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ISSN (E) 2790-9352
ISSN (P) 2790-9344

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ISI 000000524023175



ISSN (E) 2790-9352
ISSN (P) 2790-9344

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Pakistan Journal
of Health Sciences
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A Preventable Crisis: Overhauling Healthcare for Pakistan's Scorching Future

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ARTICLE INFO

How to Cite:

Mehboob, R. (2026). A Preventable Crisis: Overhauling Healthcare for Pakistan's Scorching Future: Pakistan's Heat Crisis and Healthcare. Pakistan Journal of Health Sciences, 7(6), 01-02. <https://doi.org/10.54393/pjhs.v7i6.4446>

The mercury is rising, and so is the loss of life among humans. The current and future seasons of Pakistan are not only a meteorological event, but a systemic failure that has been revealed. Today, the healthcare system lacks adequate resources and funds, and is in short supply, as the temperature regularly exceeds 49°C in cities such as Karachi and Peshawar, and this is the final line of defense in survival. This heatwave crisis needs more than a seasonal warning; it's a call for a swift and drastic restructuring of public health systems, ranging from the emergency ward to urban design [1].

The numbers put on a dark picture of an approaching collapse. In the past one season, thousands of patients with heatstroke have been reported and admitted at hospitals in Sindh and Punjab, which have been unable to cope with huge number of patients as they were overrun by the number of patients and lacked basic facilities for quick cooling [2]. A study on heat stroke in Karachi revealed that a total of over 6 thousand heat strokes had been reported, but this is a conservative estimate, given that only 5% of deaths are registered officially in the country [3]. No heat-related illness (HRI) ward or special cooling areas are available in KP, and up to 60 patients are brought to major public hospitals every day for heat-related illness, and critical patients are treated in general emergency bays. It is not because patients don't have resources; it's because patients don't prioritize them [4].

The effects of this lack of preparation are deadly, especially for the most vulnerable. Those who are elderly, children, pregnant women, and workers in the open fields, who have no other way to make a living except under the hot sun, are severely affected [5]. Chronic power shortages (otherwise known as load-shedding) and acute water scarcity combine to make homes into furnaces and people into dehydrated individuals in the fight for survival, with acute kidney injuries being just one of the many life-threatening illnesses that result. A new Amnesty International report revealed that the deaths of victims of heatwaves are often not recorded in official statistics, meaning that they are not registered as heatstroke victims. One resident of Karachi reported that his 65-year-old father died after his body overheated during a power outage when he was not able to go to an overcrowded hospital [6].

So, what is the solution? It begins with acknowledging that this is not a natural disaster but a public health emergency that demands systemic change.

First, hospitals must be engineered to be heat-resilient. This is not limited to the provision of IV fluids and ORS. There should be dedicated heatstroke wards in all major public hospitals with A/C cooling centres and crash carts that have all the necessary intubation equipment for heatstroke. Water and electricity are two critical infrastructures in hospitals that are in short supply and must be taken as an emergency failure since cooling is crucial for hospitals to operate and maintain life-saving systems. A recent advisory issued by the National Institutes of Health (NIH) for "dedicated heatstroke centres" is a positive move, but it needs to be followed by fast funding and implementation.

Second, frontline staff must be empowered with the right knowledge. Heat-related illness has long been a marginal problem

in the medical curriculum. A recent study of undergraduate medical programs in Pakistan identified no dedicated courses on climate-health connections. Emergency physicians must learn to recognize and treat heatstroke in a proactive rather than a reactive manner. In Karachi, the "Heat Emergency Awareness and Treatment" (HEAT) intervention proved that a structured training program greatly enhanced the diagnosis rate and management practices. This blueprint needs to be scaled up nationally.

Third, prevention must start long before a patient reaches the emergency room. Effective public health measures involve creating early warning systems and conducting awareness-raising campaigns in the community to educate citizens about the signs and symptoms of heat exhaustion, including dizziness and confusion. The relief camps set up by the local administration in Sukkur, where ORS and chilled water were distributed, should be replicated in all cities. Moreover, long-term resilience needs urban greening: planting trees and using reflective surfaces to counteract the so-called "urban heat island" effect.

Pakistan is on the front lines of the climate change crisis, but its healthcare system is still in reactive mode. Heatwaves remained alarming during 2024 and 2025. Pakistan cannot afford to wait for another crisis to act. The decision is stark: invest in a health system built to withstand the climate crisis, or keep tallying preventable deaths. It's essential to the health of this country.

REFERENCES

- [1] Arshad A, Ashraf M, Sundari RS, Qamar H, Wajid M, Hasan MU. Vulnerability assessment of urban expansion and modelling green spaces to build heat waves risk resiliency in Karachi. *International journal of disaster risk reduction*. 2020 Jun; 46: 101468.
- [2] Saleem MS, Fatima SZ, Kamran H, Nouman A, Bibi K. Impact of rising summer temperatures on government sector tertiary care emergency centers: addressing heatstroke and associated death rates in Karachi, Pakistan. *Environmental Health Insights*. 2024 Nov; 18: 11786302241303584.
- [3] Khan UR, Saleem SG, Shah A, Raheem A, Qadir MA, Kerai S, Parveen F, Ali S, Razzak JA, Khan NU. Long-Term Impact of HEAT Educational Intervention in the Emergency Department in Karachi, Pakistan. *Annals of Global Health*. 2025 Sep 13; 91(1): 63.
- [4] O'Connor FG. Heat-related illnesses. *Annals of Internal Medicine*. 2025 Jul;178(7):ITC97-112.
- [5] Bassey PU, Ngwu FA, Shimobi OC, Isiaka AB, God'swill CC, Hosein C, Ephraim-Emmanuel BC. Heat-related illnesses: a scoping review of health system strategies, emergency responses and interventions in heat-prone areas. *BMC Public Health*. 2025 Aug 6;25(1):2679.
- [6] Amnesty International. Uncounted: Invisible deaths of older people and children during climate disasters in Pakistan. London: Amnesty International. 2025. <https://www.amnesty.org/en/latest/news/2025/05/pakistan-climate-disasters-increasing-risks-of-death-and-disease-amongst-children-and-older-people-new-report/>



Original Article



Role of Epoetin- α in the Management of Anemia in Chronic Kidney Disease (CKD) Patients

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ARTICLE INFO

Keywords:

Anemia, Epoetin-alpha, Efficacy, Chronic Kidney Disease

How to Cite:

Afzal, H., Ahmed, A., Hussain, M., Malik, M. K., & Hussain, A. (2026). Role of Epoetin- α in the Management of Anemia in Chronic Kidney Disease (CKD) Patients: Epoetin- α in the Management of Anemia in Chronic. Pakistan Journal of Health Sciences, 7(6), 03-07. <https://doi.org/10.54393/pjhs.v7i6.3282>

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Received Date: 30th June, 2025

1st Revision Received: 6th November, 2025

2nd Revision Received: 18th December, 2025

3rd Revision Received: 28th February, 2026

Acceptance Date: 10th March, 2026

Published Date: 30th June, 2026

ABSTRACT

Anemia in chronic kidney disease (CKD) contributes to morbidity, increased transfusion requirements, and cardiovascular risk, and is mainly caused by insufficient erythropoietin (EPO) synthesis. Erythropoietin-stimulating agents (ESAs) are a crucial therapy for managing anemia associated with CKD. Before the introduction of ESAs, blood transfusions were primarily used to manage anemia in these patients. Epoetin- α was the first erythropoietin analog to be used clinically. **Objective:** To find the efficacy of epoetin- α in increasing hemoglobin in chronic kidney disease patients. **Methods:** A cross-sectional study was conducted at Pakistan Air Force Hospital Mushaf, Sargodha, including 189 CKD patients. All patients received Epoetin- α at a dose of 4000 IU subcutaneously once weekly. Baseline complete blood count (CBC) was recorded before treatment, and a follow-up CBC was performed after one month. Data were collected through a questionnaire and analyzed using SPSS version 24.0. **Results:** The study included 189 patients, of whom 121 were male and 68 were female. The mean age was 58.7 ± 14.39 years. The mean hemoglobin before Epoetin- α therapy was 7.5 ± 0.76 g/dL, which increased to 8.9 ± 1.28 g/dL after one month. Erythropoietin was found effective in 82% of patients, while 18% showed an insufficient response. Post-treatment chi-square analysis revealed statistically significant associations for age, baseline hemoglobin, and duration of dialysis ($p < 0.001$), whereas gender was not significantly associated ($p = 0.202$). **Conclusions:** Epoetin- α stands as a cornerstone in managing CKD-related anemia. Despite the efficacy, optimal dosing strategies, long-term safety profiles, and personalized treatment algorithms necessitate further research.

INTRODUCTION

Chronic kidney disease (CKD) is the most common and prevailing health issue with an overall prevalence of 21.2% in all age groups in Pakistan and 24.2% in the high-risk population [1]. Anemia in CKD leads to further morbidity, transfusion requirement, and cardiovascular risks. It has a high incidence and prevalence, with a recent study in Japan suggesting a prevalence of 40.1% in stage 4 and 60.3% in stage 5 CKD [2]. The higher prevalence among CKD stage 3 to 5 was also revealed in an Ethiopian study [3]. Human Erythropoietin (EPO), a hormone secreted by kidney, which is called a glycoprotein, under the influence of Hypoxia Inducible Transcription Factor (HIF), regulates the

production of erythrocytes. Normochromic normocytic anemia in CKD is mainly due to insufficient Erythropoietin (EPO) synthesis by the kidney as Glomerular Filtration Rate (GFR) falls and worsens with disease progression [4]. Iron and erythropoiesis-stimulating agents (ESAs) are a major form of treating anemia of chronic kidney disease and have been used for decades [4]. Treatment with erythropoietin analog was started in 1989, before which patients with symptomatic anemia were managed with blood transfusions [5, 6]. Epoetin- α was the 1st used erythropoietin analog, then darbepoetin was approved, and now other agents are being studied like Methoxy



Polyethylene Glycol-Epoetin beta, Constant Erythropoiesis Receptor Activator, Prolyl Hydroxylase Inhibitors (HIF stabilizers), and others [4, 5]. Use of Erythropoietin analogs has a clear benefit in patients with Hb < 10.0 g/dL with a possible increase of hemoglobin around 1 g/dL after 1st month of therapy [5]. A Thai study indicated the efficacy of epoetin- α , with mean Hb increased from 7.39 g/dL to 11.15 g/dL [7]. Being under-responsive and over-responsive to EPO were defined as less than 1 g/dL increase in hemoglobin level within 2 to 4 weeks and more than 1.0 g/dL during a 1- to 2-week period of treatment in an Iranian study [8]. Studies have been conducted worldwide on the management of anemia in CKD and have compared different agents.

This study was aimed to find the efficacy of epoetin- α in the management of anemia in CKD patients, as this is the only ESA currently being used in this setting and there is no previous efficacy data on epoetin- α in CKD related anemia from this particular setup. However, our study has certain limitations regarding safety profile in the long run, and individualized treatment algorithms. We can't generalize the data from a single setup of PAF hospital Mushaf. There is also a selection bias due to non-probability consecutive sampling. One month follow up is not a sufficient time to evaluate long term adverse effects.

METHODS

It was a cross-sectional study, carried out over a period of 6 months, from 1st June 2023 to 1st Dec, 2023, after getting approval from the hospital IRB (MSF(H)/308/3/1/Trg) Dated February, 2022, at Pakistan Air Force Hospital Mushaf, Sargodha. It included patients who were already on HD or not on dialysis. The method of non-probability consecutive sampling was used to select patients. A sample size of 189 patients was estimated using an efficacy of 60% from a recent Thai study [7]. The sample size was taken by using WHO's sample size calculator, with 95% confidence interval and total precision of 7. Inclusion criteria included age (20-80 years of any gender), patients with estimated GFR of less than 30 (CKD stage IV and V), CKD patients on hemodialysis or renal support medications, and patients with serum ferritin above 100 μ g/L. Exclusion criteria were CKD patients not receiving epoetin, patients who fail to follow up, Patients who deny informed consent, and patients with uncontrolled diabetes and hypertension. Permission was taken from patients. Patients were asked about their hemodialysis status and duration, as well as any comorbid conditions. All participants underwent a newly collected CBC to determine their hemoglobin concentration. CBC was performed using a Kx-21 analyzer. Epoetin was started at 4000 IU once a week, subcutaneously. Epoetin injection (Eritrogen 4000 IU) was received from the hospital medical store, where its temperature was maintained at 4°C. Before

each administration, blood pressure was checked, and patients were observed for any anaphylactic reaction. Red flag signs of thromboembolic events were explained to patients. Patients were asked for weekly follow-ups to confirm proper dosage and administration of epoetin on an outpatient basis. All of the patients received the same dose of iron and vitamin C supplements. After 1 month, CBC was repeated, and efficacy was labeled if Hb improved by ≥ 1 g/dL at the end of 1st month, as was indicated in other studies, including a recent study from Iran [8].

The data were collected by using a questionnaire and was analyzed by using SPSS version 24.0. Analysis included means and SD about quantitative data like age and hemoglobin, and frequencies for qualitative data like gender and efficacy. Data collected were stratified for age, gender, pre-treatment Hb, and duration of dialysis. Post-stratification chi-square was applied, and a p-value of < 0.05 was considered significant.

RESULTS

Out of 189 patients, 121 patients were males i.e 64% and 68 were females i.e 36%. Mean age of patients was 58.7 years (SD = 14.39; 95% CI: 56.6-60.8 years). Mean Hb before starting epoetin was 7.5 g/dL with (SD = 0.76; 95% CI: 7.39-7.61 g/dL). The mean hemoglobin level after 1 month of therapy was 8.9 g/dL (SD = 1.28; 95% CI: 8.72-9.08 g/dL). The mean change in Hb was 1.4 g/dL (95% CI: 1.2-1.6, $p < 0.001$). 140 patients (74.1%) were on dialysis at the time of study, while the remaining 49 (25.9%) were not on hemodialysis. Out of 140 patients, who were on hemodialysis, 26 (17.8%) were having dialysis for less than a month, 77 patients (52.7%) for a duration between 1-6 months, 16 (11%) between 6 months to a year, and 27 (18.5%) patients were on dialysis for more than a year. The X-axis represents HD duration, and the y-axis the proportion of patients. It shows the %age of patients in each HD category (Figure 1).

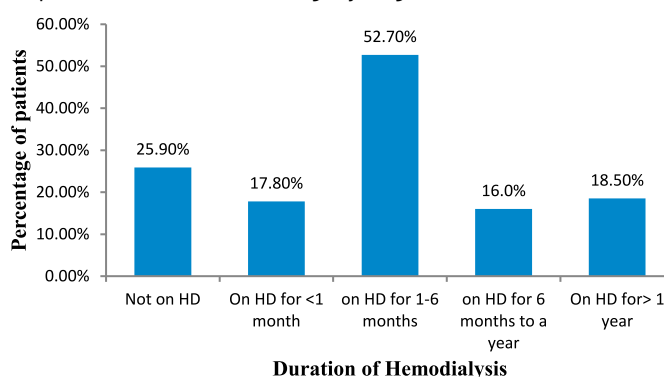


Figure 1: Distribution of Patients by Hemodialysis Status

Out of a total of 189 patients, epoetin was found efficacious (Hb improved greater than 1 g/dL in 1 month) in 155 patients i.e 82% and was not efficacious in 34 patients i.e 18%. It demonstrates the distribution of 189 patients on the y-axis

across two x-axis categories, i.e., Hb increased and not increased (Figure 2).

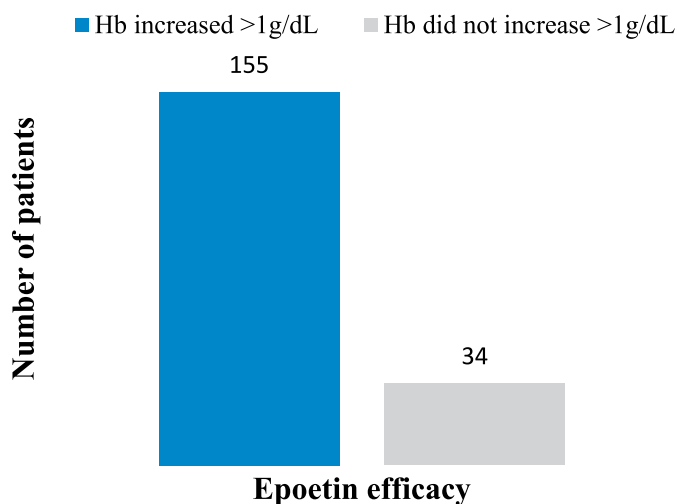


Figure 2: Epoetin Efficacy

The data were stratified for age, gender, pre-treatment Hb, and time period of dialysis, and post stratification Chi square was used to compare efficacy in different parameters. It revealed that in age groups, chi-square was statistically significant for age with a p-value of <0.001. It reveals that at both extremes of ages epoetin has higher efficacy. Epoetin- α was most effective in patients aged 20–40 years (94.7%) and 61–80 years (92.0%), but lower efficacy in the 41–60 years group (68.7%), $p < 0.001$. For gender, chi square test was not significant, and the p-value was 0.202. For hemoglobin before epoetin, chi square was significant with a p-value of <0.001. Higher Hb was associated with better outcomes. There was no significant association between dialysis and efficacy, with a p-value of 0.008. However, for the duration of dialysis, the p-value was <0.001, and the increased duration of dialysis had better results (Table 1).

Table 1: Efficacy Analysis by Various Factors (Chi-Square Test)

Factors	Category	Hb Increased >1g/dL	Hb Didn't Increase >1g/dL	Total	p-value	X ²	df
Age (Years)	20–40	18	1	19	<0.001	17.91	2
	41–60	57	26	83			
	61–80	80	7	87			
Gender	Male	96	25	121	0.202	1.71	1
	Female	59	9	68			
Hb Before Epoetin (g/dL)	6.00	0	10	10	<0.001	>60	9
	6.40	5	0	5			
	6.50	8	0	8			
	7.00	51	14	65			
	7.80	11	0	11			
	7.90	10	0	10			
	8.00	42	10	52			
	8.30	10	0	10			

Either on Dialysis or not	8.40	5	0	5	0.008	7.14	1
	9.00	13	0	13			
	Yes	121	19	140			
Duration of Dialysis	No	34	15	49	<0.001	80	3
	Less than 30 Days	9	17	26			
	1 to 6 Months	71	6	77			
	6 Months to One Year	16	0	16			
	More than One Year	27	0	27			

DISCUSSION

Chronic Kidney Disease (CKD) shows a very important world health burden, influencing millions of people globally. A meta-analysis from South Asia revealed that in South Asia, 1 in 7 adults had CKD. It further elaborated that the pooled prevalence of chronic kidney disease (CKD) in the general population was estimated at 14% (95% CI: 11–18%), with prevalence rates of 15% (95% CI: 11–20%) among adult males and 13% (95% CI: 10–17%) among adult females. Among high-risk groups, the prevalence of CKD was 27% (95% CI: 20–35%) in adults with hypertension, 31% (95% CI: 22–41%) in those with diabetes, and 14% (95% CI: 10–19%) in individuals who were overweight or obese. The prevalence of CKD of unknown origin in endemic regions was reported as 8% (95% CI: 3–16%) [9]. CKD might be associated with a lot of functional disabilities [10]. Among the myriads of complications associated with CKD, anemia is one of the major prevalent and clinically established impacts. Determinants of anemia in CKD are multifaceted [11]. A study in Ethiopia revealed overall prevalence of anemia was 85.33%. Among these patients, 28.67% had mild anemia, 40.67% had moderate anemia, and 16% had severe anemia. Stage 4 CKD, stage 5 CKD, and CKD duration of less than one year were significantly associated with anemia. Study indicated that the prevalence of anemia among patients with stage 3 to 5 CKD was notably high, and that anemia was significantly associated with both the severity and duration of CKD [3]. A systematic analysis of patients in Sub-Saharan countries revealed that more than half of the CKD patients had anemia [12]. The anemia found in CKD stems primarily from the impaired formation of erythropoietin by dysfunctional kidneys, leading to decreased red blood cell production and subsequent tissue hypoxia. ESAs like epoetin alpha and darbepoetin are used in the management of anemia in CKD [13]. A study in Thai patients revealed that Hb level increased in all enrolled patients, and 60% of patients achieved target or more than target Hb after completion of the drug [7]. The study's findings underscore the remarkable efficacy of epoetin alpha in ameliorating anemia among CKD patients. Mean levels of hemoglobin significantly increased from 7.39g/dL before therapy to 11.5 g/dL after one month of treatment,

highlighting the robust erythropoietic response elicited by epoetin alpha. A recent study in patients with myelodysplastic syndrome revealed an increase in Hb in 41.1% of patients using epoetin alpha [14]. For this study, epoetin was administered via the subcutaneous route; the study employed the SC route of administration due to the multiple advantages of the SC route over the IV route, notably a lower overall dose to get a similar target Hb level as well as the levels of hematocrit and a less frequent dosing frequency [15]. All ESAs need parenteral administration [16]. However, parenteral administration might be inconvenient for patients, which has led to novel oral therapies [17]. Other than this, a lot of anemic patients are refractory to erythropoietin effects due to inflammation, deranged iron utilization, and generation of EPO antibodies [18]. Beyond the overall efficacy of epoetin alpha therapy, our study elucidated several key factors influencing treatment outcomes in CKD-related anemia. Age emerged as a significant determinant of treatment response, with both younger and older patients demonstrating higher rates of efficacy compared to middle-aged individuals, while gender was not found as determinant of treatment response. Further exploration into age-specific treatment algorithms and considerations is warranted to optimize therapeutic outcomes and tailor interventions to individual patient needs. Contrary to age, gender did not emerge as an important predictor of treatment efficacy in the study population. Both male and female patients exhibited comparable response rates to epoetin alpha therapy, suggesting that gender may not exert a substantial influence on the erythropoietic response to treatment in CKD-related anemia. The underlying mechanisms driving the differences in age and gender-based response remain incompletely understood and warrant further investigation. Baseline hemoglobin levels emerged as a strong predictor of treatment response, with patients presenting higher baseline hemoglobin levels demonstrating more robust responses to epoetin alpha therapy. This finding underscores the significance of pre-detection and treatment in managing CKD-related anemia to prevent disease progression and optimize treatment outcomes. Moreover, the time period of dialysis emerged as a critical determinant of treatment efficacy, with longer durations of dialysis correlating with improved response rates to epoetin alpha therapy. This highlights the dynamic nature of CKD-related anemia and the need for tailored treatment strategies that account for disease progression and evolving clinical needs over time. Epoetin alpha represents a cornerstone in the management of CKD-related anemia, offering a safe and effective therapeutic option for restoring hemoglobin levels and improving clinical outcomes in affected

individuals. However, optimizing treatment outcomes requires a comprehensive understanding of the complex interplay between patient demographics, disease characteristics, and treatment modalities. Treatment with ESAs with a near-normal hemoglobin range can lead to increased risk of certain cardiovascular events, stroke, vascular access thrombosis, and death [19, 20]. Further research is warranted on the side effects of ESAs.

There were some shortcomings in our study. The current cross-sectional study design cannot establish the causality. The dose of epoetin- α should be adjusted to the individual patient needs. There was no evaluation of erythropoietin resistance variables, such as inflammation and malnutrition. An extended multi center randomized controlled trial must be conducted with an extended follow up period of 6 to 12 months for comparison between epoetin- α and newer agents as darbapoetin and HIF stabilizers. The study must also incorporate assessment of iron studies, inflammatory biomarkers, and malnutrition to identify predictors of erythropoietin resistance and to develop evidence-based, individualized dosing algorithms specifically for Pakistani CKD population.

CONCLUSIONS

The findings of current study underscored the significant efficacy of epoetin-alpha in ameliorating anemia. Our study identified several key factors influencing treatment outcomes in CKD-related anemia, including age, gender, baseline hemoglobin levels, and the duration of dialysis. Age, baseline hemoglobin, and duration of dialysis had a significant impact on the increase in hemoglobin after erythropoietin in our study.

Authors' Contribution

Conceptualization: HA

Methodology: HA, AA, MH, MKM, AH

Formal analysis: HA, MKM, AH

Writing and Drafting: HA, AA, MH, AH

Review and Editing: HA, AA, MH, MKM, AH

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All 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] Khan A, Cheema MF, Fatima R, Cheema SS, Butt Z, Gillani S et al. Prevalence of Chronic Kidney Disease in a High-Risk Population in Urban Lahore, Pakistan: A Cross-Sectional Study. *Cureus*. 2024 Jun; 16(6). doi: 10.7759/cureus.63296.
- [2] Sofue T, Nakagawa N, Kanda E, Nagasu H, Matsushita K, Nangaku M et al. Prevalence of Anemia in Patients with Chronic Kidney Disease in Japan: A Nationwide, Cross-Sectional Cohort Study Using Data from the Japan Chronic Kidney Disease Database. *PLoS One*. 2020 Jul; 15(7): e0236132. doi: 10.1371/journal.pone.0236132.
- [3] 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.00000000000031797.
- [4] Shen Y, Wang J, Yuan J, Yang L, Yu F, Wang X et al. Anemia among Chinese Patients with Chronic Kidney Disease and Its Association with Quality of Life-Results from the Chinese Cohort Study of Chronic Kidney Disease (C-STRIDE). *BioMed Central Nephrology*. 2021 Feb; 22(1): 64. doi: 10.1186/s12882-021-02247-8.
- [5] Hazin MA. Anemia in Chronic Kidney Disease. *Revista da Associação Médica Brasileira*. 2020 Jan; 66(Suppl 1): s55-8. doi: 10.1590/1806-9282.66.s1.55.
- [6] Macdougall IC. Anaemia in CKD—Treatment Standard. *Nephrology Dialysis Transplantation*. 2024 May; 39(5): 770-7. doi: 10.1093/ndt/gfad250.
- [7] Chuengsamarn P, Narenpitak S, Sritippayawan S. Efficacy and Safety of Recombinant Human Erythropoietin (Hema-Plus®) for Management of Anemia in Thai Patients on Peritoneal Dialysis. *World Journal of Nephrology*. 2021 Nov; 10(6): 109. doi: 10.5527/wjn.v10.i6.109.
- [8] Karimzadeh I, Rasekh H, Karimian A, Shabani-Borujeni M, Vazin A. Drug Utilization Evaluation of Erythropoietin at a Referral Teaching Hospital in Iran. *Advances in Pharmacological and Pharmaceutical Sciences*. 2023; 2023(1): 6685602. doi: 10.1155/2023/6685602.
- [9] Shrestha N, Gautam S, Mishra SR, Virani SS, Dhungana RR. Burden of Chronic Kidney Disease in the General Population and High-Risk Groups in South Asia: A Systematic Review and Meta-Analysis. *PLoS One*. 2021 Oct; 16(10): e0258494. doi: 10.1371/journal.pone.0258494.
- [10] Deme S, Janakiraman B, Alamer A, Wayessa DI, Yitbarek T, Sidiq M. Predictors of Functional Status and Disability Among Patients Living with Chronic Kidney Diseases at St Paul's Hospital Millennium Medical College, Ethiopia: Findings from a Cross-Sectional Study. *BioMed Central Nephrology*. 2024 Oct; 25(1): 343. doi: 10.1186/s12882-024-03783-9.
- [11] Prapaiwong P, Ruksakulpiwat S, Jariyasakulwong P, Kasetkala P, Puwarawuttipanit W, Pongsuwun K. Determinants of Anemia Among Patients with Chronic Kidney Disease: A Systematic Review of Empirical Evidence. *Journal of Multidisciplinary Healthcare*. 2025 Dec; 3765-80. doi: 10.2147/JMDH.S535423.
- [12] 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.
- [13] Hashmi MF and Shaikh H, Rout P. Anemia of Chronic Kidney Disease. In *Stat-Pearls* [Internet]. 2024 Jul. <https://www.ncbi.nlm.nih.gov/books/NBK539871/>.
- [14] Aboulela M and Collins A. Efficacy of Epoetin Alfa in Managing Symptomatic Anemia in Low-Risk Myelodysplastic Syndromes: A Retrospective Analysis. *Cureus*. 2024 Oct; 16(10). doi: 10.7759/cureus.72460.
- [15] Shahab MH and Khan SS. Erythropoietin Administration for Anemia Due to Chronic Kidney Disease-Subcutaneous or Intravenous, What Do We Know So Far? *Cureus*. 2020 Sep; 12(9). doi: 10.7759/cureus.10358.
- [16] Wish JB, Eckardt KU, Kovesdy CP, Fishbane S, Spinowitz BS, Berns JS. Hypoxia-Inducible Factor Stabilization as an Emerging Therapy For CKD-Related Anemia: Report from a Scientific Workshop Sponsored by the National Kidney Foundation. *American Journal of Kidney Diseases*. 2021 Nov; 78(5): 709-18. doi: 10.1053/j.ajkd.2021.06.019.
- [17] Singh AK, Carroll K, Perkovic V, Solomon S, Jha V, Johansen KL et al. Daprodustat for the Treatment of Anemia in Patients Undergoing Dialysis. *New England Journal of Medicine*. 2021 Dec; 385(25): 2325-35. doi: 10.1056/NEJMoa2113379.
- [18] Joharapurkar AA, Patel VJ, Kshirsagar SG, Patel MS, Savsani HH, Kajavadara C et al. Prolyl Hydroxylase Inhibitor Desidustat Improves Anemia in the Erythropoietin Hyporesponsive State. *Current Research in Pharmacology and Drug Discovery*. 2022 Jan; 3: 100102. doi: 10.1016/j.crphar.2022.100102.
- [19] Chertow GM, Pergola PE, Farag YM, Agarwal R, Arnold S, Bako G et al. Vadadustat in Patients with Anemia and Non-Dialysis-Dependent CKD. *New England Journal of Medicine*. 2021 Apr; 384(17): 1589-600. doi: 10.1056/NEJMoa2035938.
- [20] Eckardt KU, Agarwal R, Aswad A, Awad A, Block GA, Bacci MR et al. Safety and Efficacy of Vadadustat for Anemia in Patients Undergoing Dialysis. *New England Journal of Medicine*. 2021 Apr; 384(17): 1601-12. doi: 10.1056/NEJMoa2025956.



Original Article



Comparison Between Serum Electrolyte Levels in Full-Term Healthy Neonates Versus Neonates with Hypoxic Ischemic Encephalopathy

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ARTICLE INFO

Keywords:

Hypoxic Ischemic Encephalopathy, Neonates, Electrolytes, Hyponatremia, Hyperkalemia

How to Cite:Iftikhar, K., Ijaz, S. F., & Husnain, M. (2026). Comparison Between Serum Electrolyte Levels in Full-Term Healthy Neonates Versus Neonates with Hypoxic Ischemic Encephalopathy: Serum Electrolyte Levels in Healthy Neonates Versus Neonates with HIE. *Pakistan Journal of Health Sciences*, 7(6), 08-13. <https://doi.org/10.54393/pjhs.v7i6.3688>***Corresponding Author:**Muhammad Husnain
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ABSTRACT

Hypoxic ischemic encephalopathy (HIE) is a major cause of neonatal mortality and neurological disability. Hypoxia leads to multisystem involvement, causing electrolyte disturbances such as hyponatremia, hyperkalemia, and hypocalcemia, causing adverse clinical outcomes. Most studies assess these abnormalities after 24 hours of life. Detection within the first 12 hours may help reduce complications and long-term disability. **Objectives:** To compare serum sodium, potassium, and calcium levels in full-term healthy neonates versus those with HIE. **Methods:** This cross-sectional study was conducted at King Edward Medical University from June 2025 to November 2025 (IRB letter no. 512/RC/KEMU). Patients presenting to Mayo hospital over six months period were evaluated to determine the frequency of hypoxic-ischemic encephalopathy (HIE). After taking informed consent, 228 eligible subjects were identified, comprising 114 HIE and 114 non-HIE patients. Serum sodium, calcium, and potassium levels were measured within the first 12 hours of life and were compared between the two groups. Data were analyzed using SPSS version 27.0, and an independent t-test and Chi-square test were applied with a p-value <0.050. **Results:** The frequency of neonates diagnosed with HIE was 9.7%. Hyponatremia (32.3%), hyperkalemia (22.8%), and hypocalcemia (8.8%) were significantly more common in neonates with HIE. These differences were statistically significant (p<0.001). **Conclusions:** Compared to healthy neonates, neonates with HIE demonstrated significantly higher rates of electrolyte abnormalities. Identification of these electrolyte abnormalities is crucial, as timely detection and correction can play an important role in preventing further neurological damage, thereby enhancing clinical outcomes in affected neonates.

INTRODUCTION

Hypoxic Ischemic Encephalopathy is a leading cause of neonatal mortality, morbidity, and neonatal brain injury despite advancements in neonatal medicine. Approximately 17% of infants with HIE die in the neonatal period, and 25% of survivors face permanent cerebral palsy, decreased IQ, cognitive impairment, and other developmental abnormalities. The frequency of HIE ranges from 0.5 to 2% of live births [1, 2]. A study conducted in Pakistan reported the neonatal mortality rate of 64% following perinatal asphyxia (roughly 80,000 deaths/year) [2]. Hypoxic ischemic encephalopathy is an antepartum or intrapartum fetal insult causing various adverse biochemical and functional changes in the body [3]. Birth asphyxia is the most common preventable cause of

neonatal central nervous system injury [4]. The American College of Obstetricians and the American Academy of Pediatrics recommend HIE diagnosis to include the occurrence of a sentinel event immediately before or during labor, low Apgar scores, and evidence of fetal acidosis, signs of multi-organ injury affecting the heart, liver, or kidneys, and MRI findings consistent with acute intrapartum or peripartum asphyxia [3, 5]. The serum electrolyte levels play a pivotal role in the outcome of neonates with hypoxia [6]. Deviation of electrolytes from the normal levels can lead to shock, convulsions, and other types of metabolic abnormalities [7]. HIE can cause dilutional hyponatremia by causing increased secretion of antidiuretic hormone. Hyponatremia in HIE could also be



the result of elevated sodium excretion via collecting tubules [8, 9]. Hyperkalemia may occur in HIE due to increased pH of the extracellular environment that brings more potassium out. Acute kidney injury, seen in HIE, also results in hyperkalemia [10, 11]. Hypocalcemia is also observed in HIE, probably due to decreased effect of parathyroid hormone under the influence of hypoxia [1]. Early detection and immediate correction of biochemical derangements in birth asphyxia can prevent the complications and lifelong disabilities associated with it [12-14]. Although several studies elaborate on the underlying physiological association between electrolyte imbalance and hypoxic tissue damage, most of the studies determine electrolyte levels at 24h of life or later. Hyponatremia was found to be significant in all stages of birth asphyxia, hyperkalemia was associated with increased severity of birth asphyxia, whereas hypocalcemia was not found to be related to birth hypoxia [8]. The frequency of hypoxic ischemic encephalopathy in the developing world is at an alarmingly high level of 10% [15]. Early detection and immediate correction of biochemical derangements in newborns with hypoxic ischemic encephalopathy can prevent lifelong disabilities related to birth asphyxia that may occur due to injury to vital organs, particularly the brain.

There is no multicenter data available on electrolyte disturbances in HIE in Pakistan, and most research is the experience of a single center. None of the longitudinal studies have evaluated the benefits of timely electrolyte correction within 12 hours of birth on the neurodevelopmental outcome in the long run. The Mayo Hospital, Lahore, has a single-center design, which limits the generalizability throughout Pakistan. The cross-sectional design does not allow a causal or temporal correlation of HIE and electrolyte disturbances. Therefore, this study is needed to find abnormalities of serum electrolytes in hypoxic neonates within the first 12 hours of life. This study aims to compare serum sodium, potassium, and calcium levels in healthy neonates and neonates with HIE.

METHODS

This comparative cross-sectional study was carried out at Mayo Hospital, Lahore, with approval from the Institutional Review Board (IRB letter reference no. 512/RC/KEMU Dated: 28th June, 2025 and CPSP no: CPSP/REU/PED-2022-066-7108 Dated 13th April, 2025). During June 2025 to November 2025, all neonates were assessed to determine the frequency of hypoxic-ischemic encephalopathy (HIE), diagnosed based on history and examination. After completing the inclusion criteria and taking informed consent from parents, a total of 228 full-term neonates (≥ 37 weeks of gestation) were enrolled using non-

probability consecutive sampling, including 114 with HIE and 114 healthy controls. The sample size was calculated using the single population proportion formula using 95% confidence interval, 5% margin of error, and an expected percentage of HIE as 10% [15]. Inclusion criteria comprised of full-term neonates admitted within 12 hours of birth and diagnosed with HIE based on history (e.g., delayed cry, meconium-stained liquor), APGAR score of less than 7 at 5 minutes, and Sarnat staging. Syndromic babies, infants of diabetic mothers, and infants born to mothers on antiepileptics or antihypertensives were excluded from the study. Serum sodium, serum potassium, and serum calcium levels were measured within the first 12 hours of life. 3 ml venous blood was collected under aseptic conditions for serum sodium, potassium, and calcium estimation using a standard autoanalyzer. The normal reference ranges were defined according to standard laboratory reference intervals (CLSI guidelines) and Nelson's textbook as follows: serum sodium 135-145 mEq/L, serum potassium 3.5-5.0 mEq/L, and total serum calcium 8.0-10.5 mg/dL.

SPSS version 27 was used. Quantitative variables were expressed as mean $\pm$ standard deviation. Chi-square test and independent sample t-test were used with a p-value < 0.050 as statistically significant.

RESULTS

During the study period, the frequency of HIE among full-term neonates was 9.7%, with approximately 56% of cases being male and 44% female. The majority of neonates with HIE had evidence of fetal distress, as indicated by documented fetal distress during labor. In the HIE group, the mean age of gestation was 39.1 ± 1.0 weeks, with a range of 37.0 to 41.2 weeks. In the non-HIE group, the mean age of gestation was 39.0 ± 1.0 weeks, with a range of 37.0 to 41.0 weeks, indicating comparable gestational ages between the groups. Additionally, mean birth weight and mode of delivery were similar between the two groups. The comparison of mean serum electrolyte levels between patients with and without HIE is presented (Table 1).

Table 1: Comparison of Mean Serum Electrolytes Between HIE and Healthy Neonates (Group Statistics)

Electrolytes	HIE Status (Yes/No)	Number of Subjects (n)	Mean $\pm$ SD	SD Error Mean
Sodium (Na)	No	114	139.81 $\pm$ 3.772	0.353
	Yes	114	135.25 $\pm$ 5.347	0.501
Potassium (K)	No	114	4.042 $\pm$ 0.3703	0.0347
	Yes	114	4.511 $\pm$ 0.7596	0.0711
Calcium (Ca)	No	114	8.894 $\pm$ 0.5481	0.0513
	Yes	114	8.321 $\pm$ 0.9835	0.0921

An independent sample T test was performed to look for a statistically significant difference between the electrolyte levels of HIE and non-HIE groups (Table 2).

Table 2: Independent Samples t-Test Comparing Serum Electrolytes Between HIE and Non-HIE Groups

Parameters	t	df	p-value	Mean Difference	95% CI of Difference
Na	7.442	203.13	<0.001	4.561	3.353 to 5.770
K	-5.918	163.84	<0.001	-0.468	-0.624 to -0.312
Ca	5.432	177.01	<0.001	0.572	0.364 to 0.780

Among the 228 neonates studied, sodium levels showed a clear difference between those with and without hypoxic-ischemic encephalopathy (HIE). 92.1% of the healthy neonates had normal sodium levels, in comparison, only 64.9% of HIE neonates were within normal range. Hyponatremia was more frequent in HIE subjects, whereas hypernatremia was less frequent and similar in both groups (~3%)(Table 3).

Table 3: Distribution of Serum Sodium Levels in HIE and Non-HIE patients

HIE Status	Sodium within Normal Range (%)	Low (%)	High (%)	p-value
No	92.1	4.4	3.5	<0.001
Yes	64.9	32.3	1.8	
Total	78.5	18.9	2.6	

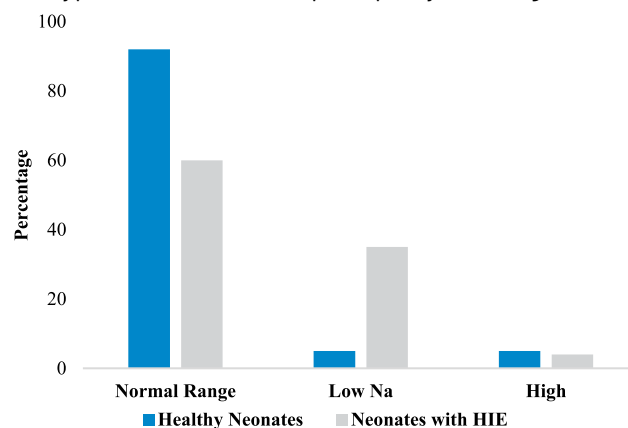
Among HIE neonates, 88.3% had normal serum calcium, while 8.8% showed hypocalcemia, and only 2.6% had hypercalcemia. In contrast, almost all healthy neonates had normal calcium levels, with only 0.9% showing low calcium. Calcium abnormalities were more frequent in the HIE group ($p=0.001$), indicating an association between HIE and calcium imbalance, particularly hypocalcemia. In addition, only 65.8% HIE neonates had normal potassium levels, while 11.4% had hypokalemia and 22.8% had hyperkalemia. In comparison, 95.6% of healthy neonates had potassium levels within the normal range, and only 1.8% having low and 2.6% having high Potassium levels. Overall, potassium abnormalities, especially hyperkalemia, were significantly more common in HIE neonates than in controls ($p<0.001$), indicating a strong association between HIE and potassium derangements (Table 4).

Table 4: Distribution of Serum Calcium Levels and Serum Potassium Levels in HIE and Non-HIE Patients

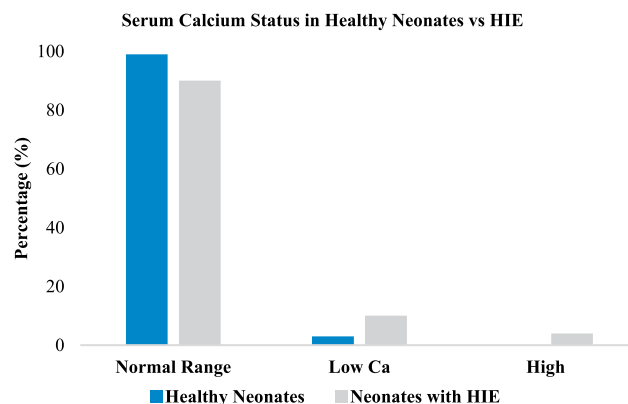
HIE Status	Within Normal Range (%)	Low (%)	High (%)	p-value
Calcium				
No	99.1%	0.9%	0.0%	0.001
Yes	88.6%	8.8%	2.6%	
Total	93.9%	4.8%	1.3%	
Potassium				
No	95.6%	1.8%	2.6%	<0.001
Yes	65.8%	11.4%	22.8%	
Total	80.7%	6.6%	12.7%	

Electrolyte disturbances were significantly more common in HIE neonates: hyponatremia (33.1% vs 3.8%),

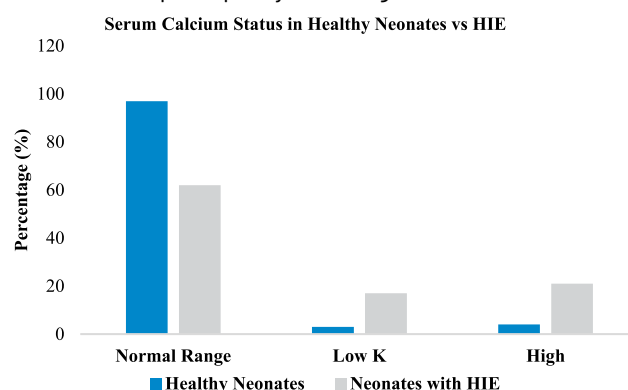
hyperkalemia (20.8% vs 2.3%), and hypocalcemia (8.5% vs 0.8%), all $p<0.001$. The study compares the distribution of serum sodium levels between healthy neonates and those with hypoxic-ischemic encephalopathy (HIE)(Figure 1).

**Figure 1:** Comparison of Serum Sodium Levels Between Healthy and HIE Neonates

The results compare the distribution of serum calcium levels between healthy neonates and those with hypoxic-ischemic encephalopathy (HIE)(Figure 2).

**Figure 2:** Comparison of Serum Calcium Levels Between Healthy and HIE Neonates

The results compare the distribution of serum potassium levels between healthy neonates and those with hypoxic-ischemic encephalopathy (HIE)(Figure 3).

**Figure 3:** Comparison of Serum Potassium Levels Between Healthy and HIE Neonates

DISCUSSION

Hypoxic Ischemic Encephalopathy remains a major cause of neonatal morbidity and mortality, especially in developing countries where the prevalence may reach up to 10% of live births [16]. This study aimed to find the frequency of neonates presenting at Mayo Hospital who are affected with HIE and to compare serum electrolyte levels, specifically sodium, potassium, and calcium, between full-term healthy neonates and those diagnosed with HIE. The findings highlight that 9.7% of the neonates had HIE, with significant electrolyte disturbances observed among the asphyxiated neonates. Study shows that the degree of hyponatremia, hyperkalemia, and hypocalcemia progressively worsened with increasing severity of HIE at baseline and subsequently [17]. In moderate to severe HIE, the most commonly mildly affected organ systems were the respiratory system, acid-base and electrolyte balance on the first day, and the cardiovascular system on the second day [18]. Neonates with HIE showed a significantly higher frequency of electrolyte disturbances, especially hyponatremia, hyperkalemia, and hypocalcemia. Hyponatremia was more frequently observed in neonates with HIE compared to healthy controls. This disturbance is likely multifactorial and may be a result of increased secretion of antidiuretic hormone in response to hypoxia, causing water retention and dilutional hyponatremia [6, 9]. Additionally, hypoxic damage causes renal tubular dysfunction that impairs sodium reabsorption, which results in increased urinary sodium loss despite low serum levels. These findings are similar to the study by Bhat *et al.* and Segar *et al.* which report hyponatremia to be a significant biochemical derangement in all stages of HIE, and it is closely linked to the severity of hypoxia and risk of seizures [8, 9]. Hyperkalemia was noted in neonates with moderate to severe HIE. The pathophysiology involves impaired renal excretion due to acute kidney injury and hypoxia-induced acidosis, leading to extracellular shifts of potassium [10, 11]. Jha *et al.* reported a strong association between hyperkalemia and asphyxia severity, suggesting its potential use as a severity marker [11]. These findings were further supported by Rajesh *et al.* who found that perinatal asphyxia significantly contributes to potassium elevation by renal compromise [10]. The correlation between hyperkalemia and the severity of asphyxia governs cardiac monitoring and timely intervention. Hypocalcemia was observed in the HIE group, which was less significantly correlated with severity compared to other electrolyte disturbances. This may be due to low parathyroid hormone responsiveness under hypoxic stress [1, 12]. Studies by Injeti *et al.* and Pyati *et al.* support this hypothesis, though the clinical significance of early hypocalcemia remains controversial [1, 12]. While some

studies show associations with poor feeding and hypotonia, other studies, such as Bhat *et al.* found no statistically significant association between hypocalcemia and birth asphyxia severity [8]. The electrolyte imbalances, such as hyponatremia, hyperkalemia, and hypocalcemia, reflect the systemic effects of perinatal hypoxia. These abnormalities demonstrate underlying pathophysiological processes affecting neurologic, endocrine, and renal systems. Acharya *et al.* emphasize that early identification and correction of these imbalances can enhance short-term clinical outcomes and lower the risk of long-term neurological complications, including cerebral palsy and developmental delay [7]. In a study conducted in 2019, 59 out of 75 newborns having HIE (78.7%) exhibited electrolyte abnormalities, including hyponatremia, hyperkalemia, hypocalcemia, or combinations of these disorders. The findings showed that electrolyte disturbances worsened with increasing severity of HIE [8]. A recent study by Nasrin *et al.* demonstrated similar electrolyte derangements [19]. Another study demonstrated similar electrolyte disturbances, which were independently associated with low Apgar scores, severe hypoxic-ischemic encephalopathy, convulsions, dehydration, need for resuscitation at birth, low birth weight, and prolonged intravenous fluid therapy [20]. Furthermore, this study highlights the importance of assessing electrolytes within the first 12 hours of life. Unlike many previous studies that assessed electrolyte levels after 24 hours, early biochemical testing allows for timely medical intervention, potentially avoiding many complications. The clinical importance of such early testing supports existing literature supporting early evaluation and stabilization in birth asphyxia management protocols [13, 14].

A limitation of this study is that the potential confounders, such as duration of birth asphyxia and early fluid or electrolyte management, were not controlled, which may have influenced the observed electrolyte abnormalities, although HIE severity was limited to moderate and severe cases. Prospective cohort studies based on multicenter studies across tertiary hospitals in Pakistan are required in order to determine the national HIE prevalence and electrolyte patterns. The need to evaluate whether early electrolyte correction positively affects neurodevelopmental outcomes should be done through longitudinal follow-up (12-24 months).

CONCLUSIONS

Neonates with HIE exhibited significantly more frequent electrolyte disturbances, particularly hyponatremia (32.3%), hyperkalemia (22.8%), and hypocalcemia (8.8%), compared with healthy neonates ($p < 0.001$). These findings highlight the strong association between HIE and electrolyte imbalance. Early detection and correction of

these disturbances is essential to minimize complications and improve outcomes. Timely electrolyte screening in neonatal resuscitation and early postnatal care in resource-limited settings with a high burden of HIE can have substantial public health benefits.

Authors' Contribution

Conceptualization: SFI

Methodology: KI

Formal analysis: MH

Writing and Drafting: KI, SFI, MH

Review and Editing: KI, SFI, MH

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All 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] Injeti G, Kher A, Taksande A, Panwar AS. Determination of Serum Electrolyte and Calcium Abnormalities in Neonates with Birth Asphyxia. *Journal of Pharmaceutical Research International*. 2021 Dec; 33(60B): 807-15. doi: 10.9734/jpri/2021/v33i60B34683.
- [2] Shamaoon M, Razzaq N, Ahsan M, Ahmad A, Maqbool T, Chaudhary AJ. Electrolyte Imbalance in Neonates with Hypoxic Ischemic Encephalopathy: A Single-Center Study. *The Professional Medical Journal*. 2020 Oct; 27(10): 2159-64. doi: 10.29309/TPMJ/2020.27.10.4128.
- [3] Shi Z, Luo K, Deol S, Tan S. A Systematic Review of Noninflammatory Cerebrospinal Fluid Biomarkers for Clinical Outcome in Neonates with Perinatal Hypoxic Brain Injury That Could be Biologically Significant. *Journal of Neuroscience Research*. 2022 Dec; 100(12): 2154-73. doi: 10.1002/jnr.24801.
- [4] Wosenu L, Worku AG, Teshome DF, Gelagay AA. Determinants of Birth Asphyxia among Live Birth Newborns in University of Gondar Referral Hospital, Northwest Ethiopia: A Case-Control Study. *Plos One*. 2018 Sep; 13(9): e0203763. doi: 10.1371/journal.pone.0203763.
- [5] Hasan BA and Al-Ani MH. Electrolyte Disturbance in Asphyxiated Neonates in Maternity Hospital in Erbil, Iraq. *Medical Journal of Babylon*. 2019 Oct; 16(4): 331-4. doi: 10.4103/MJBL.MJBL_52_19.
- [6] Bansal S, Kabra N, Singhal S, Singh S, Bassi M. A Study of Renal Parameters and Serum Electrolyte Levels in Newborns with Birth Asphyxia. *IP International Journal of Medical Pediatrics and Oncology*. 2019; 5(2): 51-3. doi: 10.18231/j.ijmpo.2019.011.
- [7] Acharya A, Swain B, Pradhan S, Jena PK, Mohakud NK, Swain A et al. Clinico-Biochemical Correlation in Birth Asphyxia and Its Effects on Outcome. *Cureus*. 2020 Nov; 12(11). doi: 10.7759/cureus.11407.
- [8] Bhat JA, Sheikh SA, Ara R. Prevalence of Electrolyte Imbalance in Hypoxic-Ischemic Encephalopathy: A Hospital-Based Prospective Observational Study. *Iran Journal of Neonatology*. 2019 Jul; 10(3).
- [9] Segar JL, Chock VY, Harer MW, Selewski DT, Askenazi DJ, Newborn Brain Society Guidelines and Publications Committee. Fluid Management, Electrolyte Imbalance, and Renal Management in Neonates with Neonatal Encephalopathy Treated with Hypothermia. In *Seminars in Fetal and Neonatal Medicine*. 2021 Aug; 26(4): 101261. doi: 10.1016/j.siny.2021.101261.
- [10] Rajesh KC, Kanodia P, Sah SN, Adhikari S. Acute Renal Failure in Newborns with Birth Asphyxia. *Journal of Nepalgunj Medical College*. 2022 Jul; 20(1): 1-3. doi: 10.3126/jngmc.v20i1.48089.
- [11] Jha G, Kumar S, Sharma S, Singh BK. Renal Profile of Asphyxiated Neonates in Relation to the Severity of Asphyxia. *International Journal of Health and Clinical Research*. 2021; 4(6): 241-244.
- [12] Pyati AK, Khanikekar PK, Shetkar NR, Patil MM, Jaju PB, Karra ML et al. Association of Cord Blood Glucose, Sodium, Potassium, and Calcium Levels with Neonatal Birth Asphyxia: A Hospital-Based Study. *Cureus*. 2022 Jun; 14(6). doi: 10.7759/cureus.26115.
- [13] Bahatkar K and Aundhakar CD. Electrolyte Status and Plasma Glucose Levels in Birth Asphyxia: A Case-Control Study. *Journal of Medical Sciences*. 2021 Jan; 41(1): 17-21. doi: 10.4103/jmedsci.jmedsci_93_20.
- [14] Islam A, Yesmin F, Islam MS, Chowdhury N, Uddin MM, Alauddin M et al. Correlation of Apgar Score with Serum Glucose, Calcium, and Electrolytes in Asphyxiated Neonates. *International Journal of Scientific Reports*. 2019 May; 5(5): 125-9. doi: 10.18203/issn.2454-2156.IntJSciRep20191859.
- [15] Hameed M, Siddiqui F, Bozdar H, Khurshid S, Sohail H, Fatima N et al. Prevalence and Pattern of Hypoxic Ischemic Encephalopathy on Magnetic Resonance Imaging among Pediatric Patients at a Tertiary Hospital in Pakistan. 2023 Mar; 17(3). doi: 10.53350/pjmhs202317310.
- [16] Odo KE, Odetunde OI, Chinawa JM, Okafor HU, Aronu AE, Adimora GN. Comparison of Plasma Electrolytes of Perinatally Asphyxiated and Normal Term Babies. *Journal of Neonatal-Perinatal Medicine*. 2020 Jan;

- 12(4): 385-9. doi:10.3233/NPM-1839.
- [17] Bhoye SV, Bhongale ND, Thorat RM, Wade PA. Biochemical Profile of Term Neonates with Perinatal Asphyxia and Their Correlation with Severity of Asphyxia. *Journal of Family Medicine and Primary Care*. 2024 Nov; 13(11): 5108-12. doi: 10.4103/jfmpc.jfmpc_676_24.
- [18] Zhang Y, Lei Y, Jiang H, Li X, Feng H. Analysis of the Correlation Between the Severity of Neonatal Hypoxic Ischemic Encephalopathy and Multiple Organ Dysfunction. *American Journal of Translational Research*. 2022 Jan; 14(1): 311.
- [19] Nasrin L, Islam MB, Mir IK, Hossain MD, Islam MS, Ahmed MU. Electrolyte Status and Plasma Calcium Levels of Birth Asphyxiated Neonates. *Scholars Journal of Applied Medical Sciences*. 2024 Jun; 6: 755-8.
- [20] Yusuf B, Ediamu T, Odoch S, Issa Ali Z, Abshir YA, Farah AA et al. Electrolyte Imbalance in Asphyxiated Term Neonates: Incidence, Predictors, and Outcomes from a Prospective Cohort Study in Northern Uganda. *medRxiv*. 2025 Oct: 2025-10. doi: 10.1101/2025.10.29.25339105.



Original Article



Comparative Efficacy of Hypertonic Versus Normal Saline Nebulization in Acute Bronchiolitis in Infants at a Tertiary Care Hospital

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ARTICLE INFO

Keywords:

Acute Bronchiolitis, Hypertonic Saline Nebulization, Normal Saline Nebulization, Infants, Respiratory Distress Assessment Instrument

How to Cite:

Emel, K., Ahmad, K., Gul, W., Khan, M. R., Pervez, K., & Ullah, Z. (2026). Comparative Efficacy of Hypertonic Versus Normal Saline Nebulization in Acute Bronchiolitis in Infants at a Tertiary Care Hospital: Hypertonic vs Normal Saline Nebulization in Infant Bronchiolitis. *Pakistan Journal of Health Sciences*, 7(6), 14-19. <https://doi.org/10.54393/pjhs.v7i6.3599>

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Received Date: 9th November, 2025

1st Revision Received: 12th December, 2025

2nd Revision Received: 31st December, 2025

3rd Revision Received: 26th February, 2026

Acceptance Date: 12th March, 2026

Published Date: 30th June, 2026

ABSTRACT

Acute bronchiolitis is a leading cause of hospitalization in infants and is managed mainly with supportive care. Nebulized 3% hypertonic saline (HS) has been used in some settings, but evidence from routine-care practice remains variable. **Objectives:** To compare short-term clinical outcomes of nebulized 3% hypertonic saline versus 0.9% normal saline administered as routine care in infants hospitalized with acute bronchiolitis at Mardan Medical Complex. **Methods:** This was a prospective quasi-experimental comparative cohort study to compare the outcomes between infants receiving 3% hypertonic saline and those receiving 0.9% normal saline. Participants were actively followed for up to 72 hours to assess clinical response, with treatment allocation based on routine clinical decisions made by the treating pediatrician. Efficacy was predefined as a ≥ 2 -point reduction in the Respiratory Distress Assessment Instrument (RDAI) score within 72 hours or discharge without supplemental oxygen. **Results:** Treatment response occurred in 27/30 (90%) in the 3% HS group versus 15/30 (50%) in the 0.9% NS group ($p < 0.001$). Mean oxygen-therapy duration was shorter (17.3 ± 4.2 vs 26.8 ± 5.6 hours; $p < 0.001$), and hospital stay was shorter (2.6 ± 0.8 vs 3.5 ± 1.0 days; $p < 0.001$) in the 3% HS group. **Conclusions:** In this routine-care setting, nebulized 3% hypertonic saline was associated with a higher treatment-response rate and shorter oxygen-therapy duration and hospital stay than 0.9% normal saline.

INTRODUCTION

Bronchiolitis is a common lower respiratory tract infection in infants and young children [1]. Most infants with bronchiolitis recover without complications, although neonates might develop respiratory failure [2]. Management of bronchiolitis is primarily supportive, focusing on hydration, oxygen supplementation when indicated, and feeding support [3]. Respiratory syncytial virus (RSV) is the most common etiologic agent of bronchiolitis. Although RSV can infect individuals across

the lifespan, bronchiolitis occurs primarily in infants and tends to be most severe in younger infants [4]. Symptomatic treatment is the key approach in managing bronchiolitis in infants [5]. It is important to thoroughly evaluate the hydration status, respiratory distress, and presence of hypoxia in all babies and children diagnosed with bronchiolitis [6, 7]. Supportive care, which involves maintaining sufficient oxygen exchange, hydration intake, and eating, is the established therapy for acute



bronchiolitis [8]. Evidence for adjunct pharmacologic therapies remains limited and inconsistent. Given that airway inflammation and mucus plugging contribute to bronchiolitis symptoms, therapies that may improve airway hydration and secretion clearance have been explored as adjuncts to supportive care. Due to its viral etiology, pharmacological treatments have not consistently demonstrated clear clinical benefit in the routine management of acute bronchiolitis. Nebulized 3% hypertonic saline may help reduce wheezing and respiratory distress in some infants with bronchiolitis [9]. Several studies have evaluated nebulized hypertonic saline as an adjunct to supportive care in bronchiolitis, with mixed findings across settings. Hypertonic saline has been studied as a potential adjunct therapy in bronchiolitis, with some studies reporting improvements in clinical severity scores and length of hospital stay; however, findings across studies and settings remain variable [10]. A study reported higher clinical improvement rates among infants receiving nebulized hypertonic saline than among those receiving normal saline in their study population [11]. It is common practice in many centers to administer inhalation therapy using salbutamol diluted in 0.9% normal saline for hospitalized children with acute bronchiolitis. However, evidence from routine-care tertiary settings in Pakistan, particularly regarding the use of hypertonic saline without bronchodilators, remains limited. In this prospective quasi-experimental comparative cohort study conducted under routine clinical care, we compared nebulized 3% hypertonic saline with 0.9% normal saline, without bronchodilators, in infants admitted with acute bronchiolitis. Treatment allocation was based on the pediatrician's clinical judgment, and participants were actively followed for 72 hours to assess clinical response. The study hypothesized that nebulized 3% hypertonic saline (without bronchodilators) would be associated with greater improvement in RDAI scores and a shorter hospital stay than 0.9% normal saline. Therefore, this study aimed to compare short-term clinical outcomes between infants receiving nebulized 3% hypertonic saline and those receiving 0.9% normal saline under routine care at Mardan Medical Complex.

METHODS

This was a prospective quasi-experimental comparative cohort study conducted under routine clinical care at the Department of Pediatrics, Mardan Medical Complex, from April to September 2024. Ethical approval was obtained from the BKMC Ethical Review Board (Ref No. BKMC/473/2024-03; Dated 29th March, 2024), and written informed consent was obtained from parents or guardians before enrollment. Treatment allocation was based on routine clinical decisions made by the treating pediatrician,

and participants were actively followed for 72 hours to assess clinical response. The study assessed differences in outcomes between infants with acute bronchiolitis who received 3% hypertonic saline nebulization and those who received 0.9% normal saline nebulization as part of routine clinical management. Sample size was calculated using the WHO Sample Size Calculator (version 2.0) at a 95% confidence level ($\alpha=0.05$, power=80%), assuming a difference in clinical response rates reported in prior studies comparing hypertonic saline and normal saline nebulization in infants with bronchiolitis [11]. Based on this, 60 infants were included, with 30 in the hypertonic saline group (Group A) and 30 in the normal saline group (Group B), using a consecutive sampling design. Infants of both genders aged 1 month to 2 years with a diagnosis of bronchiolitis of ≤ 48 hours' duration were enrolled. Bronchiolitis was defined as presentation with a persistent dry cough and noisy breathing (wheezing) with a Respiratory Distress Assessment Instrument (RDAI) score between 4 and 15 on a scale with a total possible range of 0–17. The RDAI scores wheeze (expiration, inspiration, and location) and chest retractions (supraclavicular, intercostal, and subcostal) on an ordinal scale, with higher scores indicating more severe respiratory distress. RDAI scoring followed standard published criteria. Infants suffering from congenital or acquired cardiac disease, chronic respiratory conditions, or progressive respiratory distress necessitating respiratory assistance beyond supplemental oxygen, as well as those with preterm birth (gestational age <37 weeks) or a history of neonatal mechanical ventilation, were excluded. Treatment response (operationally defined for this study) was predefined as either (i) a ≥ 2 -point reduction in total RDAI score within 72 hours of nebulization initiation, or (ii) discharge within 72 hours without supplemental oxygen. This outcome definition was used to provide a clinically interpretable RDAI-based response measure, and the RDAI has published validity and reliability data in bronchiolitis [18]. Participants were followed for 72 hours after nebulization initiation or until discharge, whichever occurred first. During follow-up, RDAI was reassessed at routine clinical reviews using the same standardized scoring criteria. Infants treated with 4 mL of 3% hypertonic saline were classified as Group A, and those treated with 4 mL of 0.9% normal saline were classified as Group B. Nebulization was generally administered three times per day at approximately 8-hour intervals, according to the treating physician's judgment, until sufficient clinical improvement for discharge. All infants received standard supportive care, including propped-up positioning, suction as required, fluid administration, routine feeding, antipyretic therapy (paracetamol) for fever, and parental counseling. Supplemental oxygen was delivered via nasal cannula or face mask and initiated when oxygen saturation

persistently fell below 90%, then titrated to maintain oxygen saturation $\geq 90\%$. Inhalation treatments were delivered using a standard nebulizer machine. No bronchodilators (e.g., salbutamol) or inhaled corticosteroids were administered during the observation period. For each infant, treatment response status and continuous outcomes, including duration of oxygen therapy (hours) and length of hospital stay (days), were recorded on the study proforma.

Data were analyzed using SPSS version 25.0. Categorical variables, such as treatment response, were summarized as frequencies and percentages and compared between groups using the Chi-square test. Effect sizes were reported as appropriate with 95% confidence intervals. Continuous variables, such as oxygen-therapy hours and length of hospital stay, were expressed as mean $\pm$ standard deviation and compared using independent-samples t-tests; normality was assessed (e.g., Shapiro-Wilk test and/or visual inspection). When normality was not satisfied, the Mann-Whitney U test was applied. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 60 infants were included in the study, with 30 in Group A (3% hypertonic saline) and 30 in Group B (0.9% normal saline). The infants were aged between 1 month and 2 years. In Group A, the mean age was 5.43 ± 3.58 months, and the mean duration of complaints was 23.23 ± 7.37 hours, whereas in Group B, the mean age was 5.83 ± 4.87 months and the mean duration of complaints was 17.50 ± 4.99 hours. Males were predominant in both groups. Baseline demographic characteristics were broadly similar between groups; however, baseline symptom duration was longer in Group A than in Group B, which may introduce residual confounding. This study was a prospective quasi-experimental comparative cohort study, where treatment allocation was based on the pediatrician's clinical judgment. Participants were actively followed for 72 hours to assess clinical response, with efficacy defined as a ≥ 2 -point reduction in RDAI or discharge without supplemental oxygen (Table 1).

Table 1: Basic Demographics of Patients and Clinical Characteristics of Infants

Demographic Characteristic	Group A (n=30), Mean $\pm$ SD	Group B (n=30), Mean $\pm$ SD
Age (Months)	5.433 $\pm$ 3.58	5.833 $\pm$ 4.87
Male	20 (66.67%)	18 (60%)
Female	10 (33.33%)	12 (40%)
Duration of Presenting Complaints (Hours)	23.233 $\pm$ 7.37	17.500 $\pm$ 4.99

Baseline symptom duration was longer in Group A than in Group B, reflecting usual-care treatment selection and potential residual confounding

In Group A, 27 of 30 infants (90%) met the predefined treatment-response criterion, compared with 15 of 30 (50%) in Group B. This difference is statistically significant ($p < 0.001$), showing a higher proportion of infants meeting the predefined treatment-response criterion in Group A than in Group B. Treatment allocation was based on the pediatrician's clinical judgment, and patients were followed for 72 hours to assess clinical response. In both groups, infants were assessed over the first 72 hours; the proportion meeting the predefined treatment-response criterion was significantly higher in the hypertonic saline group. The risk ratio for treatment response was 1.80 (27/30 vs 15/30), and the absolute risk difference was 40.0 percentage points (Table 2).

Table 2: Comparison of Treatment Response Between the Two Groups

Treatment Response	Group A (3% HS), n (%)	Group B (0.9% NS), n (%)	p-value
Yes	27 (90.0%)	15 (50.0%)	<0.001
No	3 (10.0%)	15 (50.0%)	
Total	30 (100%)	30 (100%)	

As summarized, treatment response was more frequent in the hypertonic saline group than in the normal saline group across most strata. The difference was statistically significant in infants aged 1-12 months and in both complaint-duration categories ($p = 0.016$ and $p = 0.008$); no statistically significant difference was observed in the 13-24-month subgroup, which had a small sample size. Stratified analyses suggested that the higher response rate with 3% hypertonic saline was most evident in infants aged 1-12 months and in both complaint-duration strata; interpretation remains cautious due to non-assigned usual-care treatment selection (Table 3).

Table 3: Stratification of Treatment Response by Subgroups

Age	Group	Treatment Response		p-value
		Yes	No	
1-12 Months	A	24 (88.9%)	3 (11.1%)	0.002
	B	13 (50%)	13 (50%)	
13-24 Months	A	3 (100%)	0 (0%)	0.147
	B	2 (50%)	2 (50%)	
Male	A	17 (85%)	3 (15%)	0.005
	B	8 (44.4%)	10 (55.6%)	
Female	A	8 (80%)	2 (20%)	0.055
	B	6 (50%)	6 (50%)	
Duration 1-24 Hours	A (n=13)	12 (92.3%)	1 (7.7%)	0.016
	B (n=26)	14 (53.8%)	12 (46.2%)	
Duration 25-48 Hours	A (n=17)	15 (88.2%)	2 (11.8%)	0.008
	B (n=4)	1 (25%)	3 (75%)	

Infants treated with 3% hypertonic saline required significantly fewer hours of oxygen therapy (17.3 ± 4.2 vs. 26.8 ± 5.6 hours, $p < 0.001$) and had a shorter mean hospital stay (2.6 ± 0.8 vs. 3.5 ± 1.0 days, $p < 0.001$) than those treated

with normal saline, with shorter observed oxygen-therapy duration and hospital stay in the hypertonic saline group (Table 4).

Table 4: Oxygen Therapy Duration and Length of Hospital Stay

Outcomes	Group A (3% HS)	Group B (0.9% NS)	p-value
Oxygen Therapy, Hours (Mean $\pm$ SD)	17.3 $\pm$ 4.2	26.8 $\pm$ 5.6	<0.001
Length of Stay, Days (Mean $\pm$ SD)	2.6 $\pm$ 0.8	3.5 $\pm$ 1.0	

DISCUSSION

Bronchiolitis is common among children under two years old and is a leading cause of hospitalization for respiratory illness in early childhood [12–14]. The objective of this study was to compare short-term clinical outcomes between infants receiving nebulized 3% hypertonic saline and those receiving 0.9% normal saline under routine clinical care. Both cohorts showed little demographic variation in age and sex, and clinical signs and symptoms were broadly similar at baseline. Baseline clinical features were comparable between groups; however, given the usual-care treatment selection, baseline differences in symptom duration were noted and cannot be fully excluded. Infants who received 3% hypertonic saline had a higher observed rate of clinical improvement than those who received normal saline (0.9%). The former group had an average of approximately 9 fewer hours of oxygen administration compared with the latter group. Approximately 90% of infants treated with 3% hypertonic saline met the predefined treatment-response criterion within 72 hours, compared with 50% of those treated with 0.9% normal saline [11]. No treatment-limiting adverse events were documented during hospitalization; however, adverse events were not collected using a dedicated active-surveillance tool. As the basic clinical parameters were broadly similar between the two groups, the observed variation in outcomes (with a higher treatment-response rate among those treated with nebulized 3% saline) may be associated with the type of saline used. However, causal inference is limited by the quasi-experimental study design (non-randomized treatment allocation). In this study, the utilization of 3% hypertonic saline was associated with a significantly shorter duration of hospitalization. These differences were accompanied by a significantly shorter length of hospital stay, with many patients in Group A being discharged within three days of treatment. Nonetheless, in infants with acute bronchiolitis, 3% hypertonic saline was associated with a higher RDAI-defined treatment response and shorter observed oxygen-therapy duration and hospital stay compared with 0.9% normal saline in this cohort. No treatment-limiting adverse events were documented during hospitalization. Our findings are broadly consistent with previous studies reporting reduced hospital stay in infants treated with 3% hypertonic

saline compared with normal saline [15]. The administration of oxygen should be guided by oxygen saturation. When oxygen saturation persistently falls below 90% in infants with bronchiolitis, supplemental oxygen is typically initiated and titrated according to oxygen saturation and clinical status [16]. In this study, the hypertonic saline group required fewer hours of oxygen therapy than the normal saline group (approximately 9 hours fewer on average), and a previous study reported a similar observation [17]. Prior studies have reported that nebulized 3% hypertonic saline may be associated with faster clinical improvement than 0.9% normal saline in infants with acute bronchiolitis. Several studies have also reported a shorter length of hospital stay with hypertonic saline compared with normal saline among admitted infants [18, 19]. Many investigations used bronchiolitis severity scores (including RDAI or similar validated scores) to assess changes over time. For example, studies evaluating nebulized 3% hypertonic saline administered with epinephrine every 6–8 hours reported improvements in bronchiolitis severity scores and shorter hospitalization duration compared with 0.9% saline with epinephrine. No serious adverse events were reported in those investigations [19, 20]. These findings are broadly consistent with the current study, as the oxygen-therapy duration in the hypertonic saline group was notably shorter (approximately 17 hours) compared to the normal saline group. Previous studies have reported mixed findings regarding the clinical benefit of nebulized hypertonic saline in infants with acute bronchiolitis [9]. However, another study investigating the utilization of 3% hypertonic saline in the accident and emergency room proposed that there may not be immediate therapeutic advantages seen with the administration of nebulized hypertonic saline [21]. Although hypertonic saline has been proposed to improve airway surface hydration and facilitate mucus clearance, these mechanisms were not directly assessed in the present study. Therefore, interpretation is based on observed clinical outcomes rather than physiological measures [22–24]. Nebulization with hypertonic saline (3%) was well tolerated in this cohort and was associated with a higher RDAI-defined treatment response and shorter observed oxygen-therapy duration and hospital stay than normal saline among infants hospitalized with acute bronchiolitis. No treatment-limiting adverse events were documented in routine records, although adverse events were not captured using a dedicated active-surveillance tool [18–20]. Hypertonic saline is inexpensive and widely available; however, formal cost-effectiveness was not evaluated in this study. Furthermore, our findings are consistent with the Cochrane review reporting shorter hospitalization in some settings with hypertonic saline [9].

Across both groups, respiratory rate, wheeze, retractions, overall clinical condition, and clinical severity scores improved over three days, with improved room-air oxygen saturation [25]. Our quantitative analysis shows substantially shorter oxygen use and hospital stay with hypertonic saline (both $p < 0.001$).

However, because treatment was selected as part of routine care, residual confounding (including baseline symptom duration) cannot be excluded. Baseline symptom duration differed between groups, which may reflect confounding by indication. This was a single-center, quasi-experimental comparative cohort study with a modest sample size and no blinding, which may limit generalizability and introduce selection and measurement bias. Baseline imbalances suggest possible residual confounding, and adverse events were not captured using a dedicated surveillance tool. We did not separately analyze the proportion requiring supplemental oxygen; instead, we assessed oxygen-therapy duration as a more sensitive outcome. Larger multicenter studies with more rigorous designs and systematic adverse-event monitoring are warranted to confirm these observed associations.

CONCLUSIONS

In this prospective quasi-experimental comparative cohort study, nebulized 3% hypertonic saline was associated with a higher RDAI-defined treatment response and shorter oxygen-therapy duration and hospital stay than 0.9% normal saline among infants admitted with acute bronchiolitis. These findings should be interpreted cautiously due to routine care treatment allocation, baseline differences, and potential residual confounding.

Authors' Contribution

Conceptualization: KE

Methodology: KE, KA

Formal analysis: MRK, ZU

Writing and Drafting: KE, KA, WG, MRK, KP

Review and Editing: KE, KA, WG, MRK, KP, ZU

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All 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] Moulia DL. Use of Clesrovimab for Prevention of Severe Respiratory Syncytial Virus-Associated Lower Respiratory Tract Infections in Infants: Recommendations of The Advisory Committee on Immunization Practices—United States. *Morbidity and Mortality Weekly Report*. 2025 Aug; 74(32): 508–514. doi: 10.15585/mmwr.mm7432a3.
- [2] Jo YM, Kim J, Chang J. Vaccine Containing G Protein Fragment and Recombinant Baculovirus Expressing M2 Protein Induces Protective Immunity to Respiratory Syncytial Virus. *Clinical and Experimental Vaccine Research*. 2019 Jan; 8(1): 43–53. doi: 10.7774/cevr.2019.8.1.43.
- [3] Oz-Alcalay L, Ashkenazi S, Glatman-Freedman A, Weisman-Demri S, Lowenthal A, Livni G. Hospitalization for Respiratory Syncytial Virus Bronchiolitis in the Palivizumab Prophylaxis Era: Need for Reconsideration of Preventive Timing and Eligibility. *Israel Medical Association Journal*. 2019 Feb; 21(2): 110–115.
- [4] Soudani N, Caniza MA, Assaf-Casals A, Shaker R, Lteif M, Su Y et al. Prevalence and Characteristics of Acute Respiratory Virus Infections in Pediatric Cancer Patients. *Journal of Medical Virology*. 2019 Jul; 91(7): 1191–1201. doi: 10.1002/jmv.25432.
- [5] Supino MC, Buonsenso D, Scateni S, Scialanga B, Mesturino MA, Bock C et al. Point-of-Care Lung Ultrasound in Infants with Bronchiolitis in The Pediatric Emergency Department: A Prospective Study. *European Journal of Pediatrics*. 2019 May; 178(5): 623–632. doi: 10.1007/s00431-019-03335-6.
- [6] Lodeserto FJ, Lettich TM, Rezaie SR. High-Flow Nasal Cannula: Mechanisms of Action and Adult and Pediatric Indications. *Cureus*. 2018 Nov; 10(11): 1–9. doi: 10.7759/cureus.3639.
- [7] Stobbelaar K, Kool M, de Kruijf D, Van Hoorenbeeck K, Jorens P, De Dooy J et al. Nebulised Hypertonic Saline in Children with Bronchiolitis Admitted to The Paediatric Intensive Care Unit: A Retrospective Study. *Journal of Paediatrics and Child Health*. 2019 Sep; 55(9): 1125–1132. doi: 10.1111/jpc.14371.
- [8] Petrarca L, Jacinto T, Nenna R. The Treatment of Acute Bronchiolitis: Past, Present and Future. *Breathe*. 2017 May; 13(1): 24–26. doi: 10.1183/20734735.000717.
- [9] Zhang L, Mendoza-Sassi RA, Wainwright C, Klassen TP. Nebulised Hypertonic Saline Solution for Acute Bronchiolitis in Infants. *Cochrane Database of Systematic Reviews*. 2013; 7: 1–41. doi: 10.1002/14651858.CD006458.pub3.
- [10] Máiz Carro L and Martínez-García MA. Nebulized Hypertonic Saline in Noncystic Fibrosis Bronchiectasis: A Comprehensive Review. *Therapeutic Advances in Respiratory Disease*. 2019 Aug; 13: 1–15. doi: 10.1177/1753466619866102.

- [11] Islam KT, Mollah AH, Matin A, Begum M. Comparative Efficacy of Nebulized 3% Hypertonic Saline Versus 0.9% Normal Saline in Children with Acute Bronchiolitis. *Bangladesh Journal of Child Health*. 2018 Dec; 42(3): 130-137. doi: 10.3329/bjch.v42i3.39264.
- [12] Sanghavi B and Sugapradha GR. Clinical Profile and Outcome of Bronchiolitis in Children With 1-24 Months of Age. *Cureus*. 2024 Sep; 16(9): 1-6.
- [13] Erickson EN, Bhakta RT, Tristram D, Mendez MD. Pediatric bronchiolitis. StatPearls Publishing. 2025 Jan.
- [14] Almansoor BA. Epidemiology of Hospitalization for Acute Bronchiolitis in Children: A Systematic Review. *International Journal of Medicine in Developing Countries*. 2023 Apr; 7(7): 1046. doi: 10.24911/IJMDC.51-1677868429.
- [15] Omparkash AL, Laghari TM, Sirichand MA, Aslam M. Compare the Clinical Severity and Length of Hospital Stay in Children with Bronchiolitis Treated with the 3% Hypertonic Saline Nebulization Versus Normal Saline and Salbutamol. 2023; 17(3): 448-451. doi: 10.53350/pjmhs2023173448.
- [16] Louman S, van Stralen KJ, Pijnenburg MW, Koppelman GH, Boehmer AL. Oxygen Saturation Targets for Children with Respiratory Distress: A Systematic Review. *European Respiratory Society open research*. 2023 Oct; 9(5). doi: 10.1183/23120541.00256-2023.
- [17] Jhaveri S, Patel B, Kariya PV. A Prospective Study on the Efficacy of Hypertonic Saline Nebulization in Infants with Acute Bronchiolitis. *European Journal of Cardiovascular Medicine*. 2025 Apr; 15: 593-595.
- [18] Alamer HS, Asiri AJ, Aalhassan A, Tahaeibashir SE. A retrospective study on the effect of nebulized hypertonic saline (3%) vs. epinephrine on admission rates among infants with acute moderate to severe bronchiolitis at AFHSR. *International Journal of Advanced Research*. 2025; 13(1): 1360-1368. doi: 10.21474/IJAR01/20326.
- [19] Mahjoub E, Suliman O, Alhussain Z, Alsubhi H, Altom S. Clinical Practice Guidelines for the Diagnosis and Management of Bronchiolitis in Infants and Young Children: A Systematic Review. *Vascular and Endovascular Review*. 2025 Oct; 8(5): 43-54.
- [20] Parveen A, Naureen S, Waseem R, Noor T, Malik T, Shaheen B. Comparison Between 0.9% Normal Saline and 0.3% Hypertonic Saline Nebulization in Acute Bronchiolitis in Terms of Mean Length of Hospital Stay. *Pakistan Pediatric Journal*. 2025 Aug; 49(2): 1-5.
- [21] Brown CS, Rabinstein AA, Zhao Y, Wieruszewski ED. Safety of Peripheral 3% Hypertonic Saline Bolus Administration for Neurologic Emergency. *The American Journal of Emergency Medicine*. 2023 Jul; 69: 83-86. doi: 10.1016/j.ajem.2023.04.007.
- [22] Khan Z, Naeem MO, Amin A, Amin L, Shah A, Khaliq SU et al. Effectiveness of Hypertonic Saline with or without Hyaluronic Acid Among Patients with Cystic Fibrosis: A Systematic Review and Meta-Analysis. *Annals of Medicine and Surgery*. 2024 Oct; 86(10): 6091-6096. doi: 10.1097/MS9.0000000000002450.
- [23] Kelly S, Valentine M, Chua WH, Tatkov S. Impact of High-And Low-Flow Nebulised Saline on Airway Hydration and Mucociliary Transport. *ERJ Open Research*. 2023 Jun; 9(3): 1-10. doi: 10.1183/23120541.00724-2022.
- [24] Roe T, Talbot T, Terrington I, Johal J, Kemp I, Saeed K et al. Physiology and Pathophysiology of Mucus and Mucolytic Use in Critically Ill Patients. *Critical Care*. 2025 Feb; 29(1): 68. doi: 10.1186/s13054-025-05286-x.
- [25] Ahmadi Z, Smallwood NE, Russell AM, Saggu R, Romero L, Holland AE et al. Supplemental Oxygen for Symptomatic Relief in People with Serious Respiratory Illness: A Systematic Review and Meta-Analysis. *European Respiratory Review*. 2025 Mar; 34(175): 1-19. doi: 10.1183/16000617.0025-2024.



