Socioeconomic Communities; A Cross-Sectional Study from Pakistan. 2022 Mar; 17(5): 291-303. doi: 10.2217/fvl-2021-0060.

[21] Asad M, Ahmed F, Zafar H, Farman S. Frequency and determinants of Hepatitis B and C virus in general population of Farash Town, Islamabad. Pakistan Journal of Medical Sciences. 2015 Nov; 31(6): 1394. doi: 10.12669/pjms.316.7047.

[22] Khan M, Hussain U, Irshad A, Khan A. Prevalence of hepatitis B and C seropositivity in patients presenting for dental treatment. Pakistan Oral and Dental Journal. 2015 Jun; 35(2): 250-253.

[23] Maan MA, Fatma H, Muhammad J. Epidemiology of hepatitis C viral infection in Faisalabad, Pakistan: a retrospective study (2010-2012). African Health Sciences. 2014 Dec; 14(4): 810-4. doi: 10.4314/ahs.v14i4.6.

[24] Janjua NZ and Nizamy MA. Knowledge and practices of barbers about hepatitis B and C transmission in Rawalpindi and Islamabad. Journal of Pakistan Medical Association. 2004 Mar; 54(3): 116-9.

[25] Hussain S and Ali Z. Prevalence of hepatitis B virus in the Kurram Agency, Pakistan: A 5-year observational study in a war-affected region. Journal of Clinical Virology. 2016 Sep; 82: 17-9. doi: 10.1016/j.jcv.2016.06.009.

[26] Irshad H, Aziza F, Rahman AU. Frequency and associated risk factors of hepatitis B and C infection in Tehsil fort Abbas, Pakistan. Pakistan Journal of Medical Research. 2021 May; 60(1): 44-8.

[27] Bibi S, Dars S, Ashfaq S, Qazi RA, Akhund S. Seroprevalence and risk factors for hepatitis C virus (HCV) infection in pregnant women attending public sector tertiary care hospital in Hyderabad Sindh. Pakistan Journal of Medical Sciences. 2013 Apr; 29(2): 505. doi: 10.12669/pjms.292.3211.

[28] Akhtar N, Ilyas M, Muhammad K, Shams S, Saeed K, Asadullah A. Prevalence of Hepatitis C virus infections among the general population of Buner, Khyber Pakhtunkhwa, Pakistan. Biomedical Research and Therapy. 2016 Dec; 3(12): 1003-17. doi: 10.15419/bmrat.v3i12.139.

[29] Rana NA, Munir B, Hussain N, Imtiaz N. Seroprevalence, biochemical investigation and risk factor assessment for HBV & HCV Infection in Hospital Based Patients of Islamabad, Pakistan. Journal of Bioresource Management. 2020; 7(2): 2. doi: 10.35691/JBM.0202.0127.

[30] Saleem HA, Roman U, Mughal HH. Prevalence of Hepatitis B and C and associated risk factors in rural areas of Punjab. Pakistan Journal of Medical and Health Sciences. 2020 Oct; 14(4): 2062-3.

[31] Memon AR, Shafique K, Memon A, Draz AU, Rauf MU, Afsar S. Hepatitis B and C prevalence among the high risk groups of Pakistani population. A cross sectional study. Archives of Public Health. 2012 Dec; 70: 1-6. doi: 10.1186/0778-7367-70-9.

[32] Alibrahim OA, Misau YA, Mohammed A, Faruk MB, Izzeldin SS. Prevalence of hepatitis C viral infection among injecting drug users in a Saudi Arabian hospital: a point cross sectional survey. Journal of Public Health in Africa. 2018 May; 9(1): 726. doi: 10.4081/jphia.2018.726.

[33] Fayyaz M, Ghous SM, Ullah F, Abbas I, Ahmed N, Ahmed A. Frequency of hepatitis B and C in patients seeking treatment at the dental section of a tertiary care hospital. Journal of Ayub Medical College Abbottabad. 2015 Jun; 27(2): 395-7.

[34] Akhtar AM, Majeed S, Jamil M, Rehman A. Prevalence of hepatitis C infection: General patients attending various hospitals of Lahore, Pakistan: a cross sectional study. The Professional Medical Journal. 2015 Nov; 22(11): 1390-6. doi: 10.29309/TPMJ/2015.22.11.861.

[35] Ataei B, Alavian SM, Shahriari-Fard F, Rabiei AA, Safaei A, Rabiei A *et al.* A case-control study of risk factors for hepatitis B infection: A regional report among Isfahanian adults. Journal of Research in Medical Sciences. 2019 Jan; 24(1): 22. doi: 10.4103/jrms.JRMS_761_18.

[36] IJAZ RR and Bhatti S. Risk of hepatitis C in factory workers and their relatives. Biomedica. 2013; 29(1): 42-3.

[37] Mansour-Ghanaei R, Joukar F, Souti F, Atrkar-Roushan Z. Knowledge and attitude of medical science students toward hepatitis B and C infections. International Journal of Clinical and Experimental Medicine. 2013; 6(3): 197-205.

[38] Ali A, Khan S, Malik SM, Iqbal MH, Aadil M. Comparison of knowledge and attitudes regarding hepatitis B among healthcare professionals in Pakistan. Cureus. 2017 Feb; 9(2): e1049. doi: 10.7759/cureus.1049.

Original Article

Periodontal Health and Its Association with Age and Trimester in Pregnant Women Visiting Hospitals of Prime Foundation

Farah Shah[1*], Farzeen[1], Sana Kiramat Khan[2], Khadija Bibi[1], Areeba Faheem[3] and Kanwal Nazir Arbab[2]

[1]Department of Community and Preventive Dentistry, Peshawar Dental College, Riphah International University, Peshawar, Pakistan
[2]Department of Community and Preventive Dentistry, Rehman, College of Dentistry, Peshawar, Pakistan
[3]Department of Community and Preventive Dentistry, Khyber Medical University, Peshawar, Pakistan

ARTICLE INFO

*Corresponding Author:
Farah Shah
Department of Community and Preventive Dentistry, Peshawar Dental College, Riphah International University, Peshawar, Pakistan
fara.shah@yahoo.com

ABSTRACT

Immune system and trimester-specific hormonal changes that affect the mother and baby during pregnancy raise the hazards to dental health. **Objective:** To use the Community Periodontal Index of Treatment Needs (CPITN) Index to evaluate expectant mothers' periodontal health and its association with age and trimester. **Methods:** The research used a descriptive cross-sectional survey in a number of healthcare settings, including outpatient departments for gynecology and dentistry at many hospitals were conducted from January 2022 to December 2022. 384 pregnant patients were evaluated utilizing a specially created questionnaire and the CPITN Index by non-probability sequential sampling. IBM-SPSS Statistics 23.0 was used for statistical analysis, whereby associations between age, trimester, and CPITN scores (p-value < 0.05) were investigated using chi-square tests. **Results:** The groups with the largest representation in the third trimester (68.8%) and 18–22 (33.6%) were found to be the majority in the age distribution. The majority (59.9%) had a CPITN score of 0, age and trimester has significant association with CPITN scores (p-value<0.05). **Conclusions:** The study among pregnant women visiting hospitals of Prime Foundation highlights significant associations between periodontal health and trimester, with younger age groups and the third trimester predominantly represented. Most participants exhibited normal gum health, while notable proportions showed calculus and pocket depth issues, underscoring the relevance of these factors in periodontal health during pregnancy.

INTRODUCTION

Woman's health is greatly affected by her periodontal health, notably during pregnancy when her body experiences changes which could worsen whichever dental problems she had before [1]. Pregnancy raises the chance of disease because of hormone and adjustments in the immune system [2]. Possibly risky for mom and baby, the seriousness of these problems can differ with the age of the mother and the phase of pregnancy [3]. To successfully prevent and treat, one must grasp the nature of periodontal health during pregnancy [4]. Dental research has revealed complex associations between paternal oral hygiene and infant tooth and dental development, emphasizing the importance of specialized treatment during this sensitive period of life [5]. Dental problems are common in expectant women due to mutations, increased circulation, and immune dysfunction [6]. These conditions raise the possibility of complications throughout the pregnancy including premature or preterm labor apart from her oral symptoms. Assessing the well-being of expectant women during dental procedures is important to reduce risks and enhance maternal and infant well-being [7]. A pregnant woman's dental health may be affected by her age, and that's a big deal. Periodontal diseases are common in the elderly population, and may exacerbate pre-existing health issues and poor dental hygiene [8]. Despite the fact that changes in vascular

Shah F *et al.,*

health with gestational age can affect the development of age-specific treatment regimens and preventive strategies, it can also occur as pregnancy young pregnant women with delirium have difficulty maintaining good dental health due to inadequate oral hygiene practices or erroneous information [9]. Physiological changes that occur during every trimester could affect several outcomes connected to dental health [10]. For instance, you might encounter sickness and noticeable hormonal changes in the first trimester of your pregnancy. Dental hygiene routines may be impacted by these variables, which may worsen periodontal disorders that have already happened [11]. Gingival hypertrophy and inflammation might arise during the third trimester due to increased vascularization and fluid retention, according to the proof [12]. Assessing periodontal health at every trimester might assist medical practitioners in recognizing and addressing oral health matters that might emerge during pregnancy [13]. Globally, periodontal diseases affect a substantial portion of the population, with varying prevalence rates across different regions [14]. According to the World Health Organization (WHO), periodontal diseases are among the most prevalent chronic conditions, affecting approximately 10-15% of the worldwide population. The burden of these conditions is particularly pronounced in low and middle income countries, where access to dental care and awareness about oral health may be limited [15]. Moreover, epidemiological studies have demonstrated a notable increase in the prevalence of periodontal diseases with age, indicating a potential correlation between aging and oral health [16]. During pregnancy, hormonal changes can exacerbate pre-existing periodontal conditions or even lead to the onset of new ones [17]. Research suggests that up to 70% of pregnant women experience gingivitis, an early stage of periodontal disease characterized by inflammation of the gums [18].

The study aimed to investigate the intricate relationship between periodontal health and demographic factors, particularly age and trimester, in pregnant women. Understanding this relationship is crucial, given the significant impact of periodontal health on maternal well-being, especially during pregnancy when hormonal fluctuations and immune system changes can exacerbate existing dental issues. The study acknowledges the heightened risk of complications for both mother and baby, emphasizing the need for specialized treatment and preventive strategies tailored to this sensitive period of life. By utilizing the CPITN Index to assess periodontal health at each trimester. The study aimed to provide insights that can inform medical practitioners in identifying and addressing oral health concerns throughout pregnancy, ultimately aiming to enhance maternal and infant well-being.

METHODS

Gynecological Outpatient Departments (OPDs) at hospitals including Peshawar Dentistry, Mercy, Prime Teaching, and Kuwait Teaching were the subject of our comprehensive cross-sectional research conducted from January 2022 to December 2022 (1 year). The present study has been granted ethical approval by Prime Foundation Pakistan's Institutional Review Board, with (Reference No# Prime/IRB/2021-389; Dated 8th Nov, 2021). Prior to data collection, informed permission was sought from each participant, with a focus on voluntary participation and the confidentiality of the information submitted. Convenient sampling technique was used and sample size was calculated by using Slovin's formula: $n = N / (1 + Ne2)$, where, n = Number of samples, N = Total population and e = Error tolerance (level). The sample for this research consisted of 384 pregnant individuals. The inclusion criterion was satisfied by pregnant patients between the ages of 18 and 40 who attended the gynecological OPDs of the selected hospitals and the dental OPD of Peshawar Dental Hospital. Patients who had labor pain throughout their pregnancy at the time of the assessment were not allowed to continue. Data collection for age involved obtaining demographic information from the participants, including their age at the time of enrollment, which was recorded in years. Community periodontal index of treatment needs (CPITN) scores, dental examinations were conducted to assess periodontal health status. Trained examiners evaluated participants' periodontal conditions using standardized criteria, categorizing them based on CPITN scores ranging from 0 to 4. The CPITN categorizes periodontal health based on criteria including healthy condition, bleeding, calculus, and pocket depth. These categories were formed through dental examinations by trained professionals, assessing participants' periodontal status. Trimester categories were established based on self-report or medical records. Statistical analysis was performed using IBM-SPSS version 23.0. Frequency and percentages were used to construct descriptive data connected to CPITN scores, whereas mean and standard deviation were used to calculate age-related descriptive statistics. All the quantitative data were presented by mean + SD and qualitative with frequency and percentages. The distribution of periodontal health conditions by age group and trimester in pregnant individuals was analyzed using chi-square tests. A significance level of $p < 0.05$ was used to determine statistical significance using the relevant tests.

RESULTS

A comprehensive overview of the demographic and clinical characteristics of the participants. In terms of age distribution, the majority fall within the 18-22 age group, constituting 129 (33.6) of the total sample, followed by 23-27 was 121 (31.5) and 28-32 99 (25.8) age groups. A notable

proportion of participants belong to the lower middle class 190 (49.5), followed by the upper middle class 120 (31.3). Regarding pregnancy trimesters, most participants were in their third trimester 264 (68.8). In terms of oral health, the majority exhibited normal gum health 345 (89.8) and no plaque 205 (56.4). However, 105 (27.3) reported the presence of calculus. CPITN scores reveal that the highest proportion of participants had a score of 0 was 230 (59.9), indicating healthy periodontal conditions. Overall, the distribution underscores the diversity within the sample and provides insight into the various factors influencing periodontal health among the participants (Table 1).

Table 1: Descriptive Statistics of the Demographic and Clinical Characteristics of Participants

Variables	Categories	n (%)
Age Group	18-22	129 (33.6)
	23-27	121 (31.5)
	28-32	99 (25.8)
	33-37	27 (7.0)
	38-40	12 (3.1)
	Total	384 (100.0)
Social Class	Upper Class	6 (1.6)
	Upper Middle Class	120 (31.3)
	Lower Middle Class	190 (49.5)
	Upper Lower Class	66 (17.2)
	Lower Class	2 (0.5)
	Total	384 (100.0)
Trimester	First	56 (14.6)
	Second	64 (16.7)
	Third	264 (68.8)
	Total	384 (100.0)
Gum Health	Normal	345 (89.8)
	Swollen	39 (10.2)
	Total	384 (100.0)
Plaque	Yes	179 (43.6)
	No	205 (56.4)
	Total	384 (100.0)
Calucus	Yes	105 (27.3)
	No	279 (72.7)
	Total	384 (100.0)
CPITN Score	1	18 (4.7
	2	60 (15.6)
	3	75 (19.5)
	4	1 (0.3)
	Total	384 (100.0)
CPITN	Healthy	223 (58.1)
	Bleeding	20 (5.2)
	Calculus	64 (16.7)
	Pocket Depth 3.5 to 5.5	77 (20.1)
	Total	384 (100.0)

The distribution of individuals with healthy gums, bleeding, calculus, and pocket depth of 3.5 to 5.5 mm was analyzed by the chi-square test (x_2). For age groups, x_2 yielded a significant result (x_2=268.86), df = 22, p < 0.001), indicating a statistically significant difference in periodontal conditions across ages 18-22 (129 healthy, 5 bleeding, 25 calculus, 20 with pocket depth 3.5-5.5 mm), 23-27 (121, 8, 30, 15), 28-32 (99, 3, 20, 10), 33-37 (27, 2, 10, 5), and 38-40 (12, 2, 5, 3). For trimesters, the chi-square test showed a significant difference (x_2 = 217.00), df = 2, p < 0.001) with first trimester (56 healthy, 4 bleeding, 12 calculus, 8 with pocket depth 3.5-5.5 mm), second trimester (64, 6, 18, 10), and third trimester (264, 10, 34, 23), reflecting varied periodontal health statuses in different trimesters of pregnancy. Total participants were 384 with 20 experiencing bleeding, 64 having calculus, and 41 with pocket depths of 3.5 to 5.5 mm (Table 2)

Table 2: Distribution of Periodontal Health Conditions by Age Group and Trimester in Pregnant Individuals with Chi-Square

Variable		Healthy	Bleeding	Calculus	Pocket Depth 3.5 to 5.5	x^2	p-value
Age	18-22	129	5	25	20	268.86	<0.001*
	23-27	121	8	30	15		
	28-32	99	3	20	10		
	33-37	27	2	10	5		
	38-40	12	2	5	3		
Trimester	First	56	4	12	8	217.00	<0.001*
	Second	64	6	18	10		
	Third	264	10	34	23		
	Total	384	20	64	41		

*p-value<0.05 was significant

DISCUSSION

The association between age and intermaternal health provides important new information on oral health habits in this population. The majority of participants, or 65.1% of the total sample, were in the younger age groups of 18–22 and 23–27 years. This distribution is consistent with previous research where majority of the participants belonged to the younger age group as well [19]. That although there are significant differences in periodontal health by age, these differences may not be as significant. However, a higher correlation is revealed when examining the relationship between root canal health and quarter. This result is consistent with other studies showing a high prevalence of dental abnormalities in pregnancy, especially in later stages [20, 21]. Dental examinations and treatments are important to reduce the risks to the dental health of the developing baby and the mother, especially in the later stages of pregnancy [22]. The study revealed differences in access to dental treatment during pregnancy, since the majority of respondents did not get preventative therapy for pregnant gingivitis. Dentist appointments are rare, and even fewer people say they only go when they have problems with their teeth or gums rather than as a preventative strategy. Unreliable data, budgetary restraints, and worries regarding the safety and

effectiveness of dental treatments during pregnancy are just a few of the obstacles that pregnant women face when trying to receive oral healthcare [23]. In order to overcome these challenges and achieve the best possible dental results for both the mother and her unborn child, individualized therapies are essential. Oral health screenings and recommendations for safe cavity treatment are essential components of prenatal care [24]. This study highlights the importance of a targeted health education program for a large population in terms of increasing knowledge about health problems and providing people from different socioeconomic backgrounds with tools an immediate need for learned choices action must be taken. The socioeconomic data table map highlights the need for inclusive health care, with a focus on social determinants of health and policies designed to cater to people from whom they come by meeting the specific needs of all social situations [25]. According to subsequent statistics and p-values, the study results are statistically significant. The statistical significance of the age variable (p =.002) indicates that different age groups can be identified among the groups that formed the sample. Age should be considered when assessing the effect of pregnancy on oral health because it affects response to treatment and the susceptibility to dental problems [26]. There was a significant difference observed between the trimester and periodontal health conditions. Consider the p-value of <0.001 for "Trimester"; it implies that the dependent variable is substantially impacted by the trimester of pregnancy. This data suggests that other variables have significant influence on the outcome as well, even if particular oral health concerns could differ by trimester, including a higher risk of gingivitis in the latter trimesters. The links between different oral health concerns and pregnancy-related features may be further understood by examining the correlations identified among the matched groups. When looking at Pair 1, which contains "Age" and "CPITN Score," p-value of 0.156 indicates a slightly positive connection. This is in line with other studies that shown that periodontal disease risk factors, including changes in oral health and cumulative exposure, tend to increase with age [27]. It is crucial to take a pregnant woman's age into account when assessing the necessity for periodontal therapy. Pair 2 "Trimester" and "CPITN Score" were not significantly correlated (r=0.032). This provides further evidence that the need for periodontal care may be unaffected by the third trimester of pregnancy. The risk of periodontal disease seems to change across trimesters, even though hormonal changes during pregnancy may impact oral health generally [28, 29]. In sum, these results add to what is already known about the intricate relationship between factors present during pregnancy, personal traits, and the final results of oral health care. Although there is a substantial correlation between maternal age and periodontal care throughout pregnancy, the fact that the third trimester seems to have little effect highlights the necessity to personalize oral health treatments for each patient based on their unique requirements, which include their gestational stage and other personal information. In order to improve pregnant women's dental health, further study into these links and what they mean for clinical practice is needed. This might result in better medications and preventative measures.

CONCLUSIONS

The results indicate a significant association between periodontal health and both age and trimester among pregnant women visiting hospitals of Prime Foundation. The majority of participants were in the younger and in their third trimester of pregnancy. Most exhibited normal gum health and no plaque. The CPITN scores reflected healthy periodontal conditions for the majority, though a notable proportion had calculus and pocket depths indicating periodontal issues. Chi-square tests revealed significant differences in periodontal conditions across different age groups and trimesters, suggesting that both age and stage of pregnancy are important factors influencing periodontal health among the participants. The need for therapy may be unaffected by trimester.

REFERENCES

[1] Figueiredo MG, Takita SY, Dourado BM, Mendes HD, Terakado EO, Nunes HR *et al.* Periodontal disease: repercussions in pregnant woman and newborn health—a cohort study. PLOS One. 2019 Nov; 14(11):e0225036. doi: 10.1371/journal.pone.0225036.

[2] Chen M, Zeng J, Liu X, Sun G, Gao Y, Liao J *et al.* Changes in physiology and immune system during pregnancy and coronavirus infection: A review. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2020 Dec; 255: 124-8. doi: 10.1016/j.ejogrb.2020.10.035.

[3] Davis EP and Narayan AJ. Pregnancy as a period of risk, adaptation, and resilience for mothers and infants. Development and Psychopathology. 2020 Dec; 32(5): 1625-39. doi: 10.1017/S0954579420001121.

[4] Bobetsis YA, Graziani F, Gürsoy M, Madianos PN. Periodontal disease and adverse pregnancy outcomes. Periodontology 2000. 2020 Jun; 83(1): 154-74. doi: 10.1111/prd.12294.

[5] Arora A, Lucas D, To M, Chimoriya R, Bhole S, Tadakamadla SK *et al.* How do mothers living in socially deprived communities perceive oral health of young children? A qualitative study. International Journal of Environmental Research and Public Health. 2021 Mar; 18(7): 3521. doi: 10.3390/ijerph1807 3521.

[6] Figuero E, Han YW, Furuichi Y. Periodontal diseases and adverse pregnancy outcomes: Mechanisms. Periodontology 2000. 2020 Jun; 83(1): 175-88. doi: 10.1111/prd.12295. doi: 10.1111/prd.12295.

[7] Thakur V, Thakur R, Kaur M, Kaur J, Kumar A, Virdi D *et al.* Pregnancy & oral health and dental management in pregnant patient. Journal of Current Medical Research and Opinion. 2020 Nov; 3(11): 724-31. doi: 10.15520/jcmro.v3i11.360. doi: 10.15520/jcmro.v3i11. 360.

[8] Clark D, Kotronia E, Ramsay SE. Frailty, aging, and periodontal disease: Basic biologic considerations. Periodontology 2000. 2021 Oct; 87(1): 143-156. doi: 10.1111/prd.12380.

[9] Srivastava R, Chandra C, Jha V, Dubey A, Sharma T, Goel T. Periodontal health is the key for overall health. Asian Journal of Oral Health and Allied Sciences. 2022 Feb; 12. doi: 10.25259/AJOHAS_11_2021.

[10] Goel MR, Dombre S, Bande CR, Joshi A, Singh S. Physiological Changes during Pregnancy with Oral Manifestations in Dentistry: A Review. Journal of Advanced Health Sciences and Research. 2020; 1(2): 79-91.

[11] Sedghi L, DiMassa V, Harrington A, Lynch SV, Kapila YL. The oral microbiome: Role of key organisms and complex networks in oral health and disease. Periodontology 2000. 2021 Oct; 87(1): 107-31. doi: 10.1111/prd.12393.

[12] Kumar M, Saadaoui M, Al Khodor S. Infections and pregnancy: effects on maternal and child health. Frontiers in Cellular and Infection Microbiology. 2022 Jun; 12: 873253. doi: 10.3389/fcimb.2022.873253.

[13] Fakheran O, Keyvanara M, Saied-Moallemi Z, Khademi A. The impact of pregnancy on women's oral health-related quality of life: a qualitative investigation. BMC Oral Health. 2020 Dec; 20: 1-1. doi: 10.1186/s12903-020-01290-5.

[14] Nazir M, Al-Ansari A, Al-Khalifa K, Alhareky M, Gaffar B, Almas K. Global prevalence of periodontal disease and lack of its surveillance. The Scientific World Journal. 2020; 2020(1): 2146160. doi: 10.1155/2020/21 46160.

[15] Petersen PE and Ogawa H. Strengthening the prevention of periodontal disease: the WHO approach. Journal of Periodontology. 2005 Dec; 76(12): 2187-93. doi: 10.1902/jop.2005.76.12.2187.

[16] Gera I. Periodontal treatment needs in Central and Eastern Europe. Journal of the International Academy of Periodontology. 2000 Oct; 2(4): 120-8.

[17] Gare J, Kanoute A, Meda N, Viennot S, Bourgeois D, Carrouel F. Periodontal conditions and pathogens associated with pre-eclampsia: a scoping review. International Journal of Environmental Research and Public Health. 2021 Jul; 18(13): 7194. doi: 10.3390/ijer ph18137194.

[18] Talebessy R and Cecilia S. Gingivitis and Oral Health Diseases Related to Pregnancy. Crown: Journal of Dentistry and Health Research. 2023 Oct; 1(1): 1-5. doi: 10.59345/crown.v1i1.51.

[19] Cagetti MG, Salerno C, Ionescu AC, La Rocca S, Camoni N, Cirio S, Campus G. Knowledge and attitudes on oral health of women during pregnancy and their children: an online survey. BMC Oral Health. 2024 Jan; 24(1): 85.

[20] Tedjosasongko U, Anggraeni F, Wen ML, Kuntari S, Puteri MM. Prevalence of caries and periodontal disease among Indonesian pregnant women. Pesquisa Brasileira em Odontopediatria e Clínica Integrada. 2019 Oct; 19: e4533. doi: 10.4034/PBOCI.2 019.191.90.

[21] Africa CW and Turton M. Oral health status and treatment needs of pregnant women attending antenatal clinics in KwaZulu-Natal, South Africa. International Journal of Dentistry. 2019 Mar; 2019. doi: 10.1155/2019/5475973.

[22] Favero V, Bacci C, Volpato A, Bandiera M, Favero L, Zanette G. Pregnancy and dentistry: A literature review on risk management during dental surgical procedures. Dentistry Journal. 2021 Apr; 9(4): 46. doi: 10.3390/dj9040046.

[23] Van der Zande MM, Exley C, Wilson SA, Harris RV. Disentangling a web of causation: an ethnographic study of interlinked patient barriers to planned dental visiting, and strategies to overcome them. Community Dentistry and Oral Epidemiology. 2021 Apr; 49(2): 144-57. doi: 10.1111/cdoe.12586.

[24] Bao J, Huang X, Wang L, He Y, Rasubala L, Ren YF. Clinical practice guidelines for oral health care during pregnancy: a systematic evaluation and summary recommendations for general dental practitioners.

Quintessence International. 2022 Mar; 53(4): 362-73.

[25] Whitman A, De Lew N, Chappel A, Aysola V, Zuckerman R, Sommers BD. Addressing social determinants of health: Examples of successful evidence-based strategies and current federal efforts. Office of Health Policy. 2022 Apr; 1: 1-30.

[26] Thakur V, Thakur R, Kaur M, Kaur J, Kumar A, Virdi D *et al.* Pregnancy & oral health and dental management in pregnant patient. Journal of Current Medical Research and Opinion. 2020 Nov; 3(11): 724-31. doi: 10.15520/jcmro.v3i11.360.

[27] Borsanelli AC, Viora L, Parkin T, Lappin DF, Bennett D, King G *et al.* Risk factors for bovine periodontal disease–a preliminary study. Animal. 2021 Feb; 15(2): 100121. doi: 10.1016/j.animal.2020.100121.

[28] Thomas C, Timofeeva I, Bouchoucha E, Canceill T, Champion C, Groussolles M *et al.* Oral and periodontal assessment at the first trimester of pregnancy: The Periscope longitudinal study. Acta Obstetricia et Gynecologica Scandinavica. 2023 Jun; 102(6): 669-80. doi: 10.1111/aogs.14529.

[29] Radwan-Oczko M, Hirnle L, Szczepaniak M, Duś-Ilnicka I. How much do pregnant women know about the importance of oral health in pregnancy? Questionnaire-based survey. BMC Pregnancy Childbirth. 2023 May 13; 23(1): 348. doi: 10.1186/s12884-023-05677-4.

PAKISTAN JOURNAL OF HEALTH SCIENCES

Original Article

Spectrum of Clinical Manifestations among Paediatrics and Adult Patients of Idiopathic Thrombocytopenic Purpura Presenting to Tertiary Care Hospital

Masuma Ghazanfar[1]*, Hamid Sarwar[1], Muhammad Hassan Cheema[2], Muhammad Hussain Cheema[2], Noor Fatima[3] and Ali Husnain Sheikh[4]

[1]Department of Pathology, Allama Iqbal Medical College, Lahore, Pakistan
[2]Department of Pathology, Sahara Medical College, Lahore, Pakistan
[3]Department of Medicine, District Health Quarter, Layyah, Pakistan
[4]Department of Ear, Nose and Throat, Akhtar Saeed Medical College, Lahore, Pakistan

ARTICLE INFO

ABSTRACT

Idiopathic Thrombocytopenia Purpura (ITP), an autoimmune bleeding disorder, affects both children and adults, categorized into acute, persistent or chronic types based on symptom duration. Clinical presentations vary widely, ranging from minor bleeds to severe systemic hemorrhages involving CNS, GIT and genitourinary tract. **Objective:** To assess clinical manifestations in ITP patients at a Lahore tertiary care Hematology department. **Methods:** This retrospective cross-sectional study included data from 660 diagnosed ITP patients from January 2020 to December 2022 using consecutive sampling technique at Allama Iqbal Medical College. Data were recorded after taking consent from patients. **Results:** Mean age was 31.8 ± 12.8 SD, with 10.3% children and 89.7% adults. Patients were categorized based on platelet counts into mild, moderate, and severe groups. Most children (47%) and adults (59.9%) had moderate thrombocytopenia. Common features included bruising in children (67.6%), gum bleeding (77%) in adults of both sexes and menorrhagia (67.9%) in females. **Conclusions:** ITP affects all ages but predominantly females. Clinical presentation varies, with most cases showing superficial bleeding like bruising, epistaxis, gum bleeding, or menorrhagia in females.

INTRODUCTION

Idiopathic Thrombocytopenia Purpura (ITP), also known as immune thrombocytopenic purpura is a common bleeding disorder that is encountered in healthy individuals, affecting both children and adults [1]. It is an autoimmune disorder characterized by increased destruction of platelets that is mediated by antiplatelet antibodies or decreased production resulting in thrombocytopenia. On the basis of international consensus, the term ITP should be used if platelets count is below 100 x 109 /L. Based on the duration of symptoms, it is divided into three types i.e. acute (newly diagnosed until 3 months), persistent (3 to 12 months) and chronic (more than 12 months) [2, 3]. The

clinical presentation of ITP differs from patient to patient. The bleeding pattern varies from minor superficial and mucosal bleed to life-threatening systemic bleeding involving CNS, GIT and genitourinary tract. A local study conducted by Rashid N *et al.,* concluded that petechiae (31.25%) was the most frequent manifestation, followed by bruises, gum bleed and nose bleed [4]. According to a study done in Turkey in 2002, it was found that 73.2% ITP patients between 14-78 years of age presented with initial symptom of bleeding. The frequency of bleeding in relation to platelet count was 82% with platelet count 50000/mm3 [5]. A study done to determine clinical spectrum of acute

Ghazanfar M et al.,

ITP in children between 1 month to 14 years of age in India concluded that petechiae and purpura were the most common clinical features followed by mucosal bleed in 67% of the children [1]. In a local study on ITP patients, it was found that 88% of the patients presented with only three complaints i.e., nose bleed, gum bleed and bruising. Other less frequent clinical features included hematuria and hematemesis (8%) and menorrhagia (3.2%) and cut off platelet count associated with more frequent bleeding episodes was reported to be <100000/mm [5, 6]. ITP is a very frequently occurring condition in our setup, affecting individuals of all ages. The clinical presentation varies from being asymptomatic to presenting with a wide range of symptoms. Therefore, the study aimed to provide valuable insights into the clinical spectrum of ITP in all age groups and to determine the frequency and spectrum of clinical manifestations among ITP patients presenting to our setup. Additionally, we will review relevant literature on the subject to complement our findings and place them in the context of existing knowledge [7, 8, 9]. Ultimately, this research will help to improve our understanding of the clinical presentation of ITP and provide insights into the management and treatment of this condition. The collection of studies examines the spectrum of clinical manifestations and outcomes in pediatric and adult patients with Idiopathic Thrombocytopenic Purpura (ITP) who present to tertiary care hospitals. These studies offer a comprehensive overview of the clinical features, management strategies, and therapeutic responses observed in different patient populations [10, 11]. The studies highlight that ITP can present with a wide range of clinical symptoms, from asymptomatic thrombocytopenia to severe bleeding disorders. In children, the disease often follows a viral infection and tends to be acute, whereas in adults, it is more commonly chronic and may be associated with autoimmune disorders or drug use. Common clinical manifestations include petechiae, purpura, and mucosal bleeding, with variations observed based on age and severity of the disease [12-14]. Management strategies discussed in the studies emphasize the importance of individualized treatment approaches. For pediatric patients, observation and supportive care are often sufficient for acute cases, while adults with chronic ITP may require more aggressive therapies, including corticosteroids, intravenous immunoglobulins, and splenectomy [15, 16]. Advances in diagnostic techniques, such as the use of immunobead assays, have improved the accuracy of ITP diagnosis, enabling better-targeted treatments [17]. The outcomes of ITP patients vary widely, with many children experiencing spontaneous remission, while adults may face a relapsing-remitting course. Factors affecting the prognosis include the patient's age,

initial platelet count, and response to initial treatment [18, 19]. Overall, these studies underscore the need for continued research to optimize the management and improve the outcomes for ITP patients [20].

This study was conducted to provide insights into the clinical spectrum of ITP across age group and to determine the frequency and spectrum of clinical manifestations.

METHODS

This retrospective cross-sectional study was conducted at the Haematology Department of Allama Iqbal Medical College (AIMC) Lahore. The study included data from the diagnosed ITP patients from January 2020 to December 2022. Institutional ethical review Committee gave permission (Ref No: ERB 144/6/09-06-2023/S1 ERB). Sample size was calculated using OpenEpi software which came out to be 331 keeping 95% confidence interval and 5% margin of error but we took 660 subjects for our study [11]. Inclusion criteria comprised patients aged 3-60 with confirmed ITP diagnosis, excluding those with pancytopenia, haematological malignancies, or inherited thrombocytopenia. The data of ITP patients already diagnosed on the basis of history, examination and investigations, fulfilling the inclusion criteria were obtained using convenient sampling technique. Prior written informed consent was taken from all patients authorizing the use of their personal information for research purposes. The data were presented using frequency tables, charts and figures. Data were analyzed using SPSS version 26.0. P value of ≤0.05 was taken as statistically significant.

RESULTS

The study included data of 660 ITP patients between 3 to 60 years of age. The mean age was 31.8 ± 12.8 SD. There were total 68 children (10.3%) out of which there were 30 males (12.4%) and 38 females (9.1%). The total adult population was 592 (89.7%) which included 212 males (87.6%) and 380 females (90.9%), the overall male to female ratio was 0.5:1 as shown in figure 1.
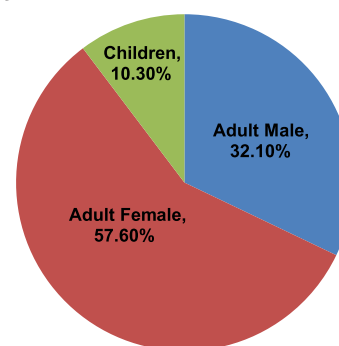
Figure 1: Study Population Statistics

Based on platelet count thrombocytopenia was divided into 3 groups' i.e. mild, moderate and severe. Most of the

children (47%) and adults (59.9%) had moderate thrombocytopenia as shown in table 1.

Table 1: Thrombocytopenia Groups and Age Distribution

Age Category	Thrombocytopenia Group		
	Mild	Moderate	Severe
Up to 12 Years	28	32	8
Above 12 Years	35	355	152
Total	113	387	160

The most common clinical feature in children was bruising and in adult's gum bleeding. In adult females, menorrhagia was observed most common clinical feature (67.9%). Apparently it appears that bruising was more common among children while gum bleed occurred more frequently in adults but when Chi-square test was applied to see any relationship between age groups and frequency of symptoms, p value came out to be 0.85 which is statistically not significant hence establishing that there exists no predilection of any symptom towards any specific age groups i.e. children and adults as shown in table 2.

Table 2: Frequency of Symptoms

Groups	Epistaxis N (%)	Gum Bleed N (%)	Bruise N (%)	p-Value
Children	41 (60.2%)	35 (51.4%)	46 (67.6%)	0.85
Adult	165 (27.8%)	456 (77%)	349 (58.9%)	

DISCUSSION

Immune Thrombocytopenia Purpura (ITP) is an acquired autoantibody-mediated bleeding condition with a frequency in adults between 1.6 and 3.9 per 100,000 person-years and is characterized by both rapid platelet destruction and reduced platelet formation [5]. ITP's actual prevalence is unknown. The male to female ratio is variable since there may be a male majority in children and a female preponderance in adults in the USA, where the prevalence was estimated at 1/10,000 in children and 5.5/100,000 people in adults In Pakistan, ITP has been reported to have an incidence of between 0.2 and 0.4 new cases per 10,000 per year, a prevalence of 0.9-2.6 per 10,000, and a female preponderance [4]. ITP has been consistently observed to be more prevalent among females as also observed in our study in which 418 (63.3%) patients were females. This female predominance was also reported by Ejaz A and Radia D [2]. However, in studies done in India in 2015 and 2016 by Godhani UR and Devaliya JJ and Shah HR *et al.,* male predominance of ITP was reported [9, 10]. The clinical features of ITP vary as observed in our study. Among children, bruising (67.6%) was the dominant clinical feature while gum bleeding was least common. This finding is in consistence with the study of Farid J *et al.,* who reported bruising (50.4%) as the most common clinical feature [6]. Similar findings were reported in the study done in Riyadh to determine the clinical characteristics and outcomes of pediatric patients with ITP where skin manifestation was

present in 92.7% and gum bleeding in only 19.5% of study population [11]. In adults, gum bleeding was the commonest presentation (77%) observed. However, our results are at odds with those of a 2017 study conducted in Nigeria, which identified epistaxis (88.9%) as the most prevalent complaint [8]. In our study, menorrhagia was present in 67.9% of adult females, being the second most common clinical feature. This finding was similar to the study done in India in 2022, where menorrhagia was reported in 79% of the females [7]. However, Hassan A *et al.,* reported menorrhagia in only 22.2% of females [8]. Our study possesses several limitations that necessitate consideration. Initially, the inclusion of only a single center raises concerns about the generalization of the findings to the entire population of ITP patients in Pakistan. To gain a more accurate estimation of the disease burden, a larger sample size collected from multiple centers would be imperative.