Original Article



Comparison of Rivaroxaban Versus Warfarin in Resolution of Left Ventricular Thrombus After Acute Anterior Wall Myocardial Infarction: A Prospective Cohort Study

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ARTICLE INFO

Keywords:

Echocardiography, Myocardial Infarction, Rivaroxaban, Thrombosis, Warfarin

How to Cite:

Siddique, M. Z., Majid, A., Nawaz, J. N., Razaq, M. K., & Faiz, S. A. (2026). Comparison of Rivaroxaban Versus Warfarin in Resolution of Left Ventricular Thrombus After Acute Anterior Wall Myocardial Infarction: A Prospective Cohort Study: Rivaroxaban vs Warfarin for Left Ventricular Thrombus. *Pakistan Journal of Health Sciences*, 7(6), 20-25. <https://doi.org/10.54393/pjhs.v7i6.3638>

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Received Date: 6th December, 2025

1st Revision Received: 17th February, 2026

2nd Revision Received: 9th March, 2026

Acceptance Date: 12th March, 2026

Published Date: 30th June, 2026

ABSTRACT

There is emerging evidence that direct oral anticoagulants like rivaroxaban are a more effective alternative for thrombus resolution after acute myocardial infarction. **Objective:** To compare the rate of left ventricular thrombus resolution between rivaroxaban and warfarin after acute anterior wall myocardial infarction. **Methods:** This prospective cohort study was conducted in the Department of Cardiology at Sheikh Zayed Hospital, Rahim Yar Khan, from May to November 2025. A total of 290 participants with left ventricular thrombus after acute anterior wall myocardial infarction were enrolled in the study. The unexposed group consisted of patients treated with warfarin, with the dose adjusted to maintain an INR of 2.0-3.0. The exposed group received rivaroxaban (20 mg daily; 15 mg if creatinine clearance was 30-50 ml/min/1.73m²). Echocardiography was performed at baseline and repeated after three months to assess thrombus resolution. Data were analyzed through SPSS version 25.0. Descriptive statistics were run, and an independent sample t-test was used for numerical comparison and a chi-square test for categorical comparison. **Results:** The mean age was 60.4 ± 6.4 years, with 73.4% males. Baseline demographics were comparable between the groups. Thrombus resolution at three months was achieved in 52.4% overall, significantly higher in rivaroxaban versus warfarin (61.4% vs. 43.4%, p-value=0.002; RR: 1.4, 95% CI: 1.1-1.8). Diabetes, hypertension, and thrombus size ≥1 cm were associated with lower thrombus resolution rates. **Conclusions:** Rivaroxaban demonstrated better efficacy over warfarin for thrombus resolution in post-myocardial infarction patients. Comorbid diabetes, hypertension, and larger thrombosis size were significant negative predictors of resolution.

INTRODUCTION

Patients with left ventricular systolic dysfunction are more likely to experience left ventricular thrombosis (LVT), mostly a fatal condition that typically develops between 1 day and 2 weeks following myocardial infarction (MI) [1]. A significant 10-40% chance of MI, acute stroke, distal embolism, and other severe cardiovascular incidents is linked to the establishment of LVT [2]. LVT is seen in 3-7% cases with significant LV dysfunction and may increase up to 20-22% in individuals with ST-elevation myocardial infarction (STEMI), even though its prevalence has declined in comparison to the pre-thrombolytic era [3]. Warfarin and other vitamin K antagonists (VKAs) are common

anticoagulant medications used to treat LVT, in cases of an international normalised ratio (INR) of 2-3, during treatment [4]. The family of Direct Oral Anticoagulants (DOACs) includes the direct factor Xa inhibitor rivaroxaban. It can be used to treat non-valvular atrial fibrillation, pulmonary embolism (PE), and deep vein thrombosis (DVT). Rivaroxaban's use in preventing atherothrombotic events after acute coronary syndrome (ACS) is one of its noteworthy features [5]. Compared to VKAs, DOACs—like rivaroxaban—have fewer dietary and medication interactions, less chance of cerebral haemorrhage, less need for frequent monitoring, and improved drug



adherence, making them promising therapies for LVT [6]. Only diverse retrospective observational studies have evaluated the safety and effectiveness of DOACs in treating LVT in individuals presenting with acute coronary syndrome (ACS) [7, 8]. Mansouri et al. enrolled 52 patients with ACS, equally divided into rivaroxaban and warfarin groups (26 patients each). The thrombus resolution rates in the rivaroxaban (76.9%) and warfarin (69.2%) groups, as well as the thrombus size reduction, did not show any major difference between the two groups [9]. Prajapati et al. studied 21 cases in the Warfarin group and 19 patients in the Rivaroxaban group. Three months after the treatment initiation, thrombus resolution in the rivaroxaban group was 47.7% vs. 33.4% in the warfarin group [10]. Current study was planned to assess the efficacy of rivaroxaban versus warfarin in managing LVT in patients with ACS. Identifying a more effective and safer anticoagulant will reduce the risk of embolic complications, improving patient outcomes after anterior wall MI. If rivaroxaban proves superior or non-inferior to warfarin, it will lead to updated treatment guidelines, simplifying LVT management. Reducing hospital visits for INR monitoring will ease the burden on healthcare systems and enhance patient convenience. We hypothesized that the thrombus resolution rate in three months would be higher in rivaroxaban compared to warfarin after acute anterior wall myocardial infarction.

There is limited evidence comparing the efficacy and safety of rivaroxaban with the traditionally used warfarin for the management of left ventricular thrombus (LVT) following acute coronary syndrome, particularly after anterior wall myocardial infarction. Warfarin therapy also requires frequent INR monitoring, which increases the burden on both patients and healthcare systems. Therefore, this study aimed to assess the efficacy of rivaroxaban compared with warfarin in the management of LVT in patients with acute coronary syndrome.

METHODS

This prospective cohort study was conducted at the Department of Cardiology of Sheikh Zayed Hospital, Rahim Yar Khan. Participants were enrolled in the study over a period of six months from 21st May 2025 to 20th November 2025, through consecutive sampling. The study was conducted after approval from the institutional ethics committee (ERC#145-/IRB/SZMC/SZH; Dated 23rd April, 2025). A total of 290 participants, 40-80 years of age, either male or female gender, admitted to the hospital due to left ventricular thrombus after acute anterior wall myocardial infarction, were included in the study after written informed consent. Participants with a history of clotting disorder, antiphospholipid syndrome, atrial fibrillation, deep venous thrombosis, pulmonary embolism, on

anticoagulation therapy, estimated GFR < 30 mL/min/1.73m², platelet count < 50,000/mm³, chronic liver disease, pregnant and breastfeeding women were excluded from the study. Patients were managed according to routine clinical practice, and the decision to prescribe rivaroxaban or warfarin was made by the treating physician in consultation with the patient, based on clinical judgment, patient preference, and drug availability. The standard/unexposed group consisted of the patients treated with Warfarin, and the exposed group was the patients treated with Rivaroxaban. After enrolment, baseline characteristics of participants, including age, gender, obesity, diabetes, hypertension, and smoking, were recorded. All the participants had baseline transthoracic echocardiography performed by a consultant cardiologist to confirm the presence and size of the thrombus before starting thrombolytic therapy. Dual antiplatelet therapy was prescribed to all the participants as per hospital protocol. All the patients in the warfarin group had baseline prothrombin time (PT) and international normalized ratio (INR) measured before starting treatment. The initial dose of 5 mg was titrated to keep INR between 2.0 and 3.0. The patients in the exposed group were prescribed 20 mg of rivaroxaban once daily at bedtime. The dose was reduced to 15 mg if creatinine clearance was between 30 - 50 mL/min/1.73m². The treatment was continued for three months with fortnightly follow-ups. All patients were verbally inquired about adverse drug reactions during each follow-up visit. After treatment, echocardiography was repeated by the same operator, not aware of the thrombolytic treatment given. The status of thrombus resolution was recorded. The primary outcome was defined as complete thrombus resolution, characterized by the absence of any visible thrombus on follow-up echocardiography. The same predefined criteria were applied consistently to all participants to ensure standardized, transparent outcome assessment. Safety assessment was limited to major adverse events, specifically stroke, pulmonary embolism, and deep vein thrombosis, identified through scheduled clinical follow-up and review of hospital records [10]. These outcomes were defined as clinically diagnosed and are imaging-confirmed events. A sample size of 290 patients, 1:1 ratio of both groups, was calculated assuming 47.7% thrombus resolution in the rivaroxaban and 33.4% in the warfarin thrombolysis treatment groups at 80% power of the study and 5% significance level. The sample size was calculated through the OpenEpi online software using the cohort study formula: $n = \frac{(Z_{\alpha/2} + Z_{1-\beta})^2 pq(r+1)}{r(p_1 - p_2)^2}$.

The data were analysed through SPSS version 25.0. Normality of age and thrombus size was assessed using the Shapiro-Wilk test, and as both variables followed a normal distribution, they were summarized as mean $\pm$ standard deviation. Frequency and percentages are reported for

categorical data. Between-group comparisons are made using an independent sample t-test for numerical data and a chi-square test for categorical data. Relative Risk with 95% confidence interval is calculated to identify factors associated with complete thrombus resolution. For all the comparisons, p-value <0.05 is considered significant. To estimate adjusted relative risks (aRR) for complete thrombus resolution, a multivariable generalized linear model with a log link function and binomial distribution was applied. Adjusted relative risk and their 95% confidence intervals were derived directly from the model coefficients. Covariates included in the multivariable model were selected a priori based on clinical relevance and variables demonstrating a p-value < 0.20 in univariate analysis. Statistical significance of individual predictors was assessed using Wald chi-square statistics. To assess potential multicollinearity among predictors, variance inflation factors (VIFs) were examined. A VIF>10 was considered indicative of significant collinearity. No substantial multicollinearity was detected in the final model. This study was conducted and reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for observational research.

RESULTS

The mean age of the participants was 60.4 ± 6.4 years, with 56.2% (n=163) 60 years and above. There were 73.4% (n=213) male patients. Obesity was prevalent in 26.6% (n=77), diabetes in 40.3% (n=117), hypertension in 44.1% (n=128), and smoking in 43.4% (n=126) of the patients. The mean thrombus size was 11.3 ± 5.0 mm, with 56.2% (n=163) having a thrombus size of one cm or above. The demographic characteristics were comparable between the warfarin and rivaroxaban thrombolysis therapy groups. No hospital-acquired infection during hospital stay was observed. No adverse drug reactions or adverse events (stroke, pulmonary embolism, DVT) were observed during the follow-up (Table 1).

Table 1: Characteristics of Patients with Left Ventricular Thrombus After Acute Anterior Wall Myocardial Infarction (n=290)

Characteristic	Overall (n=290)	Warfarin Group (n=145)	Rivaroxaban Group (n=145)	p-value*
Age (years)	60.4 ± 6.4	59.9 ± 6.6	60.9 ± 6.1	0.188 ^a
< 60-years old	127 (43.8%)	67 (52.8%)	60 (47.2%)	0.407 ^b
≥ 60-years old	163 (56.2%)	78 (47.9%)	85 (52.1%)	
Gender - Male	213 (73.4%)	107 (50.2%)	106 (49.8%)	0.894 ^b
Female	77 (26.6%)	38 (49.4%)	39 (50.6%)	
Obesity - Yes	77 (26.6%)	36 (46.8%)	41 (53.2%)	0.506 ^b
Diabetic - Yes	117 (40.3%)	58 (49.6%)	59 (50.4%)	0.905 ^b
Hypertensive - Yes	128 (44.1%)	62 (48.4%)	66 (51.6%)	0.636 ^b
Smoker - Yes	126 (43.4%)	64 (50.8%)	62 (49.2%)	0.813 ^b
Thrombus size (mm)	11.3 ± 5.0	11.6 ± 5.5	11.0 ± 4.5	0.318 ^a

< 1 cm	127 (43.8%)	65 (51.2%)	62 (48.8%)	0.723 ^b
≥ 1 cm	163 (56.2%)	80 (49.1%)	83 (50.9%)	

*Independent sample t-test for numerical comparison and chi-square for categorical b comparison

Three months after treatment, thrombus resolution was achieved in 52.4% (n=152) of all the participants. Rate of thrombus resolution was significantly higher in the rivaroxaban group compared to warfarin (61.4% vs. 43.4%, p-value=0.002) (Figure 1).

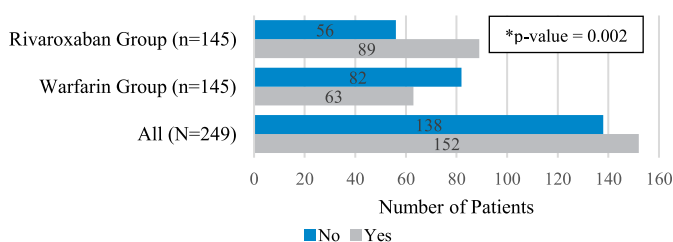


Figure 1: Thrombus Resolution After Three Months in Study Participants (n=290)

*chi-square test

Compared to warfarin therapy, the relative risk of thrombus resolution was significantly higher in rivaroxaban treatment [61.4% vs. 43.4%: RR (95%CI): 1.4 (1.1 – 1.8), p-value = 0.003]. Compared to patients without diabetes, the relative risk of thrombus resolution was significantly lower in diabetics [40.2% vs. 60.7%: RR (95%CI): 0.66 (0.5 – 0.9), p-value <0.001]. Compared to patients without hypertension, the relative risk of thrombus resolution was significantly lower in hypertensive patients [41.4% vs. 61.1%: RR (95%CI): 0.67 (0.5 – 0.8), p-value <0.001]. Incidence of thrombus resolution was significantly lower in thrombus size ≥ 1 cm compared to <1cm [28.8% vs. 82.7%: RR (95%CI): 0.35 (0.3 – 0.5), p-value <0.001] (Table 2).

Table 2: Factors Associated with Thrombus Resolution in Patients with Left Ventricular Thrombus After Acute Myocardial Infarction (n=290)

Associated Factors		Thrombus Resolution		Relative Risk (95% CI)	p-value
		Yes	No		
Treatment	Rivaroxaban	89 (61.4%)	56 (38.6%)	1.4 (1.1 – 1.8)	0.003*
	Warfarin	63 (43.4%)	82 (56.6%)		
Age groups	< 60-year	72 (56.7%)	55 (43.3%)	1.2 (0.9 – 1.4)	0.195
	≥ 60-year	80 (49.1%)	83 (50.9%)		
Gender	Male	106 (49.8%)	107 (50.2%)	0.8 (0.6 – 1.1)	0.116
	Female	46 (59.7%)	31 (40.3%)		
Obesity	Yes	34 (44.2%)	43 (55.8%)	0.8 (0.6 – 1.1)	0.110
	No	118 (55.4%)	95 (44.6%)		
Diabetes	Yes	47 (40.2%)	70 (59.8%)	0.66 (0.5 – 0.9)	<0.001*
	No	105 (60.7%)	68 (39.3%)		
Hypertension	Yes	53 (41.4%)	75 (58.6%)	0.67 (0.5 – 0.8)	<0.001*
	No	99 (61.1%)	63 (38.9%)		
Smoker	Yes	61 (48.4%)	65 (51.6%)	0.87 (0.7 – 1.1)	0.238
	No	91 (55.5%)	73 (44.5%)		

Thrombus Size	≥ 1cm	47 (28.8%)	116 (71.2%)	0.35 (0.3 – 0.5)	<0.001*
	< 1cm	105 (82.7%)	22 (17.3%)		

*chi-square test, significant p-value

Five independent predictors were identified in the multivariable model, including treatment as the primary exposure variable. Thrombus resolution was 3.7 (1.9 – 7.1) times higher in the rivaroxaban group compared to warfarin. Thrombus size of ≥ 1cm [aRR: 0.07 (0.03 – 0.14)], smoking [aRR: 0.29 (0.15 – 0.58)], hypertension [aRR: 0.27 (0.14 – 0.54)], and diabetes [aRR: 0.43 (0.23 – 0.78)] were significant negative predictors of thrombus resolution (Table 3).

Table 3: Independent Predictors of Thrombus Resolution in Patients with Left Ventricular Thrombus After Acute Myocardial Infarction (n=290)

Independent Predictors		Adjusted Relative Risk (95% CI)	Wald chi-square	P-value
Treatment	Rivaroxaban	3.7 (1.9 – 7.1)	16.1	<0.001*
	Warfarin	1		
Thrombus Size	≥ 1cm	0.07 (0.03 – 0.14)	56.7	<0.001*
	< 1cm	1		
Smoking	Yes	0.29 (0.15 – 0.58)	12.3	<0.001*
	No	1		
Hypertension	Yes	0.27 (0.14 – 0.54)	14.1	<0.001*
	No	1		
Diabetes	Yes	0.43 (0.23 – 0.78)	7.6	<0.006*
	No	1		

*Significant p-value

DISCUSSION

In our study, we found that three months after treatment, thrombus resolution was achieved in almost half of all the participants. The rate of thrombus resolution was significantly higher in the rivaroxaban group compared to warfarin. LVT is very common after STEMI, even though it can happen in conditions other than infarction. The increased risk of embolization and ischemic stroke makes medical management of LVT extremely difficult. One of the key components of managing LVT is anticoagulation therapy. For the treatment of post-ACS, LVT, current guidelines (ESC, ACCF/AHA) mainly recommend using VKAs (warfarin) for a maximum of three to six months [11]. At the same time, individuals who have poor warfarin compliance are recommended to take DOACs. However, the off-label use of DOACs among patients with LVT has increased recently due to no dietary limitations, the lack of frequent monitoring requirements, and the absence of various drug interactions associated with warfarin [12]. In a pilot randomized research, Jenab Y et al found that after 3-months, full LVT resolution was 76.0% with rivaroxaban and 54.2% with warfarin (RR ~1.40). In both groups, significant bleeding and embolic episodes were uncommon [13].

Zhang et al. demonstrated comparable or quicker LVT resolution in an observational cohort of patients receiving rivaroxaban-based triple treatment as compared to VKA-based regimens; bleeding and clinical outcomes were tolerable [7]. In comparison to VKAs, DOACs (including rivaroxaban) were linked to comparable or superior thrombus resolution and decreased bleeding/stroke risk, according to a meta-analysis of observational studies conducted by Shrestha et al. [14]. This pooled evidence supports our results. A comparative cohort analysis of DOACs versus VKAs for post-myocardial infarction LVT was carried out by Attachaipanich et al. In post-MI patients, they found that DOACs were associated with reduced risks of stroke and systemic embolism and greater LVT resolution rates than warfarin [15]. Their results also support our findings that rivaroxaban outperforms warfarin in terms of resolution at three months. Rivaroxaban lowers the period of insufficient anticoagulation that can obstruct thrombus resolution by providing rapid, predictable anticoagulation without the INR instability and dietary/drug interactions of warfarin [16]. Because DOACs don't require monitoring visits, they frequently increase adherence, which in turn results in more constant anticoagulation and greater resolution rates. In the present study, we observed that diabetes, hypertension, and thrombus size ≥ 1 cm were associated with lower thrombus resolution rates. At three months, Yang et al. discovered that a large thrombus was independently linked to a higher probability of thrombus persistence or recurrence (OR ~1.11 per unit increase). Persistence was also predicted by ventricular aneurysm and mural texture [17]. Despite anticoagulation, larger (≥ 1 cm) thrombi persist because they are more likely to be chronic or mural and are mechanically more difficult to lyse. In an observational research, Lu et al. found that characteristics of larger/older thrombi and elevated inflammatory markers (such as CRP) were associated with a decreased chance of early thrombus clearance. According to the authors, comorbid disorders that worsen inflammation and hinder healing also decrease remission [18]. It is conceivable that diabetes and hypertension decrease anticoagulant-mediated thrombus resolution because they are pro-inflammatory and pro-thrombotic conditions (and frequently linked to elevated CRP). In a similar study, a review and pooling of data by Kim et al. revealed that thrombus size/area, ventricular aneurysm presence, decreased LVEF, and inflammatory markers predicted persistence; comorbidities that resulted in endothelial dysfunction, such as diabetes and poorly controlled hypertension, were reported as significant predictors for delayed thrombus resolution [19]. LVT size was found to be an independent predictor of thrombus persistence by Ahmed et al. Concurrent antiplatelet

medication aided in resolution; a bigger thrombus area was strongly associated with non-resolution [20]. Patients with type-2 diabetes had poorer cardiovascular outcomes overall, according to a retrospective analysis by Shi et al. There was evidence of greater adverse events and possibly various types of responses to anticoagulant methods in LVT subgroups [21]. Microvascular disease, chronic inflammation, poor fibrinolysis, and platelet hyperactivity associated with diabetes may all decrease thrombus clearance and raise the chance of recurrence [22]. Current study's prospective cohort design and well-defined inclusion and exclusion criteria were its strengths. For statistical analysis to be significant, the sample size (n=290) was sufficient. In a real-world post-MI setting, rivaroxaban and warfarin were directly compared head-to-head.

Standardized follow-up evaluation was ensured using echocardiography at baseline and three months. Some of the limitations of our study were that it was a single-center study, which may limit generalizability. The imaging modality used was echocardiography, which is less sensitive than cardiac MRI for thrombus detection despite being more practical. Because of the comparatively brief follow-up (three months), long-term recurrence, embolic events, or bleeding problems might not have been detected. As treatment allocation was determined by physician judgment and patient preferences rather than randomization, the study is subject to potential selection bias and residual confounding. Although this pragmatic approach reflects real-world clinical practice, differences in baseline characteristics are unmeasured factors between groups may have influenced outcomes, thereby limiting the internal validity and causal inference of the findings. Minor bleeding events were not systematically captured as predefined study outcomes. Therefore, while no thromboembolic complications were observed, the absence of recorded bleeding events should not be interpreted as absence of bleeding risk. In the future, large multi-center randomized controlled studies will be required to confirm that rivaroxaban is superior to warfarin in a variety of populations. Future research should use cardiac MRI to detect and characterize thrombus more precisely. Studies with longer follow-up (6-12 months) should be carried out to evaluate the risk of bleeding, embolic events, recurrence, and durability of thrombus clearance.

CONCLUSIONS

We concluded that rivaroxaban was more effective than warfarin in resolving left ventricular thrombus after acute anterior wall myocardial infarction. However, diabetes, hypertension, and larger thrombus size significantly reduced resolution rates, highlighting the need for

individualized management and further large-scale, randomized studies. This study was conducted for academic and research purposes to generate preliminary evidence in a real-world clinical setting. The findings should be interpreted cautiously and are not intended to be directly replicated or implemented as a definitive treatment strategy without further validation through larger, more well-designed studies, ideally randomized controlled trials.

Authors' Contribution

Conceptualization: MZS

Methodology: MZS, JNN, SAF

Formal analysis: AM, JNN, MKR

Writing and Drafting: MZS, AM

Review and Editing: MZS, AM, JNN, MKR, SAF

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All 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] Camaj A, Fuster V, Giustino G, Bienstock SW, Sternheim D, Mehran R et al. Left Ventricular Thrombus Following Acute Myocardial Infarction: JACC State-Of-The-Art Review. *Journal of the American College of Cardiology*. 2022 Mar; 79(10): 1010-1022. doi: 10.1016/j.jacc.2022.01.011.
- [2] Jones DA, Wright P, Alizadeh MA, Fhadil S, Rathod KS, Guttman O et al. The Use of Novel Oral Anticoagulants Compared to Vitamin K Antagonists (Warfarin) in Patients with Left Ventricular Thrombus After Acute Myocardial Infarction. *European Heart Journal-Cardiovascular Pharmacotherapy*. 2021 Sep; 7(5): 398-404. doi: 10.1093/ehjcvp/pvaa096.
- [3] Zhou X, Shi R, Wu G, Zhu Q, Zhou C, Wang L, Xue C, Jiang Y, Cai X, Huang W, Shan P. The prevalence, predictors, and outcomes of spontaneous echocardiographic contrast or left ventricular thrombus in patients with HFrEF. *European Society of Cardiology heart failure*. 2021 Apr; 8(2): 1284-1294. doi: 10.1002/ehf2.13196.
- [4] Alcalai R, Butnaru A, Moravsky G, Yagel O, Rashad R, Ibrahimli M et al. Apixaban vs. Warfarin in Patients with Left Ventricular Thrombus: A Prospective Multicentre Randomized Clinical Trial. *European Heart Journal-Cardiovascular Pharmacotherapy*. 2022 Nov; 8(7): 660-667. doi: 10.1093/ehjcvp/pvab057.

- [5] Berkowitz SD, Bauersachs RM, Szarek M, Nehler MR, Debus ES, Patel MR et al. Prevention of Arterial and Venous Thrombotic Events in Symptomatic Peripheral Arterial Disease Patients After Lower Extremity Revascularization in the VOYAGER PAD Trial: Dual Anticoagulant/Antiplatelet Regimen Vs Antiplatelet Therapy Alone. *Journal of Thrombosis and Haemostasis*. 2022 May 1;20(5):1193-205. doi: 10.1111/jth.15673.
- [6] Camanho LE and Santos GV. Rivaroxaban: Does it Really Need to Monitor its Anticoagulant Effect in Clinical Practice? *International Journal of Cardiovascular Sciences*. 2021 Mar; 34(2): 122-123. doi: 10.36660/ijcs.20200373.
- [7] Zhang Z, Si D, Zhang Q, Qu M, Yu M, Jiang Z et al. Rivaroxaban Versus Vitamin K Antagonists (Warfarin) Based on the Triple Therapy for Left Ventricular Thrombus After ST-Elevation Myocardial Infarction. *Heart and Vessels*. 2022 Mar; 37(3): 374-384. doi: 10.1007/s00380-021-01921-z.
- [8] Mir T, Sattar Y, Attique HB, Hussain T, Alraies MC, Sheikh M et al. Meta-analysis of Direct Oral Anticoagulants Compared with Vitamin K Antagonist for Left Ventricular Thrombus. *Cardiovascular Revascularization Medicine*. 2022 Feb; 35: 141-146. doi: 10.1016/j.carrev.2021.03.001.
- [9] Mansouri P, Jazi ZA, Mansouri MH, Dehghan H, Zavar R, Hashemi SM et al. Evaluation of the Efficacy and Safety of Rivaroxaban Compared to Warfarin in Patients with Left Ventricular Apical Thrombus: A Randomized Clinical Trial. *Thrombosis Journal*. 2024 Jul; 22(1): 66. doi: 10.1186/s12959-024-00632-5.
- [10] Prajapati D. Comparison of Warfarin Versus Rivaroxaban in Management of Post-Myocardial Infarction Left Ventricular Thrombus in a Tertiary Cardiac Centre of Nepal: A Randomized Controlled Study. 2024 Nov: 1-32.
- [11] Levine GN, McEvoy JW, Fang JC, Ibeh C, McCarthy CP, Misra A et al. Management of Patients at Risk for and with Left Ventricular Thrombus: A Scientific Statement from the American Heart Association. *Circulation*. 2022 Oct; 146(15): 205-223. doi: 10.1161/CIR.0000000000001092.
- [12] Olie RH, Winkers K, Rocca B, Ten Cate H. Oral Anticoagulants Beyond Warfarin. *Annual Review of Pharmacology and Toxicology*. 2024 Jan; 64(1): 551-575. doi: 10.1146/annurev-pharmtox-032823-122811.
- [13] Jenab Y, Sadeghipour P, Mohseni-Badalabadi R, Kaviani R, Hosseini K, Pasebani Y et al. Direct Oral Anticoagulants or Warfarin in Patients with Left Ventricular Thrombus After ST-Elevation Myocardial Infarction: A Pilot Trial and a Prespecified Meta-Analysis of Randomised Trials. *Euro Intervention*. 2025 Jan; 21(1): 82. doi: 10.4244/EIJ-D-24-00527.
- [14] Shrestha DB, Dawadi S, Dhakal B, Shtembari J, Patel T, Shaikh R et al. Direct Oral Anticoagulants Versus Vitamin K Antagonist in Left Ventricular Thrombus: An Updated Meta-Analysis. *Health Science Reports*. 2023 Nov; 6(11): 1736. doi: 10.1002/hsr2.1736.
- [15] Attachaipanich T, Thanyaratsarun T, Attachaipanich S, Danpanichkul P, Kaewboot K. Efficacy of Direct Oral Anticoagulants Vs. Warfarin in Left Ventricular Thrombus in Myocardial Infarction: Systematic Review and Meta-Analysis. *Journal of Cardiovascular Medicine*. 2025 Jan; 26(1): 40-49. doi: 10.2459/JCM.0000000000001683.
- [16] Jiang H, Jiang Y, Ma H, Zeng H, Lv J. Effects of Rivaroxaban and Warfarin on the Risk of Gastrointestinal Bleeding and Intracranial Hemorrhage in Patients with Atrial Fibrillation: Systematic Review and Meta-Analysis. *Clinical Cardiology*. 2021 Sep; 44(9): 1208-1215. doi: 10.1002/clc.23690.
- [17] Yang Q, Quan X, Wang C, Yu L, Yang Y, Zhu J et al. A Prediction Model for Left Ventricular Thrombus Persistence/Recurrence: Based on a Prospective Study and a Retrospective Study. *Thrombosis Journal*. 2023 May; 21(1): 50. doi: 10.1186/s12959-023-00488-1.
- [18] Lu Z, Song B, Liu X, Zhang N, Li F, Xu F et al. Factors Predicting Resolution of Left Ventricular Thrombus in Different Time Windows After Myocardial Infarction. *BioMed Central Cardiovascular Disorders*. 2024 May; 24(1): 278. doi: 10.1186/s12872-024-03898-9.
- [19] Kim SE, Lee CJ, Oh J, Kang SM. Factors Influencing Left Ventricular Thrombus Resolution and Its Significance on Clinical Outcomes. *European Society of Cardiology heart failure*. 2023 Jun; 10(3): 1987-1995. doi: 10.1002/ehf2.14369.
- [20] Ahmed HS, Ede H, Mahfouz AS, Rahhal AA, Ali MA, Issa AF et al. Surrogates of the Left Ventricular Thrombus Resolution: A Retrospective Data Review. *Türk Kardiyoloji Derneği Arşivi*. 2022 Apr; 50(3): 168. doi: 10.5543/tkda.2022.21068.
- [21] Shi B, Zhang R, Song C, Cui K, Zhang D, Jia L et al. Impacts of Diabetes Mellitus on Cardiovascular Outcomes and Differential Effects of Direct Oral Anticoagulants in Patients with Left Ventricular Thrombus. *Reviews in Cardiovascular Medicine*. 2023 Feb; 24(3): 65. doi: 10.31083/j.rcm2403065.
- [22] Vaidya AR, Wolska N, Vara D, Mailer RK, Schröder K, Pula G. Diabetes and Thrombosis: A Central Role for Vascular Oxidative Stress. *Antioxidants*. 2021 Apr; 10(5): 706. doi: 10.3390/antiox10050706.



Original Article



Comparison of Video Laryngoscopy Versus Conventional Laryngoscopy in Anticipated Difficult Intubation in Patients Undergoing Thyroid Surgery

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ARTICLE INFO

Keywords:

Anticipated Difficult Intubation, Video Laryngoscopy, Direct Laryngoscopy, Thyroid Surgery, Cormack-Lehane Grade

How to Cite:

Riaz, U., Majeed, Z., Sadaf, S., Ahmed, A., Abbas, F., & Jamil, M. I. (2026). Comparison of Video Laryngoscopy Versus Conventional Laryngoscopy in Anticipated Difficult Intubation in Patients Undergoing Thyroid Surgery: Video Laryngoscopy Versus Conventional Laryngoscopy in Anticipated Difficult Intubation. *Pakistan Journal of Health Sciences*, 7(6), 26-31 <https://doi.org/10.54393/pjhs.v7i6.3692>

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Received Date: 14th December, 2025

1st Revision Received: 23rd February, 2026

2nd Revision Received: 9th March, 2026

Acceptance Date: 12th March, 2026

Published Date: 30th June, 2026

ABSTRACT

Anticipated difficult airway in thyroid surgery is associated with failed intubation, hypoxia, and airway trauma, despite structured preoperative assessment. **Objectives:** To compare video laryngoscopy with conventional direct laryngoscopy in adult patients undergoing elective thyroid surgery with anticipated difficult intubation in terms of first-attempt and overall tracheal intubation success, glottic visualization, intubation time, and immediate oropharyngeal injury. **Methods:** A randomized controlled trial was conducted in the Department of Anesthesia, Sheikh Zayed Hospital, Rahim Yar Khan, from January 2025 to June 2025. Sixty patients (18–60 years) undergoing elective thyroidectomy with anticipated difficult intubation (ASA I–II, ≥ 1 airway predictor) were enrolled by non-probability consecutive sampling and randomized (1:1) to conventional laryngoscopy or video laryngoscopy. All intubations were performed by experienced anesthetists. **Results:** Among 60 randomized patients, baseline age (44.47 ± 7.66 vs 44.60 ± 8.02 years) and gender distribution (46.7 % vs 40.0 % males) were comparable between conventional and video- laryngoscopy groups. Video laryngoscopy improved Cormack-Lehane grade I view frequency (60.0% vs 13.3%, $p=0.002$) and increased first-attempt intubation success (93.3% vs 60.0%, $p=0.002$). Overall success was 100.0% with video laryngoscopy versus 93.3% with direct laryngoscopy ($p=0.150$). Mean intubation time was longer with video laryngoscopy (45.13 ± 8.38 vs 39.20 ± 9.83 seconds, $p=0.015$). Immediate oropharyngeal injury was numerically lower with video laryngoscopy (6.7% vs 20.0%, $p=0.129$). **Conclusions:** In anticipated difficult airways during thyroid surgery, video laryngoscopy significantly improved first-attempt intubation success and glottic visualization, while overall success remained similarly high in both groups.

INTRODUCTION

Difficult tracheal intubation is a recognized challenge in thyroid surgery owing to anatomical distortion caused by large goiters, tracheal deviation, reduced cervical extension, and limited mouth opening [1]. These factors can impair glottic visualization and increase the risk of airway complications during induction [2]. Anticipated difficult intubation occurs in approximately 1.1 percent to 3.8 percent of the general surgical population, but the risk is considerably higher in thyroid surgery, where airway distortion is common [3, 4]. Conventional direct

laryngoscopy continues to be widely practiced; however, video laryngoscopy provides an indirect view that may enhance laryngeal exposure, reduce the need for optimization maneuvers, and mitigate physiologic stress responses [5]. Prior study in predicted difficult airways consistently reported superior glottic visualization and higher first-attempt success with video laryngoscopy, although findings for intubation time vary across devices and operator experience [6]. Meta-analyses further support reductions in failed or difficult intubation and



airway trauma, yet highlight heterogeneity related to technique, device, and user proficiency [7]. Evidence specific to difficult airway management demonstrates consistent performance advantages with video laryngoscopy [8]. In a randomized trial of adults with anticipated difficult intubation, video laryngoscopy produced markedly more grade-1 views, higher first-attempt success, and fewer optimization maneuvers with only a small increase in intubation time relative to direct laryngoscopy [9]. In a randomized trial during thyroid surgery, first-attempt success was 66% with direct laryngoscopy versus 96% with video laryngoscopy ($p<0.001$) [10]. Among thyroid patients with difficult airways, intubation time was shorter with the optical stylet 42.4 ± 24.1 s and video laryngoscope (29.8 ± 22.3 s) than with direct laryngoscopy 68.8 ± 26.6 s; first-attempt success was higher with the stylet 90.0% and video laryngoscope 97.5% versus direct laryngoscopy 75.0% [11]. In 360 elective cases, video laryngoscopy achieved higher first-attempt success 96.1% versus 90.1% ($p=0.024$), higher overall success 100% vs 94.5% ($p=0.004$), and fewer immediate oropharyngeal injuries 1.1% vs 5.1% ($p=0.033$) [12]. Given the anatomical complexity of thyroid surgery and the higher likelihood of encountering a difficult airway, a focused evaluation of intubation methods is warranted [13].

The present study has been designed to compare video laryngoscopy with conventional direct laryngoscopy in adult thyroid surgery patients who meet predefined clinical predictors of anticipated difficult intubation. The primary objective was to determine whether video laryngoscopy improves the first-attempt intubation success rate. Secondary objectives included comparing overall intubation success, intubation time, and the incidence of immediate oropharyngeal injuries between the two techniques. This study aims to provide procedure-specific evidence to guide optimal airway management in thyroid surgery patients with anticipated difficult intubation.

METHODS

A randomized controlled trial (NCT07113171) was conducted in the Department of Anesthesia, Sheikh Zayed Hospital, Rahim Yar Khan, after obtaining approval from the Institutional Review Board (803/IRB/SZMC/SZH; Dated 18th October, 2023) from January 2025 to June 2025. A sample size of 60 patients, with thirty allocated to each group, was calculated using an expected first-attempt intubation success rate of 66% with direct laryngoscopy and 96% with video laryngoscopy, at 80% power and a 95% confidence level [10]. Participants were enrolled through non-probability consecutive sampling. Adults aged 18 to 60 years of either sex who were scheduled for elective thyroid surgery under general anesthesia and met predefined criteria for anticipated difficult intubation were included.

Eligible patients had an ASA physical status of I or II and demonstrated at least one airway predictor such as limited neck mobility, short thyromental distance, restricted mouth opening, visibly enlarged goiter, or obesity. Patients with neck trauma, cervical spondylopathy, emergency surgical indications, pre-existing oropharyngeal or laryngeal pathology, or significant cardiovascular or respiratory disease were excluded. After written informed consent, enrolled patients were randomized into two groups using computer-generated numbers. Group A underwent endotracheal intubation with conventional direct laryngoscopy, performed by extending the proximal cervical spine and flexing the distal cervical spine to align the oral, pharyngeal, and laryngeal axes. A Macintosh blade was used to retract the tongue and expose the glottis for endotracheal tube placement. Group B underwent intubation using a video laryngoscope, which permitted visualization of the vocal cords without the need for extensive neck extension. All intubations were carried out by experienced anesthetists trained in both techniques. Baseline demographic and clinical variables, including age, gender, BMI, diabetes mellitus, hypertension, COPD or asthma, ASA class, Mallampati score, and airway predictors, were recorded. Cormack-Lehane grading, intubation method, first-attempt intubation success, overall success, number of attempts, intubation time measured in seconds, and the presence or absence of immediate oropharyngeal injuries (bleeding or soft tissue injury) were documented. The CONSORT flow diagram is given (Figure 1).

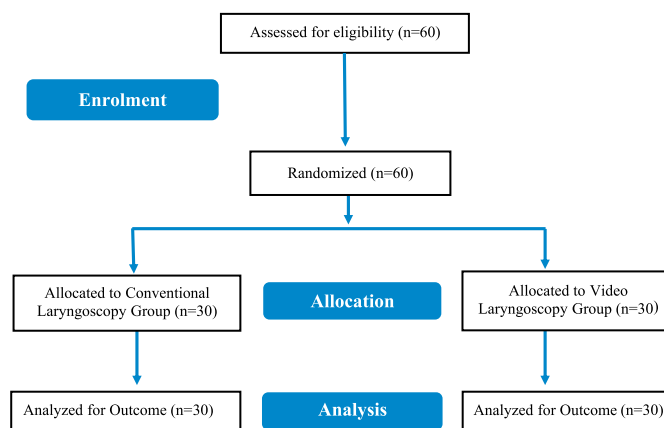


Figure 1: CONSORT Flow Diagram

Data analysis was performed using SPSS version 26. Categorical variables (gender, comorbidities, ASA class, Mallampati class, airway predictors, Cormack-Lehane grade categories, first-attempt success, overall success, number of attempts, immediate oropharyngeal injury) were expressed as frequencies and percentages, while continuous variables (age, body mass index, intubation time) were summarized as means with standard deviations. Normality of quantitative variables was assessed by using

the Shapiro–Wilk test. Differences in categorical outcomes between the two groups were analyzed using the Chi-square test. Continuous variables were compared using the Independent Samples t-test. A p-value less than 0.05 was considered statistically significant.

RESULTS

The mean age of the patients was 44.54 ± 7.78 years, with 22 (36.7%) patients aged 18 to 40 years and 38 (63.3%) aged 41 to 60 years. Gender distribution was comparable, with 26 (43.3%) males and 34 (56.7%) females overall. The mean body mass index was 27.67 ± 2.32 kg per m² in the conventional laryngoscopy group and 28.91 ± 2.04 kg per m² in the video-laryngoscopy group (Table 1).

Table 1: Baseline Demographics and Clinical Characteristics by Intubation Method

Variables	Category	Group A: Conventional Laryngoscopy (n=30), Mean $\pm$ SD/ n (%)	Group B: Video Laryngoscopy (n=30), Mean $\pm$ SD/ n (%)	p-value
Age	Years	44.47 $\pm$ 7.66	44.60 $\pm$ 8.02	0.948
Age Group	18–40 Years	12 (40.0%)	10 (33.3%)	0.592
	41–60 Years	18 (60.0%)	20 (66.7%)	
Gender	Male	14 (46.7%)	12 (40.0%)	0.602
	Female	16 (53.3%)	18 (60.0%)	
ASA Physical Status	I	10 (33.3%)	16 (53.3%)	0.118
	II	20 (66.7%)	14 (46.7%)	
Body Mass Index	kg/m ²	27.673 $\pm$ 2.320	28.907 $\pm$ 2.037	0.033
Diabetes Mellitus	Yes	8 (26.7%)	6 (20.0%)	0.542
Hypertension	Yes	10 (33.3%)	8 (26.7%)	0.573
COPD/Asthma	Yes	4 (13.3%)	6 (20.0%)	0.488

Independent t-test used for continuous variables; Pearson's Chi-square test applied for categorical variables. COPD: chronic obstructive pulmonary disease; ASA: American Society of Anesthesiologists

Airway assessment showed Mallampati Class I in 4 (13.3%) versus 2 (6.7%), Class II in 14 (46.7%) versus 6 (20.0%), Class III in 10 (33.3%) versus 16 (53.3%), and Class IV in 2 (6.7%) versus 6 (20.0%) for the conventional and video-laryngoscopy groups, respectively. Limited neck mobility was present in 10 (33.3%) versus 12 (40.0%) (Table 2).

Table 2: Airway Assessment and Predictors of Anticipated Difficult Intubation by Intubation Method

Variables	Category	Group A: Conventional Laryngoscopy (n=30)	Group B: Video Laryngoscopy (n=30)	p-value
Mallampati Class	I	4 (13.3%)	2 (6.7%)	0.064
	II	14 (46.7%)	6 (20.0%)	
	III	10 (33.3%)	16 (53.3%)	
	IV	2 (6.7%)	6 (20.0%)	
Limited Neck Mobility	Yes	10 (33.3%)	12 (40.0%)	0.592
Short Thyromental Distance <6 cm	Yes	10 (33.3%)	8 (26.7%)	0.573

Limited Mouth Opening <3 cm	Yes	6 (20.0%)	10 (33.3%)	0.243
Visibly Large Goiter	Yes	20 (66.7%)	26 (86.7%)	0.067
Obesity (BMI>30 kg/m ²)	Yes	6 (20.0%)	10 (33.3%)	0.243

Independent t-test used for continuous variables; Pearson's Chi-square test applied for categorical variables

Intubation performance showed more favorable laryngeal view with video laryngoscopy, with Cormack–Lehane grade I observed in 4 (13.3%) patients in the conventional group compared with 18 (60.0%) in the video-laryngoscopy group ($p=0.002$). First-attempt intubation success was higher with video laryngoscopy, achieved in 28 (93.3%) patients compared with 18 (60.0%) in the conventional group ($p=0.002$). Overall success remained high in both groups at 28 (93.3%) versus 30 (100.0%) ($p=0.150$). Immediate oropharyngeal injuries occurred in 2 (6.7%) patients in the video-laryngoscopy group and 6 (20.0%) in the conventional group ($p=0.129$). Mean intubation time was 45.13 ± 8.38 seconds with video laryngoscopy and 39.20 ± 9.83 seconds with conventional laryngoscopy ($p=0.015$) (Table 3).

Table 3: Intubation Performance Outcomes by Intubation Method (Group A: Conventional Laryngoscopy; Group B: Video Laryngoscopy; n=60)

Variables	Category	Group A (n=30)	Group B (n=30)	Test Statistic (χ^2 / t)	p-value
Cormack–Lehane Grade (First Attempt)	I	4 (13.3%)	18 (60.0%)	$\chi^2 = 15.366$	0.002
	IIa	8 (26.7%)	6 (20.0%)		
	IIb	10 (33.3%)	4 (13.3%)		
	III	8 (26.7%)	2 (6.7%)		
First-Attempt Intubation Success	Yes	18 (60.0%)	28 (93.3%)	$\chi^2 = 9.317$	0.002
Overall Intubation Success	Yes	28 (93.3%)	30 (100.0%)	$\chi^2 = 2.069$	0.150
Number of Intubation Attempts	1	18 (60.0%)	28 (93.3%)	$\chi^2 = 9.774$	0.008
	2	8 (26.7%)	2 (6.7%)		
	≥ 3	4 (13.3%)	0 (0.0%)		
Immediate Oropharyngeal Injury	Present	6 (20.0%)	2 (6.7%)	$\chi^2 = 2.308$	0.129
Intubation Time (Seconds)	Mean $\pm$ SD	39.20 $\pm$ 9.83	45.13 $\pm$ 8.38	t = -2.515	0.015

Independent t-test used for continuous variables; Pearson's Chi-square test applied for categorical variables

DISCUSSION

This randomized comparison of video laryngoscopy and conventional direct laryngoscopy in adults undergoing thyroid surgery with anticipated difficult intubation showed that video laryngoscopy provided a substantially better laryngeal view and a markedly higher first-attempt success rate. Cormack–Lehane grade I views were

achieved in 18 patients (60.0%) with video laryngoscopy compared with 4 (13.3%) with conventional laryngoscopy ($p=0.002$), and first-attempt success increased from 18 (60.0%) to 28 (93.3%) ($p=0.002$). Overall success remained high in both groups at 93.3% and 100.0%, whereas immediate oropharyngeal injury was numerically lower with video laryngoscopy, 2 (6.7 %) versus 6 (20.0%), and mean intubation time was modestly prolonged from 39.20 ± 9.83 seconds to 45.13 ± 8.38 seconds ($p=0.015$). The glottic visualization in the present trial is consistent with and directionally similar to previous studies. Downey et al. reported that video laryngoscopy yielded Cormack-Lehane grade I views in 98% compared with 44% with direct laryngoscopy ($p<0.001$) [14]. Mohammed et al. likewise found that video laryngoscopy converted glottic views to grade I in 51.5 % versus 9.1 % patients intubated with direct laryngoscopy ($p<0.001$) [15]. In a larger randomized series, Kriege et al. reported that video laryngoscopy shifted the Cormack-Lehane distribution to 84.6 % grade I views compared with 36.9% grade I views with direct laryngoscopy ($p<0.001$) [10]. The increase in grade I views from 13.3% to 60.0% in the present series falls within this spectrum. In this study, first-attempt success rose from 60.0% with conventional laryngoscopy to 93.3 % with video laryngoscopy ($p=0.002$). Similar patterns have been reported by Downey et al. who documented first-attempt success of 90% versus 44% for video versus direct laryngoscopy ($p<0.001$) [14]. Larger meta-analyses corroborate these findings: Vargas et al. reported that video laryngoscopes reduced difficult intubation, with a pooled risk ratio of 0.48 (95% CI 0.35–0.65) and modestly increased first-attempt success (risk ratio 1.03, 95 % CI 1.00–1.07) [16]. In the present study, first-attempt success appears greater than the pooled averages in these reviews, likely reflecting the combination of anticipated difficult anatomy and the focused use of video laryngoscopy in a high-risk thyroid surgery population. In this trial, overall success reached 93.3% with conventional laryngoscopy and 100.0 % with video laryngoscopy, comparable to the 99% versus 92% overall success and 97.8% versus 77.8% success in the difficult-view subgroup reported by Jungbauer et al. with video laryngoscopy versus direct laryngoscopy ($p=0.017$ and $p<0.001$, respectively) [17]. Polo et al. found that video laryngoscopy improved first-attempt success with a pooled risk ratio of 1.12 (95% CI 1.04–1.21) and dental injuries (risk ratio 0.32, 95% CI 0.16–0.67) across 15 randomized trials involving 4582 intubations [18]. Immediate oropharyngeal injury in the present study was less frequent with video laryngoscopy, occurring in 6.7 % compared with 20.0 %, consistent with previous literature. Liu et al. reported that lip or mucosal trauma was present in 50 % patients intubated with conventional laryngoscopy

versus 10 % with video laryngoscopy ($p<0.05$) [11]. Taboada et al. found that oral trauma occurred in 21.4% Macintosh patients versus 5% video laryngoscopy ($p=0.012$) [19]. Meta-analysis has confirmed lower airway trauma with video laryngoscopy, with Lewis et al. documenting reduced laryngeal or airway trauma (odds ratio 0.68, 95% CI 0.48–0.96) and hoarseness (odds ratio 0.57, 95 % CI 0.36–0.88) [20]. In this study, mean intubation time increased by approximately 6s with video laryngoscopy, from 39.20 ± 9.83 to 45.13 ± 8.38 seconds ($p=0.015$). Downey et al. similarly reported longer intubation times with video laryngoscopy, 37.82 ± 5.21 versus 35.18 ± 4.21 s ($p=0.006$) [14]. In contrast, Jungbauer et al. found shorter total intubation time with video laryngoscopy, 40 ± 31 versus 60 ± 77 ($p=0.017$), and Liu et al. reported that video laryngoscopy reduced intubation time from 68.8 ± 26.6 s with direct laryngoscopy to 29.8 ± 22.3 s in difficult thyroid airways [17]. In thyroid surgery with goiter and tracheal deviation, the combination of improved view and more complex tube steering likely explains the small increase in time observed here, which appears clinically acceptable in the context of much higher first-pass success. These findings carry important implications for clinical practice in thyroid surgery with anticipated difficult airways. Video laryngoscopy in this setting converted a high proportion of challenging airways with Mallampati class III–IV, large goiters, and obesity into laryngoscopies with grade I or IIa views and raised first-attempt success to over 90%, while maintaining 100% overall success and a numerically lower rate of oropharyngeal injury. The combination of fewer attempts and better views is particularly relevant in thyroid surgery, where repeated instrumentation may increase the risk of laryngeal trauma. When considered alongside the broader evidence from elective surgery, difficult airway management, and critical care, showing reduced failed intubations and less dental trauma with video laryngoscopy [18].

This trial had several methodological strengths. It was a prospective randomized comparison with clearly defined inclusion criteria for anticipated difficult intubation in thyroid surgery, with balanced baseline demographic and airway characteristics between groups. Detailed documentation of multiple airway predictors, Cormack-Lehane grades, number of attempts, success rates, and immediate oropharyngeal complications allowed a nuanced assessment in a clinically relevant high-risk population. However, the study was conducted at a single center with a relatively small sample size, which limits statistical power for less frequent outcomes and may restrict generalizability beyond elective thyroid surgery. Peri-intubation hemodynamic responses were not measured in the present trial. Future research should

include larger multicenter trials across different surgical settings, incorporate operator experience stratification, and include hemodynamic and longer-term airway outcomes.

CONCLUSIONS

In adults with an anticipated difficult airway presenting for thyroid surgery, video laryngoscopy demonstrated clear clinical advantages over conventional laryngoscopy. Video-laryngoscopy yielded better glottic visualization and higher first-attempt intubation success, while maintaining a very high overall success rate comparable to conventional laryngoscopy. Oropharyngeal trauma was not increased, and the only trade-off was a modest prolongation of intubation time, which did not appear clinically relevant in the elective setting. Taken together, these findings support the preferential use of video laryngoscopy as the primary intubation strategy in similar high-risk thyroid populations.

Authors' Contribution

Conceptualization: UR, FA

Methodology: SS, FA, MIJ

Formal analysis: UR, ZM, SS, AA

Writing and Drafting: UR, ZM, SS, AA, FA, MIJ

Review and Editing: UR, ZM, SS, AA, FA, MIJ

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All 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] Urang M, Basumatary J, Saikia A, Talukdar TK, Borgohain R. Intubation Challenges in Surgeries of Thyroid Swellings. *Asian Journal of Medical Sciences*. 2023 Sep; 14(9): 53-7. doi: 10.3126/ajms.v14i9.55535.
- [2] Putrawan IW and Widnyana IM. Difficult Airway Management in Severe Tracheal Deviation Due to Large Nodular Goiter: A Case Report. *Journal of Social Research*. 2025 Sep; 4(10): 2505-13. doi: 10.55324/josr.v4i9.2768.
- [3] Hansel J, Rogers AM, Lewis SR, Cook TM, Smith AF. Videolaryngoscopy versus Direct Laryngoscopy for Adults Undergoing Tracheal Intubation: A Cochrane Systematic Review and Meta-Analysis Update. *British Journal of Anesthesia*. 2022 Oct; 129(4): 612-23. doi: 10.1016/j.bja.2022.05.027.
- [4] Agón KA and Maldonado JF. Awake Intubation with Videolaryngoscopy and Ultrasound-Guided Percutaneous Tracheostomy in a Patient with Anaplastic Thyroid Cancer and Difficult Airway: A Case Report. *Colombian Journal of Anesthesiology*. 2018 Apr; 46(2): 159-63. doi: 10.1097/CJ9.0000000000000029.
- [5] Alwan I, Alwan M, Mahgoub I, Eghzawi A, Gharaibeh A, Goyal AV. Video Laryngoscopy Vs. Direct Laryngoscopy in Adult Patients with Difficult Airways Who Require Emergency Intubation. *Emergency Care and Medicine*. 2024 Apr; 1(2): 77-86. doi: 10.3390/ecm1020011.
- [6] Dardeer A, Alhammad MF, Zaza KJ, Shallik AN, Hammad YA, Elkarta ES et al. First-Pass Success in Video Laryngoscopy with Transcutaneous Infrared Illumination in Patients with Normal Airways—A Clinical Pilot Study. *Journal of Clinical Monitoring and Computing*. 2025 Sep: 1-9. doi: 10.1007/s10877-025-01361-4.
- [7] Vargas M, Pastore A, Aloj F, Laffey JG, Servillo G. A Comparison of Videolaryngoscopes for Tracheal Intubation in Predicted Difficult Airway: A Feasibility Study. *BioMed Central Anesthesiology*. 2017 Feb; 17(1): 25. doi: 10.1186/s12871-017-0318-2.
- [8] Khajavi M, Kazeroni R, Ramezani R, Biderafsh A, Kianpour P, Neishaboury M. Tracheal Intubation with Glidescope Vs. Sanyar Video Laryngoscopes in Adults with Predicted Difficult Intubation: A Non-Inferiority Clinical Trial. *Anesthesiology Intensive Therapy*. 2025 May; 57: e80. doi: 10.5114/ait/200292.
- [9] Bhattacharjee S, Maitra S, Baidya DK. A Comparison Between Video Laryngoscopy and Direct Laryngoscopy for Endotracheal Intubation in the Emergency Department: A Meta-Analysis of Randomized Controlled Trials. *Journal Of Clinical Anesthesia*. 2018 Jun; 47: 21-6. doi: 10.1016/j.jclinane.2018.03.006.
- [10] Kriege M, Hilt JA, Dette F, Wittenmeier E, Meuser R, Staubitz JI et al. Impact of Direct Laryngoscopy vs. Videolaryngoscopy on Signal Quality of Recurrent Laryngeal Nerve Monitoring in Thyroid Surgery: A Randomized Parallel Group Trial. *Anesthesia*. 2023 Jan; 78(1): 55-63. doi: 10.1111/anae.15865.
- [11] Liu L, Yue H, Li J. Comparison of Three Tracheal Intubation Techniques in Thyroid Tumor Patients with a Difficult Airway: A Randomized Controlled Trial. *Medical Principles and Practice*. 2014 Aug; 23(5): 448-52. doi: 10.1159/000364875.
- [12] Liu DX, Ye Y, Zhu YH, Li J, He HY, Dong L et al. Intubation of Non-Difficult Airways Using Video Laryngoscope versus Direct Laryngoscope: A Randomized, Parallel-Group Study. *BioMed Central Anesthesiology*. 2019 May; 19(1): 75. doi: 10.1186/s12871-019-0737-3.

- [13] Amaniti A, Papakonstantinou P, Gkinas D, Dalakakis I, Papapostolou E, Nikopoulou A et al. Comparison of Laryngoscopic Views Between C-MAC™ and Conventional Laryngoscopy in Patients with Multiple Preoperative Prognostic Criteria of Difficult Intubation. An Observational Cross-Sectional Study. *Medicina*. 2019 Nov; 55(12): 760. doi: 10.3390/medicina55120760.
- [14] Downey AW, Duggan LV, Law JA. A Systematic Review of Meta-Analyses Comparing Direct Laryngoscopy with Videolaryngoscopy. *Canadian Journal of Anesthesia*. 2021 May; 68(5): 706-14. doi: 10.1007/s12630-021-01921-7.
- [15] Mohammed AM, Abdel-Fatah AE, Abdul Latif HK, Farmawy MS. Study of Video Assisted Laryngoscope versus Conventional Macintosh Laryngoscope for Management of Predicted Difficult Airway in Minor Elective Surgeries. *The Egyptian Journal of Hospital Medicine*. 2022 Apr; 87(1): 1449-55. doi: 10.21608/ejhm.2022.225411.
- [16] Vargas M, Servillo G, Buonanno P, Iacovazzo C, Marra A, Putensen-Himmer G et al. Video vs. Direct Laryngoscopy for Adult Surgical and Intensive Care Unit Patients Requiring Tracheal Intubation: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *European Review for Medical and Pharmacological Sciences*. 2021 Dec; 25(24).
- [17] Jungbauer A, Schumann M, Brunkhorst V, Börgers A, Groeben H. Expected Difficult Tracheal Intubation: A Prospective Comparison of Direct Laryngoscopy and Video Laryngoscopy in 200 Patients. *British Journal of Anesthesia*. 2009 Apr; 102(4): 546-50. doi: 10.1093/bja/aep013.
- [18] Polo PP, Ramirez-Rodriguez R, Alejandro-Salinas R, Yangali-Vicente J, Rivera-Lozada O, Barboza JJ. Video versus Direct Laryngoscopy for Tracheal Intubation of Critically Ill Adults: A Systematic Review and Meta-Analysis. *Journal of Clinical Medicine*. 2025 Mar; 14(6): 1933. doi: 10.3390/jcm14061933.
- [19] Taboada M, Fernández J, Bermúdez M, Estany-Gestal A, Molins N, de los Ángeles Orallo M et al. Universal Videolaryngoscopy for Tracheal Intubation in the Operating Theatre: A Prospective Non-Randomized Clinical Trial. *Anesthesia*. 2025 Sep; 80(9): 1045-56. doi: 10.1111/anae.16643.
- [20] Lewis SR, Butler AR, Parker J, Cook TM, Schofield-Robinson OJ, Smith AF. Videolaryngoscopy versus Direct Laryngoscopy for Adult Patients Requiring Tracheal Intubation: A Cochrane Systematic Review. *BJA: British Journal of Anesthesia*. 2017 Sep; 119(3): 369-83. doi: 10.1093/bja/aex228.



Original Article



Role of Pre-Operative Single Dose Versus Double Dose Antibiotic in Prevention of UTI in Patients Undergoing Ureteroscopy with Negative Urine Culture

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ARTICLE INFO

Keywords:

Ureteroscopy, Urinary Tract Infections, Urolithiasis, Antibiotic Prophylaxis, Ureteral Stents

How to Cite:

Ramchand, M., Ali, A., Valecha, N. K., Khan, A., Mujeeb, A., Siddiqui, H., & Ahmed, F. (2026). Role of Pre-Operative Single Dose Versus Double Dose Antibiotic in Prevention of UTI in Patients Undergoing Ureteroscopy with Negative Urine Culture: Pre-Operative Dose Antibiotic: UTI in Ureteroscopy with Negative Urine Culture. *Pakistan Journal of Health Sciences*, 7(6), 32-37. <https://doi.org/10.54393/pjhs.v7i6.3708>

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Received Date: 23rd December, 2025

1st Revision Received: 7th March, 2026

2nd Revision Received: 17th March, 2026

Acceptance Date: 14th April, 2026

Published Date: 30th June, 2026

ABSTRACT

Ureteroscopy (URS) is a minimally invasive procedure for ureteral stones, strictures, and tumors. Though generally safe, it carries a risk of postoperative urinary tract infections (UTIs), particularly with instrumentation or residual fragments. The optimal prophylactic antibiotic strategy remains debated. **Objectives:** To compare single- versus double-dose intravenous Ceftriaxone for preventing post-URS UTIs in patients with sterile preoperative urine. **Methods:** A prospective cohort study was conducted from 12 June to 11 December 2025, including 86 patients aged 18-60 years undergoing URS for ureteric calculi (0.5-2.0cm) with negative urine cultures. Patients were allocated to two equal groups: Group A received a single 2g intravenous Ceftriaxone dose at anesthesia induction, and Group B received two doses, 24 hours preoperatively and at induction. Exclusion criteria included uncontrolled diabetes or hypertension, positive culture, and cephalosporin allergy. Data were collected by a standardized proforma. Postoperative UTI was defined clinically (fever >100°F, TLC >10×10⁹/L, pulse >100/min) and confirmed by urine culture. Statistical analysis was performed using SPSS version 22.0; p<0.05 was considered significant. **Results:** Baseline characteristics (age, BMI, gender) were comparable between groups (p>0.05). UTIs occurred in 11 patients (12.8%), with no significant difference between Group A (16.3%) and Group B (13.9%) (p=0.74). Isolated organisms included *E. coli*, *Enterococcus faecalis*, *Proteus mirabilis*, and *Enterobacter*. No significant associations were found with stone location, URS side, stenting, or diabetes. **Conclusions:** Single- and double-dose Ceftriaxone equally prevent post-ureteroscopy UTIs in sterile urine patients. Single-dose is a cost-effective, stewardship-friendly option. Further trials needed.

INTRODUCTION

Ureteroscopy (URS) has evolved into a fundamental minimally invasive approach for diagnosing and treating upper urinary tract conditions, including ureteral and renal stones, strictures, and urothelial tumors. This evolution has been driven in part by advancements in holmium laser technology and the widespread availability of rigid, semi-rigid, and flexible ureteroscopes with enhanced maneuverability and visualization capabilities [1]. Ureteric colic, most often caused by ureteric or migratory kidney stones, remains a common cause for emergency urological consultations. Lower pole stones, which are found in around 35% of cases, have the lowest likelihood of passing

on their own. These residual fragments can also be managed with flexible ureterorenoscopy with laser lithotripsy [2]. Clinical guidelines from the EAU and AUA recommend URS as first-line therapy for symptomatic ureteral stones in most patients, except in those with severe comorbidities or uncontrolled urinary tract infections [3]. However, URS can introduce bacteria into the urinary tract via surgical instruments or retained stone fragments, thereby increasing the risk of postoperative UTIs and urosepsis [4]. Postoperative UTIs and surgical site infections are among the most common complications and significantly impact patient morbidity. Currently,



recommended prophylaxis for URS includes antibiotics like fluoroquinolones and trimethoprim-sulfamethoxazole (TMP-SMX) as first-line options. Alternative agents include aminoglycosides (with or without ampicillin), amoxicillin/clavulanate, and first- to third-generation cephalosporins [5]. However, due to the lack of consensus and validated data, there remains a need to evaluate the efficacy of perioperative antibiotic prophylaxis in URS [6]. Multiple RCTs have shown different and inconsistent results. For instance, one study proved a significant reduction in postoperative UTI after extended antibiotic prophylaxis instead of standard fluoroquinolone-based regimens, but several other studies did not prove any significant benefit of antibiotic prophylaxis, especially in the low-risk patient group [7, 8]. In addition, guidelines in different urological societies vary due to the scarcity of randomized controlled trials and differences in their recommendations on prescribing antibiotic regimens and duration of prophylaxis needed for URS [9, 10].

Despite these differences, several studies continue to advocate for a single preoperative antibiotic dose, with extra doses deemed unnecessary. Therefore, to address this conflict in the context of clinical practice in Pakistan, and considering the rising antibiotic resistance as well as the need for cost-effective strategies in resource-limited healthcare settings, this study was conducted. This study aimed to compare the effectiveness of single-dose versus double-dose antibiotic prophylaxis in preventing postoperative UTIs in patients undergoing URS with negative preoperative urine cultures in the local population.

METHODS

This prospective cohort study was performed to assess the effectiveness of single versus double-dose antibiotic prophylaxis in preventing postoperative urinary tract infections (UTIs) in patients undergoing URS. The study was carried out in the Department of Urological Surgery and Transplantation, Ward 19, Jinnah Postgraduate Medical Centre (JPMC), Karachi, from 12th June till 11th December, 2025. Ethical approval from the Institutional Review Board was also obtained with ref no: NO.F.2-81/2025-GENL/298/JPMC; dated 29th May, 2025. A total of 86 patients were enrolled as per the inclusion criteria. Patients were allocated sequentially into two equal groups of 43 using a blindfolded allocation process to ensure balanced group distribution. The sample size was calculated using PASS 2020 Power Analysis and Sample Size Software (NCSS, LLC, Kaysville, Utah, USA), which determined that a sample of 86 would provide 83.06%. The study was powered to detect a 5% difference in postoperative UTI incidence between the two groups, with a significance level set at 0.05 with a baseline

postoperative UTI rate of 25% [11]. The inclusion criteria comprised male and female patients aged 18 to 60 years with controlled diabetes mellitus and hypertension, undergoing URS for ureteric calculi measuring between 0.5 and 2.0 cm in size, located in the upper, middle, or distal ureter. Only patients with a negative preoperative urine culture were included. Exclusion criteria were a positive urine culture, age below 18 or above 60 years, uncontrolled or severe diabetes or hypertension, known allergy to cephalosporin, or any other contraindication to the use of the study antibiotics. Written informed consent was taken, and then patients were divided into two groups based on the prophylactic antibiotic regimen. Group A consisted of patients who received a single dose of 2 grams of intravenous Ceftriaxone, which was administered at the time of anesthesia induction. Group B consisted of patients who received two doses of 2 grams of intravenous Ceftriaxone, of which one was administered 24 hours before the surgery and the second was given at the time of anesthesia induction. Data were obtained by filling out a proforma, which included demographic details, medical history, intraoperative and postoperative data, and outcomes. The primary endpoint was the rate of urinary tract infections following surgery, diagnosed clinically (TLC > 10.0 x 10⁹/L, Temp: >100°F, Pulse rate > 100 beats per minute and confirmed through urine culture and sensitivity testing. The study was conducted in accordance with all ethical standards. Before being included in the study, written informed consent was obtained from all the patients. Patient confidentiality was strictly taken care of throughout the study, and all efforts were made to avoid misconduct and to protect participants' rights and welfare. SPSS version 22.0 was used for statistical analysis. The incidence of UTIs in the two groups was compared using the chi-square test. A p-value below 0.05 was considered statistically significant.

RESULTS

Participant characteristics were comparable between the single-dose and double-dose groups. Mean age and BMI showed no statistically significant differences (Age: 41.2 ± 8.45 vs. 41.9 ± 7.76 years, p=0.77; BMI: 25.9 ± 3.56 vs. 27.7 ± 3.38, p=0.06). Gender distribution was also comparable, minimizing potential confounding effects on study outcomes, with males representing approximately half of each group (53.5% vs. 55.8%, p=0.82), as shown in table 1.

Table 1: Demographic Characteristics of the Participants (n=86)

Variables	Group	n	Mean ± SD / %	p-value
Age	Group 1 (Single Dose)	43	41.2 ± 8.45	0.77
	Group 2 (Double Dose)	43	41.9 ± 7.76	
BMI	Group 1 (Single Dose)	43	25.9 ± 3.56	0.06
	Group 2 (Double Dose)	43	27.7 ± 3.38	
Gender	Group 1 (Single Dose)	Male: 23	53.5%	0.82

	Group 2 (Double Dose)	Female: 20	46.5%	
		Male: 24	55.8%	
		Female: 19	44.2%	

A total of eleven patients developed postoperative UTIs, either clinically or based on positive urine cultures. Statistical analysis by applying the Chi-square test showed no significant variation in postoperative UTIs incidence between the groups ($p=0.74$), as shown in figure 1.

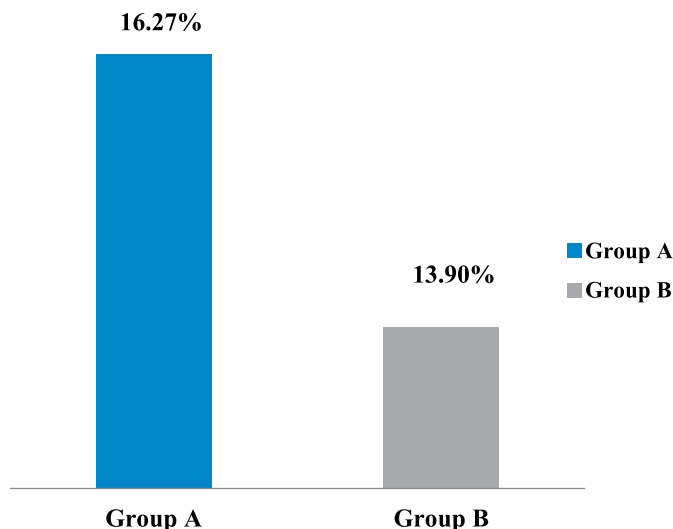


Figure 1: Frequency of Postoperative UTIs

In Group 1, seven patients (16.27%) experienced a UTI. One patient developed urosepsis, with urine culture revealing growth of *Enterobacter cloacae*. The remaining six cases reported symptoms typical of lower urinary tract issues consistent with cystitis; urine cultures identified *E. coli* in four patients, *Proteus mirabilis* in one, and one culture remained sterile, as shown in figure 2.

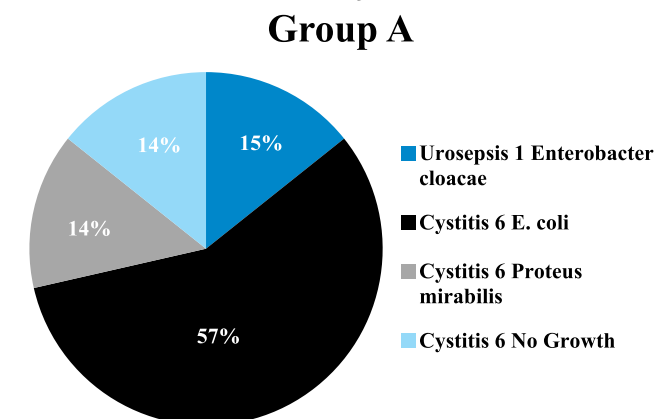


Figure 2: Number of Infected Cases and Organisms Involved in Group 1

Whereas in Group 2, six patients (13.9%) exhibited symptoms of postoperative UTIs. Pyelonephritis was diagnosed in two patients - one of them had a positive culture for *E. coli*, while the other had no growth. Four patients presented with cystitis; two cultures grew *E. coli*,

one showed *Enterococcus faecalis*, and one was negative, as shown in figure 3.

Group B

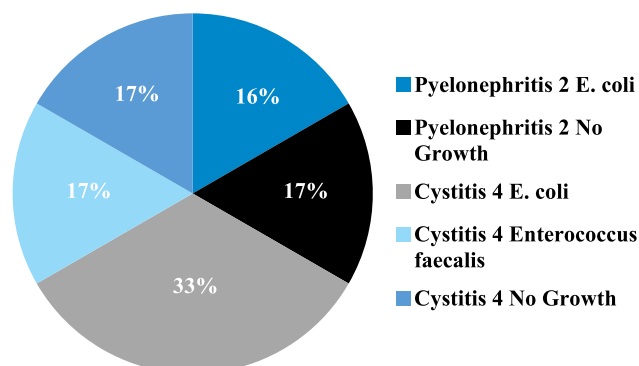


Figure 3: Number of Infected Cases and Organisms Involved in Group 2

All infections were managed successfully with appropriate antimicrobial therapy, and patients were discharged home in clinically stable condition post-therapy.

A comparative analysis of surgical factors and infection risks between Group 1 and Group 2 is presented. There were no statistically significant differences between Group 1 and Group 2 regarding stone location, URS side, postoperative stent placement, or diabetes mellitus. Chi-square tests were used for comparisons involving stone location, URS side, and stent placement. Fisher's exact test was applied for diabetes mellitus due to the low frequency of positive cases, as shown in table 2.

Table 2: Comparison of Surgical Factors and Infection Risk Factors

Variables	Category	Group 1 (n=43)	Group 2 (n=43)	p-value
Stone Location	Upper Ureter	9 (20.9%)	11 (25.6%)	0.33
	Mid Ureter	5 (11.6%)	9 (20.9%)	
	Lower Ureter	29 (67.4%)	23 (53.5%)	
URS Side	Right	22 (51.2%)	20 (46.5%)	0.67
	Left	21 (48.8%)	23 (53.5%)	
Postoperative Stent	Yes	34 (79.1%)	37 (86.0%)	0.39
	No	9 (20.9%)	6 (14.0%)	
Diabetes Mellitus	Yes	2 (4.7%)	1 (2.3%)	0.55
	No	41 (95.3%)	42 (97.7%)	

In summary, the results of this study suggest that single-dose and double-dose antibiotic prophylaxis regimens are equally effective in preventing postoperative UTIs following ureteroscopy stone management in patients with urine cultures taken pre-procedure showing no bacterial growth. The incidence of postoperative UTIs was low and statistically comparable among both groups, with no statistically significant variations observed in patient demographics, stone characteristics, or perioperative factors. These findings suggest that an antibiotic given as a single-dose regimen may be a sufficient and potentially more cost-effective approach for infection prevention in selected patients undergoing URS.

DISCUSSION

To address ureteral stone diseases, ureteroscopy is commonly used, but like every procedure, it too carries the risk of postoperative UTIs. In the current cohort, 11 of 86 patients (12.8%) developed postoperative urinary tract infections, including cystitis, pyelonephritis, and even life-threatening urosepsis; this infection rate falls within the range reported in previous studies, which vary from approximately 2% to 33% depending on patient population, study design, and the use of ureteral stents. [12, 13]. As patients with specific risk factors were included in the current study, this explains the slightly increased infection rate in the current cohort. In the patient who had a post-procedural ureteral stent placed, 5 out of 71 (7.04%) developed a postoperative UTI. This may be partially explained by microbial adherence and subsequent biofilm development on the stent external layer, a phenomenon observed in up to 25% of cases, depending on the stent dwell time [14]. However, despite bacterial presence, only around 10% of colonized stents lead to positive urine cultures [15], which is consistent with our findings as well. Multiple recent studies have demonstrated that prophylactic antibiotics do not prevent bacterial colonization of ureteral stents, indicating that antibiotics have limited utility in this context. [16-18]. Nonetheless, stent colonization does not consistently result in symptomatic infection, particularly in immunocompetent patients. The current study results indicated that 14 patients (16.3%) had preoperative ureteral stents, 9 in Group 1 (20.9%) and 5 in Group 2 (11.6%). Although this difference was not statistically significant ($p=0.21$), only one stented patient (8.5%) developed a postoperative UTI, suggesting that pre-stenting alone does not significantly increase infection risk in our cohort. These findings are in close agreement with the randomized controlled trial by Damavand et al. [19]. The current study found that preoperative ureteral stenting was not significantly associated with postoperative UTIs (8.5% infection rate in stented patients; $p=0.21$), suggesting that pre-stenting alone may not meaningfully elevate infection risk. This result aligns with Jennings et al. who compared single-dose preoperative antibiotics to combined pre- and postoperative dosing in URS: they observed postoperative UTI rates of 10% in the single-dose cohort versus 9.8% in the double-dose cohort ($p=0.15$), and reported that risk factors like preoperative stenting did not predict infection outcomes. Both studies together imply that a single preoperative antibiotic dose may be sufficient for stented patients and that extending antibiotics postoperatively has limited benefit [20]. Selection of an antibiotic for prophylaxis should be based on a variety of factors like agents' mechanism of action, site of action, tolerability,

cost effectiveness, and low resistance. Among the antibiotics that are broadly prescribed are fluoroquinolones, aminoglycosides, and cephalosporins due to their broad-spectrum coverage, long serum half-lives, lower side-effect profiles, and cost-effectiveness. Particularly in the prevention of genitourinary infections, fluoroquinolones and cephalosporins provide comparable efficacy [21, 22].

In today's world, it is necessary to create a standardized antibiotic policy based on the local resistance profile. This not only addresses local resistance trends but also avoids unnecessary antibiotic use, thereby limiting rising resistance. The emergence of resistant organisms such as MRSA, *Pseudomonas aeruginosa*, and *Stenotrophomonas maltophilia* highlights the growing challenge. Hence, prophylactic antibiotic use should be restricted to clearly indicated scenarios to preserve antimicrobial efficacy for future use.

CONCLUSIONS

Single-dose antibiotic prophylaxis regimen appears to be as effective as double-dose prophylaxis in postoperative UTIs in patients undergoing ureteroscopy with negative preoperative urine cultures. The overall infection rate remained pretty low in each group, and no statistically significant differences were observed in the occurrence of infection, demographic profiles, or perioperative risk factors. These findings support the adoption of a single-dose prophylactic strategy as a safe and cost-effective option, especially in resource-limited healthcare settings.