CONCLUSIONS

ITP can affect individuals of any age but there is a female predominance. The clinical presentation can vary from patient to patient however in majority of the cases there is no life-threatening bleed and mostly patients present with superficial bleeding like bruising, epistaxis or gum bleed.

Authors Contribution

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

REFERENCES

[1]   Champatiray J, Behera DK, Krishnamoorthy A, Bhat S. Evaluation of prevalence, clinical spectrum and outcome of acute ITP in children in a tertiary care centre in Odisha, India. International Journal of Contemporary Pediatrics. 2017 Jul; 4(4): 1470-5. doi: 10.18203/2349-3291.ijcp20172688.

[2]   Ejaz A and Radia D. Diagnosis and management of primary immune thrombocytopenia in adults. British Journal of Hospital Medicine. 2019 Apr; 80(4): C54-7. doi: 10.12968/hmed.2019.80.4.C54.

[3]   Cooper N. State of the art-how I manage immune thrombocytopenia. British Journal of Haematology. 2017 Apr; 177(1): 39-54. doi: 10.1111/bjh.14515.

[4] Rashid N, Imtiaz U, Iqbal I, Malik A, Khalid A, Mobeen S. Spectrum of skin manifestations in patients presenting with idiopathic thrombocytopenic purpura in a tertiary care hospital. Journal of Pakistan Association of Dermatologists. 2020 Sep; 30(2): 286-8.

[5] Pamuk G, Pamuk Ö, Başlar Z, Öngören Ş, Soysal T, Ferhanoğlu B *et al.* Overview of 321 patients with idiopathic thrombocytopenic purpura: retrospective analysis of the clinical features and response to therapy. Annals of Hematology. 2002 Aug; 81: 436-40. doi: 10.1007/s00277-002-0488-x.

[6] Farid J, Gul N, Idris M. Clinical presentations in immune thrombocytopenic purpura. Journal of Ayub Medical College Abbottabad. 2012 Jun; 24(2): 39-40.

[7] Chakrabarti P, George B, Shanmukhaiah C, Sharma LM, Udupi S, Ghanima W. How do patients and physicians perceive immune thrombocytopenia (ITP) as a disease? Results from Indian analysis of ITP World Impact Survey (I-WISh). Journal of Patient Reported Outcomes. 2022 Mar; 6(1): 24. doi: 10.1186/s41687-022-00429-y.

[8] Hassan A, Adebayo A, Musa AU, Suleiman AM, Ibrahim IN, Kusfa IU *et al.* Clinical feature and management of immune thrombocytopenic purpura in a tertiary hospital in Northwest Nigeria. Nigerian Medical Journal. 2017 Mar; 58(2): 68-71. doi: 10.4103/0300-1652.219343.

[9] Godhani UR and Devaliya JJ. Clinical profile of patients with thrombocytopenia attending a tertiary care hospital, Gujarat. Scholars Journal of Applied Medical Sciences. 2016 Aug; 4(8E): 3058-62. doi: 10.36347/sjams.2016.v04i08.063.

[10] Shah HR, Vaghani BD, Gohel P, Virani BK. Clinical profile review of patients with thrombocytopenia: A study of 100 cases at a tertiary care centre. International Journal of Current Research and Review. 2015 Mar; 7(6): 33.

[11] Alwadi KW, Alomari A, Alrugaib AK, Alrubayea A, Alzoman M, Alkahtani F. Clinical Characteristics and Outcomes of Pediatric Patients With Immune Thrombocytopenic Purpura in King Abdulaziz Medical City and King Abdullah Specialist Children's Hospital: A 10-Year Study. Cureus. 2020 Nov; 12(11): e11366. doi: 10.7759/cureus.11366.

[12] Thiagarajan S and Omana S. Clinical profile of immune thrombocytopenic purpua and outcome at 6 months: a South Indian observational study. International Journal of Contemporary Pediatrics. 2018 Jan; 5(1): 190. doi: 10.18203/2349-3291.ijcp20175584.

[13] Rashid N, Imtiaz U, Iqbal I. Spectrum of skin manifestations in patients presenting with idiopathic thrombocytopenic purpura in a tertiary care hospital. Journal of Pakistan Association of Dermatologists. 2020; 30(2): 286-8.

[14] Zimmer J, Andres E, Noel E, Koumarianou A, Blicklé JF, Maloisel F. Current management of adult idiopathic thrombocytopenic purpura in practice: a cohort study of 201 patients from a single center 1. Clinical & Laboratory Haematology. 2004 Apr; 26(2): 137-42. doi: 10.1111/j.1365-2257.2004.00591.x.

[15] George JN, Woolf SH, Raskob GE, Wasser JS, Aledort LM, Ballem PJ *et al.* Idiopathic thrombocytopenic purpura: a practice guideline developed by explicit methods for the American Society of Hematology. Blood. 1996 Jul; 88(1): 3-40. doi: 10.1182/blood.V88.1.3.3.

[16] Cines DB and Blanchette VS. Immune thrombocytopenic purpura. New England Journal of Medicine. 2002 Mar; 346(13): 995-1008. doi: 10.1056/NEJMra010501.

[17] Bussel J. Treatment of immune thrombocytopenic purpura in adults. InSeminars in Hematology. 2006 Jul; 43: S3-S10. doi: 10.1053/j.seminhematol.2006.04.009.

[18] Chong BH and Keng TB. Advances in the diagnosis of idiopathic thrombocytopenic purpura. InSeminars in Hematology. 2000 Jul; 37(3): 249-260. doi: 10.1053/shem.2000.8956.

[19] Cohen R, Garcia CA, Mena D, Castellanos M. Case review: idiopathic thrombocytopenic purpura. Journal of Medical Cases. 2012 Mar; 3(2): 130-4. doi: 10.4021/jmc506w.

[20] McMillan R. Autoantibodies and autoantigens in chronic immune thrombocytopenic purpura. InSeminars in Hematology. 2000 Jul; 37(3): 239-248. doi: 10.1016/S0037-1963(00)90102-1.

Original Article

Comparison of Conjunctival Autograft Using Autologous Serum Versus Suturing Technique in Primary Pterygium

Zulfiqar Ali[1*], Nadia Nazir[1], Soufia Farrukh[1], Muhammad Khalid[2], Sarfraz Ahmad Mukhtar[1] and Muhammad Jahanzaib Khan[1]

[1]Department of Ophthalmology, Bahawalpur Victoria Hospital, Quaid-e-Azam Medical College, Bahawalpur, Pakistan
[2]Department of Ophthalmology, Shahida Islam Medical College, Lodhran, Pakistan

ARTICLE INFO

ABSTRACT

Pterygium is characterized by degeneration of the subconjunctival tissue, which proliferates as vascularized granulation tissue that invades the cornea, particularly affecting the superficial layers of the stroma and bowman's membrane. **Objective:** To compare the conjunctival autografts using autologous serum versus suturing techniques in primary pterygium. **Methods:** This randomized controlled study was conducted at the ophthalmology department of Bahawal Victoria Hospital, Bahawalpur, Pakistan, from September 2023 to February 2024. Patients of either gender aged between 18-70 years with primary pterygium (either nasal or temporal) were included. Patients in Suturing group (n=16) consisted of patients receiving the traditional suturing technique, while in autologous serum group (n=16) had surgeries performed using autologous serum as tissue adhesive. **Results:** In a total of 32 patients, there were 25 (78.1%) males while overall mean age was 45.4 ± 12.6 year. The mean duration of surgery was 35.6 ± 4.8 minutes in suturing group versus 26.4 ± 2.9 minutes in autologous group (p<0.000). Evaluation of post-surgery ocular discomfort showed that significantly better results were obtained among patients of autologous serum group (p=0.024). Significantly better satisfaction scores were recorded among patients of autologous serum group when compared to patients undergoing suturing technique (p=0.001). Post-surgery complications were assessed in both study groups and no statistically significant differences were observed among patients of both study groups (p>0.05). **Conclusions:** When considering efficacy, both techniques demonstrated comparable outcomes. In terms of postoperative discomfort and surgical duration, the autologous serum method showed significant advantages by presenting reduced discomfort and shorter surgical times.

INTRODUCTION

The term "pterygium" finds its roots in the Greek word "pterygose," meaning 'wing' [1]. It appears as a wing-shaped growth of subconjunctival fibrovascular tissue that is mostly located in the interpalpebral fissure and is encroaching on the cornea. This condition is characterized by degeneration of the subconjunctival tissue, which proliferates as vascularized granulation tissue that invades the cornea, particularly affecting the superficial layers of the stroma and bowman's membrane [2]. Sunlight exposure stands as a significant modifiable risk factor for pterygium while there exists a correlation between ultraviolet light exposure and the development of pterygium, which may damage limbal stem cells and activate matrix metalloproteinase [3]. Heat, dust, and wind also contribute to its occurrence if exposed to them too much [4]. While often asymptomatic, pterygium encroaches on the visual axis, leading to vision impairment and can induce astigmatism in advanced stages [5]. Apart from visual disturbances, complications of pterygium may include recurrent inflammation, issues with contact lens fitting, and cosmetic concerns. Most cases with no symptoms require no medical attention [6]. However, surgical excision, followed by a conjunctival autograft to cover the exposed sclera, is the best mode if necessitated [7]. Various techniques are used to keep the graft in position; using a nylon 10-0 or Vicryl 8-0 suture is

considered standard. Alternatively, tissue adhesives like fibrin glue or autologous serum can secure the graft [8]. Suturing the conjunctival graft, although effective, presents complications such as prolonged surgery time, pain throughout the healing process, infection, the development of granuloma, and chronic inflammation [9]. The use of fibrin glue decreases surgery times, lessens related problems, and enhances subsequent satisfaction. However, the use of fibrin glue derived from human plasma can potentially transmit the disease and increase surgical costs. A recent popular method involves using autologous serum as a tissue adhesive, eliminating suture-related complications and disease transmission risks and proving to be cost-effective [10]. A study found post-surgery discomfort among 73.3% patients undergoing suturing technique versus 20% among autologous serum patients with primary pterygium [11].

The current research objective was to compare conjunctival autografts using autologous serum versus suturing techniques in primary pterygium. This research would be able to add significant information to the current data by comparing two techniques of securing conjunctival autografts suturing and utilizing autologous serum in treating pterygium in terms of their effectiveness, safety, patient comfort, complications, and surgical time.

METHODS

This randomized controlled study was conducted at the ophthalmology department, Bahawal Victoria Hospital, Bahawalpur, Pakistan, from September 2023 to February 2024. A prior approval from the "Institutional Ethical Committee" was obtained (Letter No.: 2350/DME/QAMC /Bahawalpur). Informed and written consents were sought from study participants. A sample size of 32 (16 in each group) was calculated taking two sided significance level as 95%, power 80%, proportion of post-surgery discomfort in suturing technique and autologous serum techniques in patients with primary pterygium as 73.3% and 20.0% respectively [11]. Inclusion criteria were patients of either gender aged between 18 and 70 years with primary pterygium (either nasal or temporal). All included patients had recurrent inflammation, induced astigmatism, encroachment over the pupillary margin, rapid pterygium growth, and cosmetic concerns. The exclusion criteria were conditions like atrophic pterygium, pseudopterygium, recurrent or double-headed pterygium, prior ocular surgery, or patients on anticoagulants. Those with known bleeding or coagulation disorders were also note included. All of the necessary demographic and clinical aspects of the patients were noted. Patients underwent a comprehensive ocular examination, including visual acuity, refraction, slit-lamp biomicroscopy, ocular movement, intraocular pressure measurement, lacrimal passage irrigation, and dilated fundoscopy, and then were

distributed randomly into two study groups. Patients in Suturing group (n=16) consisted of patients receiving the traditional suturing technique, while in autologous serum group (n=16) had surgeries performed using autologous serum as tissue adhesive. The procedure involved a peribulbar block using 2% xylocaine and adrenaline. A bridle suture was inserted under the muscle known as the superior rectus. It was followed by injecting a balanced salt solution under the pterygium to create separation from the sclera. Subsequently, excision of the pterygium was performed, and the bare scleral bed was measured. In the same eye, a conjunctival graft from the superior quadrant was prepared, somewhat bigger than the recipient bed. The graft was gently slide over the recipient bed, maintaining the limbal edge aligned with the limbus and the epithelial side up. After the procedure, various factors, such as graft edema, sub-graft hemorrhage, displacement or retraction of the graft, pterygium recurrence, formation of granulomas or cysts, and signs of infection, were observed under a slit lamp on a regular basis. Patients were interviewed post-surgery for grading pain, foreign body sensation, photophobia, hyperemia, and chemosis according to intensity. The score was graded from 0 to 3 as 0 for nothing, 1 as mild, 2 as moderate, and 3 as severe. Overall satisfaction with the procedure was also recorded after 1-month post-surgery. For overall satisfaction, 0 described unsatisfied, 1 as low satisfaction, 2 as moderate satisfaction, and 3 as highly satisfied. A specifically pre-designed proforma was used to collect all of the relevant information. The collected data were analyzed using the "IBM-SPSS Statistics", version 26.0. The qualitative data were presented as frequency and percentages. Quantitative variables were given representation through mean and standard deviation. Chi-square was employed to compare categorical data whereas independent sample t-test was performed to compare numeric data. A p-value<0.05 was considered significant.

RESULTS

In a total of 32 patients, there were 25 (78.1%) males while overall mean age was 45.4 ± 12.6 years. In the comparison of demographic and clinical characteristics between the suturing (n=16) and autologous serum (n=16) groups, the gender distribution showed 12 (75.0%) males and 4 (25.0%) females in the suturing group, while the autologous serum group exhibited 13 (81.3%) males and 3 (18.7%) females (p=0.668). The mean age were 46.8 ± 11.5 years and 44.3 ± 13.5 years in the suturing and autologous serum groups, respectively (p=0.577). Pterygium was predominantly located nasally in both groups, with 14 (87.5%) in the suturing group and 13 (81.3%) in the autologous serum group (p=0.626). Laterality distribution did not demonstrate any significant differences in between study groups (n=0.723). The mean size of the pterygium was relatively similar in both groups (p=0.709). The details about

the demographic and clinical characteristics as shown in table 1.

Table 1: Demographic and Clinical Characteristics of Patients in Both Study Groups (N=32)

| Demographic and Clinical Characteristics	Groups		p-Value
	Suturing	Autologous Serum	
Gender N (%)			
Male	12 (75.0%)	13 (81.3%)	0.668
Female	4 (25.0%)	3 (18.7%)	
Residence N (%)			
Rural	11 (68.8%)	9 (56.2%)	0.465
Urban	5 (31.2%)	7 (43.8%)	
Location N (%)			
Nasal	14 (87.5%)	13 (81.3%)	0.626
Temporal	2 (12.5%)	3 (18.7%)	
Laterality N (%)			
Left	7 (43.8%)	8 (50.0%)	0.723
Right	9 (56.2%)	8 (50.0%)	
Age (Mean ± SD)			
Age (Years)	46.8 ± 11.5	44.3 ± 13.5	0.577
Size (Mean ± SD)			
Size of Pterygium in mm^2	22.2 ± 1.6	22.4 ± 1.4	0.709

The mean duration of surgery was 35.6 ± 4.8 minutes in suturing group versus 26.4 ± 2.9 minutes in autologous group (p<0.000). Evaluation of post-surgery ocular discomfort showed that significantly better results were obtained among patients of autologous serum group (p=0.024) and the details about the distribution as shown in figure 1.
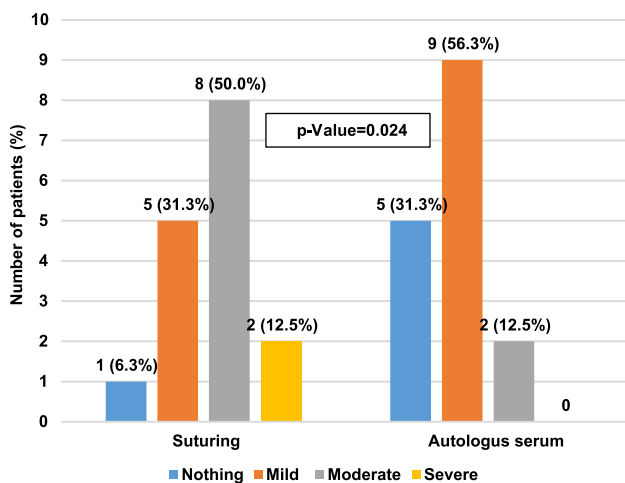
Figure 1: Comparison of Post-Surgery Ocular Discomfort Score (n=32)

Significantly better satisfaction scores were recorded among patients of autologous serum group when compared to patients undergoing suturing technique (p=0.001) and the detailed distribution as shown in figure 2.
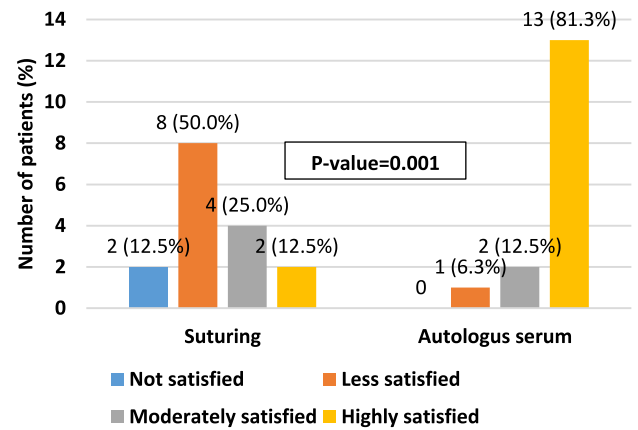
Figure 2: Satisfaction Score (n=32)

Post-surgery complications were assessed in both study groups and no statistically significant differences were observed among patients of both study groups (p>0.05), as shown in table 2.

Table 2: Post-Surgery Complications in Both Study Groups

Demographic and Clinical Characteristics	Groups		p-Value
	Suturing N (%)	Autologous Serum N (%)	
Graft Edema	6 (37.5%)	3 (18.8%)	0.238
Graft Retraction	2 (12.5%)	3 (18.8%)	0.626
Sub-Graft Hematoma	2 (12.5%)	1 (6.3%)	0.544
Graft Loss	–	1 (6.3%)	0.309
Infection	1 (6.3%)	–	0.309

DISCUSSION

The main objectives of pterygium surgery are to remove the fibrovascular membrane and prevent its recurrence. Removing the pterygium and replacing the exposed sclera with a conjunctival autograft that contains limbal stem cells is a suitable method that can effectively prevent pterygium from reoccurring [12, 13]. By acting as a barrier, these limbal stem cells inhibit the migration of conjunctival cells onto the corneal surface. In the current study, two techniques for fixing the conjunctival graft were compared. In a group of patients, the traditional suturing method was employed, whereas autologous serum as tissue adhesive was used in other patients. It was observed that, with suturing the autologous serum technique took significantly less time to complete the surgery (35.6 ± 4.8 vs. 26.4 ± 2.9 minutes, p<0.000). Suturing, while effective, increase operating time and required greater skill to carry on with it. These observations align with the findings of Elwan SA and Ti SE et al [13, 14]. Postoperative discomfort was notably lower in autologous serum patients, consistent with studies by Sharma A et al., and Khedr et al., [15, 16]. Recurrence, a major concern post-surgery, was absent in both groups in our study, mirroring findings by De Wit et al., although other studies reported recurrence rates of 4.7%-6% in sutured or sutureless methods [9, 17, 18]. Graft loss, another critical complication, was observed in

6.3% of cases in autologous group versus none in the suturing group. The primary reasons for graft dehiscence and loss were identified to be greater severity and vascular pterygium, insufficient blood supply for graft adhesion, and thicker grafts, including Tenon's capsule. Post-surgery graft edema was more frequent in suturing groups versus autologous group (37.5% vs. 18.8%, p=0.238) but typically resolved within 7-10 days post-surgery. Similar trends were noted in studies by Sharma A et al [15]. Patients treated with autologous serum showed a higher rate of graft retraction and remained stationary, not resulting in graft dehiscence, as noted in studies by Elwan SA [13]. Some other researchers have found pyogenic granuloma, although uncommon, at the edge of the conjunctival graft [11]. It may result from Tenon's reaction to sutures, localized graft loss emerged only in 1 patient from autologous serum patients. Strategies to potentially circumvent graft loss involve creating a thick film of blood over the recipient bed before graft placement and ensuring the use of thin and uniform grafts without the inclusion of Tenon's capsule [19, 20]. These modifications can enhance graft adherence and minimize the risk of graft dehiscence or loss, thus potentially mitigating this complication in the autologous serum method. Being a single center study conducted on a relatively small size were some of the limitations of this study. Studies evaluating long term outcomes of the studied approaches should be conducted to evaluate the long-term effectiveness and safety of these techniques.

CONCLUSIONS

When considering efficacy, both techniques demonstrated comparable outcomes. However, in terms of postoperative discomfort and surgical duration, the autologous serum method showed significant advantages by presenting reduced discomfort and shorter surgical times.

Authors Contribution

Conceptualization: ZA, SF, MK
Methodology: ZA, NN, SAM, MJK
Formal analysis: ZA, NN, MK, SAM, MJK
Writing, review and editing: ZA, NN, SF, MK, SAM, MJK

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

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

REFERENCES

[1] Johnson RD, Pai VC, Hoft RH. Historical approaches to pterygium surgery, including bare sclera and adjunctive beta radiation techniques. Pterygium: Techniques and Technologies for Surgical Success. 2012 Jun; 2012: 27-36. doi: 10.1201/9781003526094-2.

[2] Shahraki T, Arabi A, Feizi S. Pterygium: an update on pathophysiology, clinical features, and management. Therapeutic Advances in Ophthalmology. 2021 May; 13: 25158414211020152. doi: 10.1177/25158414211020152.

[3] Van Acker SI, Haagdorens M, Roelant E, Rozema J, Possemiers T, Van Gerwen V *et al.* Pterygium Pathology: A Prospective Case-Control Study on Tear Film Cytokine Levels. Mediators of Inflammation. 2019 Nov; 2019(1): 9416262. doi: 10.1155/2019/9416262.

[4] Fekadu SA, Assem AS, Adimassu NF. Prevalence of pterygium and its associated factors among adults aged 18 years and above in Gambella town, Southwest Ethiopia, May 2019. PLOS One. 2020 Sep; 15(9): e0237891. doi: 10.1371/journal.pone.0237891.

[5] Sharma B, Bajoria SK, Mishra M, Iqubal N. Refractive outcomes of simultaneous pterygium and cataract surgery with fibrin glue. Cureus. 2021 Nov; 13(11): e19857. doi: 10.7759/cureus.19857.

[6] Singh SK. Pterygium: epidemiology prevention and treatment. Community Eye Health. 2017; 30(99): S5.

[7] Suryawanshi MP, Isaac R, Suryawanshi MM. Pterygium excision with conjunctival autograft fixed with sutures, glue, or autologous blood. Oman Journal of Ophthalmology. 2020 Jan; 13(1): 13-7. doi: 10.4103/ojo.OJO_113_2019.

[8] Chu WK, Choi HL, Bhat AK, Jhanji V. Pterygium: new insights. Eye. 2020 Jun; 34(6): 1047-50. doi: 10.1038/s41433-020-0786-3.

[9] Bhatia J, Varghese M, Narayanadas B, Bhatia A. Cut-and-place technique of pterygium excision with autograft without using sutures or glue: Our experience. Oman Journal of Ophthalmology. 2017 May; 10(2): 81-6. doi: 10.4103/ojo.OJO_208_2015.

[10] Thatte S, Dube AB, Sharma S. Efficacy of autologous serum in fixing conjunctival autografts of various sizes in different types and grades of pterygium. Journal of Ophthalmic & Vision Research. 2019 Apr; 14(2): 136. doi: 10.4103/jovr.jovr_227_17.

[11] Minj A and Satapathy J. Conjunctival Autograft using Autologous Serum versus Suturing Technique in Primary Pterygium: A Randomised, Prospective, Comparative Study. Journal of Medical Science and Clinical Research. 2018 Apr; 6(4). doi: 10.18535/jmscr/v6i4.198.

[12] Gulani AC and Gulani AA. Cosmetic pterygium surgery: Techniques and long-term outcomes. Clinical Ophthalmology. 2020 Jun; 18: 1681–7. doi: 10.2147/OPTH.S251555.

[13] Elwan SA. Comparison between sutureless and glue free versus sutured limbal conjunctival autograft in primary pterygium surgery. Saudi Journal of Ophthalmology. 2014 Oct; 28(4): 292-8. doi: 10.1016/j.sjopt.2014.03.012.

[14] Ti SE, Chee SP, Dear KB, Tan DT. Analysis of variation in success rates in conjunctival autografting for primary and recurrent pterygium. British Journal of Ophthalmology. 2000 Apr; 84(4): 385-9. doi: 10.1136/bjo.84.4.385.

[15] Sharma A, Raj H, Gupta A, Raina AV. Sutureless and glue-free versus sutures for limbal conjunctival autografting in primary pterygium surgery: a prospective comparative study. Journal of Clinical and Diagnostic Research. 2015 Nov; 9(11): NC06–NC09. doi: 10.7860/JCDR/2015/15689.6789.

[16] Khedr Mohamed M, Rashed AE, Mahmoud Mohamed Hasan M. Sutureless versus sutured conjunctival autograft for surgical treatment of pterygium. Al-Azhar Medical Journal. 2020 Jul; 49(3): 947-56. doi: 10.21608/amj.2020.91619.

[17] De Wit D, Athanasiadis I, Sharma A, Moore J. Sutureless and glue-free conjunctival autograft in pterygium surgery: a case series. Eye. 2010 Sep; 24(9): 1474-7. doi: 10.1038/eye.2010.75.

[18] Mahdy MA and Bhatia J. Treatment of primary pterygium: role of limbal stem cells and conjunctival autograft transplantation. Oman Journal of Ophthalmology. 2009 Jan; 2(1): 23-6. doi: 10.4103/0974-620X.48418.

[19] Nuzzi R and Tridico F. How to minimize pterygium recurrence rates: clinical perspectives. Clinical Ophthalmology. 2018 Nov; 12: 2347-2362. doi: 10.2147/OPTH.S186543.

[20] Kodavoor SK, Rathi N, Dandapani R. Tuck in versus cauterisation of graft edge in pterygium management: A comparative retrospective interventional analysis. Oman Journal of Ophthalmology. 2022 May; 15(2): 193-7. doi: 10.4103/ojo.ojo_277_21.

Original Article

Comparative Analysis of Tinted X-Chrome Contact Lenses and Red Filters on Color Vision Impairment

Maryam Jabbar[1*], Amna Aslam[1], Maryam Faryad[1], Ayesha Mehboob[1], Naveera Zahid[1] and Marriam Amjad[1]

[1]Department of Optometry, The University of Faisalabad, Faisalabad, Pakistan

ARTICLE INFO

ABSTRACT

Accurate color vision is necessary for doing daily tasks efficiently. Even so, numerous individuals experience color vision impairment. **Objective:** To evaluate and compare the effect of x-chrome contact lenses (CLs) and red filters on color vision deficient. **Methods:** Cross-sectional study was conducted at Madinah Teaching Hospital, Faisalabad. Data were collected by non-probability purposive sampling technique. Congenital color blindness, 15-35 years, red-green deficient were included. Acquired color blindness, active ocular diseases, systemic diseases were excluded. 30 red-green color vision deficient, divided in 2 groups, 15 used CLs and 15 used RF. Visual acuity, contrast sensitivity, stereopsis and color vision were recorded at baseline and after wearing lenses. Data were analyzed by using SPSS version 23.0. **Results:** Mean age was 24.53 ± 6.68. After using x-chrome CL, mean number of correctly read plates increased to 22.55 ± 1.27 from the baseline evaluation of 1 ± 1.679 (p=0.00). Comparably, baseline performance was 1 ± 1.89 plates successfully read; using red filters, that number increased to 22.89 ± 1.03 (p = 0.00). With red filters, the mean contrast sensitivity decreased from 1.35 ± 0.32 to 1.31 ± 0.56 (p = 0.004), and with x-chrome lenses, it decreased from 1.34 ± 0.45 to 1.32 ± 0.97 (p = 0.02). Mean stereopsis value was 55.33 ± 13.02 prior to x-chrome contact lens insertion; this value decreases to 67.33 ± 12.47 (p = 0.00). Likewise, mean stereopsis value was 54.02 ± 11.05 before to applying red filters, it decreases significantly to 66.89 ± 11.98 (p=0.00). **Conclusions:** X-Chrome CLs and red filter has significantly improved color vision. Visual acuity remains unchanged. Contrast sensitivity and stereopsis showed slight reduction in both groups.

INTRODUCTION

A condition affecting the eyes that makes it difficult to see and differentiate between certain hues is called color vision insufficiency (CVD) [1]. Although complete color blindness where only grayscale vision is possible is exceedingly rare, the phrase "color blindness" is frequently used to describe CVD. This may be an acquired or congenital disorder [2]. Color Vision Deficiency (CVD) is a common congenital defect, more common in males [3,4]. People sometimes don't become aware of their color vision deficiency until they are subjected to pre-employment exams, or even later, when they are subjected to routine health screenings [5, 6]. Such delayed diagnoses can cause psychological strain and have a direct impact on livelihoods, which makes them very upsetting. As a result, CVD can seriously limit employment prospects and have an impact on mental health [7, 8]. To effectively carry out daily duties precisely, one needs accurate color vision [9]. It is especially significant for professionals in the medical field, industrial workers, pilots, sailors, and signalmen. Therefore, before assigning individuals to various roles in both government and private companies, color vision evaluations must be performed [10, 11]. The main cause of color vision impairment is genetics, most commonly x-linked recessive inheritance, but it can also develop as a result of diseases such retinitis pigmentosa, diabetes, glaucoma, and macular degeneration [12-18]. Medical professionals can use a variety of instruments to evaluate CVD in clinical settings. Of them, the Ishihara plates test is particularly noteworthy [19]. No cure currently exists for any type of CVD, though efforts to enhance color vision

have been made. One method is to use tinted x-chrome contact lenses, and another is to utilize red filters [20, 21]. The X-chromosome's spatial frequency is used to build tinted x-chrome contact lenses that are used to treat defects in red-green color vision [22, 23]. When worn in only one eye, the x-chrome lens is a corneal contact lens that corrects color deficiencies. It is employed in binocular viewing scenarios and functions as a broad-band filter. It is a color-coded contact lens, worn monocular in the non-dominant eye. The lens is red in center and transparent in peripheral. The principle is to create what is referred to as retinal rivalry, which results in the brain being able to better distinguish between shades of colors [23, 24]. Through the process of retinal rivalry, information from each eye is alternated such that a new perception of color discrimination is observed by an individual. Red filters have been suggested as a therapy strategy for people who are color deficient. These filters absorb other colors and preferentially transmit red wavelengths, which may improve color perception in a scene, provide it a warmer tone, and create contrast between various colors [25, 26]. The study's objectives were to evaluate and compare the effects of red filters and x-chrome contact lenses on patients who also had a red-green color vision defect in terms of their visual function (visual acuity, contrast sensitivity, and color vision). The purpose of this study is to determine the most effective modality for patients with CVD to enhance their visual functions.

METHODS

A cross sectional study design was conducted at Madinah Teaching Hospital, Faisalabad. The duration of study was from January 2024 to April 2024. IRB approval letter number is TUF/IRB/265/23 given by ethical institutional review board of The University of Faisalabad on 26 December 2023. 30 participants were included in the study's sample, which was calculated using Rao software. These individuals divided in two groups 15 individuals in each group, group 1 used x-chrome contact lenses while group 2 used red filters. Non probability purposive sampling technique was used in this study. Inclusion criteria for this study were aged 15-35 years, both genders, emmetropes, congenital color blindness, red-green deficient. Exclusion criteria was acquired color blindness, refractive errors, patient with dry eye, contact lens user, active ocular disease, systemic disease (diabetes, multiple sclerosis, alzheimer's disease and parkinson's disease), optic nerve disorders, glaucoma and macular degeneration. LogMAR chart was employed to evaluate visual acuity and the Titmus Fly Test was utilized to test stereopsis. The Pelli-Robson Chart was utilized to ascertain the contrast sensitivity. Ishihara Plates was used for the assessment of red-green color vision defiency. X-Chrome contact lenses were worn by subjects in group 1

who had a red-green color vision deficit, while red filters were used by subjects in group 2. For the collection of data, a self-structured proforma was used to investigate visual acuity, color vision, contrast sensitivity and stereopsis. Verbal consent was taken from the patients, when patients were agreed then written consent was also taken from the patients and detailed history was taken. After obtaining the subject's informed consent, the data were collected. The objective of the research was also discussed to the subject. A comprehensive eye examination using a slit lamp was performed in an attempt to recruit patients. Using a non-probability purposive sampling technique, thirty patients with color vision impairments have been selected for this study and split into two groups. Fifteen patients in group 1 used x-chrome contact lenses, and fifteen patients in group 2 wore red filters. After that, baseline pre-screening records of visual function tests were completed for both groups. These tests included visual acuity, contrast sensitivity, the Titmus fly test, and the Ishihara testing for color vision evaluation. Patients then had the intervention (red filter and x-chrome contact lenses) on for six hours, during which time visual function tests were performed afterward to analyze the post-intervention data for both groups. Patients wear x-chrome contact lenses and red filters monocularly. To determine whether using red filters or x-chrome CLs may improve color discrimination, the same color vision test (ishihara testing) from the pre-screening were performed yet again. Any modifications to visual acuity brought about by the filters or lenses were measured. X-Chrome CLs and red filters were used, and their possible effects on stereopsis were assessed in light of how they may affect color perception. On a scale of 0 to 10, patients in both groups were asked to rate how satisfied they were with the intervention either the red filter or the x-chrome contact lenses. The minimal degree of satisfaction or dissatisfaction with the intervention was represented by a score of 0, and the highest level of satisfaction was indicated by a score of 10. Descriptive statistics was used to analysed age distribution, gender distribution, occupation, family history and color vision interpretation. Paired t-test was used to analyse contrast sensitivity and stereopsis with and without both interventions. The contrast sensitivity and stereopsis of both groups were compared using an independent t-test to determine which modality red filters or x-chrome contact lenses.

RESULTS

Descriptive statistics analysis was used to investigate the age distribution; the selected age range was 15-35 years. Total number of color vision deficient subjects was 30. In this study 15 was the minimum age while 35 was maximum age. The mean of the age distribution was 24.53 ± 6.68. Descriptive statistics analysis was used to investigate the gender distribution among 30 subjects. The gender

distribution reveals that there were 20 males (66.7%) and 10 females (33.3%). Frequency distribution showed that 4 (13.33%) patients had no family history on record, while 26 participants (86.66%) had a family history of color vision impairment. A descriptive statistical analysis of the 30 individuals' occupations indicated that 14 were students, 12 were office workers (including teachers and administrative staff), and 4 were factory workers (Table 1).

Table 1: Demographic Variable Analysis

Variables	Frequency (%)
Age Distribution (n=30)	
Age (Mean ± SD)	24.53 ± 6.68
Gender Distribution N (%)	
Male	20 (66.66%)
Female	10 (33.33%)
Family History of Color Vision Impairment N (%)	
No	26 (86.66%)
Yes	4 (13.33%)
Occupation N (%)	
Others (Students)	14 (46.67)
Office Worker (Teachers, Administrative Staff)	12 (40 %)
Factory Worker	4 (13.33 %)

Ishihara's plates were used for assessment of color vision deficiency. A paired t-test analysis for Group 1 demonstrated that the mean number of correctly read plates at baseline was 1 ± 1.67, which significantly increased to 22.55 ± 1.27 with the use of x-chrome contact lenses (p = 0.00). Similarly, the red filter group's mean number of correctly read plates at baseline was 1 ± 1.89, but after applying the red filters, that number increased significantly to 22.89 ± 1.03 (p = 0.00). These results show that wearing red filters and x-chrome contact lenses improved color vision in both groups. There was no reduction in binocular visual acuity with x-chrome contact lens and red filter remains same in all CVD patients. Contrast sensitivity was examined using a paired t-test both with and without intervention (x-chrome and red filters). The outcomes demonstrated that both therapies significantly reduced contrast sensitivity. The mean contrast sensitivity dropped (p = 0.004) for the red filter intervention, going from 1.35 ± 0.32 to 1.31 ± 0.56. Comparably, the mean contrast sensitivity for the x-chrome intervention dropped from 1.34 ± 0.45 to 1.32 ± 0.97 (p = 0.02). This suggests that contrast sensitivity is greatly decreased by both x-chrome and red filters. Titmus fly test was used for assessment of stereopsis. The results of the analysis indicate that there were differences in the stereopsis. Prior to the x-chrome contact lens insertion, Group 1's mean value was 55.33 ± 13.02. Following insertion, the average values were 67.33 ± 12.47, with a p-value of 0.00. Likewise, prior to employing red filters, Group 2's mean value was 54.02 ± 11.05. Following the application of red filters, the mean values were 66.89 ± 11.98, with a p-value 0.00. The mean stereopsis

values decreased after both therapies in comparison to the baseline. Significant results were found using paired t-tests, suggesting that both x-chrome contact lenses and red filters reduce stereopsis (Table 2).

Table 2: Comparisons of Color Vision, Contrast Sensitivity, Stereopsis With and Without Contact Lenses and Red Fillers

Groups	Group 1 (X-Chrome CL) (Mean ± SD)			Group 2 (Red Filters) (Mean ± SD)		
Intervention	Baseline	With X-Chrome CL	p-value	Baseline	With RF	p-value
Color Vision Assessment	1 ± 1.67	22.55 ± 1.27	0.00	1 ± 1.89	22.89 ± 1.03	0.00
Contrast Sensitivity	1.34 ± 0.45	1.32 ± 0.97	0.02	1.35 ± 0.32	1.31 ± 0.56	0.004
Stereopsis	55.33 ± 13.03	67.33 ± 12.47	0.00	54.02 ± 11.05	66.89 ± 11.98	0.00

X-Chrome contact lenses and red filters were compared for efficacy using the Ishihara test with an independent t-test. Both treatments help patients distinguish between colors and improve their perception of color, according to the highly non-significant results (0.71). An independent t-test was conducted to compare the contrast sensitivity for group 1 (X-chrome contact lens) and group 2 (red filter). There was no significant difference p=0.61 in the score. Mean value for group 1 mean=1.32 ± 0.97 for group 2 mean=1.31 ± 0.56. Contrast sensitivity was reduced after use of CLs and red filter. An independent t test was conducted to compare the steropsis for group 1 (X-chrome contact lens) and group 2 (red filter). There was no significant difference p=0.98 in the score. Mean value for group 1 mean= 67.33 ± 12.47 for group 2 mean= 66.89 ± 11.98. Contrast sensitivity was reduced after use of CLs and red filter (Table 3).