Authors' Contribution

Conceptualization: MR

Methodology: MR, AA, NKV

Formal analysis: MR, AA, AK, HS

Writing and Drafting: MR, AA, NKV, AK, AM, HS

Review and Editing: MR, AA, NKV, AK, AM, HS, FA

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All 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] Li Z, Tang X, Wu S, Liu S, Wang X, He Z et al. Efficacy and Safety of Semirigid Ureteroscopy Combined with Holmium: Yttrium-Aluminum-Garnet Laser Lithotripsy for the Treatment of Proximal Ureteral Calculi: A Single-Arm Meta-Analysis. *European Urology Open Science*. 2024 Dec; 70: 124-34. doi:

- 10.1016/j.euros.2024.10.006.
- [2] McClinton S, Starr K, Thomas R, MacLennan G, Lam T, Hernandez R et al. The Clinical and Cost Effectiveness of Surgical Interventions for Stones in the Lower Pole of the Kidney: The Percutaneous Nephrolithotomy, Flexible Ureterorenoscopy and Extracorporeal Shockwave Lithotripsy for Lower Pole Kidney Stones Randomized Controlled Trial (Pure RCT) Protocol. *Trials*. 2020 Jun; 21(1): 479. doi: 10.1186/s13063-020-04326-x.
 - [3] Türk C, Petřík A, Sarica K, Seitz C, Skolarikos A, Straub M et al. EAU Guidelines on Interventional Treatment for Urolithiasis. *European Urology*. 2016 Mar; 69(3): 475-82. doi: 10.1016/j.eururo.2015.07.041.
 - [4] Scotland KB and Lange D. Prevention and Management of Urosepsis Triggered by Ureteroscopy. *Research and Reports in Urology*. 2018 Jul; 43-9. doi: 10.2147/RRU.S128071.
 - [5] Bhojani N, Miller LE, Bhattacharyya S, Cutone B, Chew BH. Risk Factors for Urosepsis After Ureteroscopy for Stone Disease: A Systematic Review with Meta-Analysis. *Journal of Endourology*. 2021 Jul; 35(7): 991-1000. doi: 10.1089/end.2020.1133.
 - [6] Ivan SJ and Sindhwani P. Comparison of Guideline Recommendations for Antimicrobial Prophylaxis in Urologic Procedures: Variability, Lack of Consensus, and Contradictions. *International Urology and Nephrology*. 2018 Nov; 50(11): 1923-37. doi: 10.1007/s11255-018-1971-1.
 - [7] Hsieh CH, Yang SS, Lin CD, Chang SJ. Are Prophylactic Antibiotics Necessary in Patients with Preoperative Sterile Urine Undergoing Ureterorenoscopic Lithotripsy? *British Journal of Urology International*. 2014 Feb; 113(2): 275-80. doi: 10.1111/bju.12502.
 - [8] El-Agamy ES, Elhelaly MA, Abouelgreed TA, Abdrabuh AM, Elebiary MF, Elatreisy A et al. Randomized Comparison of the Effect of Standard Antibiotic Prophylaxis Versus Enhanced Prophylactic Measures on the Rate of Urinary Tract Infection After Flexible Ureteroscopy. *Archivio Italiano di Urologia e Andrologia*. 2023 Mar; 95(1): 11084. doi: 10.4081/aiua.2023.11084.
 - [9] Lightner DJ, Wymer K, Sanchez J, Kavoussi L. Best Practice Statement on Urologic Procedures and Antimicrobial Prophylaxis. *The Journal of Urology*. 2020 Feb; 203(2): 351-6. doi: 10.1097/JU.0000000000000509.
 - [10] Sui W, Yang H, Pepic L, Chang K, Shee K, Rompsaithong U et al. Longer Preoperative Antibiotic Duration Before High-Risk Ureteroscopy Does Not Decrease Infectious Complications. *Journal of Endourology*. 2025 Jan; 39(1): 34-41. doi: 10.1089/end.2024.0487.
 - [11] Shaikh AA, Chand K, Soomro MI, Pirzade AG, Shaikh NA, Abassi A. Urinary Tract Infection in Patients with Ureteric Stone, Before and After Ureteroscopy. *Rawal Medical Journal*. 2023 Sep; 48(3): 722-.
 - [12] Veeratterapillay R, Gravestock P, Harding C, Shaw M, Fitzpatrick J, Keltie K et al. Infection After Ureteroscopy for Ureteric Stones: Analysis of 71,305 Cases in the Hospital Episode Statistics Database. *British Journal of Urology International*. 2023 Jan; 131(1): 109-15. doi: 10.1111/bju.15850.
 - [13] Girgin R and Demirkiran ED. Postoperative Fever and Systemic Inflammatory Response Syndrome after Ureteroscopy for Stone Disease in the Geriatric Population: Risk Factors and Determinants. *Journal of Urological Surgery*. 2020 Aug; 7(3):177-183. doi: 10.4274/jus.galenos.2020.3366.
 - [14] Ozgur BC, Ekici M, Yuceturk CN, Bayrak O. Bacterial Colonization of Double J Stents and Bacteriuria Frequency. *The Kaohsiung Journal of Medical Sciences*. 2013 Dec; 29(12): 658-61. doi: 10.1016/j.kjms.2013.01.017.
 - [15] Shaker EK and Chaloob FA. Risk Factors in Bacterial Colonization of Internal Ureteral Stent. *Bionatura*. 2021; 6: 2022-6. doi: 10.21931/RB/2021.06.03.22.
 - [16] Westhoff N, Anokhin A, Patroi P, Neuberger M, Siegel F, Pfalzgraf D. Prospective Evaluation of Antibiotic Management in Ureteral Stent and Nephrostomy Interventions. *Urologia Internationalis*. 2022 Apr; 106(4): 411-8. doi: 10.1159/000517546.
 - [17] Samir M, Mahmoud MA, Tawfik A. Does bacterial Colonization Influence Ureteral Stent-Associated Morbidity? A Prospective Study. *Arab Journal of Urology*. 2023 Jul; 21(3): 156-61. doi: 10.1080/2090598X.2022.2164124.
 - [18] Cornette J, Lange D, Chew BH, Taily T. Bridging the Knowledge Gap: Past, Present, and Future of Antibiotic Use for Ureteral Stents. *British Journal of Urology International*. 2024 Dec; 134(6): 858-68. doi: 10.1111/bju.16515.
 - [19] Damavand RS, Esmaeili S, Bateni BH, Tavakoli AA, Kazemnezhad E. Comparing the Effect of Peri-Operative Antibiotic Prophylaxis Only with Continuous Low-Dose Antibiotic Treatment on the Incidence of Urinary Tract Infection and Stent-Related Symptoms in Patients Undergoing Double-J (DJ) Stent Insertion Following Transurethral Lithotripsy (TUL). *World Journal of Urology*. 2023 Nov; 4(11): 3027-32. doi: 10.1007/s00345-023-04585-8.
 - [20] Chew BH, Flannigan R, Kurtz M, Gershman B, Arsovska O, Paterson RF et al. A Single Dose of Intraoperative Antibiotics Is Sufficient to Prevent Urinary Tract Infection During Ureteroscopy. *Journal of*

- Endourology. 2016 Jan; 30(1): 63-8. doi: 10.1089/end.2015.0511.
- [21] Rosen GH, Wright CC, Murray KS. Antibiotic Stewardship in Urological Procedures: Are Prophylactic Recommendations Appropriate? American Urological Association. 2023.
- [22] Asmarawati TP, Djodimedjo T, Andhika DP, Rusli M, Qibtiyah M, Mahdi BA *et al.* The Use of Antibiotic Prophylaxis in Patients Undergoing Urologic Procedures in an Academic Hospital Surabaya: A Retrospective Study. Journal of Infection in Developing Countries. 2023; 17(6): 874-880. doi: 10.3855/jidc.17180.



Original Article



Knowledge, Practices, and Barriers Related to Informed Consent Among Postgraduate Medical and Surgical Residents in Peshawar

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ARTICLE INFO

Keywords:

Informed Consent, Postgraduate Residents, Knowledge, Safety Practice, Barriers, Ethics, Training, Language Barriers, Decision Capacity

How to Cite:

Hamza, M., Ahmed, D., Amin, I., Khan, A. W., Hussain, S., Zahir, S., Wazir, F., & Nisar, M. (2026). Knowledge, Practices, and Barriers Related to Informed Consent Among Postgraduate Medical and Surgical Residents in Peshawar: Informed Consent Knowledge and Practices Among Residents. *Pakistan Journal of Health Sciences*, 7(6), 38-44. <https://doi.org/10.54393/pjhs.v7i6.3891>

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Received Date: 26th January, 2026

1st Revision Received: 19th February, 2026

2nd Revision Received: 4th March, 2026

3rd Revision Received: 10th March, 2026

Acceptance Date: 16th March, 2026

Published Date: 30th June, 2026

ABSTRACT

Informed Consent is well-established and standard protocol in clinical practice, ensuring that patients are autonomous in making decisions and know about the benefits, risks, and alternatives to the procedure. **Objectives:** To determine the knowledge, practices, and barriers of informed consent among medical and surgical postgraduate residents of the tertiary care hospitals in Peshawar, Khyber Pakhtunkhwa (KP), Pakistan. **Methods:** An analytical cross-sectional study was conducted from July 2025 to September 2025 among 294 medical and surgical postgraduate residents in public and private hospitals in Peshawar through a self-structured questionnaire, using convenience sampling, and analyzed by SPSS version 27.0. **Results:** 65% of postgraduate residents were aware of informed consent, especially legal requirements and ethical principal 92.9% and 91.8% respectively, while lower for assessing decision capacity (36.7%) and voluntariness (21.4%). Practice levels were lower than the knowledge level, despite the frequent use of standardized forms and verification of understanding. Language barriers (74.1%) and time constraints (58.5%) were key obstacles in obtaining informed consent. Knowledge significantly correlated with department ($p=0.018$), while practice significantly correlated with formal training in informed consent ($p=0.010$), but not age. Barriers showed no significant associations with department or training year. **Conclusions:** Regardless of the high knowledge of informed consent among residents, it was moderately practiced in hospitals, with a weakness in assessing decision-making and voluntariness. Language barriers and time constraints embarrass the practice of informed consent. Structured training and barrier mitigation could bridge this knowledge-practice gap and strengthen the practice of informed consent.

INTRODUCTION

Informed consent is one of the most important topics in bioethics literature, which emphasizes the patient's involvement in health decisions, embodying their opinion and viewpoints to strengthen the doctor-patient relationship. Informed Consent is well-established and standard protocol in clinical practice. [1] The concept of informed consent is more linked to a surgical specialty than to other therapeutic fields because it is mandatory to take

informed consent from the patient before a surgical procedure. While the indication and necessity for obtaining consent in clinical practice are the same worldwide, the process of taking it differs from place to place [2, 3]. Many perceive informed consent as a mere medicolegal ritual rather than a fully participatory decision-making process, which is usually carried out as a short preparatory routine. Most of the respondents in a study indicated that informed



consent feels foreign to the African psyche, yet they did not consider insistence on informed consent by doctors as constituted cultural insensitivity. While most Nigerian surgeons demonstrate understanding of the informed consent process, they often lack practical experience, highlighting the need to modernize the surgeon-patient connection [1]. Obtaining informed consent is a vital and required skill in medical training, yet many residents receive minimal formal training regarding the importance and necessity of informed consent. and [4-6]. Some senior medical students in New Zealand admitted to performing sensitive examinations on patients without their knowledge or agreement [7]. Similarly, a study conducted in the United States of America found that the lack of confidence and competence in their abilities to obtain informed consent in undergraduate and postgraduate medical students [8]. A study conducted in Cairo, Egypt, indicated that informed consent in hospitals is often treated as a formal procedure rather than a genuine connection between physician and patient [9]. Earlier research suggests that many healthcare professionals believe providing full information to the patient renders formal consent unnecessary [10, 11]. A U.S study of first-year surgical residents showed that few could accurately identify the risks, advantages, and alternatives for any of the procedures, with less than half addressing common patient queries correctly. Surgical faculty must dedicate more time to training first-year residents on the challenges involved in providing informed consent for treatments [12]. Despite many surgical residents and faculty understanding the significance of the informed consent process, they still faced persistent challenges, including inadequate communication, legal pressures, time constraints, and poor scheduling of informed consent discussions [13]. Despite high global knowledge of informed consent as a fundamental ethical requirement in medical practice, no prior studies in Peshawar, Khyber Pakhtunkhwa, Pakistan, have systemically evaluated postgraduate medical and surgical residents knowledge, real-world practices and barriers to effective implementation in tertiary care hospitals. Local research elsewhere in Pakistan and nearby regions highlight discrepancies between theoretical understanding and application such as inadequate documentation, time constraints, training gaps or cultural factors yet leaves this critical group explored, potentially comprising patient safety and exposing institution to medicolegal risks. This study aimed to evaluate knowledge and practices of informed consent among medical and surgical postgraduate residents of the tertiary care hospitals in Peshawar, identify barriers to effective implementation, and provide insights to enhance training programs and improve patient care in the region.

METHODS

This analytical cross-sectional study was conducted from July to September 2025 across public and private teaching hospitals in Peshawar, Pakistan, to evaluate informed consent competency among 294 postgraduate residents in Medicine and Allied specialties and Surgery and Allied specialties. A sample size of 278 residents was calculated using OpenEpi (95% confidence level and a finite population of 1000. To account for potential incomplete responses or data loss, data were collected from 294 residents. Postgraduate trainees who consented to participate were included, while those unwilling to participate or working in the emergency department were excluded. Data were collected through a convenience sampling technique using a self-structured questionnaire with closed-ended questions (Figure 1).

Sample Size for Frequency in a Population	
Population size (for finite population correction factor or fpc)(N):	1000
Hypothesized % frequency of outcome factor in the population (p):	50% +/- 5
Confidence limits as % of 100 (absolute +/- %)(d):	5%
Design effect (for cluster surveys-DEFF):	1
Sample Size(n) for Various Confidence Levels	
Confidence Level(%)	Sample Size
95%	278
80%	142
90%	214
97%	321
99%	400
99.9%	521
99.99%	603
Equation	
Sample size $n = [DEFF * Np(1-p)] / [(d^2 / Z^2_{1-\alpha/2} * (N-1) + p * (1-p)]$	
Results from OpenEpi, Version 3, open source calculator--SSPropor Print from the browser with ctrl-P or select text to copy and paste to other programs.	

Figure 1: Sample Size Calculation Using Openepi Showing a Minimum Required Sample of 278 Participants at a 95% Confidence Level and 5% Margin of Error

The questionnaire was developed by the study authors based on a review of prior literature on informed consent among healthcare professionals [14-16]. No single existing validated instrument was fully adopted, as available tools were primarily designed for general healthcare workers or surgical patients in other regions and required adaptation to focus on postgraduate medical and surgical residents in Pakistani tertiary hospitals. The final questionnaire comprised four sections: (1) sociodemographic variables, (2) knowledge of informed consent (9 items), (3) practice related to obtaining informed consent (11 items), and (4) perceived barriers (10 items). Knowledge and practice items were scored binarily (1 point for "yes" responses indicating correct knowledge or reported good practice, 0

for negative responses), enabling computation of total scores categorized as low, moderate, or high. Item-level responses informed detailed profiles of specific components. Total scores for knowledge (9 items, maximum 9) and practice (11 items, maximum 11), and Perceived Barriers (10 items, maximum 10) were converted to percentages of the maximum possible score. Levels were categorized using widely adopted standard cut-offs in similar knowledge, attitude, and practice (KAP) studies: low (<50%), moderate (50–69%), and high (≥70%). Ethical approval was obtained from the Institutional Review Board and Ethical Committee of Alliance Healthcare Private Ltd (Northwest General Hospital & Research Centre Ethics Committee) (Ref: IRB&EC/2025-GH/0261; dated 30th June, 2025). A pilot study was conducted with 20 residents (excluded from the final analysis) at Northwest General Hospital and Research Centre, Peshawar, to assess the validity and reliability of the self-structured questionnaire. Cronbach's alpha was used to ensure internal consistency of the items, yielding $\alpha=0.80$ for the overall questionnaire, indicating good reliability. Informed consent was obtained from all participants through a consent form placed at the beginning of the questionnaire, and the confidentiality of the participants was maintained. Data were collected using Google Forms and a paper-based questionnaire. Data were analysed in SPSS version 27.0. Descriptive statistics included frequencies, percentages for categorical variables, and means with standard deviation for continuous variables. Normality of age and total scores was assessed using the Shapiro-Wilk tests, which indicated non-normal distribution ($p<0.05$). Therefore, non-parametric tests were applied where appropriate. Chi-square test was used to examine the association between nominal categorical variables (gender, training hospital, training department) and ordinal outcome levels (knowledge, practices, barrier). Kruskal-Wallis tests were applied for ordinal (training year) across the three outcome levels. Mann-Whitney U tests were used for two-group comparisons (medicine vs surgery department) on ordinal outcomes. All tests were two-tailed, with $p<0.05$ considered statistically significant.

RESULTS

Among the 294 participants, the mean age was 28.78 ± 2.56 years, with 59.9% male and balanced representation across public (52%) and private (48%) hospitals, as well as medicine/allied (50%) and surgery/allied (50%) departments (Table 1).

Table 1: Sociodemographic Characteristics of the Participants (n=294)

Variables	Category	Frequency (%age)
Age	Mean $\pm$ SD	28.78 $\pm$ 2.56
Gender	Male	176 (59.9%)
	Female	118 (40.1%)
Training Hospital	Public	153 (52%)
	Private	141 (48%)
Training Department	Medicine and Allied	147 (50%)
	Surgery and Allied	147 (50%)
Training Year	First	108 (36.7%)
	Second	65 (22.1%)
	Third	68 (23.1%)
	Fourth	48 (16.3%)
	Fifth	05 (1.7%)
Formal Training in Informed Consent	Yes	160 (54.4%)
	No	134 (45.6%)

Among participants, 65.0% demonstrated high knowledge of informed consent, 29.9% moderate, and 5.1% low. In contrast, practice levels were more evenly distributed, with high 43.9% (n=129), moderate 38.1% (n=112), and low 18.0% (n=53), indicating a clear gap between higher knowledge than practice (Table 2).

Table 2: Knowledge and Practice Level and Barrier Perceived Level of Postgraduate Trainees Regarding Informed Consent

Variables	Low	Moderate	High
Knowledge level	15 (5.1%)	88 (29.9%)	191 (65.0%)
Practice level	53 (18%)	112 (38.1%)	129 (43.9%)
Barrier Perceived level	8 (2.7%)	72 (24.5%)	214 (72.8%)

Knowledge was strongest for core formal aspects, such as legal requirements and ethical principles, but substantially weaker for critical ethical principles, including the assessment of decision-making capacity and voluntariness. Similarly, most residents reported good adherence to basic procedural practices such as using standardized forms, disclosure of risk, benefit, or alternative, verification of understanding, and following institution protocol, yet considerably fewer utilized supportive tools and strategies such as visual aids, translators when needed, encouragement of patient questions, or routine involvement of family/guardians. The most common reported barriers to effective informed consent were language difficulties and time constraints for detailed discussion, followed by patient anxiety related to risk disclosure. Less frequently cited were cultural or institutional norms that minimize the consent process and are perceived as inadequate training. The results indicated that the training department was significantly associated with the knowledge of informed consent at the postgraduate residents' level ($p=0.018$), with a higher percentage of high knowledge in the medicine department

(34.7%) compared to the surgery department (20.4%). On the other hand, the training hospital, the training year, and the formal training were not statistically significant for the knowledge levels ($p>0.05$). In terms of the practice domain, the results indicated that the formal training was statistically significant for the practice domain ($p = 0.010$), with a higher percentage for the high practice group in the

formal training group (51.9%) compared to the non-formal training group (34.3%). On the other hand, the training hospital, the training department, and the training year were not statistically significant for the practice domain ($p>0.05$), with a higher percentage for good practice in the medicine department and the senior years (Table 3).

Table 3: Association of Knowledge and Practice Level Regarding Informed Consent Using Chi-Square Test

Variables		Categories	Low	Moderate	High	Chi-square χ^2	p-value
Knowledge	Training Hospital	Public	10 (6.5%)	101 (66%)	42 (27.5%)	0.190	0.909
		Private	11 (7.8%)	91 (64.5%)	39 (27.7%)		
	Training Department	Medicine	11 (7.5%)	85 (57.8%)	51 (34.7%)	8.013	0.018
		Surgery	10 (6.8%)	107 (72.8%)	30 (20.4%)		
	Training Year	1 st	7 (6.5%)	72 (66.7%)	29 (26.9%)	10.164	0.254
		2 nd	6 (9.2%)	49 (75.4%)	10 (15.4%)		
		3 rd	6 (8.8%)	38 (55.9%)	24 (35.3%)		
		4 th	2 (4.2%)	29 (60.4%)	17 (35.4%)		
		5 th	0 (0%)	4 (80%)	1 (20%)		
	Formal Training	Yes	13 (8.1%)	102 (63.8%)	45 (28.1%)	0.646	0.724
		No	8 (6.0%)	90 (67.2%)	36 (26.9%)		
Practice	Training Hospital	Public	23 (15.0%)	56 (36.6%)	74 (48.4%)	3.23	0.198
		Private	30 (21.2%)	56 (39.8%)	55 (39%)		
	Training Department (Medicine/Surgery)	Medicine	27 (18.4%)	47 (32%)	73 (49.7%)	5.152	0.076
		Surgery	26 (17.7%)	65 (44.2%)	56 (38.1%)		
	Formal Training	Yes	25 (15.6%)	52 (32.5%)	83 (51.9%)	9.126	0.010
		No	28 (20.9%)	60 (44.8%)	46 (34.3%)		
	Training Year (1 st -5 th)	1 st	25 (23.1%)	35 (32.4%)	48 (44.4%)	12.274	0.139
		2 nd	9 (13.8%)	33 (50.8%)	23 (35.4%)		
		3 rd	7 (10.3%)	29 (42.6%)	32 (47.1%)		
		4 th	11 (22.9%)	14 (29.2%)	23 (47.9%)		
		5 th	1 (20%)	1 (20%)	3 (60%)		

There was a significant association found between the level of Knowledge and the level of practice of informed consent. It was interesting to note that among the participants with a high level of Knowledge, 33.3% showed a low level of practice, and only 53.1% showed a high level of practice. On the other hand, among the participants with a moderate level of Knowledge, the majority showed a moderate level of practice (48.4%), and a significant number showed a low level of practice (12.0%). This shows that though the level of Knowledge among the participants is generally moderate to high, the level of practice of informed consent is still low. Among postgraduate trainees, Knowledge regarding informed consent showed a strong and highly significant relationship with perceived barriers. Trainees with greater Knowledge were noticeably more likely to experience fewer barriers in obtaining or applying informed consent, while those with low Knowledge consistently reported the highest levels of perceived barriers. This clear pattern suggests that a better understanding of informed consent principles is closely linked to feeling fewer practical, ethical, or systemic obstacles in clinical or research settings. In contrast, trainees with higher levels of practice did not show a strong reduction in perceived barriers compared to those with lower levels of practice. The correlation between the two was less direct and varied. This implies that doing the process more often does not guarantee perceiving fewer barriers (Table 4).

Table 4: Association of Knowledge and Practice Levels with Perceived Barrier Levels regarding Informed Consent among Postgraduate Residents (n=294)

Variables	Category	Low Barrier, n (%)	Moderate Barrier, n (%)	High Barrier, n (%)	Low Practice, n (%)	Moderate Practice, n (%)	High Practice, n (%)	Total, n (%)	Chi-square (df)	p-value
Knowledge	Low	0 (0%)	6 (28.6%)	15 (71.4%)	3 (14.3%)	8 (38.1%)	10 (47.6%)	21 (100%)	$\chi^2=40.101$	<0.001
	Moderate	0 (0%)	34 (17.7%)	158 (82.3%)	23 (12.0%)	93 (48.4%)	76 (39.6%)	192 (100%)		
	High	8 (9.9%)	32 (39.5%)	41 (50.6%)	27 (33.3%)	11 (13.6%)	43 (53.1%)	81 (100%)		

Practice Level	Low	4 (7.5%)	20 (37.7%)	29 (54.7%)	—	—	—	53	$\chi^2=17.708$	0.001
	Moderate	2 (1.8%)	17 (15.2%)	93 (83.0%)	—	—	—	112		
	High	2 (1.6%)	35 (27.1%)	92 (71.3%)	—	—	—	129		

Overall, the results of this study have shown that knowledge of informed consent has a more powerful impact on reducing perceived barriers than simply increasing the frequency of practice alone

DISCUSSION

According to this study, postgraduate residents in Peshawar are typically informed of the legal and intellectual foundations of informed consent; however encounter it difficult to deal with some of its ethical and practical aspects. Most people (65%) had high knowledge scores overall, especially when it came to legal criteria for consent (92.9%) and ethical standards (91.8%). Conversely, fewer residents showed knowledge of voluntariness (21.4%) and decision-making capacity (36.7%), which are essential elements of true consent. Despite the extensive use of standard consent forms (82.7%) and routine validation that patients comprehended information (95.6%), only 43.9% of respondents reported consistently high-quality consent processes in practice. Time restrictions (58.5%) and language barriers (74.1%) were the most frequently encountered barriers. Our data show that a majority (65.0%) of postgraduate residents reported high knowledge of informed consent. Consistent with our findings, numerous studies reveal that medical trainees typically have a thorough understanding of consent theory despite their lack of practical experience. In the Ugandan survey, almost all senior dentistry students (>97%) showed a good level of understanding of consent principles [18]. While qualitative research in Somalia showed fairly high knowledge of informed consent [19]. In comparison, some settings report significantly less professional competence. An Ethiopian study found that around two-thirds of medical personnel had sufficient understanding of surgical informed consent [14]. In northeast India, just over half (56%) of junior physicians reported having "good knowledge" about the process for obtaining research consent [15]. Taken together, these comparisons indicate that although the general knowledge of residents is relatively high, there are still significant gaps globally, particularly in low-resource settings. Residents were particularly aware of formal consent requirements, as seen by the 92.9% recognition of legal/medico-legal requirements and the 91.8% recognition of ethical consent standards. The crucial ideas of voluntariness (21.4%) and patient decision capacity (36.7%), however, were far less well understood. This absence is concerning because obtaining valid consent necessitates not just disclosing information but also guaranteeing the patient's competence and autonomy [19]. To put it another way, our findings point to a discrepancy: practically all trainees are aware of the procedural guidelines, almost all are aware

that consent must be documented, yet only a small percentage understood that consent must be provided voluntarily and properly. This is consistent with international clinical ethics recommendations that highlight capacity and voluntariness as essential components of legitimate consent [16]. The contradiction between action and knowledge is a significant problem. Although the majority of the residents in our sample were aware of consent procedures, they only indicated a moderate level of adherence in practice (43.9%). However, in an Italian survey, 71% of physicians followed consent procedures completely [20]. According to an audit, even though the majority of patients had signed consent forms, only 64% of them comprehended the information completely, and only 24% were made aware of the risks associated with surgery 76% did not receive a risk discussion [21]. Such data reveals how often the consent procedure in practice diverges from ethical principles. Similarly, another research of emergency operations in Lahore found that only 59.5% of patients felt at ease with the consent process and that almost all forms were signed by family members rather than patients (only 1.6% of patients signed themselves) [22]. In contrast, some research indicates that self-reported consent processes are substantial. Likewise, 88.8% of Anaesthetists in Tertiary Care Hospitals of Karachi who participated in a survey reported following official consent procedures, including disclosure and documentation. [23] Together, these findings imply that consistent application of consent often fails due to practical obstacles, even in cases where doctors are aware of it. Systemic pressures and communication challenges are the main barriers to appropriate consent in all contexts. Language barriers were the most frequently reported barrier in our sample (74.1%), which is consistent with earlier research on Pakistan. An Ethiopian study of healthcare professionals finds that language barriers and a lack of interaction time were specifically the two main obstacles to getting appropriate informed consent [15]. Clinicians claim that language or literacy barriers prevent clear communication and that patients' families frequently control decision-making [23]. Current results support a trend seen in recent research: while understanding of informed consent is often sufficient, systemic and practical barriers prevent its application. Crucially, ethical and educational interventions can have an impact in areas where

knowledge and practice disagree.

The analytical cross-sectional study design limits causal inference and temporal tracking of competency changes, while convenience sampling from Peshawar hospitals risks selection bias and restricts generalizability. Complications of noncompliance with informed consent practices and patient perspectives in their health decision were not addressed. Self-reported data are susceptible to social desirability and recall bias. Patient perspectives were not included, and department-specific subgroup analyses were not performed, representing areas for future research. Residency training programs must integrate mandatory and structured education on informed consent, including decision-making capacity. Simulation training and case discussion should target the inclusion of aspects of voluntariness verification, simplification of multilingual communication, and the inclusion of the family. Hospitals should adopt standardized multilingual consent forms (in Pashto, Urdu, and English), a time and space (such as a Consent/Counselling room) dedicated to consent, especially in busy departments, and interpreters or culturally competent staff. Audits of consent practices should be encouraged, and feedback from residents should be taken regularly. This will ensure continuous improvement and patient-centred ethical practice in hospitals.

CONCLUSIONS

Our study concludes that postgraduate residents in Peshawar possess a high level of knowledge regarding informed consent. However, actual clinical implementation is lacking in high-patient-inflow hospitals. In the Pakistani tertiary care hospital, the most significant barriers to the compliance of informed consent are the language barrier, lack of time, and high patient volume. There is a requirement for structured training of postgraduate residents, consent forms in multiple languages, and assignment at the policy level for consent discussions.

Authors' Contribution

Conceptualization: MH, DA

Methodology: MH, DA, IA, AWK, SH, SZ, FW, MN

Formal analysis: MH, DA, IA, AWK, SH, SZ, FW, MN

Writing and Drafting: MH, DA, IA, AWK, SH, SZ, FW, MN

Review and Editing: MH, DA, IA, AWK, SH, SZ, FW, MN

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All 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] Ogundiran TO and Adebamowo CA. Surgeons' Opinions and Practice of Informed Consent in Nigeria. *Journal of Medical Ethics*. 2010 Dec; 36(12): 741-745. doi: 10.1136/jme.2010.037440.
- [2] Aisuodionoe-Shadrach OI, Ogunlade OS, Amoran OE. An Evaluation of the Informed Consent Process for Elective Surgery at a University Hospital. *Nigerian Journal of Medicine*. 2006; 15(3): 281-284. doi: 10.4314/njm.v15i3.37229.
- [3] Jochum SB, Venkatramani M, Ritz EM, Favuzza J, Hayden DM, Saclarides TJ *et al*. Surgical Residents' Perspective on Informed Consent—How Does It Compare With Attending Surgeons? *Journal of Surgical Research*. 2021 Apr; 260: 88-94. doi: 10.1016/j.jss.2020.10.019.
- [4] Hassan IN, Ibrahim M, Yaqub S, Abdalla H, Aljaili G, Osman W *et al*. Perceptions, Practices, and Barriers in Surgical Informed Consent: A Cross-Sectional Study from Sudan: *Surgical Informed Consent in Sudan*. *Surgery in Practice and Science*. 2025 Sep; 23: 100309. doi: 10.1016/j.sipas.2025.100309.
- [5] Nono D, Mwebesa E, Bagenda G, Okullo I, Rwenyonyi CM, Williams S. Assessment of the Knowledge, Attitude, and Practices of the Informed Consent Process in Oral Healthcare Among Dental Students in Makerere University Dental Hospital, Uganda. *BMC Medical Education*. 2024 May; 24(1): 516. doi: 10.1186/s12909-024-05520-0.
- [6] Loughran D. Surgical Consent: The World's Largest Chinese Whisper? A Review of Current Surgical Consent Practices. *Journal of Medical Ethics*. 2015 Feb; 41(2): 206-210. doi: 10.1136/medethics-2013-101931.
- [7] Malpas PJ, Bagg W, Yelder J, Merry AF. Medical Students, Sensitive Examinations and Patient Consent: A Qualitative Review. *The New Zealand Medical Journal (Online)*. 2018 Sep; 131(1482): 29-37.
- [8] Tang AB, Childers CP, Dworsky JQ, Maggard-Gibbons M. Surgeon Work Captured by the National Surgical Quality Improvement Program Across Specialties. *Surgery*. 2020 Mar; 167(3): 550-555. doi: 10.1016/j.surg.2019.11.013.
- [9] Galal YS. Knowledge, Practice, and Perception Towards the Informed Consent Process Among Physicians And Patients in General Surgical

- Departments at Cairo University Hospitals. The Egyptian Journal of Community Medicine. 2016 Apr; 34(2): 1-7. doi: 10.21608/ejcm.2016.649.
- [10] Putrihamidah DA, Adhayati B, Louisa M. Physician Knowledge and Training as Determinants of Informed Consent Implementation: A Cross-Sectional Study in Two Indonesian Hospitals. Journal of Health and Nutrition Research. 2025 Dec; 4(3): 1175-1183. doi: 10.56303/jhnresearch.v4i3.689.
- [11] Paterick TJ, Carson GV, Allen MC, Paterick TE. Medical informed consent: general considerations for physicians. In Mayo Clinic Proceedings. Elsevier. 2008 Mar; 83(3): 313-319. doi: 10.4065/83.3.313.
- [12] Oberoi SS, Sharma N, Rastogi S, Kumar S, Suresh A. Informed Consent: An Essential Tool for Medical Practice and Research. Amrita Journal of Medicine. 2025 Apr; 21(2): 50-56. doi: 10.4103/AMJM.AMJM_62_24.
- [13] Newman N, McKenzie F, Wells JM, Wilkinson T, Dean J, Doogue M et al. Consent to Medical Student Teaching: An Observational, Cross-Sectional Study Exploring the Patient View. BioMed Central Medical Education. 2024 Dec; 24(1): 1525. doi: 10.1186/s12909-024-06557-x.
- [14] Bolado GN, Ataro BA, Feleke MG, Gadabo CK, Kebamo TE, Minuta WM. Informed Consent Practice and Associated Factors Among Healthcare Professionals In Public Hospitals of Southern Ethiopia, 2023: A Mixed-Method Study. Biomed Central Nursing. 2024 Jan; 23(1): 77. doi: 10.1186/s12912-024-01748-9.
- [15] Rajkumari B, Devi SP, Chanu LR, Gairanlung T. Knowledge and Practices Regarding Informed Consent Process For Research Among Junior Doctors of a Tertiary-Care Institution in Northeast India: A Cross-Sectional Study. International Journal of Community Medicine and Public Health. 2025 Jul; 12(7): 3131. doi: 10.18203/2394-6040.ijcmph20252107.
- [16] Memon R, Asif M, Shah BA, Kiran T, Khoso AB, Tofique S et al. Clinicians' experiences of obtaining informed consent for research and treatment: a nested qualitative study from Pakistan. BioMed Central Medical Ethics. 2024 Nov; 25(1): 131. doi: 10.1186/s12910-024-01119-8.
- [17] Aweis A, Mauma M, Afrah A, Guled IA, Kulane A. Doctors' Experiences on Dealing with Informed Consent Required for Lifesaving Interventions for Pregnant Women in Somalia. Frontiers in Global Women's Health. 2025 Aug; 6: 1584113. doi: 10.3389/fgwh.2025.1584113.
- [18] Turillazzi E and Neri M. Informed Consent and Italian Physicians: Change Course or Abandon Ship—From Formal Authorization to a Culture of Sharing. Medicine, Health Care, and Philosophy. 2015 Aug; 18(3): 449-453. doi: 10.1007/s11019-015-9637-6.
- [19] Shafique MU, Saleem MS, Saghir M, Javaid MS, Saad M, Sadiq A et al. An Audit of Preoperative Informed Consent in Surgical Patients at a Tertiary Care Hospital in Lahore, Pakistan. Cureus. 2023 Dec; 15(12): 1-6. doi: 10.7759/cureus.50122.
- [20] Munawar T, Ismail F, Qadri HM, ul Haq A, Munawar A, Zahid AS et al. Practices of Informed Consent for Emergency Procedures at a Tertiary Care Hospital in Lahore, Pakistan. Cureus. 2023 Dec 11; 15(12): 1-8. doi: 10.7759/cureus.50322.
- [21] Zewudie BT, Tenaw SG, Mesfin Y, Abebe H, Mekonnen Z, Mengist ST et al. Practice and Factors Affecting Informed Consent Among Healthcare Workers for Major Surgical Procedures at Gurage Zone Hospitals, South Ethiopia, 2022: a facility-based cross-sectional study. BMJ Open. 2025 Jan; 15(1): 83253. doi: 10.1136/bmjopen-2023-083253.
- [22] Hassan A, Wanwari M, ur Rehman A, Aziz T, Naeem K. Application of Standard Informed Consent Procedure Amongst Practicing Anesthetists in Tertiary Care Hospitals of Karachi: Informed Consent Practices Among Anesthetists. Journal of Health and Rehabilitation Research. 2024 Sep; 4(3): 1-5. doi: 10.61919/jhrr.v4i3.1497.
- [23] Fatima A. Informed consent process: Ethical and Practical Challenges in Clinical Trials Regarding Subject Enrollment, Protection, and Informed Consent in Developing Countries (India, Pakistan, and Iran). History and Philosophy of Medicine. 2021; 3(2): 7. doi: 10.53388/HPM20210409029.



Original Article



Comparative Evaluation of Classical Inferior Alveolar Nerve Block and Gow-Gates Nerve Block for Surgical Removal of Mandibular Third Molar

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ARTICLE INFO

Keywords:

Inferior Alveolar Nerve Block, Gow-Gates Nerve Block, Surgical Removal, Mandibular Third Molar

How to Cite:

Khan, M. M., Ilyas, M., Sheikh, T., Sohail, A., Ahmad, S. S., & Khalid, F. (2026). Comparative Evaluation of Classical Inferior Alveolar Nerve Block and Gow-Gates Nerve Block for Surgical Removal of Mandibular Third Molar: IANB vs Gow-Gates for Mandibular Third Molar Surgery. *Pakistan Journal of Health Sciences*, 7(6), 45-50. <https://doi.org/10.54393/pjhs.v7i6.3661>

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ABSTRACT

Effective anesthesia is essential for the surgical removal of mandibular third molars. While the classical inferior alveolar nerve block is widely used, its success may be limited by anatomical variations. The Gow-Gates technique is considered a potential alternative offering broader mandibular anesthesia. **Objectives:** To evaluate and compare the classical inferior alveolar nerve block and Gow-Gates nerve block for surgical removal of mandibular third molars in terms of Anesthetic success rate, Onset and duration of anesthesia, and patient-reported pain using a visual analog scale. **Methods:** A quasi-experimental, comparative study was performed in which a total of 160 patients were selected and randomly allocated to receive Gow-Gates (GG) nerve block or inferior alveolar nerve block (IANB) for the extraction of mandibular molars. Onset time, pain levels, and volume of anesthesia were recorded as data. SPSS statistical analysis version 26.0 was used for data analysis. **Results:** Regarding gender, females were counted more, 87, comprised 54.43 % of the sample, whereas 73 men accounted for 45.57 %. The onset time of the Gow-Gates group took 6.16 minutes, which is slower than IANB, 2.78 minutes; however, the success rate of both techniques is about the same, 87.5%. Furthermore, the mean volume of local anesthesia used to anesthetize tissues was higher in the IANB group than in the GG group. **Conclusions:** Both methods are useful in mandibular anesthesia, and Gow-Gates has a high rate of success and less chance of aspiration, though IANB has a quicker onset. Patient and clinician factors determine the technique to be used.

INTRODUCTION

One of the greatest aspects of oral and maxillofacial surgery is pain control, and local anesthesia represents an essential step to its achievement. The mechanism of action of a local anesthetic is that they temporarily affect the nerve conduction of nerve impulses, like they temporarily block the feeling of pain [1]. Globally, the prevalence of impacted third molars ranges from approximately 16% to 68%, making their surgical removal one of the most common oral surgical procedures. Effective local anesthesia is essential for pain control during these procedures, with the classical inferior alveolar nerve block (IANB) being the most widely used technique.

However, IANB has been reported to have a failure rate ranging from 15% to 25%, which may compromise patient comfort and surgical efficiency. The Gow-Gates mandibular nerve block has been proposed as an alternative technique with potentially higher success rates and lower incidence of positive aspiration. Despite these advantages, comparative evidence regarding the efficacy of these techniques during mandibular third molar surgery remains limited, particularly in the regional and local population. Therefore, this study was conducted to compare the effectiveness of the classical inferior alveolar nerve block and Gow-Gates nerve block for the surgical



removal of mandibular third molars [2]. Two percent lidocaine is the most widespread local anesthetic drug in dentistry and is frequently mixed with a vasoconstriction agent, adrenaline (epinephrine) [3]. Vasoconstrictor also increases the life of an anesthetic, not only by decreasing vascular pick-up but also in terms of reducing systemic toxicity, and gives a clean, hemorrhage-free surgical field. All these contribute greatly to the general efficiency and safety of dental surgical operations [4]. Successful local anesthesia is an achievement towards the success of any oral surgery. But the working of anesthesia depends upon various factors [5]. These encompass the method adopted and employed by the clinician during the procedure of anesthesia, plus the individualized conditions of the patient, such as variations of anatomy, the existence of infection or inflammation, psychological factors, including fear or anxiety, and so on [6]. With the rather thin and porous bone containing the tooth roots, which is present in the maxilla, the local anesthetic solutions have a tendency to diffuse easily, thereby making the local infiltration technique a highly successful technique. Consequently, maxillary anesthesia is expected to be associated with a positive success rate in common dental practices [7]. Contrary to this, a more difficult procedure is mandibular anesthesia, especially among adults. Mandibular teeth have dense cortical bone around the roots, leading to poor infiltration, and in such cases, it requires the application of nerve block procedures [8]. The inferior alveolar nerve block (IANB), despite its widespread use, does not ensure an effective pulpal anesthesia. The failure rates reported are comparatively high, and the result can be affected by a variety of factors [6]. These are: anatomical variation, e.g., bifid mandibular nerves or supernumerary foramina, wrong injecting technique, individual differences in drug response, and factors such as intravascular injection or injection-site infection [10]. Alternative techniques, such as the Gow-Gates mandibular nerve block, have been developed to address these issues. By injecting the anesthetic solution closer to the neck of the mandibular condyle, a higher anatomical location than that of the standard IANB, he aimed to provide a more thorough and efficient anesthesia of the branches of the mandibular nerve in 1973 [11]. This enables anesthesia of the inferior alveolar nerve and related nerves, including lingual, buccal, and mylohyoid. The Gow-Gates technique depends upon the accuracy of needle placement based on both extraoral and intraoral landmarks of the anatomy and on more technical skill; however, the benefit of the technique is extension and more consistent distribution of anesthesia [12].

Despite widespread use of the inferior alveolar nerve block, high failure rates and variable anesthesia success highlight the need for more effective techniques. Limited

comparative evidence exists on the efficacy of the Gow-Gates versus classical IANB, particularly in local populations. Therefore, this study aimed to compare the effectiveness of the classical inferior alveolar nerve block and Gow-Gates nerve block for the surgical removal of mandibular third molars in patients presenting to Dow University of Health Sciences Karachi.

METHODS

This study was designed as a quasi-experimental, comparative study involving two independent groups. Group 1 received the classical inferior alveolar nerve block, while Group 2 received the Gow-Gates mandibular nerve block. Patients in each group were different, and outcomes were compared between the groups was carried out at the Department of Dental and Maxillofacial Surgery, Dr. Ishrat-ul-Ebad Khan Institute of Oral Health Sciences, Dow University of Health Sciences, Karachi in time frame of six months from (April to September 2024) following the institutional ethical review committee of Dow University of Health Sciences Karachi's synopsis approval (Ref: IRB-334-/DUHS/Approval/2024/99; dated 28th March, 2024). Written informed consent was obtained from each patient using a non-probability sequential (convenience) sampling technique. Using a proportion of positive aspiration in Group 1 (P_1) = 2.5% and Group 2 (P_2) = 15% [13], power ($1-\beta$) = 80%, and a 95% confidence level, the sample size was determined using WHO sample-size software to be 80 patients per group ($n=80$). Consequently, a total of 160 patients will be included, 80 in each of the two groups. The primary outcome of this study was anesthetic success rate, defined as the ability to complete surgical removal of the mandibular third molar without supplemental anesthesia, assessed intraoperatively and using a 0-10 Visual Analog Scale (VAS). Secondary outcomes included the onset time of anesthesia and the duration of anesthesia. Inclusion Criteria consisted of patients undergone extractions of mandibular molars requiring different local anesthesia techniques, having an age of 18-60 years, and patients with known allergy to local anesthetics, local inflammation, or tenderness at the injection site. Current users of antidepressant or antipsychotic medication were excluded from the study. The primary outcome of the study was anesthetic success rate, defined as the ability to complete the surgical extraction of the mandibular third molar without the need for supplemental anesthesia. A nerve block was considered successful if the patient achieved adequate lip numbness and the procedure was completed without significant pain or the need for additional anesthetic injections. Pain perception was assessed using a Visual Analog Scale (VAS) ranging from 0 to 10, where 0 indicated no pain, and 10 indicated the worst imaginable pain.

Patients were instructed to indicate their pain intensity on the scale during the surgical procedure. Pain scores were recorded at the time of tooth extraction, and any score ≥ 4 was considered indicative of inadequate anesthesia, requiring supplemental anesthesia and recorded as anesthetic failure. Participants were randomly allocated into two equal groups using a computer-generated randomization method. Group A received the classical inferior alveolar nerve block, while Group B received the Gow-Gates mandibular nerve block. Allocation concealment was ensured using sealed opaque envelopes opened at the time of intervention. The study followed a single-blind design, while outcome assessment was performed by an independent investigator blinded to group allocation. To ensure procedural standardization, all injections were administered by the same experienced operator using the same armamentarium and local anesthetic solution (2% lidocaine with 1:100,000 epinephrine), following standardized protocols for both techniques. Outcome variables were monitored intraoperatively and postoperatively using standardized assessment criteria. During the surgical procedure, patients were observed for signs of inadequate anesthesia, and pain was assessed using a Visual Analog Scale (VAS, 0–10). If a patient reported moderate to severe pain (VAS ≥ 4) or showed signs of discomfort during the procedure, supplemental anesthesia was administered, and this was recorded as anesthetic failure. Intraoperative monitoring also included observation for the onset of anesthesia, and patients were followed for 24–48 hours to assess complications such as pain, swelling, trismus, or any adverse reactions to the anesthetic technique. Outcome assessments were recorded immediately after anesthesia administration, during the surgical procedure, and at the postoperative follow-up visit to ensure consistent evaluation of all study parameters. A complete medical and dental history was recorded. The principal investigator (PI) will leave the operatory while a consultant administers the assigned block. After injection, the PI will re-enter, double-blinded to the technique, and assess the following parameters: Onset time of anesthesia (minutes), Maximum mouth openness (mm) prior to and following each block, and Surgical pain (visual analogue scale). A 27-gauge long dental needle attached to a standard aspirating syringe was used for both the classical inferior alveolar nerve block and Gow-Gates mandibular nerve block techniques. Approximately 1.8 mL of anesthetic solution was deposited following the standard protocol for each technique. All injections and surgical procedures were performed by a single experienced oral surgeon with more than five years of clinical experience to minimize operator variability. The surgical removal of mandibular third molars was carried out

using a standardized surgical protocol, including mucoperiosteal flap elevation, bone removal, when necessary, tooth sectioning if required, and wound closure with sutures, ensuring consistency across all participants. Following administration of the anesthetic, the onset of anesthesia was assessed clinically by the presence of lip numbness and soft-tissue anesthesia. To control potential confounders, the same anesthetic agent, surgical protocol, operator, and assessment criteria were used for all participants. Patient confidentiality was maintained by assigning unique identification codes and storing data in password-protected files accessible only to the research team. After data collection, information was entered and analyzed using SPSS version 26.0. Continuous variables were expressed as mean $\pm$ standard deviation and compared using the independent-sample t-test, while categorical variables were analyzed using the Chi-square test. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Among the 160 patients whose gender was recorded in the dataset, the gender distribution where females outnumbered males: 87 women comprised 54.43 % of the sample, whereas 73 men accounted for 45.57 %. In the conventional IANB group 44 (55%) patients were female, while 36 (45%) were male, with a mean age of 35 ± 36.89 years, while the Gow-Gates group had a mean age of 35.37 ± 34.71 years, with 52 (65%) female patients and 28 (35%) male patients (Table 1).

Table 1: Distribution of Gender and Age

Techniques	Female (%)	Male (%)	Mean Age
IANB	44 (55%)	36 (45%)	34 ± 36.89
Gow-Gates	52 (65%)	28 (35%)	35.37 ± 34.71

Seventy patients (87.5%) and ten (12.5%) in each group attained complete anesthesia after receiving an Inferior Alveolar Nerve Block (IANB) and a Gow-Gates block, respectively. Direct comparison of the two methods yields the same overall success rate ($140/160=87.5\%$), and the corresponding p-value of 0.35 suggests that the difference is not statistically significant. To put it briefly, both the Gow-Gates method and the IANB are equally successful in achieving pulpal anesthesia (Table 2).

Table 2: Comparison of Success Rate between Two Groups

Success Status	Techniques	IANB (n=80)	Gow-Gates (n=80)	Total (n=160)	p-value
Successful	Inferior Alveolar Nerve Block	70 (87.5%)	70 (87.5%)	140 (87.5%)	0.350
	Gow-Gates	70 (87.5%)	70 (87.5%)	140 (87.5%)	
Un-successful	Inferior Alveolar Nerve Block	10 (12.5%)	10 (12.5%)	20 (12.5%)	
	Gow-Gates	10 (12.5%)	10 (12.5%)	20 (12.5%)	

It indicates that the average time of onset of Gow-Gates is 5.77 ± 1.28 minutes, and of IANB, it is 4.87 ± 1.34 minutes. The IANB group's mean time of action was significantly earlier than the GG group's (p-value of <0.002). (Table 2). Additionally, the IANB group employed a larger mean volume of local anesthetic to anaesthetize tissues than the GG group. The p-value for the independent samples t-test was 0.004.

Table 3: Comparison of Two Groups' Anesthesia Onset Times

Techniques	N	Onset Time Mean $\pm$ S.D (min)	p-value
Gow-Gates	80	5.77 ± 1.28	0.002
IANB	80	4.87 ± 1.34	0.002
Volume Mean $\pm$ S.D (ml)			
Gow-Gates	80	4.0 ± 3.49	0.004
IANB	80	4.3 ± 1.56	

The majority of patients, or 30 (37.5%) cases in the IANB group, experienced moderate pain during the administration of anaesthesia, whereas the majority of patients, or 50 (62.5%) cases in the GG group, experienced mild pain, which compares the intensity of pain during the administration of anaesthesia between the two groups. The chi-square test revealed a significant difference between the two groups (p-value=0.001) (Table 4).

Table 4: Pain Comparison of Two Groups during LA Administration

Pain Status	IANB (%)	Gow-Gates (%)	Total (%)	p-value
No pain	10 (12.5%)	12 (15%)	22 (13.75%)	0.001
Mild	20 (25%)	50 (62.5%)	70 (43.75%)	
Moderate	30 (37.5%)	13 (16.25%)	43 (26.9%)	
Severe	20 (25%)	5 (6.25%)	25 (15.6%)	
Total	80 (100%)	80 (100%)	160 (100%)	

DISCUSSION

A successful procedure in oral surgery specifically requires proper anesthetizing of the mandible, which can be achieved through a few injection methods. One of the most used methods is the Classical Inferior Alveolar Nerve block (IANB) [13]. This is one of the methods that was developed in the late 19th century and has served as a basis in oral surgery during the provision of anesthesia to the teeth in the mandible. Nevertheless, it is said to be associated with a greater rate of clinical errors, though this procedure is quite easy to conduct [14, 15]. The challenge posed by IANB is mainly the anatomical variability of the patients, besides the dense thickness of the cortical bone around the teeth in the mandible, which may render the block procedure less predictable [16, 17]. To eliminate the shortcomings of the approach, Gow-Gates proposed a more thorough method of blocking the mandibular nerve in 1973. This method is used when the needle is brought near the mandibular condyle, giving a wider and higher span of anesthesia in

several branches of the mandibular nerve [18, 19]. Gow-Gates has exhibited some usefulness since there have been increased success rates, lower proportions of positive aspiration, and good distribution of overall anesthetic [20]. It is, however, more technically demanding and may be more difficult to learn, especially for clinicians who have been using IANB. Other research conducted by Valenzuela et al. there was a shorter induction time using IANB, whereby the average period was 2.78 minutes as compared to 6.16 minutes by Gow-Gates [21]. This concurs with the findings of other research studies, such as Sarfaraz et al. which found that IANB had a higher onset speed [1]. The rapidity of onset of IANB can be attributed to the fact that the practitioner precisely placed the technique near the inferior alveolar nerve, which gives a quicker numbness. The two methods exhibited equal success rate in respect to quality of the anesthesia, as 87.5 percent of the patients in both cases experienced effective anesthesia. Although the amount of anesthetic used was equal between the two groups, other researchers, such as Saatchi et al. have proposed that a higher amount of the anesthetic may enhance the success rate and, in that regard, the Gow-Gates technique [22]. But this difference between the two techniques regarding the success rate was not significant in our study, which confirms the thought that both techniques work equally well when the required dose is administered [23]. The openness of the mouth showed one of the distinctions between the techniques, as the mouth opening was not measured accurately using one of the techniques. The Gow-Gates group developed a significant increase in mouth opening (0.5 mm), which was not noticed in the IANB group. This modest increase in mouth opening with the Gow-Gates technique can be explained by the fact that it covers all the anesthetic areas, as compared to the decrease in the number of muscles relaxed around the mandible [24]. In general, although the two methods have their merits, the preference of Gow-Gates and IANB can be based on the clinical condition, which should be comprised of patient anatomy and clinician experience. These two ways are both reliable forms of anesthesia, and Gow-Gates can induce a more consistent and broader block, especially in difficult cases [25].

The research had limitations that included a single-center design and a small sample, which can be used to indicate a limitation in the generalization of the research. Moreover, the operators might have been biased by the Gow-Gates technique experience. Further studies are necessary to involve more and more multi-centers and more populations, and also to conduct research to understand training protocols in order to enhance clinical acceptance and effectiveness of advanced mandibular nerve block methods.

CONCLUSIONS

In general, the study comes to the conclusion that both the IANB and Gow-Gates methods are safe and accurate when it comes to mandibular anesthesia, and neither one has a serious advantage over the other, actually. However, patients who received GG block reported much less discomfort when anesthesia was administered, and less LA solution was needed to produce a sufficient level of anesthesia. Consequently, GG can be regarded as a good substitute anesthetic approach for the widely utilized IANB technique in the extraction of mandibular molars.

Authors' Contribution

Conceptualization: MMK, MI

Methodology: MMK, TS

Formal analysis: MI, SSA

Writing and Drafting: TS, AS, SSA, FK

Review and Editing: MMK, MI, TS, AS, SSA, FK

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All 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] Sarfaraz I, Pascoal S, Macedo JP, Salgado A, Pereira J. Anesthetic Efficacy of Gow-Gates Versus Inferior Alveolar Nerve Block for Irreversible Pulpitis: A Systematic Quantitative Review. *Journal of Dental Anesthesia and Pain Medicine*. 2021 Jul; 21(4): 269. doi: 10.17245/jdamp.2021.21.4.269.
- [2] Pandey S, Yadav P, Roychoudhury A, Bhutia O, Goswami D. A Randomized Controlled Trial to Compare Functional, Combined Rigid and Functional, and Rigid Fixation in Double Mandibular Fractures. *Journal of Oral Biology and Craniofacial Research*. 2022 Mar; 12(2): 233-237. doi: 10.1016/j.jobcr.2022.02.003.
- [3] Calatayud J and Saraghi M. Local Anesthesia in Dentistry: A Locoregional Approach. John Wiley and Sons; 2024 Jan: 23. doi: 10.1002/9781394180189.
- [4] Kumar N and Shankar R. Evaluation of a Nishit-Rama Modification of a Gow-Gates Technique for Giving Mandibular Nerve Block: A Randomized Controlled Trial. *Journal of Maxillofacial and Oral Surgery*. 2023 Jun; 22(2): 359-364. doi: 10.1007/s12663-023-01901-y.
- [5] Rehman S, Channar KA, Memon W, Kumbhar AA, Bilgrami A, Javed F. Comparison Between Gow-Gates Mandibular Nerve Block Versus Inferior Alveolar Nerve Block in Extraction of Mandibular Third Molars: Gow-Gates Mandibular Nerve Block Versus Inferior Alveolar Nerve Block. *Pakistan Journal of Health Sciences*. 2024 Jul; 52-6: 1-5. doi: 10.54393/pjhs.v5i07.1621.
- [6] Chauhan N. Current Practices Used to Increase the Success Rate of The Inferior Alveolar Nerve Block in Mandibular Molars with Symptomatic Irreversible Pulpitis. West Virginia University. 2022: 1-15.
- [7] Naz S, Shah SA, Sattar R, Akbar N, Gul F. Anesthetic Effectiveness of Buccal Infiltration Alone Vs Combined Buccal and Palatal Infiltration on Symptomatic Maxillary Teeth. *Indus Journal of Bioscience Research*. 2025 Mar; 3(3): 215-220. doi: 10.70749/ijbr.v3i3.843.
- [8] NyoDu T, Saha N, Sil S, GhoSh S. Role of Age, Gender and Vertical Facial Type on Anatomical Location of Mandibular Foramen in Paediatric Population: A Cross-sectional Study. *Journal of Clinical & Diagnostic Research*. 2024 May; 18(5). doi: 10.7860/JCDR/2024/68925.19418.
- [9] Afridi RU, Shah SA, Khattak IU, Shah FA, Zain M, Ali F. Comparison of Anesthetic Efficacy of Conventional Inferior Alveolar Nerve Block and Gow Gates Technique in Patients with Symptomatic Irreversible Pulpitis Randomized Control Trail. *Journal of Khyber College of Dentistry*. 2019 Jun; 9(02): 58-64.
- [10] Dias-Junior LC, Bezerra AP, Schuldt DP, Kuntze MM, de Luca Canto G, da Fonseca Roberti Garcia L et al. Effectiveness of Different Anesthetic Methods for Mandibular Posterior Teeth with Symptomatic Irreversible Pulpitis: A Systematic Review and Meta-Analysis. *Clinical Oral Investigations*. 2021 Dec; 25(12): 6477-500. doi: 10.1007/s00784-021-04145-7.
- [11] Usama MM, Ashar A, Zafar KJ, Janjua OS, Khalid MU, Ghauri N. Comparison of Efficacy of Gow-Gates Mandibular Nerve Block Technique with Inferior Alveolar Nerve Block for Pain Management during Extraction of Mandibular Teeth. *Foundation University Journal of Dentistry*. 2022 Jan; 2(1): 64-70. doi: 10.33897/fujd.v2i1.277.
- [12] Nurjanah N, Herijulianti E, Putri MH, Sukmasari S. Eugenia Polyantha (Wight) Infusion Against Oral Microorganisms on Toothbrushes. *Scientific Dental Journal*. 2020 Sep; 4(3): 105-109. doi: 10.4103/SDJ.SDJ_38_20.
- [13] Thomas AM, Mangalath U, Abida R, Aslam S, Soman S, Nair RB. Comparative Evaluation of Classical Inferior Alveolar Nerve Block and Gow-Gates Nerve Block for Surgical Removal of Mandibular Third Molar: A Prospective Study. *Journal of Pharmacy and*

- Bioallied Sciences. 2021 Nov; 13(2): 1011-1014. doi: 10.4103/jpbs.jpbs_279_21.
- [14] Laham A, Clouet R, Del Valle GA, Gaudin A, Prud'homme T. Anaesthetic Efficacy and Influence on Cardiovascular Parameters Change of Intraosseous Computerised Anaesthesia Versus Inferior Alveolar Nerve Block Anaesthesia in Acute Irreversible Pulpitis of Mandibular Molars: Study Protocol for a Prospective Randomised Controlled Trial. *Trials*. 2022 Dec; 23(1): 979. doi: 10.1186/s13063-022-06915-4.
- [15] Sayahpour B, Nucci L, Eslami S, Talaeipour A, Ahmadi Ranani S, Mafi R et al. Three - Dimensional Evaluation of Mandibular Lingula: Comparisons of Skeletal Angle Classifications and Growth Patterns. *Orthodontics and Craniofacial Research*. 2024 Jun; 27(3): 494-503. doi: 10.1111/ocr.12757.
- [16] Karthikeyan T, Subramanian A, Narayanan V, Seetaram M. Does Peripheral Nerve Stimulator-Guided Extraoral Mandibular Nerve Block Provide Effective Anaesthesia for Third Molar Surgery: A Prospective Interventional Study. *Journal of Maxillofacial and Oral Surgery*. 2025 Feb; 24(1): 267-273. doi: 10.1007/s12663-024-02418-8.
- [17] Fauziya D, Anantanarayanan P, Shankar DP. Effectiveness and Distribution of Anesthesia for a Modified Extra Oral Maxillo-Mandibular Nerve Block for Dento-Alveolar Procedures: A Prospective Cohort Study. *Journal of Maxillofacial and Oral Surgery*. 2024 Jun; 23(3): 561-567. doi: 10.1007/s12663-022-01755-w.
- [18] Sonare S and Nikam P. Morphometric Analysis of the Human Mandibular Foramen and Its Implications in Inferior Alveolar Nerve Block. *European Journal of Cardiovascular Medicine*. 2025 May; 15(5).
- [19] Karamifar K, Shirali D, Saghiri MA, Abbott PV. Retromolar Canal Infiltration as a Supplement to the Inferior Alveolar Nerve Block Injection: An Uncontrolled Clinical Trial. *Clinical Oral Investigations*. 2021 Sep; 25(9): 5473-5478. doi: 10.1007/s00784-021-03855-2.
- [20] Jha AK. Evaluation of Mandibular Nerve Block: A Clinical Study. *International Journal of Oral Care and Research*. 2016; 4(1): 1-3. doi: 10.5005/jp-journals-10051-0001.
- [21] Valenzuela-Fuenzalida JJ, Cariseo C, Gold M, Díaz D, Orellana M, Iwanaga J. Anatomical Variations of the Mandibular Canal and their Clinical Implications in Dental Practice: A Literature Review. *Surgical and Radiologic Anatomy*. 2021 Aug; 43(8): 1259-1272. doi: 10.1007/s00276-021-02708-7.
- [22] Saatchi M, Shafiee M, Khademi A, Memarzadeh B. Anesthetic Efficacy of Gow-Gates Nerve Block, Inferior Alveolar Nerve Block, and their Combination in Mandibular Molars with Symptomatic Irreversible Pulpitis: A Prospective, Randomized Clinical Trial. *Journal of Endodontics*. 2018 Mar; 44(3): 384-388. doi: 10.1016/j.joen.2017.10.008.
- [23] Celikgun B and Derinsu U. Standardization of the Transient Evoked Otoacoustic Emissions Contralateral Suppression Test in Terms of Stimulus Intensity and Contralateral Noise Duration in Individuals with Normal Hearing. *Journal of the American Academy of Audiology*. 2022 Jan; 33(1): 29-35. doi: 10.1055/s-0041-1735523.
- [24] Noguchi T, Odaka K, Fukuda KI. Challenge of creating an inferior alveolar nerve block device that allows for safe, secure, and successful performance by any operator: Non-clinical studies on models. 2022 Oct: 1-11. doi: 10.21203/rs.3.rs-2141206/v1.
- [25] Chen Z and Li X. Measurement of mandibular anatomy associated with inferior alveolar nerve block anesthesia using 3D mandible models reconstructed by Cone Beam Computed. *Quintessence International*. 2025 Jan; 56(1).



Original Article



Frequency of Human Immunodeficiency Virus, Hepatitis B, and Hepatitis C Among Antenatal Women at a Tertiary Care Hospital

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ARTICLE INFO

Keywords:

Hepatitis B, Hepatitis C, Human Immunodeficiency virus, Antenatal Care

How to Cite:

Mallick, R., Baloch, F. N., Rashed, F., Nazir, N., Ismail, A., & Maryam, H. (2026). Frequency of Human Immunodeficiency Virus, Hepatitis B, and Hepatitis C Among Antenatal Women at a Tertiary Care Hospital: HIV, HBV, and HCV Prevalence in Antenatal Women. *Pakistan Journal of Health Sciences*, 7(6), 51-56. <https://doi.org/10.54393/pjhs.v7i6.3017>

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ABSTRACT

Human Immunodeficiency Virus (HIV), Hepatitis B (HBV), and Hepatitis C (HCV) are major blood-borne infections. In Pakistan, the prevalence of HCV is predicted to range from 8% to 15%, while the combined frequency of HBV and HCV affects 7.6% of the population. Prenatal HIV screening is recommended to prevent mother-to-child transmission. **Objectives:** This study aimed to determine the frequency of HIV, HBV, and HCV among antenatal patients at a tertiary healthcare facility. **Methods:** A descriptive cross-sectional study was carried out at the Civil Hospital Karachi Obstetrics and Gynecology unit 3 over 6 months, from October 7, 2022, to April 8, 2023. Pregnant women aged between 15-49 years, with a gestational age >20 weeks, presenting for routine antenatal care were enrolled using non probability consecutive sampling. All participants were screened for HIV, HBV, and HCV. Data were analyzed using SPSS version 25.0. **Results:** Among 187 women, the mean age was 32.29 ± 3.91 years, and the mean gestational age was 22.87 ± 1.34 weeks. The prevalence rates of HIV, HBV, and HCV were 13 (7%), 23 (12.3%), and 43 (23%), respectively. **Conclusions:** Among antenatal patients, the prevalence of HIV, HBV, and HCV was 13 (7%), 23 (12.3%), and 43 (23%), respectively. This underscores the need for regular screening during pregnancy. Regular screening during pregnancy is mandatory to prevent these infections from being transferred from the mother to the child.

INTRODUCTION

Infections caused by HIV, HBV, and HCV are major contributors leading to chronic viral infections, posing a significant public health burden worldwide. All share a common route of transmission by parenteral transmission [1-3]. Globally, around 248 million people are suffering from chronic HBV, while 150 million are affected by HCV, resulting in a mortality rate of 780,000 and 350,000 per year, for the first and second, respectively [1, 2]. These infections often coexist due to shared transmission routes, including parenteral, sexual, and perinatal, particularly among vulnerable populations [4]. HBV and HCV infections are most commonly found in territories of Asia and Africa, where healthcare services are limited, due to barriers

including economic, geographic, and social [2, 5]. Studies have shown a global variation rate in viral hepatitis endemicity, with sub-Saharan Africa (SSA) identified as a high-endemic region [6]. Recent information from Somalia also indicates a high antibody positivity rate of HBV, HCV, and HIV among expectant mothers presenting to tertiary care hospitals, highlighting the fact that these infections are a persistent burden in low-resource settings [7]. As per the WHO Global Health, about 36.9 million people are affected with HIV, with more than 50% of these cases affecting women, and this results in perinatal transmission being the predominant route for HIV infection in children, as around 1.8 million children [2, 3]. Recent antenatal



studies conducted in Pakistan show regional variation in viral hepatitis prevalence. For example, Qureshi et al. reported HBV prevalence of 5% and HCV prevalence of 2% among pregnant women in Multan, Pakistan, in 2025, while Ehsan et al. reported comparable findings among women attending a military hospital in Hyderabad in 2020 [8, 9]. Previous national estimates from Pakistan's 2008 hepatitis survey indicated that HBsAg has a prevalence of approximately 2.5% and anti-HCV has a prevalence of about 5%, contributing a substantial burden of chronic liver viral infections in the affected population [10, 11]. Coinfection of HBV and HCV during pregnancy may lead to severe maternal complications and increase the likelihood of transmission from mother to the newborn, potentially leading to hepatitis in fetuses and neonates [3]. Assessing the seroprevalence of HBsAg and anti-HCV antibodies universally during pregnancy is important because identifying infected women during antenatal care allows timely interventions to prevent perinatal transmission of these infections in case of Hepatitis B infections [12]. As recommended in the evidence-based management guidelines, universal screening for hepatitis B during pregnancy and active and passive immunization of the newborn after delivery, preferably within the first 24 hours of life, significantly reduce the chances of mother-to-child transmission [13]. Current HIV diagnostic testing algorithms begin with a sensitive antigen-antibody combination assay, such as an ELISA-based test for HIV-1/2, with positive results confirmed using more specific assays to ensure correct diagnosis [14]. Universal HIV screening is recommended during pregnancy to identify infected women early and initiate antiretroviral therapy, which along with appropriate obstetric management such as planned cesarean section if viral load is high or CD4 count is low and avoidance of breastfeeding, can reduce perinatal transmission rates from as high as 15–45% in the absence of intervention to less than 1% with effective treatment and preventive measures [15].

Existing research studies, both nationally and internationally, have explored the development of HIV, HBV, and HCV infections in expectant mothers, and seroprevalence varies widely depending on geographic location, population risk groups, and exposure types. Early detection during antenatal care is very important, as it can prevent mother-to-child transmission, which further increases the occurrence of these infections in a vicious circle. Hence, antenatal screening is a golden opportunity to identify these infections in a population that could serve as a reservoir for future transmissions. Therefore, this study aimed to assess the seroprevalence of HIV, HBV, and HCV among expectant mothers presenting to antenatal clinics for check-ups and to determine the frequency of these infections among antenatal patients at a tertiary

healthcare facility, to inform strategies for their prevention, screening, and management during pregnancy.

METHODS

This was a descriptive cross-sectional study and was initiated in the Department of Obstetrics and Gynecology, Unit 3, Civil Hospital Karachi, over six months, from October 7, 2022, to April 8, 2023. This study aimed to evaluate the proportion of individuals with hepatitis B, hepatitis C, and HIV infections in antenatal patients and to identify correlated risk factors. Pregnant females aged 15 to 49 years presenting with a gestational age of >20 weeks attending routine antenatal care were enrolled. Exclusion criteria included pregnant women unable to provide reliable data due to major disability or life-threatening illness, as well as patients with chronic liver disease or end-stage renal failure. The number of participants (187) was estimated using the WHO sample size calculator, with an estimated HBV prevalence of 8.5% based on previously reported seroprevalence among pregnant women in antenatal care settings, a margin of error of 4%, and a confidence level of 95%. Non-probability consecutive sampling was employed to select the study population [14]. Ethical approval was taken from the College of Physicians and Surgeons, Pakistan (CPSP Approval Letter No: CPSP/REU/OBG-2020-183-9946; dated October 7, 2022). Each participant provided informed consent before enrollment. Initial sociodemographic and medical information, including age, place of living, family monthly earnings, gestational age, parity, gravida, and associated risk factors (such as history of working in a healthcare institution, surgery, blood transfusion, tooth extraction, family history of HBV, HCV, or HIV, nose piercing, ear piercing, body tattooing, history of unsafe abortion, polygamous husband, and multiple sexual partners), were recorded. All participants were screened for HIV, HBV, and HCV infections in the central laboratory of Civil Hospital Karachi using standard, validated, commercially available kits. HIV screening was conducted using Abbott Determine and Immunocomplex II HIV 1&2, and reactive or indeterminate results were confirmed by indirect immunofluorescence (IIF) using kits supplied by the Oswaldo Cruz Foundation. HBV and HCV infections were identified using standard ELISA kits available in the hospital laboratory. Specific kit numbers were not recorded; however, all kits are routinely used for clinical diagnostics and are validated for hospital use.

Body mass index (BMI) was calculated using the formula to divide weight in kilograms by the square of height in meters (kg/m^2). Data analysis was performed using SPSS version 25.0. Quantitative variables were presented as mean and standard deviation or median and interquartile range,

based on the data's normality, which was assessed using the Shapiro-Wilk test. Qualitative variables were analyzed using frequency and percentage. Qualitative variables were analyzed using frequency and percentage. Participant characteristics and infection status were summarized using counts and percentages. No inferential statistical tests were performed, as the study was descriptive in nature.

RESULTS

Among the 187 women who participated in the study, the mean age was 32.29 ± 3.91 years. A total of 120 (64.2%) participants were aged 25–30 years, while 67 (35.8%) were between 31–40 years. The mean gestational age was 22.87 ± 1.34 weeks. Gestational age between 21+1 and 22+0 weeks was recorded in 117 (62.6%) women, whereas 70 (37.4%) were between 22+1 and 25+0 weeks. The average monthly family income was $65,417 \pm 10,115$ rupees; 108 (57.8%) participants reported an income between 52,000–65,000 rupees, and 79 (42.2%) reported 65,001–84,000 rupees. Urban residence was noted in 136 (72.7%) women, while 51 (27.3%) resided in rural areas. Illiteracy was observed in 56 (29.9%) participants. Regarding obstetric characteristics, 80 (42.8%) women were primiparous and 107 (57.2%) were multiparous (Table 1).

Table 1: Sociodemographic and Clinical Characteristics of Study Participants (n=187)

Variables	Category	n (%)
Age (Years)	25–30	120 (64.2%)
	31–40	67 (35.8%)
Gestational Age (Weeks)	21+1 – 22+0	117 (62.6%)
	22+1 – 25+0	70 (37.4%)
Family Income (PKR)	52,000 – 65,000	108 (57.8%)
	65,001 – 84,000	79 (42.2%)
Residence	Urban	136 (72.7%)
	Rural	51 (27.3%)
Education	Illiterate	56 (29.9%)
Parity	Primiparous	80 (42.8%)
	Multiparous	107 (57.2%)

Frequency of HIV was observed in 13 (7%), HBV in 23 (12.3%), and HCV in 43 (23%) women (Figure 1).

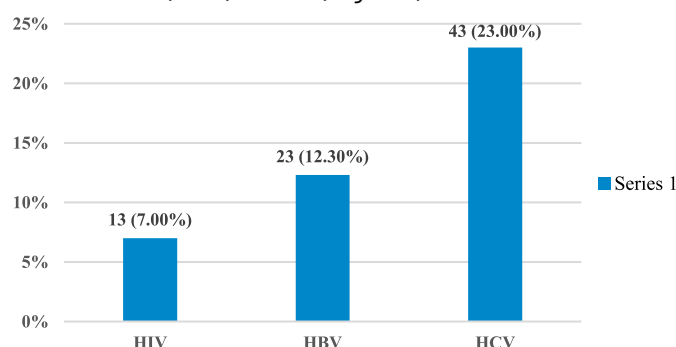


Figure 1: Prevalence of HIV, HBV, and HCV Among Antenatal

Patients (n=187). Values Represent Number of Cases and Corresponding Percentages

Among all participants, 27 (14.4%) reported a history of working in a healthcare institute, 43 (23%) had a history of surgery, 19 (10.2%) had received a blood transfusion, 22 (11.8%) had a history of tooth extraction, 19 (10.2%) reported a family history of viral infections, 14 (7.5%) had nose piercings, 15 (8%) had ear piercings, and 10 (5.3%) had body tattoos. The characteristics among women who tested positive for HIV (n=13), HBV (n=23), and HCV (n=43). Frequencies and percentages are presented for each factor, and no inferential statistical tests were performed, as the study is descriptive in nature (Table 2).

Table 2: Factors Related to HIV, Hepatitis B, and Hepatitis C Virus Infections (descriptive analysis only)

Variables	Total (n=187)	HIV Positive (n=13)	HBV Positive (n=23)	HCV Positive (n=43)
History of Working in a Healthcare Institute	27 (14.4%)	1 (7.7%)	9 (39.1%)	18 (41.9%)
History of Surgery	43 (23.0%)	5 (38.5%)	4 (17.4%)	18 (41.9%)
History of Blood Transfusion	19 (10.2%)	4 (30.8%)	9 (39.1%)	8 (18.6%)
History of Tooth Extraction	22 (11.8%)	2 (15.4%)	4 (17.4%)	0 (0%)
Family History of HIV, HBV, or HCV	19 (10.2%)	2 (15.4%)	0 (0%)	0 (0%)
Nose Piercing	14 (7.5%)	5 (38.5%)	5 (21.7%)	1 (2.3%)
Ear Piercing	15 (8.0%)	4 (30.8%)	4 (17.4%)	3 (7.0%)
Body Tattooing	10 (5.3%)	0 (0%)	3 (13.0%)	3 (7.0%)
History of Unsafe Abortion	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Polygamous Husband	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Multiple Sex Partners	0 (0%)	0 (0%)	0 (0%)	0 (0%)

DISCUSSION

The findings of this study focus on the occurrence and associated determinants for HIV, HBV, and HCV infection among antenatal clients presenting for routine checkups at a tertiary care hospital at their booking appointment. This highlights the importance of including thorough checks for these risk factors in routine antenatal care by the healthcare providers, allowing for early detection and appropriate interventional strategies to prevent mother-to-child transmission rates. Of 13 HIV positive cases, a history of working in a healthcare institute was observed in 7.7% women, a history of surgery in 38.5%, a previous blood transfusion history in 30.8%, a previous tooth extraction history in 15.4%, a family history 15.4%, nose piercing 38.5%, and ear piercing 30.8% women. Of 23 HBV positive cases, a history of working in a healthcare institute was observed in 39.1% women, a history of surgery in 17.4%, a history of blood transfusion in 39.1%, a history of tooth extraction in 17.4%, nose piercing 21.7%, ear piercing 17.4%, and body tattooing 13% women. Of 43 HCV positive cases, a history of working in a healthcare institute was observed in 41.9% women, a history of surgery in 41.9%, a

history of blood transfusion in 18.6%, nose piercing 2.3%, ear piercing 7%, and body tattooing 7% women. A study by Roble et al. found that 8.5% of expectant women seeking antenatal care in Jigjiga, Ethiopia, tested positive for HBsAg [16]. Significant contributing factors for HBV infection included a history of surgery (AOR=3.41, 95% CI: 1.26–9.24), history of HBV infection in the family (AOR=4.96, 95% CI: 2.11–10.60), sharing sharp objects (AOR=2.78, 95% CI: 1.13–6.83), and engagement in multiple sexual encounters (AOR=6.12, 95% CI: 2.12–17.64). A study conducted in Enugu, Nigeria, reported that 12.4% of antenatal clients were seropositive for HIV, 3.4% for hepatitis B virus (HBV), 2.6% for hepatitis C virus (HCV), and 0.08% for syphilis. The co-infection rates were 0.24% for HIV/HBV and 0.16% for HIV/HCV. This study observed no cases of concurrent infection with both hepatitis B and C viruses within the HIV-positive and HIV-negative antenatal population [17]. Studies from Sub-Saharan Africa show that HIV and hepatitis infections remain a significant concern among pregnant women. In Luanda, Angola, HIV and HBV were found to be common, with rates influenced by social and obstetric factors [18]. In Yirgalem Hospital, Ethiopia, HBV prevalence was linked to surgery, family history, and exposure to sharp objects [19]. Similarly, research conducted in Zambia shows varying HIV rates among young women, reflecting differences in behavior, socio-economic status, and healthcare access as important determinants [20]. These observations highlight the importance of universal antenatal screening and careful risk management to prevent infections in both mothers and babies. One of the studies showed that the occurrence of anti-HIV antibodies was found to be 13.4%, which is comparable to findings from studies conducted in Ethiopia (10.1%), Zambia (11.3%), and the Democratic Republic of Congo (11%) [21]. However, these numbers are higher than those reported in the research conducted in Nigeria (6.1%) and Cameroon (5.1%) [22, 23]. In Tanzania, the prevalence ranged between 5.1% and 5.6% among expectant women [24, 25]. In Latin America, HIV prevalence among expectant mothers is generally below 1% in countries such as Brazil, while in several Caribbean countries, including the Dominican Republic, HIV prevalence among pregnant women has been reported to reach or exceed 2%, reflecting regional differences in epidemic dynamics [26, 27]. In India, earlier reports indicated antenatal HIV prevalence around 0.88% in specific regions, while more recent hospital-based surveillance from western India reported a prevalence of 0.22% among expectant mothers, reflecting declining trends in HIV among antenatal populations [28]. A study reported that infectious diseases such as HIV, HBV, and syphilis are a societal health burden among expectant

mothers, which highlights the need to strengthen biomedical interventions. Understanding the demographic and behavioral factors that contribute to the emergence of infectious agents is essential for reducing planning costs, controlling the spread of infectious diseases, preventing vertical transmission, and mitigating negative outcomes in neonates [2]. A recent systematic review and meta-analysis reported the worldwide pooled prevalence of HIV, HBV, HCV, and syphilis among expectant mothers to be 2.9% (95% CI: 2.4–3.4%), 4.8% (95% CI: 3.8–5.8%), 1.0% (95% CI: 0.8–1.3%), and 0.8% (95% CI: 0.7–0.9%), respectively. In financially constrained nations, the combined prevalence of these infections exceeds the global average, with HIV at 5.2% (1.6–10.5%), HBV at 6.6% (5.4–7.9%), HCV at 2.7% (1.6–4.1%), and syphilis at 3.3% (2.2–4.6%). In lower-middle-income countries, the pooled prevalence rates exceed global averages, with HIV at 2.9% (0.8–6.1%), HBV at 4.9% (3.8–6.1%), HCV at 2.3% (1.2–3.6%), and syphilis at 1.5% (1.0–2.2%). The author asserts that the frequency of these infections is significantly higher among pregnant women in resource-limited environments. Assessing the applicability and practicality of existing global guidelines for preventing perinatal transmission of these infections in countries with lower-middle-income status is crucial. This evaluation should include an assessment of timely access to both screening and therapeutic interventions. Another systematic review and meta-analysis reported that, among maternal-neonatal pairs with single infection, the combined perinatal infection transfer rates were 2.74% for HIV and 55.49% for hepatitis B virus, respectively. There is no available information on the perinatal transfer rate of the hepatitis C virus in cases of single infection, nor on the transmission rates of HIV, hepatitis B virus, and hepatitis C virus among maternal-neonatal pairs with double or triple infections [29].

Certain limitations should be considered when interpreting the results of this study. The comparatively small sample size of 187 women may limit the generalizability of the conclusion. Additionally, given that this study was conducted at a single center, the results may not fully reflect the broader population trends. The cross-sectional design allows a snapshot, but a more comprehensive understanding is needed through longitudinal studies, exploring trends in infections and associated factors over the course of pregnancy. Despite these limitations, one of the strengths of this research is its relevance to maternal healthcare practices and the prevention of mother-to-child transmission rates. The identified risk factors provide insights for healthcare practitioners, highlighting the importance of action points, including counseling and interventions. Furthermore, research in the future could be

strengthened by including larger and more diverse samples, encompassing various socio-economic backgrounds and geographical locations, to give more generalized results. Longitudinal studies can provide a dynamic perspective on infection trends during pregnancy, while interventional studies can be conducted to evaluate the effectiveness of preventive measures in reducing transmission rates. While this study contributes valuable insights, ongoing research should be carried out for a more comprehensive understanding and the development of evidence-based strategies in maternal healthcare.

CONCLUSIONS

The frequency of HIV was observed in 7%, HBV in 12.3%, and HCV in 23% women. The history of nose piercing, ear piercing, blood transfusion, and body tattooing was observed among women with these infections.