Table 3: Comparative Analysis of Color Vision, Contrast Sensitivity, Stereopsis Both Groups

Variable	Group 1 (X-chrome CL) Mean ± SD	Group 2 (Red Filters) Mean ± SD	p-value
Color Vision Assessment	22.55 ± 1.27	22.89 ± 1.03	0.71
Contrast Sensitivity	1.31 ± 0.56	1.32 ± 0.97	0.61
Stereopsis	67.33 ± 12.47	66.89 ± 11.98	0.98

Following the evaluation of the mean number of correctly read plates by patients in the two groups, the number of subjects was also assessed according to pass/fail responses. However, all subjects passed the Ishihara test monocularly when red filters and x-chrome contact lenses were placed in the non-dominant eye. However, 2 patients in group 1 using x-chrome lenses and 3 subjects in group 2 using red filters failed the test binocularly. If a CVD subject answers "pass," it means they properly identified the Ishihara plate; if they answer "fail," it means they either didn't identify the plate at all or identified it wrongly, classifying them as either protanopia or deuteranopia. The color vision of CVD individuals was analyzed using descriptive statistics both before and after they wore x-chrome contact lenses and red filters (Table 4).

Table 4: Color Vision Assessment of Both Groups

Number of Subjects	Group 1 (With X-Chrome Contact Lens)		Group 2 (With Red Filters)	
Interpretation	Pass	Fail	Pass	Fail
Monocular	15	0	15	0
Binocular	13	2	12	3

Both the red filter users and the x-chrome contact lens users were asked to rate their level of satisfaction on a 0–10 scale after the evaluation. A score of 0 represented the least amount of satisfaction or dissatisfaction while a score of 10 represented the highest level of contentment. A mean satisfaction score of 7.01 with a standard deviation of 1.01 was recorded by users of x-chrome contact lenses, while a mean satisfaction score of 5.7 with a standard deviation of 1.32 was reported by users with red filters (Table 5).

Table 5: Level of Satisfaction

Level of Satisfaction	Group 1 (Mean ± SD)	Group 2 (Mean ± SD)
	7.01 ± 1.01	5.7 ± 1.32

D I S C U S S I O N

Almutairi N *et al.,* conducted study in which red filter significantly improved color discrimination, particularly the deutan subjects. Improved subjects improved from severe deutan to mild deutan in all deutan subjects and from severe protan to mild deutan in one subject when tested with ColorDx with mean value of 34.9 ± 2.5 and 50 ± 9.34 and p=0.006, respectively, Red filter was a highly clinically significant in improvement of color perception of CVD subjects while in addition performance with red filter was significantly better compared to enchroma 34.9 ± 2.5 and 49.6 ± 7.8 p=0.004, respectively and green filter 34.9 ± 2.5 and 51.0 ± 8.8 p =0.003 respectively [27]. Current study concluded that in a comparable manner, the mean number of plates correctly read at baseline with red filters was 1 ± 1.89; after putting red filters, the number ascended to 22.89 ±1.03. These results show that wearing red filters improved color vision. Both studies concluded that wearing red filter improve the color vision of CVD subjects (Red-Green Deficient) so both studies correlate with each other by showing significant improvement in color vision. Sodhi PK *et al.,* conducted in which the mean number of "TES/plates not read" was 8.23 ± 6.04 and following use of red-tinted lenses, the TES reduced to 6.16 ± 6.27 the mean reduction in errors was 2.11 ± 4.54 (P value = 0.001). In category 22-25 plates, the mean number of TES/plates not read was 1.58 ± 1.67 and following the use of red-tinted lenses, this reduced to 1.14 ± 1.53 the mean reduction in errors was 0.47 ± 1.05 (p=0.001) which showed significant improvement in color vision deficient subjects [28]. Present study concluded Group 1, at baseline 1 ± 1.67 plates were correctly read on mean. This mean increased to 22.55 ± 1.27 with x-chrome contact lenses. These results show that wearing x-chrome

contact lenses improved color vision, so both studies correlate and shown significant results. Brinda HS *et al.,* conducted study that 7 patients were having protanomaly while 3 were having deutranomaly. Mean value and standard deviation for the contrast sensitivity after wearing chrome lens was 0.07 and 0.057 respectively with p value = 0.010 shows that there was no significant change in contrast sensitivity with wearing a x-chrome contact lens [29]. Current study concluded that the mean contrast sensitivity dropped (p = 0.004) for the red filter intervention, going from 1.35 ± 0.32 to 1.31 ± 0.56. Comparably, the mean contrast sensitivity for the x-chrome intervention dropped from 1.34 ± 0.45 to 1.32 ± 0.97 (p = 0.02). Previous study showed that no significant change in contrast sensitivity after wearing x-chrome contact lens while current study revealed that there was reduction in contrast sensitivity after wearing x-chrome contact lens and red filter. Mutalib HA *et al.,* conducted study that showed that the mean value and standard deviation value of stereopsis at baseline was 2.62 ± 0.6. While after wearing type 1 light red contact lens the means value and standard deviation value increases to 5.10 ± 1.4 while wearing type 2 dark red contact lens the mean values and standard deviation increases to 5.76 ± 1.51 which shows reduction in stereopsis [30]. The current study showed that Prior to the x-chrome contact lens insertion, Group 1's mean value was 55.33 ± 13.02. Following insertion, the average values were 67.33 ± 12.47, with a p-value of 0.00. Likewise, prior to employing red filters, Group 2's mean value was 54.02 ± 11.05. Following the application of red filters, the mean values were 66.89 ± 11.98, with a 0.00 p-value. The mean stereopsis values decreased after both therapies in comparison to the baseline. Both studies concluded that stereopsis shows reduction after wearing contact lens and red filter. A significant gap in this research is the lack of subsequent assessments. More specifically, the impact of using red filters and contact lenses on participants' daily activities was not evaluated. A thorough understanding of the long-term efficacy and useful uses of these medicines is hampered by this lack of follow-up. In order to assess the long-term efficacy and practicality of red filters and x-chrome contact lenses in improving daily tasks and general visual function particularly color vision further research should examine follow-up assessments. The sample size in this study is limited, necessitating future research with a larger sample size to better understand the implications. Participants also differed in their preferences based on factors other than functioning. Beauty-obsessed people frequently selected x-chrome contact lenses. Red filters were preferred by those who found it difficult to adjust to these contact lenses but desired effectiveness despite the fact they weren't appealing either when worn on a single lens. Red filters and x-chrome contact lenses should be regarded as potential

therapy choices for those with red-green color vision insufficiency, according to the study's findings. It has been demonstrated that these therapies enhance color perception and the capacity to differentiate between different color tones. Consequently, it is advised that people with color vision deficits use red filters or x-chrome contact lenses to improve their color vision, especially if they work in fields like fine art or graphic design where accurate color discrimination is necessary.

CONCLUSIONS

Red filters and x-chrome contact lenses have been demonstrated to improve color vision deficiencies in CVD patients when compared to baseline findings. The two treatment options showed promise in improving the individuals' color vision impairment associated with CVD. Both before and after wearing contact lenses and filters, visual acuity remains unaltered. On the other hand, using red filters with x-chrome contact lenses reduced contrast sensitivity and stereopsis.

Authors Contribution

Conceptualization: MJ
Methodology: AA, AM, MA
Formal analysis: NZ
Writing, review and editing: MJ, MF

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

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1]   Hosein C. Review article on color vision defect. 2020 Jun.

[2]   Bartolomeo P. Color vision deficits. Current Neurology and Neuroscience Reports. 2021 Oct; 21: 1-7. doi: 10.1007/s11910-021-01137-8.

[3]   Mitiku RG, Tolera BS, Tolesa ZG. Prevalence and allele frequency of congenital color vision deficiency (CCVD) among students at Hawassa University, Ethiopia. Journal of the Egyptian Public Health Association. 2020 Dec; 95: 1-6. doi: 10.1186/s42506-020-00037-y.

[4]   Hashemi H, Khabazkhoob M, Pakzad R, Yekta A, Heravian J, Nabovati P *et al.* The prevalence of color vision deficiency in the northeast of Iran. Journal of Current Ophthalmology. 2019 Mar; 31(1): 80-5. doi: 10.1016/j.joco.2017.05.005.

[5]   Hathibelagal AR. Implications of inherited color vision deficiency on occupations: A neglected entity!. Indian Journal of Ophthalmology. 2022 Jan; 70(1): 256-60. doi: 10.4103/ijo.IJO_1100_21.

[6]   Hewett R and Ellis L. An investigation into factors contributing towards employment outcomes for individuals with vision impairment. Available from: An-investigation-intofactors-contributing-towards-employment-outcomes-for-individuals-with-vision-impairment-Final-clean. docx(live. com). 2021.

[7]   Chakrabarti S. Psychosocial aspects of color vision deficiency: Implications for a career in medicine. National Medical Journal of India. 2018 Mar; 31(2). doi: 10.4103/0970-258X.253167.

[8]   Klooster S. The inclusion of individuals with color vision deficiencies. 2016 May.

[9]   Ikeuchi K, editor. Computer vision: A reference guide. Cham: Springer International Publishing. 2021. doi: 10.1007/978-3-030-63416-2.

[10]   Barbur JL and Rodriguez-Carmona M. Color vision requirements in visually demanding occupations. British Medical Bulletin. 2017 Jun; 122(1): 51-77. doi: 10.1093/bmb/ldx007.

[11]   Stoianov M, de Oliveira MS, dos Santos Ribeiro Silva MC, Ferreira MH, de Oliveira Marques I, Gualtieri M. The impacts of abnormal color vision on people's life: an integrative review. Quality of Life Research. 2019 Apr; 28: 855-62. doi: 10.1007/s11136-018-2030-1.

[12]   Basta M and Pandya AM. Genetics, X-linked inheritance. 2024 Jan.

[13]   Abeshi A, Bruson A, Beccari T, Dundar M, Colombo L, Bertelli M. Genetic testing for color vision deficiency. The EuroBiotech Journal. 2017 Oct; 1(1): 32-4. doi: 10.24190/ISSN2564-615X/2017/S1.10.

[14]   Couser NL, editor. Ophthalmic Genetic Disease: A Quick Reference Guide to the Eye and External Ocular Adnexa Abnormalities. Elsevier Health Sciences. 2018 Sep.

[15]   Cross N, van Steen C, Zegaoui Y, Satherley A, Angelillo L. Retinitis pigmentosa: Burden of disease and current unmet needs. Clinical Ophthalmology. 2022 Jun; 16: 1993-2010. doi: 10.2147/OPTH.S365486.

[16]   Ouchi J, Kunikata H, Omodaka K, Sato H, Sato H, Ito A *et al.* Color visual acuity in preperimetric glaucoma and open-angle glaucoma. PLOS One. 2019 Apr; 14(4): e0215290. doi: 10.1371/journal.pone.0215290.

[17]   Saeed R, Iqbal I, Bajwa JA, Falak S. Evaluation of color vision and contrast sensitivity in diabetic patients without retinopathy. Advances in Ophthalmology & Visual System. 2019 May; 9(3): 71-6. doi: 10.15406/aovs .2019.09.00349.

[18]   Vemala R, Sivaprasad S, Barbur JL. Detection of early loss of color vision in age-related macular

degeneration-with emphasis on drusen and reticular pseudodrusen. Investigative Ophthalmology & Visual Science. 2017 May; 58(6): BIO247-54. doi: 10.1167/iovs. 17-21771.

[19] Perez A. Color Vision Testing with Readily Available Materials [Doctoral Dissertation]. The University of Alabama at Birmingham; 2021.

[20] Sato K, Inoue T, Tamura S, Takimoto H. Discrimination of colors by red-green color vision-deficient observers through digitally generated red filter. Visual Neuroscience. 2019 Jan; 36: E001. doi: 10.1017/S0952523818000068.

[21] Oli A and Joshi D. Efficacy of red contact lens in improving color vision test performance based on Ishihara, Farnsworth D15, and Martin Lantern Test. Medical Journal Armed Forces India. 2019 Oct; 75(4): 458-63. doi: 10.1016/j.mjafi.2018.08.005.

[22] Sodhi DP, Saraf S, Kishore J. Are X-chrome lenses an occupational succor for the color vision defectives? Journal of Advanced Research in Medical Science and Technology. 2017; 1: 1-6. doi: 10.24321/2394.6539. 201701.

[23] Lakkis C and Weidemann K. Evaluation of the performance of photochromic spectacle lenses in children and adolescents aged 10 to 15 years. Clinical and Experimental Optometry. 2006 Jul; 89(4): 246-52. doi: 10.1111/j.1444-0938.2006.00056.x.

[24] Wendt G and Faul F. Binocular luster-A review. Vision Research. 2022 May; 194: 108008. doi: 10.1016/j.visres .2022.108008.

[25] Huertas R, Valero EM, Gómez-Robledo L, Martínez-Domingo MA, Hernández-Andrés J. Congenital red-green color deficiency: study of the efficacy of commercial color filters. Journal of the International Color Association. 2024; 35: 24-8.

[26] Martínez-Domingo MA, Gómez-Robledo L, Valero EM, Huertas R, Hernández-Andrés J, Ezpeleta S *et al.* Assessment of VINO filters for correcting red-green Color Vision Deficiency. Optics Express. 2019 Jun; 27(13): 17954-67. doi: 10.1364/OE.27.017954.

[27] Almutairi N, Kundart J, Muthuramalingam N, Hayes J, Citek K, Aljohani S. Assessment of EnChroma filter for correcting color vision deficiency. Pacific University (Oregon). 2017 Jul.

[28] Sodhi PK, Gautam A, Rao KC, Archana TR, Sharma N, Marimuthu Y. Color perception on Ishihara plates with red lenses in subjects with low vision due to retinal diseases. Indian Journal of Ophthalmology. 2023 Nov; 71(11): 3534-8. doi: 10.4103/IJO.IJO_2532_22.

[29] Brinda HS, Optom B, Optom M, Partha HC. Functional Vision with X Chrome Lenses. Optom Open Access. 2017 Nov; 2(125): 2476-075. doi: 10.4172/2476-2075.1000125.

[30] Mutilab HA, Sharanjeet-Kaur KL, Choo PF. Special tinted contact lens on color-defects. Clinical Therapeutics. 2012 Jan; 163(3): 199-204.

Original Article

Medical Student's Attitudes towards Implementation of National Licensing Exam (NLE) – A Qualitative Exploratory Study

Saima Bashir[1*] and Rehan Ahmed Khan[2]

[1]Department of Pathology, Gomal Medical College, Dera Ismail Khan, Pakistan
[2]Department of Surgery, Riphah International University, Islamabad, Pakistan

ARTICLE INFO

ABSTRACT

The introduction of the post-qualification National Licensing Examination (NLE) in Pakistan has been met with resistance from the medical students. They are the main stakeholders of medical colleges. **Objective:** To explore the opinions of medical students regarding the feasibility of NLE. **Methods:** An exploratory, qualitative study was conducted at Riphah International University, Islamic international medical college, Rawalpindi and Gomal Medical College, D.I. Khan, KP using in-depth interviews. A sample of 12 medical students from different medical colleges in Pakistan was included. The recorded interviews transcribed verbatim. Thematic analysis was then conducted using NVivo V2 and coded into nodes and daughter nodes, of which 5 themes and 17 subthemes emerged. **Results:** A total of five themes and 17 themes were created. NLE was deemed as a good standardization tool for assessing the competence of medical graduates. Students believed that current MBBS assessment lacks in clinical skills assessment and did not prepare to treat patients upon graduation. However, they did not want to take another exam after the professional exams especially when no incentives are offered to graduates upon clearing. They suggested NLE should be used as a means of constructive feedback for institutions and students to allow them to work on weak areas. **Conclusions:** There were mixed opinions regarding the acceptance of the exam. If medical institutions across the country focus their curricula on developing clinical skills and incentives are provided to the doctors upon clearing, the students would readily accept the exam.

INTRODUCTION

After studying medicine at a medical institute or university, entering the clinical workplace is indeed a crucial part of the medical profession. However, a minimum standard of protocol is required to treat patients and because of this need, several academics and educators believe that all new physicians should be evaluated to ensure they meet a minimum standard of competency [1]. Since every country differs in the core medical education systems such as curriculum design and assessment methods, they differ in the measures required to ensure the quality of medical graduates as well. Nonetheless, the common goal of medical education is to produce physicians who can provide quality care and patient safety. In order to assure quality, several approaches are implemented in medical education including accreditation systems and assessment programs such as the NLE [2]. Recently, NLE has been introduced in South Asia including in Pakistan to assess medical graduates before allowing practice on real patients [3]. The National Medical Authority in Pakistan effectively carried out the NLE test, comprising 200 multiple choice questions as well as 20 Clinical Skilled Examination stations [4]. Moreover, in Pakistan, the growth of private medical colleges over the past two decades has exceeded the capacity of the regulatory system due to weakened regulations by the regulatory authority. Teachers, policymakers, and medical students in Pakistan have been somewhat divided about the National Licensing Exam. Though supporters argue that the NLE would standardize medical education and improve the quality of healthcare generally, critics point out that the

NLE would burden students more and that current curricula are inadequate to prepare them for such assessments [5, 6]. The NLE is planned as a two-step assessment. The initial step is the Multiple-Choice Questions (MCQ) based theory part containing 70% MCQs from clinical sciences and 30% MCQs from basic sciences. A student needs to pass this first step to meet all requirements for the second Clinical Skills Examination (CSE). The students can show up in the first theory component solely after securing their MBBS qualification. The two stages should be passed to accomplish a permanent clinical permit from PMC [4]. There are several stakeholders involved in the implementation of this exam including the government, medical schools, endowment bodies, employers, medical teachers, and students. We believe that students are valuable stakeholders in process of assessment [7]. The NLE is a high-cost policy; therefore, there is a need to understand its impact; what changes it has brought, and what further changes it would bring to medical education [8].

The aim of the study was to explore the attitudes & perceptions of undergraduate medical students in medical colleges in Pakistan regarding the national licensing exam as stakeholders.