Authors' Contribution

Conceptualization: RM

Methodology: FR, HM

Formal analysis: FNB, NN, AI

Writing and Drafting: FNB

Review and Editing: RM, FNB, FR, NN, AI, HM

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All 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] Dagnew M, Million Y, Gizachew M, Eshetie S, Yitayew G, Asrade L et al. Hepatitis B and C Virus Infection and Associated Factors Among Pregnant Women Attending Antenatal Care in Hospitals in the Amhara National Regional State, Ethiopia. *International Journal of Microbiology*. 2020; 2020: 8848561. doi: 10.1155/2020/8848561.
- [2] Wu S, Wang J, Guo Q, Lan H, Sun Y, Ren M et al. Prevalence of Human Immunodeficiency Virus, Syphilis, and Hepatitis B and C Virus Infections in Pregnant Women: A Systematic Review and Meta-Analysis. *Clinical Microbiology and Infection*. 2023; 29(8): 1000-1007. doi: 10.1016/j.cmi.2023.03.002.
- [3] Beard N and Hill A. Combined "Test and Treat" Campaigns for Human Immunodeficiency Virus, Hepatitis B, and Hepatitis C: A Systematic Review to Provide Evidence to Support World Health Organization Treatment Guidelines. *Open Forum Infectious Diseases*. 2024; 11(2):. 666. doi: 10.1093/ofid/ofad666
- [4] Arbune M, Iancu AV, Padurariu-Covit MD, Plesea-Condratovici A, Arbune AA, Plesea-Condratovici C. Triple Burden of HIV, HBV, and HDV in Adults with Childhood Parenterally Acquired Infections: A Romanian Single-Center Study. *Pathogens*. 2025; 14(12): 1261. doi: 10.3390/pathogens14121261.
- [5] World Health Organization. *Global Hepatitis Report 2024: Action for Access in Low- And Middle-Income Countries*. Geneva: WHO; 2024.
- [6] Sticher JS, Csermak KR, Otsyula N, Turkson M, Aubrun E, Oshagbemi OA. Prevalence of Viral Hepatitis in Sub-Saharan Africa Among the General Population: An Umbrella Review of Systematic Reviews and Meta-Analyses. *British Medical Journal Open*. 2025; 15(9) :101029. doi: 10.1136/bmjopen-2025-101029.
- [7] Hassan-Kadle MA, Keles E, Nor MA, Hassan MA, Karaketir S, Hussein AI et al. Seroprevalence of Hepatitis B, Hepatitis C, and HIV in Pregnant Women Attending a Tertiary Care Hospital in Mogadishu, Somalia, 2017-2021. *BioMed Central Infectious Diseases*. 2025; 25(1): 885. doi: 10.1186/s12879-025-11268-9.
- [8] Qureshi HZ, Khan B, Iftikhar A, Imran H, Iqbal MA. Prevalence and Risk Factors of Hepatitis B and C in Pregnant Women at Bakhtawar Amin Trust Hospital, Multan, Pakistan. *Life Science*. 2025; 6(3): 387-393. doi: 10.37185/LnS.1.1.569.
- [9] Ehsan A, Robert H, Nabi I, Abbas M. Prevalence of Hepatitis B and C in Female Population Reporting for Antenatal Screening at Combined Military Hospital, Hyderabad, Sindh, Pakistan. *Pakistan Armed Forces Medical Journal*. 2020; 70(2): 385-389.
- [10] World Health Organization. Prevalence of hepatitis and HIV in Pakistan. *East Mediterr Health Journal*. 2024; 30(10). doi: 10.26719/2024.30.10.689.
- [11] Tanveer Z, Ahmad I, Javed MS, Malik SA, Kakar NH, Ahmad M et al. Screening for Hepatitis B and C Viral Infections Among Pregnant Women Attending Bolan Medical Complex Hospital and Sandeman Provincial Civil Hospital, Quetta, Pakistan. *The Professional Medical Journal*. 2020; 27(7): 1328-1334. doi: 10.29309/TPMJ/2020.27.08.3129.
- [12] Rios J, Alpert L, Mehra S, Schmidt N, Kushner T. Overview of Hepatitis C in Pregnancy: Screening, Management, and Treatment. *Journal of the Pediatric Infectious Diseases Society*. 2024; 13(5): 171-178. doi: 10.1093/jpids/piae070.
- [13] Society for Maternal-Fetal Medicine. SMFM consult series #69: Hepatitis B in Pregnancy: Updated Guidelines. *American Journal of Obstetrics and*

- Gynecology. 2024; 230(4): 2–11. doi: 10.1016/j.ajog.2023.12.023.
- [14] Duncan D, Duncan J, Kramer B, Nilsson AY, Haile B, Butcher A et al. An HIV Diagnostic Testing Algorithm Using the Cobas HIV-1/HIV-2 Qualitative Assay for HIV Type Differentiation and Confirmation. *Journal of Clinical Microbiology*. 2021; 59(7): 0303020. doi: 10.1128/JCM.03030-20.
- [15] Fleşeriu T, Meliţ LE, Mărginean CO, Pop AV, Văsieşiu AM. Maternal HIV Infection and Antiretroviral Therapy in Pregnancy: Implications for Vertical Transmission and Outcomes. *Pathogens*. 2025; 14(8): 818. doi: 10.3390/pathogens14080818.
- [16] Roble AK, Roba KT, Mengistie B, Abdurke Kure M. Seroprevalence of Hepatitis B Virus and Associated Factors Among Pregnant Women Attending Antenatal Care in Public Health Facilities in Jigjiga Town, Eastern Ethiopia. *International Journal of Women's Health*. 2021; 12: 1299–1310. doi: 10.2147/IJWH.S276526.
- [17] Ikeako L, Ezegwui H, Ajah L, Dim C, Okeke T. Seroprevalence of Human Immunodeficiency Virus, Hepatitis B, Hepatitis C, Syphilis, and Co-Infections Among Antenatal Women in a Tertiary Institution in South East, Nigeria. *Annals of Medical and Health Sciences Research*. 2014; 4(6): 954–958. doi: 10.4103/2141-9248.144925.
- [18] Vueba AN, Almendra R, Santana P, Faria C, do Céu Sousa M. Prevalence of HIV and Hepatitis B Virus Among Pregnant Women in Luanda (Angola): Geospatial Distribution and Association with Socio-Demographic and Clinical-Obstetric Determinants. *Virology Journal*. 2021; 18(1): 1–9. doi: 10.1186/s12985-021-01698-7.
- [19] Amsalu A, Ferede G, Eshetie S, Tadewos A, Assegu D. Prevalence, Infectivity, and Associated Risk Factors of Hepatitis B Virus Among Pregnant Women in Yirgalem Hospital, Ethiopia: Implication of Screening to Control Mother-To-Child Transmission. *Journal of Pregnancy*. 2018: 8435910. doi: 10.1155/2018/8435910.
- [20] Nakazwe C, Michelo C, Sandøy IF, Fylkesnes K. Contrasting HIV Prevalence Trends Among Young Women and Men in Zambia in the Past 12 Years: Data from Demographic and Health Surveys 2002–2014. *BioMed Central Infectious Diseases*. 2019; 19(1): 432. doi: 10.1186/s12879-019-4059-3.
- [21] Pour M, James L, Singh K, Mampunza S, Baer F, Scott J et al. Increased HIV in Greater Kinshasa Urban Health Zones, Democratic Republic of Congo (2017–2018). *AIDS Research and Therapy*. 2020; 17(1): 67. doi: /10.1186/s12981-020-00322-y.
- [22] Gbadamosi SO, Itanyi IU, Menson WNA, Olawepo JO, Bruno T, Ogidi AG et al. Targeted HIV Testing for Male Partners of HIV-Positive Pregnant Women in a High Prevalence Setting in Nigeria. *PLoS One*. 2019; 14(1): 211022. doi: 10.1371/journal.pone.0211022.
- [23] Dionne-Odom J, Tita ATN, Silverman NS. Hepatitis B in Pregnancy: Screening, Treatment, and Prevention of Vertical Transmission. *American Journal of Obstetrics and Gynecology*. 2016; 214(1): 6–14. doi: 10.1016/j.ajog.2015.09.100.
- [24] Mboya E, Mizinduko M, Balandya B, Mushi J, Sabasaba A, Amani DE et al. HIV Burden and Global Fast-Track Targets Progress Among Pregnant Women in Tanzania: Analysis Of 2020 Antenatal Clinics HIV Sentinel Site Surveillance. *PLoS One*. 2023; 18(10): 285962. doi: 10.1371/journal.pone.0285962.
- [25] Njau AF, Robert M, Rwebembera A, Kisendi R, Maro C, Dennis G et al. Prevalence and Associated Factors for HIV, HBV, and Syphilis Co-Infections Among Pregnant Women Attending Antenatal Care in Tanzania. *PLoS One*. 2025; 20(8): 329068. doi: 10.1371/journal.pone.0329068.
- [26] Pereira GF, Sabidó M, Caruso A, Oliveira SB, Mesquita F, Benzaken AS. HIV Prevalence Among Pregnant Women in Brazil: A National Survey. *Revista Brasileira de Ginecologia e Obstetrícia*. 2016; 38(8): 391–398. doi: 10.1055/s-0036-1592102.
- [27] UNFPA Caribbean. HIV and AIDS Overview for the Caribbean region. UNFPA; 2025.
- [28] Karena ZV, Padaliya D, Viradia DS. Trend of HIV Prevalence in Antenatal Women in a Tertiary Care Hospital in the Western Region of India. *Cureus*. 2024; 16(3): 57125. doi: 10.7759/cureus.57125.
- [29] Eleje GU, Onubogu CU, Fiebai PO, Mbachu II, Akaba GO, Loto OM et al. Mother-to-Child Transmission of HIV, Hepatitis B, and Hepatitis C Among Pregnant Women with Single, Dual, or Triplex Infections in Nigeria: A Systematic Review and Meta-Analysis. *SAGE Open Medicine*. 2022; 10. doi: 10.1177/20503121221095411.



Original Article



Frequency and Types of Seizures among Patients Presenting with Stroke

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ARTICLE INFO

Keywords:

Stroke, Post-Stroke Seizures, Early Seizures, Late Seizures, Epilepsy, CT Brain

How to Cite:

Jamil, S., Khan, Z. U., Khan, S., Ullah, A., Khan, S. F., & Khan, J. (2026). Frequency and Types of Seizures among Patients Presenting with Stroke: Seizure Frequency and Types in Stroke Patients. *Pakistan Journal of Health Sciences*, 7(6), 57-62. <https://doi.org/10.54393/pjhs.v7i6.3878>

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Received Date: 21st January, 2026

1st Revision Received: 4th March, 2026

Acceptance Date: 16th March, 2026

Published Date: 30th June, 2026

ABSTRACT

Stroke is a leading cause of death and disability worldwide, particularly in low- and middle-income countries. Post-stroke seizures represent an important neurological complication that may occur early or late after the event. However, limited data are available regarding their frequency and characteristics in the local population. **Objective:** To determine the frequency and types of seizures among patients presenting with stroke. **Methods:** This analytical cross-sectional study was conducted in the Department of Emergency Medicine, Lady Reading Hospital, Peshawar, over six months from May 2023 to November 2023. A total of 177 patients aged 20–80 years with radiologically confirmed stroke were enrolled using non-probability consecutive sampling. Patients with prior epilepsy or metabolic derangements known to precipitate seizures were excluded. Post-stroke seizures were classified as early (≤ 14 days) or late (> 14 days to 3 months). Data were analyzed using SPSS version 26.0. Frequencies, percentages, chi-square tests, and logistic regression were applied, with $p < 0.05$ considered statistically significant. **Results:** The mean age was 49.7 ± 18.1 years, and 61.0% were male. Ischemic stroke occurred in 73.4% of patients. Post-stroke seizures were observed in 14.1% ($n=25$). Among these, 48.0% were early, and 52.0% were late seizures. No statistically significant associations were found between seizures and stroke subtype ($p=0.197$), gender ($p=0.150$), or age category ($p=0.320$). **Conclusions:** Post-stroke seizures occurred in 14.1% of patients, with nearly equal early and late distribution. Structured surveillance during acute and subacute phases is warranted.

INTRODUCTION

Stroke is a major cause of both death and disability worldwide and represents a significant public health burden, particularly in low- and middle-income countries (LMICs) [1]. Approximately 16 million first-ever strokes occur annually, resulting in nearly 5.7 million deaths globally. The burden of stroke is disproportionately higher in LMICs, where limited access to early diagnosis, acute stroke care, and rehabilitation services contributes to increased morbidity and mortality. In Pakistan, the prevalence of stroke has been reported to be approximately 6.4%, underscoring its substantial impact on the national healthcare system [2, 3]. Stroke is associated with numerous systemic and neurological complications, including aspiration pneumonia, dehydration, urinary tract infections, deep vein

thrombosis, and pulmonary embolism [4]. Among neurological complications, epileptic seizures represent an important yet often under-recognized consequence. Post-stroke seizures may occur in the acute phase or during the chronic recovery period, reflecting distinct underlying pathophysiological mechanisms [5, 6]. Early post-stroke seizures are generally attributed to acute neuronal injury resulting from cerebral ischemia or hemorrhage. Mechanisms include excitotoxic glutamate release, disruption of ionic homeostasis, blood-brain barrier breakdown, cytotoxic edema, and acute inflammatory responses leading to transient cortical hyperexcitability. In contrast, late post-stroke seizures are believed to arise from chronic structural and functional alterations such as gliosis, synaptic reorganization,



cortical remodeling, and the formation of permanent epileptogenic foci following neuronal injury [7, 8]. Thus, early seizures are typically considered acute symptomatic events, whereas late seizures may reflect the development of post-stroke epilepsy due to long-term cortical reorganization. Stroke is recognized as one of the leading causes of newly acquired seizures in older adults. Large cohort studies report that approximately 10–20% of stroke survivors experience seizures, including both early and delayed manifestations [5, 9]. However, reported prevalence varies widely across regions, with higher variability observed in LMICs due to delayed presentation, limited neuroimaging access, underutilization of electroencephalography (EEG), and suboptimal follow-up systems. In countries such as Pakistan, where healthcare resources may be constrained, post-stroke seizures may be underdiagnosed or inadequately documented, potentially leading to delayed treatment and worse neurological outcomes.

Despite the recognized clinical importance of post-stroke seizures, there is limited published data from Pakistan regarding their frequency, temporal distribution, and association with demographic and clinical variables. Most available evidence originates from high-income settings with advanced neurodiagnostic facilities, limiting generalizability to local populations. The absence of region-specific epidemiological data restricts the development of context-appropriate surveillance strategies and management protocols. Therefore, the present study was conducted to determine the frequency and temporal distribution (early versus late) of post-stroke seizures among patients presenting with radiologically confirmed stroke at a tertiary-care hospital in Peshawar. Additionally, the study aimed to evaluate the association between post-stroke seizures and selected demographic and clinical variables.

METHODS

This analytical cross-sectional study was conducted in the Department of Emergency Medicine at Medical Teaching Institution (MTI), Lady Reading Hospital (LRH), Peshawar, a tertiary-care referral center serving the population of Khyber Pakhtunkhwa. The study was conducted over 6 months, from May 2023 to November 2023. Ethical approval was obtained from the Institutional Review Board of Lady Reading Hospital (Ref No: 764/LRH/MTI; dated 25th May, 2023). The study was conducted in accordance with the Declaration of Helsinki, and written informed consent was obtained from all participants or their legal guardians before enrollment. The sample size was calculated using the WHO sample size calculator to estimate a single population proportion. A previously reported prevalence of 8% early post-stroke seizures was used as the expected

frequency [10]. With a 95% confidence interval and a margin of error of 4%, the minimum required sample size was calculated to be 177 patients. A non-probability consecutive sampling technique was employed, whereby all eligible patients presenting during the study period were enrolled until the required sample size was achieved. Patients aged between 20 and 80 years of either gender presenting with clinical features suggestive of acute stroke were eligible for inclusion, provided that the diagnosis was confirmed radiologically by computed tomography (CT) scan of the brain. Stroke was operationally defined as the sudden onset of focal or global neurological deficit persisting for more than 24 hours due to a vascular cause. Ischemic stroke was identified by the presence of hypodense lesions or normal early CT findings consistent with ischemia, whereas hemorrhagic stroke was diagnosed based on hyperdense intracranial lesions on CT imaging. To minimize confounding bias and ensure that seizure events were attributable to stroke rather than metabolic abnormalities, patients with a prior history of epilepsy were excluded. In addition, patients with metabolic derangements known to precipitate seizures, including hypoglycemia (fasting blood glucose <80 mg/dL or random blood glucose <120 mg/dL), hyponatremia (serum sodium <135 mmol/L), hypocalcemia (serum calcium <9 mg/dL), and uremia (serum urea >50 mg/dL), were excluded from the study. Post-stroke seizures were defined clinically as transient episodes of abnormal motor activity, altered consciousness, sensory disturbance, or autonomic manifestations suggestive of abnormal cortical electrical activity, as determined by clinical history and neurological examination. Seizures were temporally classified into early and late categories. Early seizures were defined as those occurring within 14 days (≤ 2 weeks) of stroke onset, whereas late seizures were defined as those occurring after 14 days and up to three months following the stroke [11]. These temporal definitions were based on contemporary neurological literature and established clinical classifications of post-stroke seizures. All enrolled patients received standard institutional stroke management and were admitted for stabilization and treatment as per hospital protocol. Following discharge, patients were followed for a total duration of three months to identify seizure occurrence. Follow-up was conducted through scheduled outpatient department visits as well as weekly telephonic contact to ensure systematic monitoring. Any reported seizure episode was documented in a structured proforma, and the timing (early versus late) and clinical characteristics of the seizure were recorded. All clinical assessments and follow-up evaluations were supervised by a consultant physician with a minimum of five years of clinical experience. Demographic data, clinical findings, laboratory

investigations, imaging results, and seizure characteristics were recorded using a pre-designed structured data collection form. CT brain scans were reviewed by qualified radiologists for confirmation of stroke subtype. Detailed imaging parameters such as lesion size, cortical versus subcortical involvement, and stroke severity scores were not consistently available in emergency records and, therefore, were not included in the analysis.

Data were entered and analyzed using the Statistical Package for Social Sciences (SPSS) version 26.0. Continuous variables were summarized as mean $\pm$ standard deviation, while categorical variables were presented as frequencies and percentages. Associations between post-stroke seizures and categorical variables such as gender, age category, and stroke subtype were assessed using the Chi-square test, and Fisher's exact test was applied where appropriate. Effect size was evaluated using Cramer's V to assess the strength of associations. To adjust for potential confounding variables, binary logistic regression analysis was performed, including age (continuous), gender, and stroke subtype. Odds ratios with 95% confidence intervals were calculated. A p-value of less than 0.05 was considered statistically significant. The study was powered to estimate the frequency of post-stroke seizures rather than detect subgroup differences; therefore, multivariable analysis was interpreted cautiously due to the limited number of seizure events.

RESULTS

A total of 177 patients with radiologically confirmed stroke were included in the study. The demographic characteristics are presented in Table 1. The mean age was 49.7 ± 18.1 years (range 20–80 years). The majority of patients belonged to the 40–59 years age group (35.0%), followed by 60–80 years (33.3%) and 20–39 years (31.6%). Males constituted 61.0% of the study population (Table 1).

Table 1: Demographic Characteristics of Stroke Patients (n=177)

Variables	n (%)
Age (Years)	
Mean $\pm$ SD	49.7 $\pm$ 18.1
Minimum–Maximum	20–80
Age Category	
20–39 years	56 (31.6%)
40–59 years	62 (35.0%)
60–80 years	59 (33.3%)
Gender	
Male	108 (61.0%)
Female	69 (39.0%)

The distribution of stroke subtype and CT findings is shown in Table 2. Ischemic stroke was observed in 73.4% of patients, while 26.6% had hemorrhagic stroke. CT brain

findings corresponded with stroke subtype (Table 2).

Table 2: Stroke Characteristics of Patients (n=177)

Variables	n (%)
Type of Stroke	
Ischemic	130 (73.4%)
Hemorrhagic	47 (26.6%)
CT Brain Finding	
Hypodense lesion	130 (73.4%)
Hyperdense lesion	47 (26.6%)

The overall frequency of post-stroke seizures was 14.1% (n=25) among the studied patients (Table 3).

Table 3: Frequency of Post-Stroke Seizures (n=177)

Post-Stroke Seizures	n (%)
Yes	25 (14.1%)
No	152 (85.9%)
Total	177 (100.0%)

Among patients who developed seizures, 48.0% experienced early seizures (≤ 14 days), while 52.0% had late seizures (> 14 days to 3 months) (Table 4).

Table 4: Types of Post-Stroke Seizures (n=25)

Types of Seizure	n (%)
Early seizures	12 (48.0%)
Late seizures	13 (52.0%)
Total	25 (100.0%)

No statistically significant association was observed between seizures and gender ($\chi^2=2.074$, $p=0.150$; Fisher's exact $p=0.185$). The effect size was small (Cramer's $V=0.108$). Females demonstrated a higher seizure proportion (18.8%) compared to males (11.1%), but the difference was not statistically significant (OR=0.538, 95% CI: 0.230–1.261). Similarly, no significant association was observed between seizure occurrence and age category ($\chi^2=2.281$, $p=0.320$). The effect size was small (Cramer's $V=0.114$), indicating minimal practical association. Stroke subtype was not significantly associated with seizure development ($p=0.197$) (Table 5).

Table 5: Association of Post-Stroke Seizures with Demographic and Clinical Variables (n=177)

Variables	Categories	Seizures Yes, n (%)	Seizures No, n (%)	Total, (n)	χ^2 (df)	p-value
Type of Stroke	Ischemic	21 (16.2%)	109 (83.8%)	130	1.66 (1)	0.197
	Hemorrhagic	4 (8.5%)	43 (91.5%)	47		
Gender	Male	12 (11.1%)	96 (88.9%)	108	2.07 (1)	0.150
	Female	13 (18.8%)	56 (81.2%)	69		
Age Category	20–39 years	7 (12.5%)	49 (87.5%)	56	2.28 (2)	0.320
	40–59 years	12 (19.4%)	50 (80.6%)	62		
	60–80 years	6 (10.2%)	53 (89.8%)	59		
Total		25 (14.1%)	152 (85.9%)	177	—	

To adjust for potential confounding, binary logistic

regression was performed, including age (continuous), gender, and stroke subtype. The overall model was not statistically significant ($\chi^2=4.329$, $df=3$, $p=0.228$), explaining 4.3% of the variance (Nagelkerke $R^2=0.043$). Age was not independently associated with post-stroke seizures (OR = 1.005, 95% CI: 0.981-1.030, $p=0.672$). The female gender showed higher odds compared to males (OR=2.021, 95% CI: 0.843-4.841, $p=0.115$), although this did not reach statistical significance. Hemorrhagic stroke demonstrated lower odds compared to ischemic stroke (OR=0.453, 95% CI: 0.146-1.411, $p=0.172$) (Table 6).

Table 6: Binary Logistic Regression Analysis for Predictors of Post-Stroke Seizures

Variables	OR	95% CI	p-value
Age	1.005	0.981-1.030	0.672
Female Gender	2.021	0.843-4.841	0.115
Hemorrhagic Stroke	0.453	0.146-1.411	0.172

DISCUSSION

Current study determined the frequency and temporal pattern of post-stroke seizures in patients presenting with radiologically confirmed stroke at a tertiary-care hospital in Peshawar. Post-stroke seizures were observed in 14.1% of patients, a finding that falls within the globally reported range of 10-20%. This consistency supports the external validity of our findings and suggests that the burden of post-stroke seizures in our setting is comparable to international data. Misra *et al.* reported a similar prevalence of seizures after stroke and highlighted their association with poorer functional outcomes and increased mortality [11]. Likewise, Freiman *et al.* documented post-stroke seizures in approximately 15% of stroke survivors in a hospital-based cohort [12]. These comparisons reinforce that post-stroke seizures remain a clinically significant neurological complication across diverse populations. Regarding temporal distribution, late seizures (52.0%) were slightly more frequent than early seizures (48.0%). The nearly equal distribution between early and late events is clinically important, as it reflects the dual-phase pathophysiology of seizure development following stroke. Early seizures are primarily attributed to acute biochemical disturbances, excitotoxic neurotransmitter release, and transient cortical hyperexcitability, whereas late seizures are associated with chronic structural remodeling, gliosis, synaptic reorganization, and formation of epileptogenic foci. Tanaka *et al.* emphasized that late post-stroke seizures are often markers of long-term cortical reorganization and may predict the development of post-stroke epilepsy [13]. Similarly, Ryu *et al.* reported that delayed seizures frequently reflect irreversible neuronal network alterations [14]. Current findings therefore support the need for continued surveillance beyond the

acute hospitalization period, as seizure risk persists during the subacute recovery phase. In our cohort, seizures were more frequent in ischemic stroke (16.2%) compared to hemorrhagic stroke (8.5%), although the difference did not reach statistical significance ($p=0.197$). This lack of statistical significance may be explained by the relatively small number of seizure events ($n=25$), which limits statistical power for subgroup comparisons. The literature regarding stroke subtype and seizure risk remains heterogeneous. Guo *et al.* in a meta-analysis of seizures following intracerebral hemorrhage, reported considerable variability across cohorts [9]. Lin *et al.* similarly observed inconsistent associations between hemorrhagic stroke and seizure occurrence [15]. These findings suggest that seizure risk is multifactorial and may depend more strongly on cortical involvement, lesion size, and stroke severity rather than stroke subtype alone. Since detailed imaging variables were not systematically available in our dataset, subtype-specific differences should be interpreted cautiously. Gender-based analysis demonstrated a higher proportion of seizures among females (18.8%) compared to males (11.1%), although this difference was not statistically significant ($p=0.150$). Logistic regression showed approximately two-fold higher adjusted odds among females (OR=2.021), but the confidence interval was wide and crossed unity, indicating statistical uncertainty. The small effect size (Cramer's $V=0.108$) further suggests minimal practical association. Previous studies have shown inconsistent gender effects. Sarfo *et al.* reported no independent association between gender and post-stroke seizures in a multicenter African cohort [16]. Similarly, Federico *et al.* found no significant sex-related differences in seizure risk following ischemic stroke [17]. Thus, our findings align with the broader evidence indicating that gender alone is unlikely to be a strong independent predictor of post-stroke seizures. Age-stratified analysis showed the highest seizure proportion in the 40-59-year group (19.4%), followed by 20-39 years (12.5%) and 60-80 years (10.2%), but these differences were not statistically significant ($p=0.320$). The absence of age-related significance may reflect the multifactorial nature of seizure development and the limited statistical power for subgroup detection. Lidetu and Zewdu similarly reported no independent age-based association after adjusting for stroke characteristics [18]. Smigelskyte *et al.* also concluded that age alone does not reliably predict early post-stroke seizures following ischemic stroke [19]. These findings collectively suggest that demographic variables may have limited predictive value when considered independently. Importantly, the 14.1% overall seizure incidence and the nearly equal early-late distribution have practical implications. These

findings highlight the necessity for structured seizure surveillance not only during the acute admission period but also throughout the early recovery phase. Routine follow-up and patient education regarding seizure recognition are essential components of post-stroke care. Furthermore, the absence of routine electroencephalographic monitoring in our study may have resulted in under-detection of subclinical or non-convulsive seizures. Gururangan *et al.* demonstrated that point-of-care EEG can improve detection of occult epileptiform activity in acute stroke settings [20]. AlGaeed *et al.* emphasized the value of continuous EEG monitoring in identifying epileptiform discharges among ischemic stroke patients [21].

Strengths of this study include radiologically confirmed stroke diagnosis, clearly defined operational seizure classifications, exclusion of metabolic confounders, and a structured three-month follow-up to capture both early and late events. The use of logistic regression further allowed adjustment for potential confounding variables. However, several limitations should be acknowledged. First, the single-center design may limit generalizability. Second, the study was powered to estimate seizure frequency rather than detect subgroup differences, and the relatively small number of seizure events (n=25) limits statistical power for multivariable modeling. Third, detailed imaging parameters such as lesion size, cortical versus subcortical involvement, and standardized stroke severity scores were not available. Finally, electroencephalography was not routinely performed, which may have resulted in an underestimation of seizure burden. These limitations should be considered when interpreting the findings. Future studies incorporating systematic EEG evaluation may provide more accurate seizure incidence estimates and better risk stratification.

CONCLUSIONS

Post-stroke seizures were observed in 14.1% of patients presenting with radiologically confirmed stroke, with a nearly equal distribution between early and late seizure onset. Although ischemic stroke and female gender showed numerically higher seizure proportions, no statistically significant independent predictors were identified. These findings suggest that post-stroke seizures are relatively frequent but may not be strongly predicted by basic demographic or subtype variables alone. The observed incidence underscores the importance of structured surveillance during both the acute and subacute phases of stroke recovery. Future multicenter studies incorporating detailed neuroimaging parameters, stroke severity assessment, and routine electroencephalographic monitoring are warranted to better define seizure risk profiles and improve post-stroke neurological care strategies.

Authors' Contribution

Conceptualization: SJ, AU

Methodology: ZUK, SK, SFK

Formal analysis: ZUK, SK, AU, SFK, JK

Writing and Drafting: SJ, JK

Review and Editing: SJ, ZUK, SK, AU, SFK, JK

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All 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] Alsaad F, Alkeneetir N, Almatroudi M, Alatawi A, Alotaibi A, Aldibasi O *et al.* Early Seizures in Stroke-Frequency, Risk Factors, and Effect on Patient Outcomes in a Tertiary Center in Saudi Arabia. *Neurosciences Journal*. 2022 Apr; 27(2): 104-110. doi: 10.17712/nsj.2022.2.20210144.
- [2] Nandan A, Zhou YM, Demoe L, Waheed A, Jain P, Widjaja E. Incidence and Risk Factors of Post-Stroke Seizures and Epilepsy: Systematic Review and Meta-Analysis. *Journal of International Medical Research*. 2023 Nov; 51(11): 1-18. doi: 10.1177/03000605231213231.
- [3] Querdien A, Messelmani M, Derbali H, Mansour M, Zaouali J, Mrissa N *et al.* Post-Stroke Seizures: Risk Factors and Management After Ischemic Stroke. *Acta Neurologica Belgica*. 2023 Feb; 123(1): 145-152. doi: 10.1007/s13760-021-01742-x.
- [4] Qazi TR, Siddiqui AI, Lakhair MA, Mahesar SA. Frequency of Early Seizures in Patients of Acute Ischemic Stroke. *Seizure*. 2016 Jul; 1(7): 3-59.
- [5] Franco AC, Fernandes T, Peralta AR, Basílio G, Carneiro I, Melo TP *et al.* Frequency of Epileptic Seizures in Patients Undergoing Decompressive Craniectomy After Ischemic Stroke. *Seizure: European Journal of Epilepsy*. 2022 Oct; 101: 60-66. doi: 10.1016/j.seizure.2022.07.011.
- [6] Kühne Escolà J, Bozkurt B, Brune B, Chae WH, Milles LS, Pommeranz D *et al.* Frequency and Characteristics of Non-Neurological and Neurological Stroke Mimics in The Emergency Department. *Journal of Clinical Medicine*. 2023 Nov; 12(22): 7067. doi: 10.3390/jcm12227067.
- [7] Sinka L, Abaira L, Imbach LL, Zieglgänsberger D, Santamarina E, Álvarez-Sabín J *et al.* Association of Mortality and Risk of Epilepsy with Type of Acute Symptomatic Seizure After Ischemic Stroke and an

- Updated Prognostic Model. *JAMA Neurology*. 2023 Jun; 80(6): 605-613. doi: 10.1001/jamaneurol.2023.0611.
- [8] Lasek-Bal A, Dewerenda-Sikora M, Binek Ł, Student S, Łabuz-Roszak B, Krzystanek E et al. Epileptiform Activity in the Acute Phase of Stroke Predicts the Outcomes in Patients Without Seizures. *Frontiers in Neurology*. 2023 Mar; 14: 1-8. doi: 10.3389/fneur.2023.1096876.
- [9] Guo X, Zhong R, Han Y, Zhang H, Zhang X, Lin W. Incidence and Relevant Factors for Seizures After Spontaneous Intracerebral Hemorrhage: A Systematic Review and Meta-Analysis. *Seizure: European Journal of Epilepsy*. 2022 Oct; 101: 30-38. doi: 10.1016/j.seizure.2022.06.016.
- [10] Mecarelli O, Pro S, Randi F, Dispenza S, Correnti A, Pulitano P et al. Electroencephalogram patterns and epileptic seizures in acute phase stroke. *Cerebrovascular Diseases*. 2011 Dec; 31(2): 191-198. doi: 10.1159/000321872.
- [11] Misra S, Kasner SE, Dawson J, Tanaka T, Zhao Y, Zaveri HP et al. Outcomes in Patients with Poststroke Seizures: A Systematic Review and Meta-Analysis. *JAMA Neurology*. 2023 Nov; 80(11): 1155-1165. doi: 10.1001/jamaneurol.2023.3240.
- [12] Freiman S, Hauser WA, Rider F, Yaroslavskaya S, Sazina O, Vladimirova E et al. Post-Stroke Seizures, Epilepsy, and Mortality in a Prospective Hospital-Based Study. *Frontiers in Neurology*. 2023 Dec; 14: 1-11. doi: 10.3389/fneur.2023.1273270.
- [13] Tanaka T, Ihara M, Fukuma K, Mishra NK, Koepp MJ, Guekht A et al. Pathophysiology, Diagnosis, Prognosis, And Prevention of Poststroke Epilepsy: Clinical and Research Implications. *Neurology*. 2024 Jun; 102(11): 1-12. doi: 10.1212/WNL.000000000000209450.
- [14] Ryu HU, Kim HJ, Shin BS, Kang HG. Clinical Approaches for Poststroke Seizure: A Review. *Frontiers in Neurology*. 2024 Apr; 15: 1337960. doi: 10.3389/fneur.2024.1337960.
- [15] Lin HY, Wei QQ, Huang JY, Pan XH, Liang NC, Huang CX et al. Relationship Between Mortality and Seizures After Intracerebral Hemorrhage: A Systematic Review and Meta-Analysis. *Frontiers in Neurology*. 2022 Jun; 13: 922677. doi: 10.3389/fneur.2022.922677.
- [16] Sarfo FS, Akinyemi J, Akpalu A, Wahab K, Yaria J, Adebayo O et al. Frequency and Factors Associated with Post-Stroke Seizures in a Large Multicenter Study in West Africa. *Journal of the Neurological Sciences*. 2021 Aug; 427: 117535. doi: 10.1016/j.jns.2021.117535.
- [17] Federico EM, Carroll K, McGrath M, Walker M, Stafstrom I, Skinner E et al. Incidence and Risk Factors of Post-Stroke Seizure Among Ischemic Stroke Patients. *Journal of Stroke and Cerebrovascular Diseases*. 2024 Dec; 33(12): 108072. doi: 10.1016/j.jstrokecerebrovasdis.2024.108072.
- [18] Lidetu T and Zewdu D. Incidence and Predictors of Post-Stroke Seizure Among Adult Stroke Patients Admitted at Felege Hiwot Comprehensive Specialized Hospital, Bahir Dar, North West Ethiopia, 2021: A Retrospective Follow-Up Study. *BioMed Central Neurology*. 2023 Jan; 23(1): 40. doi: 10.1186/s12883-023-03083-z.
- [19] Šmigelskytė A, Gelžinienė G, Jurkevičienė G. Early Epileptic Seizures After Ischemic Stroke: Their Association with Stroke Risk Factors and Stroke Characteristics. *Medicina*. 2023 Aug; 59(8): 1433. doi: 10.3390/medicina59081433.
- [20] Gururangan K, Kozak R, Dorris PJ. Time is Brain: Detection of Nonconvulsive Seizures and Status Epilepticus During Acute Stroke Evaluation Using Point-Of-Care Electroencephalography. *Journal of Stroke and Cerebrovascular Diseases*. 2025 Jan; 34(1): 108116. doi: 10.1016/j.jstrokecerebrovasdis.2024.108116.
- [21] AlGaeed M, Grewal M, Hareesh P, Sadeghikhah S, Chen H, Gholipour T et al. Diagnostic Yield of Electroencephalography When Seizure Is Suspected in Acute Ischemic Stroke. *The Neurohospitalist*. 2022 Jan; 12(1): 8-12. doi: 10.1177/19418744211021224.



Original Article



Frequency of Pneumonia in Children Presenting with Measles at DHQ Hospital, Dera Ismail Khan

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ARTICLE INFO

Keywords:

Measles, Pneumonia, Pediatric, Vaccination, Malnutrition

How to Cite:

Javed, F., Ibrahim, M., Khan, A. M., Burki, F. U., Ullah, F., & Ullah, I. (2026). Frequency of Pneumonia in Children Presenting with Measles at DHQ Hospital, Dera Ismail Khan: Frequency of Pneumonia in Children Presenting with Measles. *Pakistan Journal of Health Sciences*, 7(6), 63-68. <https://doi.org/10.54393/pjhs.v7i6.3922>

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Received Date: 3rd February, 2026

1st Revision Received: 2nd March, 2026

Acceptance Date: 24th March, 2026

Published Date: 30th June, 2026

ABSTRACT

Measles remains a significant cause of pediatric morbidity and mortality worldwide, particularly in low- and middle-income countries. Pneumonia is one of the most frequent and serious complications of measles, contributing substantially to adverse outcomes in affected children.

Objectives: To determine the frequency of pneumonia among children presenting with measles at DHQ Hospital, Dera Ismail Khan, and to assess associated demographic and clinical factors.

Methods: This cross-sectional analytical study was conducted in the Department of Pediatrics, District Headquarters Hospital, Dera Ismail Khan, from September 2024 to January 2025. A total of 169 children aged 2–15 years with laboratory-confirmed measles were enrolled using consecutive non-probability sampling. Pneumonia was diagnosed based on clinical findings and radiographic confirmation. Data on age, gender, vaccination status, nutritional status, socioeconomic status, and residence were collected using a structured proforma. Statistical analysis was performed using SPSS version 25.0. Associations were evaluated using chi-square and Fisher's exact tests, and multivariable logistic regression was conducted. **Results:** Among 169 children, 54 (32.0%) developed pneumonia. Pneumonia was significantly associated with malnutrition ($p < 0.001$), younger age ($p < 0.001$), rural residence ($p = 0.028$), and lack of immunization ($p < 0.001$). No pneumonia cases were observed among immunized children.

Conclusions: Pneumonia was observed in approximately one-third of children with measles. Malnutrition, younger age, and non-immunization were associated with higher pneumonia frequency.

INTRODUCTION

Measles remains one of the most contagious viral diseases affecting children worldwide, despite the availability of a safe and effective vaccine for more than five decades. Globally, measles continues to contribute substantially to pediatric morbidity and mortality, particularly in low- and middle-income countries [1]. Recent global estimates indicate approximately 100,000 measles-related deaths annually, with the majority occurring in children under five years of age [2]. The virus is transmitted through respiratory droplets and aerosols and has an exceptionally high basic reproduction number (R_0), with one infected

individual capable of transmitting the infection to 12–18 susceptible persons [3]. Although widespread immunization has significantly reduced disease burden in many regions, suboptimal vaccination coverage, population displacement, and vaccine hesitancy continue to fuel recurrent outbreaks, threatening global elimination goals [4]. The World Health Organization reported a substantial resurgence of measles cases during 2022–2023, reflecting persistent immunity gaps in vulnerable populations [5]. Beyond its characteristic clinical manifestations of fever and maculopapular rash,



measles is associated with profound transient immunosuppression that may persist for weeks to months following acute infection [6]. This immunological impairment increases susceptibility to secondary infections, among which pneumonia represents the most frequent and life-threatening complication [7]. Measles-associated pneumonia may occur as primary viral pneumonia resulting from direct viral involvement of pulmonary tissue, secondary bacterial pneumonia due to impaired mucosal immunity, or a mixed viral-bacterial process. Clinically, affected children commonly present with cough, tachypnea, chest indrawing, and hypoxemia, often necessitating prompt medical intervention [8]. Reported case-fatality rates vary considerably depending on nutritional status and access to healthcare, remaining below 1% in well-resourced settings but exceeding 10% in resource-limited environments [9].

Despite the recognized burden of measles-associated pneumonia globally, there is limited contemporary data from southern Khyber Pakhtunkhwa, particularly from district-level referral hospitals serving predominantly rural populations. Furthermore, the interaction between vaccination status, nutritional status, socioeconomic conditions, and pneumonia occurrence among children with laboratory-confirmed measles has not been adequately explored in this setting. Addressing this gap is essential to inform targeted preventive strategies and optimize clinical management. Therefore, this study aims to determine the frequency of pneumonia among children aged 2–15 years presenting with measles at DHQ Hospital, Dera Ismail Khan, and to examine its association with key demographic, vaccination, nutritional, socioeconomic, and residential factors.

METHODS

This cross-sectional analytical study was conducted in the Department of Pediatrics, District Headquarters (DHQ) Hospital, Dera Ismail Khan, the main public-sector tertiary referral center for pediatric infectious diseases in the district, serving an estimated population of approximately 1.7 million in southern Khyber Pakhtunkhwa, Pakistan. The study was carried out from September 2024 to January 2025 following approval from the Ethical Review Committee of Gomal Medical College (Reference No. 146/GJMS/JC; dated 25th September, 2024) and registration with the Research Training and Monitoring Cell of the College of Physicians and Surgeons Pakistan (RTMC Registration No. CPSP/REU/PED-2023-029-7549; dated 25th October 2024). The sample size was calculated using the World Health Organization (WHO) sample size calculator for descriptive studies, assuming an expected pneumonia frequency of 31.13% [10] among measles cases, a 95% confidence level, and a 7% margin of error, resulting

in a required sample of 169 participants. Consecutive non-probability sampling was used to recruit eligible participants presenting to the Department of Pediatric Emergency, Outpatient Department, and inpatient wards during the study period. Inclusion criteria comprised children aged 2–15 years of either gender presenting with clinically suspected measles, defined as fever $\geq 38.3^{\circ}\text{C}$, maculopapular rash, and at least one of cough, coryza, or conjunctivitis, with laboratory confirmation by detection of measles-specific IgM antibodies in serum. Measles IgM testing was performed for all enrolled patients using the enzyme-linked immunosorbent assay (ELISA) method at the DHQ Hospital Dera Ismail Khan laboratory, following manufacturer protocols and internal quality control procedures. Exclusion criteria included children with pre-existing congenital heart disease, chronic respiratory disorders (including bronchial asthma), documented neurological disorders, known immunodeficiency, or those receiving immunosuppressive therapy, as these conditions may independently increase the risk of pneumonia and confound study outcomes. After obtaining written informed consent from parents or legal guardians, demographic and clinical data were recorded using a structured proforma. Collected variables included age (in years), gender, weight, vaccination status (verified through immunization cards or parental recall), residence (urban/rural), and socioeconomic status. Nutritional status was operationally defined using weight-for-age Z-scores according to WHO growth standards. Children with a weight-for-age Z-score ≥ -2 standard deviations were categorized as well-nourished, while those with a Z-score < -2 standard deviations were classified as malnourished [11]. Socioeconomic status was assessed using the Modified Kuppuswamy Socioeconomic Scale (2023 updated version) [12], with income categories adapted to Pakistani Rupees (PKR) according to prevailing economic standards during the study period. Participants were classified into lower, middle, and upper socioeconomic groups based on composite scores. Pneumonia was operationally defined as the presence of cough, fever $\geq 38.3^{\circ}\text{C}$, and age-adjusted tachypnea, confirmed radiographically by chest X-ray demonstrating alveolar opacity, patchy infiltrates, or pleural effusion. Radiographs were interpreted independently by consultant radiologists blinded to clinical data.

Data were entered and analyzed using IBM SPSS Statistics version 25. Categorical variables were summarized as frequencies and percentages, while continuous variables were reported as mean $\pm$ standard deviation and range. Associations between categorical variables and pneumonia were assessed using the chi-square test. Fisher's exact test was applied when expected cell counts were less than five or when zero-cell frequencies were

observed. Multivariable logistic regression analysis was performed to identify factors independently associated with pneumonia. Adjusted odds ratios (AORs) with 95% confidence intervals were reported. Model fit was evaluated using the Hosmer–Lemeshow goodness-of-fit test and Nagelkerke R^2 . A two-tailed p-value < 0.05 was considered statistically significant.

RESULTS

A total of 169 children diagnosed with measles were enrolled in this study. Pneumonia was observed in 54 children, yielding an overall prevalence of 32.0% (95% CI: 25.0%–39.0%). The mean age of participants was 7.1 ± 3.6 years (range: 2–15 years), with the largest proportion belonging to the 6–10 years age group (42.6%), followed by 2–5 years (40.2%) and 11–15 years (17.2%). Male children constituted 55.0% of the sample. The mean weight was 21.2 ± 8.5 kg. Most participants were malnourished (58.0%), belonged to lower socioeconomic households (63.9%), and resided in rural areas (62.1%). Detailed demographic and baseline characteristics are presented in table 1.

Table 1: Demographic Characteristics of Stroke Patients (n=177)

Variables	Categories	n (%) / Mean $\pm$ SD
Age (years)	Mean $\pm$ SD	7.1 ± 3.6
	Range	2–15
Age Groups	2–5 Years	68 (40.2%)
	6–10 Years	72 (42.6%)
	11–15 Years	29 (17.2%)
Gender	Male	93 (55.0%)
	Female	76 (45.0%)
Weight (kg)	Mean $\pm$ SD	21.2 ± 8.5
	Range	9.1–41.8
Vaccination Status	Immunized	47 (27.8%)
	Not Immunized	122 (72.2%)
Nutritional Status	Well-Nourished	71 (42.0%)
	Malnourished	98 (58.0%)

Socioeconomic Status	Lower Class	108 (63.9%)
	Middle Class	49 (29.0%)
	Upper Class	12 (7.1%)
Place of Residence	Urban	64 (37.9%)
	Rural	105 (62.1%)

The mean fever temperature at presentation was $38.9 \pm 0.4^\circ\text{C}$, and the mean duration of symptoms before hospital presentation was 4.4 ± 1.3 days. Cough was reported in 89.9% of children, and tachypnea was observed in 35.5%. Pneumonia occurred in 32.0% of cases. Clinical features are summarized in table 2.

Table 2: Clinical Characteristics and Pneumonia Frequency (n=169)

Variables	Categories/Values	n (%) / Mean $\pm$ SD
Pneumonia	Present	54 (32.0%)
	Absent	115 (68.0%)
Fever Temperature	$^\circ\text{C}$	38.9 ± 0.4
	Range	38.3–39.8
Duration of Measles	Days	4.4 ± 1.3
	Range	3–7
Cough	Present	152 (89.9%)
	Absent	17 (10.1%)
Tachypnea	Present	60 (35.5%)
	Absent	109 (64.5%)

In bivariate analysis, significant associations were observed between pneumonia and age group ($\chi^2 = 19.432$, $p < 0.001$), nutritional status ($\chi^2 = 52.536$, $p < 0.001$), and place of residence ($\chi^2 = 4.811$, $p = 0.028$). Malnourished children demonstrated markedly higher pneumonia frequency (54.1%) compared with well-nourished children (1.4%). Pneumonia was most common among children aged 2–5 years (45.6%) and was not observed in adolescents aged 11–15 years. No significant association was found between gender or socioeconomic status and pneumonia occurrence. These findings are detailed in table 3.

Table 3: Bivariate Association Between Risk Factors and Pneumonia (n=169)

Variables	Categories	Pneumonia Present, n (%)	Pneumonia Absent, n (%)	χ^2 (p-value)*	Cramer's V
Age Group	2–5 Years	31 (45.6%)	37 (54.4%)	19.432 (<0.001)	0.339
	6–10 Years	23 (31.9%)	49 (68.1%)		
	11–15 Years	0 (0.0%)	29 (100.0%)		
Gender	Male	33 (35.5%)	60 (64.5%)	1.186 (0.276)	0.084
	Female	21 (27.6%)	55 (72.4%)		
Nutritional Status	Well-Nourished	1 (1.4%)	70 (98.6%)	52.536 (<0.001)	0.558
	Malnourished	53 (54.1%)	45 (45.9%)		
Socioeconomic Status	Lower	38 (35.2%)	70 (64.8%)	1.448 (0.485)	0.093
	Middle	13 (26.5%)	36 (73.5%)		
	Upper	3 (25.0%)	9 (75.0%)		
Place of Residence	Urban	14 (21.9%)	50 (78.1%)	4.811 (0.028)	0.169
	Rural	40 (38.1%)	65 (61.9%)		

*Chi-square test applied; $p < 0.005$ considered statistically significant

Pneumonia occurred exclusively among non-immunized children (44.3%) and was not observed among immunized children (0%). Because of a zero-cell frequency, Fisher's exact test was applied, demonstrating a statistically significant association ($p < 0.001$). Using the Haldane-Anscombe continuity correction to account for the zero cell, non-immunized children had significantly higher odds of pneumonia compared with immunized children (crude OR = 75.6; 95% CI: 4.6–1254.2) as shown in table 4.

Table 4: Association Between Vaccination Status and Pneumonia (n=169)

Vaccination Status	Pneumonia (Yes), n (%)	Pneumonia (No), n (%)	Total, n (%)	p-value
Immunized	0 (0.0%)	47 (100.0%)	47 (27.8%)	<0.072*
Not immunized	54 (44.3%)	68 (55.7%)	122 (72.2%)	
Total	54 (32.0%)	115 (68.0%)	169 (100%)	

*Fisher's exact test applied due to zero cell frequency. †Crude odds ratio calculated using Haldane-Anscombe continuity correction (OR=75.6; 95% CI: 4.6–1254.2)

To identify independent factors associated with pneumonia, multivariable logistic regression analysis was performed. Vaccination status was excluded from the regression model due to complete separation (no pneumonia events among immunized children). The overall model was statistically significant (Omnibus test $\chi^2 = 97.051$, $p < 0.001$) and demonstrated good fit (Hosmer-Lemeshow $p = 0.460$; Nagelkerke $R^2 = 0.612$). After adjustment for confounders Malnutrition remained strongly associated with pneumonia (AOR = 125.96, 95% CI: 15.70–1010.86, $p < 0.001$). Rural residence was independently associated with higher odds of pneumonia (AOR = 2.91, 95% CI: 1.04–8.12, $p = 0.041$). Increasing age was protective, with each additional year associated with a 27% reduction in odds of pneumonia (AOR = 0.73, 95% CI: 0.63–0.85, $p < 0.001$). Gender and socioeconomic status were not independently associated with pneumonia. Multivariable results are presented in table 5.

Table 5: Multivariable Logistic Regression Analysis of Factors Associated with Pneumonia (n=169)

Variables	Adjusted OR	95% CI	p-value
Age (Per Year Increase)	0.73	0.63 – 0.85	<0.001
Male Gender	1.62	0.65 – 4.07	0.305
Malnourished vs Well-Nourished	125.96	15.70 – 1010.86	<0.001
Rural Residence vs Urban	2.91	1.04 – 8.12	0.041
SES – Lower vs Upper	2.65	0.44 – 16.13	0.289
SES – Middle vs Upper	0.92	0.14 – 6.12	0.931

DISCUSSION

This frequency is comparable to findings reported in similar hospital-based studies from low- and middle-income countries. Turaiche et al. reported pneumonia in

28.4% of unvaccinated children with measles in Romania [2], while Mehta et al. documented a frequency of 35.2% among pediatric measles cases in India [13]. Regional Pakistani data have reported pneumonia frequencies ranging from approximately 29% to 42% among hospitalized children with measles [14, 15]. These comparisons suggest that the burden observed in Dera Ismail Khan is broadly consistent with patterns reported in comparable socioeconomic and healthcare contexts. Younger children demonstrated higher pneumonia frequency in bivariate analysis, particularly those aged 2–5 years. This observation aligns with existing literature indicating that younger children may be more vulnerable to severe measles complications due to immature immune responses and higher baseline rates of malnutrition [16]. However, in multivariable logistic regression, age was analyzed as a continuous variable and demonstrated a protective association, with increasing age associated with lower odds of pneumonia. This finding should be interpreted cautiously, as cross-sectional data cannot establish temporal or causal relationships. Vaccination status showed a strong inverse association with pneumonia in bivariate analysis, with no pneumonia cases observed among immunized children. Because of complete separation, vaccination status was excluded from the multivariable model. Using Fisher's exact test and Haldane-Anscombe correction, non-immunized children had significantly higher crude odds of pneumonia (OR = 75.6; 95% CI: 4.6–1254.2). Although the magnitude of this association appears large, the wide confidence interval reflects statistical imprecision related to the zero-cell frequency and sample size limitations. Therefore, the strength of association should be interpreted with caution. These findings are biologically plausible and consistent with evidence that measles vaccination reduces the risk of severe complications and case-fatality [17, 18]. However, given the study design, causality cannot be inferred. Malnutrition demonstrated the strongest independent association with pneumonia after adjustment (AOR = 125.96; 95% CI: 15.70–1010.86). Despite the large adjusted odds ratio, the wide confidence interval suggests variability and possible overestimation influenced by event distribution and sample size. The association between undernutrition and severe measles outcomes has been consistently reported in the literature [14, 19]. Malnutrition impairs cell-mediated immunity, reduces mucosal barrier integrity, and predisposes children to secondary bacterial infections. Furthermore, vitamin A supplementation has been shown to reduce measles-related morbidity and mortality in children [20]. These study findings support existing evidence emphasizing the importance of nutritional assessment and supportive care in children with

measles. Rural residence was independently associated with higher odds of pneumonia (AOR = 2.91; 95% CI: 1.04–8.12). This association may reflect disparities in healthcare access, delayed presentation, lower immunization coverage, and higher prevalence of malnutrition in rural communities. Similar patterns have been observed in regional studies examining measles complications in underserved populations [14, 15]. These findings highlight the potential influence of social determinants of health on complication severity.

The present study contributes district-level data from southern Khyber Pakhtunkhwa, where contemporary hospital-based evidence remains limited. Nevertheless, several limitations should be acknowledged. First, the cross-sectional design does not allow assessment of temporal sequence or causal inference. Second, the single-center setting may limit generalizability to other regions. Third, the zero-cell frequency in vaccination status limited regression modeling and resulted in wide confidence intervals for crude estimates. Despite these limitations, laboratory confirmation of measles and multivariable adjustment strengthen the internal validity of the findings.

CONCLUSIONS

In conclusion, pneumonia was observed in approximately one-third of children hospitalized with measles at DHQ Hospital, Dera Ismail Khan. Malnutrition and rural residence were independently associated with higher odds of pneumonia, while increasing age demonstrated a protective association. Vaccination status showed a strong inverse association with pneumonia in bivariate analysis; however, due to complete separation and study design limitations, this finding should be interpreted cautiously. These findings suggest that strengthening routine immunization coverage and addressing childhood malnutrition may contribute to reducing the burden of severe measles-related complications in similar settings. Further multicenter prospective studies are recommended to confirm these associations and provide more precise effect estimates.

Authors' Contribution

Conceptualization: FJ

Methodology: MI, FUB, FU, IU

Formal analysis: FU, IU

Writing and Drafting: FJ, MI, AMK, FUB, FU, IU

Review and Editing: FJ, MI, AMK, FUB, FU, IU

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All 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] Riabokon OV, Bilokobyla SO, Korniienko OO, Riabokon YY, Vynokurova AV. Diagnostic Significance of Immunological Parameters in Predicting the Development of Pneumonia in Adult Patients with Measles. *Current Issues in Pharmacy and Medicine: Science and Practice*. 2024 Jun; 17(2): 160-8. doi: 10.14739/2409-2932.2024.2.299489.
- [2] Turaiche M, Grigoras ML, Bratosin F, Bogdan I, Bota AV, Cerbu B et al. Disease Progression, Clinical Features, and Risk Factors for Pneumonia in Unvaccinated Children and Adolescents with Measles: A Re-Emerging Disease in Romania. *International Journal of Environmental Research and Public Health*. 2022 Oct; 19(20): 13165. doi: 10.3390/ijerph192013165.
- [3] Kulsoom S, Soomro S, Junejo S, Anjum M, Waseem H, Akram M. Clinical Presentation, Complications, and Outcome of Measles in Pediatric Population at Tertiary Care Hospital: Measles in Pediatric Population. *Pakistan Journal of Health Sciences*. 2023 Mar; 50-3. doi: 10.54393/pjhs.v4i03.624.
- [4] Khan IU, Shehzad A, Ahmad Z. Frequency of Myocarditis in Children Presenting with Measles at Tertiary Care Hospital. *Medical and Experimental Research Articles - Journal of Combined Military Hospital Lahore Medical College and Institute of Dentistry*. 2024 Dec; 6(2).
- [5] Gul J, Gul H, Asma B, Ali I, Ullah MZ. Frequency of Pneumonia in Children Presenting with Measles at Bacha Khan Medical College, Swabi. *Indus Journal of Bioscience Research*. 2025 Jul; 3(7): 1240-4. doi: 10.70749/ijbr.v3i7.2528.
- [6] Bursal B, Çelik T, Bingöl İ, Tosun D, Tuncay SA, Dağtekin ZK et al. Resurgent Measles in Türkiye: Predictors of Severe Disease in a Nationwide Pediatric Cohort, 2023. *European Journal of Pediatrics*. 2025 Nov; 184(11): 1-1. doi: 10.1007/s00431-025-06539-1.
- [7] Zhao L, Wang Y, Chen X, Yang L, Cai M, Zhang Z et al. Clinical Characteristics of Adult Inpatients with Measles in Beijing from 2010 to 2021: A Retrospective Analysis. *BioMed Central Infectious Diseases*. 2023 May; 23(1): 312. doi: 10.1186/s12879-023-08256-2.
- [8] Mawlood SD, Al-Ani MM, Al-Ani RM, Alshibib A. Impact of Measles Vaccination on Clinical Characteristics

- and Outcomes in Children in Ramadi, Iraq. *World Journal of Clinical Pediatrics*. 2025 Sep; 14(3): 107253. doi: 10.5409/wjcp.v14.i3.107253.
- [9] Ullah F, Muhammad T, Ullah F, Naz R, Bashir Khan, Shaista Qazi. Frequency of Measles-Related Complications in Hospitalized Children. *Pakistan Journal of Medical and Health Sciences*. 2023; 17(01): 548. doi: 10.53350/pjmhs.2023171548.
- [10] Khan A, Khan AM, Akbar A, Akram M, Ahmad F, Nawaz A. Prevalence of Pneumonia Associated with Measles among Infants and Children. *Children*. 2021; 90: 60. doi: 10.19045/bspab.2021.100072.
- [11] Lin Y, Shi Q, Yang J, Huang G, Yan J. Association of Anthropometric Z Score with Complications and Length of Hospital Stay in Children with Severe Pneumonia Aged 3 Months to 5 Years. *Nutrition in Clinical Practice*. 2024 Apr; 39(2): 459-69. doi: 10.1002/ncp.11067.
- [12] Wani RT. Socioeconomic Status Scales-Modified Kuppuswamy and Udai Pareekh's Scale Updated for 2019. *Journal of Family Medicine and Primary Care*. 2019 Jun; 8(6): 1846-9. doi: 10.4103/jfmpc.jfmpc_288_19.
- [13] Mehta KP, Patel A, Patel A. Clinical Profile, Complications and Outcomes of Measles among Children: An Observational Study from a Tertiary Care Hospital, South Gujarat, India. *Journal of Clinical and Diagnostic Research*. 2023 Jan; 17(1). doi: 10.7860/JCDR/2023/59480.17410.
- [14] Aurangzeb B, Fatmee A, Waris R, Haider N, Berjees A, Raza SH. Risk Factors for Mortality Among Admitted Children with Complications of Measles in Pakistan: An Observational Study. *The Journal of the Pakistan Medical Association*. 2021 Feb; 71(2(A)): 497-501.
- [15] Khan S, Iqbal J, Tayyeb M, Fahad S, Ullah A, Khan H. Prevalence of pneumonia associated with measles among infants and children hospitalized in Khyber Teaching Hospital, Peshawar, KPK, Pakistan. *Pure and Applied Biology*. 2021 Jul; 10(3): 703-12. doi: 10.19045/bspab.2021.100072.
- [16] Chen W, Du M, Deng J, Liu M, Liu J. Global, Regional, and National Trends of Measles Burden and Its Vaccination Coverage among Children Under 5 Years Old: An Updated Systematic Analysis from the Global Burden of Disease Study 2021. *International Journal of Infectious Diseases*. 2025 Jul; 156: 107908. doi: 10.1016/j.ijid.2025.107908.
- [17] Gastañaduy PA, Goodson JL, Panagiotakopoulos L, Rota PA, Orenstein WA, Patel M. Measles in the 21st century: Progress Toward Achieving and Sustaining Elimination. *The Journal of Infectious Diseases*. 2021 Oct; 224(Supplement_4): S420-8. doi: 10.1093/infdis/jiaa793.
- [18] Sbarra AN, Mosser JF, Jit M, Ferrari M, Ramshaw RE, O'Connor P et al. Estimating National-Level Measles Case-Fatality Ratios in Low-Income and Middle-Income Countries: An Updated Systematic Review and Modelling Study. *The Lancet Global Health*. 2023 Apr; 11(4): e516-24. doi: 10.1016/S2214-109X(23)00043-8.
- [19] Nezhoda II, Havryliuk AO, Asaulenko AA, Kholod LP, Onofriychuk Ye S. Measles Pneumonia in Children: Clinical and Morphological Features of the Course. *The World of Medicine and Biology*. 2020; 16(1(71)): 88-93. doi: 10.26724/2079-8334-2020-1-71-88-93.
- [20] Kakoullis L, Sampsonas F, Giannopoulou E, Kalogeropoulou C, Papachristodoulou E, Tsiamita M et al. Measles-Associated Pneumonia and Hepatitis During the Measles Outbreak of 2018. *International Journal of Clinical Practice*. 2020 Feb; 74(2): e13430. doi: 10.1111/ijcp.13430.



Original Article



Diagnostic Accuracy of Magnetic Resonance Cholangiopancreatography (MRCP) in Differentiating Benign and Malignant Causes of Obstructive Jaundice Using Histopathology as the Reference Standard

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ARTICLE INFO

Keywords:

Obstructive Jaundice, Magnetic Resonance Cholangiopancreatography, Biliary Obstruction, Histopathology, Diagnostic Accuracy

How to Cite:

Begum, T., Orakzai, Z. J., Khan, L., Noureen, S., Baig, H., & Azam, N. (2026). Diagnostic Accuracy of Magnetic Resonance Cholangiopancreatography (MRCP) in Differentiating Benign and Malignant Causes of Obstructive Jaundice Using Histopathology as the Reference Standard: MRCP in Benign and Malignant Causes of Obstructive Jaundice Using Histopathology. *Pakistan Journal of Health Sciences*, 7(6), 69-74. <https://doi.org/10.54393/pjhs.v7i6.3912>

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ABSTRACT

Obstructive jaundice requires accurate differentiation between benign and malignant causes to guide management and prognosis. Magnetic resonance cholangiopancreatography (MRCP) is increasingly used as a non-invasive diagnostic modality; however, local evidence comparing MRCP findings with histopathology remains limited. **Objectives:** To evaluate the diagnostic accuracy of MRCP in differentiating benign from malignant obstructive jaundice using histopathology as the reference standard. **Methods:** This retrospective cross-sectional study included 103 patients with obstructive jaundice who underwent MRCP followed by histopathological confirmation between June and December 2025. Biochemical parameters and imaging findings were analyzed. Sensitivity, specificity, predictive values, overall accuracy, and area under the receiver operating characteristic curve (AUC) were calculated. **Results:** Histopathology confirmed 54 (52.4%) benign and 49 (47.6%) malignant cases. Total bilirubin, direct bilirubin, ALT, AST, ALP, and CA 19-9 levels were significantly higher in malignant cases (all $p < 0.001$), while duration of jaundice, GGT, and stricture length showed no significant difference ($p > 0.005$). MRCP demonstrated a sensitivity of 95.9%, specificity of 96.3%, positive predictive value of 95.9%, negative predictive value of 96.3%, and overall accuracy of 96.1%. ROC analysis showed excellent diagnostic performance (AUC = 0.961; 95% CI: 0.918-1.000; $p < 0.001$). **Conclusions:** MRCP demonstrates excellent diagnostic accuracy in differentiating malignant from benign obstructive jaundice and serves as a reliable non-invasive imaging modality for clinical decision-making

INTRODUCTION

Obstructive jaundice is a common clinical condition encountered in hepatobiliary practice and results from mechanical obstruction of the biliary tract, leading to impaired bile flow and conjugated hyperbilirubinemia [1]. Globally, obstructive jaundice accounts for a significant proportion of hepatobiliary admissions, with malignant causes reported in approximately 40-60% of adult cases, particularly in patients above 50 years of age [2]. The etiology ranges from benign conditions such as choledocholithiasis, benign strictures, and chronic

pancreatitis to malignant diseases, including cholangiocarcinoma, ampullary carcinoma, and pancreatic carcinoma [3]. Differentiating benign from malignant obstruction is crucial because management strategies, surgical planning, and prognosis differ markedly between the two groups [4]. Biochemical assessment and imaging studies form the cornerstone of evaluation [5]. Serum biomarkers, including total and direct bilirubin, alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), transaminases (ALT, AST), and



tumor marker CA 19-9, are commonly used in clinical practice [6]. Elevated CA 19-9 levels have been associated with biliary malignancy; however, false elevation may occur in benign obstructive and inflammatory conditions, limiting its specificity. Therefore, no single biochemical marker can reliably distinguish malignant from benign obstruction. Ultrasonography is often the first-line imaging modality, but its diagnostic accuracy is limited by operator dependency and suboptimal visualization of distal bile ducts [7]. Endoscopic retrograde cholangiopancreatography (ERCP) has traditionally served both diagnostic and therapeutic roles, but carries procedure-related risks such as pancreatitis and cholangitis [8]. Magnetic resonance cholangiopancreatography (MRCP) has emerged as a non-invasive imaging modality that provides high-resolution visualization of the biliary and pancreatic ducts without contrast injection or instrumentation [8, 9]. Several studies have reported high sensitivity and specificity of MRCP in differentiating malignant from benign biliary strictures; however, variability in diagnostic performance has been observed across different populations and healthcare settings [10, 11]. In resource-limited environments, access to advanced diagnostic modalities may be constrained, making accurate non-invasive tools even more critical. Histopathology remains the definitive method for confirming malignancy [12]. It was hypothesized that MRCP demonstrates high diagnostic accuracy in differentiating malignant from benign obstructive jaundice when compared with histopathology as the reference standard.

Despite increasing use of MRCP, there is limited local evidence directly correlating MRCP findings with histopathological outcomes in patients with obstructive jaundice. Furthermore, the combined diagnostic value of MRCP alongside routinely available biochemical parameters has not been adequately explored in our setting. This represents an important research gap. Therefore, the present study aimed to evaluate the diagnostic performance of MRCP by determining its sensitivity, specificity, predictive values, overall accuracy, and area under the ROC curve, and to correlate imaging findings with biochemical parameters and final histopathological diagnosis.

METHODS

In this retrospective cross-sectional study, patients were assessed between June and December 2025 in the Department of Radiology, MTI Bacha Khan Medical College and Mardan Medical Complex, Mardan, Pakistan. The study aimed to determine the diagnostic performance of magnetic resonance cholangiopancreatography (MRCP) in distinguishing between benign and malignant causes of

obstructive jaundice using histopathology as the reference (gold) standard. The study included all patients who underwent MRCP for evaluation of obstructive jaundice and subsequently had histopathological confirmation within the study period. The study received ethical approval from the Ethical Review Board of MTI Bacha Khan Medical College, Mardan (Ref No. 937/BKMC; dated 14th January 2026), prior to data extraction and analysis and was conducted in accordance with the Declaration of Helsinki. Written informed consent had been obtained from all patients at the time of hospital admission and before undergoing radiological and surgical procedures, and this was documented in their medical records. Although the present analysis was retrospective, patient confidentiality was strictly maintained, and all data were anonymized before statistical analysis. The sample size was calculated using the World Health Organization (WHO) sample size calculator for diagnostic test evaluation. Assuming an expected sensitivity of MRCP of 90% [9], a confidence level of 95%, and an absolute precision of 5%, the minimum required sample size was estimated to be 92 patients. To compensate for incomplete records and improve the precision of diagnostic estimates, a total of 103 patients were included in the final analysis. Consecutive sampling was employed. Adult patients aged 18 years and above with clinical and biochemical features suggestive of obstructive jaundice who underwent MRCP followed by histopathological confirmation were included in the study. Patients with incomplete biochemical records, absence of histopathological confirmation, prior biliary reconstructive surgery altering normal anatomy, or poor-quality MRCP images were excluded. MRCP was performed using a 1.5 Tesla high-field MRI scanner following a standardized hepatobiliary imaging protocol. Axial and coronal heavily T2-weighted sequences were acquired to optimally visualize the biliary tree and pancreatic ductal system. Imaging parameters, including slice thickness and field of view, were kept uniform for all patients to ensure consistency. All MRCP images were independently evaluated by two consultant radiologists with more than five years of experience in hepatobiliary imaging who were blinded to the histopathological findings, and any discrepancies were resolved by consensus to enhance reliability. The radiological parameters documented included the level of obstruction (intrahepatic or extrahepatic), distal common bile duct involvement, hilar involvement, degree of biliary dilatation, morphology of stricture, presence of abrupt cut-off, mass lesion, pancreatic head mass, lymphadenopathy, vascular invasion, gallstones, and stricture length. The degree of biliary dilatation was categorized as mild, moderate, or severe based on duct diameter measurements. Stricture length was measured in millimeters on coronal reformatted

MRCP images using electronic calipers available in the radiology workstation software. Measurements were taken from the proximal to distal margins of luminal narrowing along the bile duct axis. Predefined radiological criteria were used to classify lesions as benign or malignant. Features suggestive of malignancy included irregular or asymmetric strictures, abrupt cut-off, associated mass lesion, lymphadenopathy, vascular invasion, and marked upstream biliary dilatation, whereas smooth tapered strictures without invasive features were categorized as benign. Clinical and biochemical data were retrieved from hospital records. The laboratory parameters analyzed included total bilirubin (mg/dL), direct bilirubin (mg/dL), alanine aminotransferase (ALT, U/L), aspartate aminotransferase (AST, U/L), alkaline phosphatase (ALP, U/L), gamma-glutamyl transferase (GGT, U/L), and carbohydrate antigen 19-9 (CA 19-9, U/mL). Venous blood samples were collected under aseptic conditions at the time of initial clinical presentation before any surgical or endoscopic intervention. Serum bilirubin, ALT, AST, ALP, and GGT levels were measured using an automated clinical chemistry analyzer based on standardized enzymatic colorimetric methods in the hospital laboratory. CA 19-9 levels were determined using a chemiluminescent immunoassay technique. All measurements were performed according to manufacturer guidelines and internal laboratory quality control protocols, and results were recorded in standard international units. The definitive reference standard was histopathological diagnosis obtained from biopsy or surgical specimens. All tissue samples were processed in the Department of Pathology using standard hematoxylin and eosin staining techniques and examined by consultant pathologists. Cases were categorized as benign or malignant based on microscopic evaluation, and specific histopathological diagnoses were documented. MRCP findings were compared with histopathological results to determine true-positive, true-negative, false-positive, and false-negative outcomes.

Data were entered and analyzed using SPSS version 25.0. The Shapiro-Wilk test was applied to assess the normality of quantitative variables. Variables with normal distribution were presented as mean $\pm$ standard deviation, whereas non-normally distributed variables were presented as median and interquartile range. Independent samples t-test or Mann-Whitney U test was used to compare benign and malignant groups, as appropriate. Categorical variables were expressed as frequencies and percentages and compared using the chi-square test. Sensitivity, specificity, positive predictive value, negative predictive value, and overall diagnostic accuracy were calculated using standard 2 $\times$ 2 contingency tables. Receiver operating characteristic (ROC) curve analysis was performed to

evaluate the discriminative ability of MRCP, and the area under the curve (AUC) with 95% confidence interval was reported. A p-value of less than 0.005 was considered statistically significant.

RESULTS

A total of 103 patients with obstructive jaundice were included in the study. The mean age was 55.63 ± 15.93 years (range 28–82 years), and the mean duration of jaundice was 6.47 ± 3.67 weeks. Males constituted 53.4% of the study population. Pruritus, abdominal pain, weight loss, and fever were reported in 53.4%, 55.3%, 50.5%, and 51.5% of patients, respectively. Diabetes mellitus and hypertension were present in 49.5% and 54.4% of cases (Table 1).

Table 1: Baseline Characteristics of Patients (n=103)

Variables	Mean $\pm$ SD / n (%)
Age (Years)	55.63 $\pm$ 15.93
Duration of Jaundice (Weeks)	6.47 $\pm$ 3.67
Male Gender	55 (53.4%)
Pruritus	55 (53.4%)
Weight Loss	52 (50.5%)
Abdominal Pain	57 (55.3%)
Fever	53 (51.5%)
Diabetes Mellitus	51 (49.5%)
Hypertension	56 (54.4%)

Histopathological examination classified 54 (52.4%) cases as benign and 49 (47.6%) as malignant. There was no statistically significant difference in age between benign and malignant groups ($p=0.883$). Duration of jaundice, GGT levels, and stricture length also did not differ significantly ($p>0.05$). However, total bilirubin, direct bilirubin, ALT, AST, ALP, and CA 19-9 levels were significantly elevated in patients with malignant obstruction compared to benign cases (all $p<0.001$), indicating more severe cholestatic and hepatocellular injury in malignant disease (Table 2).

Table 2: Comparison of Clinical and Biochemical Variables by Histopathology

Variables	Benign (n=54)	Malignant (n=49)	p-value
Age (years), Mean $\pm$ SD	55.85 $\pm$ 16.50	55.39 $\pm$ 15.45	0.883†
Duration (weeks), Median (IQR)	6.5 (7.0%)	6.0 (7.0%)	0.979‡
Total Bilirubin (mg/dL)	6.25 (4.08%)	13.10 (4.40%)	<0.001‡
Direct Bilirubin (mg/dL)	3.75 (2.45%)	9.20 (3.10%)	<0.001‡
ALT (U/L)	97.5 (39.5%)	164.0 (44.5%)	<0.001‡
AST (U/L)	97.5 (47.25%)	143.0 (48.5%)	<0.001‡
ALP (U/L)	348.0 (160.5%)	676.0 (218.5%)	<0.001‡
GGT (U/L)	222.0 (136.5%)	230.0 (121.5%)	0.577‡
CA 19-9 (U/mL)	83.5 (43.5%)	451.0 (428.5%)	<0.001‡
Stricture Length (mm)	22.5 (19.0%)	22.0 (16.5%)	0.399‡

† Independent t-test. ‡ Mann-Whitney U test

MRCP identified extrahepatic obstruction in 59.2% of cases and intrahepatic obstruction in 40.8%. Distal

common bile duct involvement was observed in 53.4% and hilar involvement in 42.7% of patients. Moderate biliary dilatation was the most common pattern (42.7%), followed by mild (30.1%) and severe (27.2%). Irregular strictures and abrupt cut-off were observed in 53.4% and 54.4% of cases, respectively. A mass lesion was detected in 38.8% of patients. Pancreatic head mass, lymphadenopathy, and vascular invasion were present in 47.6%, 53.4%, and 49.5% of patients, respectively. The mean stricture length was 21.47 ± 10.70 mm (Table 3).

Table 3: MRCP Imaging Characteristics (n=103)

Variables	n (%) / Mean $\pm$ SD
Extrahepatic Obstruction	61 (59.2%)
Intrahepatic Obstruction	42 (40.8%)
Distal CBD Involvement	55 (53.4%)
Hilar Involvement	44 (42.7%)
Moderate Dilatation	44 (42.7%)
Irregular Stricture	55 (53.4%)
Abrupt Cut-Off	56 (54.4%)
Mass Lesion Detected	40 (38.8%)
Pancreatic Head Mass	49 (47.6%)
Lymphadenopathy	55 (53.4%)
Vascular Invasion	51 (49.5%)
Gallstones	53 (51.5%)
Stricture Length (mm)	21.47 ± 10.70

Definitive histopathological diagnosis revealed 54 (52.4%) benign and 49 (47.6%) malignant cases. Among benign causes, benign stricture was most frequent (21.4%), followed by chronic pancreatitis (17.5%) and choledocholithiasis (13.6%). Among malignant etiologies, cholangiocarcinoma was the most common (19.4%), followed by ampullary carcinoma (16.5%) and pancreatic carcinoma (11.7%) (Table 4).

Table 4: Histopathological Spectrum (n=103)

Category	Diagnosis	n (%)
Benign	Benign Stricture	22 (21.4%)
	Chronic Pancreatitis	18 (17.5%)
	Choledocholithiasis	14 (13.6%)
Malignant	Cholangiocarcinoma	20 (19.4%)
	Ampullary Carcinoma	17 (16.5%)
	Pancreatic Carcinoma	12 (11.7%)

Using histopathology as the reference standard, MRCP correctly identified 47 true-positive and 52 true-negative cases, with 2 false-positive and 2 false-negative results. MRCP demonstrated a sensitivity of 95.9% and specificity of 96.3% in differentiating malignant from benign obstruction. The positive predictive value and negative predictive value were 95.9% and 96.3%, respectively. The overall diagnostic accuracy was 96.1%. Receiver operating characteristic (ROC) curve analysis further confirmed excellent diagnostic performance, with an area under the

curve (AUC) of 0.961 (95% CI: 0.918–1.000; $p < 0.001$) (Table 5).

Table 5: Diagnostic Performance of MRCP Compared with Histopathology

Parameters	Value
True positive	47
True negative	52
False positive	2
False negative	2
Sensitivity	95.9%
Specificity	96.3%
PPV	95.9%
NPV	96.3%
Accuracy	96.1%
AUC (95% CI)	0.961 (0.918–1.000)

ROC curve of MRCP for differentiating malignant from benign obstructive jaundice using histopathology as a reference standard. Receiver operating characteristic (ROC) curve of MRCP for differentiating malignant from benign obstructive jaundice using histopathology as the gold standard. The area under the curve (AUC) was 0.961 (95% CI: 0.918–1.000; $p < 0.001$), indicating excellent diagnostic performance (Figure 1).

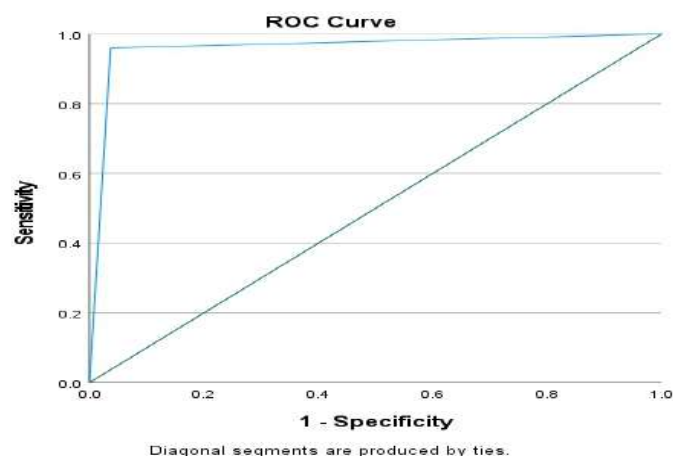


Figure 1: ROC Curve of MRCP for Differentiating Malignant from Benign Obstructive Jaundice Using Histopathology as Reference Standard

DISCUSSION

Obstructive jaundice remains a clinically challenging condition in which early differentiation between benign and malignant etiologies is essential for appropriate management and prognosis. Current international guidelines recommend a structured diagnostic approach integrating biochemical evaluation with high-quality cross-sectional imaging before proceeding to invasive procedures [13–15]. In this context, MRCP has gained recognition as a reliable non-invasive modality for the evaluation of biliary obstruction. In the present study, MRCP demonstrated excellent diagnostic performance, with a sensitivity of 95.9%, specificity of 96.3%, overall

accuracy of 96.1%, and an AUC of 0.961 when compared with histopathology. These findings are consistent with recent regional and international studies reporting sensitivity ranging from 90% to 96% and specificity exceeding 90% in differentiating malignant from benign biliary obstruction [16, 17]. The high AUC observed in this study further confirms the strong discriminative ability of MRCP in clinical practice. Radiological patterns observed in malignant cases, including irregular strictures, abrupt cut-off, associated mass lesion, lymphadenopathy, and vascular invasion, align with established imaging characteristics of biliary malignancy described in contemporary literature [18, 19]. Extrahepatic and distal common bile duct involvement was frequently observed in malignant cases, which corresponds with known distribution patterns of cholangiocarcinoma and pancreatic malignancies. These findings reinforce the reliability of morphological criteria in MRCP-based assessment. Biochemical parameters also showed significant differences between benign and malignant groups. Elevated total and direct bilirubin, transaminases, ALP, and CA 19-9 levels were associated with malignant obstruction. The significant elevation of CA 19-9 in malignant cases is consistent with recent evidence supporting its adjunctive role in cholangiocarcinoma and pancreatic cancer diagnosis [19, 20]. However, as reported in previous studies, CA 19-9 lacks absolute specificity due to false elevation in benign cholestatic and inflammatory conditions, limiting its independent diagnostic utility. In the present study, MRCP demonstrated superior discriminative performance compared with individual biochemical markers, supporting its role as the primary non-invasive diagnostic modality. A major strength of this study is the use of histopathology as the reference standard, minimizing diagnostic misclassification. The nearly balanced distribution of benign and malignant cases enhances the reliability of sensitivity and specificity estimates. Furthermore, ROC curve analysis adds robust statistical validation to the reported diagnostic performance.

Nevertheless, certain limitations must be acknowledged. The study was conducted at a single tertiary care center, which may limit generalizability. A small number of false-positive and false-negative cases were observed, likely due to overlapping imaging features between inflammatory strictures and malignancy. Advanced imaging modalities such as PET/MRI or diffusion-weighted imaging were not evaluated and may further refine diagnostic pathways in future research. Multicenter studies with larger sample sizes and standardized reporting criteria are recommended to validate these findings. Overall, the findings support current guideline recommendations

positioning MRCP as a first-line imaging modality in the evaluation of obstructive jaundice. Its high sensitivity, specificity, and negative predictive value make it an effective non-invasive gatekeeper investigation before invasive diagnostic procedures such as ERCP or surgical exploration, particularly in resource-constrained settings.

CONCLUSIONS

MRCP demonstrated excellent diagnostic accuracy in differentiating benign from malignant causes of obstructive jaundice when compared with histopathology as the reference standard. With high sensitivity, specificity, predictive values, and strong ROC performance, MRCP represents a reliable non-invasive imaging modality that supports accurate clinical decision-making and may reduce unnecessary invasive procedures.

Authors' Contribution

Conceptualization: TB

Methodology: LK

Formal analysis: TB, HB,

Writing and Drafting: TB, ZJO, LK, SN, HB, NA

Review and Editing: TB, ZJO, LK, SN, HB, NA

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All 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] Hanif H, Khan SA, Muneer S, Adil SO. Diagnostic Accuracy of Ultrasound in Evaluation of Obstructive Jaundice with MRCP as Gold Standard. *Pakistan Journal of Medical Sciences*. 2020 May; 36(4): 652. doi: 10.12669/pjms.36.4.1665.
- [2] Isram J, Haider E, Khan RS, Hafeez M, e Hinna R, Baig I et al. Diagnostic Accuracy of Magnetic Resonance Cholangiopancreatography in Comparison with Endoscopic Retrograde Cholangiopancreatography for Detection of the Etiology of Obstructive Jaundice. *Cureus*. 2023 Feb; 15(2): e34484. doi: 10.7759/cureus.34484.
- [3] Gupta M, Pattanaik R, Agarwal BD, Bahinipati P, Das S. A Comparative Study of Ultrasound, Computed Tomography, and Magnetic Resonance Cholangiopancreatography in Detecting the Etiology of Obstructive Jaundice. *International Journal of Medicine and Health Development*. 2025 Oct; 30(4): 388-96. doi: 10.4103/ijmh.ijmh_21_25.
- [4] Shimu F, Ahmed A, Shahriar S, Yasmin T, Amin MB,

- Hasan AF. Comparison of the Diagnostic Accuracy of Magnetic Resonance Cholangiopancreatography (MRCP) with Ultrasound and Computed Tomography (CT) in Evaluation of Patients with Obstructive Jaundice. *Journal of Shaheed Suhrawardy Medical College*. 2022; 14(1): 32-6. doi: 10.3329/jssmc.v14i1.70116.
- [5] Mustafa W and Alawamy S. Diagnostic Role of Magnetic Resonance Cholangiopancreatography in Evaluation of Obstructive Jaundice. *Libyan Medical Journal*. 2026 Jan; 48-55.
- [6] Katariya P, Vaishnani B, Gamit H, Vaghela S, Jasani K, Gamit Sr HH et al. Comparative Diagnostic Accuracy of Ultrasonography and Magnetic Resonance Cholangiopancreatography (MRCP) in the Evaluation of Obstructive Jaundice: A Prospective Study in Western India. *Cureus*. 2025 Dec; 17(12). doi: 10.7759/cureus.100312.
- [7] Sherpa NT, Manandhar S, Karki A, Karki P. Accuracy of Magnetic Resonance Cholangiopancreatography in the Diagnosis of Benign and Malignant Cause of Obstructive Jaundice. *Journal of Patan Academy of Health Sciences*. 2022 Jun; 9(1): 65-71. doi: 10.3126/jpahs.v9i1.43896.
- [8] Chawla S, Sharma M, Makkar A, Tripathi N, Gupta P, Pahal N. Comparative Assessment to Establish the Accuracy of MRCP Over USG and CT in Diagnosing the Case of Obstructive Jaundice. *European Journal of Molecular and Clinical Medicine*. 2022 Jan; 9(1): 1113-9.
- [9] Khalid MS, Arooj S, Ahmed A, Mansoor A, Masood M. Diagnostic Accuracy of Ultrasound Sonography Test and Computed Tomography Compared with Magnetic Resonance Cholangio Pancreatography in Patients with Obstructive Jaundice Considering Endoscopic Retrograde Cholangio Pancreatography as Gold Standard. *Journal of Postgraduate Medical Institute*. 2023 Aug; 37(3): 201-7. doi: 10.54079/jpmi.37.3.3226.
- [10] Rațiu I, Lupușoru R, Lungeanu D, Popescu A, Sporea I, Goldiș A et al. Diagnosis of Malignant Biliary Obstruction: Pondering Over the ERCP, MRCP and Histology. *Journal of International Medical Research*. 2022 Feb; 50(2): 03000605221076924. doi: 10.1177/03000605221076924.
- [11] Chhettri P and Rana H. Ultrasonography and Magnetic Resonance Cholangiopancreatography in Patients with Obstructive Jaundice. *Journal of College of Medical Sciences-Nepal*. 2020 Mar; 16(1): 6-11. doi: 10.3126/jcmsn.v16i1.26641.
- [12] Samier HM, Selim AF, Sarhan ME, Dawoud TM. Diagnostic Accuracy of Magnetic Resonance Cholangiopancreatography (MRCP) Combined with Multidetector Computed Tomography (MDCT) in Determining the Nature of Biliary Stricture. *Egyptian Journal of Radiology and Nuclear Medicine*. 2025 Sep; 56(1): 168. doi: 10.1186/s43055-025-01585-z.
- [13] European Association for the Study of the Liver. EASL-ILCA Clinical Practice Guidelines on the management of intrahepatic cholangiocarcinoma. *Journal of Hepatology*. 2023 Jul; 79(1): 181-208. doi: 10.1016/j.jhep.2023.03.010.
- [14] Dar FS, Abbas Z, Ahmed I, Atique M, Aujla UI, Azeemuddin M et al. National Guidelines for the Diagnosis and Treatment of Hilar Cholangiocarcinoma. *World Journal of Gastroenterology*. 2024 Mar; 30(9): 1018. doi: 10.3748/wjg.v30.i9.1018.
- [15] Facciorusso A, Crinò SF, Gkolfakis P, Spadaccini M, Arvanitakis M, Beyna T et al. Diagnostic Work-Up of Bile Duct Strictures: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy*. 2025 Feb; 57(02): 166-85. doi: 10.1055/a-2481-7048.
- [16] Patel VB, Musa RK, Patel N, Patel SD. Role of MRCP to Determine the Etiological Spectrum, Level, and Degree of Biliary Obstruction in Obstructive Jaundice. *Journal of Family Medicine and Primary Care*. 2022 Jul; 11(7): 3436-41. doi: 10.4103/jfmpc.jfmpc_2362_21.
- [17] Rashid S, Mehmood S, Suqrat H. Comparison of Diagnostic Usefulness of Magnetic Resonance Cholangiopancreatography (MRCP) with Endoscopic Retrograde Cholangiopancreatography (ERCP) in Evaluation of Patients with Obstructive Jaundice. *The Professional Medical Journal*. 2023 Aug; 30(08): 977-81. doi: 10.29309/TPMJ/2023.30.08.7639.
- [18] Samanvitha H, Shivagange SP, Sajjan SS, Sajjan Sr SS. When the Gut Took a Wrong Turn to the Right: A Case Report of a Rare Complication of Closed Loop Small Bowel Obstruction with Small Bowel Volvulus in a Right Paraduodenal Hernia with Midgut Malrotation. *Cureus*. 2024 Jan; 16(1).
- [19] Liu B, Wang S, Wen T, Qiu H, Xiang L, Huang Z et al. Developing a Prognostic Model for Intrahepatic Cholangiocarcinoma Patients with Elevated Preoperative Carbohydrate Antigen 19-9 Levels: Volume-Adjusted CA19-9 (VACA) as a Novel Biomarker. *Cancer Control*. 2025 Jan; 32: 10732748251317692. doi: 10.1177/10732748251317692.
- [20] Luo G, Jin K, Deng S, Cheng H, Fan Z, Gong Y et al. Roles of CA19-9 in Pancreatic Cancer: Biomarker, Predictor and Promoter. *Biochimica et Biophysica Acta (BBA)-Reviews on Cancer*. 2021 Apr; 1875(2): 188409. doi: 10.1016/j.bbcan.2020.188409.



Original Article



Visual Outcome and Topographic Parameters Stability after Corneal Ring Segment Surgery in Keratoconus

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ARTICLE INFO

Keywords:

Keratoconus, Ring Segments, Femtolaser, Kmax, Topography

How to Cite:

Khan, S. Z., Khan, A. A., Rasheed, A., Saeed, R., Saeed, A., Ali, S., Malik, A. M., & Ahmed, W. (2026). Visual Outcome and Topographic Parameters Stability after Corneal Ring Segment Surgery in Keratoconus: Topographic Parameters Stability after Corneal Ring Segment Surgery in Keratoconus. Pakistan Journal of Health Sciences, 7(6), 75-80. <https://doi.org/10.54393/pjhs.v7i6.3908>

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Received Date: 30th January, 20261st Revision Received: 11th March, 20262nd Revision Received: 18th March, 2026Acceptance Date: 31st March, 2026Published Date: 30th June, 2026

ABSTRACT

Keratoconus is a bilateral, non-inflammatory disease that leads to the bulging outward of a cone-shaped cornea affecting both genders. The major symptoms are blurring of vision, distortion of images, and difficulty in night driving. **Objectives:** To find the improvement in distance best corrected visual acuity (BCVA) and maximum keratometry (Kmax) from the baseline values up to three months following the implantation of ICRS. **Methods:** This study was employed as a retrospective consecutive cohort, which included all eligible keratoconus subjects visiting Out Patient Department, Fatima Memorial Hospital. All twenty-five cases underwent a comprehensive clinical ocular examination followed by Pentacam corneal topography. Those willing for the Kerrara ring segment implant for visual rehabilitation were enrolled. All surgeries were performed by a single surgeon with Femtolaser technology. **Results:** A total of twenty-five subjects were implanted with Ferrara Rings. Regarding the visual outcome, a statistically significant improvement in uncorrected visual acuity (UCVA) was observed following implantation of the Ferrara cornea rings ($p < 0.001$). Similarly, the K max values also demonstrated a decreasing trend from 52.88 ± 4.80 preoperatively to 50.42 ± 4.61 postoperatively ($p < 0.001$). Hence, it was documented that a reduction in Kmax values indicates a significant flattening in corneal regularity and topographic stability after Ferrara segment implantation. **Conclusions:** The results of this observational study showed a significant improvement in visual acuity and a reduction in K max values due to the spacer effects of ICRS, resulting in an overall improvement in the quality of life of Keratoconus patients.

INTRODUCTION

Keratoconus (KC) is a non-inflammatory, progressive disorder that causes the cornea to thin and bulge outward into a cone shape. This consequently distorts both the anterior and posterior surfaces of the cornea, leading to irregular astigmatism and myopia. As a result, light entering the eye is not properly focused on the retina, causing blurry, distorted vision. The condition usually develops in the late teens or early twenties and continues

to progress for the next ten to twenty years before stabilizing, although the degree of progression of the disease may vary widely. These patients commonly experience various symptoms like blurring and distortion of images, increased sensitivity to light and glare, and driving at night becomes difficult due to halos around bright light. Moreover, subjects complain of frequent changes in the prescription of eyeglasses and intolerance



to contact lenses [1]. Multiple factors have been implicated in the pathophysiology of keratoconus. In the past, it was considered primarily as a biomechanical disorder leading to bulging of the cornea. However, recent research highlighted that structural abnormalities within the cornea, disruptions in collagen lamellae, reduced levels of collagen crosslinking, and deranged lysosomal enzyme activity were the main pillars of etiology and progression of Keratoconus [2]. In addition, very recently, the significant role of immunologic changes and oxidative stress has been implicated as a causative factor. The increased levels of cytokines, including IL-1 β , IL-6, IL-17, and TNF- α , along with increased apoptosis of keratocytes, have supported it [3]. Furthermore, it was postulated that high oxidative stress stimulated the collagenase and gelatinase enzymes, contributing to collagen degradation. There is a high rate of cousin marriages in this country; consequently, the role of genetic predisposition is an important risk factor leading to the development of disease in young people. Additionally, multiple environmental factors, such as high levels of humidity, wind, dust, and dirt, can lead to chronic allergic responses in the eyes. Consequently, it is associated with frequent and forceful rubbing of the eyes. All these factors have been strongly implicated, possibly by inducing mechanical stress that triggers the release of pro-inflammatory mediators, ultimately contributing to structural modifications and ectasia. Despite advancements in operative techniques for managing corneal diseases, keratoconus remains a frequent indication for penetrating keratoplasty in underdeveloped countries of Southeast Asia. Hence, there was a dire need for effective, minimally invasive interventions to manage visually debilitating conditions like keratoconus. Intrastromal Corneal Ring Segments (ICRS), Ferrara rings, are small, clear devices made up of polymethylmethacrylate (PMMA). The fundamental mechanism of ICRS involves the implantation within the mid-corneal peripheral part of the stroma. It is usually placed at approximately two-thirds of the corneal depth, outside the central optical zone. The rings act as spacer elements between corneal lamellae; these segments induce an arc-shortening effect, which effectively shortens the central arc length of the cornea and consequently flattens the central anterior conical surface of the cornea [4]. Due to this reshaping, it will regularize the irregular astigmatism and reduce the associated myopia, thereby improving visual acuity. It has been observed that the degree of corneal flattening achieved is directly proportional to the thickness and inversely proportional to the diameter of the intracorneal ring segments [5]. In addition, patient counseling, such as reduced eye rubbing and avoiding dusty, windy environments, might also contribute to perceived stability. ICRS implantation has

been considered a minimally invasive and reversible procedure for keratoconus treatment [6]. Moreover, it provided a valuable option to more invasive surgical procedures like corneal transplantation, especially for cases where visual acuity could no longer be adequately corrected with glasses and subjects were intolerant to contact lenses [7].

Even though it has been shown that intrastromal corneal ring segments (ICRS) have been effective in terms of enhancing the visual acuity and corneal topography, little has been done in terms of enduring results, extensive population-based results, and even comparative outcomes with other methods of the surgery, particularly in the local population with a low socioeconomic status and with short follow-up periods. Keratoconus causes cumulative visual impairment, and most patients in developing countries have no access to effective, least invasive, and sustainable methods of treatment. As such, there is a need to assess the short-term effectiveness and safety of using ICRS implantation in enhancing the visual and topographic performance among these populations. This study aimed to evaluate the efficacy and safety of ICRS implantation. The findings contributed preliminary data to the existing literature regarding the impact on visual, refractive, and topographic parameters and complications in patients with Keratoconus in the local population.

METHODS

This retrospective observational cohort study design was based on reviewing the electronic medical records of keratoconus patients who underwent Ferrara ring segment implantation in the cornea. The study was conducted at Fatima Memorial Hospital College of Medicine and Dentistry, Lahore. The data collection was initiated before the approval of the institutional review board. In light of this methodology, the consecutive sampling technique was employed. The study was approved by the IRB of the hospital vide reference no FMH-05/08/2025-IRB-1701 dated 15th September 2025. The sample size was calculated by using the WHO sample size formula, taking a standard deviation of nearly 3 to 4 diopters of Kmax after the implantation of Ferrara rings in the cornea. With a 95% confidence level and precision of 1.5 diopters, the minimum sample size was calculated as 21 eyes. With consideration of potential loss to follow-up, the final sample size of 25 eyes was selected [8]. After the approval, those patients who fulfilled the inclusion and exclusion criteria underwent implantation of Ferrara rings between 16 September 2025 and January 2026. The surgery was performed under topical anesthesia, with a dedicated Department of Corneal and Refractive Surgery on the Femtosecond LDV Z6 Platform at Amanant Eye

Centre, Lahore. The inclusion criteria for each patient were a history of intolerance to glasses and contact lenses, aged more than eighteen years, best-corrected visual acuity (BCVA) less than 6/12 in both eyes, Pentacam topography confirmed the presence of keratoconus, and progression was documented on two consecutive scans at least one month apart from the previous examination. Moreover, a corneal thickness of 380 microns or greater at the 5 mm zone of the placement of stromal ring segments was established. Patients with conditions, such as a history of glaucoma and cataract surgeries, corneal cross-linking, other refractive surgeries, and keratoplasty, were also not considered for this procedure. Presence of corneal hydrops or significant central corneal scarring and active ocular infection, especially bacterial and viral keratitis or uncontrolled inflammation in either eye at the time of surgery. Moreover, known systemic collagen vascular diseases, pregnancy, autoimmune disorders, or immunodeficiency diseases were excluded from the study. In this study, visual acuity was assessed by using the Snellen charts and converted to Log MAR values for data analysis. Pentam Topograph was used for corneal topography. On line Ferrara ring calculator was used to assess the number and size of the segments [9]. To ensure reproducibility, all measurements were conducted by a single Pentacam machine and the same professionally trained optometrist. For the safety of the subjects, broad-spectrum Moxifloxacin topical drops were initiated a week before the surgery, and a sterile environment was ensured in the operating room. A close post-operative follow-up scheduled at 1st, 2nd weeks, 1 month, and 3 months was maintained.

In this study, statistical analysis was performed by using the SPSS Statistics platform with version 23.0. Continuous variables like BCVA, pachymetry readings, Kmax values were expressed as mean $\pm$ SD to check the normal distribution. Normality was assessed using the Shapiro-Wilk tests. To compare the pre- and post-operative values after Ferrara ring implantation using paired t-test was employed. In addition, the categorical variables were tabulated as frequencies and percentages. As per standardized practice, a p-value < 0.050 was considered statistically significant.

RESULTS

A total of 25 patients who underwent corneal Ferrara Rings implantation for mild to moderate visually compromising keratoconus were included in this study. The mean age of patients in this series was 20.50 ± 2.75 SD years. There was a male predominance among the enrolled subjects, as 68% were male and 32% were female. During the postoperative follow-up of these cases, clinical complications were generally mild and self-limited. After the femtosecond

laser docking of the footplate on the eye, subconjunctival hemorrhage occurred in 56% of patients, which resolved within a week with topical treatment. All these patients underwent a surgical procedure under short-acting topical anesthesia. During the ring insertion, due to corneal tissue handling and manipulation to implant the ring, corneal epithelial defects were observed in 11(44%) patients. However, none of these cases had developed active stromal keratitis. In addition, no segment extrusion and segment decentration were observed throughout the follow-up period. Moreover, during the early post-operative follow-up, glare or haloes were reported by 14 (56%) patients, which progressively diminished. Regarding the visual outcome, a statistically significant improvement in uncorrected visual acuity (UCVA) was observed following implantation of the Ferrara corneal rings (Table 1).

Table 1: Demographics of Study Participants

Variables	n (%)
Gender	
Male	17 (68%)
Female	8 (32%)
Complications	
Hemorrhage	14 (56%)
Corneal Lesion	11 (44%)
Keratitis	0 (0%)
Extrusion	0 (0%)
Decentration	0 (0%)
Glare/Haloes	14 (56%)

The pre-operative right-eye visual acuity assessed by the Log Mar chart showed a mean of 1.15 ± 1.43 , which improved significantly postoperatively to 0.34 ± 0.16 ($p < 0.001$). In addition, the left-eye post-operative visual assessment also demonstrated a mean of 0.35 ± 0.16 , compared with a pre-operative mean of 0.85 ± 0.18 . Both these improvements in the indices indicated a remarkable visual gain in both eyes following minimally invasive surgery. There was a significant flattening of corneal curvature as demonstrated on post-operative topographic measurements (Table 2).

Table 2: Comparison between Pre and Post Visual Outcomes

Visual Outcome	Mean $\pm$ SD	p-value
VA Right Eye Pre-Op	1.15 ± 1.43	<0.001
VA Right Eye Post-Op	0.34 ± 0.16	
VA Left Eye Pre-Op	0.85 ± 0.17	<0.001
VA Left Eye Post-Op	0.35 ± 0.16	

The preoperative K max for the right eye was 52.58 ± 4.12 , which decreased statistically significantly to 50.42 ± 3.81 postoperatively ($p < 0.001$). Similarly, the left-eye K max also demonstrated a decreasing trend from 52.88 ± 4.80 preoperatively to 50.42 ± 4.61 postoperatively ($p < 0.001$). Hence, it was inferred that a reduction in Kmax values

would indicate an improvement in corneal regularity and topographic stability after Ferrara segment implantation (Table 3).

Table 3: Comparison Between Pre-Op and Post Op Kmax Readings

K max Cornea	Mean $\pm$ SD	Minimum	Maximum	p-value
Kmax RE Pre-Op	52.58 $\pm$ 4.12	45.00	62.40	<0.001
Kmax RE Post-op	50.42 $\pm$ 3.81	45.00	59.20	
Kmax LE Pre-Op	52.88 $\pm$ 4.80	45.00	62.40	<0.001
Kmax LE Post-Op	50.42 $\pm$ 4.61	45.20	59.20	

DISCUSSION

The present study demonstrated that Ferrara corneal ring segment implantation resulted in a marked improvement in visual acuity and a meaningful reduction in corneal steepening among patients with keratoconus. The arc shortening effect on keratoconus patients following ring implantation has also been reported in previous studies, which consequently resulted in an improvement of visual status and anterior corneal topographic parameters [10]. Colin et al. implanted the Intacs rings. They followed the post implantation Pentacam topographic scans and revealed a favourable improvement in best corrected visual acuity (BCVA) and significant reduction in Kmax in both eyes, which resulted in flattening of the cornea by approximately 1.5 to 3.75 D. The same observation was inferred in this study with BCVA improved from 1.1 ± 1.43 to 0.34 ± 0.16 ($p=0.001$) and Kmax 52.58 ± 4.12 to 50.42 ± 3.81 ($p=0.001$) [11]. In the published series by Ertan et al. also used Femtosecond laser for the management of Keratoconus and reported a substantial improvement in vision and decreased corneal irregularity following Ferrara and Intacs segment implantation. These findings were synchronous with our findings [12]. In addition, in a case series by Sandes et al. evaluated the visual status after concentric ring implantation in cases of asymmetric Keratoconus. They documented better corneal regularity and a favourable visual outcome post-operatively [13]. These findings were similar to the present study as ectatic corneas had achieved good regularity, hence improved vision post-operatively. Moreover, in keratoconus management, corneal topographic stability, even after placing the single segment Intacs ICRS implantation, played a significant role in predicting the post-operative visual outcome. The study by Vega-Estrada et al. analysed the clinical and Pentacam topography parameters and reported that they remained stable during the six-month to one-year follow-up [14]. In the present study, all cases were followed both clinically and with Pentam topography and had a good, stable visual and refractive outcome. However, due to social and economic constraints, most of the patients were followed 3 months postoperatively. During

post-operative follow-up, no vision-threatening complications like infectious keratitis, segment migration, or extrusion were observed. However, Bautista-Llamas reviewed post-operative data of Keratoconus cases and reported a minimum rate of complications, which led to migration and explantation of intrastromal corneal ring segments [15]. Moreover, two large series analysed the post-operative complications and documented that 6.1% ICRS were explanted from a total cohort of 572 eyes. They divided it into two groups; out of these, 2.6% were explanted for medical complications, and 3.5% for unfavourable refractive outcomes [16, 17]. Contrary to this, no device was explanted in this study. This difference might be due to the strict sterilization measures practiced in the operating room and meticulous refractive and topographic assessment by modern Pentacam topography. In addition, we performed all the procedures by using a Femtosecond laser with a predefined precise depth of the corneal tunnel [18]. In contrast, due to meticulous pre and post-operative monitoring, not a single case of migration or extrusion, or infectious keratitis of the device was reported in this study. Izquierdo et al. formalised a series of 40 eyes of central Keratoconus operated with Femtolaser z6 with good visual status. It was substantiated that both visual acuity and mean keratometry readings had statistically significant improvement ($p<0.001$) after 1 year follow-up [19]. In the present study, the same methodology was practiced, and good visual and keratometry outcomes were inferred by using Femtolaser in ectatic corneas. In another retrospective study, Monterosso et al. opted for deep lamellar keratoplasty in Keratoconus patients. They authored a BCVA of 0.9 ± 0.08 Log MAR and zero rate of graft failure post-operatively. On the contrary, the safety and efficacy of the Ferrara corneal ring documented in this study strengthen the evidence supporting ICRS as a viable option in the management of keratoconus, particularly in countries where a cornea bank system does not exist and donor corneal tissue availability is very limited [20].

There were a few limitations in this study. Due to the socioeconomic constraints, most of the keratoconus patients resort to non-surgical options like glasses and contact lenses. However, due to the progressive nature of the disease, it usually progresses to an advanced form of ectatic cornea. This resulted in a small sample size for intra-stroma rings, which were indicated for mild to moderate cases of keratoconus. Moreover, our patients belonged to far-flung areas of the province, and due to difficulty in boarding and lodging in a cosmopolitan city, we had short follow-ups with the patients. In future studies, a larger sample size, longer follow-up, and a comparison between Femtolaser-coupled deep lamellar keratoplasty and femtosecond-assisted ring implantation are

recommended to validate the stability and adaptability of ICRS by the ophthalmologist.

CONCLUSIONS

Ferrara corneal ring segment implantation demonstrated significant improvement in visual outcome and reduced corneal topographic evidence of steepening in patients with keratoconus. This procedure has proven its effectiveness as a minimally invasive method for visual rehabilitation in keratoconus patients.

Authors' Contribution

Conceptualization: SZK

Methodology: SZK, RS

Formal analysis: AAK, AR, SA, WA

Writing and Drafting: SZK, AAK, AS, AMM

Review and Editing: SZK, AAK, AR, RS, AS, SA, AMM, WA

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All 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] Moscovici BK, Rodrigues PF, Rodrigues RA, Rios LC, Simoncelli R, Freitas MM et al. Evaluation of Keratoconus Progression and Visual Improvement After Intrastromal Corneal Ring Segments Implantation: A Retrospective Study. *European Journal of Ophthalmology*. 2021 Nov; 31(6): 3483-9. doi: 10.1177/11206721211000646.
- [2] Navel V, Malecaze J, Pereira B, Baker JS, Malecaze F, Sapin V et al. Oxidative and Antioxidative Stress Markers in Keratoconus: A Systematic Review And Meta-Analysis. *Acta Ophthalmologica*. 2021 Sep; 99(6): e777-94. doi: 10.1111/aos.14714.
- [3] D'Souza S, Nair AP, Sahu GR, Vaidya T, Shetty R, Khamar P et al. Keratoconus Patients Exhibit A Distinct Ocular Surface Immune Cell and Inflammatory Profile. *Scientific Reports*. 2021 Oct; 11(1): 20891. doi: 10.1038/s41598-021-99805-9.
- [4] Dal A, Canleblebici M, Kutluksaman B, Erdağ M. Effects and Safety of Combined Corneal Collagen Crosslinking and Intrastromal Corneal Ring Segment Treatment in Patients with Keratoconus: A Retrospective Study. *BioMed Central Ophthalmology*. 2024 Oct; 24(1): 473. doi: 10.1186/s12886-024-03745-7.
- [5] Costa JV, Monteiro T, Franqueira N, Faria-Correia F, Alfonso J, Vaz F. Five-Year Long-Term Outcomes of Intrastromal Corneal Ring Segment Implantation Using the Manual Technique for Keratoconus Management. *Journal of Cataract and Refractive Surgery*. 2021 Jun; 47(6): 713-21. doi: 10.1097/j.jcrs.000000000000500.
- [6] Friedrich M, Auffarth GU, Soiberman U, Augustin VA, Khoramnia R, Son HS. Visual and Topographic Outcomes After Corneal Allogeneic Intrastromal Ring Segments for Keratoconus: A Systematic Review and Meta-Analysis. *American Journal of Ophthalmology*. 2025 Aug; 276: 81-91.
- [7] Elbassiouny KA, Hafez TA, Osman IA, Elmassry AA. Evaluation of Long-Term Outcomes of Simultaneous Corneal Collagen Cross-Linking and Femtosecond Laser-Assisted Intracorneal Ring Segment Implantation For Keratoconus. *Journal of the Egyptian Ophthalmological Society*. 2022 Apr; 115(2): 49-53. doi: 10.4103/ejos.ejos_65_21.
- [8] Coskunseven E, Kymionis GD, Tsiklis NS, Atun S, Arslan E, Jankov MR et al. One-Year Results of Intrastromal Corneal Ring Segment Implantation (Keraring) Using Femtosecond Laser in Patients with Keratoconus. *American Journal of Ophthalmology*. 2008 May; 145(5): 775-9. doi: 10.1016/j.ajo.2007.12.022.
- [9] Torquetti L and Ferrara P. The Ferrara Intrastromal Corneal Ring Segment Nomogram. In *Keratoconus: A Comprehensive Guide to Diagnosis and Treatment*. Cham: Springer International Publishing. 2022 Oct: 507-514. doi: 10.1007/978-3-030-85361-7_43.
- [10] Alió JL, Shabayek MH, Artola A. Intracorneal Ring Segments for Keratoconus Correction: Long-Term Follow-Up. *Journal of Cataract and Refractive Surgery*. 2006 Jun; 32(6): 978-85. doi: 10.1016/j.jcrs.2006.02.044.
- [11] Colin J and Malet FJ. Intacs for the Correction of Keratoconus: Two-Year Follow-Up. *Journal of Cataract and Refractive Surgery*. 2007 Jan; 33(1): 69-74. doi: 10.1016/j.jcrs.2006.08.057.
- [12] Ertan A and Kamburoğlu G. Intacs Implantation Using A Femtosecond Laser for Management of Keratoconus: Comparison of 306 Cases In Different Stages. *Journal of Cataract and Refractive Surgery*. 2008 Sep; 34(9): 1521-6. doi: 10.1016/j.jcrs.2008.05.028.
- [13] Sandes J, Ferrara P, Moscovici BK. Concentric Intrastromal Corneal Ring Implantation for Asymmetric Keratoconus: A Case Series. *International Journal of Keratoconus and Ectatic Corneal Diseases*. 2025 Apr; 11(1): 54-9. doi: 10.5005/jp-journals-10025-1210.

- [14] Vega-Estrada A, Del Barrio JA, Alio JL. Intracorneal Ring Segments and Keratoconus. In *Controversies in the Management of Keratoconus*. Cham: Springer International Publishing. 2018 Dec; 221-234. doi: 10.1007/978-3-319-98032-4_19.
- [15] Bautista-Llamas MJ, Sánchez-González MC, López-Izquierdo I, López-Muñoz A, Gargallo-Martínez B, De-Hita-Cantalejo C et al. Complications and Explantation Reasons in Intracorneal Ring Segments (ICRS) Implantation: A Systematic Review. *Journal of Refractive Surgery*. 2019 Nov; 35(11): 740-7. doi: 10.3928/1081597X-20191010-02.
- [16] D'Oria F, Abdelghany AA, Ledo N, Barraquer RI, Alio JL. Incidence and Reasons for Intrastromal Corneal Ring Segment Explantation. *American Journal of Ophthalmology*. 2021 Feb; 222: 351-8. doi: 10.1016/j.ajo.2020.09.041.
- [17] Larco P, Larco Jr P, Torres D, Piñero DP. Intracorneal Ring Segment Implantation for the Management of Keratoconus in Children. *Vision*. 2020 Dec; 5(1): 1. doi:10.3390/vision5010001.
- [18] Prisant O, Pottier E, Guedj T, Xuan TH. Clinical Outcomes of an Asymmetric Model of Intrastromal Corneal Ring Segments for the Correction of Keratoconus. *Cornea*. 2020 Feb; 39(2): 155-60. doi: 10.1097/ICO.0000000000002160.
- [19] Izquierdo Jr L, Rodríguez AM, Sarquis RA, Altamirano D, Henriquez MA. Intracorneal Circular Ring Implant with Femtosecond Laser: Pocket Versus Tunnel. *European Journal of Ophthalmology*. 2022 Jan; 32(1): 176-82. doi:10.1177/1120672121994729.
- [20] Monterosso C, Antonini M, Di Zazzo A, Gaudenzi D, Caretti L, Coassin M et al. Femtosecond Laser-Assisted Deep Anterior Lamellar Keratoplasty: A Safer Option in Keratoconus Surgery. *European Journal of Ophthalmology*. 2022 Jan; 32(1): 59-65. doi:10.1177/11206721211059023.



Original Article



Association of Plasma Fibrinogen Levels with Severity of Postpartum Hemorrhage: A Cross-Sectional Study

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ARTICLE INFO

Keywords:

Postpartum Hemorrhage, Fibrinogen, Hemostasis, Obstetric Bleeding

How to Cite:Zainab, A., Naz, M. K., Fawad, E., Fawad, R., Osaf, H., & Hamdani, S. S. Q. (2026). Association of Plasma Fibrinogen Levels with Severity of Postpartum Hemorrhage: A Cross-Sectional Study: Fibrinogen Levels in Postpartum Hemorrhage. *Pakistan Journal of Health Sciences*, 7(6), 81-86. <https://doi.org/10.54393/pjhs.v7i6.3979>***Corresponding Author:**Arfa Zainab
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ABSTRACT

Postpartum hemorrhage (PPH) significantly contributes to maternal morbidity and mortality worldwide. Identifying women at risk for severe PPH early is essential for timely intervention. **Objective:** To compare the mean plasma fibrinogen level between women with severe and non-severe postpartum hemorrhage (PPH). **Methods:** This comparative cross-sectional study was performed after its approval from the ethical committee with approval number Admin/PF/722A dated 2nd July 2025 in the Department of Obstetrics and Gynecology at Cantt General Hospital, Rawalpindi, from July 3, 2025, to December 30, 2025. A total of 60 women with postpartum hemorrhage were enrolled using a consecutive sampling technique and categorized into non-severe PPH (n=30) and severe PPH (n=30) based on predefined clinical criteria. Plasma fibrinogen levels were assessed at the time of postpartum hemorrhage diagnosis with IBM SPSS version 25.0. A p-value of less than 0.05 was considered statistically significant. **Results:** Women experiencing severe PPH exhibited significantly lower fibrinogen levels in comparison to those with non-severe hemorrhage. The mean fibrinogen level in the non-severe postpartum hemorrhage group was 4.55 ± 1.06 g/L, but in the severe PPH group it was 3.53 ± 0.66 g/L, indicating a statistically significant difference ($p=0.001$). The findings demonstrate an inverse association between fibrinogen concentration and the severity of PPH, showing that lower fibrinogen levels are associated with an increased likelihood of severe bleeding. **Conclusions:** Reduced fibrinogen levels were significantly associated with severe PPH. Early measurement of fibrinogen may assist in identifying patients at increased risk of severe hemorrhage and ensure prompt management.

INTRODUCTION

Postpartum hemorrhage (PPH) is one of the most common causes of maternal morbidity and mortality worldwide, especially in low- and middle-income countries. Defined as a blood loss of 500mL or more after vaginal delivery or 1000mL or more after cesarean section, PPH is responsible for a considerable number of preventable maternal deaths [1]. Statistics show that 99% of all maternal deaths occurred in developing countries, and of them, 27.1% are caused by postpartum hemorrhage [2]. Early recognition and prompt management are vital for counteracting the negative effects that this condition can lead to. Amid the slew of determinants that affect the severity of PPH,

fibrinogen status has become a hugely important determinant in recent years [3]. Fibrinogen is a glycoprotein predominantly produced in the liver and is integral to the hemostatic mechanism. It serves as the substrate for thrombin, facilitates platelet aggregation, and generates fibrin clots crucial for hemostasis. During pregnancy, the fibrinogen levels usually increase to compensate for the hypercoagulable state needed to prevent hemorrhage during delivery [4]. However, in cases of severe PPH, hypofibrinogenemia is an early marker of coagulopathy that is associated with increased bleeding severity and poor clinical outcome. Despite this known



relationship between fibrinogen and PPH, consensus exists only to a limited extent on exactly how low fibrinogen levels are predictive of critical PPH and the extent to which they should shape the clinical decision process [5]. Fibrinogen plasma levels can predict the likelihood of significant bleeding in patients with postpartum hemorrhage; nevertheless, it remains uncertain whether the association between fibrinogen and PPH is causal or associative [6]. A retrospective cohort study of 103 patients indicated that early fibrinogen replacement based on shock index and lactate levels improves hemostatic control and reduces intensive care unit admissions in major postpartum hemorrhage [7]. This study was designed to assess the mean fibrinogen level and severity of PPH, focusing on the identification of possible thresholds for intervention and the prognostic implications of hypofibrinogenemia. By clarifying this relationship, we hope to yield insights that will lead to improved risk stratification and lead to evidence-based management protocols for PPH, which ultimately lead to improved maternal outcomes.

Despite growing evidence that fibrinogen is an early indicator of hemorrhage severity, low- and middle-income countries (LMICs), such as Pakistan, where PPH is a prominent cause of maternal mortality, have inadequate data, highlighting a critical gap in context-specific evidence. Early laboratory predictors that assist doctors in quickly identifying women at risk of severe bleeding are especially useful in resource-limited settings, where delayed recognition contributes to poor maternal outcomes. Therefore, this study compared plasma fibrinogen levels in women with severe and non-severe PPH to assess their therapeutic relevance in early risk stratification, especially in Pakistani healthcare.

METHODS

After receiving approval from the Ethical Review Committee (Ref. No. Admin/PF/722A; dated 2nd July, 2025), a comparative cross-sectional study was undertaken in the Department of Obstetrics and Gynecology of Cantt General Hospital, Rawalpindi, for 6 months from 3rd July 2025 to 30th December 2025. A total of 60 women were included in the study, with 30 patients in each group. The sample size was calculated using the World Health Organization sample size calculator version 2.0 for comparison of two means, assuming a power of 80% and a significance level of 5%. The calculation was based on previously reported mean fibrinogen levels of 4.2 ± 1.2 g/L in non-severe postpartum hemorrhage and 3.4 ± 0.9 g/L in severe postpartum hemorrhage [8]. Study participants were recruited using consecutive sampling from all eligible women presented with PPH during the study duration. Women aged between 18 and 45 years with postpartum

hemorrhage (PPH) as per the operational definition presented for the study. PPH was defined as blood loss of ≥ 500 mL after vaginal delivery or cesarean delivery within 24 hours after childbirth. Non-severe PPH was considered when bleeding would only necessitate medical handling without hemodynamic instability (i.e., hemodynamic instability defined as systolic blood pressure < 90 mmHg or heart rate > 100 beats/min) or operative treatment. Severe PPH was defined as hemorrhage that was characterized by hemodynamic instability, blood transfusion of two or more units, or surgery, such as uterine artery embolization or hysterectomy. Women with pre-existing coagulopathies, liver dysfunction or incomplete medical records were excluded from the study. After informed consent, eligible patients were included. The patients were predominantly divided into two groups, namely, non-severe and severe PPH, based on predefined operational definitions. Fibrinogen levels were checked at the time of diagnosis for the PPH with standard laboratory methods. The mode of delivery (spontaneous vaginal delivery, assisted delivery, or cesarean section) was recorded. Data was collected on a structured questionnaire, and it contained patient identification information (serial number, registration number, name, and age), obstetric history (gestational age and parity), physical parameters (BMI), classification of PPH (severe or non-severe), and clinical outcomes (mean fibrinogen levels). To minimize potential confounding, stratification was conducted based on age, gestational age, body mass index (BMI), parity, and mode of delivery. Post-stratification statistical comparisons were then conducted to assess whether these variables affected the association between fibrinogen levels and the severity of PPH. Normality of continuous variables was evaluated using the Shapiro-Wilk test before applying parametric statistical tests.

Data were analyzed using IBM SPSS version 25.0. Continuous variables were presented as Mean $\pm$ SD, while categorical variables were expressed as frequencies and percentages. An independent sample t-test was applied to compare mean fibrinogen levels between severe and non-severe postpartum hemorrhage groups. Furthermore, binary logistic regression analysis was conducted to evaluate the association between fibrinogen levels and the severity of postpartum hemorrhage while controlling for potential confounders. A p-value of less than 0.05 was considered statistically significant.

RESULTS

The demographic and obstetric characteristics of women with non-severe (Group A) and severe (Group B) postpartum hemorrhage. The mean age was 30.60 ± 8.04 years for Group A and 31.20 ± 7.04 years for Group B. Gestational ages ≤ 39 weeks were found in 70.0% of Group A and 73.3% of

Group B, with mean gestational ages of 38.97 ± 1.47 weeks. Group A had a mean BMI of 25.90 ± 3.81 kg/m². Most study participants (56.7% Group A, 63.3% Group B) had normal BMIs. Multiparous women were the largest subgroup (43.3% in Group A, 46.7% in Group B), and vaginal deliveries were most common (Table 1).

Table 1: Baseline Demographic and Obstetric Characteristics of Study Participants

Variables	Group A (Non-severe PPH) n=30	Group B (Severe PPH) n=30	p-value
Age Groups			
≤30 years	17 (56.7%)	16 (53.3%)	0.790
>30 years	13 (43.3%)	14 (46.7%)	
Mean Age (Years)	30.60 ± 8.04	31.20 ± 7.04	0.760
Gestational Age			
≤ 39 weeks	21 (70.0%)	22 (73.3%)	0.770
>39 weeks	9 (30.0%)	8 (26.7%)	
Mean Gestational age (weeks)	38.97 ± 1.47	38.50 ± 1.58	0.230
BMI Category			
Normal	17 (56.7%)	19 (63.3%)	0.740
Overweight	8 (26.7%)	8 (26.7%)	
Obese	5 (16.6%)	3 (10.0%)	
Mean BMI (kg/m ²)	25.90 ± 3.81	25.47 ± 3.42	0.640
Parity			
Nulliparous	5 (16.7%)	3 (10.0%)	0.810
Primiparous	12 (40.0%)	13 (43.3%)	
Multiparous	13 (43.3%)	14 (46.7%)	
Mode of Delivery			
Vaginal	14 (46.7%)	15 (50.0%)	0.850
Assisted Vaginal	7 (23.3%)	8 (26.7%)	
Cesarean section	9 (30.0%)	7 (23.3%)	

The comparison of mean fibrinogen levels between women with non-severe and severe postpartum hemorrhage. The mean fibrinogen level in Group A (non-severe PPH) was 4.55 ± 1.06 g/L, whereas it was significantly lower in Group B (severe PPH) at 3.53 ± 0.88 g/L. The mean difference of 1.03 g/L reveals that non-severe PPH patients had much higher fibrinogen levels. The true difference in fibrinogen levels between groups is probably within the 95% confidence interval (CI) (0.52-1.52). The difference between the two groups was statistically significant ($p = 0.001$). These findings showed a significant difference in mean fibrinogen levels between severe and non-severe PPH groups (Table 2).

Table 2: Comparison of Mean Plasma Fibrinogen Levels Between Study Groups

Variables	Group A (Non-severe PPH) n=30	Group B (Severe PPH) n=30	Mean difference	95% CI	p-value
Fibrinogen Level (g/L)	4.55 ± 1.06	3.53 ± 0.88	1.02	0.52-1.52	0.001

In the stratified study, significant postpartum hemorrhage was associated with decreased fibrinogen levels across

most categories. In women aged ≤30, fibrinogen levels were higher in the non-severe group (4.46 ± 0.97 g/L) than in the severe group (3.39 ± 0.64 g/L) ($p=0.001$). Similar patterns were seen for gestational age ≤39 weeks (4.57 ± 1.16 versus 3.60 ± 0.89 ; p -value = 0.004) and normal BMI (4.54 ± 1.11 versus 3.54 ± 0.95 ; p -value = 0.008). Assisted deliveries showed a significant difference ($p=0.005$), but vaginal deliveries did not ($p=0.083$) (Table 3).

Table 3: Stratification of Mean Fibrinogen Levels Between Groups with Respect to Different Variables

Variables	Groups		p-value
	Group A (Non-severe PPH), Mean Difference	Group B (Severe PPH), Mean Difference	
Age Groups			
≤30 years	4.46 ± 0.97	3.39 ± 0.64	0.001
>30 years	4.67 ± 1.19	3.69 ± 1.10	0.035
Gestational Age			
≤ 39 weeks	4.57 ± 1.16	3.60 ± 0.89	0.004
>39 weeks	4.52 ± 0.81	3.34 ± 0.89	0.012
BMI			
Normal	4.54 ± 1.11	3.54 ± 0.95	0.006
Overweight	4.92 ± 1.07	3.64 ± 0.73	0.015
Obese	4.01 ± 0.73	3.15 ± 1.00	0.039
Parity			
Nulliparous	4.94 ± 0.78	2.92 ± 0.54	0.008
Primiparous	4.27 ± 1.01	3.50 ± 0.63	0.031
Multiparous	4.67 ± 1.19	3.69 ± 1.10	0.035
Mode of Delivery			
Vaginal	4.48 ± 1.18	3.83 ± 0.70	0.083
Assisted Vaginal	4.80 ± 0.90	3.23 ± 0.90	0.005
Cesarean section	4.47 ± 1.05	3.23 ± 1.09	0.037

DISCUSSION

This study proved a significant relationship between low fibrinogen levels and the severity of PPH. The average fibrinogen level in women with severe PPH (3.53 ± 0.88 g/L) was significantly lower than the fibrinogen level in women with non-severe PPH (4.55 ± 1.06 g/L). These findings add to the literature, which has previously suggested that fibrinogen concentration is a strong predictor of hemorrhage severity and the need for aggressive management interventions. Cui et al. performed a multicenter study addressing fibrinogen dynamics in obstetrical disseminated intravascular coagulation (DIC), which showed that women with severe PPH had a high incidence of fibrinogen deficiency (less than 3g/L) and marked the importance of fibrinogen as an important biomarker in assessing risk of maternal bleeding, with low fibrinogen being associated with adverse maternal outcome [9]. Obaro and Heazell also attach importance to fibrinogen as a crucial biomarker in maternal bleeding risk assessment, showing that low fibrinogen is associated with poor outcomes [10]. A recent analysis by Kobayashi et

al. concluded that fibrinogen levels tend to be rapidly depleted in severe obstetric bleeding owing to consumption coagulopathy, in which mean values of 3.2 ± 0.6 g/L were reported, corresponding to our result [11]. Similar to our work, Tardy-Poncet *et al.* concluded that maintaining fibrinogen concentrations of more than 3.5 g/L optimized transfusion requirements and improved clinical outcomes [12]. The association between fibrinogen depletion and hemorrhage severity was also backed up by Daikuara *et al.* who showed that fibrinogen below 3 g/L after it was associated with a three times higher risk of uncontrolled bleeding at delivery [13]. Ren *et al.* also highlighted the importance of fibrinogen measurement as part of coagulation screening; it provides important prognostic information for early intervention [14]. The average fibrinogen value in severe PPH in our study (3.53 g/L) is slightly higher than those reported by Cui *et al.* (3 g/L) and Daikuara *et al.* (2.9 g/L) [9, 13]. This difference could potentially be due to differences in patient selection, timing of measurement, and management protocols. In our study setting, samples were taken immediately upon diagnosis of PPH, possibly before total consumption of clotting factors, whereas in other studies, levels were measured later during active hemorrhage. Moreover, our population was made up of women without pre-existing coagulopathies, which may explain the rather higher baseline fibrinogen levels. Kiani *et al.* both reaffirmed that fibrinogen rises physiologically throughout pregnancy to reach levels of 4–6 g/L by the third trimester of pregnancy, and a rapid decrease below 3 g/L during delivery is suggestive of pathological bleeding. These physiological considerations are consistent with our findings in which non-severe cases of PPH maintained mean levels within the expected range for late pregnancy (4.55 g/L) [15]. In comparison, another study conducted by Kaur *et al.* showed that the mean fibrinogen levels in patients needing surgical interventions for PPH were 2.95 ± 0.97 g/L (almost at the same level as in our severe PPH group). Another study conducted by Hofer *et al.* reinforced that women with persistent hemodynamic instability after PPH had significantly low fibrinogen and platelet count, further supporting fibrinogen's hemostatic role in the management of maternal recovery [2, 16]. A study by Park *et al.* supported the importance of early guiding laboratory management and fibrinogen as a rapid response indicator in massive transfusion protocols [17]. After postpartum hemorrhage, decreased fibrinogen is the earliest hemostatic sign of coagulopathy [18]. Significant PPH is predicted by lower fibrinogen levels before delivery and upon postpartum hemorrhage onset. In severe conditions, early goal-directed fibrinogen concentrate treatment [19]. Among reviewed studies, the mean fibrinogen levels in severe cases of PPH were 2.8 to 3.6 g/L, and in non-severe cases were 4.2 to 4.8 g/L. Our results (3.53 g/L and 4.55 g/L,

respectively) are well within these ranges, implying external validity and concomitance with international findings. This strengthens the validity of our study results and may help the increasing consensus that fibrinogen concentration provides an early biomarker that predicts the severity of PPH and can guide clinical modalities. A comparative cross-sectional study of 60 patients found that severe postpartum hemorrhage has much lower mean fibrinogen levels, 200 mg/dL, than mild PPH (more than 250 mg/dL) [20].

The findings suggest the potential use of fibrinogen level estimation as a quick, cheap, and effective predictor that can be used at bedside to identify patients at risk of developing severe PPH. Inclusion of routine fibrinogen testing as a component of protocols around obstetric hemorrhage can facilitate early targeted therapy and include early use of fibrinogen concentrate or cryoprecipitate. Larger multicentric trials are needed to provide optimal cut-off levels for fibrinogen, dependent on the population and the healthcare setting. This study was limited in its single-center design with a relatively small sample size ($n = 60$), which may limit the study's generalizability. Fibrinogen was only measured (single measurement) at the time of diagnosis, and not serially over time to examine dynamic trends. In addition, the effects of factors that influence the production of fibrinogen (liver synthetic function, nutrition, and genetic variation) were not investigated. Longitudinal sampling is needed; consideration should be given to the kinetics of fibrinogen to bleeding ratio, and the use of POC technologies would enable quick decision-making in low-resource settings. Limited sample sizes in some stratified subgroups may reduce statistical power and/or violate assumptions of parametric tests.

CONCLUSIONS

Low levels of fibrinogen were significantly associated with severe PPH. Estimating the levels of fibrinogen at an early stage could be a valuable indicator of patients who are likely to present with serious haemorrhage and enable prompt intervention with management strategies.

Authors' Contribution

Conceptualization: AZ, MKN

Methodology: AZ, EF

Formal analysis: RF, SSQH

Writing and Drafting: HO, SSQH

Review and Editing: AZ, MKN, EF, RF, HO, SSQH

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All 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] Li YT, Chang WH, Wang PH. Postpartum Hemorrhage. *Taiwanese Journal of Obstetrics and Gynecology*. 2022 Jan; 61(1): 5-7. doi: 10.1016/j.tjog.2021.11.003.
- [2] Kaur K, Grover S, Kukar N, Tapasvi I, Garg M, Singla R. The Association of Serum Fibrinogen Levels with the Severity of Primary Postpartum Hemorrhage: A Prospective Study. *Cureus*. 2024 Oct; 16(10): 1-11. doi: 10.7759/cureus.71397.
- [3] Federspiel JJ, Eke AC, Eppes CS. Postpartum hemorrhage protocols and benchmarks: improving care through standardization. *American Journal of Obstetrics and Gynecology Maternal-Fetal Medicine*. 2023 Feb; 5(2): 100740. doi: 10.1016/j.ajogmf.2022.100740.
- [4] Zou Y, Jiang Y, Zhu D, Liu L, Zheng X, Gu X et al. Fibrinogen as a potential diagnostic marker for prediction and evaluation of postpartum hemorrhage: a retrospective study. *The Journal of Maternal-Fetal and Neonatal Medicine*. 2024 Jan; 37(1): 2300418. doi: 10.1080/14767058.2023.2300418.
- [5] Grottke O, Mallaiah S, Karkouti K, Saner F, Haas T. Fibrinogen supplementation and its indications. In *Seminars in thrombosis and hemostasis*. Thieme Medical Publishers. 2020 Feb; 46(1): 38-49. doi: 10.1055/s-0039-1696946.
- [6] Hosseini MS, Abtahi D, Tajbakhsh A, Farzaneh F, Sayadi S, Amjadi N et al. Evaluation of the Differences in Plasma Fibrinogen Levels Before and After Cesarean Section and its Association with Intra- and Postoperative Bleeding. *Journal of Obstetrics, Gynecology and Cancer Research*. 2023 Feb; 8(2): 157-166. doi: 10.30699/jogcr.8.2.157.
- [7] Küçükbaş M, Özen EG, Özen S, Selçuk S, Polat M, Karateke A. Early Fibrinogen Replacement Based on Shock Index and Lactate Levels in Massive Postpartum Hemorrhage: A Retrospective Cohort Study. *Blood Transfusion*. 2025 Jul; 23(6): 527.
- [8] Cortet M, Deneux-Tharaux C, Dupont C, Colin C, Rudigoz RC, Bouvier-Colle MH et al. Association Between Fibrinogen Level and Severity of Postpartum Haemorrhage: Secondary Analysis of a Prospective Trial. *British journal of anaesthesia*. 2012 Jun; 108(6): 984-989. doi: 10.1093/bja/aes096.
- [9] Cui J, Liu Z, He W, Su R, Ma R, Tao H et al. Multicenter Retrospective Evaluation of the Chinese Expert Consensus Scoring System for the Diagnosis of Obstetrical DIC. *Maternal-Fetal Medicine*. 2025 Oct; 7(4): 216-227. doi: 10.1097/FM9.0000000000000313.
- [10] Obaro J and Heazell A. Investigation and Management of Stillbirth. *Obstetrics, Gynaecology and Reproductive Medicine*. 2023 Aug; 33(8): 209-216. doi: 10.1016/j.ogrm.2023.05.001.
- [11] Kobayashi H, Matsubara S, Imanaka S. The Role of Tissue Factor Pathway Inhibitor 2 in The Coagulation and Fibrinolysis System. *Journal of Obstetrics and Gynaecology Research*. 2023 Jul; 49(7): 1677-1683. doi: 10.1111/jog.15660.
- [12] Tardy-Poncet BP. Potential Roles of TFPI in Both Thrombotic and Hemorrhagic Diseases (Doctoral dissertation, Université Jean Monnet-Saint-Etienne). 2015 Mar: 1-151.
- [13] Daikuara LY. Fabricating delivery platforms for wound management and tissue regeneration (Doctoral dissertation, University of Wollongong). 2021: 1-201.
- [14] Ren B, Zhang Y, Chen S, Dai J, Chong J, Chang Z. Association Between Fibrinogen Levels and Prognosis in Critically Bleeding Patients: Exploration of the Optimal Therapeutic Threshold. *European Journal of Trauma and Emergency Surgery*. 2025 Dec; 51(1): 219. doi: 10.1007/s00068-025-02886-8.
- [15] Kiani MT, Khan AQ, Khan YQ, Hameed M, Hussain ST, Asghar R. D-Dimers and Fibrinogen in Third Trimester of Normal Pregnancy and Pregnancy Complicated by Gestational Hypertension or Preeclampsia. *International Journal of Pathology*. 2023 May: 13-17.
- [16] Hofer S, Blaha J, Collins PW, Ducloy-Bouthors AS, Guasch E, Labate F et al. Haemostatic Support in Postpartum Haemorrhage: A Review of the Literature and Expert Opinion. *European Journal of Anaesthesiology | European Journal of Anaesthesiology*. 2023 Jan; 40(1): 29-38. doi: 10.1097/EJA.0000000000001744.
- [17] Park S, Sohn C, Kwon H, Kim S, Ryoo S, Ahn S et al. Association Between Initial Fibrinogen Levels and The Need for Massive Transfusion in Emergency Department Patients with Primary Postpartum Hemorrhage: A Retrospective Study from a Single Center in Korea. *Journal of Personalized Medicine*. 2024 Mar; 14(4): 344. doi: 10.3390/jpm14040344.
- [18] Diguisto C, Baker E, Stanworth S, Collins PW, Collis RE, Knight M. Management and Outcomes of Women with Low Fibrinogen Concentration During Pregnancy or Immediately Postpartum: A UK national population-based cohort study. *Acta Obstetrica et Gynecologica Scandinavica*. 2024 Jul; 103(7): 1339-47. doi: 10.1111/aogs.14828.

- [19] Vermeulen T, Van de Velde M. The Role of Fibrinogen in Postpartum Hemorrhage. *Best Practice and Research Clinical Anaesthesiology*. 2022 Dec; 36(3-4): 399-410. doi: 10.1016/j.bpa.2022.10.002.
- [20] Abbas M, Bukhari MM, Sardar F, Azhar H, Shabbar S. Association of Fibrinogen Levels with Severity of Postpartum Hemorrhage and Contributing Risk Factors. *Pakistan Journal of Pathology*. 2025 Jun; 36(2): 138-143. doi: 10.55629/pakjpathol.v36i2.907.



Original Article

Investigating the Psychosocial Impact and Quality of Life in Gyne Cancer Survival Patients

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ARTICLE INFO

Keywords:

Cancer Survivors, Gynecology, Anxiety, Depression

How to Cite:

Aslam, Y., Naqvi, Z., & Khan, Y. Q. (2026). Investigating the Psychosocial Impact and Quality of Life in Gyne Cancer Survival Patients : Psychosocial Impact and Quality of Life Among Gynecological Cancer Survivors. *Pakistan Journal of Health Sciences*, 7(6), 87-92. <https://doi.org/10.54393/pjhs.v7i6.4004>

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Received Date: 21st February, 20261st Revision Received: 16th March, 2026Acceptance Date: 14th April, 2026Published Date: 30th June, 2026

ABSTRACT

Gynecologic cancers are on the rise globally. Survivors frequently encounter physical distress aggravated by psychological instability, anxiety, and depression. Quality of life (QoL) includes physical, emotional, social, and functional well-being, rendering it a crucial patient-reported outcome in cancer. **Objective:** To investigate the psychosocial impact and quality of life in gynaecological cancer survival patients. **Methods:** A descriptive cross-sectional study was conducted in the Department of Obstetrics and Gynecology, Liaquat National Hospital, Karachi. This study comprised 178 women with ovarian, endometrial, and cervical cancer who were undergoing active therapy at the time data were collected. Psychological well-being was measured by using the Hospital Anxiety and Depression Scale and the Distress Thermometer. The collected data were analyzed with IBM SPSS version 27.0. A p-value of ≤ 0.050 was deemed statistically significant. **Results:** The abnormal anxiety was highly prevalent (110; 61.8%) compared to depression (27; 15.2%). Patients ≤ 50 years showed significantly higher abnormal anxiety (66.2%) (p-value=0.025) and depression (18.5%). Treatment modality was significant, with combined surgery and chemoradiotherapy showing the highest abnormal depression (32.3%). Patients with abnormal anxiety showed significantly poorer functional status compared with normal anxiety (median FACT score versus 18, with a p-value < 0.001). **Conclusions:** Gynecological cancer survivors face significant psychosocial challenges, with anxiety being more prevalent than depression. Quality of life was markedly impaired, and functional limitations were strongly linked to psychological morbidity.

INTRODUCTION

Globally, cancer is a leading cause of morbidity and mortality [1]. Cancer effect expected to rise significantly soon [2]. Gynecological cancers represent a significant part of this burden among women, representing approximately 15.3% of newly diagnosed cancer cases and 15.8% of deaths due to cancer worldwide [3]. Gynecological cancers are a type of cancer that affects women's reproductive organs, such as the cervix, uterus, ovaries, vagina, and vulva [4]. The evaluation of health-related QoL in survivors of gynecological cancers has become increasingly significant and is recognized as an essential patient-reported outcome, in addition to traditional metrics such as overall survival and disease-free survival [5]. Traditionally, the treatment of gynecological cancers mainly aimed at prolonging life expectancy, with insufficient emphasis on the quality of life (QoL) of patients

during and post-treatment [6]. Over the years, other measures have been utilized to evaluate how well patients are doing, such as mortality rates, survival rates, and levels of discomfort. These indicators give important clinical information, but they do not show how disease and treatment affect a patient's physical health. Health-based QoL provides a more holistic view by evaluating both the physical and psychological dimensions of health [7]. In the past twenty years, clinical research has put more focus on mental health and QoL, recognizing that they are important parts of good patient care and recovery [8]. Evaluating the psychosocial impact and quality of life in gynecologic cancer survivor patients is crucial for holistic patient care and well-being. Although increasing evidence is available on psychological distress in gynecological cancer patients, there is a paucity of data on low- and middle-income



countries especially Pakistan which cover combined psychosocial impact and quality of life using validated instruments.

The previous researches concentrate on individual types of cancer (e.g., cervical cancer) or individual outcomes (e.g., anxiety or depression) but not a wholesome quality of life. Moreover, the demographic and treatment-related factors are not studied as related to psychosocial morbidity. This shows that multidimensional studies on this population require context-specific research. The survivors of gynecological cancer often have a severe psychological distress and poor quality of life; nevertheless, it has not been a topic of research in the local clinical practice. The magnitude of anxiety, depression, and the quality of life of such patients in Pakistan in general and the determinants of these outcomes has a dearth of evidence. This study aimed to evaluate the psychosocial effect, anxiety and depression, and quality of life in gynecological cancer survivors, as well as to determine the relationship between demographic and clinical factors and psychological morbidity and functional status.

METHODS

This description cross-sectional study was carried out in the Department of Obstetrics and Gynecology at Liaquat National Hospital in Karachi. It was carried out over a minimum period from 15th July to 31st December 2025, following approval of the synopsis by the institutional research and evaluation committee (IRB # 1068-2024-LNH-ERC; dated 11th July 2024). A World Health Organization sample size calculator was used to collect data with a 95% confidence interval (CI), 6% precision, 80% power, and a reported prevalence of depression of 21% [9]. The final sample size was calculated was 178 participants. Women aged 18 years and above with a confirmed diagnosis of gynecological cancer, including ovarian, endometrial, or cervical cancer, and undergoing active oncological treatment were included in this study. Those patients who were above 70 years and to reduce bias, people who had a history or who were currently suffering from psychological problems were not included in the study. Age was classified as ≤50 years and >50 years based on epidemiological parameters that represent menopausal transition and psychosocial issues faced by younger and older cancer survivors. Because the data were not normally distributed, continuous variables like age and FACT scores were summarized using the median and interquartile range (Q1-Q3). Every study participant provided written informed consent before enrolling in the study. Participants were told of the study's goal, the confidentiality of their responses, and their freedom to withdraw at any time without compromising their medical treatment. Psychosocial impact was defined as the presence of

psychological distress, anxiety, depression, post-traumatic stress symptoms, and perceived social support, measured using validated scales. Quality of life was evaluated through physical functioning, emotional well-being, social functioning, and overall life satisfaction, employing established tools such as the FACT scales. Data were collected prospectively. Participants received validated questionnaires upon ward or day hospital admission. Anxiety and depression were assessed by using the Hospital Anxiety and Depression Scale. This self-report measure had 14 items, 7 for anxiety (HADS-A) and depression (HADS-D). A 4-point Likert scale from 0 (no symptoms) to 3 (highest severity) yielded subscale scores between 0 and 21. Scores between 0-7 were normal, 8-10 were borderline abnormal, and 11-21 were abnormal. Psychosocial distress was assessed using the Distress thermometer, a single-item visual analogue scale from 0 to 10, and a problem checklist with practical, family, emotional, spiritual-religious, and physical domains. Oncology researchers utilize the validated FACT scale to assess quality of life. The scale examines physical, emotional, functional, and social health-related quality of life. Low scores indicate poor quality of life, whereas high scores indicate better quality.

This study used IBM SPSS version 27.0 to analyze the data. To describe quantitative data, descriptive statistics were utilized. This study employed inferential statistics, like chi-square tests/Fisher's exact test, and the Kruskal-Wallis's test, to look at the association and differences in means between demographic and clinical variables and psychosocial findings. In this study, a probability value of less than or equal to 0.050 was considered significant.

RESULTS

The current study shows the demographic and psychosocial profile of women who have survived gynecological cancer. The median age was 55 years (IQR 12; range 32-78), and 63.5% of the study participants were over 50 years old. The median FACT score was 16 (IQR 9; range 4-32), highlighting marked impairment in QoL among the study participants. Anxiety levels were comparatively elevated, exhibiting a median score of 11 (IQR 4; range 4-21), indicative of significant psychological distress, but depression scores were lower, presenting a median of 4 (IQR 5; range 0-14) (Table 1).

Table 1: Demographic Characteristics and FACT Score of Gynecological Cancer Survivors

Variables	Category	n (%) / Median
Age	—	55.0 (12.0; 32.0-8.0)
FACT Scale	—	16.0 (9.0; 4.0-2.0)
Anxiety Subscale	—	11.0 (4.0; 4.0-1.0)
Depression Subscale	—	4.0 (5.0; 0.0-14.0)

Age Groups	≤ 50 Years	65 (36.5%)
	> 50 Years	113 (63.5%)
Education	Matric or below	46 (25.8%)
	Intermediate	59 (33.1%)
	Graduation	31 (17.4 %)
	Master or above	42 (23.6%)
Monthly Income	< 50K per month	68 (38.2%)
	50K – 100K per month	60 (33.7%)
	> 100K per month	50 (28.1%)
Occupation	Unemployed	33 (18.5%)
	Private Job	50 (28.1%)
	Govt. Job	44 (24.7%)
	Business	15 (8.4%)
	Shopkeeper	16 (9.0%)
	Labour	20 (11.2%)
Working Status	Yes	125 (70.2%)
	No	53 (29.8%)
Time Since Diagnosis	< 1 Year	57 (32.0%)
	1 – 5 Years	70 (39.3%)
	> 5 Years	51 (28.7%)
Treatment	Surgery	47 (26.4%)
	Chemoradiotherapy	53 (29.8%)
	Surgery and Chemotherapy	29 (16.3%)

Anxiety Severity	Surgery and Chemoradiotherapy	31 (17.4%)
	Surgery and Radiotherapy	18 (10.1%)
	Normal	43 (24.2%)
Depression Severity	Borderline Abnormal	25 (14.0%)
	Abnormal	110 (61.8%)
	Normal	130 (73.0%)
Depression Severity	Borderline Abnormal	21 (11.8%)
	Abnormal	27 (15.2%)
	Normal	130 (73.0%)

It shows that age was significantly associated with anxiety, with a p-value of 0.025 and depression, with more abnormal depression in persons less than 50 years old and higher borderline depression in older people. Education was associated with anxiety severity, with a p-value of 0.018, with graduates having the highest rate of abnormal anxiety, but not depression, with a p-value of 0.141. Monthly income is significantly associated with anxiety and depression, showing higher psychological morbidity in low-and middle-income groups. Both anxiety and depression were significantly associated with occupation and working status, with a p-value > 0.01. Time since diagnosis was associated with anxiety but not depression, while treatment modality was linked to anxiety and depression (Table 2).

Table 2: Association of Demographic Variables with Anxiety and Depression Severity

Variables	Category	Anxiety Normal, n (%)	Borderline Abnormal, n (%)	Abnormal, n (%)	p-value	Depression Normal, n (%)	Borderline Abnormal, n (%)	Abnormal, n (%)	p-value
Age Groups	≤ 50 Years	9 (13.8%)	13 (20.0%)	43 (66.2%)	0.025	51 (78.5%)	2 (3.1%)	12 (18.5%)	0.018
	> 50 Years	34 (30.1%)	12 (10.6%)	67 (59.3%)		79 (69.9%)	19 (16.8%)	15 (13.3%)	
Education	Matric or below	13 (28.3%)	10 (21.7%)	23 (50.0%)	0.018	33 (71.7%)	7 (15.2%)	6 (13.0%)	0.141
	Intermediate	18 (30.5%)	9 (15.3%)	32 (54.2%)		45 (76.3%)	2 (3.4%)	12 (20.3%)	
	Graduation	5 (16.1%)	0 (0.0%)	26 (83.9%)		24 (77.4%)	5 (16.1%)	2 (6.5%)	
	Master or above	7 (16.7%)	6 (14.3%)	29 (69.0%)		28 (66.7%)	7 (16.7%)	7 (16.7%)	
Monthly Income	< 50K per month	20 (29.4%)	7 (10.3%)	41 (60.3%)	<0.001	44 (64.7%)	9 (13.2%)	15 (22.1%)	0.008
	50K–100K per month	13 (21.7%)	2 (3.3%)	45 (75.0%)		41 (68.3%)	7 (11.7%)	12 (20.0%)	
	> 100K per month	10 (20.0%)	16 (32.0%)	24 (48.0%)		45 (90.0%)	5 (10.0%)	0 (0.0%)	
Occupation	Un-employed	13 (39.4%)	9 (27.3%)	11 (33.3%)	<0.001	31 (93.9%)	0 (0.0%)	2 (6.1%)	<0.001
	Private Job	13 (26.0%)	7 (14.0%)	30 (60.0%)		37 (74.0%)	5 (10.0%)	8 (16.0%)	
	Govt. Job	10 (22.7%)	0 (0.0%)	34 (77.3%)		29 (65.9%)	7 (15.9%)	8 (18.2%)	
	Business	0 (0.0%)	9 (60.0%)	6 (40.0%)		15 (100.0%)	0 (0.0%)	0 (0.0%)	
	Shopkeeper	0 (0.0%)	0 (0.0%)	16 (100.0%)		4 (25.0%)	5 (31.3%)	7 (43.8%)	
	Labor	7 (35.0%)	0 (0.0%)	13 (65.0%)		14 (70.0%)	4 (20.0%)	2 (10.0%)	
Working Status	Yes	30 (24.0%)	11 (8.8%)	84 (67.2%)	0.006	84 (67.2%)	16 (12.8%)	25 (20.0%)	0.008
	No	13 (24.5%)	14 (26.4%)	26 (49.1%)		46 (86.8%)	5 (9.4%)	2 (3.8%)	
Time Since Diagnosis	< 1 Year	15 (26.3%)	15 (26.3%)	27 (47.4%)	0.002*	44 (77.2%)	9 (15.8%)	4 (7.0%)	0.094
	1–5 Years	15 (21.4%)	10 (14.3%)	45 (64.3%)		53 (75.7%)	7 (10.0%)	10 (14.3%)	
	> 5 years	13 (25.5%)	0 (0.0%)	38 (74.5%)		33 (64.7%)	5 (9.8%)	13 (25.5%)	
Treatment	Surgery	7 (14.9%)	12 (25.5%)	28 (59.6%)	<0.001	37 (78.7%)	2 (4.3%)	8 (17.0%)	0.001
	Chemoradiotherapy	10 (18.9%)	6 (11.3%)	37 (69.8%)		34 (64.2%)	12 (22.6%)	7 (13.2%)	
	Surgery and Chemotherapy	10 (34.5%)	0 (0.0%)	19 (65.5%)		24 (82.8%)	5 (17.2%)	0 (0.0%)	
	Surgery and Chemoradiotherapy	15 (48.4%)	0 (0.0%)	16 (51.6%)		19 (61.3%)	2 (6.5%)	10 (32.3%)	
	Surgery and Radiotherapy	1 (5.6%)	7 (38.9%)	10 (55.6%)		16 (88.9%)	0 (0.0%)	2 (11.1%)	

It shows the comparison of age and functional scores with anxiety and depression severity, further elucidating the psychosocial burden. Median age did not differ significantly across anxiety severity groups ($p=0.251$), but depression severity was significantly associated with age ($p=0.006$), with borderline abnormal depression clustering in younger patients (median age 48 years). Functional scores demonstrated a robust association with both anxiety and depression severity ($p<0.001$ for each) (Table 3).

Table 3: Comparison of Age and FACT Scores Based on Anxiety and Depression Severity

Variables	Statistic	Anxiety Normal	Anxiety Borderline	Anxiety Abnormal	Depression Normal	Depression Borderline	Depression Abnormal
Age Years	Median	55.0	48.0	56.0	55.0	48.0	56.0
	Q1	54.0	43.0	47.0	54.0	43.0	47.0
	Q3	58.0	57.5	60.0	57.5	56.0	60.0
	p-value	(0.251)	(0.006)	—	—	—	—
FACT Score	Median	9	12	18	9	12	18
	Q1	8	11	16	8	11	16
	Q3	12	14.5	22	12	14	22
	p-value	<0.001	<0.001	—	—	—	—

DISCUSSION

A diagnosis of cervical cancer can exert significant psychological impacts, especially in underdeveloped countries. Numerous women endure profound emotional distress, feelings of humiliation, and societal stigma, which can harm their mental health and general health [10]. The initial course of action to cervical cancer identification is frequently characterized by shock, fear, and confusion, which can rapidly escalate to anxiety and despair. Numerous women additionally face feelings of shame and embarrassment, especially when cervical cancer is frequently associated with human papillomavirus (HPV), a sexually transmitted illness [11]. A study of thirty women undergoing therapy for cervical cancer revealed that over half 56.6% had clinically significant amounts of anxiety and depression. The mental health issues were intricately associated with challenges, including disturbed marital relationships and a reduction in sexual engagement post-treatment, both of which adversely impacted their emotional wellness [12]. A study conducted in Tunisia revealed that 40 women in relapse revealed that numerous patients persisted in experiencing anxiety and despair post-treatment. Psychological problems were more prevalent in women with late stages and those who had received intense treatments such as hysterectomy/external radiotherapy, highlighting the long-lasting emotional effects of both the disease and its management [13]. In another study of 83 patients, 75.7% of women of fertile age exhibited clinically significant anxiety, whereas 57.5% demonstrated clinically expressed depression [14]. A Korean study intended to evaluate the prevalence of anxiety and depression in eight hundred and twenty-eight cervical cancer survivors and to find related factors. The study found an anxiety prevalence of 39.5%, considerably elevated among women aged below or up to fifty and a depression prevalence of 34.6% [15]. Despite a statistically significant association between age and depression

severity, normal and abnormal depression groups had equal median ages. The statistical significance may have been driven by the smaller borderline group rather than by a clinically relevant difference between normal and abnormal cases. Population-based research in France investigated cancer-related fatigue, QoL, and anxiety in long-lasting survivors of breast cancer, cervical cancer, and colorectal cancers, around 15 years post-diagnosis. The results indicated that survivors exhibited elevated amounts of fatigue, especially mental fatigue and overall exhaustion, alongside increased anxiety, in comparison to the population without a previous history of cancer. But even with these chronic physical and emotional problems, their quality of life was about the same as that of the overall population. These findings showed that the impacts of cancer can last for decades, which makes it even more important to keep getting psychological and supportive care after treatment is completed [16]. Patients with locally advanced cervical cancer experience significant impacts on their quality of life due to the disease and its therapies, affecting their physical health and mental wellness. According to a study, although some patients do better after treatment, many more experience long-term problems that affect many parts of their lives [17]. This study's moderate quality of life scores, especially in the physical and psychological domains, show how cervical cancer affects many parts of patients' lives. Furthermore, the study confirmed the previously developed association between mental health and quality of life in cancer patients by showing that higher levels of emotional distress, which is measured by HADS scores, were associated with lower levels of physical and psychological health [10]. The Global health status was 68.20 ± 23.61 , which was deemed good. This is similar to the findings in Egypt, which had a QoL score of 70.16 [18]. When the sub-domain of functional scales was evaluated, the physical function score

(81.77±16.43), Cognitive function score (78.91±25.18) and social function score (71.43±27.85) were good, whereas the role function score (66.67±24.76) and emotional function score (64.79±26.53) were moderate. Emotional score had the lowest functional scale score; this may be related to the diagnosis and prognosis of gynecological cancers, as most of the patients presented with stage 3 disease, coupled with financial difficulties. The emotional aspect is the most difficult to manage in cancer patients, particularly those with children. Patients with low socio-economic status are frequently more difficult to manage than those with high socio-economic status in this regard [19]. A study has shown that anxiety and depression are highly prevalent among cancer patients and significantly affect their QoL [20].

Although valuable findings, this study has numerous limitations. A cross-sectional study design makes establishing causal relationships difficult. Second, the study was confined to a single tertiary care hospital. Third, response bias may influence self-reported psychological measurements. Future research should explore psychosocial trajectories and target psychosocial therapies to enhance quality of life (QoL) in gynecological cancer survivors using longitudinal and multicenter approaches.

CONCLUSIONS

This study shows that survivors of gynecological cancer encounter considerable psychosocial challenges, with anxiety occurring more frequently than depression. The quality of life was markedly impaired, and functional limitations were significantly associated with psychological morbidity. Younger age, lower income, and integrated treatment approaches associated with elevated anxiety and depression, while socioeconomic and occupational variables additionally affected outcomes.

Authors' Contribution

Conceptualization: YA

Methodology: ZN

Formal analysis: YQK

Writing and Drafting: YA, ZN, YQK

Review and Editing: YA, ZN, YQK

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All 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] Ogamba CF, Joseph A, Adefemi AK, Ezegwui CO, Major A, Jimoh RO et al. Factors Associated with Health-Related Quality of Life and Financial Toxicity among Gynecological Cancer Patients in Southern Nigeria. *Scientific Reports*. 2025 Jul; 15(1): 28041. doi: 10.1038/s41598-025-13763-0.
- [2] Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I et al. *Global Cancer Statistics 2022: GLOBOCAN Estimates of Incidence and Mortality Worldwide For 36 Cancers In 185 Countries*. CA: A Cancer Journal for Clinicians. 2024 May; 74(3): 229-63. doi: 10.3322/caac.21834.
- [3] Zhu B, Gu H, Mao Z, Beeraka NM, Zhao X, Anand MP et al. Global Burden of Gynaecological Cancers in 2022 and Projections to 2050. *Journal Of Global Health*. 2024 Aug; 14: 04155. doi: 10.7189/jogh.14.04155.
- [4] Alegbeleye JO and John CO. An Appraisal of the Quality of Life of Gynaecological Cancer Patients at a Teaching Hospital in Southern Nigeria. *International Journal of Research and Reports in Gynaecology*. 2024; 7(1): 31-46. doi: 10.9734/ijrrgy/2024/v7i198.
- [5] Gil-Ibanez B, Davies-Oliveira J, Lopez G, Diaz-Feijoo B, Tejerizo-Garcia A, Sehoul J. Impact of Gynecological Cancers on Health-Related Quality of Life: Historical Context, Measurement Instruments, and Current Knowledge. *International Journal of Gynecological Cancer*. 2023 Nov; 33(11): 1800-6. doi: 10.1136/ijgc-2023-004804.
- [6] Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A et al. *Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide For 36 Cancers In 185 Countries*. CA: A Cancer Journal for Clinicians. 2021 May; 71(3): 209-49. doi: 10.3322/caac.21660.
- [7] Shirali E, Yarandi F, Ghaemi M, Montazeri A. Quality of Life in Patients with Gynecological Cancers: A Web-Based Study. *Asian Pacific Journal of Cancer Prevention*. 2020 Jul; 21(7): 1969. doi: 10.31557/APJC P.2020.21.7.1969.
- [8] Yen KY, Cheng JY, Li JQ, Toh ZA, He HG. The Effectiveness of Digital Psychosocial Interventions on Psychological Distress, Depression, Anxiety, and Health-Related Quality of Life in Patients with Gynaecological Cancer: A Systematic Review and Meta-Analysis. *Supportive Care in Cancer*. 2024 Apr; 32(4): 240. doi: 10.1007/s00520-024-08415-4.
- [9] Modares Gilani M, Mousavi AS, Akhavan S, Sheikhhasani S. Investigating the Quality of life of patients with cervical cancer in Iran. *Journal of Obstetrics, Gynecology and Cancer Research*. 2022 Sep; 7(6): 530-5. doi: 10.30699/jogcr.7.6.530.

- [10] Samia K, Yassine B, El Mehdi S, Wissal H, Zahra FF, Zenab A et al. Psychosocial Impact of Cervical Cancer Diagnosis: A Study Conducted in the Radiotherapy Department at CHU Hassan II, Fez, Morocco. *ecancermedicalscience*. 2025 Aug; 19: 1976. doi: 10.3332/ecancer.2025.1976.
- [11] Raj R and Bhagat N. Psychiatric Morbidity in Newly Diagnosed Carcinoma Cervix and its Comparison with Benign Condition. *Int J Reprod Contracept Obstet Gynecol*. 2017; 6(11): 4990. doi: 10.18203/2320-1770.ijrcog20175014.
- [12] Bouzid N, Abdallah HH, Tebessi S, Zanzouri R, Fayala R, Tebra S. 1210 Assessment of Anxiety and Depression in Women Treated for Cervical Cancer. *International Journal of Gynecological Cancer*. 2024 Mar; 34: A484. doi: 10.1136/ijgc-2024-ESGO.953.
- [13] Zanzouri R, Bouzid N, Jaafer RB, Fayala R, Tbessi S, Kanoun S et al. 1335 Depression and anxiety among women treated for cervical cancer. *International Journal of Gynecological Cancer*. 2024 Mar; 34: A489. doi: 10.1136/ijgc-2024-ESGO.964.
- [14] Burgoeva MN and Zhumabaev AR. Psychological Disorders in Women of Fertile Age and Postmenopausal Women with Advanced Cervical Cancer. *Tumors of Female Reproductive System*. 2023 May; 18(4): 98-102. doi: 10.17650/1994-4098-2022-18-4-98-102.
- [15] Kim SH, Kang S, Kim YM, Kim BG, Seong SJ, Do Cha, et al. Prevalence and Predictors of Anxiety and Depression Among Cervical Cancer Survivors in Korea. *International Journal of Gynecological Cancer*. 2010 Jul; 20(6): 1017-24. doi: 10.1111/IGC.0b013e3181e4a704.
- [16] Gernier F, Joly F, Klein D, Mercier M, Velten M, Licaj I. Cancer-Related Fatigue Among Long-Term Survivors of Breast, Cervical, and Colorectal Cancer: A French Registry-Based Controlled Study. *Supportive Care in Cancer*. 2020 Dec; 28(12): 5839-49. doi: 10.1007/s00520-020-05427-8.
- [17] Sari S, Sukista N, Agustini TT, Ghozali MT. Analysis of Health-Related Quality of Life (Hrql) in Advanced Stage Cervical Cancer Patients in Riau Province, Indonesia. *Research Journal of Pharmacy and Technology*. 2024 May; 17(5): 2265-70. doi: 10.52711/0974-360X.2024.00356.
- [18] El Ghazaly H, Saad AS, Samy N, Kamal KA, Medhat D, Tawfic AM. Follow up of Quality of Life and Sexual Wellbeing in Gynaecological Cancers: A Cross-Sectional Study. *Ain Shams Medical Journal*. 2023 Mar; 74(1): 111-22. doi: 10.21608/asmj.2023.298215.
- [19] Edianto D, Yaznil MR, Chartyansari AA, Effendi IH. Assessment of the Quality of Life for Gynecologic Cancer Patients Using Functional Assessment of Cancer Therapy-General (Fact-G) Questionnaire At Haji Adam Malik Hospital. *Open Access Macedonian Journal Of Medical Sciences*. 2019 Jul; 7(16): 2569. doi: 10.3889/oamjms.2019.391.
- [20] Fasoi G, Bourazani M, Papatheodorou D, Vlachou E, Toylia G, Kaba E, et al. Exploration the Quality of Life and the Related Factors in Women with Recent Diagnosis of Gynecological Cancer, Before the Surgical Treatment, in Greece. *Health and Research Journal*. 2020 Dec; 6(4): 114-22. doi: 10.12681/healthresj.25628.