METHODS

Ethical approval (Ref No: Riphah/IIMC/ IRC/22/2013) was taken at 27th January, 2022 from the ERC, Riphah international university (Islamic international medical college), Rawalpindi. Written and verbal consent was taken prior to the interviews. Confidentiality and anonymity were assured to the participants. RIU (Riphah International University, Islamic international medical college, Rawalpindi). Gomal Medical College,D.I. Khan, KPK. This research study was carried out in two medical institutions from 1st February, 2022 to 31st July, 2022: The study design was "Qualitative Exploratory". A total of 12 students from both institutions were interviewed. Purposive sampling with maximum variance technique was used. Inclusion criteria was Final year MBBS students (two with top score, two with average & two with failed attempts in the class without gender discrimination) on the basis of the senior class who were about to graduate and appear in NLE in near future to provide the most relevant information.One public-sector medical college in a remote area & one private medical college in the capital city were selected to provide variation in data collection. Exclusion criteria wasAll students not falling in the inclusion criteria as mentioned above were not included in the study to avoid irrelevant data extraction. In-depth semi-structured one-to-one interviews were arranged face-to-face and through zoom meetings depending on the feasibility of the participants. The interviews were audio-recorded. Open-ended questions were used to let the participants have freedom of expression including emotions and gestures. The interview started using the introductory open-ended question "What do you know about licensing examinations nationally and internationally?". The researcher used probes during the interview to get in-depth details as and when required. Afterward, the recorded interviews were transcribed verbatim. Before transcription, the participants were assigned numbers with codes to maintain anonymity and confidentiality. The transcripts were saved on the researcher's laptop hard disk. These transcribed interviews were sent back to participants for checking to ensure credibility and support triangulation. After this stage, the data was transferred to NVivo software v 12 for windows, which is qualitative data management software. Computer-Assisted Qualitative Data Analysis: Computer-Assisted Qualitative Data Analysis (CAQDA) was done using NVivo software version 12.0. All interview files were initially added to a new NVivo file. Then, an Inductive thematic analysis was done. Similar content was exported to individual nodes in NVivo. Then these nodes were re-assessed to evaluate emergent patterns. Recoding was then performed to identify themes and subthemes. The final node files were then exported to MS Word.

RESULTS

In Table 1 total of five themes and 17 subthemes were identified.

Feasibility of NLE: All the participants were well-versed in the concept of a licensing exam. They were somewhat familiar with international licensing exams conducted abroad such as the USMLE in the US and PLAB in the UK. The students made an argument that they are already being assessed by the Pakistan Medical Council (PMC) during the duration of MBBS program, there should not be any standardized exam to check whether the students graduating from these institutions are competent enough or equally competent. While some students deemed NLE unnecessary, many students believed that NLE could bring about a positive change in medical education and practice. They believed that such exams are imperative as the medical profession is a high-risk profession that deals directly with human lives. These students believed that NLE could serve as a platform to validate the medical education program the students go through and put forth the shortcomings in the infrastructure. They were hopeful that the NLE would break the cycle of rote learning common in Pakistan: "The biggest advantage of this is that we will know our system at the MBBS level. Often, our system is rote learning based. We just passed the papers and got the degree"(M1).

Reasons for Having NLE: Two types of learning were identified; rote learning and learning through application of

knowledge & skills. In the medical colleges with curricula higher on the Integration ladder, the curriculum assessed the application of knowledge more efficiently, as compared to medical colleges that still have their curricula closer to the traditional systems. The students expressed that they feel very nervous and unprepared when asked to interact with a real patient. Consequently, fresh medical graduates are not competent enough to practice on real patients: "The thing is that we do not have exposure to the patient directly. We don't know how to deal with the patient. We are just practicing on the dummies. We get more anxious than the patient sometimes while doing."(M3).

Demerits of NLE: Some students stated that they did not understand the point of having an additional assessment instead of improving the assessment system that already exists. The imposition of continuous exams might discourage prospective students from taking up medical education and practice: "We are continuously examined to prove our knowledge; and continuously tested to see our abilities in every aspect, whether it's practical or theoretical. I believe it (NLE) is not necessary. It is just deterring people away from doing medicine." (M5). Moreover, they might neglect patient care and focus more on studying well for the exam and the stress of the exam and getting a passing percentage overshadows everything else.

Areas for Improvement in NLE: The students were quick to embrace the idea of constructive feedback. Through feedback, the students can not only recognize their weak areas which might not have been brought to their attention but it can also aid in improving patient care in the future as it would help work on weak areas and polish already existent skills: "This is going to help because he will know where I need improvement or where I am going well and where I do not need to worry about."(M7). While the majority of the students believed that NLE should be focused more on professional identity formation and competencies instead of just knowledge, two students believed that professional identity cannot be developed through NLE. The majority of the students were in favor of NLE being conducted after house job as they believed that most of the clinical skills are acquired during house job and if NLE is going to assess the graduates based on skills, after house job would be the right time.

Resistance to NLE: Medical students across the country showed great resistance against NLE in Pakistan. The exam does not guarantee a good job and would not add any value to their profession. Similarly, the exam would not guarantee a better income in the future, improve their quality of life, or working conditions, or improve their skills: "The Quality of Life (QoL) "in our country is not what everyone wants. So, a lot of people leave for income and QoL." (M3). Moreover, many students were not willing to take NLE in Pakistan as they believe that the medical system is corrupt and lacks opportunities which are accentuated by the fact that bribery to get jobs is a common practice in Pakistan.

Table 1: Themes and Subthemes

Themes	Subthemes
Feasibility of NLE	Defining Licensing Examinations
	Compared with International Examinations
	Self-Sufficiency of MBB
	Validation of MBBS
	Social Accountability
	Assuring High-Quality Patient Care
Reasons of Having NLE	Curricular Infrastructure
	Competence to Practice
Demerits	Additional Hardships
	Deterrence from Studying Medicine
	Patient Care Affected
Areas of Improvement	Constructive Feedback
	Professionalism
	Timing
Resistance	Incentives Abroad
	Corrupt System in Pakistan
	Deterring from Learning Skills in House Job

DISCUSSION

However, not much is known about the actual effect NLE has on protecting the public from substantial clinical practice and improvements in a country's healthcare system. Literature already in publication shows that responses to licensure tests vary widely. Studies conducted, for example, in the US and the UK have shown that, while students often express concern and tension about the high stakes involved, they typically see licensure tests as essential[9]. Many of the students emphasized the possible advantages of the NLE, which include the possibility of improving the level of medical education and guaranteeing uniformity for medical graduates. This viewpoint is consistent with studies from other nations where excellent standards in healthcare are seen to depend on licensure tests[10, 11]. Significant worry among students about the extra demands the NLE will place was also found by the research. This is consistent with research from across the world that show medical students experience a great deal of stress from the high stakes of licensure tests. This worry is heightened in Pakistan, however, by worries about the uneven quality of education offered by various medical schools, which students worry might make test performance and job prospects even more unequal[12]. About 93% of the students surveyed nationally in the UK on their opinions on the general medical councils' suggested reform of undergraduate medical assessment said that they supported uniformity in the assessment method across medical schools[13].

Similarly, Study by Siddique *et al.,* on stakeholders' perception on the Indonesian Medical Doctor National Competency exam showed that the exam was perceived as a standardization tool to decrease the disparity among various medical schools in the country [14]. Hidayah *et al.,* reported that when NLE was introduced in Indonesia, a large number of students from private colleges failed the exam. The students upon failing multiple times started a protest against NLE. The Indonesian government held the medical institutions to be responsible for the students' failure which forced the medical schools to be more diligent regarding their quality of education. They also restricted the number of students allowed to be admitted to universities that did not meet the accreditation criteria and whose students performed poorly in NLE [13, 15]. With the modular system, the students have to be exposed to the clinical environment beginning from their first year and the students need to study more subjects in one year as opposed to the conventional system which demanded more work from the teachers. This was not feasible for all medical colleges in Pakistan and since the modular system was not mandated, many institutions across Pakistan still use the conventional mode of education [16]. The bulk of students in the current survey believed that their MBBS program does not provide them with sufficient clinical experience to build their confidence in their clinical abilities. Jeyaraju *et al.,* said that because of unprofessional training techniques at hospitals, medical graduates lack easily available practical information and abilities, which make them, unfit to perform on actual patients [15, 17]. Students' recommendations for addressing these issues such as proposals for curriculum changes and better preparation materials were also emphasized by the qualitative data. These suggestions are consistent with methods used in other nations to help students preparing for national examinations, such as thorough review courses and the inclusion of exam-related material into normal courses [18]. Moreover, Rahim F pointed out in his study, the introduction of NLE during house job would make the students and even educators lose focus on developing competencies essential to treating real-life patients which would affect patient care [19]. The licensing exam should focus on assessing the competency of students through a balance in assessing knowledge and clinical skills. In the study by Huwendiek *et al.,* the combination of MCQs and clinical skills assessment was perceived to be appropriate for NLE as it allowed assessing the applied clinical knowledge in addition to practical and communication skills. This was perceived as a shift towards competency-based assessment [17, 20]. NLE has faced resistance from students in Pakistan as it doesn't offer the students any benefits. International licensing exams like the USMLE are taken by thousands of

CONCLUSIONS

The study explores the students' feelings and opinions about the National Licensing Exam as stakeholders. The students were familiar with the value and significance of conducting a high-stakes exam nationwide. The students expressed mixed opinions regarding the acceptance of exams.

Authors Contribution

Conceptualization: SB
Methodology: SB
Formal analysis: SB, RAK
Writing, review and editing: SB, RAK

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

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

REFERENCES

[1]   Saleem S and Afzal S. Implementation of National Licensing Examination (NLE) and its Impact on Global Healthcare: A Systematic Review. Annals of King Edward Medical University. 2022 May; 28(1): 128-34. doi: 10.21649/akemu.v28i1.5022.

[2]   Prihatiningsih TS. The role of Indonesian Medical Council in assuring the quality of medical education. Jurnal Pendidikan Kedokteran Indonesia: The Indonesian Journal of Medical Education. 2016 Nov; 5(3): 181-91. doi: 10.22146/jpki.25452.

[3]   Jawaid W. The National Licensing Examination: A Comparison with Other Major Medical Licensing Examinations and Practical Suggestions for Wider Acceptance. Khyber Medical University Journal. 2021 Dec; 13(4): 185-6. doi: 10.35845/kmuj.2021.22251.

[4] Flores-Cohaila JA. Factors associated with medical students' scores on the National Licensing Exam in Peru: a systematic review. Journal of Educational Evaluation for Health Professions. 2022 Dec; 19. doi: 10.3352/jeehp.2022.19.38.

[5] Archer J, Lynn N, Coombes L, Roberts M, Gale T, Price T *et al.* The impact of large scale licensing examinations in highly developed countries: a systematic review. BioMed Central Medical Education. 2016 Dec; 16: 1-1. doi: 10.1186/s12909-016-0729-7.

[6] Demmer I, Selgert L, Altiner A, Baum E, Becker A, Schmittdiel L *et al.* Implementation of a uniform nationwide medical licensing examination in general practices. A feasibility study. German Medical Sciences Journal for Medical Education. 2021 Jun; 38(5). doi: 10.3205/zma001492.

[7] Iqbal T. Rapid changes are deleterious for health profession. Pakistan Journal of Physiology. 2020 Dec; 16(4): 1-2.

[8] Alam DW, Amin A, Hussain N. Religiosity and Quality of Life and Well-being in districts of Khyber Pakhtunkhwa, Pakistan. International Journal of Business and Management Sciences. 2021 Dec; 2(4): 109-121.

[9] Cho HB, Sung WS, Hong J, Kang Y, Kim EJ. A Survey on Perceptions of the Direction of Korean Medicine Education and National Licensing Examination. InHealthcare. 2023 Jun; 11(12): 1685. doi: 10.3390/healthcare11121685.

[10] Reid H, Gormley GJ, Dornan T, Johnston JL. Harnessing insights from activity system–OSCEs past and present expanding future assessments. Medical Teacher. 2021 Jan; 43(1): 44-9. doi: 10.1080/0142159X.2020.1795100.

[11] Price T, Lynn N, Coombes L, Roberts M, Gale T, de Bere SR *et al.* The international landscape of medical licensing examinations: a typology derived from a systematic review. International Journal of Health Policy And Management. 2018 Sep; 7(9): 782. doi: org/10.15171/ijhpm.2018.32.

[12] Almazan JU. Nursing student's academic performance and success in nursing licensure examination: A narrative literature review. Majmaah Journal of Health Sciences. 2019 May; 7(2): 75-84. doi: 10.5455/mjhs.2019.02.008.

[13] Hidayah RN, Fuller R, Roberts TE. Licensing examinations in southeast asia: Lesson learnt from exploring changes in education policy. Asia Pacific School. 2020 Sep; 5(3): 5-9. doi: 10.29060/TAPS.2020-5-3/GP2178.

[14] Siddique H, Hasnain S, Minhas R, Shahid N, Hanif R, Sidhu MJ. Hybrid versus Traditional Teaching in the Subject of Anatomy: A Comparison Based On Results of Students. Pakistan Armed Forces Medical Journal. 2024 Apr; 74(2): 459-63. doi:10.51253/pafmj.v74i2.10879.

[15] Jeyaraju M, Linford H, Mendes TB, Caufield-Noll C, Tackett S. Factors leading to successful performance on US National Licensure exams for Medical students: a scoping review. Academic Medicine. 2023 Jan; 98(1): 136-48. doi: 10.1097/ACM.0000000000004877.

[16] Rahim F. National Licensing Examination: Are We Ready For It?. Kashmir Journal of Medical Sciences. 2021 Jul; 14(3): 136. doi: 10.35845/kmuj.2021.22251.

[17] Huwendiek S, Jung D, Schirlo C, Huber P, Balestra G, Guttormsen S *et al.* The introduction of a standardised national licensing exam as a driver of change in medical education: A qualitative study from Switzerland. Medical Teacher. 2020 Oct; 42(10): 1163-70. doi: 10.1080/0142159X.2020.1798911.

[18] Ekarattanawong S, Chamod P, Thuppia A, Mathuradavong N, Pattharanitima P, Bhamarapravatana K *et al.* Using Facebook for ongoing learning promotes higher national licensing examination success. Medical Science Educator. 2019 Mar; 29: 241-5. doi: 10.1007/s40670-018-00677-y.

[19] Swanson DB and Roberts TE. Trends in national licensing examinations in medicine. Medical Education. 2016 Jan; 50(1): 101-14. doi: 10.1111/medu.12810.

[20] Saleem S, Afzal S. Implementation of National Licensing Examination (NLE) and its Impact on Global Healthcare: A Systematic Review. Annals of King Edward Medical University. 2022 May; 28(1): 128-34. doi: 10.21649/akemu.v28i1.5022.

Original Article

High Doses of Dexamethasone Improved Hemoglobin Levels Lowered by Corona Virus in COVID-19 Infected Patients

Zunnera Rashid Chaudhry[1]*, Sabeen Shakir[1], Sana Rasheed[2], Erum Rashid[3], Hifza Noor Lodhi[4] and Naima Shakeel[5]

[1]Department of Pharmacology, Akhtar Saeed Medical College, Rawalpindi, Pakistan
[2]Department of Physiology, Ameer-Ud-Din Medical College, Lahore, Pakistan
[3]Department of Biochemistry, Watim Medical College, Rawalpindi, Pakistan
[4]Department of Physiology, Rashid Latif Khan University, Lahore, Pakistan
[5]Department of Physiology, Postgraduate Medical Institute, Ameer-Ud-Din Medical College, Lahore General Hospital, Lahore, Pakistan

ARTICLE INFO

ABSTRACT

Corona virus an infectious disease caused by SARS–CoV-2 virus that lower hemoglobin level leading to worsening of the conditions. The respiratory symptoms are treated by steroids and patients are rapidly recovered. **Objective:** To study the effect of high and low doses of dexamethasone on hemoglobin level in COVID-19 infected patients. **Methods:** This experimental study was carried out in Rawal Institute of Health Sciences, Islamabad and Pakistan Institute of Medical Sciences, Islamabad between May 2021 to Sep 2021 on 100 adult male and female of COVID-19 patients having blood hemoglobin level < 10 g/dl. For different doses of dexamethasone patients were divided into two groups of 50 patients in each group. Blood samples were taken on day 01 and day 15 for hemoglobin analysis. Mean and standard deviation of both groups was calculated and p-value of < 0.05 was considered significant. **Results:** At the time of admission 74% of the patients had a cough, 89% of the patients presented with fever, 98% had increased heart rate whereas 100% of the patients presented with the complaint of fatigue. Mean Hemoglobin (Hb) levels of both groups were compared on day 01 and day 15 respectively. The comparison of Hb levels showed a significant difference on day 15, there was a marked increase in Hb levels in the group which was taking 12mg/day of dexamethasone as compared to the group which was taking 6mg/day of dexamethasone (P-value <0.05). **Conclusions:** Administration of high doses of Dexamethasone caused a pronounced increase in hemoglobin levels in COVID-19 patients.

INTRODUCTION

The global pandemic disease COVID-19 caused by "SARS–CoV-2" virus presented with flu and common cold like symptom mainly effecting the respiratory tract , If not treated properly leads to death. This positive RNA strand coronavirus produces cytokines and chemokine's damage lungs and causes cough with fever [1]. Coronavirus targets the ACE-2 receptors for entering in host cell mucosa, after replication, it damages the respiratory passage, lungs, trachea, pharynx, nasal cavity and conjunctiva [2]. The mode of transmission of this virus is by contact with infected individual, droplets and aerosol [3, 4]. Hemoglobin contains porphyrin on which coronavirus damages and gains porphyrin required for its replication. The deranged hemoglobin are unable to deliver oxygen to the tissues [5]. Coronavirus binds and interacts with the receptors located on red blood cells and causes further destruction of hemoglobin and reduces oxygen supply [6]. Steroids have effective role in controlling and reducing the symptoms of COVID-19 patients. One of the corticosteroid with similarity to natural hormones is dexamethasone. It has anti-inflammatory effects relieves respiratory symptoms, itching, rhinitis and asthma in coronavirus infected

patients. It also inhibits expression of inflammatory proteins and transcription factors necessarily for cell proliferation [7, 8]. Different doses of dexamethasone ranging from 6-12mg once daily are used for treating respiratory and allergic symptoms in COVID-19 patients [9]. Dexamethasone also improves hemoglobin level. Steroids increases blood hemoglobin level in the body by stimulating the synthesis of a hormone erythropoietin which leads to increased production of red blood cells and hemoglobin [10].

The present study was conducted to see the effect of high dose of dexamethasone in improving blood hemoglobin levels compared to low dose in coronavirus infected patients.

METHODS

After approval from the ethical committee of RIHS Islamabad with reference no: RIHS-REC/ 062/21 dated: 29-01-21. This study was carried out in Rawal Institute of Health Sciences, Islamabad and Pakistan Institute of Medical Sciences, Islamabad from May 2021 till September 2021. It is an experimental study conducted on 100 adult patients suffering from COVID-19 disease. The sample size was calculated by using expected prevalence of COVID-19 in Pakistan was 6.67% by taking 5% margin of error and 95% confidence interval [11]. Male and female patients with low hemoglobin (<10 g/dl) were included. The patient with anemia due to blood disorders, or diseases causing anemia were excluded. Blood hemoglobin was seen from the records on the day of admission. Patients with blood hemoglobin level less than 10 g/dl were considered anemic and selected. Prior to study, all the patients provided informed consent. Patients were taking dexamethasone prescribed by the physician. On the basis of the doses, patients were divided into two groups with 50 patients in each group. Group 1 was taking dexamethasone in a dose of 6 mg once daily and group 2 was taking dexamethasone 12 mg once daily. Blood hemoglobin was analyzed on day 01 and on day 15 after taking dexamethasone Change in blood hemoglobin level was recorded. Data were entered using SPSS version 26.0. Results were given in mean ± standard deviation (mean ± SD). Hemoglobin levels on day 01 and day 15 of both groups were compared by applying unpaired t-test and paired sample t-test was used to find out difference of mean hemoglobin of each group before and after taking the dexamethasone. P value < 0.05 was considered significant.

RESULTS

At the time of admission 74% of the patients had a cough, 89% of the patients presented with fever, 98% had increased heart rate whereas, 100% of the patients presented with the complaint of fatigue. Group wise distribution of presenting complaints was in table 1.