Original Article



Frequency of Cognitive Impairment in Multiple Sclerosis: Association with Neuro-Imaging Parameters and Disease Duration

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ARTICLE INFO

Keywords:

Multiple Sclerosis, Cognitive Impairment, Cortical Lesions, Brain Atrophy

How to Cite:

Shehzad, A., Gul, Q., Ashraf, M. S., Naeem, I., Zaheer, M., & Ather, F. (2026). Frequency of Cognitive Impairment in Multiple Sclerosis: Association with Neuro-Imaging Parameters and Disease Duration : Cognitive Impairment in Multiple Sclerosis: Association with Neuro-Imaging Parameters. Pakistan Journal of Health Sciences, 7(6), 91-98. <https://doi.org/10.54393/pjhs.v7i6.3694>

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ABSTRACT

Cognitive impairment is a frequent but underrecognized feature of multiple sclerosis and contributes to functional decline. Early identification and association with clinical and neuroimaging markers may guide management. **Objectives:** To determine the frequency of cognitive impairment and its relationship with demographic, clinical, and MRI characteristics in multiple sclerosis. **Methods:** This cross-sectional study was conducted at the Department of Neurology, Punjab Institute of Neurosciences, Lahore, from May to December 2025. Seventy-one adults aged 18–50 years with multiple sclerosis, diagnosed according to the 2017 Revised McDonald Criteria, were enrolled. Brain MRI on a 3-Tesla system was evaluated for lesion characteristics and atrophy by a radiologist. Cognitive function was assessed using the Montreal Cognitive Assessment. **Results:** The mean age of participants was 35.08 ± 7.71 years, and the mean disease duration was 6.53 ± 3.24 years. The mean Montreal Cognitive Assessment (MoCA) score was 22.91 ± 5.87 , and the mean total MRI lesion count was 16.07 ± 8.98 . Cognitive impairment was found in 40.8%, including 21.1% mild, 12.7% moderate, and 7.0% severe impairment. Relapsing–remitting multiple sclerosis was most common (69.0%), followed by secondary progressive (19.7%) and primary progressive (11.3%). Patients with impairment had older age ($p=0.016$) and longer disease duration ($p=0.012$). Cortical lesions and brain atrophy were significantly related to cognitive impairment. **Conclusions:** Cognitive impairment appeared as a frequent feature of multiple sclerosis and was related to advancing age, longer disease duration, and neuroimaging abnormalities.

INTRODUCTION

Multiple sclerosis (MS) is a chronic, immune-mediated, demyelinating disorder of the central nervous system that typically affects adults in early to mid-adulthood and produces cumulative neurological disability [1, 2]. Asian estimates remain heterogeneous, with a regional analysis reporting an age-standardized prevalence of 10.96 per 100,000 population [3]. In Pakistan, available contemporary sources indicate a low to intermediate but rising burden, with an estimated prevalence of approximately 5 to 10 per 100,000 population and

increasing recognition of service needs within neurology practice [4]. In this disease, cognitive impairment signifies a clinically related nonmotor manifestation that disturbs functional independence, work productivity, and health-related quality of life [5, 6]. Cognitive impairment in MS is multifactorial, representing inflammatory injury, axonal loss, and grey matter pathology that interrupt distributed neural tissue [7]. Screening studies using the Montreal Cognitive Assessment (MoCA) have shown that a considerable proportion of patients may have measurable



impairment even when routine clinical follow-up attention on relapse activity and physical disability [8]. In a study assessing cognitive function, 48% patients met criteria for cognitive impairment with a lower mean MoCA score in patients than in healthy individuals (24.58 ± 4.29 vs 28.14 ± 0.73) [9]. Neuroimaging findings provide added biological support for cognitive impairment, mainly cortical involvement and neurodegeneration. Longitudinal studies have shown that cortical lesions identified at diagnosis are associated with cognitive impairment over long-term follow-up, suggesting the significance of lesion location rather than lesion quantity alone [10]. The present study was designed to generate clinically useful evidence to support earlier recognition of cognitive impairment and targeted monitoring in patients at higher risk.

Despite these observations, limitations remain in routine clinical practice where detailed neuropsychological assessment and advanced volumetric magnetic resonance imaging are not available. In many low and middle-income regions, cognitive screening is not regularly added to multiple sclerosis care, and local data relating practical screening tools to routinely reported magnetic resonance imaging features remain scarce. The present study aims to determine the frequency of cognitive impairment among patients with multiple sclerosis using the Montreal Cognitive Assessment and to assess its connotations with demographic factors, disease duration, and MRI markers recorded in everyday practice, including lesion burden, lesion location, cortical lesion presence, and radiological evidence of brain atrophy.

METHODS

This cross-sectional study was carried out in the Department of Neurology, Punjab Institute of Neurosciences, Lahore, over a duration of six months from May to December 2025. Ethical approval of the study was obtained from the institutional review committee (1991/IRB/PINS/Approval/2024; dated 13th December 2024). Patients were enrolled through a non-probability consecutive sampling technique from both the outpatient and inpatient neurology services, and a brain MRI was arranged through the Department of Radiology as part of routine patient care. All scans were interpreted by a consultant radiologist who remained unaware of the patients' cognitive assessment. A sample size of 71 was calculated on the basis of an expected cognitive impairment frequency of 18.3%, with a 95% confidence level and 9% margin of error [11]. Adults between 18 and 50 years of age with multiple sclerosis diagnosed according to the 2017 Revised McDonald Criteria [12] and disease duration of at least 12 months were eligible for inclusion. Only clinically stable patients were enrolled, defined as no relapse and no high-dose corticosteroid use within the

preceding 30 days. Participants had to be able to undergo a brain MRI and complete the Montreal Cognitive Assessment under standardized conditions, with satisfactory hearing, vision, and language comprehension. Patients were excluded if they had any other neurological disorders, such as stroke, traumatic brain injury, or epilepsy, psychiatric illness affecting cognitive assessment, systemic illnesses to influence cognition or imaging findings, or contraindications to MRI, including metallic implants or severe claustrophobia, or recent use of medications recognized to affect cognition. After obtaining written informed consent, baseline demographic information, including age, sex, and education level, was recorded, followed by detailed assessments of clinical, neurological, and cognitive functions, including the type of multiple sclerosis and disease duration in years. Baseline laboratory investigations, including complete blood count, erythrocyte sedimentation rate, liver and renal function tests, thyroid profile, cerebrospinal fluid analysis, and vitamin B12 levels, were performed to exclude secondary causes of cognitive impairment. Brain magnetic resonance imaging was performed on a 3-Tesla scanner using routine clinical T2-weighted and fluid-attenuated inversion recovery sequences. Total lesion count and lesion location were recorded based on radiology review. Cortical lesions were coded as present or absent when identifiable on the MRI. Brain atrophy was recorded as present or absent based on the consultant radiologist's report. Cognitive screening was performed using the Montreal Cognitive Assessment by a trained neurologist in a quiet, distraction-free environment. Scores range from 0 to 30, with cognitive impairment defined a priori as a score below 26 [13]. For descriptive reporting, scores were grouped as normal (26–30), mild impairment (20–25), moderate impairment (10–19), and severe impairment (<10). Data were entered and analyzed using SPSS version 26.0. Quantitative variables were reported as mean and standard deviation, while categorical variables were noted as frequencies and percentages. Between-group comparisons for continuous variables were conducted using independent sample t-tests. Associations between categorical variables and cognitive status were assessed using Pearson's chi-square test. All tests were two-tailed, and a p-value <0.005 was considered statistically significant.

RESULTS

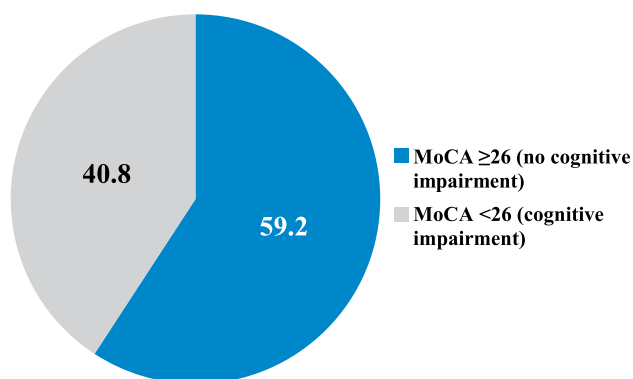
The mean age of the patients was 35.08 ± 7.71 years, and the mean disease duration was 6.53 ± 3.24 years. There were 23 males (32.4 %) and 48 females (67.6 %). Cognitive impairment severity showed 59.2 % were normal, 21.1 % had mild, 12.7 % had moderate, and 7.0 % had severe impairment (Table 1).

Table 1: Baseline Demographic, Cognitive, and Neuro-Imaging Characteristics of Patients with Multiple Sclerosis (n=71)

Variables	Category	Mean $\pm$ SD / n (%)
Age (years)	Years	35.08 $\pm$ 7.71
Disease Duration	Years	6.53 $\pm$ 3.24
Age Group	18–35 Years	35 (49.3%)
	36–50 Years	36 (50.7%)
Sex	Male	23 (32.4%)
	Female	48 (67.6%)
Education Level	No Formal Education	8 (11.3%)
	Primary	15 (21.1%)
	Secondary	28 (39.4%)
	Higher	20 (28.2%)
Moca Score	Mean $\pm$ SD	22.91 $\pm$ 5.87
Cognitive Impairment Severity	Normal (≥ 26)	42 (59.2%)
	Mild (20–25)	15 (21.1%)
	Moderate (10–19)	9 (12.7%)
	Severe (<10)	5 (7.0%)
Type of MS	Relapsing-Remitting MS	49 (69.0%)
	Primary Progressive MS	8 (11.3%)
	Secondary Progressive MS	14 (19.7%)
Disease Duration	<5 Years	27 (38.0%)
	5–10 Years	32 (45.1%)
	>10 Years	12 (16.9%)

MoCA: Montreal Cognitive Assessment; MS: Multiple Sclerosis

Out of 71 patients, 42 (59.2 percent) had no cognitive impairment, while 29 (40.8 percent) were classified as cognitively impaired (Figure 1).

**Figure 1:** Frequency of Cognitive Impairment Based on MoCA Score**Table 1:** Association of Cognitive Impairment with Demographic, Clinical, and Neuroimaging Parameters

Variables	Category	MoCA ≥ 26 (No Impairment), n (%)	MoCA < 26 (Impairment), n (%)	Test statistic (χ^2 / t-value)	p-value
Age in years	Mean $\pm$ SD	33.26 $\pm$ 7.47	37.72 $\pm$ 7.39	t = -2.49	0.016
Age Group	18–35 Years	25 (59.5%)	10 (34.5%)	$\chi^2 = 4.304$	0.038
	36–50 Years	17 (40.5%)	19 (65.5%)		
Disease Duration in Years	Mean $\pm$ SD	5.73 $\pm$ 3.02	7.70 $\pm$ 3.25	t = -2.58	0.012
Sex	Male	14 (33.3%)	9 (31.0%)	$\chi^2 = 0.041$	0.839
	Female	28 (66.7%)	20 (69.0%)		
Education Level	No Formal Education	5 (11.9%)	3 (10.3%)	$\chi^2 = 6.095$	0.107

Cortical lesions (72.4% vs. 38.1%, $p=0.004$) and brain atrophy (48.3% vs. 16.7%, $p=0.004$) were significantly associated with cognitive impairment (Figure 2).

**Figure 1:** Representative Axial Fluid-Attenuated Inversion Recovery Brain Magnetic Resonance Image Demonstrating Periventricular and Juxtacortical Demyelinating Lesions in Multiple Sclerosis

Patients with cognitive impairment had a higher mean age (37.72 ± 7.39 vs. 33.26 ± 7.47), longer disease duration (7.70 ± 3.25 vs. 5.73 ± 3.02), lower MoCA score (20.15 ± 6.25 vs. 24.81 ± 4.81), and greater total MRI lesions (19.45 ± 10.74 vs. 13.74 ± 6.72), with significant t-values (all $p < 0.005$). Cognitive impairment was more frequent in the older age group (36–50 years: 65.5% vs. 40.5%, $p=0.038$) and with longer disease duration (>10 years: 27.6% vs. 9.5%, $p=0.022$) (Table 2).

	Primary	12 (28.6%)	3 (10.3%)		
	Secondary	12 (28.6%)	16 (55.2%)		
	Higher	13 (31.0%)	7 (24.1%)		
Disease Duration Groups	<5 Years	21 (50.0%)	6 (20.7%)	$\chi^2 = 7.668$	0.022
	5–10 Years	17 (40.5%)	15 (51.7%)		
	>10 Years	4 (9.5%)	8 (27.6%)		
Moca Score	Mean $\pm$ SD	24.81 $\pm$ 4.81	20.15 $\pm$ 6.25	t = 3.54	0.001
Total MRI Lesions	Mean $\pm$ SD	13.74 $\pm$ 6.72	19.45 $\pm$ 10.74	t = -2.76	0.007
Periventricular Lesions	Yes	30 (71.4%)	24 (82.8%)	$\chi^2 = 1.209$	0.271
Juxtacortical Lesions	Yes	25 (59.5%)	23 (79.3%)	$\chi^2 = 3.067$	0.080
Infratentorial Lesions	Yes	12 (28.6%)	12 (41.4%)	$\chi^2 = 1.258$	0.262
Spinal Cord Lesions	Yes	10 (23.8%)	11 (37.9%)	$\chi^2 = 1.642$	0.200
Cortical Lesions	Yes	16 (38.1%)	21 (72.4%)	$\chi^2 = 8.096$	0.004
Brain Atrophy	Yes	7 (16.7%)	14 (48.3%)	$\chi^2 = 8.229$	0.004

MoCA: Montreal Cognitive Assessment. χ^2 : Pearson chi-square statistic. t: independent samples t-test. SD: standard deviation. Independent t-test used for continuous variables; Pearson's Chi-square test applied for categorical variables. p-value <0.005 was considered statistically significant

DISCUSSION

The present study demonstrated that cognitive impairment is a frequent complication of multiple sclerosis, with a mean age of 35.08 ± 7.71 years and a mean disease duration of 6.53 ± 3.24 years. The overall mean Montreal Cognitive Assessment (MoCA) score was 22.91 ± 5.87 , and 40.8% of patients had cognitive impairment defined as MoCA <26, whereas 59.2% remained cognitively intact. Total MRI lesion burden averaged 16.07 ± 8.98 , and cognitive impairment was significantly associated with higher age, longer disease duration, lower MoCA scores, greater total lesion counts, as well as the presence of cortical lesions and brain atrophy. Given the cross-sectional design, temporal change in cognition could not be evaluated, and the findings should be interpreted as associations at a single assessment rather than evidence of progression. Age and disease duration emerged as important correlates of cognition in the present Study. Patients with cognitive impairment were older ($p=0.016$) and had longer disease duration ($p=0.012$). These findings are consistent with the meta-regression from Wu *et al.* who found that the prevalence of impairment increased with older age ($p=0.017$) and longer disease duration ($p=0.005$) [14]. The present findings therefore reinforce robust evidence that age and especially disease duration are key determinants of cognitive decline in multiple sclerosis, even when absolute disability levels may still be moderate. The frequency of cognitive impairment in this study (40.8%) falls within the upper range of estimates reported in the international literature and is remarkably close to the 40% of patients with MoCA <26 described by Taub *et al.* whose mean MoCA score was higher at 25.86 ± 2.92 [13]. Al-Falaki *et al.* observed MoCA-defined impairment in 48% of patients, with a mean total MoCA of 24.58 ± 4.29 compared with 28.14 ± 0.73 in healthy controls [9]. The pooled prevalence of cognitive impairment in relapsing–remitting

multiple sclerosis in the meta-analysis by Wu *et al.* was 32.5% (95% CI 29.3–36.0%), somewhat lower than the 40.8 percent observed here, but within the heterogeneity range of 10.2–60.0% across included studies [14]. By contrast, Bouman *et al.* described a much higher burden of impairment, with 73.6% of patients classified as cognitively impaired and only 26.4% preserved, reflecting longer disease duration (11.6 ± 6.9 years) and older age (48 ± 11 years) in that cohort [15]. Taken together, the current prevalence aligns with the notion that approximately one-third to one-half of adults with multiple sclerosis exhibit clinically relevant cognitive deficits, with higher rates in progressive and long-standing disease. The proportional distribution of clinical phenotypes in this study, with relapsing–remitting multiple sclerosis in 69.0%, primary progressive in 11.3%, and secondary progressive in 19.7%, aligns with the typical dominance of relapsing–remitting disease in clinic-based samples. Taub *et al.* reported that MoCA impairment rates were higher in secondary progressive (55%) and primary progressive (56%) than in relapsing remitting disease (33%) [13]. Brochet and Ruet noted that the prevalence in relapsing remitting disease tends to be around 31–45% [16]. A study by Brochet *et al.* confirmed higher impairment rates in secondary progressive disease, with representative figures of 79.4% versus 44.5% in relapsing–remitting [17]. Sabanagic-Hajric *et al.* also reported worse MoCA performance in progressive types, with significant correlations between progressive phenotype and executive and language dysfunction [18]. Thus, although causal inference is limited in the present cross-sectional design, the relatively high overall prevalence of impairment and the strong imaging associations are biologically congruent with a sample that includes a substantial proportion of progressive disease [19]. A key contribution of this study is the demonstration

that total MRI lesion burden, cortical involvement, and brain atrophy are strongly associated with cognitive impairment. Patients with MoCA <26 had significantly higher total lesion counts ($p=0.007$), and cortical lesions and brain atrophy were represented in the impaired group (72.4% and 48.3%, both $p=0.004$). Curti *et al.* reported a similar mean lesion count (22.7 ± 16.42 overall) and demonstrated higher lesion burden in patients with cortical lesions ($p=0.002$) and in progressive versus relapsing–remitting disease ($p=0.001$) [11]. Bouman *et al.* further linked multi-domain impairment to smaller cortical grey matter, thalamic, and hippocampal volumes [15]. Van Doninck *et al.* observed that impaired patients had lower raw hippocampal, thalamic, cortical, and grey matter volumes, although only normalized cortical volume remained significantly different after correction for intracranial volume [20]. From a clinical perspective, the findings support the routine use of MoCA as a practical screening tool to detect cognitive impairment in multiple sclerosis, mainly in older patients, have longer disease duration or exhibit cortical lesions and radiological atrophy Al-Falaki *et al.* and Taub *et al.* both noted that MoCA is useful to identify cognitive impairment in multiple sclerosis, with abnormalities most frequently involving memory, attention, visuospatial functions, and executive processing [9, 13]. The study has several strengths, including standardized cognitive screening with the Montreal Cognitive Assessment, which was done along with brain MRI within the same clinical setting, allowing individual patient-level relation of cognitive status with lesion burden and atrophy. Recruitment from both inpatient and outpatient neurology services increases clinical relevance, and radiological evaluation was done by qualified specialists, reducing the likelihood of error in identifying lesion types and brain atrophy. The inclusion of disease duration and age stratification further supports the interpretation of associations.

Important limitations exist. Disability scores, fatigue, depression, and medication effects were not assessed, even though these factors are recognized to influence cognitive outcomes. MoCA offers a global screen but does not substitute detailed neuropsychological testing. Since the study was conducted at a single center, the findings may not be fully applicable to other clinical settings. Future studies should implement long follow-up with standardized disability scoring, validated measures of depression and fatigue, and quantitative volumetric imaging to model cognitive trajectories and determine whether imaging markers add prognostic value beyond clinical measures.

CONCLUSIONS

Cognitive impairment was common in patients with multiple sclerosis and associated with many demographic and disease-related factors. Poorer cognition on screening was common in those with old age, longer disease duration,

and those showing structural changes on brain imaging. These findings suggest that cognitive decline should be regarded as an important part of the overall disease burden rather than an isolated complication. Integrating cognitive assessment into routine neurological follow-up may improve patient monitoring, allow earlier identification of decline, and may support timely rehabilitation and supportive care aimed at maintaining daily functioning and quality of life.

Authors' Contribution

Conceptualization: AS, MSA

Methodology: AS, IN, FA

Formal analysis: QG, MSA, IN, MZ, FA

Writing and Drafting: QG, MSA, IN, MZ, FA

Review and Editing: AS, QG, MSA, IN, MZ, FA

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All 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] Eva L, Pleş H, Covache-Busuioc RA, Glavan LA, Bratu BG, Bordeianu A *et al.* A Comprehensive Review on Neuroimmunology: Insights from Multiple Sclerosis to Future Therapeutic Developments. *Biomedicines*. 2023 Sep; 11(9): 2489. doi: 10.3390/biomedicines11092489.
- [2] Boutitah-Benyaich I, Eixarch H, Villaceros-Álvarez J, Hervera A, Cobo-Calvo Á, Montalbán X *et al.* Multiple Sclerosis: Molecular Pathogenesis and Therapeutic Intervention. *Signal Transduction and Targeted Therapy*. 2025 Oct; 10(1): 324. doi: 10.1038/s41392-025-02415-4.
- [3] Aliyev RR, Mehtiyeva SN, Shiraliyeva RK. Clinical and Epidemiological Characteristics of Multiple Sclerosis in the Southern Region of the Republic of Azerbaijan. *Pakistan Journal of Medical Sciences*. 2025 Feb; 41(2): 437. doi: 10.12669/pjms.41.2.11373.
- [4] Rathore MF and Mansoor SN. Multiple Sclerosis Management in Pakistan: A Call for Comprehensive Multidisciplinary Rehabilitation Strategies. *Journal of the College of Physicians and Surgeons—Pakistan*. 2025 May; 35(5): 553-5. doi: 10.29271/jcpsp.2025.05.553.
- [5] Gómez-Melero S, Caballero-Villarraso J, Escribano BM, Galvao-Carmona A, Túnez I, Agüera-Morales E. Impact of Cognitive Impairment on Quality of Life in Multiple Sclerosis Patients—A Comprehensive

- Review. *Journal of Clinical Medicine*. 2024 Jun; 13(11): 3321. doi: 10.3390/jcm13113321.
- [6] Jakimovski SB, Zivadinov S, Morrow R, H. Benedict, F, Zipp, B, Weinstock-Guttman. Multiple Sclerosis. *Lancet*. 2024; 403: 183-202. doi: 10.1016/S0140-6736(23)01473-3.
- [7] Pitteri M, Galazzo IB, Brusini L, Cruciani F, Dapor C, Marastoni D et al. Microstructural MRI Correlates of Cognitive Impairment in Multiple Sclerosis: The Role of Deep Gray Matter. *Diagnostics*. 2021 Jun; 11(6): 1103. doi: 10.3390/diagnostics11061103.
- [8] Scheenen ME, van den Brink RH, Konstantinidou S, Lugtenburg A, Spit J, Hendriks GJ et al. Montreal Cognitive Assessment (MoCA) Norms for Older Patients with a Depressive Disorder. *Medical Sciences*. 2025 Dec; 13(4): 312. doi: 10.3390/medsci13040312.
- [9] Al-Falaki TA, Hamdan FB, Sheaaheed NM. Assessment of Cognitive Functions in Patients with Multiple Sclerosis. *The Egyptian Journal of Neurology, Psychiatry and Neurosurgery*. 2021 Sep; 57(1): 127. doi: 10.1186/s41983-021-00383-4.
- [10] Ziccardi S, Pisani AI, Schiavi GM, Guandalini M, Crescenzo F, Colombi A et al. Cortical Lesions at Diagnosis Predict Long-Term Cognitive Impairment in Multiple Sclerosis: A 20-Year Study. *European Journal of Neurology*. 2023 May; 30(5): 1378-88. doi: 10.1111/ene.15697.
- [11] Curti E, Graziuso S, Tsantes E, Crisi G, Granella F. Correlation Between Cortical Lesions and Cognitive Impairment in Multiple Sclerosis. *Brain and Behavior*. 2018 Jun; 8(6): e00955. doi: 10.1002/brb3.955.
- [12] Thompson AJ, Banwell BL, Barkhof F, Carroll WM, Coetzee T, Comi G et al. Diagnosis of Multiple Sclerosis: 2017 Revisions of the McDonald Criteria. *The Lancet Neurology*. 2018 Feb; 17(2): 162-73. doi: 10.1016/S1474-4422(17)30470-2.
- [13] Taub ES, Cersosimo BH, Krupp L, Rosicki C, Melville P, Charvet L. The Montreal Cognitive Assessment (MoCA) in multiple sclerosis: relation to clinical features. *Journal of Multiple Sclerosis*. 2015; 2(02). doi: 10.4172/2376-0389.1000135.
- [14] Wu W, Francis H, Lucien A, Wheeler TA, Gandy M. The Prevalence of Cognitive Impairment in Relapsing-Remitting Multiple Sclerosis: A Systematic Review and Meta-Analysis. *Neuropsychology Review*. 2025 Jun; 35(2): 233-53. doi: 10.1007/s11065-024-09640-8.
- [15] Bouman PM, Van Dam MA, Jonkman LE, Steenwijk MD, Schoonheim MM, Geurts JJ et al. Isolated Cognitive Impairment in People with Multiple Sclerosis: Frequency, MRI Patterns and Its Development Over Time. *Journal of Neurology*. 2024 May; 271(5): 2159-68. doi: 10.1007/s00415-024-12185-8.
- [16] Brochet B and Ruet A. Cognitive Impairment in Multiple Sclerosis with Regards to Disease Duration and Clinical Phenotypes. *Frontiers in Neurology*. 2019 Mar; 10: 261. doi: 10.3389/fneur.2019.00261.
- [17] Brochet B, Clavelou P, Defer G, De Seze J, Louapre C, Magnin E et al. Cognitive Impairment in Secondary Progressive Multiple Sclerosis: Effect of Disease Duration, Age, and Progressive Phenotype. *Brain Sciences*. 2022 Jan; 12(2): 183. doi: 10.3390/brainsci12020183.
- [18] Sabanagic-Hajric S, Memić-Serdarević A, Sulejmanpasić G, Salihović-Besirović D, Kurtović A, Bajramagić N et al. Cognitive Impairment in Multiple Sclerosis: Relation to Disability, Duration, and Type of Disease. *Materia Socio-Medica*. 2023; 35(1): 23. doi: 10.5455/msm.2023.35.23-28.
- [19] Goodin DS. The Epidemiology, Pathology, and Pathogenesis of MS: Therapeutic Implications. *Neurotherapeutics*. 2025 Feb; e00539. doi: 10.1016/j.neurot.2025.e00539.
- [20] Van Doninck E, De Keersmaecker AV, D'hooghe M, Van Wijmeersch B, Perrotta G, El Sankari S et al. Cognitive Functioning in Multiple Sclerosis with Focus on Brainstem Volume. *Acta Neurologica Belgica*. 2025 Nov; 1-0. doi: 10.1007/s13760-025-02928-3.



Original Article



Efficacy and Safety of Topical Spironolactone Versus Topical Clindamycin in the Treatment of Acne Vulgaris: A Split-Face Study

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ARTICLE INFO

Keywords:

Acne Vulgaris, Topical Spironolactone, Topical Clindamycin, Global Acne Assessment Score

How to Cite:

Khan, A., Hanif, S., Shaukat, R., Hamadani, A., Kausar, I., Chattha, A. A., Nabi, H., Pavin, O., & Rao, B. (2026). Efficacy and Safety of Topical Spironolactone Versus Topical Clindamycin in the Treatment of Acne Vulgaris: A Split-Face Study: Topical Spironolactone Versus Topical Clindamycin in the Treatment of Acne Vulgaris. *Pakistan Journal of Health Sciences*, 7(6), 99-104. <https://doi.org/10.54393/pjhs.v7i6.4125>

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Received Date: 23rd February, 2026

1st Revision Received: 3rd April, 2026

2nd Revision Received: 11th April, 2026

Acceptance Date: 16th April, 2026

Published Date: 30th June, 2026

ABSTRACT

This study compares the effectiveness and safety of topical Spironolactone 5% versus topical Clindamycin 2% in treating acne vulgaris in the same patient. **Objective:** To assess the effectiveness and safety of topical spironolactone 5% versus topical clindamycin 2% in the treatment of mild to moderate acne vulgaris in the same patient through a controlled evaluation. **Methods:** A double-blind, split-face comparative study was conducted at the Department of Dermatology, Ghurki Trust Teaching Hospital (October 2023-September 2024). Participants used 5% Spironolactone on one side of the face and 2% Clindamycin on the other for 12 weeks. Both patients and the assessing dermatologist remained blind. Improvement was measured by Total Lesion Count, Acne Severity Index, and Global Acne Assessment Score (GAAS), with a GAAS score of 0 or 1 indicating treatment success. **Results:** Both therapies effectively reduced papules, pustules, and comedones in 42 participants over 12 weeks, achieving Total Lesion Count Reductions of approximately 77.5 % for topical Spironolactone and 79.2% for topical Clindamycin ($p=0.877$). Clindamycin demonstrated faster initial improvement in total lesion count at week 6 ($p=0.043$) and week 8 ($p=0.012$), but Spironolactone showed comparable improvement by Week 12; however, the difference was not statistically significant ($p=0.057$). Clindamycin reduced pustules more efficiently at Week 12 ($p=0.007$). **Conclusions:** Both topical spironolactone and clindamycin were effective in treating mild to moderate acne vulgaris. Clindamycin showed a quicker initial improvement, but both treatments had similar results after 12 weeks.

INTRODUCTION

Acne vulgaris is a recurrent inflammatory skin disorder that affects sebaceous glands and hair follicles [1]. Comedones, papules, pustules, nodules, and scars are its prominent features [2]. While the disease is thought to mostly affect adolescents and young adults, it can develop and persist long into adulthood [3, 4]. Around the world, 87% of adults suffer from acne vulgaris. Acne can significantly affect mental health and psychosocial growth [5]. The formation of acne involves a multifaceted process inside the pilosebaceous unit, incorporating numerous factors.

These factors encompass hormonal balance alterations, excessive production of sebum, and changes in its composition and follicular hyperkeratinisation. The combination of these complex mechanisms leads to dysfunction in the pilosebaceous unit, facilitating the formation of microcomedones, which subsequently develop into non-inflammatory and inflammatory lesions [6]. Treatment options encompass topical retinoids (Isotretinoin, Tretinoin, Adapalene, Tazarotene), topical antibiotics (Clindamycin, Tetracycline, Erythromycin),



systemic antibiotics (Azithromycin, Minocycline, Doxycycline, Tetracycline), systemic retinoids, and hormone therapy, based upon the degree of severity [7]. Resistance to antibiotics in acne presents a significant concern [8]. Anti-androgens appear to be an acceptable approach to the treatment of acne vulgaris because androgen hormones cause sebaceous gland hyperplasia and increased sebum production [9, 10]. As a result, several anti-androgen medications have been used for acne vulgaris, including Androgen Receptor Blockers (spironolactone, combined oral contraceptive pills, and topical clascoterone), Non-steroidal anti-androgens (flutamide), and 5 alpha reductase inhibitors (finasteride, dutasteride) [11]. Spironolactone exerts its effects via the following mechanisms: Androgen Receptor blockade acts as a competitive inhibitor of testosterone and dihydrotestosterone (DHT), blocking their binding. Suppression of 5 alpha reductase leads to reduced DHT formation, resulting in decreased size and activity of sebaceous glands. Side effects include menstrual irregularities, postural hypotension, and hyperkalaemia. Breast enlargement and alterations in libido are specific to males. Topical preparations can be utilized to obtain the benefits of their action while minimising significant side effects [12]. Clindamycin diminishes the development of acne lesions by inhibiting the growth of *Cutibacterium* acnes and preventing the synthesis of bacterial proteins [13].

Direct comparative studies between topical spironolactone and topical clindamycin in acne vulgaris are limited. While randomized controlled trials (RCTs) are the standard design for clinical trials, ethical and practical considerations make a non-randomized split-face design more achievable. This approach minimizes inter-individual variability, allows for direct within-patient comparisons, and ensures no patient is deprived of standard therapy. The current study used double-blinding and standardized application to limit biases that will improve clinical decision-making and acne management protocols. This study aimed to assess the effectiveness and safety of topical spironolactone 5% versus topical clindamycin 2% in the treatment of mild to moderate acne vulgaris in the same patient through a controlled evaluation.

METHODS

A double-blind split-face comparative study was conducted at the Department of Dermatology, Ghurki Trust Teaching Hospital, from October 2023 to September 2024 after taking ethical approval from the Institutional Review Board (LMDC/16989/23; dated 9th October 2023). A third party made both formulations and made sure they had the same color, texture, and smell. The participants and the dermatologist who was judging the treatment did not know

which treatment was given to each person. The study protocol followed the Declaration of Helsinki's ethical guidelines and Good Clinical Practice (GCP) guidelines. Participants were selected using consecutive sampling from patients presenting to the department during the study duration. The study included 42 patients, aged 12-39 years, with mild to moderate acne vulgaris. Patients who had hypersensitivity to either clindamycin or spironolactone, Individuals who had used systemic or topical acne medications during the month before beginning therapy, pregnant or lactating women, and patients with nodulocystic acne were excluded from the study. All patients provided written informed consent before participating in the trial. The sample size was calculated by the WHO sample size calculator using a 95% confidence interval and 80% power of the study. The mean Acne severity index of the cases was taken from a previous study with (Group A) = 5.1 ± 5.3 , the mean Acne severity index of the controls (Group B) = 7.7 ± 6.2 [14]. Acne lesions were evaluated by type (comedones, papules, pustules), number, and severity using the Global Acne Assessment Score (GAAS) and Acne Severity Index (ASI). Acne severity was assessed using the Global Acne Assessment Score (GAAS), a validated and widely used clinical grading tool with demonstrated reliability and applicability across different populations [15, 16]. Based on GAAS scores, patients were classified into mild, moderate, and severe. Photographic evaluation of the lesion was carried out at each visit with the patient's consent. The effectiveness of both treatments was determined by Total Lesion Count, GAAS, and ASI, and it was evaluated biweekly at 2, 4, 6, 8 and 12 weeks by a single investigator who is blinded to the treatment allocation. The formulations of the study creams were as follows: 5% Spironolactone Cream: Spironolactone 5%, cetyl alcohol 1.5%, croda wax 10%, polawax 3%, glycerine 5%, propylene glycol 5%, white soft paraffin 10%, phenoxyethanol 1%, lactic acid 2%, methylparaben 0.2%, propyl paraben 0.02%, reverse osmosis water to 100g. 2% Clindamycin Cream: Clindamycin phosphate 2%, cetostearyl alcohol 2%, pola wax 5%, 2-phenoxy ethanol 1%, liquid paraffin 5%, white soft paraffin 20%, reverse osmosis water to 100g. To ensure blinding, both study formulations were prepared by a third party that was independent and standardized to match in colour, texture, and Odor. The creams were poured into identical coded containers, which allowed neither the participants nor the assessing dermatologist to identify which cream was used. The outcome assessor was not aware of treatment assignment during the study period. A simple randomization method (a coin toss) was used to decide which side of the face would get treatment. Spironolactone went to one side and clindamycin went to the other. Patients were directed to cleanse their face with a mild

cleanser, gently pat it dry, and apply an equal number of designated creams to each side of the face twice daily. To minimize cross-contamination, participants were given directions to clean their hands between applications. Treatment adherence was assessed through patient self-reporting and verification of medication usage at each follow-up visit. Clinical evaluations were conducted biweekly over the 12 weeks. The patients were instructed to discontinue medication after 12 weeks and undergo re-evaluation after one month to check for relapse. Acne Severity Index (ASI) was calculated using the following formula: $ASI = \text{papules} + (2 \times \text{pustules}) + (\text{comedones} / 2)$ [16]. Participants with a GAAS score of 0 (none) or 1 (minimal) will be classified as having achieved "success". Side effects were also noted at each follow-up visit. At the conclusion of the follow-up period, participants rated their satisfaction level by using a 4-point scale: 1 = Excellent (very satisfied), 2 = Good (moderately satisfied), 3 = Fair (slightly satisfied), and 4 = Poor (not satisfied). The Global Acne Grading System (GAGS) was initially created in 19973. The GAGS breaks the face (forehead, each cheek, nose, and chin) into six parts, and the severity of each area is rated on a scale of 0 to 4 (0, there are no lesions; 1, comedones; 2, papules; 3, pustules; and 4, nodules). The sum of the six zones is then added, and the severity of acne is determined as mild (118), moderate (1930), severe (3138), and very severe (>39) [15]. The primary outcome of the study was a reduction in total lesion count, while secondary outcomes included changes in Acne Severity Index (ASI), Global Acne Assessment Score (GAAS), patient satisfaction, side effects, and relapse. Data were analysed using SPSS version 27.0. Qualitative variables were represented as numbers and percentages, whereas quantitative data were presented as mean $\pm$ standard deviation (SD). The Wilcoxon signed rank test was used for comparison between the spironolactone-treated side and the clindamycin-treated side at each follow-up visit. The Kolmogorov-Smirnov test was applied to check the normality of data and found that p-values were <0.005, so non-parametric testing was applied. As it was a split-face study, the Wilcoxon test was used for comparison. All p-values less than 0.005 were considered statistically significant.

RESULTS

In this study with 42 participants, 85.7% were female, 90.5% were between the ages of 18 and 29, and 71.4% were unmarried. All participants were non-smokers, with 14.3% having comorbidities. Disease duration exhibited variability: 45.2% experienced it for 6 to 12 months, 35.7% for three to six months, and 19% for more than one year. All participants completed the study and were included in the final analysis, with no dropouts reported. At baseline, there was no statistically significant difference between the two

treatment groups regarding papules, pustules, comedones, total lesion count, and Acne Severity Index ($p > 0.005$), indicating similar initial conditions. By week 12, no significant difference in total lesion count (TLC) was observed between the treatments ($p = 0.877$), suggesting comparable long-term effectiveness. The comparison of lesion counts and ASI between the two treatments. The Acne Severity Index ASI was comparable between the groups (spironolactone 17.06 ± 2.66 versus clindamycin: 18.02 ± 2.68 , $p = 0.103$). Both treatments resulted in a decrease in ASI over time, with clindamycin demonstrating significantly greater reductions starting from week 6 ($p < 0.005$). However, at week 12, clindamycin demonstrated a lower ASI (3.43 ± 2.26) in comparison to spironolactone (4.50 ± 1.63 , $p = 0.014$). The magnitude of this difference was small, suggesting limited clinical significance despite statistical significance (Table 1).

Table 1: Comparative Clinical Profile of Patients from Baseline to 12 weeks Between Treatment with Topical Spironolactone and Topical Clindamycin (Split face n=42)

Parameters	Visit (Weeks)	Spironolactone, (Mean $\pm$ SD)	Clindamycin, (Mean $\pm$ SD)	p-value
Papules	0	6.71 $\pm$ 2.08	7.07 $\pm$ 1.80	0.398
	2	5.50 $\pm$ 1.77	5.24 $\pm$ 1.39	0.456
	4	4.24 $\pm$ 1.72	3.12 $\pm$ 1.02	<0.001
	6	3.29 $\pm$ 1.64	1.98 $\pm$ 0.84	<0.001
	8	2.60 $\pm$ 1.71	1.36 $\pm$ 1.08	<0.001
	12	1.50 $\pm$ 1.37	0.98 $\pm$ 1.09	0.058
Pustules	0	1.93 $\pm$ 1.20	2.19 $\pm$ 1.19	0.322
	2	1.86 $\pm$ 1.16	2.05 $\pm$ 1.25	0.468
	4	1.55 $\pm$ 0.99	1.60 $\pm$ 1.01	0.819
	6	1.40 $\pm$ 0.99	1.31 $\pm$ 0.98	0.677
	8	1.17 $\pm$ 0.88	0.76 $\pm$ 0.82	0.030
	12	0.88 $\pm$ 0.74	0.38 $\pm$ 0.54	<0.001
Comedones	0	12.98 $\pm$ 2.91	13.14 $\pm$ 2.51	0.788
	2	10.90 $\pm$ 3.09	10.45 $\pm$ 3.27	0.519
	4	8.98 $\pm$ 3.65	8.83 $\pm$ 3.20	0.842
	6	7.12 $\pm$ 3.26	7.00 $\pm$ 3.16	0.884
	8	4.93 $\pm$ 3.11	4.74 $\pm$ 3.06	0.779
	12	2.48 $\pm$ 2.55	3.38 $\pm$ 2.58	0.112
Total Lesion Count	0	21.62 $\pm$ 3.41	22.40 $\pm$ 2.34	0.225
	2	18.26 $\pm$ 3.40	17.74 $\pm$ 3.53	0.494
	4	14.76 $\pm$ 3.41	13.55 $\pm$ 3.39	0.107
	6	11.81 $\pm$ 3.30	10.29 $\pm$ 3.47	0.043
	8	8.69 $\pm$ 2.92	6.86 $\pm$ 3.59	0.012
	12	4.83 $\pm$ 2.34	4.74 $\pm$ 2.95	0.877
Acne Severity Index (ASI)	0	17.06 $\pm$ 2.66	18.02 $\pm$ 2.68	0.103
	2	14.67 $\pm$ 2.67	14.56 $\pm$ 3.19	0.864
	4	11.82 $\pm$ 2.19	10.73 $\pm$ 2.85	0.053
	6	9.65 $\pm$ 2.26	8.10 $\pm$ 2.83	0.007
	8	7.39 $\pm$ 2.02	5.25 $\pm$ 5.06	0.014
	12	4.50 $\pm$ 1.63	3.43 $\pm$ 2.26	0.015

Both spironolactone and clindamycin therapies

significantly decreased the presence of papules, pustules, and comedones; however, Clindamycin demonstrated faster initial improvement in total lesion count at week 6 ($p=0.043$) and week 8 ($p=0.012$). The reduction in lesion count over time for both treatments is shown (Figure 1).

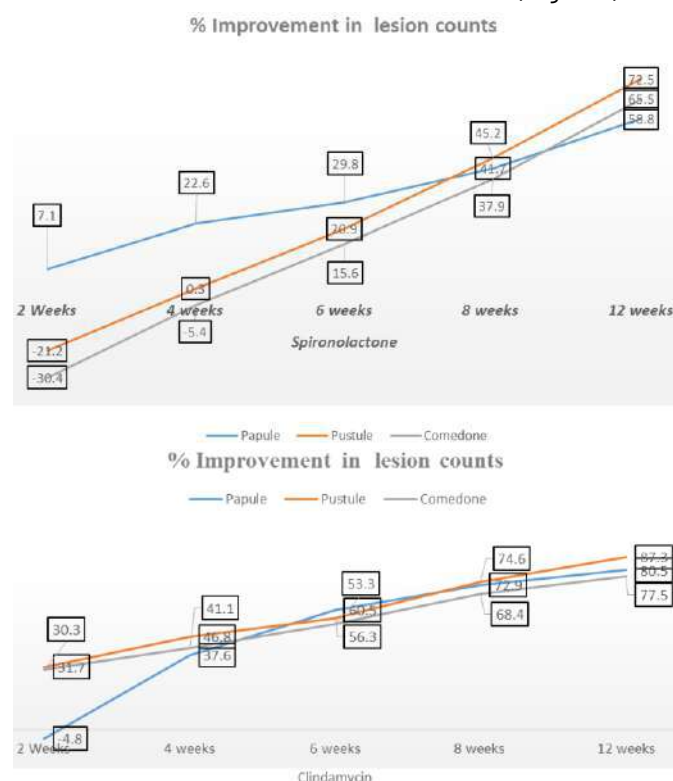


Figure 1: Improvement in Lesion Count in the Spironolactone Side and Clindamycin Side from Baseline to 12 Weeks

The two treatments demonstrated progressive improvements. None of the patients succeeded during baseline and week 2. By week 6, there were equal success rates (7.1% each). Clindamycin demonstrated a quicker response at week 8 (45.2% vs 19.0%). But by week 12, the two treatments showed similar effectiveness, with clindamycin and spironolactone success rates of 81.0 and 78.6, respectively (Table 2).

Table 2: Comparison of the Number of Patients Who Achieved Success on the Global Acne Assessment Score

Visit (Weeks)	Spironolactone Success, n (%)	Spironolactone Failure, n (%)	Clindamycin Success, n (%)	Clindamycin Failure, n (%)
0	0 (0%)	42 (100%)	0 (0%)	42 (100%)
2	0 (0%)	42 (100%)	0 (0%)	42 (100%)
4	0 (0%)	42 (100%)	1 (2.4%)	41 (97.6%)
6	3 (7.1%)	39 (92.9%)	3 (7.1%)	39 (92.9%)
8	8 (19.0%)	34 (81.0%)	19 (45.2%)	23 (54.8%)
12	33 (78.6%)	9 (21.4%)	34 (81.0%)	8 (19.0%)

The Global Acne Assessment Score indicates that the success rates for both groups were similar at week 12. The treatment success based on GAAS at each follow-up visit is presented, with 33 of 42 individuals in the spironolactone

group attaining success (78.6%) and 34 of 42 participants in the clindamycin group achieving success (81.0%). This shows that both therapies were equally successful in reaching success by the conclusion of the study even though clindamycin exhibited faster improvement early. Both treatments were generally well tolerated, with only mild side effects reported during the study period. The difference in treatment success between the two sides was minimal and appeared comparable at week 12 (Figure 2).

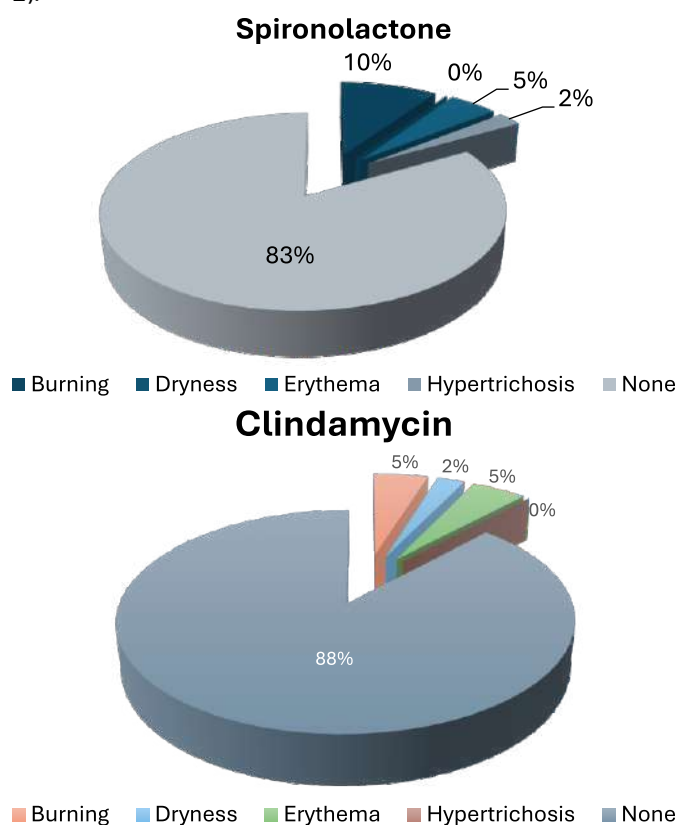


Figure 2: Side Effects Observed During Study

Patient satisfaction was high in both treatment groups, with most participants reporting good to excellent outcomes. The distribution of patient satisfaction scores is presented (Figure 3).

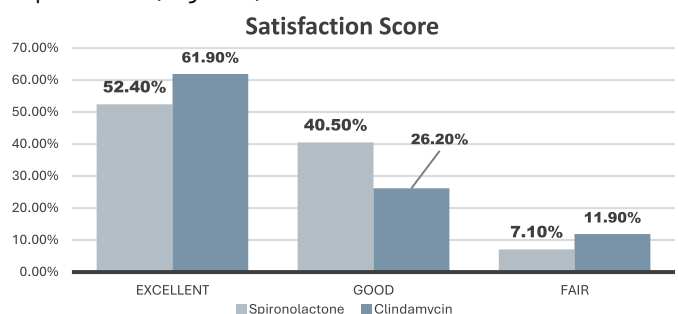


Figure 3: Patient Satisfaction Score of Spironolactone and Clindamycin

Before and after, the picture of the spironolactone side effects was shown (Figure 4).



Figure 4: Before and After Pictures of the Patient (Spironolactone Side)

DISCUSSION

This study demonstrated that both topical spironolactone 5% and clindamycin 2% are effective in reducing acne severity, with comparable outcomes at 12 weeks, although clindamycin showed a relatively faster onset of action. These results are in line with the emerging evidence of the topical spironolactone being an effective anti-androgen therapy. The clinical efficacy of topical spironolactone formulations has been recently documented by significant decreases in the Acnes Severity Index (ASI) and total lesion count (TLC), which validates its use [17]. But these comparisons are to be approached with caution because of variations in formulation, study design, and severity of baseline. The effectiveness of topical clindamycin we observed is in line with the previous literature showing that it is effective in the treatment of inflammatory lesions, especially papules and pustules [18]. But its slower and less prolonged action in later weeks than spironolactone may indicate its dominance as an antibacterial agent and not an action on the hormonal part of acne. Importantly, comparisons in this discussion are restricted to topical therapies with similar routes of administration to ensure methodological consistency. Although oral spironolactone is effective in moderate-severe acne, these results cannot be directly compared because they vary in systemic exposure and pharmacokinetics [19]. Conversely, topical spironolactone, with its localized anti-androgenic effect and low systemic absorption, is a factor in its good safety profile. The growing importance of topical antiandrogenic treatments, such as spironolactone and clascoterone, in the management of acne has also been noted in the recent literature. These agents have shown considerable decreases in inflammatory and non-inflammatory lesions, and are better tolerated than systemic treatments [20]. This justifies the topical spironolactone use over prolonged use of antibiotics, especially given the current trend of increasing antimicrobial resistance. In terms of safety, the localized adverse effects that were mild and registered in

our study are in line with other reports that suggest that topical spironolactone is well tolerated [17]. On the contrary, adverse effects of systemic spironolactone have been reported to include menstrual abnormalities and dizziness, further highlighting the safety benefit of topical preparations [19].

This research has a number of weaknesses. Small sample size and single-center design could limit generalizability. The use of mild to moderate acne only limits the generalizability to severe cases, and the duration of the follow-up does not allow evaluation of long-term effectiveness and relapse. Though the split-face design minimizes inter-individual variability, there is still a risk of cross-contamination. Also, possible confounders like hormonal status, diet, use of cosmetic and menstrual variations were not controlled, and no subgrouping based on age or gender was done. According to these gaps, future research ought to be performed on larger multicenter randomized trials with longer follow-up and including severe acne.

CONCLUSIONS

Both topical spironolactone 5% and clindamycin 2% showed considerable clinical improvement over 12 weeks in the severity of acne. Clindamycin exhibited a more rapid action and was more successful in weeks 6 and 8, but at week 12, the two treatments had similar efficacy. Spironolactone was found to have significant decreases in both lesion counts and severity indices, suggesting the agent as an effective topical antandrogen agent. Both interventions were tolerated well, and there were minimal localized adverse effects noted.

Authors' Contribution

Conceptualization: AK

Methodology: SH, RS, AH

Formal analysis: AH, HN

Writing and Drafting: AK, SH, RS, AH, IK, AAC, HN, OP, BR

Review and Editing: AK, SH, RS, AH, IK, AAC, HN, OP, BR

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All 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] Guleria P, Joshi S, Parmar S, Sharma T, Chaudhary A, Kumar P et al. Decoding Acne Vulgaris: Insights into Pathogenesis, Treatment Modalities, Diagnosis, and Recent Advancements. *Recent Advances in Inflammation & Allergy Drug Discovery*. 2025 Mar;

- 19(1): 18-30. doi: 10.2174/0127722708312980240718093537.
- [2] Cruz S, Vecerek N, Elbuluk N. Targeting Inflammation in Acne: Current Treatments and Future Prospects. *American Journal of Clinical Dermatology*. 2023 Jun; 24(5): 681. doi: 10.1007/s40257-023-00789-1.
 - [3] Dhurat R, Shukla D, Lim RK, Wambier CG, Goren A. Spironolactone in Adolescent Acne Vulgaris. *Dermatologic Therapy*. 2021 Jan; 34(1): e14680. doi: 10.1111/dth.14680.
 - [4] Rehan ST, Khan Z, Abbas S, Imran L, Munir S, Tahir MJ et al. Role of Topical Spironolactone in the Treatment of Acne: A Systematic Review of Clinical Trials—Does This Therapy Open A Path Towards Favorable Outcomes? *The Journal of Dermatology*. 2023 Feb; 50(2): 166-74. doi: 10.1111/1346-8138.16637.
 - [5] Dawson AL and Dellavalle RP. Acne vulgaris. *British Medical Journal*, 346 (may 08 1), f2634–f2634 [Internet]. 2013. doi: 10.1136/bmj.f2634.
 - [6] Noaimi A, Al-Saadi SR, Al-Saadi S. Treatment of Acne Vulgaris by Topical Spironolactone Solution Compared with Clindamycin Solution. *Cureus*. 2021 Aug; 13(8). doi: 10.7759/cureus.17606.
 - [7] Qayyum N, Mashhood AA, Farid A, Azam M, Komal S, Syeda H. Efficacy of Topical 2% Clindamycin Gel Versus 5% Nicotinamide Gel in Patients with Mild to Moderate Acne. *Pakistan Armed Forces Medical Journal*. 2022 Dec; 72(6): 1899. doi: 10.51253/pafmj.v72i6.3743.
 - [8] Adler BL, Kornmehl H, Armstrong AW. Antibiotic Resistance in Acne Treatment. *Journal of the American Medical Association Dermatology*. 2017 Aug; 153(8): 810-1. doi: 10.1001/jamadermatol.2017.1297.
 - [9] Del Rosso JQ and Kircik L. The Cutaneous Effects of Androgens and Androgen-Mediated Sebum Production and Their Pathophysiologic and Therapeutic Importance in Acne Vulgaris. *Journal of Dermatological Treatment*. 2024 Dec; 35(1): 2298878. doi: 10.1080/09546634.2023.2298878.
 - [10] Trifu V, Tiplica GS, Naumescu E, Zalupca L, Moro L, Celasco G. Cortexolone 17 α -Propionate 1% Cream, A New Potent Antiandrogen for Topical Treatment of Acne Vulgaris. A Pilot Randomized, Double-Blind Comparative Study vs. Placebo and Tretinoin 0.05% Cream. *British Journal of Dermatology*. 2011 Jul; 165(1): 177-83. doi: 10.1111/j.1365-2133.2011.10332.x.
 - [11] Azarchi S, Bienenfeld A, Sicco KL, Marchbein S, Shapiro J, Nagler AR. Androgens in Women: Hormone-Modulating Therapies for Skin Disease. *Journal of the American Academy of Dermatology*. 2019 Jun; 80(6): 1509-21. doi: 10.1016/j.jaad.2018.08.061.
 - [12] Layton AM, Eady EA, Whitehouse H, Del Rosso JQ, Fedorowicz Z, van Zuuren EJ. Oral Spironolactone for Acne Vulgaris in Adult Females: A Hybrid Systematic Review. *American Journal of Clinical Dermatology*. 2017 Apr; 18(2): 169-91. doi: 10.1007/s40257-016-0245-x.
 - [13] Armillei MK, Lomakin IB, Del Rosso JQ, Grada A, Bunick CG. Scientific Rationale and Clinical Basis for Clindamycin Use in the Treatment of Dermatologic Disease. *Antibiotics*. 2024 Mar; 13(3): 270. doi: 10.3390/antibiotics13030270.
 - [14] Ayatollahi A, Samadi A, Bahmanjahromi A, Robati RM. Efficacy and Safety of Topical Spironolactone 5% Cream in the Treatment of Acne: A Pilot Study. *Health Science Reports*. 2021 Sep; 4(3): e317. doi: 10.1002/hsr2.317.
 - [15] Doshi A, Zaheer A, Stiller MJ. A Comparison of Current Acne Grading Systems and Proposal of a Novel System. *International Journal of Dermatology*. 1997 Jun; 36(6): 416-8. doi: 10.1046/j.1365-4362.1997.00099.x.
 - [16] Alsulaimani H, Kokandi A, Khawandanh S, Hamad R. Severity of Acne Vulgaris: Comparison of Two Assessment Methods. *Clinical, Cosmetic and Investigational Dermatology*. 2020 Sep; 711-6. doi: 10.2147/CCID.S266320.
 - [17] Santer M, Lawrence M, Renz S, Eminton Z, Stuart B, Sach TH et al. Effectiveness of Spironolactone for Women with Acne Vulgaris (SAFA) in England and Wales: Pragmatic, Multicentre, Phase 3, Double Blind, Randomised Controlled Trial. *British Medical Journal*. 2023 May; 381. doi: 10.1136/bmj-2022-074349.
 - [18] Pelet del Toro NM, Strunk A, Wu JJ, Stein Gold L, Del Rosso JQ et al. Topical Clindamycin for Acne Vulgaris: Analysis of Gastrointestinal Events. *Journal of Dermatological Treatment*. 2024 Dec; 35(1): 2325603. doi: 10.1080/09546634.2024.2325603.
 - [19] Kow CS, Ramachandram DS, Hasan SS, Thiruchelvam K. Spironolactone for the Treatment of Moderate to Severe Acne in Adult Women: A Systematic Review and Meta-Analysis of Randomised Controlled Trials. *Australasian Journal of Dermatology*. 2025 May; 66(3): 165-8. doi: 10.1111/ajd.14428.
 - [20] Santhosh P and George M. Clascoterone: A New Topical Anti-Androgen for Acne Management. *International Journal of Dermatology*. 2021 Dec; 60(12): 1561-5. doi: 10.1111/ijd.15752.



Original Article



Cleft Lip and Palate: Analyzing the Impact of Family History and Cousin Marriages

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ARTICLE INFO

Keywords:

Cleft Lip and Palate, Family History, Cousin Marriages, Maternal Folic Acid Intake

How to Cite:

Anjum, R., Mahmood, S., Nagi, A. H., & Chaudhry, S. (2026). Cleft Lip and Palate: Analyzing the Impact of Family History and Cousin Marriages: Cleft Lip and Palate: Family History and Cousin Marriages. *Pakistan Journal of Health Sciences*, 7(6), 105-110. <https://doi.org/10.54393/pjhs.v7i6.2814>

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oralpathology@uhs.edu.pkReceived Date: 29th January, 20251st Revision Received: 11th December, 20252nd Revision Received: 19th December, 20253rd Revision Received: 23rd December, 2025Acceptance Date: 18th April, 2026Published Date: 30th June, 2026

ABSTRACT

Cleft lip and palate (CLP) are prevalent birth disorders and have significant impacts on the individuals and their families. **Objectives:** To identify the trends of cleft lip and palate and to examine the effects of family history and the marriage of cousins. **Methods:** This cross-sectional study was carried out in the Department of Oral Pathology, University of Health Sciences, Lahore. Four hundred children between the ages of 0 and 20 years were included. The following data were taken: demographic and clinical, such as age, sex, type of cleft, maternal folic acid intake, family history of cleft lip and/or palate or other congenital anomalies, and parental consanguinity. **Results:** The mean age of the participants was 55.79 ± 54.3 months. Among them, 214 (53.5%) were male, and 186 (46.5%) were female. In terms of cleft pattern, cleft lip and palate were most common, affecting 247 (61.8%) individuals, compared to those with only cleft lip or cleft palate. A positive family history was reported in 89 (22.3%) of the cases. Only 60 (15%) of the mothers had taken folic acid during pregnancy, and cousin marriages were noted among the parents of 309 (77.3%) children. **Conclusions:** CLP is more commonly observed in individuals with a positive family history and those whose parents are biologically related. A considerable proportion of affected children had parents who were cousins, suggesting that consanguinity may be a contributing factor to CLP. Additionally, a significant number of mothers did not receive folic acid supplementation during pregnancy, which is a modifiable risk factor.

INTRODUCTION

A cleft of the lips, palate, or both is the most common congenital anomaly of the orofacial complex in a newborn. CLP is a serious health issue with more than 10 million victims worldwide [1]. The greatest number of these anomalies concerns the Chinese births; the next ones are India and Indonesia. Pakistan has the largest number of infants born with a cleft lip or cleft palate after Indonesia [2]. One of the numerous affected craniofacial elements and oral structures is the hard palate due to these congenital defects [3]. The world is experiencing an alarming trend of the total number of people with clefts in their mouths and cheeks as the population continues to

grow and the overall life expectancy is rising [4]. These conditions are being encountered at different frequencies across geographical areas among all ethnicities, sexes, and socioeconomic strata. The management involves several surgical procedures and extended multidisciplinary treatment that cause great psychological stress to the afflicted individuals and their families [5]. Cleft lip and palate are a multifactorial and complex development in its formation, which incorporates both a genetic predisposition and environmental exposures. In some cases, chromosomal abnormalities related to inheritable syndromes can also contribute to it [6]. A



positive family history of CLP is an established risk factor of CLP; exposures to environmental risk factors like cigarettes and alcohol, prescription drugs, and illicit drugs, and an advanced maternal age at birth are some of the established risk factors of CLP [7]. Eighty-seven patients with orofacial clefts were studied in an Iranian study, and considerable relationships were observed between the presence of an orofacial cleft and consanguineous marriage of the parents, aggregation of clefts in families, and folic acid intake [8]. These patterns in the framework of hereditary background and consanguinity are analyzed as bringing important information to the genetic and environmental aspects of cleft lip and palate to develop more effective interventions, early diagnostics, and optimal management strategies.

Although the association of consanguineous marriage and congenital anomalies is well established, little data are available about the contribution of cousin marriage and maternal folic acid consumption to the occurrence and prevalence of cleft lip (CL) and cleft palate (CP) in Pakistan. This study aims to determine the distribution patterns of cleft lip and palate as well as to evaluate the influence of familial history and cousin marriages on the incidence of cleft lip and palate.

METHODS

A cross-sectional study was conducted in the Department of Oral Pathology at the University of Health Sciences, Lahore, from January 2020 to December 2021, after getting formal institutional approval (Approval No. UHS/REG-20/ERC/146; dated 15th January 2020), and the research was conducted in accordance with the Declaration of Helsinki. A non-probability convenience sampling approach was used to enroll children diagnosed with non-syndromic cleft lip and/or palate (NSCL/P) who presented to CLAP Hospital, Lahore. The study consisted of 400 participants between 0 and 20 years of age. Despite the fact that the sample size was determined by practical considerations and not as a result of a statistical power calculation, it is comparable to those reported in related published studies. All ethical requirements were carefully observed. As the study population consisted of minors, written informed consent was obtained from parents or legal guardians, and verbal or written assent was obtained from children capable of comprehension, generally those older than seven years. Participants with syndromic cleft lip and/or palate, incomplete clinical documentation, or unclear diagnostic information were excluded. The data collected were composed of demographic and clinical variables, including age, gender, cleft type, folic acid intake by mothers, and positive family history of cleft lip and/or palate or other birth defects. An established criterion was used for categorization of Parental consanguinity into

first-cousin, second-cousin, or more distantly related unions and was determined through structured interviews with parents without any genetic testing or official medical documentation, and classifications were based entirely on self-reported familial data.

SPSS version 26 was used to record and analyze the data. Descriptive statistics were performed to summarize age, gender distribution, cleft types, folic acid intake, and family history. Associations between cleft type and variables such as folic acid intake and family history were assessed using Chi-square tests or Fisher's exact tests, and assumptions for these tests (such as minimum expected cell counts) were checked before analysis. A p -value ≤ 0.05 was set as statistically significant.

RESULTS

The mean age was 55.79 ± 54.3 months. Out of 400 patients, there were 214 (53.5%) male and 186 (46.5%) female. Regarding the pattern of cleft lip and palate, CLP was the most prevalent, observed in 247 cases (61.8%), exceeding the occurrences of cleft lip only and cleft palate only. A familial occurrence of the condition was reported by 89 participants, accounting for 22.3% of the study population. Folic acid was taken by the mothers of 60 (15%) children only, and cousin marriages were observed in the parents of 309 (77.3%) children (Table 1).

Table 1: Distribution of Demographic Variables

Variables	Frequency (%)
Gender	
Male	214 (53.5%)
Female	186 (46.5%)
Cleft Lip and Palate Pattern	
Cleft Lip and Palate	214 (53.5%)
Cleft Lip Only	117 (29.3%)
Cleft Palate Only	69 (17.3%)
Family History	
Positive	89 (22.3%)
Negative	311 (77.8%)
Folic Acid	
Yes	60 (15%)
No	340 (85%)
Cousin Marriages	
Yes	309 (77.3%)
No	91 (22.8%)

The study presents the distribution of CLP patterns based on gender, family history, maternal folic acid intake, and cousin marriages; however, no significant associations were found (Table 2).

Table 2: Association among the Demographic Variables

Variables	Cleft Lip and Palate	Cleft Lip Only	Cleft Palate only
Gender			
Male	121 (56.5%)	57 (27%)	36 (16.3%)

Female	93 (50.5%)	60 (32.2%)	33 (17.2%)
p-value	0.13	0.17	0.71
RR (CI)	1.35 (0.913-2.01)	0.744 (0.48-1.14)	0.90 (0.538-1.52)
Folic Acid Intake by Mothers			
Yes	35 (60%)	15 (25%)	10 (15%)
No	179 (52.6%)	102 (3.8%)	59 (17%)
p-value	0.41	0.40	0.94
RR (CI)	1.2 (0.72-2.1)	767 (0.40-1.43)	0.9729 (0.466-2.02)
Cousin Marriages			
Yes	167 (54%)	91 (29.7%)	51 (16.2%)
No	47 (52.7%)	26 (28.5%)	18 (18.6%)
p-value	0.68	0.82	0.42
RR (CI)	1.01 (0.689-1.75)	1.06 (0.633-1.77)	0.783.43-1.4)
Family History			
Yes	49 (55%)	25 (28%)	15 (16.8%)
No	165 (53.3%)	92 (30%)	54 (16.7%)
p-value	0.73	0.74	0.96
RR (CI)	1.084 (0.675-1.7)	0.91 (0.54-1.54)	98 (0.52-1.85)

RR: Relative Risk CI: Confidence Interval

Analysis of gender, maternal folic acid intake, cousin marriage, and family history showed no statistically significant association with the type of orofacial cleft. The distribution of cleft lip and palate, cleft lip only, and cleft palate only was similar in both males and females, with all p-values > 0.05. Likewise, maternal folic acid use did not significantly influence cleft type, and relative risks for all categories crossed unity. No meaningful differences were observed between children from consanguineous versus non-consanguineous marriages, nor between those with or without a positive family history, as reflected by non-significant p-values and wide confidence intervals. Overall, none of the evaluated factors demonstrated a significant association with cleft subtype in this cohort.

DISCUSSION

Cleft lip and palate are widely occurring congenital anomalies that are caused by a complex interplay between a predisposition that is hereditary and the environmental exposures, whereby the underlying mechanisms are not always well understood. The children who are affected often face self-esteem issues and difficulty getting along with others. They may have scars on their face and talk differently, which could influence their attitude towards themselves. They may become awkward with the people around them or may be regarded as being treated unjustly or bullied. As well, communicating well due to difficulty in speaking may be a challenge and have an impact on friendship and school performance. The best thing to do is begin speech therapy at the earliest stage, and with the help of medical care and encouragement from others, a majority of individuals are capable of leading a normal, successful life. Stigmatization and increased acceptance of people can also be achieved by assisting the community

to understand more about cleft conditions. In this research, the boys (as compared to girls) were more affected by cleft lip and palate, with an average age of 55.79 and a standard deviation of 54.3 months. This is unlike some other studies, which have found more girls being affected. The variations in the way the body parts develop in both boys and girls, such as hormones that influence the formation, may be behind the fact that more boys are affected. There is research that claims the palate may take longer to form in early growth in girls, making them prone to a cleft palate. The delayed palatal fusion in embryogenesis in females has been postulated to predispose to developmental disturbances, and therefore, predispose the onset of cleft palate malformation [9]. Conversely, research conducted in Pakistan has similarly documented a higher frequency of orofacial clefts in males, who comprised 60% of cases compared with 40% in females [10]. Similarly, another study identified a total of 2,089 children meeting the inclusion criteria, with 1,311 male and 778 female. In female, orofacial clefts primarily occur during the late embryonic period and usually involve only the secondary palate, often due to fusion defects. In contrast, clefts in male are more prevalent during both the early and late embryonic stages. These clefts often affect both the primary and secondary palates and are typically caused by differentiation abnormalities or a combined fusion and differentiation disturbance [11]. The cases of cleft lip and cleft palate were found in the current study in a larger number based on palate, and then cleft lip, and finally cleft palate. A study carried out in Pakistan depicted a higher prevalence of cleft lip only, then cleft palate only, and cleft lip and palate, respectively. Out of the 540 patients with the condition of the OFC, 123 were afflicted with cleft lip alone, 233 with cleft lip and palate, and 178 with cleft palate. Cleft lip and cleft lip and palate patients were characterized by a greater number of male patients, whereas cleft palate was characterized by more female patients [12]. A different study illustrated the CL:CLP: CP ratio to be 4.7:7.1:1 [13]. The existing evidence also points to the idea that women of children with orofacial clefts (OFC) tend to have nutritional deficiencies and a lack of folic acid. Prenatal vitamins and folic acid are advised for women of childbearing age, both before and during pregnancy, in case of an unplanned pregnancy [14]. In the current study, only 60 (15%) female took folic acid during their pregnancy. Samuel Trezena noted a slight trend in the occurrence of complete non-syndromic cleft palate (NSCP) among children with a family history of NSCP, those whose mothers took some form of medication in pregnancy, or those with certain systemic alterations. Although these differences were statistically insignificant, they should still be considered while examining the development of cleft types [15]. They reported that 25% of patients had oral clefts in their families, which is significantly more than the

2.9 % prevalence in Spain and 7 % in Brazil [16, 17]. In a study conducted in Brazil, the predominance of a family history of non-syndromic oral clefts (NSOC) among individuals with non-syndromic cleft palate (NSCP) was 33.2%. Probably, this could have been due to differences in sample size of the studies [18]. The present research could not find any significant correlation between CP and consanguineous marriages. The other studies also highlight consanguineous marriage as a risk factor with an OR of nearly 3, meaning that children born to such marriages are more susceptible to developing complex cleft lip [19, 20]. It is possible that the absence of meaningful association between consanguineous marriages and cleft lip and palate reported in this research could be explained by a number of methodological and population-related factors. These are a lack of adequate sample size to elicit minor effects, a more inclusive definition of consanguinity, and an inherent genetic heterogeneity in the study sample in comparison to previous studies. Also, the outstanding confounding variables, reporting or categorizing relationships with family members, and potential selection bias because of a hospital-based sample could have diminished the capacity to find a true association. The discrepancy with the previously published results could also be due to variability caused by gene-environment interaction and natural differences between studies. Autosomal recessive disorders, such as rare or novel syndromes, can be caused by consanguineous marriages, and thus, it is vital to create awareness among the population on the dangers involved. Consanguinity in rural settings also offers various social gains, including increased female autonomy, better marriage stability, less domestic violence and violence, improved knowledge with the in-laws, and economic benefits, including reduced dowry payments, lower divorce rates, and land retention [21, 22]. Genetically, consanguinity arises from a reduced genetic diversity caused by a limited pool of close relatives. Given that more than 90% of the human genome is shared among individuals, the impact of consanguineous marriages on genomic sequencing is minimal. If two siblings have children, the resulting child will have fewer unique genetic contributions, increasing the likelihood of inheriting harmful recessive genes [23]. Offspring of consanguineous parents tend to have higher rates of homozygosity. Loss-of-function (LoF) mutations, which cause complete gene inactivation or malfunction, often occur in autozygous regions of the genome. Studying consanguineous offspring with specific clinical traits can help identify mutations responsible for diseases. However, most genes in the human genome are either unrelated to established disorders or have undiscovered roles, which is a major focus of extensive sequencing research. While many genes are associated with orofacial clefts, only a few are linked to well-defined cleft phenotypes [24].

Consistent with other studies, research in Iran showed a statistically significant link between consanguinity and the occurrence of oro-facial clefts [20]. However, a study from Saudi Arabia did not establish this relationship [25]. Additionally, a significant link between the incidence of cleft defects and family history was reported in another study conducted in Brazil and Saudi Arabia, which is also observed in the present study [26]. First and second-degree family histories of clefts had a higher risk compared to third-degree relatives. However, a study from India reported a significant correlation between cleft defects and family history [27]. Among 538, consanguinity was found in 284 parents; more of the patients were reported with cleft lip and palate [22]. In other countries, including Iran, where consanguineous marriage is common and culturally valued, the acceptance of consanguineous marriages in society contributes to the increased risk of congenital anomalies. To overcome this challenge, the policymakers in the health sector ought to issue preventive policies to reduce consanguineous marriages. It is important to adopt genetic counseling and involve prominent leaders in the community in the design and implementation of health programs [28]. Increased incidents of cleft lip and palate (CLP) are being observed in children born to similar parents, and this has significant implications for health care and society. When a child has CLP, families tend to have huge financial and social problems due to the high costs of surgeries, continuous medical treatment, and other auxiliary services. These problems demonstrate the significance of providing more genetic guidance and enhancing the health activities of the population. Informing the population about the genetic risks of close family marriages and providing them with access to counseling can be used to lessen the effects of CLP and other genetic issues in societies where such marriages are prevalent.

Although this research did not show any decisive relationship, the number of individuals that were researched was too low, and the manner in which the research was conducted may have made it difficult to notice an actual relationship. This must be taken as a limitation, and further research on bigger groups is required to prove these findings.

CONCLUSIONS

This study did not find a strong link between close family relationships or the mother taking folic acid during pregnancy and the occurrence of cleft lip and/or palate. Although many affected children were born to closely related parents and a lot of mothers didn't take folic acid, these factors didn't clearly increase the risk of CLP in this group. The lack of clear results could be because of a small sample size, how relationships were classified, or other factors not considered. So, when

interpreting these results, it's important to be careful, and larger, more detailed studies are needed to better understand the role of consanguinity and folic acid in CLP. Overall, the study shows that cleft lip and palate are influenced by many factors, both genetic and environmental. It's important to address both inherited risks and other influences in preventing and managing this condition. Improving genetic counseling, increasing awareness about close family marriages, and encouraging folic acid use during pregnancy are key steps. More research is needed to understand the biological reasons behind CLP and to develop better ways to prevent and treat it.

Acknowledgement

The authors acknowledge the staff at Cleft Lip and Plate Hospital (CLAP), Lahore, Pakistan, for their support and cooperation.

Authors' Contribution

Conceptualization: SM, SC

Methodology: RA, AHN, SC

Formal analysis: RA, SM, SC

Writing and Drafting: RA

Review and Editing: RA, SM, AHN, SC

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All 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] AlHayyan WA, Al Hayek S, Alotaibi SS, AlGhanim SA. Birth Prevalence of Orofacial Cleft in A Tertiary Hospital in Riyadh, Saudi Arabia: A Retrospective Audit. *The Saudi Dental Journal*. 2021 Dec; 33(8): 954-7. doi: 10.1016/j.sdentj.2021.08.005.
- [2] Fayyaz GQ, Gill NA, Ishaq I, Ganatra MA, Mahmood F, Kashif M et al. A Model Humanitarian Cleft Mission: 312 Cleft Surgeries in 7 Days. *Plastic and Reconstructive Surgery-Global Open*. 2015 Mar; 3(3): e313. doi: 10.1097/GOX.0000000000000282.
- [3] Vyas T, Gupta P, Kumar S, Gupta R, Gupta T, Singh HP. Cleft of Lip and Palate: A Review. *Journal of Family Medicine and Primary Care*. 2020 Jun; 9(6): 2621-5. doi: 10.4103/jfmpc.jfmpc_472_20.
- [4] Al Jadidi L, Sabrish S, Shivamurthy PG, Senguttuvan V. The Prevalence of Malocclusion and Orthodontic Treatment Need in Omani Adolescent Population. *Journal of Orthodontic Science*. 2018 Jan; 7(1): 21. doi: 10.4103/jos.JOS_44_18.
- [5] Emeka CI, Adeyemo WL, Ladeinde AL, Butali A. A Comparative Study of Quality of Life of Families with Children Born with Cleft Lip and/or Palate Before and After Surgical Treatment. *Journal of the Korean Association of Oral and Maxillofacial Surgeons*. 2017 Aug; 43(4): 247. doi: 10.5125/jkaoms.2017.43.4.247.
- [6] AlHammad Z, Suliman I, Alotaibi S, Alnofaie H, Alsaadi W, Alhusseini S et al. The Prevalence of Non-Syndromic Orofacial Clefts and Associated Congenital Heart Diseases of A Tertiary Hospital in Riyadh, Saudi Arabia. *The Saudi Dental Journal*. 2021 Mar; 33(3): 137-42. doi: 10.1016/j.sdentj.2019.12.002.
- [7] Baig S, Bhutta MF, Hashmi FP, Khan K, Iqbal UA, Bhatti ZI. Frequency of Cleft Lip and Cleft Palate in Pakistan. *The Professional Medical Journal*. 2022 Apr; 29(05): 671-5. doi: 10.29309/TPMJ/2022.29.05.6908.
- [8] Jamilian A, Sarkarat F, Jafari M, Neshandar M, Amini E, Khosravi S et al. Family History and Risk Factors for Cleft Lip and Palate Patients and Their Associated Anomalies. *Stomatologija*. 2017 Jan; 19(3): 78-83.
- [9] Burg ML, Chai Y, Yao CA, Magee III W, Figueiredo JC. Epidemiology, Etiology, and Treatment of Isolated Cleft Palate. *Frontiers in Physiology*. 2016 Mar; 7: 67. doi: 10.3389/fphys.2016.00067.
- [10] Moeed K, Ahmad W, Haris M, Muzadar S, Wazir NU, Imran S. Epidemiological Trends in Cleft Lip and Cleft Palate Frequency: An Analytical Perspective. *Annals of Punjab Medical College*. 2023 Dec; 17(4): 550-3. doi: 10.29054/apmc/2023.1371.
- [11] Pool SM, der Lek LM, de Jong K, Vermeij-Keers C, Mouës-Vink CM. Embryologically Based Classification Specifies Gender Differences in the Prevalence of Orofacial Cleft Subphenotypes. *The Cleft Palate Craniofacial Journal*. 2021 Jan; 58(1): 54-60. doi: 10.1177/1055665620935363.
- [12] Saeed OB, Moore MG, Zawahrah H, Tayem M, Kavoosi T, Van Aalst JA. The Influence of Consanguinity on Familial Clefting among Palestinians. *The Cleft Palate-Craniofacial Journal*. 2019 Sep; 56(8): 1072-9. doi: 10.1177/1055665619838381.
- [13] Belachew FK, Gerbu DG, Woldesenbet EB, Abay ES, Maswime S, Eshete M. Clinical Profiles of Individuals with Orofacial Clefts: Results from Fourteen Eastern African countries. *Global Pediatrics*. 2023 Sep; 5: 100067. doi: 10.1016/j.gped.2023.100067.
- [14] Kianifar H, Hasanzadeh N, Jahanbin A, Ezzati A, Kianifar H. Cleft Lip and Palate: A 30-Year Epidemiologic Study in North-East of Iran. *Iranian Journal of Otorhinolaryngology*. 2015 Jan; 27(78): 35.
- [15] Trezena S, Machado RA, de Almeida Reis SR, Scariot R, Rangel AL, de Oliveira FE et al. Isolated

- Nonsyndromic Cleft Palate: Multicenter Epidemiological Study in Brazil. *BioMed Central Oral Health*. 2023 Jul; 23(1): 486. doi: 10.1186/s12903-023-03197-3.
- [16] Yáñez-Vico RM, Iglesias-Linares A, Gómez-Mendo I, Torres-Lagares D, González-Moles MÁ, Gutierrez-Pérez JL et al. A Descriptive Epidemiologic Study of Cleft Lip and Palate in Spain. *Oral Surgery, Oral Medicine, Oral Pathology, and Oral Radiology*. 2012 Nov; 114(5): S1-4. doi: 10.1016/j.tripleo.2011.07.046.
- [17] Martelli DR, Machado RA, Swerts MS, Rodrigues LA, de Aquino SN, Júnior HM. Non-Syndromic Cleft Lip and Palate: Relationship Between Sex and Clinical Extension. *Brazilian Journal of Otorhinolaryngology*. 2012 Sep; 78(5): 116-20. doi: 10.5935/1808-8694.20120018.
- [18] Ferrari-Piloni C, Barros LA, Jesuíno FA, Valladares-Neto J. Prevalence of Cleft Lip and Palate and Associated Factors in Brazil's Midwest: A Single-Center Study. *Brazilian Oral Research*. 2021 Apr; 35: e039. doi: 10.1590/1807-3107bor-2021.vol35.0039.
- [19] Silva CM, de Moraes Pereira MC, de Queiroz TB, das Neves LT. Can Parental Consanguinity be a Risk Factor for the Occurrence of Nonsyndromic Oral Cleft? *Early Human Development*. 2019 Aug; 135: 23-6. doi: 10.1016/j.earlhumdev.2019.06.005.
- [20] Sakran KA, Abotaleb BM, Al-Rokhami RK, Hsieh TY, Al-Wesabi MA, Mohammed AA et al. Analysis of Environmental Exposures for Nonsyndromic Cleft Lip and/or Palate: A Case-Control Study. *Iranian Journal of Public Health*. 2022 Mar; 51(3): 578.
- [21] El Goundali K, Chebabe M, Laamiri FZ, Hilali A. The Determinants of Consanguineous Marriages among the Arab Population: A Systematic Review. *Iranian Journal of Public Health*. 2022 Feb; 51(2): 253. doi: 10.18502/ijph.v51i2.8679.
- [22] Sadiq H, Ijaz R, Ayub A. Patterns of Orofacial Clefts and Associated Risk Factors in Pakistan: An Institutional Experience. *Journal of Cleft Lip Palate and Craniofacial Anomalies*. 2022 Jul; 9(2): 145-50. doi: 10.4103/jclpca.jclpca_1_22.
- [23] Kurniati M, Pramono RC, Sosiawan A, Tirtaningsih NW. The Genetic Aspect of Non-Syndromic Cleft Lip and Palate Towards Candidate Genes in the Etiology: A Literature Review. *Indian Journal of Forensic Medicine and Toxicology*. 2021; 15(3): 3604-8. doi: 10.37506/ijfmt.v15i3.15859.
- [24] Slavec L, Karas Kuželički N, Locatelli I, Geršak K. Genetic Markers for Non-Syndromic Orofacial Clefts in Populations of European Ancestry: A Meta-Analysis. *Scientific Reports*. 2022 Jan; 12(1): 1214. doi: 10.1038/s41598-021-02159-5.
- [25] Alyami B, Ali-Hassan M, Al-Mahri M, Alyami F, Alharieth S. Risk Indicators for Syndromic and Nonsyndromic Orofacial Clefts in Southern Province of Saudi Arabia. *Journal of Cleft Lip Palate and Craniofacial Anomalies*. 2019 Jan; 6(1): 51-5. doi: 10.4103/jclpca.jclpca_31_18.
- [26] Maranhão SC, Sá J, Cangussú MC, Coletta RD, Reis SR, Medrado AR. Nonsyndromic Oral Clefts and Associated Risk Factors in the State of Bahia, Brazil. *European Archives of Paediatric Dentistry*. 2021 Apr; 22(2): 121-7. doi: 10.1007/s40368-020-00522-0.
- [27] Neogi SB, Singh S, Pallepogula DR, Pant H, Kolli SR, Bharti P et al. Risk Factors for Orofacial Clefts in India: A Case-Control Study. *Birth Defects Research*. 2017 Oct; 109(16): 1284-91. doi: 10.1002/bdr2.1073.
- [28] Bakhshani S. Consanguineous Marriage and the Risk of Parents Having Children with Cleft Lip and Palate. *International Journal of High-Risk Behaviors and Addiction*. 2021 Jan; 10(10). doi: 10.5812/ijhrba.114912.