Table 1: Presenting Complaints of Patients in Group 1 and 2 at the Time of Admission

Presenting Complaints	Group 1 (n=50) N (%)	Group 2 (n=50) N (%)
Cough	33 (66%)	41 (82%)
Fever	40 (80%)	49 (98%)
Increased Heart Rate	50 (100%)	48 (96%)
Fatigue	50 (100%)	50 (100%)

In table 2, Group 1 levels of serum hemoglobin on day 15 were compared with day 01 their mean were 8.99 ± 0.562 g/dl versus 8.95 ± 0.497 g/dl, a slight increase was observed but the difference was not significant with a p-Value of 0.64 i.e., p>0.05. However group 2 showed a remarkable increase in hemoglobin levels when recorded on day 15 as compared to day 01, i.e., 9.46 ± 0.67 g/dl versus 8.07 ± 0.32 g/dl. The difference was observed as significant with a p<0.05.

Table 2: Comparison of Effect of Dexamethasone (6mg and 12mg)/Day in Individual Groups on Serum Heamoglobin Levels in Covid 19 Patients

Groups	Day 1 (Serum Hb) g/dL	Day 15 (Serum Hb) g/dL	p-Value
Group 1	8.95 ± 0.497	8.99 ± 0.562	0.64
Group 2	8.07 ± 0.32	9.46 ± 0.67	0.00 *

P Value < 0.05 = Significant (*)
P Value > 0.05 = Non Significant (NS)
1n = 50, Results are expressed as mean (Paired t test)

On day 01 the hemoglobin level of group -1 was 8.95 ± 0.497 g/dl and group 2 was 8.07 ± 0.32 g/dl. The difference among the two groups was observed significant having p< 0.01. with a p < 0.05.

In table 3, day 15 showed the hemoglobin level of group 1 was 8.99 ± 0.562 g/dl and group 2 was 9.46 ± 0.67 g/dl. A significant rise was observed on comparing the two groups with a p < 0.05.

Table 3: Comparison of Effect of Dexamethasone (6mg and 12mg)/Day among Two Groups on Serum Heamoglobin Levels in Covid 19 Patients

Test (g/dl)	Time Points	Group 1	Group 2	p-Value
Serum Hb	Day 1	8.95 ± 0.497	8.07 ± 0.32	0.00
	Day 15	8.99 ± 0.562	9.46 ± 0.67	0.00

P Value < 0.05 = Significant (*)
P Value > 0.05 = Non Significant (NS)
1n = 50, Results are expressed as mean (Unpaired t test)

The result below shows on day 01 the hemoglobin level of group 1 was 8.95 ± 0.49 g/dl and hemoglobin level of group 2 was 8.07 ± 0.32 g/dl after taking 6 mg and 12 mg of Dexamethasone There was improvement in the hemoglobin levels in both groups. There is 0.4 % increase in hemoglobin level in group 1 and 17 % increase in hemoglobin level in group 2 patients after two weeks. The percentage improvement in hemoglobin levels is seen in table 4.

Table 4: Percentage Increase in Hemoglobin Levels in Both Groups on Day 15

Groups (n=100)	Hb (g/dl) Day 01	Hb (g/dl) Day 15	Increase in Hb (%)
Group 1 (n=50)	8.95 ± 0.497	8.99 ± 0.562	0.4 %
Group 2 (n=50)	8.07 ± 0.32	9.46 ± 0.67	17%

DISCUSSION

In our study we have seen that at the time of admission 100 % of the patients presented with fatigue and 98% of them presented with increased heart rate. Although fatigue and increased heart rate are also seen in corona patients but since these patients had hemoglobin level less than 10 g/dl and are anemic these two symptoms increased to such a high percentage. Salari N et al., in one of his research said that the global prevalence of chronic fatigue is 45.2% in corona patient [10]. In one of the study it is said that coronavirus causes inflammation of heart leading to increased heart rate [12, 13]. The causes of fatigue and increased heart rate in anemic patient are low hemoglobin levels leading to reduced oxygen delivery causing tiredness and fatigue. To provide oxygen to the rest of the body the heart works rapidly, increasing heart rate [14]. In our experimental study we have seen the effect of high and low doses of dexamethasone for two weeks and noted the changes in hemoglobin levels. Karam D et al., in one of his research used high doses of steroids for two weeks and suggested that high doses caused the improvement in hemoglobin levels [14, 15]. We have seen the effect of 6mg and 12 mg of dexamethasone in COVID -19 infected patient. Russell L et al., used the same doses of dexamethasone in coronavirus infected patients and concluded that rapid improvement in symptoms was seen in patients taking high doses compared to low dose [15, 16]. From our results we have seen although there was insignificant difference in hemoglobin levels in group 1 patients on day 01 and day 15 but on finding out the percentage increase in hemoglobin level after two weeks of taking 6mg/day of dexamethasone there is 0.4% increase in hemoglobin level. In group 2 anemic patients they had significant difference on day 01 and day 15 but after taking 12 mg /day of dexamethasone for two weeks there was 17% increase in hemoglobin levels. A research conducted by Anai M et al., on hemoglobin levels in corona virus infected patients, concluded that in severe infection there is reduction in hemoglobin level reduced oxygen delivery, further worsening the conditions [16, 17]. After destruction of red blood cells corona virus acts on the hemoglobin and deranges its structure. Nóbrega F et al., and Russo A et al., in one of his study said that coronavirus acts on the beta chain of hemoglobin and code its protein, the hemoglobin oxygen transport ability is lowered and there is more hypoxia [17-19]. Steroids have shown a positive effect in COVID-19 patients leading to rapid recovery and improvement in the symptoms. They improve the respiratory symptoms, relieves body aches and pains.

Bahsoun A et al., said that one of the beneficial outcomes of steroids is that they reduce morbidity, mortality and have anti-inflammatory effect preventing further complication in COVID-19 patients [19, 20]. In our study we have seen that high dose of dexamethasone caused more increase in hemoglobin level compared to low dose Karam D et al., used high dose of steroids for correction of anemia and concluded that hemoglobin level was not improving but after increasing the dose of steroids there was improvement in the hemoglobin levels [20, 21]. The steroids are used in multiple blood disorder diseases and it was seen that they increase red cell production Ashley R et al., in one of his research said that dexamethasone augments hemoglobin by increasing the expansion and average size of erythrocyte colony forming units causing increase in red cell production [21, 22]. A study conducted on the physiological and pharmacological effects of corticosteroids suggested that the increase in blood hemoglobin by steroids may be due to retarding or reducing phagocytosis of erythrocytes [23]. Steroids improve hemoglobin and correct anemia this may be due to their effect on bone marrow causing an increase in erythropoiesis [24]. In this study although the patients were using pain killers and antibiotics for the treatment of corona but their hemoglobin levels and symptoms improved rapidly after taking steroids. In future we can recommend steroids to be added in the treatment of anemia and correction of hemoglobin level.

CONCLUSIONS

Dexamethasone in high doses of 12mg /day caused more improvement in hemoglobin levels lowered by corona virus compared to low dose of dexamethasone 6mg/day in COVID-19 infected patients.

Authors Contribution

Conceptualization: ZRC
Methodology: ZRC, SS[1], SS[2], SS[3], NS
Formal analysis: ZRC, SS[1] SS[2], SS[3], ER, HNL
Writing, review and editing: ZRC, SS[1] SS[2], SS[3], ER, HNL

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

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

REFERENCES

[1] Keam S, Megawati D, Patel SK, Tiwari R, Dhama K, Harapan H. Immunopathology and immunotherapeutic strategies in severe acute respiratory syndrome coronavirus 2 infection.

Reviews in Medical Virology. 2020 Sep; 30(5): e2123. doi: 10.1002/rmv.2123.

[2] Li H, Wang Y, Ji M, Pei F, Zhao Q, Zhou Y *et al.* Transmission routes analysis of SARS-CoV-2: a systematic review and case report. Frontiers in Cell and Developmental Biology. 2020 Jul; 8: 618. doi: 10.3389/fcell.2020.00618.

[3] Jin YH, Cai L, Cheng ZS, Cheng H, Deng T, Fan YP *et al.* A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). Military Medical Research. 2020 Dec; 7: 1-23. doi: 10.1186/s40 779-020-0233-6.

[4] Rahman HS, Aziz MS, Hussein RH, Othman HH, Omer SH, Khalid ES *et al.* The transmission modes and sources of COVID-19: A systematic review. International Journal of Surgery Open. 2020 Jan; 26: 125-36. doi: 10.1016/j.ijso.2020.08.017.

[5] Hopp MT, Domingo-Fernández D, Gadiya Y, Detzel MS, Schmalohr BF, Steinbock F *et al.* Unravelling the debate on heme effects in COVID-19 infections. bioRxiv 2020 Jun; 10: 2020-06. doi: 10.1101/2020.06.0 9.142125.

[6] Cavezzi A, Troiani E, Corrao S. COVID-19: hemoglobin, iron, and hypoxia beyond inflammation. A narrative review. Clinics and Practice. 2020 May; 10(2): 1271. doi: 10.4081/cp.2020.1271.

[7] Mehta J, Rolta R, Mehta BB, Kaushik N, Choi EH, Kaushik NK. Role of Dexamethasone and Methylprednisolone Corticosteroids in Coronavirus Disease 2019 Hospitalized Patients: A Review. Frontiers in Microbiology. 2022 Feb; 13:813358. doi: 10.3389/fmicb.2022.813358.

[8] Seo SJ and Priefer R. Dexamethasone Mechanism in Inflammatory Immune Mediated Disease and its Application in Treating 2019 Coronavirus Disease (COVID-19). Medical Research Archives. 2020 Dec; 8(12): 2020. doi: 10.18103/mra.v8i12.2267.

[9] Zhang G, Su L, Wu W, Qiao Q, Gao S, Zhang Y *et al.* Efficacy of different doses of corticosteroids in treating severe COVID-19 pneumonia. Virology Journal. 2024 Mar; 21(1): 74. doi: 10.1186/s12985-024-02345-7.

[10] Salari N, Khodayari Y, Hosseinian-Far A, Zarei H, Rasoulpoor S, Akbari H, Mohammadi M. Global prevalence of chronic fatigue syndrome among long COVID-19 patients: A systematic review and meta-analysis. BioPsychoSocial Medicine. 2022 Oct; 16(1): 21. doi: 10.1186/s13030-022-00250-5.

[11] Saeed U, Uppal SR, Piracha ZZ, Khan AA, Rasheed A, Zaheer H, Aftab Z, Uppal R. Effectivity analysis of SARS-CoV-2 nasopharyngeal swab rapid testing kits in Pakistan: A scenario of inadequate COVID-19 diagnosis. Research Square. 2021 Mar. [Preprint].

[12] Shiravi AA, Saadat M, Abdollahi Z, Miar P, Khanahmad H, Zeinalian M. Vitamin D can be effective against COVID-19 and other similar viral infections: a review on molecular aspects. Zenodo. 2020 Mar; 92(2): 134-146. doi: 10.1024/0300-9831/a000676.

[13] Paul P, Maiti D, Adhikary T. Iron deficiency anemia-An updated overview. International Journal of Research in Pharmacy and Pharmaceutical Sciences. 2021 Sep; 6(4): 28-33.

[14] Miwa T, Hatano Y, Kochi T, Aiba M, Toda K, Goto H, *et al.* Spur cell anemia related to alcoholic liver cirrhosis managed without liver transplantation: a case report and literature review. Clinical Journal of Gastroenterology. 2020 Oct; 13: 882-90. doi: 10.1007/s12328-020-01142-3.

[15] Russell L, Uhre KR, Lindgaard AL, Degn JF, Wetterslev M, Sivapalan P *et al.* Effect of 12 mg vs 6 mg of dexamethasone on the number of days alive without life support in adults with COVID-19 and severe hypoxemia: the COVID steroid 2 randomized trial. The Journal of the American Medical Association. 2021 Nov; 326(18): 1807-17.

[16] Anai M, Akaike K, Iwagoe H, Akasaka T, Higuchi T, Miyazaki A *et al.* Decrease in hemoglobin level predicts increased risk for severe respiratory failure in COVID-19 patients with pneumonia. Respiratory Investigation. 2021 Mar; 59(2): 187-93. doi: 10.1016/j.resinv.2020.10.009.

[17] Nóbrega F, Mauad VA, Borducchi DM. Does COVID-19 really impact on the oxy-hemoglobin dissociation curve? eJHaem. 2020 Nov; 1(2): 604-7. doi: 10.1002/jha2.126.

[18] Russo A, Tellone E, Barreca D, Ficarra S, Lagana G. Implication of COVID-19 on erythrocytes functionality: red blood cell biochemical implications and morpho-functional aspects. International Journal of Molecular Sciences. 2022 Feb; 23(4): 2171. doi: 10.3390/ijms23042171.

[19] Bahsoun A, Fakih Y, Zareef R, Bitar F, Arabi M. Corticosteroids in COVID-19: pros and cons. Frontiers in Medicine. 2023 Aug; 10: 1202504. doi: 10.3389/fmed.2023.1202504.

[20] Karam D, Swiatkowski S, Purohit P, Agrawal B. High-dose steroids as a therapeutic option in the management of spur cell haemolytic anaemia. Case Reports. 2018 Jan; 2018: bcr-2017. doi: 10.1136/bcr-2017-223281.

[21] Ashley R, Yan H, Wang N, Hale J, Dulmovits BM, Papoin J, Olive M, Udeshi N, Carr S, Vlachos A, Lipton JM. Glucocorticoids Induce the Maintenance and Expansion of an Immature CFU-E Erythroid

Progenitor Population in Humans. Blood. 2019 Nov; 134: 943. doi: 10.1182/blood-2019-130710.

[22] Al-Ansari RY, Alromaih L, Osman M. Steroid induced hypertriglyceridemia in pregnant women with immune thrombocytopenia-case report. Annals of Medicine and Surgery. 2022 May; 77: 103636. doi: 10.1016/j.amsu.2022.103636.

[23] NB, Bonne TC, Sørensen H, Bejder J. Glucocorticoids accelerate erythropoiesis in healthy humans-should the use in sports be reevaluated?. Medicine and Science in Sports and Exercise. 2023 Feb; 55(7): 1334-1341. doi: 10.1249/MSS.0000000000003156.

[24] Hsu RJ, Yu WC, Peng GR, Ye CH, Hu S, Chong PC et al. The role of cytokines and chemokines in severe acute respiratory syndrome coronavirus 2 infections. Frontiers in Immunology. 2022 Apr; 13: 832394. doi: 10.3389/fimmu.2022.832394.

Original Article

Pattern of Temporomandibular Joint Disorders and Associated Intra-Oral Findings Among Patients Reporting To Oral and Maxillofacial Surgery OPD, with History of Psychiatric Illness in a Tertiary Care Hospital of Taxila Cantt

Syed Zuhair Mehdi[1*], Maimoona Siddiq[2], Sadia Moin[2], Sarosh Khan[3], Syeda Rabia Rahat Gillani[4] and Umar Farooq Khan[5]

[1]Department of Oral Medicine, Frontier Medical and Dental College, Abbottabad, Pakistan
[2]Department of Oral and Maxillofacial Surgery, Dental College, HITEC-Institute of Medical Sciences, Taxila, Pakistan
[3]Frontier Medical and Dental College, Abbottabad, Pakistan
[4]Department of Oral and Maxillofacial Surgery, Foundation University College of Dental, Islamabad, Pakistan
[5]Department of Periodontology, HBS Medical and Dental College, Islamabad, Pakistan

ARTICLE INFO

ABSTRACT

Temporomandibular joint illness impairs normal existence. Many disagree on this condition's cause. To comprehend this illness, know the signs. Understanding the prevalence of temporomandibular disorder will help people prevent them and schedule regular temporomandibular joint exams. **Objective:** To observe the pattern of temporomandibular joint disorders and associated intra-oral signs and symptoms among patients who are being treated for psychiatric illnesses and mental health issues. **Methods:** This prospective, cross-sectional study was conducted at the dental college HITEC-IMS Taxila Cantt from 1st September 2022 to 31st December 2023 and comprised of 181 patients. A detailed history of para-functional habits, headache, otalgia, smoking and stress was acquired along with a clinical examination of joint clicking, and occlusal variation. Fisher's exact test and pearson's chi-square found factor connections. **Results:** There were 112 (61.9%) females and 69 (38.1%) males in all patients. The patients mean age was 33.7 ± 10.47 years and had a mean BMI 24.12 ± 6.26 kg/m2. Among the symptoms that patients experienced, 125 (69.1%) heard noises in their joints, while 116 (64.1%) of the total reported feelings of emotional stress or strain. Most symptoms were more common in women. Men showed a substantial connection (p<0.005) between para-functional habits and stress/tension. Age also correlated with occlusal variation, joint sound, missing teeth, mastication side, parafunctional behaviors, tension, and stress. **Conclusions:** The study indicated that temporomandibular disorders were more common in women. Psychiatric patients most often complained of headache, clicking, and limited mouth opening.

INTRODUCTION

There is evidence that the effective functioning of the TMJ which includes the mandibular condyles, meniscus, glenoid fossa, ligaments, and muscles depends on the harmony of these components [1, 2]. Until mechanical, psychological, occupational, or habitual factors disrupt the normal functioning of the joint, the TMJ continues its normal function [3]. The body keeps trying to fix aggressiveness, but eventually, it stops being able to fix aggressiveness and symptoms start to show. Orofacial and preauricular discomfort, difficulty opening the mouth, noise from the TMJ when chewing, and disc displacement are all indications of TMJ disorder [4]. Symptoms are often experienced between the ages of 20 and 40, making this demographic another risk factor for masticatory system disorders among students. The vast majority of TMD cases occur in reproductive-aged women [5]. During

adolescence, the incidence of TMD rises worldwide and can range from 7–30% [5]. The symptoms related to the masticatory system are more common in women than in males, according to many researchers [5, 6]. Hormonal shifts in biology and mental factors could be to blame. Literature supports that, students are more prone to TMD and oral dysfunction due to the high levels of stress they endure [5]. A few examples of possible sources of stress include exams, research paper presentations, the desire to become self-reliant, money problems, studying in an awkward position, and low academic achievement. New research from the Orofacial Pain: Prospective Evaluation and Risk Assessment (OPPERA) study provide credence to the biopsychosocial theory of illness and the multifactorial origins of TMD. On the other hand, malocclusion's significance has been diminished, despite it being previously believed to be one of the main etiological consequences of TMD symptoms. The likelihood of TMD is higher in patients with crossbite, maximum intercuspal instability, and Class II malocclusion [5]. Occlusal changes may also increase the likelihood that a person with a history of TMD may experience TMD symptoms. Thus, TMD and malocclusion are entangled in a complicated chain of causes and effects [5-7]. One must not underestimate the significance of maintaining a healthy TMJ. Pain in the face and mouth can be caused by TMDs. Limitations in jaw mobility, clicking or crepitation noises, discomfort felt when moving the jaw, and pain felt when palpating the masticatory muscles are all symptoms that can be identified during a clinical examination for a diagnosis of TMJ disorders. The mandible can develop TMDs for a variety of reasons, such as occlusal interferences, tumor growth, misalignment of the condylar head and temporal fossa, destructive movement (nonfunctional movement), emotional stress, anxiety, tooth misalignment or loss, and grinding or clenching habits [8, 9]. An estimated 3- 10% of the population seeks medical attention [10]. More than 60% of patients with orofacial discomfort, including 95% of those with TMD, had tried non-dental treatments, with physiotherapy being the most common (42.2%), according to a research by Schiffman E et al [11]. Not only that, physiotherapy wasn't the only non-dental therapy that most patients received; osteopathy and relaxation training were among the others. With 27.7% being either very unhappy or unsatisfied and just 18.5% being extremely satisfied, patient satisfaction with treatment outcomes and provided care was modest [12]. Thus it is evident from the literature that there is a strong relationship between stress, anxiety, and temporomandibular joint disorders.