Original Article



Incidence of Contrast-Induced Nephropathy in Post-Renal Transplant Recipients

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ARTICLE INFO

Keywords:

Contrast-Induced Nephropathy, Diabetes Mellitus, Iodinated Contrast Media, Kidney Transplantation

How to Cite:

Naseer, A., Ahmed, E., Anmol, ., & Kumari, A. (2026). Incidence of Contrast-Induced Nephropathy in Post-Renal Transplant Recipients: Contrast-Induced Nephropathy in Post-Renal Transplant Recipients. *Pakistan Journal of Health Sciences*, 7(6), 111-115. <https://doi.org/10.54393/pjhs.v7i6.3752>

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Received Date: 10th January, 20261st Revision Received: 17th January, 2026Acceptance Date: 21st April, 2026Published Date: 30th June, 2026

ABSTRACT

Contrast-induced nephropathy (CIN) is a widely occurring, although possibly preventable, complication after the use of iodinated contrast media. **Objectives:** To identify CIN incidence in patients who have undergone renal transplants and also to see the risk factors involved. **Methods:** The cross-sectional research was carried out at the Sindh Institute of Urology and Transplantation (SIUT), Karachi, within six months after ethical consent of the College of Physicians and Surgeons Pakistan (CPSP). The sample size was 174 renal transplant recipients (aged 18 years and above) with an estimated glomerular filtration rate (eGFR) of over 20 ml/min, and these individuals were pre-exposed to 50 ml of iodinated contrast. Data analysis was done by use of SPSS version 25.0. Associations were evaluated using the chi-square test and multivariate logistic regression, with $p \leq 0.005$ being taken as statistically significant. **Results:** The average age of the interviewees was 44.2 ± 11.6 years old. The mean serum creatinine increased to 1.76 ± 0.49 mg/dl at the end of the experiment and correspondingly decreased to 55.6 ± 12.3 ml/min to 49.8 ± 13.1 ml/min. CIN appeared in 26 patients (14.9%). Its occurrence was much higher among those patients who had diabetes mellitus (23.8%, $p=0.021$) and hypertension (19.2%, $p=0.045$). On multivariate analysis, independent predictors of CIN were diabetes mellitus and contrast volume more than 100 ml ($p<0.001$). **Conclusions:** CIN is very prevalent among the post-renal transplant recipients. Higher contrast volume and diabetes mellitus are the best independent predictors.

INTRODUCTION

Contrast-induced nephropathy (CIN), also known as contrast-induced acute kidney injury (CI-AKI), is a major cause of iatrogenic kidney dysfunction, especially in individuals who have underlying kidney dysfunction, including renal transplant recipients. Even though iodinated contrast agents have significantly improved diagnostic and interventional radiology, their usage is linked with the high likelihood of acute kidney injury, even when the kidney is transplanted and is thought to be in stable baseline performance [1, 2]. Kidney transplant recipients (KTRs) could be a unique population vulnerable to CIN since a combination of several factors can increase their vulnerability to the condition, such as dependence on one functioning kidney, persistent exposure to immunosuppressive agents, which can be nephrotoxic, and changes in renal hemodynamics [3]. There is some

inconsistent evidence on contrast exposure in this population, though. Chotkan *et al.* showed that pre-transplant contrast administration to deceased kidney donors did not have a significant effect on the long-term graft survival, but transient impairment of early renal functioning was reported [1]. However, other reports have indicated quantifiable incidence of CIN after exposure to contrast in transplant patients, which demands close observation and preventive measures in this high-risk patient population [4, 5]. There is a wide range of reported incidence of CIN, with much of the variation being a result of heterogeneity in patient populations, diagnostic criteria, and preventive protocols. A huge meta-analysis found a combined worldwide incidence of 2-30 percent, with most of the cases found in persons who have already had dysfunction of the kidney [6]. There are no particular data



on renal transplant groups, but argue in favor of a clinically important risk as potentially negative outcomes on graft functionality and patient outcome [7]. Pathophysiology of CIN comprises of renal vasoconstriction, medullary hypoxia, and direct tubular toxicity induced by oxidative stress and inflammatory mechanisms [8]. Increase in molecular knowledge has led to possible preventive measures, such as optimized hydration, antioxidant therapy, and pharmacologic vasodilation, but CIN remains a clinical problem, especially in cases where contrast-enhanced imaging is inevitable in transplant recipients [9]. The recent activities have been aimed at minimizing contrast-associated nephrotoxicity in the use of alternative imaging modalities and risk stratification. Contrast-enhanced ultrasound (CEUS) has become a safer imaging tool to assess kidney transplant complications without making use of the iodinated contrast media [4]. Also, recent recommendations by the American College of Radiology support the customized risk evaluation and preventive actions in case of necessity of contrast administration in patients with kidney disease [10].

Although there has been an increased awareness and preventive strategies developed, their use in daily clinical practice has been inconsistent. Timely intervention and early detection of the risk of CIN are thus important, especially in the transplant population. This study hypothesized that contrast-induced nephropathy events are clinically significantly frequent in post-renal transplant recipients and that the risk of it is related to certain clinical factors, such as comorbidities and contrast volume. This study aimed to establish the occurrence of CIN and determine the predictors of CIN among post-renal transplant individuals who are exposed to contrast.

METHODS

The study is cross-sectional research done with a group of patients visiting the outpatient and inpatient department of the Transplant Unit of the Sindh Institute of Urology and Transplantation (SIUT), Karachi, between 6 months of August 2025 and January 2026. The research began following ethical consent of the College of Physicians and Surgeons Pakistan (CPSP) (CPSP/REU/NEP-2023-198-1082; dated 28th June 2025) and permission of its Research Evaluation Unit (REU) (IRB approval number: SIUT-ERC-2025/A-563; dated 22nd May 2025). All participants had given informed consent in written form before enrolling. The sample size was estimated with the help of the Open Epi software, whose assumptions were based on the predicted incidence of a contrast-induced nephropathy (CIN) of 13 percent in post-renal transplant recipients, according to Abu Jawdeh et al. [11]. The sample size of 174 was determined by using a 95% confidence interval and a 5 percent margin of error. A non-probability consecutive

sampling method was used in the recruitment. Included were patients who had a history of renal transplant, whose estimated glomerular filtration rate (eGFR) was stable (over 20 ml/min/1.73 m² when calculated according to the CKD-EPI equation), and had received at least 50 ml of intravenous iodinated contrast media during diagnostic or interventional procedures. Patients would not be included in the study if they had any dialysis within the previous week before contrast exposure, had suffered an acute rejection episode within the past week, were on inotropic or ventilatory support, or were undergoing acute rejection or active infection at the time of contrast. Age, gender, medical record number, education level, residence, and monthly income were all collected by use of a pre-designed proforma. Body mass index (BMI) was calculated by dividing the weight of a person in kilograms by height in meters squared, and anthropometric measurements were taken with the help of a calibrated digital weighing scale and a standard height chart. The time taken after renal transplantation and comorbid conditions like diabetes mellitus, hypertension, obesity, anemia, coronary artery disease, congestive heart failure, and smoking status were recorded and confirmed with the help of medical records. The kind of contrast media used and the amount of the media used were noted in relation to each participant. Baseline (day 1) and repeated (72-96 hours, day 4) serum creatinine were determined after exposure to the contrast. The level of hemoglobin and HbA1c was also recorded. All laboratory values were recorded by the investigator with the help of an estimation of glomerular filtration rate before and after contrast exposure. The definition of contrast-induced nephropathy was a 25% increase in serum creatinine relative to baseline during 72-96 hours of exposure to contrast without any other known etiologies of acute kidney injury.

The Statistical Package of Social Sciences (SPSS) version 25.0 was used in the analysis of the data. Mean and standard deviation were used to represent quantitative variables, whereas frequencies and percentages were used to represent qualitative variables. They stratified to adjust for potential effect modifiers, including age, gender, BMI categories, socioeconomic variables, and comorbid conditions. Categorical variables were compared using the chi-square test, and those variables that were statistically significant on univariate analysis were included in a multivariate logistic regression model to determine independent predictors of CIN. The p-value of less than 0.005 was taken to have been statistically significant.

RESULTS

The final analysis had 174 post-renal transplant recipients who received contrast-enhanced imaging. Continuous variables were described in terms of mean $\pm$ standard deviation; this was done by ensuring that there was

approximate normality, and categorical variables were stated in terms of frequencies and percentages. Categorical variable associations were evaluated with the Chi-square test, and continuous variable comparisons across groups were evaluated with independent-sample tests in situations where normality and homogeneity of variance conditions were satisfied. This study provides a summary of the baseline demographic, anthropometric, and renal function traits of the participants in the study. The average age of the participants was 44.211.6 (19-70 years). 112 (64.4%) of the cohort were males. The average serum creatinine was raised to 1.76 ± 0.49 mg/dl at 72-96 hours after contrast exposure, and the mean eGFR was reduced to 49.8 ± 13.1 ml/min/1.73 m². The volume of contrast that was administered was 92.6 ± 21.8 ml (Table 1).

Table 1: Baseline Demographic, Anthropometric, and Renal Function Characteristics of Post-Renal Transplant Recipients (n=174)

Variables	Mean $\pm$ SD / n (%)
Age (years)	44.2 $\pm$ 11.6
Gender (Male/Female)	112 (64.4%) / 62 (35.6%)
BMI (kg/m ²)	25.7 $\pm$ 3.9
Duration Since Transplantation (months)	38.5 $\pm$ 22.4
Baseline Serum Creatinine (mg/dl)	1.48 $\pm$ 0.37
Post-Contrast Serum Creatinine (mg/dl)	1.76 $\pm$ 0.49
Baseline eGFR (ml/min)	55.6 $\pm$ 12.3
Post-contrast eGFR (ml/min)	49.8 $\pm$ 13.1
Contrast Volume (ml)	92.6 $\pm$ 21.8

The study gives the prevalence of comorbid conditions in the study population. The most common comorbidities included hypertension and diabetes mellitus (Table 2).

Table 2: Frequency of Comorbid Conditions among Post-Renal Transplant Recipients (n=174)

Comorbidity	n (%)
Hypertension	78 (44.8%)
Diabetes Mellitus	63 (36.2%)
Anemia	24 (13.8%)
Coronary Artery Disease	16 (9.2%)
Congestive Heart Failure	10 (5.7%)
Smoking	27 (15.5%)

A 25% increase in serum creatinine levels compared to baseline (contrast-induced nephropathy, CIN) was noted in 26 patients (14.9%), 72 to 96 hours after the exposure to contrast. Within a week, renal function came back to normal in 22 of them (84.6%). None of the patients needed renal replacement therapy, and it was considered to be an observed clinical outcome in the course of follow-up. The results demonstrate the correlation between CIN and the possible risk variables. The prevalence of CIN was much higher among diabetes mellitus patients than among non-diabetic patients (23.8% vs. 9.8%; $p=0.021$). Similarly, hypertensive patients were found to have a greater

incidence of CIN when compared to non-hypertensive patients (19.2% vs. 10.2; $p=0.045$). There was a significantly greater incidence of CIN in patients who were given a contrast volume more than 100 ml (26.1% vs. 9.8; $p=0.008$). Statistically significant correlation between CIN and gender/BMI category was not found (Table 3).

Table 3: Association of Contrast-Induced Nephropathy with Demographic and Clinical Risk Factors

Variables	Total (n)	CIN Present, n (%)	CIN Absent, n (%)	p-value
Male	112	18 (16.1%)	94 (83.9%)	0.570
Female	62	8 (12.9%)	54 (87.1%)	
Diabetes Mellitus	63	15 (23.8%)	48 (76.2%)	0.021*
Hypertension	78	15 (19.2%)	63 (80.8%)	0.045*
Contrast Volume >100 ml	69	18 (26.1%)	51 (73.9%)	0.008*
BMI >25 kg/m ²	98	13 (13.3%)	85 (86.7%)	0.310

* $p \leq 0.005$ is considered statistically significant

The study provides a comparison of the continuous variables in the patients who succumbed to CIN and those who did not. CIN patients possessed much higher post-contrast serum creatinine values and were administered much more contrast media. There was no statistically significant difference in the age, BMI, or baseline serum creatinine between the two groups. In the multivariate logistic regression analysis, diabetes mellitus and contrast volume over 100 ml were independent predictors of CIN ($p < 0.001$) (Table 4).

Table 4: Comparison of Continuous Variables Between CIN and Non-CIN Groups

Variables	CIN Present (n=26), Mean $\pm$ SD	CIN Absent (n=148), Mean $\pm$ SD	p-value
Age (years)	46.5 $\pm$ 12.3	43.8 $\pm$ 11.5	0.290
BMI (kg/m ²)	26.2 $\pm$ 4.1	25.6 $\pm$ 3.8	0.480
Baseline Serum Creatinine (mg/dl)	1.56 $\pm$ 0.39	1.47 $\pm$ 0.36	0.330
Post-contrast Serum Creatinine (mg/dl)	2.02 $\pm$ 0.41	1.71 $\pm$ 0.45	0.001*
Contrast Volume (ml)	103.1 $\pm$ 18.5	90.7 $\pm$ 22.1	0.008*

* $p \leq 0.005$ is considered statistically significant

DISCUSSION

The current paper assessed this incidence and the determinants of contrast-induced nephropathy (CIN) in post-renal transplant patients receiving contrast-enhanced imaging and showed the overall incidence of 14.9%. This observation is in line with already established rates in transplant populations and supports the increased vulnerability of renal allografts to contrast-related renal injury despite the increased safety of imaging methods and preventive measures. Contrast-enhanced imaging continues to play a vital role in post-transplant care, especially in evaluating vascular patency, graft perfusion, and post-operative complications. Nevertheless, the problem of the safety of iodinated contrast agents in such a

high-risk population remains a significant issue. Fernández *et al.* stressed that modern contrast agents are comparatively safer, but the renal transplant patients are still at risk because of low renal reserve and due to the exposure to nephrotoxic immunosuppressive agents [12]. This issue can be justified by the baseline and renal function alterations that were experienced by our cohort, where the decrease in renal functioning was measurably observed after the exposure to contrast. Recent studies have also paid more attention to the early diagnosis of CIN by other types of biochemical markers. Zywno *et al.* have mentioned the importance of biomarkers like neutrophil gelatinase-associated lipocalin (NGAL), cystatin C, and interleukin-18 that can identify the presence of acute kidney injury earlier than serum creatinine [13]. In the present case, even though the serum creatinine-based definitions were applied, the temporary rise of creatinine levels in the vast majority of affected patients indicates that the introduction of new biomarkers into the post-contrast monitoring regimens can enable the timely detection and treatment of transplant recipients. The stratification of risks and personal contrast control is highly promoted in modern guidelines. In a collaborative statement of the Polish Society of Nephrology and Radiology, Chmielewski *et al.* suggested risk evaluation and cautious contrast application in patients with defective renal function should be personalized [14]. These recommendations are consistent with our findings, with diabetes mellitus, hypertension, and greater contrast volume being significantly related to CIN, and diabetes mellitus and contrast volume >100 ml continuing to be independent predictors on multivariate analysis. Other imaging modalities are also being considered as a way of minimizing contrast-induced nephrotoxicity in patients who have undergone renal transplants. David *et al.* proved that contrast-enhanced ultrasound (CEUS) provides better evaluation of graft perfusion, and no patients are exposed to iodinated contrast agents [15]. Further implementation of CEUS in the follow-up of routine transplantation would have the potential to decrease the incidence of CIN among this at-risk group. Preventative measures remain critical in reducing the risk of CIN. Kellum focused on the fact that acute kidney injury, such as CIN, can be prevented in most cases by proper hydration, careful use of contrast doses, and close observation after the procedure [16]. The lack of dialysis-inducing CIN in our cohort refers to the efficiency of such preventive interventions and indicates that the contrast-related renal damage in transplant patients is often mild and reversible if the relevant precautions are taken. The incidence of CIN that was observed during our study is very similar to that of the study by Abu Jawdeh *et al.* who described the incidence of CIN at around 13% in their study population of post-transplant patients [11]. Likewise, Fananapazir *et al.* reported temporary elevations of serum

creatinine in cases of intra-arterial contrast administration without irreversible graft dysfunction [17], which were observed to match current findings that 84.6% of patients returned to baseline renal functioning within one week. Image practices quality assurance is also of great essence. Research by Roohi *et al.* Taher *et al.* and Owusu-Banahene *et al.* have demonstrated that improper use of imaging and repeat exposure are some of the reasons leading to avoidable radiation and contrast utilization [18–20]. The application of standardized imaging protocols and personnel education in the transplant radiology services can further help to decrease preventable cases of CIN.

There are some limitations of this study. It has a cross-sectional design that restricts causal determination between observed risk factors and the development of CIN. It was based on serum creatinine-based definitions without any additions of early kidney injury biomarkers, which could not have given an accurate picture of subclinical renal injury. Also, the study was carried out in one center, and this might limit the extrapolation of the research to other transplant populations that have different clinical practices.

CONCLUSIONS

To sum up, it was found that contrast-induced nephropathy was present in 14.9% of those who have undergone post-renal transplant, which proves that the incidence of CIN is clinically significant in this group. The best independent predictors of CIN were diabetes mellitus and increased contrast volume. These findings highlighted the necessity of personalized risk evaluation, the reduction of contrasts, and the need to consider other imaging modalities in order to maintain long-term graft function in recipients of renal transplants despite mildly adverse cases.

Authors' Contribution

Conceptualization: AN

Methodology: AN, A, AK

Formal analysis: AN, A

Writing and Drafting: AN, EA, AK

Review and Editing: AN, EA, A, AK

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All 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] Chotkan KA, Hilbrands LB, Putter H, Konjin C, Schaefer B, Beenen LF et al. Transplant Outcomes After Exposure of Deceased Kidney Donors to Contrast Medium. *Transplantation*. 2024 Jan; 108(1): 252-60. doi: 10.1097/TP.0000000000004745.
- [2] Zahid U, Hayat A, Bedi P, Spitalewitz S. Contrast Induced Nephropathy in Kidney Transplant Recipients: A Systematic Review and Meta-Analysis: SA-PO138. *Journal of the American Society of Nephrology*. 2023 Nov; 34(11S): 761-2. doi: 10.1681/ASN.20233411S1761d.
- [3] Gheith OA, Nagib AM, Halim MA, Mahmoud T, Nair P et al. Contrast-induced Nephropathy in Kidney Transplant Recipients: A Single-center Experience. *Iranian Journal of Kidney Diseases*. 2023; 17(1): 47. doi: 10.6002/ect.MESOT2018.P6.
- [4] Bodard S, Pierce TT, Sertic M, Lafargue MC, Samir AE, Riella LV. Advancements in Imaging Modalities for Post-Kidney Transplant Monitoring: A Focus on Contrast-Enhanced Ultrasound. *American Journal of Transplantation*. 2025 Sep. doi: 10.1016/j.ajt.2025.08.035.
- [5] Wang Z, Wang Q, Gong X. Unveiling the Mysteries of Contrast-Induced Acute Kidney Injury: New Horizons in Pathogenesis and Prevention. *Toxics*. 2024 Aug; 12(8): 620. doi: 10.3390/toxics12080620.
- [6] Kaliyaperumal Y, Sivadasan S, Aiyalu R. Contrast-Induced Nephropathy: An Overview. *Dr. Sulaiman Al Habib Medical Journal*. 2023 Dec; 5(4): 118-27. doi: 10.1007/s44229-023-00040-3.
- [7] Wu MY, Lo WC, Wu YC, Lin TC, Lin CH, Wu MS et al. The Incidence of Contrast-Induced Nephropathy and the Need of Dialysis in Patients Receiving Angiography: A Systematic Review and Meta-Analysis. *Frontiers in Medicine*. 2022 Apr; 9: 862534. doi: 10.3389/fmed.2022.862534.
- [8] Mahapatro A, Nobakht S, Mukesh S, Daryagasht AA, Korsapati AR, Jain SM et al. Evaluating Biomarkers for Contrast-Induced Nephropathy Following Coronary Interventions: An Umbrella Review on Meta-Analyses. *European Journal of Medical Research*. 2024 Apr; 29(1): 210. doi: 10.1186/s40001-024-01782-y.
- [9] Theofilis P and Kalaitzidis R. Navigating Nephrotoxic Waters: A Comprehensive Overview of Contrast-Induced Acute Kidney Injury Prevention. *World Journal of Radiology*. 2024 Jun; 16(6): 168. doi: 10.4329/wjr.v16.i6.168.
- [10] Davenport MS, Perazella MA, Yee J, Dillman JR, Fine D, McDonald RJ et al. Use of Intravenous Iodinated Contrast Media in Patients with Kidney Disease: Consensus Statements from the American College of Radiology and the National Kidney Foundation. *Radiology*. 2020 Mar; 294(3): 660-8. doi: 10.1148/radiol.2019192094.
- [11] Abu Jawdeh BG, Leonard AC, Sharma Y, Katipally S, Shields AR, Alloway RR et al. Contrast-Induced Nephropathy in Renal Transplant Recipients: A Single Center Experience. *Frontiers in Medicine*. 2017 May; 4: 64. doi: 10.3389/fmed.2017.00064.
- [12] Fernández T, Sebastià C, Paño B, Corominas Muñoz D, Vas D et al. Contrast-Enhanced US in Renal Transplant Complications: Overview and Imaging Features. *Radiographics*. 2024 May; 44(6): e230182. doi: 10.1148/rgr.230182.
- [13] Zywno H, Figiel W, Grat M, Nazarewski S, Galazka Z, Malyszko J. Can Novel Biomarkers Effectively Predict Acute Kidney Injury in Liver or Kidney Transplant Recipients? *International Journal of Molecular Sciences*. 2024 Nov; 25(22): 12072. doi: 10.3390/ijms252212072.
- [14] Chmielewski M, Serafin Z, Kamińska D, Skrobisz K, Kozak O, Olczyk P et al. The Use of Intravascular Contrast Media in Patients with Impaired Kidney Function—Joint Clinical Practice Position Statement of the Polish Society of Nephrology and the Polish Medical Society of Radiology. *Polish Journal of Radiology*. 2024 Mar; 89: e161. doi: 10.5114/pjr.2024.136950.
- [15] David E, Del Gaudio G, Drudi FM, Dolcetti V, Pacini P, Granata A et al. Contrast-Enhanced Ultrasound Compared with MRI And CT in the Evaluation of Post-Renal Transplant Complications. *Tomography*. 2022 Jun; 8(4): 1704-15. doi: 10.3390/tomography8040143.
- [16] Kellum JA. AKI: The Myth of Inevitability Is Finally Shattered. *Nature Reviews Nephrology*. 2017 Mar; 13(3): 140-1. doi: 10.1038/nrneph.2017.11.
- [17] Fananapazir G, Munoz NM, Crown MT, Bent CK, Vu CT, Lamba R. Incidence of Contrast-Induced Nephropathy After Renal Graft Intra-arterial Contrast Infusion. *American Journal of Roentgenology*. 2016; 206(4): 819-24. doi: 10.2214/AJR.15.15501.
- [18] Roohi Shalemaei R. Films Reject Analysis for Conventional Radiography in Iranian Main Hospitals. *Radiation Protection Dosimetry*. 2011 Sep; 147(1-2): 220-2. doi: 10.1093/rpd/ncr306.
- [19] Taher Ali R. Assessment of X-ray Films and Image Quality in Diagnostic Radiology Departments of Teaching Hospitals in Iraq. *Radiation Effects and Defects in Solids*. 2024 Mar; 179(3-4): 292-300. doi: 10.1080/10420150.2023.2265018.
- [20] Owusu-Banahene J, Darko EO, Hasford F, Addison EK, Asirifi JO. Film Reject Analysis and Image Quality in Diagnostic Radiology Department of a Teaching Hospital in Ghana. *Journal of Radiation Research and Applied Sciences*. 2014 Oct; 7(4): 589-94. doi: 10.1016/j.jrras.2014.09.012.



Original Article



Cone Beam Computed Tomography Analysis of the Correlation Between Gingival Biotype and Schneiderian Membrane

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ARTICLE INFO

Keywords:

Cone Beam Computed Tomography, Gingival Biotype, Gingival Thickness, Schneiderian Membrane, Maxillary Sinus

How to Cite:

Sherani, H., Chachar, Z. H., Khan, Z. A., Vishal, V., Jagirani, S. A., & Kumar, K. (2026). Cone Beam Computed Tomography Analysis of the Correlation Between Gingival Biotype and Schneiderian Membrane: CBCT: Gingival Biotype and Schneiderian Membrane. *Pakistan Journal of Health Sciences*, 7(6), 116-121. <https://doi.org/10.54393/pjhs.v7i6.3866>

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ABSTRACT

The Schneiderian membrane plays a critical role in maxillary sinus health and implant planning. Although odontogenic and periodontal factors are known to influence membrane thickening, the role of the gingival phenotype remains unclear. **Objectives:** To evaluate the relationship between gingival biotype, gingival thickness, and Schneiderian membrane thickness and pathology using cone-beam computed tomography (CBCT). **Methods:** This analytical cross-sectional study included 96 CBCT scans obtained from Altamash Institute of Dental Medicine, Karachi. Gingival thickness was measured radiographically and classified as thin or thick biotype. Schneiderian membrane thickness was measured at corresponding posterior maxillary sites and categorized as normal (≤ 2 mm) or thickened (> 2 mm). Sinus pathology was recorded. Independent-samples t-test, chi-square test, and Pearson correlation were applied ($p < 0.005$). **Results:** Mean gingival thickness was 1.06 ± 0.18 mm, and mean membrane thickness was 2.23 ± 0.85 mm. Membrane thickening was observed in 61.5% of cases, while sinus pathology was present in 29.2%. No significant difference in membrane thickness was found between thin and thick biotypes (mean difference = 0.22 mm; $p = 0.203$). Gingival biotype was not associated with membrane category ($p = 0.340$) or sinus pathology ($p = 0.107$). Gingival thickness showed a weak, non-significant correlation with membrane thickness ($r = 0.084$; $p = 0.416$). **Conclusions:** Gingival phenotype was not significantly associated with Schneiderian membrane thickness or pathology. Sinus membrane alterations appear to be influenced predominantly by anatomical and odontogenic factors.

INTRODUCTION

The maxillary sinus is lined by the Schneiderian membrane, a specialized pseudostratified ciliated respiratory epithelium that plays a critical role in sinus physiology and mucociliary clearance. The thickness and integrity of this membrane are clinically important during sinus lift procedures, implant placement, and other surgical interventions involving the posterior maxilla [1]. Alterations in Schneiderian membrane thickness have been associated with odontogenic infections, periodontal disease, anatomical variations, and inflammatory processes, which may compromise surgical outcomes and implant success [2, 3]. Cone-beam computed tomography

(CBCT) has emerged as a reliable three-dimensional imaging modality for evaluating maxillary sinus anatomy and pathology. Compared with conventional radiography, CBCT allows accurate measurement of sinus membrane thickness and identification of incidental findings such as mucosal thickening, retention cysts, and polypoid changes [4]. Recent CBCT-based studies have reported a high prevalence of incidental sinus findings in asymptomatic dental patients, with mucosal thickening being the most common radiographic presentation. These findings highlight the importance of understanding the factors influencing Schneiderian membrane alterations [5, 6].



Several odontogenic and periodontal factors, including periapical lesions, periodontal bone loss, and proximity of posterior teeth to the sinus floor, have been implicated in sinus membrane thickening. Emerging evidence suggests that periodontal soft-tissue phenotype, particularly gingival biotype and gingival thickness, may reflect underlying tissue morphology and inflammatory susceptibility, potentially influencing adjacent sinus mucosa [7,8]. Thin gingival phenotype has been associated with reduced tissue resilience and increased vulnerability to inflammation, while the thick phenotype is generally considered more resistant to mechanical and inflammatory challenges [9]. However, the relationship between gingival phenotype and Schneiderian membrane thickness remains controversial. Some CBCT-based investigations have reported positive correlations between thin gingival biotype and increased sinus membrane thickness, whereas others have found weak or non-significant associations. Differences in measurement techniques, biotype classification criteria, anatomical reference points, and population characteristics contribute to these inconsistencies. Moreover, most available evidence originates from non-South Asian populations, limiting the generalizability of findings to Pakistani dental patients, where periodontal disease burden and sinus pathology prevalence may differ.

Despite increasing interest in periodontal phenotype as a potential predictor of sinus membrane alterations, there remains a lack of standardized CBCT-based research evaluating this relationship within the Pakistani population. Furthermore, existing studies often demonstrate methodological heterogeneity, small sample sizes, and inconsistent operational definitions for membrane thickening. The objective was to determine whether gingival phenotype independently influences sinus mucosal thickness or whether Schneiderian membrane changes are primarily governed by broader anatomical and odontogenic determinants. By addressing this gap, the study seeks to contribute region-specific evidence to improve preoperative assessment and clinical decision-making in implant dentistry and sinus-related procedures. This study aimed to evaluate, using standardized CBCT measurements, the relationship between gingival biotype, gingival thickness, and Schneiderian membrane thickness and pathology in a Pakistani dental population.

METHODS

This analytical cross-sectional study was conducted at the Altamash Institute of Dental Medicine, Karachi, Pakistan, from 6th June 2024 to December 2024, using archived cone-beam computed tomography (CBCT) records to evaluate the relationship between gingival biotype, gingival

thickness, and Schneiderian membrane thickness and pathology. Ethical approval was obtained from the Research Ethics and Review Committee of Altamash Institute of Dental Medicine (ERC Code: AIDM/ERC/06/2024/02; dated 6th June 2024). The study adhered to the Declaration of Helsinki. As archived CBCT scans were used, patient confidentiality was maintained through anonymization and removal of personal identifiers before analysis. Sample size was calculated using Fisher's Z transformation formula for correlation studies. Assuming a two-sided alpha of 0.05, a power of 80%, and an anticipated correlation coefficient of 0.30 based on previous radiographic periodontal sinus studies [9], the minimum required sample was 85. After adding a 10% margin for incomplete scans and exclusions, a total of 96 CBCT scans were included. A non-probability consecutive sampling technique was employed, and eligible scans were selected from the institutional radiology archive based on predefined inclusion and exclusion criteria. Inclusion criteria comprised patients aged 15 years and above, scans demonstrating adequate visualization of the posterior maxillary region and maxillary sinus, at least one measurable premolar or molar site, and diagnostic image quality with minimal artifacts. Exclusion criteria included previous maxillary sinus surgery or trauma, extensive sinus pathology obscuring standardized measurement sites, severe CBCT artifacts affecting anatomical landmarks, and the presence of maxillofacial tumors or conditions that could alter gingival architecture. Written informed consent was taken. All CBCT scans were acquired using the Planmeca ProMax 3D Mid system (Planmeca Oy, Helsinki, Finland), operating at 90 kVp and 10 mA, with a voxel size of 0.2 mm and a field of view of 8x8 cm, following standardized institutional imaging protocols. Digital Imaging and Communications in Medicine (DICOM) files were analyzed using calibrated radiographic software equipped with linear measurement tools. All measurements were performed under standardized viewing conditions to ensure consistency. A structured data collection proforma was specifically designed for this study after a literature review and expert consultation in oral radiology and periodontology [10]. The proforma included demographic variables (age and gender), gingival thickness, gingival biotype, Schneiderian membrane thickness, membrane category, sinus pathology (presence and type), and anatomical location (premolar or molar region). No previously validated questionnaire was used, as data were extracted directly from radiographic measurements. Gingival thickness was measured in millimeters at the mid-buccal aspect of the posterior maxillary region on cross-sectional CBCT slices at a standardized reference point. Gingival biotype was categorized as thin or thick based on radiographically measured gingival thickness using a predefined threshold. Schneiderian membrane thickness

was measured perpendicular to the bony sinus floor at the point of maximum mucosal thickness corresponding to the evaluated site. Measurements were stratified according to premolar and molar regions. Membrane thickness was categorized as normal (≤ 2 mm) and thickened (> 2 mm). This operational cut-off was adopted based on previously established CBCT diagnostic thresholds for sinus mucosal thickening reported in the literature [11]. Sinus pathology was recorded as present or absent, and when present, classified as retention cyst, polypoid mucosal change, or diffuse mucosal thickening based on CBCT morphology. To ensure measurement reliability, examiner calibration was conducted before data extraction. Approximately 10–15% of scans were reassessed to determine intra-observer reliability, and an independent assessor evaluated a subset for inter-observer reliability. Intraclass correlation coefficient (ICC) was calculated for continuous variables, including gingival thickness and Schneiderian membrane thickness. All eligible scans were assigned unique study identification numbers. Data were entered into a computerized database and verified through random cross-checking.

Statistical analysis was performed using SPSS version 25.0. Continuous variables were expressed as mean $\pm$ standard deviation, while categorical variables were presented as frequencies and percentages. Normality was assessed using histograms, Q-Q plots, and the Shapiro-Wilk test. Since variables were normally distributed ($p > 0.005$), parametric tests were applied. An independent-samples t-test was used to compare mean membrane thickness between gingival biotypes. Chi-square test was used to assess associations between gingival biotype and membrane category as well as sinus pathology. Pearson correlation coefficient (r) was calculated to evaluate the relationship between gingival thickness and Schneiderian membrane thickness. Statistical significance was set at $p < 0.005$.

RESULTS

Participant demographics and scan characteristics are summarized. A total of 96 participants were included, with a mean age of 36.92 ± 13.59 years. Females comprised 50 (52.1%) and males 46 (47.9%). CBCT measurements were equally distributed between the left and right sides. The majority of measurements were recorded in the molar region (66.7%). Periodontal status showed a relatively balanced distribution, with 31.3% healthy, 35.4% gingivitis, and 33.3% periodontitis cases (Table 1).

Table 1: Baseline Characteristics of the Study Participants (n=96)

Variables	Overall (n=96), n (%)
Age (Years)	
Mean $\pm$ SD	36.92 $\pm$ 13.59

Gender	
Female	50 (52.1%)
Male	46 (47.9%)
Side Examined	
Left	48 (50.0%)
Right	48 (50.0%)
Region Measured	
Molar	64 (66.7%)
Premolar	32 (33.3%)
Periodontal Status	
Healthy	30 (31.3%)
Gingivitis	34 (35.4%)
Periodontitis	32 (33.3%)

Gingival phenotype findings are presented. A slight predominance of thin gingival biotype (52.1%) was observed compared to thick biotype (47.9%). The mean gingival thickness was 1.06 ± 0.18 mm, ranging from 0.72 to 1.44 mm. Mean gingival thickness was comparable between thin (1.05 ± 0.19 mm) and thick (1.07 ± 0.17 mm) biotypes (Table 2).

Table 2: Gingival Biotype and Gingival Thickness (n=96)

Variables	n (%) / Mean $\pm$ SD
Gingival Biotype	
Thin	50 (52.1%)
Thick	46 (47.9%)
Gingival thickness (mm)	1.06 $\pm$ 0.18
Gingival thickness (mm), min-max	0.72 - 1.44
Gingival Thickness by Biotype (mm)	
Thin biotype	1.05 $\pm$ 0.19
Thick biotype	1.07 $\pm$ 0.17

Schneiderian membrane characteristics are shown. The mean membrane thickness was 2.23 ± 0.85 mm (range 0.33–3.99 mm). Membrane thickening (> 2 mm) was observed in 61.5% of cases. Sinus pathology was identified in 29.2% of participants, with diffuse mucosal thickening being the most frequent finding. Membrane thickness was greater in the molar region (2.48 ± 0.81 mm) compared to the premolar region (1.85 ± 0.77 mm) (Table 3).

Table 3: Schneiderian Membrane Characteristics (n=96)

Variables	n (%) / Mean $\pm$ SD
Membrane Thickness (mm)	2.23 $\pm$ 0.85
Membrane Thickness (mm), min-max	0.33 - 3.99
Membrane Category	
Normal (≤ 2 mm)	37 (38.5%)
Thickened (> 2 mm)	59 (61.5%)
Sinus Pathology	
Yes	28 (29.2%)
No	68 (70.8%)
Pathology Type	
Retention Cyst	10 (10.4%)
Polypoid Mucosal Change	6 (6.3%)

Diffuse Mucosal Thickening	12 (12.5%)
Membrane Thickness by Location (mm)	
Premolar Region	1.85 ± 0.77
Molar Region	2.48 ± 0.81

Comparison of Schneiderian membrane findings between gingival biotypes is presented. Mean membrane thickness did not differ significantly between thin and thick biotypes (2.34 ± 0.72 mm vs 2.12 ± 0.97 mm). The mean difference was 0.22 mm (95% CI: -0.12 to 0.56; $t(94) = 1.28$; $p = 0.203$). The effect size was small (Cohen's $d = 0.26$). Gingival biotype was not significantly associated with membrane category ($\chi^2(1) = 0.91$, $p = 0.340$; Cramer's $V = 0.097$). Similarly, no significant association was observed between gingival biotype and sinus pathology ($\chi^2(1) = 2.59$, $p = 0.107$; Cramer's $V = 0.164$) (Table 4).

Table 4: Comparison of Schneiderian Membrane Findings Between Gingival Biotypes (n=96)

Outcomes	Thin (n=50)	Thick (n=46)	p-value
Membrane Thickness (mm), Mean ± SD	2.34 ± 0.72	2.12 ± 0.97	0.203
Membrane Category, n (%)			
Normal	17(34.0)	20(43.5)	0.340
Thickened	33(66.0)	26(56.5)	
Sinus Pathology, n (%)			
Yes	11(22.0)	17(37.0)	0.107
No	39(78.0)	29(63.0)	

Correlation analysis between gingival thickness and Schneiderian membrane thickness is presented. Pearson correlation demonstrated a weak, non-significant association ($r = 0.084$; 95% CI: -0.118 to 0.278; $p = 0.416$) (Table 5).

Table 5: Correlation Between Gingival Thickness and Schneiderian Membrane Thickness (n=96)

Variable	Pearson's r	95% CI	p-value
Gingival thickness vs membrane thickness	0.084	-0.118 to 0.278	0.416

DISCUSSION

The present CBCT-based cross-sectional study demonstrated that the gingival biotype was not significantly associated with Schneiderian membrane thickness. Furthermore, gingival thickness showed only a weak and non-significant correlation with membrane thickness ($r = 0.084$; $p = 0.416$). These findings suggest that sinus mucosal alterations are likely influenced by multifactorial anatomical and odontogenic determinants rather than the gingival phenotype alone [12]. This study findings are consistent with previous CBCT-based investigations reporting weak or non-reproducible associations between periodontal phenotype and sinus membrane thickness. De Souza Fernandes et al. similarly observed only a minimal association between gingival biotype and maxillary sinus membrane thickness,

concluding that anatomical and odontogenic factors may play a more dominant role [13]. Likewise, Diaz et al. in a systematic review, highlighted substantial methodological heterogeneity across studies, limiting definitive conclusions regarding the impact of periodontal phenotype on Schneiderian membrane thickness [10]. In contrast, some studies have reported positive correlations between thin gingival phenotype and increased membrane thickness. For example, Javed et al. demonstrated a statistically significant association in a Pakistani cohort [14]. However, the discrepancy between their findings and ours may be attributed to differences in biotype classification criteria, radiographic measurement landmarks, regional sampling, and variation in periodontal disease severity among study populations. Another important finding of our study was the significantly greater membrane thickness observed in the molar region compared to the premolar region. This supports the concept that posterior maxillary teeth, particularly molars, exert a stronger odontogenic influence on sinus mucosa due to their anatomical proximity to the sinus floor. Sökmen and Sökmen similarly reported that root proximity and periodontal parameters significantly influenced Schneiderian membrane thickness [15]. Saquib et al. also emphasized that regional anatomical variations and lateral sinus wall thickness contribute substantially to mucosal thickness variability [16]. Although the gingival phenotype did not demonstrate a significant association, sinus membrane thickening and incidental sinus pathology were frequently observed in our study. Membrane thickening (>2 mm) was present in 61.5% of cases, while sinus pathology was identified in 29.2%. These findings are comparable with regional CBCT prevalence studies [17]. İspir et al. reported mucosal thickening and retention cysts as common incidental findings in the asymptomatic dental population [17]. Similarly, Madfa et al. observed that radiographic mucosal thickening on CBCT does not necessarily indicate clinically significant sinus disease [18]. Existing literature also suggests that periodontal bone loss and periapical pathology are more strongly associated with sinus membrane thickening than with the gingival phenotype. Eksi and Seker demonstrated a significant association between the severity of periodontal bone loss and Schneiderian membrane thickness [19]. while AlRowis et al. reported a strong correlation between periodontitis and maxillary sinus changes on CBCT [20]. These findings reinforce our observation that sinus membrane alterations are multifactorial and may be more closely related to inflammatory and anatomical factors than to isolated soft-tissue phenotype. Clinically, this study's results suggest that CBCT-detected Schneiderian membrane thickening should be interpreted within a broader anatomical and odontogenic context rather than relying solely on gingival phenotype assessment. This has

particular relevance in sinus lift planning and implant placement in the posterior maxilla, where accurate risk stratification is essential.

Current study has certain limitations. First, its cross-sectional design precludes causal inference. Second, variables such as periapical status, smoking history, sinus ostium patency, and detailed periodontal bone loss measurements were not included, which may act as potential confounders. Third, gingival biotype classification was based on radiographic measurement rather than clinical translucency assessment. Future multicenter longitudinal studies with larger samples incorporating detailed periodontal parameters, anatomical sinus variations, and additional inflammatory markers are recommended to better elucidate the independent role of gingival phenotype in sinus membrane alterations. Standardization of CBCT measurement protocols and biotype classification criteria would further enhance comparability across studies.

CONCLUSIONS

In this CBCT-based study of 96 participants, gingival biotype and gingival thickness were not significantly associated with Schneiderian membrane thickness. Sinus membrane thickening and incidental sinus pathology were common, particularly in the molar region, suggesting a stronger influence of anatomical and odontogenic factors than gingival phenotype alone. These findings emphasize the importance of comprehensive radiographic assessment in implant and sinus-related procedures.

Authors' Contribution

Conceptualization: HS

Methodology: HS, ZHC, V, KK

Formal analysis: ZHC, SAJ

Writing and Drafting: HS, ZHC, ZAK, V, SAJ, KK

Review and Editing: HS, ZHC, ZAK, V, SAJ, KK

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All 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] Takalkar S, Girotra C, Kini Y, Padhye M, Tomar G, Acharya S et al. Evaluation of Sexual Dimorphism in Schneider Membrane Thickness Using Cone-Beam Computed Tomography (CBCT) for its Clinical and Forensic Implications. *Journal of Maxillofacial and Oral Surgery*. 2024 Dec; 23(6): 1528-34. doi: 10.1007/s12663-021-01531-2.
- [2] Al-Bahrani ZM and Al-Ghurabi ZH. Cone Beam Computed Tomographic Evaluation of Schneiderian Membrane Thickness. *Journal of Craniofacial Surgery*. 2024 Jan; 35(1): e36-8. doi: 10.1097/SCS.00000000000009767.
- [3] Delantoni A, Şengün DN, Bayındır A, Orhan K. Risk Factors, Consequences and Treatment Alternatives of Schneiderian Membrane Perforation: Case Report and Review of the Literature. *ADO Klinik Bilimler Dergisi*. 2024 Jan; 13(1): 256-63. doi: 10.54617/adoklinikbilimler.1352345.
- [4] Sun S, Wang Y, Gong Z, Zhao W, Jia L, Wen Y. A comparative Study of the Application of Three Digital Imaging Techniques to Assess the Thickness of the Palatal Mucosa of the Maxillary Anterior Teeth. *BioMed Central Oral Health*. 2024 Sep; 24(1): 1137. doi: 10.1186/s12903-024-04896-1.
- [5] Cui X, Reason T, Pardi V, Wu Q, Martinez Luna AA. CBCT Analysis of Crestal Soft Tissue Thickness Before Implant Placement and Its Relationship with Cortical Bone Thickness. *BioMed Central Oral Health*. 2022 Dec; 22(1): 593. doi: 10.1186/s12903-022-02629-w.
- [6] Alalshaikh M, Tabasum A, Alotaibi N, Alesawy A, Ahmad S, Almas K et al. Risk Factors Contributing to Membrane Perforation in Lateral Window Maxillary Sinus Elevation: Systematic Review and Meta-Analysis. *Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology*. 2025 Jun; 139(6): 642-59. doi: 10.1016/j.oooo.2024.12.008.
- [7] Kus-Bartoszek A, Lipski M, Jarząbek A, Manowiec J, Marek E, Drożdżik A. Evaluation of Gingival Phenotype in the Early Transitional Dentition Phase in Children—Comparison of Three Non-Invasive Methods. *Journal of Clinical Medicine*. 2023 Sep; 12(18): 5897. doi: 10.3390/jcm12185897.
- [8] Ibrahim M. Mucosal Phenotype as A Multidisciplinary Approach: A Narrative Review. *Khalij-Libya Journal of Dental and Medical Research*. 2024 Aug; 187-200. doi: 0.47705/kjdmr.248207.
- [9] Huser SM, Larson RL, Taxis TM, Almaraz JM, Reif KE, Weaver B et al. Cross-Sectional Study to Describe Bovine Leukemia Virus Herd and Within-Herd ELISA Prevalence and Bovine Leukemia Virus Proviral Load Of Convenience-Sampled Kansas Beef Cow-Calf Herds. *American Journal of Veterinary Research*. 2023 Feb; 84(2). doi: 10.2460/ajvr.22.09.0156.
- [10] Diaz L, Fan S, Urrutia P, Uriarte X, Fodich I, Torres A et al. Correlation Between Periodontal Phenotype and Sinus Membrane Thickness: A Systematic Review. *Clinical Oral Implants Research*. 2023 Sep; 34(9): 881-91. doi: 10.1111/clr.14121.

- [11] Sarıbaş E, Kandemir M, Tuncer MC. Does Periodontal Bone Loss Play a Significant Role in Schneiderian Membrane Thickening? A Cone-Beam Computed Tomography Evaluation. *Medicina*. 2025 Aug; 61(9): 1529. doi: 10.3390/medicina61091529.
- [12] Kemcha N, Andrés-Veiga M, Hurtado-Celotti D, Meniz-García C, Beca-Campoy T, Martínez-Rodríguez N. Diagnostic Assessment of Maxillary Sinus Membrane Thickening Associated with Dental Implant Perforation Using Cone-Beam Computed Tomography: A Retrospective Cross-Sectional Pilot Study. *Diagnostics*. 2025 Nov; 15(21): 2809. doi: 10.3390/diagnostics15212809.
- [13] De Souza Fernandes AC, Júnior GI, de Souza Pereira F, Galil KA, Farias IO et al. Gingival Biotype and Its Relationship with the Maxillary Membrane and Lateral Wall Thickness. *Journal of Oral Implantology*. 2021 Aug; 47(4): 280-6. doi: 10.1563/aaid-joi-D-19-00247.
- [14] Javed S, Maqbool M, Warraich UM, Ullah KA, Khan ZA, Qureshi F. Relationship of Gingival Biotype with Schneiderian Membrane Thickness Using Cone Beam Computed Tomography (CBCT). *Pakistan Journal of Medical and Health Sciences*. 2023 Apr; 17(4). doi: 10.53350/pjmhs2023174105.
- [15] Sökmen K and Sökmen N. Evaluation of the Relationship Between Periodontal Bone Loss and Schneiderian Membrane Thickness in Upper Posterior Teeth with Root Tips Associated with the Maxillary Sinus: A Retrospective Cone Beam Computed Tomography Study. *BioMed Central Oral Health*. 2025 Aug; 25(1): 1340. doi: 10.1186/s12903-025-06684-x
- [16] Saquib Abullais S, AlQahtani SM, Alqahtani S, Alaamri A, Azhar Dawasaz A, Alqahtani A et al. Radiographic Assessment of Maxillary Sinus Membrane and Lateral Wall Thickness Using Cone-Beam CT in Different Facial Types in Southwestern Saudi Arabia. *Plos One*. 2024 Mar; 19(3): e0298403. doi: 10.1371/journal.pone.0298403.
- [17] İspir NG, Zor ZF, Alkurt MT. Assessment of the Relationship Between Maxillary Sinus Membrane Thickness and Various Anatomical Factors Before Implant Treatment. *Clinical and Experimental Health Sciences*. 2024 Dec; 14(4): 1076-83. doi: 10.33808/clinexphealthsci.1498706.
- [18] Madfa AA, Alshammari AF, Alenezi YE, Alshammari BB, Al-Haddad A, Aledaili EA et al. Comprehensive Analysis of Maxillary Sinus Anatomical Features and Associated Characteristics: A CBCT-Based Study in a Saudi Subpopulation. *BioMed Central Oral Health*. 2025 Nov; 25(1): 1755. doi: 10.1186/s12903-025-07152-2.
- [19] Eksi C and Seker B. Evaluating the Relationship Between Periodontal Bone Loss in Maxillary Posterior Teeth and Schneiderian Membrane Thickness. *BioMed Central Oral Health*. 2025 Apr; 25(1): 477. doi: 10.1186/s12903-025-05871-0.
- [20] AlRowis RM, Alzahrani AH, Alzuhair SH, Almalhook KA, Almasry AW, Hamdan HM et al. Assess the Association Between Periodontitis and Maxillary Sinusitis: A Cross-Sectional Cone-Beam Computerized Tomography (CBCT) Study. *Cureus*. 2023 Nov; 15(11). doi: 10.7759/cureus.48587.



Original Article



Descriptive Cross-Sectional Study on Menstrual Irregularities in Patients Undergoing Tubal Ligation

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ARTICLE INFO

Keywords:

Tubal Ligation, Menstrual Disturbances, Polymenorrhea, Gonadotropin

How to Cite:Liaquat, S., Abbas, A., Batool, S. M., Perveen, A., Fatima, A., & Shabbir, S. (2026). Descriptive Cross-Sectional Study on Menstrual Irregularities in Patients Undergoing Tubal Ligation: Menstrual Irregularities After Tubal Ligation. *Pakistan Journal of Health Sciences*, 7(6), 122-126. <https://doi.org/10.54393/pjhs.v7i6.3222>***Corresponding Author:**

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ABSTRACT

Menstrual abnormalities continue to be a problematic consequence of tubal ligation, despite conflicting results from pertinent studies. Menorrhagia, metrorrhagia, polymenorrhagia, and dysmenorrhea are common disorders that may require a hysterectomy. **Objective:** To ascertain how frequently women who had tubal ligation experienced irregular menstruation. **Methods:** The Department of Obstetrics and Gynecology at Government Maula Baksh Hospital in Sargodha carried out this descriptive cross-sectional study between August 1, 2023, and January 31, 2024. Ethical approval for this study was obtained from the Research Evaluation Unit, CPSP (Reference No. CPSP/REU/OBG-2020-147-10091; dated 1st August 2023). Using non-probability consecutive sampling, 303 women between the ages of 20 and 40 who were having tubal ligation were included. Women with gynecological conditions (polycystic ovarian syndrome, endometriosis, adenomyosis, fibroid uterus), diabetes mellitus, hypertension, thyroid or cardiovascular disorders, or thyroid dysfunction were excluded. Tubal ligation was performed by a consultant gynecologist using the standard method. Patients were followed 6 months post-ligation, with menstrual irregularities self-reported via a specially designed proforma and clinically validated through menstrual diaries where possible. **Results:** This study found oligomenorrhea in 83 (27.4%), abnormal uterine bleeding in 61 (20.1%), dysmenorrhea in 55 (18.2%), and polymenorrhea in 37 (12.2%) post-TL. **Conclusion:** Oligomenorrhea is the most common menstrual irregularity post-tubal ligation, followed by abnormal uterine bleeding.

INTRODUCTION

Although many options exist for postpartum contraception, tubal sterilization/ligation remains one of the most widely used techniques globally, particularly among women who have had two or more children [1]. Women may seek reversal for reasons such as child loss or remarriage [2]. Approximately 30% of women completing family planning opt for tubal ligation as a safe, efficient, permanent fertility control method [3]. In the 1960s in the United States, female sterilization was primarily for

medical reasons (e.g., risky subsequent pregnancies). Many centers used a formula requiring that age multiplied by parity ≥ 120 for elective sterilization, which was endorsed by the American College of Obstetricians and Gynecologists until 1969 [4, 5]. Annually, about 700,000 bilateral tubal procedures occur in the US, half of which are postpartum and half are interval operations [6]. Family planning considers desired children, timing, and contraception for sexually active individuals [7].



Preconception counseling, STI prevention and treatment, sexuality education, and infertility management are all included [3]. The average menstrual cycle is 21-35 days long, with 25-80 mL of flow volume and 7 days of bleeding [8, 9]. Menorrhagia must be distinguished from polymenorrhea (less than 21-day intervals), metrorrhagia (irregular flow), menometrorrhagia (frequent excessive flow), and dysfunctional uterine bleeding (abnormal bleeding without pathology) [9]. Due to expenses and the aim to preserve the uterus, treatment has changed from surgical to conservative [10]. Treatment approaches and result measurement are complicated by the subjective definition of severe menstrual bleeding [11]. Despite the procedure's safety, there is a dispute regarding post-tubal sterilization syndrome, which includes vaginal bleeding [12]. Research on changes in ovarian reserve after sterilization has yielded conflicting results [13]. One troublesome side effect of tubal ligation (TL) is menstrual disruptions, which may be caused by hormonal alterations, altered gonadotropin signaling, and reduced follicular growth as a result of a disrupted ovarian blood supply [14]. Menstrual disturbances are a problematic effect of tubal ligation (TL), potentially due to disrupted ovarian blood supply leading to impaired follicular growth, altered gonadotropin signaling, and hormonal changes [14].

There is a dearth of evidence on menstrual abnormalities after tubal ligation (TL), especially in local communities where the procedure is widely practiced, leaving a knowledge gap in evidence-based counseling and reproductive health over the long term. Irregular menstruation following TL poses a clinical problem as it impacts physical, mental, and reproductive health, quality of life, and increases medical needs. The study aimed to assess post-TL menstrual changes and use them to inform counseling on the advantages/disadvantages. Irregular menstruation impacts physical, mental, and reproductive health, quality of life, and medical needs. The knowledge of the effects of TL can support informed decision-making, counseling, and care. It recognizes the risk factors and correlations and provides evidence-based practices, which will enhance knowledge in long-term reproductive health in areas where TL occurs frequently.

METHODS

This descriptive cross-sectional study was carried out in the Department of Obstetrics and Gynecology, Government Maula Baksh Hospital, Sargodha, between August 1, 2023, and January 31, 2024. Ethical approval for this study was obtained from the Research Evaluation Unit, CPSP (Reference No. CPSP/REU/OBG-2020-147-10091; dated 1st August 2023). After outlining the goals of the study and guaranteeing data confidentiality, each participant gave their informed consent. Using non-probability consecutive

sampling, 303 women between the ages of 20 and 40 who were having tubal ligation and had at least three regular cycles before the procedure were included. The formula $n = Z^2 p(1-p)/e^2$ was used to determine the sample size. $Z=1.96$ for 95% confidence, $p=0.269$ and $e=0.05$ (margin of error) yielded $n \approx 99$. Women with gynecological conditions (polycystic ovarian syndrome, endometriosis, adenomyosis, fibroid uterus), chronic conditions (diabetes mellitus, hypertension, thyroid, cardiovascular), or thyroid dysfunction were not included. A consultant gynecologist used the conventional technique to conduct tubal ligation. After ligation, patients were monitored for six months. When possible, menstruation diaries were used to validate the self-reported monthly irregularities on a specifically created proforma. Monthly clinic visits or phone calls were used to guarantee compliance, and there were no losses to monitor. Every piece of information was noted on the proforma. A structured, pre-tested Menstrual Disorder Assessment Questionnaire (MDAQ), modified from the Menstrual Disorder Questionnaire (MDQ), was used to evaluate menstrual irregularities. Menstrual cycle length, bleeding duration, flow pattern, and related symptoms, including dysmenorrhea and polymenorrhea, were all covered by the tool. Self-reported information was checked using menstrual diaries when available. The MDAQ has demonstrated strong psychometric properties, with a reported Cronbach's alpha of 0.84 in prior studies. In the present study, internal consistency was satisfactory (Cronbach's alpha=0.82). Content validity was confirmed through review by three obstetric and gynecological experts.

Data analysis was performed using SPSS version 26.0. Normality of quantitative variables (age, BMI) was checked using the Shapiro-Wilk test; since normal, they were presented as mean $\pm$ standard deviation. Qualitative variables (education level, parity, menstrual irregularities: oligomenorrhea/dysmenorrhea/polymerorrhea/AUB, previous contraceptive method) were presented as frequencies and percentages. Effect modifiers (age, BMI, education, parity, and previous contraceptive use) were controlled for by stratification. Post-stratification chi-square test was applied; $p < 0.05$ was significant.

RESULTS

The demographic characteristics of the 303 participants. The mean age was 29.10 ± 4.23 years, with 178 (58.70%) aged 20-30 years and 125 (41.30%) aged 31-40 years. Mean parity was 3.19 ± 0.89 , with 199 (65.7%) having ≤ 3 parity and 104 (34.3%) > 3 . Mean BMI was 28.25 ± 2.53 kg/m², with 205 (67.7%) ≤ 30 kg/m² and 98 (32.3%) > 30 kg/m². Education levels were: illiterate 34 (11.20%), primary 37 (12.2%), middle 119 (39.3%), matric & above 113 (37.3%). Previous contraceptive methods: pills 187 (61.7%), condom 116 (38.3%) (Table 1).

Table 1: Demographic Characteristics of Patients(n=303)

Variables	Category	Frequency (%)
Age (Years)	20-30	178 (58.7%)
	31-40	125 (41.3%)
	Mean $\pm$ SD	29.10 $\pm$ 4.23
Parity	≤ 3	199 (65.7%)
	> 3	104 (34.3%)
	Mean $\pm$ SD	3.19 $\pm$ 0.89
BMI (kg/m ²)	≤ 30	205 (67.7%)
	> 30	98 (32.3%)
	Mean $\pm$ SD	28.25 $\pm$ 2.53
Education Level	Illiterate	34 (11.2%)
	Primary	37 (12.2%)
	Middle	119 (39.3%)
	Matric & above	113 (37.3%)
Previous Contraceptive Method	Pills	187 (61.7%)
	Condom	116 (38.3%)

The frequency of menstrual irregularities post-tubal ligation. Oligomenorrhea occurred in 83 patients, abnormal uterine bleeding in 61, dysmenorrhea in 55, and polymenorrhea in 37 (Table 2).

Table 2: Frequency of Menstrual Irregularities(n=303)

Type of Irregularity	Yes, n (%)	No, n (%)
Oligomenorrhea	83 (27.4%)	220 (72.6%)
Abnormal Uterine Bleeding	61 (20.1%)	242 (79.9%)
Dysmenorrhea	55 (18.2%)	248 (81.8%)
Polymenorrhea	37 (12.2%)	266 (87.8%)

Stratification analysis demonstrated that oligomenorrhea, abnormal uterine bleeding, dysmenorrhea, and polymenorrhea were distributed across age, parity, BMI, contraceptive use, and educational status, with no significant associations ($p > 0.05$) between irregularities and modifiers (Table 3).

Table 3: Stratification of menstrual irregularities by demographic and clinical variables

Variables	Categories	Yes, n (%)	No, n (%)	p-value
Presence of Oligomenorrhea				
Age (years)	20-30	40 (22.5%)	138 (77.5%)	0.197
	31-40	43 (34.4%)	82 (65.6%)	
Parity	≤ 3	58 (29.1%)	141 (70.9%)	0.545
	> 3	25 (24.0%)	79 (76.0%)	
BMI (kg/m ²)	≤ 30	61 (29.8%)	144 (70.2%)	0.405
	> 30	22 (22.4%)	76 (77.6%)	
Previous Contraceptive	Pills	49 (26.2%)	138 (73.8%)	0.768
	Condom	34 (29.3%)	82 (70.7%)	
Education	Illiterate	6 (17.6%)	28 (82.4%)	0.792
	Primary	9 (24.3%)	28 (75.7%)	
	Middle	31 (26.1%)	88 (73.9%)	
	Matric & above	37 (32.7%)	76 (67.3%)	

Presence of Abnormal Uterine Bleeding				
Age (years)	20–30	37 (20.8%)	141 (79.2%)	0.886
	31–40	24 (19.2%)	101 (80.8%)	
Parity	≤3	37 (18.6%)	162 (81.4%)	0.551
	>3	24 (23.1%)	80 (76.9%)	
BMI (kg/m ²)	≤30	49 (23.9%)	156 (76.1%)	0.187
	>30	12 (12.2%)	86 (87.8%)	
Previous Contraceptive	Pills	37 (19.8%)	150 (80.2%)	0.868
	Condom	24 (20.7%)	92 (79.3%)	
Education	Illiterate	6 (17.6%)	28 (82.4%)	0.947
	Primary	9 (24.3%)	28 (75.7%)	
	Middle	21 (17.6%)	98 (82.4%)	
	Matric & above	25 (22.1%)	88 (77.9%)	
Presence of Dysmenorrhea				
Age (years)	20–30	31 (17.4%)	147 (82.6%)	0.773
	31–40	24 (19.2%)	101 (80.8%)	
Parity	≤3	37 (18.6%)	162 (81.4%)	0.921
	>3	18 (17.3%)	86 (82.7%)	
BMI (kg/m ²)	≤30	37 (18.0%)	168 (82.0%)	0.919
	>30	18 (18.4%)	80 (81.6%)	
Previous Contraceptive	Pills	28 (15.0%)	159 (85.0%)	0.263
	Condom	27 (23.3%)	89 (76.7%)	
Education	Illiterate	6 (17.6%)	28 (82.4%)	0.157
	Primary	9 (24.3%)	28 (75.7%)	
	Middle	9 (7.6%)	110 (92.4%)	
	Matric & above	31 (27.4%)	82 (72.6%)	
Presence of Polymenorrhea				
Age (years)	20–30	22 (12.4%)	156 (87.6%)	0.985
	31–40	15 (12.0%)	110 (88.0%)	
Parity	≤3	31 (15.6%)	168 (84.4%)	0.169
	>3	6 (5.8%)	98 (94.2%)	
BMI (kg/m ²)	≤30	24 (11.7%)	181 (88.3%)	0.936
	>30	13 (13.3%)	85 (86.7%)	
Previous Contraceptive	Pills	22 (11.8%)	165 (88.2%)	0.803
	Condom	15 (12.9%)	101 (87.1%)	
Education	Illiterate	3 (8.8%)	31 (91.2%)	0.939
	Primary	6 (16.2%)	31 (83.8%)	
	Middle	15 (12.6%)	104 (87.4%)	
	Matric & above	13 (11.5%)	100 (88.5%)	

DISCUSSION

The most common form of family planning is tubal ligation. In 1990, the percentage of married women of reproductive age who were sterilized was 22% in developing countries and 11% in industrialized countries, corresponding to 44% and 18% of contraceptive users, respectively. Menstrual irregularities associated with post-tubal ligation syndrome continue to raise concerns. Decades of discussion followed by initial observation of Stein et al. increased menorrhagia and metrorrhagia following sterilization [15]. Following TL, this study discovered oligomenorrhea in 83 (27.4%), atypical uterine bleeding in 61 (20.1%), dysmenorrhea in 55 (18.2%), and polymenorrhea in 37 (12.2%). The abnormal uterine bleeding 24.35%,

polymenorrhea 13.46%, dysmenorrhea 19.87%, and oligomenorrhea 26.92%. In a local study of 200 patients, 41% were between the ages of 32 and 40, 53% had parity 4–6, and 47% had heavy bleeding, 28% had irregular cycles, 13% had polymenorrhea, 5% had dysmenorrhea, and 7% had oligomenorrhea [16]. Menstrual disorders did not significantly change after TL, according to Zhu et al. [17]. With comparable bleeding durations, flow volumes, cycle lengths, and irregularities in sterilized and non-sterilized women, concluded that TL does not cause menstruation issues [18]. Age at sterilization influences abnormalities; it is more common in those aged 20 to 29 than in those over 30, and it may be a risk factor for menorrhagia and irregular bleeding [19]. Although tubal ligation is one of the most used permanent contraceptive techniques in the world, there is ongoing debate regarding its potential link to subsequent irregular menstruation. Without aiming to demonstrate causality, the current descriptive cross-sectional study was carried out to record the prevalence and pattern of menstrual irregularities among women after tubal ligation. The results of this study show that a significant percentage of women experienced irregular menstruation following tubal ligation. The most commonly reported abnormality was oligomenorrhea, which was followed by polymenorrhea, dysmenorrhea, and irregular uterine hemorrhage. International and regional literature has documented similar trends. Similar rates of oligomenorrhea and irregular uterine hemorrhage after tubal sterilization were reported in studies by Abbas et al. confirming the consistency of findings across various populations [14]. Uncertainty surrounds the underlying mechanism of post-tubal ligation menstruation problems. One theory is that tubal ligation disrupts the mesosalpinx, changing the ovarian blood flow and potentially impacting hormone control and follicular growth. Changes in estrogen levels and gonadotropin secretion have also been proposed as important causes. These biological theories are still up for debate, though, because several controlled trials have not shown any appreciable changes in hormones or menstruation following the surgery. There is evidence in the literature to the contrary. There is no statistically significant change in menstrual cycle characteristics between sterilized and non-sterilized women, according to certain large cohort and case-control studies. Variations in study design, age at sterilization, parity, baseline menstrual cycles, and follow-up time may account for these disparities. Although no significant correlations were found in the current investigation, younger age at the time of tubal ligation and higher parity have been proposed as potential risk modifiers for post-procedural menstrual abnormalities. Menstrual changes after tubal ligation may be multifactorial rather than directly related to a single factor, as evidenced by the lack of statistically significant correlations between menstrual irregularities and clinical

or demographic variables like age, body mass index, parity, education level, and previous use of contraceptives. Menstrual patterns following sterilization may also be influenced by psychological variables, recollection bias, and age-related hormonal changes. By offering local data on menstrual disruptions after tubal ligation in a Pakistani population—where such data are still scarce—this study adds to the body of existing knowledge. While stressing that the evidence is still equivocal, these findings may help doctors counsel women contemplating tubal ligation on potential menstrual abnormalities. Because of decreased follicles and ovarian non-responsiveness to FSH, Burger et al. connected high E2 and FSH to menstruation issues [20]. Current study (mean age study group 44.4 ± 5.7 , control 45.2 ± 5.3 ; $p=0.424$; mean parity 3.8 ± 1.8 vs. 3.5 ± 1.4 ; $p=0.220$) found no significant difference in hysterectomy for irregular bleeding (RR=0.85; 95% CI: 0.56–1.28; $p=0.418$). When analyzing the results, it is important to take into account the many constraints of this case series. Since it is a descriptive case series without a control group, it is impossible to establish a causal link between menstrual abnormalities and tubal ligation. Despite reflecting the whole accessible population during the study period, the very small sample size ($n=99$) lowers the results' statistical power and generalizability. Selection bias is a possibility in this single-center study that uses non-probability consecutive sampling. The majority of menstrual irregularities were self-reported, which raises the risk of reporting bias and memory. Furthermore, the six-month follow-up period might not be long enough to record long-term or delayed menstruation changes.

CONCLUSIONS

The most frequent menstrual irregularity following tubal ligation is oligomenorrhea, which is followed by irregular uterine bleeding. In order to avoid anomalies and community morbidity, public awareness campaigns should inform the public about the importance of prompt clinician consultation.

Authors' Contribution

Conceptualization: SL

Methodology: AP, AF, SS

Formal analysis: AA, SMB

Writing and Drafting: SM

Review and Editing: SL, AA, SMB, AF, SS, SM

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All 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] Goldberg JM, Falcone T, Diamond MP. Current Controversies in Tubal Disease, Endometriosis, and Pelvic Adhesion. *Fertility and Sterility*. 2019 Sep; 112(3): 417-425. doi: 10.1016/j.fertnstert.2019.06.021.
- [2] March CM. Female tubal sterilization: traditional and research methods. In *The Handbook of Contraception: Evidence-Based Practice Recommendations and Rationales*. Cham: Springer International Publishing. 2020 Sep: 193-238. doi: 10.1007/978-3-030-46391-5_11.
- [3] Nash R, Johnson CE, Harris HR, Peres LC, Joslin CE, Bethea TN et al. Race Differences in the Associations Between Menstrual Cycle Characteristics and Epithelial Ovarian Cancer. *Cancer Epidemiology, Biomarkers and Prevention*. 2022 Aug; 31(8): 1610-1620. doi: 10.1158/1055-9965.EPI-22-0115.
- [4] Bansal A, Dwivedi LK, Ali B. The Trends of Female Sterilization in India: An Age-Period-Cohort Analysis Approach. *BioMed Central Women's Health*. 2022 Jul; 22(1): 272. doi: 10.1186/s12905-022-01857-0.
- [5] Zucchini C, De Sanctis P, Facchini C, Di Donato N, Montanari G, Bertoldo V et al. Performance of Circulating Placental Growth Factor as a Screening Marker for Diagnosis of Ovarian Endometriosis: A Pilot Study. *International Journal of Fertility and Sterility*. 2015 Dec; 9(4): 483.
- [6] Verma P, Saxena S, Hiremath RN, Sinha P. Comparative Study on Menstrual Disorders in Post-Tubal Ligated and Non-Ligated Women. *Journal of Family Medicine and Primary Care*. 2023 Oct; 12(10): 2482-7. doi: 10.4103/jfmpc.jfmpc_880_23.
- [7] Glasier A, Bhattacharya S, Evers H, Gemzell-Danielsson K, Hardman S, Heikinheimo O et al. Contraception After Pregnancy. *Acta Obstetrica Et Gynecologica Scandinavica*. 2019 Nov; 98(11): 1378-1385. Doi: 10.1111/aogs.13627.
- [8] Itriyeve K. The Normal Menstrual Cycle. *Current Problems in Pediatric and Adolescent Health Care*. 2022 May; 52(5): 101183. doi: 10.1016/j.cppeds.2022.101183.
- [9] Dreisler E, Frandsen CS, Ulrich L. Perimenopausal Abnormal Uterine Bleeding. *Maturitas*. 2024 Jun; 184: 107944. doi: 10.1016/j.maturitas.2024.107944.
- [10] Harini R, Gowri S, Vinayakamurthy N. Impact of BMI on Puberty Menorrhagia in the Modern Era: A Prospective Analysis in a Tertiary Care Centre. *Journal of Contemporary Clinical Practice*. 2025 Jan; 11: 95-102.
- [11] Rodriguez MB, Lethaby A, Low C, Cameron IT. Cyclical Progestogens for Heavy Menstrual Bleeding. *Cochrane Database of Systematic Reviews*. 2019; 8.
- [12] Akgör U, Kırat S, Tok C. The Effects of Tubal Sterilization on Menopausal Age in a Cohort of Postmenopausal Women. *Deneyisel ve Klinik Tıp Dergisi*. 2021 Sep; 38(4): 589-593. doi: 10.52142/omujecm.38.4.34.
- [13] Shaikh S. Assessment of Menstrual Disturbances Resulting from Tubal Sterilization. *Journal of Surgery Pakistan*. 2019 May; 24(1): 34-37.
- [14] Abbas HY, Liaqat F, Memon E, Qureshi ZU, Karim K, Ali N. Menstrual Irregularities Post Tubal Ligation: Menstrual Irregularities Post Tubal Ligation. *Pakistan Bio-Medical Journal*. 2022 Jul: 89-93. doi: 10.54393/pbmj.v5i7.631.
- [15] Stein RI, Ma Y, Phelan J, Roberts ET, Johnston KJ, Orav EJ et al. Growth of Chronic Condition Special Needs Plans Among Dual-Eligible Beneficiaries, 2011-24: *Health Affairs*. 2025 Mar; 44(3): 304-312. doi: 10.1377/hlthaff.2024.00651.
- [16] Chen K, Bai Y, Ma Y, Chen J, Huang Y, Yang F et al. Subsequent Pregnancy Outcomes Following Conservative Management for Placenta Accreta Spectrum Disorders: An Ambispective Cohort Study. *The Journal of Maternal-Fetal and Neonatal Medicine*. 2025 Dec; 38(1): 2477782. doi: 10.1080/14767058.2025.2477782.
- [17] Zhu Y, Gong Y, Liu P. Supportive Care Needs, Quality of Life, And Social Support Among Laryngeal Cancer Patients Undergoing Total Laryngectomy: A Cohort Study. *The Journal of Laryngology and Otology*. 2025 Nov: 1-23. doi: 10.1017/S0022215125103770.
- [18] Uppal T, Lanzarone V, Mongelli M. Sonographically Detected Caesarean Section Scar Defects and Menstrual Irregularity. *Journal of Obstetrics and Gynaecology*. 2011 Jul; 31(5): 413-416. doi: 10.3109/01443615.2011.577252.
- [19] Bagga SS, Tayade S, Lohiya N, Tyagi A, Chauhan A. Menopause Dynamics: From Symptoms to Quality of Life, Unraveling the Complexities of the Hormonal Shift. *Multidisciplinary Reviews*. 2025; 8(2): 2025057. doi: 10.31893/multirev.2025057.
- [20] Orisaka M, Kawamura H, Yoshida Y. COVID-19 Testing of Pregnant Women in Japan. *Journal of Obstetrics and Gynaecology Research*. 2021 Jan; 47(464): 10-111. doi: 10.1111/jog.14567.



Original Article



Comparison of the Six-Minute Walk Test and the One-Minute Sit-To-Stand Test for Assessing Exercise Tolerance in Patients with Chronic Obstructive Pulmonary Disease

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ARTICLE INFO

Keywords:

Six-Minute Walk Test, Chronic Obstructive Pulmonary Disease, One-Minute Sit-To-Stand Test, Dyspnea

How to Cite:

Sajjad, S., Ashraf, S., Anwar, R., Ullah, A., Younas, M., & Rehman, K. (2026). Comparison of the Six-Minute Walk Test and the One-Minute Sit-To-Stand Test for Assessing Exercise Tolerance in Patients with Chronic Obstructive Pulmonary Disease: Six-Minute Walk and the Sit-To-Stand Test for Exercise Tolerance in Patients with COPD. *Pakistan Journal of Health Sciences*, 7(6), 127-132. <https://doi.org/10.54393/pjhs.v7i6.3558>

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ABSTRACT

Exercise tolerance assessment plays an important role in the management of chronic obstructive pulmonary disease (COPD). The Six-Minute Walk Test (6-MWT) and One-Minute Sit-to-Stand Test (1-MSTST) are commonly used, although few studies have compared their relative value in COPD. **Objective:** To compare 6-MWT and 1-MSTST in assessing exercise tolerance in patients with COPD. **Methods:** This analytical cross-sectional study was conducted in the Department of Pulmonology, Khyber Teaching Hospital, Peshawar, from March 29 to September 28, 2024. 98 participants were included in the study using a non-probability convenience sampling technique. Exercise tolerance was assessed in both tests, using heart rate (beats/min) and oxygen saturation (SpO₂%) measured with a pulse oximeter. Data were analyzed using SPSS version 23.0. **Results:** Out of the 98 patients with COPD (50 males, 48 females; mean age, 58.98 ± 7.75 years), the 6MWT, pulse rate rose from 88.92 ± 6.84 to 93.15 ± 7.73 bpm, and SpO₂ fell from 93.99 ± 1.97% to 91.24 ± 2.72%. In the 1MSTST, pulse rate increased from 88.38 ± 6.48 to 90.02 ± 6.37 bpm, and SpO₂ declined from 94.01 ± 2.07% to 92.94 ± 2.34%, with changes significant for SpO₂ (p-value < 0.001) and modest for pulse rate (p = 0.002). The 6MWT induced greater tachycardia and desaturation, reflecting higher cardiopulmonary demand. **Conclusions:** Both tests effectively assessed exercise tolerance in COPD, but the 6MWT demonstrated greater desaturation, making it more sensitive for evaluating functional limitation.

INTRODUCTION

Chronic Obstructive Pulmonary Disease, or COPD, is the third leading cause of death globally and is defined by phlegm, cough, and progressive airway obstruction [1, 2]. COPD is considered a public health problem by the Global Initiative for Chronic Obstructive Lung Disease GOLD, and its prevalence is increasing steadily because of the ageing of the population, tobacco exposure, and other environmental risk factors [3]. COPD has been said to affect more than 300 million individuals worldwide

according to the World Health Organization, and it is expected to be the third leading cause of death worldwide by the year 2030 [4]. In South Asia, this creates a higher burden of COPD because tobacco use, indoor air pollution, and late diagnosis are all prevalent [5, 6]. The prevalence of COPD has been estimated to be between 3-6% in the general Pakistani population, increasing among those living in rural areas and those exposed to biomass fuel sources [7, 8]. Though the disease is a burden, knowledge



and early diagnosis are lacking, resulting in late presentations and worse outcomes [9]. Evaluating functional capacity is fundamental to COPD diagnosis, staging, disease monitoring, and developing a treatment plan [10]. The most used and accepted submaximal exercise test, the 6-Minute Walk Test (6MWT), is not practical in all types of resource-limited situations as it requires physical space and a trained staff [11]. Alternatively, the 1-Minute Sit-to-Stand Test (1MSTST) is a simple and practical tool to assess exercise tolerance and has been proposed as a valid alternative [12, 13].

Although the two tests have been validated separately, little is known about the performance and applicability of the 6MWT and the 1MSTST in a local COPD population, especially in a low-tech environment. Also, the impact of demographic and clinical variables, including age, gender, and comorbidity, on test results is not well understood in Pakistani patients either. It is important to choose valid and reliable instruments that are feasible and cost-efficient for the assessment of COPD in clinical practice. Thus, the present study aimed to compare the performance of pre- and post-6MWT and 1MSTST in COPD patients and to analyze the influence of demographic and clinical variables on test performance.

METHODS

This was an analytical cross-sectional study conducted in the Department of Pulmonology, Khyber Teaching Hospital, Peshawar, from March 29 to September 28, 2024. The ethical approval was taken from the institutional review board with ref no: 277/DME/KMC issued on 5th October 2023. The sample size was calculated using the formula for comparing two means: $n = 2(Z_{1-\alpha/2} + Z_{1-\beta})^2 \sigma^2 / (\mu_1 - \mu_2)^2$. Using $Z_{1-\alpha/2} = 1.96$, $Z_{1-\beta} = 0.84$, $\mu_1 = 110 \pm 20$ bpm (6MWT), and $\mu_2 = 98 \pm 22$ bpm (1MSTST) in COPD patients, the pooled SD was 21 [11]. Substituting these values yielded $n = 49$ per group, giving a total sample of 98 patients. Using a non-probability consecutive sample collection method, all eligible patients who presented during the study period and satisfied the eligibility criteria were included in the study until the desired sample size was reached. All patients of either gender, aged 40 to 75 years, with a confirmed diagnosis of chronic obstructive pulmonary disease (COPD) of mild to moderate severity according to the GOLD criteria, were included in the study. Patients were not included in the study if they had any orthopedic condition, previously diagnosed arrhythmia or heart failure, neurological deficit, arthritis of the knee, or end-stage renal failure. COPD patients with acute infections concomitant to the diagnosis were also excluded. After receiving permission from the ethical review board of the hospital, as well as the Department of Research in CPSP Karachi, the study was started. Those who fulfilled the study criteria were informed about the

study objectives and potential benefits and risks, and written informed consent was obtained. The demographic and clinical characteristics recorded at baseline included age, gender, occupation, education, monthly income, and socioeconomic status, residence (rural/urban), duration of COPD, and associated comorbidities, including hypertension, diabetes, anemia, hyperthyroidism, and cor pulmonale. All patients underwent a thorough physical examination and a detailed medical history. The One-Minute Sit-to-Stand Test was performed first, and the Six-Minute Walk Test was performed after one hour of rest. Oxygen saturation ($SpO_2\%$) and pulse rate (beats/min) were measured pre- and post each testing using a pulse-oximeter. A senior postgraduate resident working in the pulmonology ward led all evaluations and used a proforma to document the findings.