The aim of the study was to investigate the pattern of temporomandibular joint disorders and other intraoral signs and symptoms like para-functional habits, missing teeth, occlusal variations, headache, and joint sound among patients who are being treated for psychiatric illnesses.

METHODS

This prospective cross-sectional study was conducted at Dental College HITEC-IMS Taxila Cantonment from 1st September 2022 to 31st December 2023 with REF# Dental/HITEC/IRB/30 approved on 19th August, 2022. Non probability consecutive sampling technique was used for data collection. Using an assumed percentage of patients with TMJDs, a 95% confidence interval, and an acceptable difference of 0.08%, a sample size of 181 was calculated. The study included both male and female adult patients who reported to the Oral and Maxillofacial Surgery Department with complaints of discomfort in the temporomandibular joint and also gave a positive history of psychiatric illness. The exclusion criteria were individuals who were experiencing discomfort or pain as a result of eruption or impacted wisdom teeth or any other gum disease. Individuals who ever had orthodontic work done as well as those who suffer from neurological or musculoskeletal conditions. Patients who have had a history of face trauma, TMJ surgeries, TMJ trauma, fractures, or craniofacial deformities were also excluded. Informed consent was acquired from all subjects. A detailed history was acquired and a clinical examination was performed for each subject. A two-part self-explanatory screening questionnaire was used to gather data through in-person interviews. Demographic information, including age and sex, was recorded in the first section. Section 2 asked patients to indicate if they engaged in a variety of parafunctional habits by checking either patient involved in bruxism, thumb sucking or nail bitting [28]. The information gathered was entered into a data extraction sheet. Information regarding patient's demographics, etiology, symptoms, joint discomfort, occlusal variations, missing teeth, parafunctional habits, chewing with one, emotional stress, treatment, referrals from other medical specialties, and total visits were documented. Numbers and percentages were used to represent categorical data, whereas means and standard deviations (SD) were used to represent quantitative variables. Using either Fisher's exact or Pearson's Chi-square test, we looked for a correlation between gender and variables like age and symptoms. Statistical significance was defined as a p-value below 0.05. Excel was utilized for both data entry and analysis.

RESULTS

There were 112 (61.9%) females and 69 (38.1%) males in all patients. The patients mean age was 33.7 ± 10.47 years and had mean BMI 24.12 ± 6.26 kg/m2. Majority of the cases 108 (59.7%) were from urban areas. There were 43 (23.8%) patients had smoking history. Referral cases were 17 (9.4%). 45 (24.9%) cases had 4 number of visits and 136

(75.1%) cases had 6 visits to hospital as shown in table 1.

Table 1: Demographics of the Enrolled Cases

Variables	N (%) (n=181)
Gender N (%)	
Male	69 (38.1%)
Female	112 (61.9%)
Age (Mean ± SD)	
Mean Age (Years)	33.7 ± 10.47
Mean BMI (Kg/m^2)	24.12 ± 6.26
Residence N (%)	
Urban	108 (59.7%)
Rural	73 (40.3%)
Smoking History N (%)	
Yes	43 (23.8%)
No	138 (76.2%)
Referral Cases N (%)	
Yes	17 (9.4%)
No	164 (90.6%)
Total Visits N (%)	
6	136 (75.1%)
4	45 (24.9%)

Regarding the main complaint, pain was the most prevalent complain followed by clicking and limited mouth opening. Most common etiology was stress followed by facial trauma, bruxism stress, trauma stress and bruxism as shown in table 2.

Table 2: Complaint and Etiology of TMJD's

Variables	N (%)
Pain	115 (63.5%)
Clicking	40 (22.1%)
Limited Mouth Opening	26 (14.4%)
Etiology of TMJD's N (%)	
Stress	70 (38.7%)
Facial Trauma	48 (26.5%)
Bruxism Stress	25 (13.85)
Trauma Stress	13 (7.2%)
Bruxism	6 (3.3%)
Other	19 (10.5%)

Among the symptoms that patients experienced, 125 (69.1%) had joint sounds, while 116 (64.1%) of the total reported feelings of emotional stress or strain as shown in figure 1.
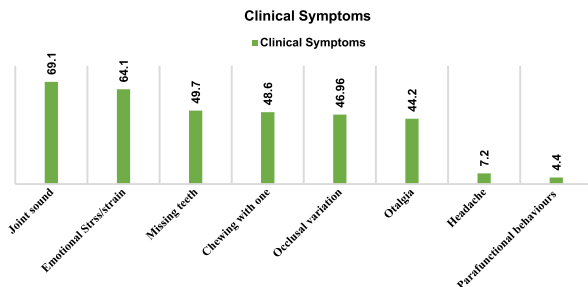
Figure 1: Clinical Symptoms of the Enrolled Cases

The frequency of most symptoms was higher in females compared to males. The correlation between parafunctional habits and stress/tension was statistically significant (p<0.005) in men as shown in table 3.

Table 3: Clinical Symptoms with Respect to Gender

Symptoms	Male N (%)	Female N (%)	Total N (%)	p-value
Joint Sounds	40 (22.1%)	85 (46.96%)	125 (69.1%)	<0.004
Stress/Strain	36 (19.9%)	80 (44.2%)	116 (64.1%)	<0.005
Missing Teeth	35 (19.3%)	55 (30.4%)	90 (49.7%)	<0.102
Chewing With One	40 (22.1%)	48 (26.5%)	88 (48.6%)	<0.215
Occlusal Variation	33 (18.2%)	52 (28.7%)	85 (46.96%)	<0.112
Otalgia	38 (20.9%)	42 (23.2%)	80 (44.2%)	0.000
Headache	5 (2.8%)	8 (4.4%)	13 (7.2%)	<0.004
Parafunctional Behaviours	2 (1.1%)	6 (3.3%)	8 (4.4%)	<0.005

Furthermore, there were correlations between age and occlusal variation, joint sound, missing teeth, side chewing, parafunctional behaviours, tension, and stress levels as shown in table 4.

Table 4: Various Clinical Signs and Symptoms are Seen Throughout Different Age Groups.

Symptoms	18-30 Years N (%)	31-60 Years N (%)	Total N (%)	p-value
Joint Sounds	34 (18.8%)	91 (50.3%)	125 (69.1%)	<0.005
Stress/Strain	20 (11.04%)	96 (53.03%)	116 (64.1%)	<0.005
Missing Teeth	30 (16.6%)	60 (33.1%)	90 (49.7%)	<0.005
Chewing With One	35 (19.3%)	53 (29.3%)	88 (48.6%)	<0.003
Occlusal Variation	23 (12.7%)	62 (34.3%)	85 (46.96%)	<0.005
Otalgia	33 (18.2%)	47 (25.96%)	80 (44.2%)	<0.002
Headache	4 (2.2%)	9 (4.97%)	13 (7.2%)	<0.005
Parafunctional Behaviours	3 (1.7%)	5 (2.8%)	8 (4.4%)	<0.005

DISCUSSION

The masticatory muscles and joint function can be impacted by TMJDs. Pain in the Temporomandibular Joint (TMJ) could originate from issues with the joint itself, nearby structures, or both. This study's results are in line with those of earlier research showing that females, not males, are more likely to experience TMJ discomfort and symptoms [13]. Several variables contribute to the development of Temporomandibular Disorders (TMDs), including a robust bio-psychosocial component [14]. Those between the ages of 45 and 64 had the highest documented prevalence of TMJ problems [15]. Among the participants in this study, those between the ages of 31 and 60 made up the largest proportion (59.1%), followed by those between the ages of 18 and 30 (40.9%). Findings from this study are in line with those from Alhussini DA *et al.,* where the average age of TMJ patients was 33.7 years [16]. A quarter to half of the population may have temporomandibular joint noises, according to a recent study [17]. The therapeutic relevance of these noises is a matter of debate, with some arguing that they indicate joint

165

disease and others that they indicate mechanical interference inside the joint. Crepitus and tenderness are common symptoms of intra-articular derangement, whereas headaches and referred pain together with discomfort when moving the jaw indicate a problem with the muscles [18]. Compared to Miyake R *et al.,* the current investigation revealed that 69.1% of TMJ patients had joint noises [19]. Still up for debate is the question of whether or not tooth loss causes TMJ discomfort. An absence of molar teeth may cause discomfort due to mandibular overclosure and auriculotemporal nerve entrapment, according to some [20]. Five patients with missing molar teeth in the current investigation experienced TMJ discomfort. A person's standard of living is greatly diminished when they are in constant agony. Compared to men, girls and adult women experience a higher prevalence of orofacial discomfort, which includes TMJ pain [21]. Anxieties, melancholy, and stress are on the rise among young people, which might explain why orofacial discomfort is so common among this age group. 64.1% of participants in this research acknowledged experiencing stress on their own. Bruxism, clenching and other parafunctional habits, as well as occlusal irregularities, might aggravate TMJ discomfort of the patients with TMJ discomfort who participated in this study, 46.96% had occlusal abnormalities and 4.4% had parafunctional habits [22]. Common symptoms of TMD include headaches, especially tension headaches. Studies conducted by RamachanDRan S discovered a positive link between TMD and the occurrence of headache, suggesting that TMD might be a cause of headaches [23]. Among the 44.2 patients surveyed for this study, otalgia was most common in those between the ages of 31 and 60. The enhanced sensitivity to biological cues and hormonal variables may explain why TMJ issues are more common in women [24]. Cultural norms and social expectations regarding the expression of suffering may also be relevant [25]. Consistent with earlier research, this study found that TMJ problems are more common in women that they tend to affect people of a certain age, that they are connected with certain noises made by the joints and differences in their occlusal surfaces, and that they can cause other symptoms such as headaches and otalgia. Symptoms of TMDs extend beyond just the jaw joint and can manifest in various areas of the body, including the neck, head, and other joints. Systemic conditions including fibromyalgia, IBS, and sleep problems are frequently linked to TMDs [26]. As a degenerative kind of TMJ dysfunction is common in rheumatoid patients, joint noises may be due to less synovial fluid and condylar wear. The current investigation indicated that 48.6% of patients chewed on one side, although a previous study by Souza RC *et al.,* did not find any relationship between unilateral mastication and mouth opening crepitus, myofascial discomfort, or joint locking [27, 28].

CONCLUSIONS

Individuals suffering from psychiatric illnesses have a greater prevalence of temporomandibular joint discomfort. Female patients are more inclined to TMJ discomfort than male patients. Joint noises (clicking, crepitus) were reported by patients at a higher rate than any other symptom. There was a statistically significant correlation between gender and parafunctional behaviors as well as stress and tension. Patients ranging in age from 31 to 60 made up the bulk of the patient population.

Authors Contribution

Conceptualization: SRRG
Methodology: SM
Formal analysis: SZM
Writing, review and editing: MS, SK, UFK

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

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

REFERENCES

[1] Fehrenbach MJ. Dental Anatomy Coloring Book. 2nd Edition. Elsevier Health Sciences; 2013.

[2] Moss-Salentijn L. Biology of Mineralized Tissues: Prenatal Skull Development. 2007.

[3] Lee JY, Kim YK, Kim SG, Yun PY. Evaluation of Korean teenagers with temporomandibular joint disorders. Journal of the Korean Association of Oral and Maxillofacial Surgeons. 2013 Oct; 39(5): 231. doi: 10.5125/jkaoms.2013.39.5.231.

[4] List T and Jensen RH. Temporomandibular disorders: Old ideas and new concepts. Cephalalgia. 2017 Jun; 37(7): 692-704. doi: 10.1177/0333102416686302.

[5] Dworkin SF. Research diagnostic criteria for temporomandibular disorders: current status & future relevance 1. Journal of Oral Rehabilitation. 2010 Oct; 37(10): 734-43. doi: 10.1111/j.1365-2842.2010.02090.x.

[6] Look JO, Schiffman EL, Truelove EL, Ahmad M. Reliability and validity of Axis I of the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) with proposed revisions. Journal of Oral Rehabilitation. 2010 Oct; 37(10): 744-59. doi: 10.1111/j.1365-2842.2010.02121.x.

[7] Loster JE, Osiewicz MA, Groch M, Ryniewicz W, Wieczorek A. The prevalence of TMD in Polish young

adults. Journal of Prosthodontics. 2017 Jun; 26(4): 284-8. doi: 10.1111/jopr.12414.

[8] Emodi-Perlman A, Eli I, Smardz J, Uziel N, Wieckiewicz G, Gilon E *et al.* Temporomandibular disorders and bruxism outbreak as a possible factor of orofacial pain worsening during the COVID-19 pandemic-concomitant research in two countries. Journal of Clinical Medicine. 2020 Oct; 9(10): 3250. doi: 10.3390/jcm9103250.

[9] Scelza G, Amato A, Rongo R, Nucci L, D'Ambrosio F, Martina S. Changes in COVID-19 Perception and in TMD Prevalence after 1 Year of Pandemic in Italy. European Journal of Dentistry. 2023 Jul; 17(03): 771-6. doi: 10.1055/s-0042-1755192.

[10] Abbasi S, Mubeen N, Ayub T, Khan M, Abbasi Z, Baig N. Comparison of stress levels among medical and dental students in the clinical years of training and their coping strategies. Journal of the Pakistan Medical Association. 2020 Jun; 70(6): 1006-1008.. doi: 10.5455/JPMA.294959.

[11] Schiffman E, Ohrbach R, Truelove E, Look J, Anderson G, Goulet JP *et al.* Diagnostic criteria for temporomandibular disorders (DC/TMD) for clinical and research applications: recommendations of the International RDC/TMD Consortium Network and Orofacial Pain Special Interest Group. Journal of Oral & Facial Pain and Headache. 2014; 28(1): 6-27. doi: 10.11607/jop.1151.

[12] Alamri A, Shahin S, Bakhurji EA, Alsulaiman AA, Salloot Z, Nazir M. Association of Test Anxiety with Temporomandibular Disorder in Health Professions Students: A Cross-Sectional Study. International Journal of Dentistry. 2020 Dec; 2020(1): 8833804. doi: 10.1155/2020/8833804.

[13] Khan MW and Zaigham AM. Prevalence and Severity of Temporomandibular Disorders in Medical/Dental Undergraduate Students. Journal of the Pakistan Dental Association. 2021 Apr; 30(2): 94-98. doi: 10.25 301/JPDA.302.94.

[14] AlHussaini AA, AlHudithy LH, AlHadlaq MA, AlAzzam NF, Abahussain NW, AlDukhiel SA *et al.* The prevalence and severity of temporomandibular disorder (TMD) among female dental students in Riyadh, Saudi Arabia. The Saudi Dental Journal. 2019 Jan; 31: S55-6. doi: 10.1016/j.sdentj.2019.02.015.

[15] Atsü SS, Güner S, Palulu N, Bulut AC, Kürçüoğlu I. Oral parafunctions, personality traits, anxiety and their association with signs and symptoms of temporomandibular disorders in the adolescents. African Health Sciences. 2019 Apr; 19(1): 1801-10. doi: 10.4314/ahs.v19i1.57.

[16] Alhussini DA, Mominkhan DM, Alhamed FJ, Saklou RA, Alim HM. Prevalence and awareness of temporomandibular joint disorders among patients in king abdulaziz university, dental hospital. Journal of dental health, oral disorders & therapy. 2017 Nov; 8(5): 603-8. doi: 10.15406/jdhodt.2017.08.00300.

[17] Ryan J, Akhter R, Hassan N, Hilton G, Wickham J, Ibaragi S. Epidemiology of temporomandibular disorder in the general population: a systematic review. Advances in Dentistry & Oral Health. 2019 Feb; 10(3): 1-3. doi: 10.19080/ADOH.2019.10.555787.

[18] Hanna K, Nair R, Armfield J, Brennan D. Temporomandibular dysfunction among working Australian adults and association with workplace effort-reward imbalance. Community Dent Health. 2020 Nov; 37(4): 253-9. doi: 10.1922/CDH_000051 Hanna07.

[19] Miyake R, Ohkubo R, Takehara J, Morita M. Oral parafunctions and association with symptoms of temporomandibular disorders in Japanese university students. Journal of Oral Rehabilitation. 2004 Jun; 31(6): 518-23. doi: 10.1111/j.1365-2842.2004.01269.x.

[20] Valesan LF, Da-Cas CD, Réus JC, Denardin AC, Garanhani RR, Bonotto D *et al.* Prevalence of temporomandibular joint disorders: a systematic review and meta-analysis. Clinical oral investigations. 2021 Feb; 25: 441-53. doi: 10.1007/s00 784-020-03710-w.

[21] AlShaban KK and Gul Abdul Waheed Z. Prevalence of TMJ disorders among the patients attending the dental clinic of Ajman University of Science and Technology-Fujairah Campus, UAE. International Journal of Dentistry. 2018 May; 2018(1): 9861623. doi: 10.1155/2018/9861623.

[22] Alrizqi AH and Aleissa BM. Prevalence of temporomandibular disorders between 2015-2021: a literature review. Cureus. 2023 Apr; 15(4): e37028. doi: 10.7759/cureus.37028.

[23] RamachanDRan S and RavichanDRan K. Prevalence of Temporomandibular Joint Pain among Patients who Reported to Dental OPD at a Tertiary Hospital in Pondicherry, India: A Cross-sectional Study. Journal of Clinical & Diagnostic Research. 2023 Nov; 17(11). ZC40-ZC44. doi: 10.7860/JCDR/2023 /64885.18743.

[24] De Leeuw R and Klasser GD. Differential diagnosis and management of TMDs. Orofacial pain: guidelines for assessment, diagnosis, and management/Americ an Academy of Orofacial Pain. 6th Edition. 2018.

[25] van Linschoten CP, van Holland BJ, te Velde BP. Integratie patiëntervaringen Paramedische zorg.A RGO BV. 2018.

[26] Srivastava KC, Shrivastava D, Khan ZA, Nagarajappa AK, Mousa MA, Hamza MO *et al.* Evaluation of temporomandibular disorders among dental students of Saudi Arabia using Diagnostic Criteria for

Temporomandibular Disorders (DC/TMD): a cross-sectional study. BioMed Central Oral Health. 2021 Dec; 21: 1-1. doi: 10.1186/s12903-021-01578-0.

[27] Souza RC, de Sousa ET, Sousa D, Sales M, dos Santos Oliveira R, Mariano MH *et al*. Prevalence of temporomandibular joint disorders in patients with ankylosing spondylitis: a cross-sectional study. Clinical, Cosmetic and Investigational Dentistry. 2021 Nov; 13: 469-478. doi: 10.2147/CCIDE.S320537.

[28] Motta LJ, Guedes CC, De Santis TO, Fernandes KP, Mesquita-Ferrari RA, Bussadori SK. Association between parafunctional habits and signs and symptoms of temporomandibular dysfunction among adolescents. Oral Health Preventive Dentistry. 2013 Jan; 11(1): 3-7. doi: 10.3290/j.ohpd.a29 369.