Data were analyzed using SPSS version 23.0. Normality of continuous variables (heart rate, oxygen saturation) was assessed using the Shapiro-Wilk test. All variables showed $p > 0.050$, indicating normal distribution. Therefore, continuous variables are presented as mean $\pm$ SD, and parametric tests were applied. The paired sample t-test was used to compare pre- and post-test heart rate and oxygen saturation in both exercise tests. Categorical variables, such as gender, were expressed as frequencies and percentages. A p -value < 0.050 was considered statistically significant.

RESULTS

Ninety-eight patients with COPD were enrolled in the study. Distribution by gender was approximately balanced: 50 were male (51.02%), and 48 were female (48.98%). Participants ranged in age from 40 to 85 years, with a mean age of 58.98 ± 7.75 years. The majority of patients, 54.1%, were aged between 51 and 60 years, 18.4% were younger than 50 years, and 27.6% older than 60 years. As for residence, 53 patients (54.1%) were from an urban area and 45 (45.9%) from a rural area. Housewives comprised the majority of the population, at 46.9%, followed by Labourers at 24.5%, farmers at 14.3%, and "other" professions like driving, teaching, and shopkeeping at 11.2%. Three patients (3.1%) were electricians. About education status, there were more uneducated participants with 89.8%, as compared to 10 (10.2%) educated population. Regarding socioeconomic status, 69.4% were lower-class, 29.6% were middle-class, and only 1 patient (1.0%) belonged to the upper-class. Regarding disease duration, 54 patients (55.1%) had COPD for 5 years or less, while 44 patients (44.9%) had it for more than 6 years (Table 3).

Table 1: Demographic and Clinical Characteristics of COPD Patients(n=98)

Variables	Category	n (%)
Gender	Male	50 (51.02%)
	Female	48 (48.98%)
Age Group (Years)	≤ 50	18 (18.4%)
	51-60	53 (54.1%)
	≥ 61	27 (27.6%)
Mean Age ± SD	—	58.98 ± 7.75
Residence	Urban	53 (54.1%)
	Rural	45 (45.9%)
Profession	Labour	24 (24.5%)
	Housewife	46 (46.9%)
	Electrician	3 (3.1%)
	Farmer	14 (14.3%)
	Driver/Teacher/Shopkeeper	11 (11.2%)
Education	Educated	10 (10.2%)
	Uneducated	88 (89.8%)
Socioeconomic Status	Lower	68 (69.4%)
	Middle	29 (29.6%)
	Upper	1 (1.0%)
Duration of COPD (years)	≤ 5	54 (55.1%)
	≥ 6	44 (44.9%)

The study displays the difference between pre- and post-test results of the Six-Minute Walk Test (6MWT) and the One-Minute Sit-to-Stand Test (1MSTST) in 98 COPD patients. The average pre-test pulse rate was the same in both groups (88.93 ± 6.84 bpm for 6MWT vs. 88.39 ± 6.48 bpm for 1MSTST, $p=0.571$), with no statistically significant difference. Similarly, pre-test SpO₂ levels were not statistically different ($93.99 \pm 1.98\%$ for 6MWT vs. $94.02 \pm 2.07\%$ for 1MSTST, $p=0.916$). However, the 6MWT group had higher post-test measurements compared to the 1MSTST group. The post-test pulse rate was greater in the 6MWT group (93.15 ± 7.74 vs. 90.02 ± 6.37 bpm, $p=0.002$). Likewise, desaturation of oxygen was more evident following the 6MWT, where mean SpO₂ decreased to $91.24 \pm 2.72\%$ from $92.93 \pm 2.34\%$ in the 1MSTST ($p<0.001$). In general, these results suggest that although the baseline parameters were similar, the 6MWT elicited more elevated rises in heart rate and larger falls in oxygen saturation than the 1MSTST (Table 2).

Table 2: Comparison of Pre- and Post-Findings in Both the Test (n=98)

Groups	n	Mean ± SD	p-value
Pre Pulse Rate	6MWT	88.9286 ± 6.84	0.571
	1MSTST	88.3878 ± 6.48	
Pre SP02%	6MWT	93.9898 ± 1.97	0.916
	1MSTST	94.0204 ± 2.06	
Post Pulse Rate	6MWT	93.1531 ± 7.73	0.002*
	1MSTST	90.0204 ± 6.36	

Post SP02	6MWT	98	91.2449 ± 2.73	<0.001*
	1MSTST	98	92.9286 ± 2.33	

asterisk(*)denotes statistical significance at $p \leq 0.050$

Normality of continuous variables (heart rate, oxygen saturation) was assessed using the Shapiro-Wilk test. All variables showed $p > 0.050$, indicating normal distribution (Table 3).

Table 3: Normality Test Results for Continuous Variables (Shapiro-Wilk test, n=98)

Variables	Shapiro-Wilk Statistic (W)	p-value	Distribution
Pre-test Pulse Rate (6MWT)	0.983	0.214	Normal
Pre-test Pulse Rate (1MSTST)	0.981	0.198	Normal
Pre-test SpO ₂ (6MWT)	0.987	0.266	Normal
Pre-test SpO ₂ (1MSTST)	0.985	0.241	Normal
Post-test Pulse Rate (6MWT)	0.979	0.187	Normal
Post-test Pulse Rate (1MSTST)	0.982	0.205	Normal
Post-test SpO ₂ (6MWT)	0.988	0.272	Normal
Post-test SpO ₂ (1MSTST)	0.986	0.258	Normal

The study shows a comparison between the tests, with the independent-samples t-test showing no difference between the tests in terms of pre-test pulse rate ($p=0.571$) and pre-test SpO₂ ($p=0.916$), while pulse rate post-test ($p=0.002$) and SpO₂ post-test ($p<0.001$) were different between the 6MWT and 1MSTST.

Table 4: Independent Samples t-Test Comparing Physiological Parameters Between 6MWT and 1MSTST (n=98)

Variables	n	Mean ± SD	p-value
Pre-test Pulse Rate	6MWT	88.93 ± 6.84	0.571
	1MSTST	88.39 ± 6.48	
Pre-test SpO ₂ (%)	6MWT	93.99 ± 1.97	0.916
	1MSTST	94.02 ± 2.06	
Post-test Pulse Rate	6MWT	93.15 ± 7.73	0.002*
	1MSTST	90.02 ± 6.36	
Post-test SpO ₂ (%)	6MWT	91.24 ± 2.73	<0.001*
	1MSTST	92.93 ± 2.33	

All variables showed $p > 0.05$, confirming normal distribution and validating the use of parametric tests (paired t-test). asterisk (*) denotes statistical significance at $p \leq 0.050$

As shown in the bar chart, in the study's 98 patients with COPD, there was a high rate of concomitant illnesses. Ten patients (10.2%) were hypertensive, while 88 patients (89.8%) did not have hypertension. Six patients (6.1%) were diabetic, and 92 patients (93.9%) were not diabetic. Anemia, hyperthyroidism, and Cor pulmonale were excluded in all patients, leaving no case of any of the three conditions out of 98 (100%). Hypertension was more prevalent overall, and both conditions were the only meaningful comorbidities present among the study population (Figure 1).

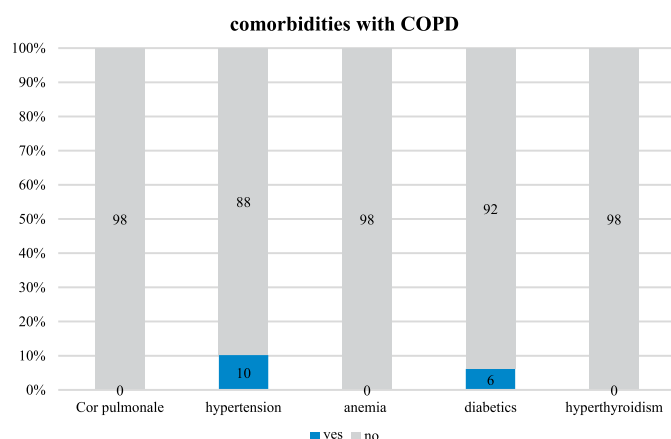


Figure 1: Distribution of Comorbid Conditions among Patients with COPD (n=98)

DISCUSSION

In the present study, both the Six-Minute Walk Test (6MWT) and One-Minute Sit-to-Stand Test (1MSTST) effectively assessed exercise tolerance in COPD patients; however, the 6MWT produced a significantly greater increase in heart rate (from 88.92 ± 6.84 to 93.15 ± 7.73 bpm) and a larger decrease in oxygen saturation (from $93.99 \pm 1.97\%$ to $91.24 \pm 2.72\%$) compared to the 1MSTST, where heart rate rose modestly (from 88.38 ± 6.48 to 90.02 ± 6.37 bpm) and SpO_2 declined slightly (from $94.01 \pm 2.07\%$ to $92.94 \pm 2.34\%$). Similarly, the study found that the 6MWT induced greater physiological stress, with a mean SpO_2 drop of $3.1 \pm 1.6\%$ compared to $1.5 \pm 0.8\%$ in the 1MSTST group ($p < 0.050$). Both previous studies, therefore, support the present study's conclusion that the 6MWT elicits higher cardiopulmonary demand and provides a more sensitive measure for detecting exertional desaturation in COPD patients [14]. But the practicality and feasibility of 1MSTST, particularly in low-resource clinical settings, make it a useful option. On top of that, it has been previously established that 1MSTST is well correlated with 6MWT as functional capacity predictors and, therefore, is especially useful when space and time are limited [15]. Hypertension and diabetes were the most common among all other documented comorbidities, but the overall prevalence was lower compared to other cohorts [16]. This difference may be due to underdiagnosis or our sample being biased against patients with more severe disease. But even small comorbidity prevalence is of clinical significance as it may also contribute to a faster progression of COPD and increased complexity of its management [17]. The need for and advantage of a systematic screening process for the identification of comorbidities among patients with COPD was recently highlighted by other authors [18] and is in line with our findings. An additional relevant finding was that more than half of the patients were diagnosed within the last five years. On top of that, early intervention is key as benefits to treatment such as smoking cessation,

medication therapy, and pulmonary rehabilitation have been shown to improve outcomes when initiated early [19]. Nonetheless, ignorance and difficult access to healthcare represent all of them, and remain as barriers to being diagnosed also in other areas, mainly rural ones [20]. These study results further highlight the complementary purposes of 6MWT and 1MSTST for the assessment of people with COPD. While the 6MWT continues to be considered the gold standard for assessment of exercise capacity and prognosis, the 1MSTST might be a better alternative in outpatient and primary care settings where the necessary infrastructure for the 6MWT is not available [21]. The sensitivity vs. convenience trade-off is one example of how the way functional assessment is done must conform to the healthcare world.

There are some limitations to this study. First, it was conducted at a tertiary care hospital, and the sample may not reflect the general population, particularly in rural areas, in which access to health and exposure risk might be different. Second, the sample was relatively small, which limits the power to identify weak correlations among demographic variables, comorbidities, and functional outcomes. Third, patients with multiple or severe comorbidities were not included, which may have reduced the overall effect of COPD-related comorbidities. Longitudinal outcomes such as frequency of exacerbation and rate of hospitalization, both important indicators of disease progression, were also not assessed. Lastly, functional assessment was limited to 6MWT and 1MSTST; other measures, such as spirometry or cardiopulmonary exercise testing, could have provided a more detailed breath assessment. Given the study findings, the One-Minute Sit-to-Stand Test (1MSTST) and the Six-Minute Walk Test (6MWT) should be incorporated as part of the usual assessment of patients with COPD, since in outpatient clinics or in developing countries where 6MWT requires space and/or several materials are not available, the 1MSTST represents a practical alternative. Similarly, it is going to be important to pursue awareness also for low-literacy and socioeconomic groups to promote early diagnosis and risk management of COPD. Periodic screening for such comorbidities as hypertension and diabetes would be necessary to improve patient outcomes. Also, formal exercise programs and rehabilitation should be promoted as a means to achieve optimal functional capacity, while policy interventions aimed at reducing exposure to environmental risk factors, such as biomass fuel use or urban air pollution exposure, remain essential in preventing overall disease progression.

CONCLUSIONS

The 1MSTST is more convenient, space-saving, and a valid alternative to be used for functional assessment, especially in resource-limited settings or outpatient use. These findings support the clinical use of both tests as complementary, considering the 6MWT as the gold standard and the 1MSTST as a feasible alternative when the 6MWT is not feasible.

Authors' Contribution

Conceptualization: RA

Methodology: SA, MY, KR

Formal analysis: SS

Writing and Drafting: AU

Review and Editing: SS, SA, RA, AU, MY, KR

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All 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] Thu HN, Le Khac B, Poncin W. Reliability of the 1-Minute Sit-To-Stand Test in Chronic Obstructive Pulmonary Disease. *Annals of Physical and Rehabilitation Medicine*. 2024 Oct; 67(7): 101866. doi: 10.1016/j.rehab.2024.101866.
- [2] Briand J, Behal H, Chenivresse C, Wêmeau-Stervinou L, Wallaert B. The 1-Minute Sit-To-Stand Test to Detect Exercise-Induced Oxygen Desaturation in Patients with Interstitial Lung Disease. *Therapeutic Advances in Respiratory Disease*. 2018 Aug; 12: 1753466618793028. doi: 10.1177/1753466618793028.
- [3] Adeloye D, Song P, Zhu Y, Campbell H, Sheikh A, Rudan I. Global, Regional, And National Prevalence of, and Risk Factors for, Chronic Obstructive Pulmonary Disease (COPD) in 2019: A Systematic Review and Modelling Analysis. *The Lancet Respiratory Medicine*. 2022 May; 10(5): 447-58.
- [4] Chae G, Ko EJ, Lee SW, Kim HJ, Kwak SG, Park D et al. Stronger Correlation of Peak Oxygen Uptake with Distance of Incremental Shuttle Walk Test Than 6-Min Walk Test in Patients with COPD: A Systematic Review and Meta-Analysis. *BioMed Central Pulmonary Medicine*. 2022 Mar; 22(1): 102. doi: 10.1186/s12890-022-01897-0.
- [5] Spence JG, Brincks J, Løkke A, Neustrup L, Østergaard EB. One-Minute Sit-To-Stand Test as a Quick Functional Test for People with COPD in General Practice. *Nature Research Journal: Primary Care Respiratory Medicine*. 2023 Mar; 33(1): 11. doi: 10.1038/s41533-023-00335-w.
- [6] Mellaerts P, Demeyer H, Blondeel A, Vanhoutte T, Breuls S, Wuyts M et al. The One-Minute Sit-to-Stand Test: A Practical Tool for Assessing Functional Exercise Capacity in Patients with COPD in Routine Clinical Practice. *Chronic Respiratory Disease*. 2024 Oct; 21: 14799731241291530. doi: 10.1177/14799731241291530.
- [7] Farley C, Phillips SM, Smith-Turchyn J, Brooks D. Measurement Properties of the Sit-to-Stand Test in People with Chronic Obstructive Pulmonary Disease: Protocol for a Systematic Review and Meta-Analysis Using the COSMIN Guidelines. *Plos One*. 2024 Dec; 19(12): e0316451. doi: 10.1371/journal.pone.0316451.
- [8] Strassmann A, Steurer-Stey C, Lana KD, Zoller M, Turk AJ, Suter P et al. Population-Based Reference Values for the 1-Min Sit-to-Stand Test. *International Journal of Public Health*. 2013 Dec; 58(6): 949-53. doi: 10.1007/s00038-013-0504-z.
- [9] Tsai MY, Huang KT, Hsu CY, Yu YH, Fu PK. Reference Values for the 1-Minute Sit-To-Stand Test to Assess Functional Capacity and Short-Term Mortality in People with Idiopathic Pulmonary Fibrosis and Fibrotic Connective Tissue Related Interstitial Lung Diseases: A Prospective Real-World Cohort Study. *BioMed Central Pulmonary Medicine*. 2025 Feb; 25(1): 61. doi: 10.1186/s12890-025-03521-3.
- [10] Jones SE, Kon SS, Canavan JL, Patel MS, Clark AL, Nolan CM et al. The Five-Repetition Sit-to-Stand Test as a Functional Outcome Measure in COPD. *Thorax*. 2013 Nov; 68(11): 1015-20. doi: 10.1136/thoraxjnl-2013-203576.
- [11] Crook S, Büsching G, Schultz K, Lebert N, Jelusic D, Keusch S et al. A Multicentre Validation of the 1-Min Sit-to-Stand Test in Patients with COPD. *European Respiratory Journal*. 2017 Mar; 49(3). doi: 10.1183/13993003.01871-2016.
- [12] Chambellan A, Nusinovi S, Vaidya T, Gourraud PA, De Bisschop C. The Validation of the Sit-To-Stand Test for COPD Patients. *European Respiratory Journal*. 2017 Sep; 50(3). doi: 10.1183/13993003.01203-2017.
- [13] Vilarinho R, Montes AM, Noites A, Silva F, Melo C. Reference Values for the 1-Minute Sit-To-Stand and 5 Times Sit-to-Stand Tests to Assess Functional Capacity: A Cross-Sectional Study. *Physiotherapy*. 2024 Sep; 124: 85-92. doi: 10.1016/j.physio.2024.01.004.
- [14] Jenkins AR, Burtin C, Camp PG, Lindenauer P, Carlin B, Alison JA et al. Do Pulmonary Rehabilitation Programmes Improve Outcomes in Patients with

- COPD Posthospital Discharge for Exacerbation: A Systematic Review and Meta-Analysis. *Thorax*. 2024 May; 79(5): 438-47. doi: 10.1136/thorax-2023-220333.
- [15] Golpe R, Pérez-de-Llano LA, Méndez-Marote L, Veres-Racamonde A. Prognostic Value of Walk Distance, Work, Oxygen Saturation, and Dyspnea During 6-Minute Walk Test in COPD Patients. *Respiratory Care*. 2013 Aug; 58(8): 1329-34. doi: 10.4187/respcare.02290.
- [16] Moorthy A, Mohapatra PR, Bhuniya S, Panigrahi MK, Bal SK, Patro M et al. Agreement Between the One-Minute Sit-To-Stand Test and the Six-Minute Walk Test in Assessing Exercise Capacity in Patients with Interstitial Lung Disease. *Monaldi Archives for Chest Disease*. 2026. doi: 10.4081/monaldi.2025.3577.
- [17] Reyhler G, Boucard E, Peran L, Pichon R, Le Ber-Moy C, Oukseil H et al. One Minute Sit-to-Stand Test Is an Alternative to 6MWT to Measure Functional Exercise Performance in COPD Patients. *The Clinical Respiratory Journal*. 2018 Mar; 12(3): 1247-56. doi: 10.1111/crj.12658.
- [18] Wakeham L, McDonnell L, Brown G, Watling B, Osman L. P175 Comparing Exertional Desaturation Between the 6-Minute Walk Test (6MWT) and 1-Minute Sit to Stand Test (1MSTST) in Those Prescribed Ambulatory Oxygen (AO). *British Medical Journal*. 2022; 17(1). doi: 10.1136/thorax-2022-BTSabstracts.309.
- [19] Dourado IM, Goulart CD, Santos-de-Araújo AD, Marinho RS, Garcia-Araujo AS, Roscani MG et al. Distance Travelled in the Six-Minute Walk Test in Patients with Chronic Obstructive Pulmonary Disease as a Predictor of Mortality. *BioMed Central Pulmonary Medicine*. 2025 May; 25(1): 258. doi: 10.1186/s12890-025-03721-x.
- [20] ATS. Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS Statement: Guidelines for the Six-Minute Walk Test. *American Journal of Respiratory and Critical Care Medicine*. 2002; 166: 111. doi: 10.1164/ajrccm.166.1.at1102.
- [21] Singh SJ, Puhan MA, Andrianopoulos V, Hernandez NA, Mitchell KE, Hill CJ et al. An Official Systematic Review of the European Respiratory Society/American Thoracic Society: Measurement Properties of Field Walking Tests in Chronic Respiratory Disease. *European Respiratory Journal*. 2014 Nov; 44(6): 1447-78. doi: 10.1183/09031936.00150414.



Original Article



Clinical Features and Prognosis of Cancer Patients Requiring Intensive Care Unit Admission

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ARTICLE INFO

Keywords:

Cancer, Critical Illness, Intensive Care Units, Prognosis, Treatment Outcome

How to Cite:

Sunil, R. K., Alvi, A., Baloch, S. A., & Khan, T. (2026). Clinical Features and Prognosis of Cancer Patients Requiring Intensive Care Unit Admission: Clinical Features and Prognosis in ICU Cancer Patients. *Pakistan Journal of Health Sciences*, 7(6), 133-139. <https://doi.org/10.54393/pjhs.v7i6.3904>

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ABSTRACT

Cancer patients are at risk of admission to the critical care unit either due to primary illness or as a consequence of treatment. **Objectives:** To determine clinical features and cancer patients' prognosis necessitating ICU (Intensive Care Unit) admission. **Methods:** This cross-sectional analytical study at the critical care unit of Ziauddin Medical University Hospital was done on cancer patients fulfilling eligibility criteria between July 2023 and December 2023. Along with demographics, Acute Physiology and Chronic Health Evaluation (APACHE) II score, Sequential Organ Failure Assessment (SOFA) score, and ECOG were reported. SPSS version 23.0 was used for data analysis. For comparing clinical characteristics and outcomes between different subgroups, the t-test and chi-square test were applied, keeping $p < 0.05$ as statistically significant. **Results:** Patients having hematological malignancy had a significantly lengthier hospital stay before ICU admittance compared to those with solid tumors ($p = 0.01$). Chemotherapy use was significantly more frequent ($p < 0.01$), and sepsis/septic shock was a more common cause of ICU admission ($p = 0.05$). On ICU admission, renal dysfunction ($p < 0.01$), leukocyte count ($p = 0.04$), thrombocyte count ($p = 0.05$), and C-reactive protein levels ($p < 0.01$) showed significant differences between the groups. During ICU stay, sepsis/septic shock remained significantly different between groups ($p < 0.01$). Additionally, overall survival outcomes differed significantly, with higher survival observed in patients with solid tumors ($p < 0.01$). **Conclusion:** The type of malignancy significantly influenced ICU outcomes, with hematological cancers associated with greater disease severity and poorer prognosis, while solid tumors showed better survival.

INTRODUCTION

Since cancer leads to a substantial effect on an individual's health, a profound understanding of its clinical manifestations and prognosis is a necessity [1]. Worldwide, estimates show around 20 million new cases in the last decade, with around 10 million deaths due to cancer. The increasing burden of cancer is predicted to reach approximately 60 % in the next 20 years, which will lead to further adverse effects on the health care system [2]. Diagnosis and treatment of cancers in their early phases are critical for patient survival throughout the globe [3]. Many cancer patients require admission to the highest

medical interventional levels, i.e., necessitating ICU admittance [4]. The purpose of admitting cancer patients to the ICU is probably due to a life-threatening situation/s or an increase in the complexity of such patients [5]. Such critical care scenarios require an in-depth comprehension of the clinical features demonstrated by cancer patients and carefully need to be evaluated for prognostic features that influence outcomes [6]. Research has demonstrated varied clinical presentations in cancer patients that were admitted to the ICU, including evaluation of stage, type of cancer, and complications associated with treatment [7].



Concurrently, it remains vital to evaluate prognostic determinants that will shape the future of such cases, including cancer's characteristics, dysfunctional organs, severity of the cancer, status of immunity, and influences of age and co-morbidities [8]. Through assessment of clinical characteristics and prognostic factors among cancer patients requiring ICU, it will aid in refining current guidelines, helping to provide enhanced healthcare and improve overall outcomes. Complications in cancer patients occur either in non-septic or in septic type overall, the duration of their cancer, and during therapies [9]. A timely, accurate, and proper evaluation can be made by proper evaluation. There is always a possibility of recovery from such complications if managed in a timely and careful manner. But if we labeled these cancer patients as they have deadly disease and marked them as not aggressive just because the malignancy has no outcome (as previously thought), then it ultimately affects the survival of these patients. It is vital to evaluate which cancer patients need ICU care the most, how they respond, and what their outcome is [10, 11]. Cancer patients account for up to 15% of all ICU admissions [12]. However, admitting cancer patients to the ICU may be fraught with controversy. Despite the fact that advances in oncology and supportive care appear to be associated with improved patient survival rates, many intensivists are still hesitant to admit these patients to the ICU [13, 14].

Limited local data exists on the clinical profile and outcomes of cancer patients admitted to the ICU, particularly in low- and middle-income settings like Pakistan, where findings from high-income countries may not be generalizable. Cancer patients requiring ICU care have high morbidity and mortality, yet the lack of local evidence limits effective risk stratification and clinical decision-making. The study aimed to assess and identify the clinical features, outcome, and prognosis of cancer patients requiring ICU admission.

METHODS

This research used an analytical cross-sectional study design that was carried out at the critical care unit of Ziauddin Medical University Hospital, Karachi, Pakistan [reference number: 7390623RKONC; dated 12th July 2023]. The study duration was for 6 months after approval of the research proposal. Using non-probability convenient sampling, all cancer patients fulfilling the inclusion criteria between July 2023 and December 2023, including patients of either gender and above 18 years of age with diagnosed cases of malignancy, were included in the study, whereas patients who were admitted on more than one occasion to the ICU during the same stay in hospital, only their first data point was included in the study. Moreover, patients who died within 24 hours of admission to the ICU, as well as

patients having a length of hospitalization stay in the ICU <24 hours, were excluded from the study. To minimize survivorship bias, ICU stays of patients <24 hours were excluded, since such cases seldom represent either extreme in terms of early death and transient admission to ICU without adequate clinical evaluation. The required sample size was estimated using a two-group comparison of proportions (solid vs. hematological malignancies), assuming a difference in mortality of 25% between groups, a confidence level of 95%, and a power of 80%. A total of 80 samples were calculated using the formula. After approval of the research proposal, data were collected from electronic medical records of the critical care unit of the hospital during the study period. The demographics included age, gender, duration of hospital stay, duration of ICU stay, characteristics of cancer on ICU admission, type of cancer, its stage, primary site of cancer, status of metastasis, treatment status, cause of ICU admission, any bacterial, fungal, pulmonary or blood stream infection, mortality and co-morbidities both on pre-hospital admission and on ICU admission and Glasgow Coma Scale (GCS). APACHE II, SOFA, and ECOG scores for pre-admission performance status were reported. In addition, laboratory data included complete blood counts, C-reactive protein, liver function tests (ALT, LDH), procalcitonin, calcium, albumin, glucose, and creatinine. ICU-associated morbidities included septic shock or sepsis, renal or hepatic dysfunction, renal replacement therapy, neutropenia, mechanical ventilation, blood transfusion, chemotherapy, culture-proven or suspected infection, catheterization, use of vasopressors or steroids, and all were recorded.

For data analysis, SPSS version 23.0 was used. The data included demographical characteristics, cancer-associated factors, and clinical data, which were presented as frequencies and percentages for qualitative variables, while means and standard deviations were used for quantitative variables. To compare clinical characteristics and outcomes on the basis of cancer subtypes, independent t-tests and chi-square tests were applied. A p-value of <0.05 was considered statistically significant.

RESULTS

There was a total of 510 admissions that took place during the study, amongst which 81 (15.88 %) were patients with cancer who met the inclusion criterion for this study. Median age was 58 (43-69) years, with the majority being females (59.26 %). The most common cause of patient admission into the ICU was due to septic shock/sepsis in about 64.2% of patients, followed by respiratory failure in 58 % of patients. Median length of hospital stay before ICU admission was 3.8 (1-19) days, and median length of ICU stay was 6.2 (4-14) days. In terms of the characteristics of cancer on admission into ICU, 34.57 % of patients were

newly diagnosed, 32.1 % with relapse of progressive disease, 23.46 % with complete or partial remission, while 9.88 % with end-stage disease. 71.6 % of patients reported a good ECOG score on pre-admission performance status. 70.37 % of patients underwent chemotherapy, while 51.9 % patients had cancer therapy within 30 days before ICU admission. Radiation therapy was carried out in 24.7 % of patients, while surgery was carried out in 27.2 % of patients. 26 % of patients in this study were diabetic, followed by hypertension in 24.7 %, cardiovascular disease in 14.8 %, and COPD in 11.11 % of patients. The most common morbidity in patients on ICU admission was either suspected or culture-proven infection, in about 84 % of patients, followed by thrombocytopenia in 50.62 %, and renal dysfunction in 48.14 % patients. The most common type of infection was pulmonary, in 70.37 % of patients (Table 1).

Table 1: Demographical characteristics of included patients (n=81)

Variables		Frequency (%) / Median $\pm$ IQR
Age (years)		58 (43-69)
Gender	Male	33 (40.74 %)
	Female	48 (59.26 %)
Hospital stay before admission to ICU (days)		3.8 (1-19)
Length of ICU stay (days)		6.2 (4-14)
Stage of Cancer	Recently diagnosed	28 (34.57 %)
	Complete or partial remission	19 (23.46 %)
	Relapse or progressive disease	26 (32.1 %)
	End stage	08 (9.88 %)
Performance Status	Good (ECOG 0-2)	58 (71.6 %)
	Poor (ECOG 3 and 4)	23 (28.4 %)
Treatment	Chemo	57 (70.37 %)
	Radiation	20 (24.7 %)
	Surgery	22 (27.2 %)
	Therapy < 30 days before ICU admit	42 (51.9 %)
Comorbidities	COPD	09 (11.11 %)
	Diabetes mellitus	21 (26 %)
	Hypertension	20 (24.7 %)
	Cardiovascular diseases	12 (14.8 %)
Reason for ICU Admission	Sepsis/septic shock	52 (64.2 %)
	Respiratory failure	47 (58 %)
	Acute renal failure	27 (33.33 %)
	Renal Dysfunction	39 (48.14 %)
ICU-Associated Comorbidities	Neutropenia	24 (29.63 %)
	Thrombocytopenia	41 (50.62 %)
	Mechanical ventilation	36 (44.44 %)
	Hepatic Dysfunction	27 (33.33 %)
	Vasopressors	28 (34.57 %)
	>2 organ dysfunction	39 (48.14 %)
	Infection	68 (84 %)
	Bacterial Infection	36 (44.44 %)
	Fungal Infection	11 (13.58 %)
	Pulmonary Infection	57 (70.37 %)

Bloodstream Infection	16 (19.75 %)
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A total of 50 patients were reported to have solid tumors, amongst which the most common type of cancer was Non-Hodgkin Lymphoma (Figure 1).

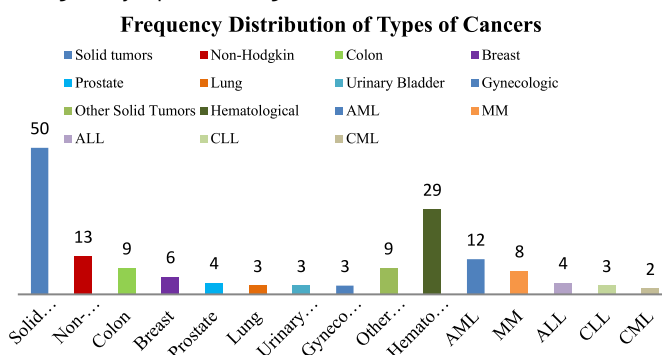


Figure 1: Frequency distribution of Cancer Types in the Study Population

The clinical features of the included patients when admitted to the ICU (Table 2).

Table 2: Clinical Features of Included Patients (n=81)

Clinical Features on ICU Admission	Median $\pm$ IQR
APACHE II score	22 (16-27)
GCS	13 (9-15)
SOFA score	9 (4-11)
Hemoglobin level (g/dL)	9.7 (7.9-10.2)
Leukocytes (/mm ³)	7,980 (3375-14450)
Thrombocytes (/mm ³)	112,000 (42000-228000)
C-reactive protein (mg/L)	144 (72.7-272.5)
ALT (IU/L)	19 (11.2-31.2)
LDH (IU/L)	410 (244.25-690.50)
Procalcitonin (ng/mL)	3.1 (0.78-18)
Calcium (mg/dL)	7.4 (6.9-9.1)
Albumin (g/dL)	2.7 (1.9-3.1)
Glucose (mg/dL)	134 (110-190)
Creatinine (mg/dL)	1.2 (0.68-2.3)

Overall, 46 (56.8 %) patients survived while 35 (43.2 %) of the patients died during the course of the study (Table 3).

Table 3: Morbidities Observed During ICU Stay and Prognosis (n=81)

ICU-Associated Comorbidities	Frequency (%)
Septic shock / Sepsis	35 (43.2 %)
Hepatic dysfunction	14 (17.28 %)
Neutropenia	14 (17.28 %)
Renal Dysfunction	24 (29.63 %)
Renal Replacement Therapy	27 (33.33 %)
Mechanical Ventilation	54 (66.67 %)
Chemotherapy	08 (9.87 %)
Blood Transfusion	52 (64.2 %)
Central Venous Catheterization	28 (34.57 %)
Arterial Catheterization	41 (50.62 %)
Infection (proven or suspected)	30 (37 %)

Bacterial Infection		28(34.57 %)
Pulmonary Infection		29(35.8 %)
Steroid Usage		59(72.8 %)
Vasopressor Use		50(61.72 %)
Final Outcome (Mortality)	Survived	46(56.8 %)
	Died	35(43.2 %)

Patients with hematological malignancies had a significantly longer hospital stay before ICU admission compared to those with solid tumors (6 vs. 2.5 days; $p=0.01$). Chemotherapy use was significantly higher in patients with solid tumors (41.98% vs. 28.4%; $p<0.01$). Sepsis/septic shock as a cause of ICU admission showed borderline significance between groups (39.5% vs. 24.7%; $p=0.05$) (Table 4).

Table 4: Cross Tabulation of Various Parameters According to Type of Cancers (n=81)

Variables		Solid Tumors	Hematological Malignancies	p-value
Age (years)		59 (37-69)	51.5 (34-61)	*0.050
Gender	Male	15 (18.5%)	18 (22.22%)	0.720
	Female	32 (39.5%)	16 (19.75%)	
Hospital stay before admission to ICU (days)		2.5 (1-9.5)	6 (1.5-12.5)	*0.010
Length of ICU stay (days)		4.5 (2-12)	4.5 (3.2-8.75)	0.100
Stage of Cancer	Recently diagnosed	11 (13.6%)	17 (21%)	0.560
	Complete or partial remission	9 (11.11%)	10 (12.35%)	
	Relapse or progressive disease	14 (17.28%)	12 (14.8%)	
	End stage	03 (3.7%)	05 (6.17 %)	
Performance Status	Good (ECOG 0-2)	40 (49.38%)	18 (22.22 %)	0.620
	Poor (ECOG 3 and 4)	10 (12.35%)	11 (13.58 %)	
Treatment	Chemo	34 (41.98%)	23 (28.4 %)	*<0.010
	Radiation	11 (13.58%)	09 (11.11 %)	
	Surgery	12 (14.8%)	10 (12.35 %)	
	Therapy < 30 days before ICU admit	28 (34.57%)	12 (14.8 %)	
Comorbidities	COPD	05 (6.17%)	04 (4.94 %)	0.550
	Diabetes mellitus	11 (13.58%)	10 (12.35 %)	
	Hypertension	09 (11.11%)	11 (13.58 %)	
	Cardiovascular diseases	04 (4.9 %)	08 (9.87 %)	
Reason for ICU Admission	Sepsis/septic shock	32 (39.5 %)	20 (24.7 %)	*0.050
	Respiratory failure	30 (37 %)	17 (21 %)	
	Acute renal failure	12 (14.8 %)	15 (18.5 %)	
ICU-Associated Comorbidities	Renal Dysfunction	24 (29.63 %)	15 (18.5 %)	*<0.010
	Neutropenia	06 (7.4 %)	18 (22.22 %)	
	Thrombocytopenia	22 (27.2 %)	19 (23.46 %)	
	Mechanical ventilation	20 (24.7 %)	16 (19.75 %)	
	Hepatic Dysfunction	12 (14.8 %)	15 (18.5 %)	
	Vasopressors	18 (22.22 %)	10 (12.35 %)	

	>2 organ dysfunction	30 (37 %)	09 (11.11 %)	
	Infection	40 (49.4 %)	18 (22.22 %)	
Bacterial Infection		22 (27.2 %)	16 (19.75 %)	0.540
Fungal Infection		04 (4.9 %)	07 (8.64 %)	
Pulmonary Infection		38 (46.9 %)	19 (23.46 %)	
Bloodstream Infection		08 (9.87 %)	08 (9.87 %)	

On admission to the ICU, renal dysfunction was significantly more common in solid tumor patients (29.63% vs. 18.5%; $p<0.01$). Hematological parameters also differed significantly, with higher leukocyte counts ($p=0.04$) and platelet counts ($p=0.05$), while C-reactive protein levels were significantly elevated in hematological malignancies ($p<0.01$). During ICU stay, sepsis/septic shock remained significantly different between groups (24.7% vs. 18.5%; $p<0.01$). Final outcomes showed a significant difference in survival, with higher survival in patients with solid tumors (37% vs. 19.75%; $p<0.01$) (Table 5).

Table 5: Cross Tabulation of Various Parameters After Admission to ICU (n=81)

Variables	Solid Tumors	Hematological Malignancies	p-value
APACHE II score	20 (16-26)	24 (17-27)	0.440
GCS	14 (9-15)	14 (10-15)	0.950
SOFA score	8 (5-10)	9 (4-11)	0.620
Hemoglobin level (g/dL)	9.9 (8.1-10.2)	9.5 (7.9-9.9)	0.080
Leukocytes (/mm ³)	7,250 (3375-12000)	8,850 (4750-14450)	*0.040
Thrombocytes (/mm ³)	98,000 (48000-185000)	124,000 (42000-228000)	*0.050
C-reactive protein (mg/L)	110 (72.7-181)	180 (87-272.5)	*<0.010
ALT (IU/L)	17 (11.2-28.1)	20 (12.8-31.0)	0.500
LDH (IU/L)	420 (244.25-585)	430 (290-690)	0.730
Procalcitonin (ng/mL)	2.8 (0.78-1.65)	3.2 (0.8-1.8)	0.120
Calcium (mg/dL)	7.6 (6.9-8.8)	7.2 (6.9-9.1)	0.500
Albumin (g/dL)	2.5 (1.92-2.9)	2.5 (1.9-3)	0.780
Glucose (mg/dL)	128 (110-164)	137 (111-190)	0.230
Creatinine (mg/dL)	1.1 (0.78-1.9)	1.3 (0.68-2.3)	0.540
Morbidities during ICU stay			
Sepsis/septic shock	20 (24.7 %)	15 (18.5 %)	*<0.010
Neutropenia	06 (7.4 %)	08 (9.87 %)	
Hepatic dysfunction	07 (8.64 %)	07 (8.64 %)	
Renal dysfunction	16 (19.75 %)	08 (9.87 %)	
Renal replacement therapy	13 (16 %)	14 (17.3 %)	
Requirement of mechanical ventilation	38 (46.9 %)	16 (19.75 %)	
Chemotherapy in ICU	04 (4.9 %)	04 (4.9 %)	
Blood transfusion	23 (28.4 %)	29 (35.8 %)	
Central venous catheterization	16 (19.75 %)	12 (14.8 %)	
Arterial catheterization	22 (27.2 %)	19 (23.46 %)	
Suspected or culture-proven infection	16 (19.75 %)	14 (17.28 %)	
Bacterial Infection	18 (22.22 %)	10 (12.36 %)	
Pulmonary Infection	10 (12.35 %)	19 (23.46 %)	
Steroid use	31 (38.27 %)	28 (34.57 %)	

Vasopressor use		31 (38.27 %)	19 (23.46 %)	
Final Outcome	Survived	30 (37 %)	16 (19.75 %)	*<0.010
	Died	20 (24.7 %)	15 (18.5 %)	0.230

DISCUSSION

Cancer patients tend to be more ill than non-cancerous patients, resultantly causing higher admissions into the ICU and an increase in hospital mortality rates. Likewise, the mortality rate in this study was 43 %, higher than the mean mortality rate reported in studies (32 %), with mortality among all ICU admission patients [15]. The difference in mortality rates can be owed to the fact that variations exist in terms of the composition of underlying diseases, the criteria used for admission and discharge of patients from the ICU, treatment decisions, and in implementing end-of-life decisions [16]. A significant difference was observed in this study between solid tumor patient group and hematological malignancy patient group in terms of median age ($p=0.05$), length of hospital stay ($p=0.01$), cancer treatment status ($p<0.01$), cause of ICU admission ($p=0.005$), morbidities on ICU admission ($p<0.001$), leukocytes ($p=0.04$), thrombocytes ($p=0.05$), C-reactive protein ($p<0.01$), morbidities during ICU stay ($p<0.001$) and in the outcome of patients who survived ($p<0.01$). As the prevalence of cancer continues to rise globally, the demand for intensive care unit (ICU) admission among cancer patients has grown, necessitating a comprehensive understanding of the clinical features and prognostic factors associated with this unique population [17, 18]. Several studies have investigated the clinical features that characterize cancer patients requiring ICU admission [19, 20]. A retrospective analysis found that hematologic malignancies, particularly acute leukemia, were associated with a higher likelihood of ICU admission compared to solid tumors. This underscores the heterogeneity of cancer types and their distinct impact on critical illness [21]. Likewise, chemotherapy-induced complications have also emerged as significant contributors to ICU admissions among cancer patients. Studies have highlighted the role of treatment-related immunosuppression, suggesting a complex interplay between cancer therapies and susceptibility to severe infections [22]. A study demonstrated that higher Sequential Organ Failure Assessment (SOFA) scores on ICU admission were associated with increased mortality among cancer patients [23]. Similar to this study, the presence of sepsis further complicates the prognosis for cancer patients in the ICU. Recent meta-analyses underscored the association between sepsis and higher mortality rates, emphasizing the need for prompt recognition and targeted management of infectious complications. Additionally, the effectiveness of cancer treatment has been implicated as a pivotal determinant of outcomes [24]. A review highlighted the importance of

considering treatment response and the impact of ongoing therapies on the overall prognosis of cancer patients admitted to the ICU. The type and stage of cancer play a crucial role in shaping the clinical course of critically ill cancer patients. Over half of the ICU-admitted patients in this study survived, potentially indicating the potential benefit of ICU care in selected patients. Published literature indicates mortality rates among ICU cancer patients tend to vary widely, ranging from 30 to 60 %. This depends upon the stage of disease and co-morbidities [22-24]. This research's mortality rate falls within the ranges of international literature.

Comprehensive data collection was one of the main highlights of this study. Comprehensive data enabled the performance of detailed subgroup analyses, identifying trends, exploring potential confounding variables, and strengthening the internal validity of the study. Since the prognostic values were not tested using multivariate analysis, the study cannot claim the predictive or prognostic outcomes of the patients. This study was limited by its single-center design and observational design, which might have affected generalizability. The relatively small sample size and lack of long-term follow-up restricted the ability to fully assess outcomes beyond ICU discharge. Additionally, heterogeneity in cancer types and prior treatments could have confounded the observed associations. Studies with higher sample sizes, having a multi-centered approach, would help in developing predictive models for ICU outcomes in cancer patients. Research should also explore interventions targeting early sepsis detection, organ dysfunction management, and optimized ICU resource allocation to improve survival in high-risk groups.

CONCLUSIONS

Cancer patients requiring ICU admission showed distinct clinical patterns based on malignancy type. Patients with hematological malignancies had longer pre-ICU hospital stays, higher inflammatory markers, and a greater burden of sepsis and organ dysfunction. In contrast, patients with solid tumors demonstrated better survival outcomes. These findings highlight the prognostic significance of malignancy type and associated clinical parameters in guiding risk stratification and ICU management.

Authors' Contribution

Conceptualization: RKS

Methodology: RKS

Formal analysis: AA, SAB, TK

Writing and Drafting: RKS, TK

Review and Editing: RKS, AA, SAB, TK

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All 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] Pal SK, Miller MJ, Agarwal N, Chang SM, Chavez-MacGregor M, Cohen E et al. Clinical Cancer Advances 2019: Annual Report on Progress Against Cancer from the American Society of Clinical Oncology. *Journal of Clinical Oncology*. 2019 Apr; 37(10): 834-49. doi: 10.1200/JCO.18.02037.
- [2] Dyba T, Randi G, Bray F, Martos C, Giusti F, Nicholson N et al. The European Cancer Burden in 2020: Incidence and Mortality Estimates for 40 Countries and 25 Major Cancers. *European Journal of Cancer*. 2021 Nov; 157: 308-47. doi: 10.1016/j.ejca.2021.07.039.
- [3] Santucci C, Carioli G, Bertuccio P, Malvezzi M, Pastorino U, Boffetta P et al. Progress in Cancer Mortality, Incidence, and Survival: A Global Overview. *European Journal of Cancer Prevention*. 2020 Sep; 29(5): 367-381. doi: 10.1097/CEJ.0000000000000594.
- [4] Han XP, Mei X, Zhang J, Zhang TT, Yin AN, Qiu F, Liu MJ. Validation of the Chinese Version of the Quality of Dying and Death Questionnaire for Family Members of ICU Patients. *Journal of Pain and Symptom Management*. 2021 Sep; 62(3): 599-608. doi: 10.1016/j.jpainsymman.2020.12.022.
- [5] Zampieri FG, Romano TG, Salluh JI, Taniguchi LU, Mendes PV, Nassar Jr AP et al. Trends in Clinical Profiles, Organ Support Use and Outcomes of Patients with Cancer Requiring Unplanned ICU Admission: A Multicenter Cohort Study. *Intensive Care Medicine*. 2021 Feb; 47(2): 170-179. doi: 10.1007/s00134-020-06184-2.
- [6] Vigneron C, Charpentier J, Valade S, Alexandre J, Chelabi S, Palmieri LJ et al. Patterns of ICU Admissions and Outcomes in Patients with Solid Malignancies Over the Revolution of Cancer Treatment. *Annals of Intensive Care*. 2021 Jan; 11(1): 182. doi: 10.1186/s13613-021-00968-5.
- [7] Koo MM, Swann R, McPhail S, Abel GA, Elliss-Brookes L, Rubin GP et al. Presenting Symptoms of Cancer and Stage at Diagnosis: Evidence from A Cross-Sectional, Population-Based Study. *The Lancet Oncology*. 2020 Jan; 21(1): 73-79. doi: 10.1016/S1470-2045(19)30595-9.
- [8] van der Velden NC, van Laarhoven HW, Burgers SA, Hendriks LE, de Vos FY, Dingemans AM et al. Characteristics of Patients with Advanced Cancer Preferring Not to Know Prognosis: A Multicenter Survey Study. *BioMed Central cancer*. 2022 Sep; 22(1): 941. doi: 10.1186/s12885-022-09911-8.
- [9] Wilhelms SB, Walther SM, Sjöberg F, De Geer L. Causes of Late Mortality Among ICU-Treated Patients with Sepsis. *Acta Anaesthesiologica Scandinavica*. 2020 Aug; 64(7): 961-966. doi: 10.1111/aas.13592.
- [10] García de Herreros M, Laguna JC, Padrosa J, Barreto TD, Chicote M, Font C et al. Characterisation and Outcomes of Patients with Solid Organ Malignancies Admitted to the Intensive Care Unit: Mortality and Impact on Functional Status and Oncological Treatment. *Diagnostics*. 2024 Mar; 14(7): 730. doi: 10.3390/diagnostics14070730.
- [11] Nazer LH, Lopez-Olivo MA, Brown AR, Cuenca JA, Sirimaturros M, Habash K et al. A Systematic Review and Meta-Analysis Evaluating Geographical Variation in Outcomes of Cancer Patients Treated in ICUs. *Critical Care Explorations*. 2022 Sep; 4(9): 757. doi: 10.1097/CCE.0000000000000757.
- [12] Alishahi Tabriz A, Turner K, Hong YR, Gheytsvand S, Powers BD, Elston Lafata J. Trends and Characteristics of Potentially Preventable Emergency Department Visits Among Patients with Cancer in the US. *JAMA Network Open*. 2023 Jan; 6(1): 2250423. doi: 10.1001/jamanetworkopen.2022.50423.
- [13] Carmona-Bayonas A, Jiménez-Fonseca P, de Castro EM, Mata E, Biosca M, Custodio A et al. SEOM Clinical Practice Guideline: Management and Prevention of Febrile Neutropenia in Adults with Solid Tumors (2018). *Clinical and Translational Oncology*. 2019 Jan; 21(1): 75-86. doi: 10.1007/s12094-018-1983-4.
- [14] Kiehl MG, Beutel G, Böll B, Buchheidt D, Forkert R, Fuhrmann V et al. Consensus Statement for Cancer Patients Requiring Intensive Care Support. *Annals of Hematology*. 2018 Jul; 97(7): 1271-1282. doi: 10.1007/s00277-018-3312-y.
- [15] Odera JO. Abstract C025: Integrating Health Disparities and AI/ML-Driven Survival Prediction in Critically Ill Patients with Multiple Primary Malignancies. *Cancer Epidemiology, Biomarkers and Prevention*. 2025 Sep; 34(9): 25. doi: 10.1158/1538-7755.DISP25-C025.
- [16] Hawari FI, Nazer LH, Addassi A, Rimawi D, Jamal K. Predictors of ICU Admission in Patients with Cancer and the Related Characteristics and Outcomes: A 5-Year Registry-Based Study. *Critical Care Medicine*. 2016 Mar; 44(3): 548-553. doi: 10.1097/CCM.0000000000001429.

- [17] Gutierrez C, McEvoy C, Munshi L, Stephens RS, Detsky ME, Nates JL et al. Critical Care Management of Toxicities Associated with Targeted Agents and Immunotherapies for Cancer. *Critical Care Medicine*. 2020 Jan; 48(1): 10-21. doi: 10.1097/CCM.00000000000004087.
- [18] do Amaral Paes TC, de Oliveira KC, de Carvalho Padilha P, Peres WA. Phase Angle Assessment in Critically Ill Cancer Patients: Relationship with the Nutritional Status, Prognostic Factors and Death. *Journal of Critical Care*. 2018 Apr; 44: 430-435. doi: 10.1016/j.jcrc.2018.01.006.
- [19] Vijenthira A, Gong IY, Fox TA, Booth S, Cook G, Fattizzo B et al. Outcomes of Patients with Hematologic Malignancies and COVID-19: A Systematic Review and Meta-Analysis Of 3377 Patients. *Blood, The Journal of the American Society of Hematology*. 2020 Dec; 136(25): 2881-2892. doi: 10.1182/blood.2020008824.
- [20] Ma J, Yin J, Qian Y, Wu Y. Clinical Characteristics and Prognosis in Cancer Patients with COVID-19: A Single Center's Retrospective Study. *The Journal of Infection*. 2020 Apr; 81(2): 318. doi: 10.1016/j.jinf.2020.04.006.
- [21] Pramanik R, Gupta R, Suvvari P, Mishra S. Management of Complications and Toxicities Related to Chemotherapy in ICU. In *Onco-critical Care: An Evidence-based Approach* Singapore: Springer Nature Singapore. 2022 Jun: 279-291. doi: 10.1007/978-981-16-9929-0_25.
- [22] Assi H, Halim NA, Alameh I, Khoury J, Nahra V, Sukhon F et al. Outcomes of Patients with Malignancy Admitted to the Intensive Care Units: A Prospective Study. *Critical Care Research and Practice*. 2021; 2021(1): 4792309. doi: 10.1155/2021/4792309.
- [23] Nathan N, Sculier JP, Ameye L, Paesmans M, Bogdan-Dragos G, Meert AP. Sepsis and Septic Shock Definitions in Patients with Cancer Admitted in ICU. *Journal of Intensive Care Medicine*. 2021 Mar; 36(3): 255-261. doi: 10.1177/0885066619894933.
- [24] Botticelli A, Cirillo A, Scagnoli S, Cerbelli B, Strigari L, Cortellini A et al. The Agnostic Role of Site of Metastasis in Predicting Outcomes in Cancer Patients Treated with Immunotherapy. *Vaccines*. 2020 Apr; 8(2): 203. doi: 10.3390/vaccines8020203.



Original Article

Internal Mammary Artery Perforator Flap to Cover Sternotomy Wounds:
A Prospective StudyMuhammad Bilal¹, Imran Shahzad^{1,2}, Kamran Khalid¹, Farrukh Aslam Khalid^{1,2}, Abdul Malik Mujahid¹ and Ahmad Saeed³¹Department of Plastic Surgery, Jinnah Burn and Reconstructive Surgery Centre, Allama Iqbal Medical College, Lahore, Pakistan²Department of Plastic Surgery, King Edward Medical University, Mayo Hospital, Lahore, Pakistan³Department of Plastic Surgery, Royal Devon and Exeter Hospital, Devon, United Kingdom

ARTICLE INFO

Keywords:

Internal Mammary Artery Perforator Flap, Sternotomy Wound, Mediastinal Defect, Conventional Reconstructive Flaps

How to Cite:

Bilal, M., Shahzad, I., Khalid, K., Khalid, F. A., Mujahid, A. M., & Saeed, A. (2026). Internal Mammary Artery Perforator Flap to Cover Sternotomy Wounds: A Prospective Study: Internal Mammary Artery Perforator Flap to Cover Sternotomy Wounds. Pakistan Journal of Health Sciences, 7(6), 140-145. <https://doi.org/10.54393/pjhs.v7i6.3950>

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ABSTRACT

The issue of sternotomy wounds is a continued challenge in cardiac and thoracic vascular surgery, especially in patients who have various comorbidities and are infected. Functional morbidity is linked to traditional muscle flaps that are effective. IMAP flap provides an alternative to other conventional flaps and the internal mammary perforator (IMAP) flap, which maintains muscle functionality while also producing well-vascularized tissue. **Objectives:** To determine the clinical results of the internal mammary artery perforator flap to reconstruct presternal and mediastinal sternotomy wound defects. **Methods:** This prospective observational study was conducted during the period of August 2024 and February 2025 at the Department of Plastic Surgery, Jinnah Burn Reconstruction Surgery Centre/Allama Iqbal Medical College. Institutional ethical approval was obtained No.6117/ED/JB&RSC. **Results:** In this study, the mean age of the cases was 56.4 ± 10.8 years. There were 21 (70%) males and 9 (30%) females enrolled. Complete reconstructive success was achieved in 10 patients, partial success was achieved in 15 on 29th July 2024 patients, and non-healing wounds were found in 5 patients. Recurrent infection was found in 5 patients (16.7%), and mortality associated with sepsis was observed in 4 patients (13.3%). **Conclusions:** IMAP flap is a secure reconstruction of the defects present on the presternal and mediastinal sternotomy wounds, which has a good healing outcome even in high-risk patients. IMAP flap is a better alternative to the conventional muscle flap for chest wound coverage.

INTRODUCTION

Sternal wound dehiscence during cardiac surgery is a significant complication, affecting 1% of patients having coronary artery bypass grafting [1]. A prevalent cause is wound infection; nonetheless, mechanical dehiscence of the skin may sometimes transpire, especially in situations with heightened chest wall movement (e.g., patients experiencing respiratory crisis) [2]. The primary therapeutic approach is surgical debridement of necrotic tissues, followed by the extraction of sternal cables.

Following wound debridement, negative pressure wound therapy (NPWT) is used until closure by tertiary aim is achieved. At this juncture, soft tissue must be translocated into the incision as a flap to facilitate healing [3]. Conventional reconstructive flaps, including pectoralis flaps, are either ineffective in covering the entire defect or necessitate laparotomy in the case of the omental flap as a sternal wound closure [4]. To repair large incisions, it is necessary to employ several flaps in conjunction, as each



flap is insufficient to cover the entire length of a sternal defect, despite its effectiveness in addressing significant weaknesses [5]. Furthermore, the atrophy of these muscles may result in functional deficits, possible hernias (particularly of the rectus muscle), seromas, and further complications. Moreover, significant dissection of the pectoral muscles at that level may impede chest mobility during the postoperative period owing to discomfort. Alternative therapeutic modalities include topical negative pressure therapy to facilitate wound healing [6]. A recent technique for closing sternal wounds is the deep superior epigastric perforator (DSEP) flap [7, 8]. Using a single perforator from the DSEP and rotating it 90 degrees, this fasciocutaneous perforator flap may successfully repair large defects. Among the documented benefits are the potential for a hidden submammary incision in females, muscle function retention, and less dissection [9]. It is necessary to have an intact internal mammary artery (IMA) axis, as the DSEP flap's maximal harvesting length restricts its application. This article delineates the utilisation of the internal mammary artery perforator (IMAP) flap to reconstruct various presternal and mediastinal lesions under specific circumstances [10]. The primary benefit is that a single fasciocutaneous or musculocutaneous IMAP flap can effectively address any three-dimensional sternotomy wound defect. Previously used for tracheostoma, head and neck reconstruction, and correcting moderate to medium-sized chest wall abnormalities after tumour excision, the IMAP flap is reliable and well-researched. In a selected group of non-infected wounds with a stable sternal wound, Lupon et al. employed the IMAP flap in both fasciocutaneous and musculocutaneous designs to reconstruct sternal wound dehiscence [11]. Likewise, in a case of anterior chest wall defects, the IMAP flap was proven to be a reliable and effective procedure with minimal donor-site morbidity and good healing [12].

Despite advancements in reconstructive techniques for post-sternotomy wound defects, the optimal method that balances effective wound coverage with minimal functional morbidity remains inadequately defined. Traditional muscle flaps, although reliable, are associated with donor-site morbidity and impaired muscle function. Recently, perforator-based flaps such as the IMAP flap have emerged as promising alternatives; however, the available literature is limited, with few prospective studies and insufficient comparative data evaluating their clinical outcomes, reliability, and complication rates, particularly in resource-limited settings. Moreover, there is a lack of regional data assessing the effectiveness of IMAP flaps in diverse patient populations with varying comorbidities. Therefore, further evidence is required to establish the clinical utility and outcomes of IMAP flap reconstruction in

sternotomy wound management. This research will clarify our experience with the internal mammary artery perforator flap for managing sternotomy wounds and provide a novel approach for correcting these issues. This study aimed to evaluate the clinical outcomes associated with the use of the IMAP flap in patients with sternotomy wound defects, particularly with respect to wound healing, infection control, and postoperative complications.

METHODS

This prospective observational study was conducted at the Department of Plastic Surgery, Jinnah Burn and Reconstructive Surgery Centre, Allama Iqbal Medical College, Lahore, after obtaining institutional ethical approval (No. 6117/ED/JB&RSC, dated 29th July 2024). This study was conducted from August of 2024 to February of 2025. A sample size of 30 patients was determined using the single population proportion formula, based on an expected success rate of 70% as determined in previous literature, an 80% confidence level ($Z = 1.96$), and a margin of error of 10% [13]. Patients aged 45–80 years who developed sternotomy wound complications following open heart surgery and required soft tissue reconstruction were included in the study using a consecutive sampling technique. Patients who had wounds on the chest wall that were not associated with post-sternotomy complications, traumatic chest wall defects, malignant wounds, medical contraindications for reconstruction surgery, or who declined to have reconstruction surgery were not included. Informed consent was obtained from all participants in writing before screening. The study population included 22 males and 8 females, that is, 2.75:1. Previous surgical operations performed on the patients included 2 patients who had received a carotico-subclavian bypass, 3 patients who had received a thoracic endoprosthesis after a carotico-subclavian bypass, 5 patients who had undergone combined cardiac valve replacement and coronary artery bypass grafting (CABG), and 20 patients who had received isolated CABG. The majority of patients had several comorbidities such as diabetes mellitus, hypertension, ischemic heart disease, and immunosuppression. Sternal wound dehiscence was evaluated using the Pairolero and Arnold classification scale as part of the pre-operative evaluation. The Type II wounds were intermediate infections that were seen during 2–3 weeks after surgery and included drainage, cellulitis, and mediastinitis, while the Type III wounds were late infections months or years after surgery with chronic sinus tracts or osteomyelitis. Patients were also classified by the American Society of Anesthesiologists (ASA) Physical Status Classification System (PSCS) I–VI [14]. Internal mammary artery perforators were preoperatively located using handheld Doppler ultrasonography, with a dominant perforator

typically found in the second or third intercostal space 1-2 cm from the sternal border. Depending on the nature of the defect, the IMAP flap was raised as a fasciocutaneous flap. The skin paddle was elevated subfascial/subcutaneously from lateral to medial until the perforator was located, with preservation or minimal skeletonization of the perforator, which enabled safe skin paddle rotation. A portion of the pectoralis major muscle was attached to the flap in patients with mediastinal defects and substantial dead space, with the IMAP system maintaining perfusion. The flap was usually turned around 90 degrees, and donor sites were primarily closed in all patients. Each procedure was carried out by the same experienced plastic surgeon. Patients with suspected fungal wound infection based on clinical presentation or non-resolving infection underwent microbiological assessment, including direct microscopy and fungal culture, to guide appropriate antimicrobial management. Postoperative management was performed as per institutional protocols, which included culture-directed antibiotic therapy. Microbiological examination consisted of direct microscopy and KOH preparation (fungal identification). Where necessary, calcofluor white staining was used under ultraviolet light for better visualization of fungal elements. Selected cases were also confirmed by fungal culture, histopathology, serological assays, and molecular diagnostic techniques. The results of the study were classified as success, partial success, non-healing, and recurrent infection. Complete primary wound healing after surgery was deemed a success. Partial success was defined as wounds that became infected but were treated conservatively. Non-healing was considered as having a chronic chest wound that caused infection and osteomyelitis for more than three months. Recurrent infection was defined as when infection returned to a previously healed wound within 3 months.

The data were entered and analyzed in SPSS version 26.0. Data analyzed quantitatively were presented as mean $\pm$ SD, and qualitative data were presented as frequency and percentage. Descriptive analysis was conducted.

RESULTS

A total of 30 patients who were reconstructed using an internal mammary artery perforator flap to treat complicated sternotomy wounds. The average age of the population under study was 56.4 ± 10.8 years, with the largest number of patients falling within the 45-54 years category. The majority of patients were male (70%), and females made up 30% of the patients. The comorbid conditions were very high. The most common risk factors were hypertension and ischemic heart disease (86.7% and 76.7%), and then diabetes mellitus (60%). Fungal infection (36.7%) and immunosuppression (23.3%) had a smaller percentage of patients reported to affect wound healing

outcomes. In this study, the mean age of the cases was 56.4 ± 10.8 years; there were 21 (70%) males and 9 (30%) females enrolled. In this study, there were 18 (60%) diabetic, 26 (86.7%) hypertensive, 23 (76.7%) patients with ischemic heart disease, 7 (23.3%) immunosuppression, 11 (36.7%) patients with fungal infection enrolled (Table 1).

Table 1: Demographic Characteristics and Comorbidities (n=30)

Variables	n (%) / Mean $\pm$ SD
Age (years)	56.4 $\pm$ 10.8
Age Categories	
45-54 Years	13 (43.3%)
55-64 Years	6 (20%)
65-74 Years	7 (23.3%)
≥ 75 Years	4 (13.3%)
Gender	
Male	21 (70%)
Female	9 (30%)
Others	
Diabetes Mellitus	18 (60%)
Hypertension	26 (86.7%)
Ischemic Heart Disease	23 (76.7%)
Immunosuppression	7 (23.3%)
Fungal Infection	11 (36.7%)

As to the main surgical procedure, the most frequent indication was the coronary artery bypass grafting (CABG) with two-thirds (66.7 percent), and the second reason was the combined valve replacement with CABG (20 percent). The patients who had undergone carotico-subclavian bypass or thoracic endoprosthesis were few. Mediastinal defects were a bit more present (53.3%) than presternal defects (46.7%). Most of the patients were ASA grade III (46.7%), which is moderate anesthetic risk, and ASA grade II and IV were 36.7% and 16.7%, respectively (Table 2).

Table 2: Operative and Defect-Related Findings

Variables	n (%)
Original Cardiac / Vascular Procedure	
CABG	20 (66.7%)
Valve Replacement + CABG	6 (20%)
Carotico-Subclavian Bypass	3 (10%)
Thoracic Endoprosthesis Procedure	3 (10%)
Type of Defect	
Presternal	14 (46.7%)
Mediastinal	16 (53.3%)
ASA Grade	
Grade II	11 (36.7%)
Grade III	14 (46.7%)
Grade IV	5 (16.7%)

In the patients who underwent reconstruction, partial success was the most common reconstructive outcome (50%), followed by complete success (33.3%). A lesser number of patients (5, 16.7%) were left with non-healing

wounds after reconstructive surgery, suggesting a lower rate of wound failure. In terms of general clinical results, most patients (21 cases, 70%) had healed wounds, indicating good wound healing in a majority of the participants after surgery. However, there was a small number of patients who developed recurrent infection (5, 16.7%) and several patients who died from sepsis (4, 13.3%), showing that there were serious postoperative complications in a subset of patients (Table 3).

Table 3: Reconstructive Procedure Success and Overall Outcome

Outcomes	n(%)
Reconstructive Outcome	
Success	10 (33.3%)
Partial Success	15 (50%)
Non-Healing Wound	5 (16.7%)
Overall Clinical Outcome	
Healed wound	21 (70%)
Recurrent infection	5 (16.7%)
Death due to sepsis	4 (13.3%)

A chronic post-sternotomy wound four months after coronary artery bypass grafting is shown, followed by surgical debridement and flap planning. The internal mammary artery perforator is identified (arrow) and incorporated into the flap design. The flap is then inset over closed-suction drains to achieve stable coverage of the sternal defect, with a six-month follow-up image demonstrating complete wound healing and durable soft-tissue reconstruction (Figure 1).



Figure 1: A Chronic Post-Sternotomy Wound Four Months After Coronary Artery Bypass Grafting Followed by Surgical Debridement and Flap Planning

A second patient presenting with chronic discharging sinuses over the sternum is shown. Following surgical debridement, flap markings are demonstrated. A combined musculofasciocutaneous flap based on the internal mammary artery perforator is raised and rotated to cover the defect, with the final image showing successful inset of the flap and restoration of soft-tissue continuity (Figure 2).

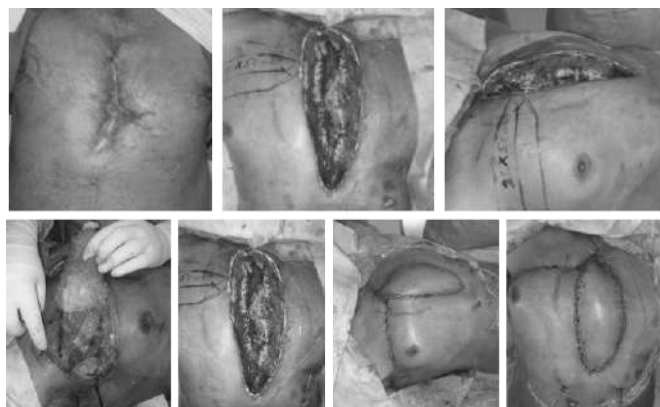


Figure 2: Patient Presenting with Chronic Discharging Sinuses Over the Sternum

DISCUSSION

The IMAP flap has transitioned from its original characterization as a perforator flap using the deltopectoral axis for tracheostomal repair to a multifaceted solution for many anterior chest and neck abnormalities [15]. Subsequent studies have shown its reliability in addressing minor to moderate-sized lesions with little donor-site morbidity. This prospective multicenter research has shown that the IMAP flap is a reliable reconstructive solution for presternal and mediastinal sternotomy wound defects in a high-risk population [16]. The majority of patients finally attained wound healing despite considerable comorbidities and active infection, demonstrating the ability of this flap to provide well-vascularized tissue to impaired surgical areas [17]. The advantageous results seen may be ascribed to many technical and anatomical benefits of the IMAP flap. The perforator-based design facilitates primary closure of the donor site, prevents exposure of deeper holes, and reduces functional loss relative to conventional muscle flaps [18, 19]. In contrast to the pectoralis major, rectus abdominis, or omental flaps, the IMAP flap may rebuild the whole extent of a sternotomy lesion from the suprasternal notch to the xiphisternum with less dissection and decreased morbidity. This characteristic makes it especially appealing for stable patients with infected sternotomy wounds and defect widths of up to 7 cm, a group for which the IMAP flap may be regarded as a primary reconstructive alternative [13]. Nonetheless, its use is restricted in individuals necessitating vasopressor assistance, and the resultant subclavicular scar may be seen as less acceptable by younger female patients. This work broadens the use of the IMAP flap in sternotomy wound restoration by implementing it in both fasciocutaneous and musculocutaneous forms, according to the defect's depth. Fasciocutaneous IMAP flaps offered enhanced shape and skin compatibility for presternal defects but exhibited heightened vulnerability to pedicle torsion and distal venous compromise, notwithstanding

preoperative perforator identification. The delayed elevation of the fasciocutaneous flap appeared to enhance survival, possibly due to gradual expansion of the perforator over time. A direct comparison between fasciocutaneous and musculocutaneous variations was impracticable due to the limited sample size; nonetheless, indirect evidence suggests greater reliability of the musculocutaneous IMAP flap [20]. Anatomical factors help explain the observed disparities among flap forms. The suprafascial width of the internal mammary artery perforator is less than that of its deeper submuscular portion, making it more vulnerable to torsion-related damage when used as a solely fasciocutaneous flap [11]. Finelle and colleagues showed that the length of the second IMAP approximately doubles when traced to its origin, with similar results for the first and third perforators [12]. Extended perforator dissection or the retention of a minor segment of the pectoralis major muscle may therefore decrease torsional stress and improve flap dependability, especially for fasciocutaneous configurations. Despite these advantages, there are inherent weaknesses of the IMAP flap, including a limited range of motion, the need for precise perforator dissection, and the inability to cover large or complicated defects. These restrictions indicate the necessity of careful patient selection and surgical planning [21]. The main strengths of this study are that it has a prospective design as well as multicenter participation, and it has a uniform surgical procedure, whereas the main weaknesses include the small sample size and lack of a comparison control group. To define the best indicators, maximize the technology modifications, and clarify the importance of the IMAP flap in the reconstruction algorithms of sternotomy wound issues, future studies with larger cohorts and comparative designs are needed.

This study was conducted at a single center with a lack of randomization, which may introduce bias and limit the external validity of the results; the relatively small sample size may limit the generalizability of the findings and reduce the statistical power. Short follow-up duration restricts the assessment of long-term outcomes, including flap durability and late complications. No control or comparison group limits the ability to directly compare the effectiveness and complication rates of the IMAP flap with other established reconstructive techniques. Additionally, potential confounding variables such as patient comorbidities (e.g., diabetes, obesity, smoking status) were not fully controlled or stratified. Future studies should include larger, multicenter samples, and randomized controlled trials with longer follow-up periods to improve the generalizability and robustness of the findings. Further comparative studies between IMAP flaps and conventional muscle flaps are warranted to establish standardized guidelines for optimal management of sternotomy wound defects.

CONCLUSIONS

IMAP flap is a secure reconstruction of the defects present on the presternal and mediastinal sternotomy wounds, which has a good healing outcome even in high-risk patients. IMAP flap is a better alternative to the conventional muscle flap for chest wound coverage.

Authors' Contribution

Conceptualization: MB

Methodology: MB, IS, AMM

Formal analysis: KK

Writing and Drafting: MB, KK, FAK, AMM, AS

Review and Editing: MB, IS, KK, FAK, AMM, AS

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All 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] De Tymowski C, Provenchère S, Para M, Duval X, Grall N, Sahnoun T et al. Deep Sternal Wound Infection After Cardiac Surgery: A Combination of 2 Distinct Infection Types, Deep Incisional Surgical-Site Infection and Mediastinitis: Results of a Retrospective Study. *Surgery*. 2025 May; 181: 109255. doi: 10.1016/j.surg.2025.109255.
- [2] Banda CH, Wilson E, Malata CM, Narushima M, Ogawa T, Hassanein ZM et al. Clinical Application and Outcomes of Reconstructive Microsurgery in Africa: A Systematic Review and Meta-Analysis. *Journal of Plastic, Reconstructive and Aesthetic Surgery*. 2022 Jul; 75(7): 2035-48. doi: 10.1016/j.bjps.2022.04.028.
- [3] Chen CY, Kuo SM, Tarng YW, Lin KC. Immediate Application of Negative Pressure Wound Therapy Following Lower Extremity Flap Reconstruction in Sixteen Patients. *Scientific Reports*. 2021 Oct; 11(1): 21158. doi: 10.1038/s41598-021-00369-5.
- [4] Wyckman A, Abdelrahman I, Steinvall I, Zdolsek J, Granfeldt H, Sjöberg F et al. Reconstruction of Sternal Defects After Sternotomy with Postoperative Osteomyelitis, Using a Unilateral Pectoralis Major Advancement Muscle Flap. *Scientific Reports*. 2020 May; 10(1): 8380. doi: 10.1038/s41598-020-65398-y.
- [5] Khashkhusha A, Butt S, Abdelghaffar M, Wang W, Rajanathanan A, Roy S et al. Sternal Wound Reconstruction Following Deep Sternal Wound Infection: Past, Present and Future: A Literature Review. *Journal of Cardiovascular Development and*

- Disease. 2024 Nov; 11(11): 361. doi: 10.3390/jcdd11110361.
- [6] Fallah N, Rasouli M, Amini MR. The Current and Advanced Therapeutic Modalities for Wound Healing Management. *Journal of Diabetes and Metabolic Disorders*. 2021 Dec; 20(2): 1883-99. doi: 10.1007/s40200-021-00868-2.
- [7] Bertheuil N, Leclere FM, Bekara F, Watier E, Flecher E, Duisit J. Superior Epigastric Artery Perforator Flap for Reconstruction of Deep Sternal Wound Infection. *Microsurgery*. 2021 Jul; 41(5): 405-11. doi: 10.1002/micr.30743.
- [8] Angrigiani C, Rancati A, Nahabedian MY, Spinelli E, Breppe P, Rancati A. Perforator-Based Cross-Midline Flaps of the Trunk: A Paradigm Shift in Flap Design. *Plastic and Reconstructive Surgery*. 2023 Dec; 152(6): 1333-48. doi: 10.1097/PRS.00000000000010567.
- [9] Charboub S, El Kamch H, Laabarta H, Hafidi J, Gharib N, Abbassi A et al. Perforator Flaps in Reconstructive Surgery: Report of Our Service's Experience. *South Asia Research Journal of Surgery*. 2025; 6(4): 76-84. doi: 10.36346/sarjs.2025.v06i04.003.
- [10] Marsden N, Shukla L, Grinsell D. Case Report: Revisiting the Internal Mammary Artery Perforator Flap: Salvage Option for Circumferential Pharyngo-Esophageal Defects. *Frontiers in Surgery*. 2021 Mar; 8: 638345. doi: 10.3389/fsurg.2021.638345.
- [11] Lupon E, Njessi P, Camuzard O, Chaput B, Gandolfi S. Preserving Function in Sternal Reconstruction: Complementary Roles of Pectoralis Major and Internal Mammary Artery Perforator Flaps. *Annals of Plastic Surgery*. 2025 Nov; 10-97. doi: 10.1097/SAP.0000000000004618.
- [12] Finelle L, Meresse T, Chaput B, Lupon E, Gandolfi S. Reconstruction of the Anterior Chest Wall Using the Internal Mammary Artery Perforator Flap (IMAP): About A Series of 23 Cases. In *Annales de Chirurgie. Plastique Esthétique*. 2024 Jul; 69(4): 286-293. doi: 10.1016/j.anplas.2024.05.003.
- [13] Oyuntogos A, Njessi P, Camuzard O, Lupon E. The Internal Mammary Artery Perforator Flap as a Reliable Option for Thoracic Osteoradionecrosis Reconstruction: A Case Report. *International Journal of Surgery Case Reports*. 2026; 10-97. doi: 10.1097/RC9.0000000000000496.
- [14] Horvath B, Kloesel B, Todd MM, Cole DJ, Prielipp RC. The Evolution, Current Value, and Future of the American Society of Anesthesiologists Physical Status Classification System. *Anesthesiology*. 2021 Oct; 135(5): 904-19. doi: 10.1097/ALN.0000000000003947.
- [15] Sharbel D, Lin C, Topf MC, Mannion K. The Internal Mammary Artery Perforator Flap in Pharyngoesophageal, Cervical Tracheal, and Cutaneous Neck Reconstruction. *Head and Neck*. 2024 Jul; 46(7): 1835-40. doi: 10.1002/hed.27769.
- [16] Scarabosio A, Tel A, Contessi Negrini F, Albanese R, Robiony M, Parodi P. The Shark Flap: A Modified Internal Mammary Artery Perforator Flap for Composite Defects in Head and Neck Reconstruction. *Case Reports in Plastic Surgery and Hand Surgery*. 2023 Dec; 10(1): 2178924. doi: 10.1080/23320885.2023.2178924.
- [17] Hom DB and Ostrander BT. Reducing Risks for Local Skin Flap Failure. *Facial Plastic Surgery Clinics*. 2023 May; 31(2): 275-87. doi: 10.1016/j.fsc.2023.01.006.
- [18] *Facial Plastic Surgery Clinics*. 2023 May.
- [19] Pirozzi N, Rocco N, Nava MB, Dória MT, Weigert CV, de Andrade Urban C. Internal Mammary Artery Perforator-Based Plug Flap. *International Journal of Surgery Case Reports*. 2024 Dec; 125: 110567. doi: 10.1016/j.ijscr.2024.110567.
- [20] Gonzalez-Martinez CA, Castro-Govea Y, Tellez-Rodriguez BJ, Palomo-Barbosa KV, Rico-Padilla MA, Vidal-Torres O et al. Safe and Time-Saving Method for Pharyngeal Reconstruction Using an Internal Mammary Artery Perforator Flap. *Archives of Plastic Surgery*. 2026 Feb; 53(03): 241-246. doi: 10.1055/a-2780-1488.
- [21] Shimbo K, Kawamoto H, Koshima I. Muscle/Musculocutaneous Versus Fasciocutaneous Free Flap Reconstruction in the Lower Extremity: A Systematic Review And Meta-Analysis. *Microsurgery*. 2022 Nov; 42(8): 835-47. doi: 10.1002/micr.30961.



Original Article



Ocular Manifestations in Patients with Facial Seborrhic Dermatitis

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ARTICLE INFO

Keywords:

Seborrhic Dermatitis, Ocular Manifestations, Tear Film Instability, Dry Eye

How to Cite:

Kumar, P. J., Kumar, V., Khan, B., Shams, A., Das, N., & Devi, V. (2026). Ocular Manifestations in Patients with Facial Seborrhic Dermatitis : Ocular Manifestations in Facial Seborrhic Dermatitis. Pakistan Journal of Health Sciences, 7(6), 146-151. <https://doi.org/10.54393/pjhs.v7i6.3873>

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Received Date: 20th January, 2026

1st Revision Received: 27th March, 2026

2nd Revision Received: 18th April, 2026

3rd Revision Received: 4th May, 2026

Acceptance Date: 22nd May, 2026

Published Date: 30th June, 2026

ABSTRACT

Seborrhic dermatitis (SD) is a chronic inflammatory disorder, especially including the peri-orbital region, which leads to different types of ocular surface abnormalities. **Objective:** To assess the prevalence and pattern of ocular manifestations in patients having facial SD and to evaluate its correlation with the severity of disease. **Methods:** An analytical case-control study was conducted from January 2024 to June 2025 in the Department of Dermatology and Ophthalmology at Al-Tibri Medical College and Hospital. Ninety-one patients with clinically diagnosed facial SD and ninety-one age and sex-matched healthy controls were enrolled in the study. All participants underwent a detailed ophthalmic examination, including TBUT, Schirmer's test, and slit-lamp evaluation. Data were analyzed by using SPSS version 26.0, and a p-value < 0.05 was taken as statistically significant. **Results:** Ocular symptoms were reported in 68.1% SD patients compared to 30.8% in controls (p < 0.001). Lid margin telangiectasia (50.5%), conjunctival hyperemia (48.4%), and meibomian gland dysfunction (57.1%) were significantly more common in SD patients (all p < 0.001). Mean TBUT (6.2 ± 2.1 s) and Schirmer's scores (9.5 ± 4.3 mm) were lower in SD patients than in controls (13.1 ± 3.9 s and 14.8 ± 4.5 mm; p < 0.001). Disease severity showed a strong negative correlation with TBUT and Schirmer's test and a positive correlation with ocular surface staining (p < 0.001). **Conclusion:** Facial seborrhic dermatitis is frequently associated with significant ocular involvement. Early ophthalmologic evaluation is recommended.

INTRODUCTION

Seborrhic dermatitis (SD) is a chronic, relapsing inflammatory skin disorder which mainly involves sebaceous gland-rich areas like the scalp, eyebrows, nasolabial folds, retroauricular regions, and upper chest. It usually presents with erythematous, greasy, scaly patches, and patients often complain of itching and irritation, although the severity is not the same in all cases. The condition affects around 5% of the adult population worldwide. Higher prevalence has been reported in immunocompromised individuals and also in patients

having neurological disorders such as Parkinson's disease and epilepsy [1]. Although SD is generally considered a dermatological condition, it is now becoming evident that its effects are not limited to the skin only. In recent years, ocular involvement has been increasingly recognized, particularly affecting eyelid margins and tear film stability. The periorbital region is commonly affected, likely due to dense sebaceous glands and their close anatomical relation with the ocular adnexa. In routine clinical practice, it is often seen that persistent facial inflammation extends



towards eyelid margins and sometimes involves the meibomian glands as well [2, 3]. This extension has clinical importance; some recent studies have suggested that SD may contribute to blepharitis and meibomian gland dysfunction (MGD), both of which are important contributors to evaporative dry eye disease (DED) [4]. One important issue is that early ocular involvement is usually mild and often remains unnoticed either by dermatologists or even ophthalmologists. Despite this, patients may still complain of dryness, burning sensation, and fluctuating vision, which sometimes appear more disturbing than expected [5]. The pathogenesis of SD is not completely understood and is likely multifactorial. It involves *Malassezia* species, disturbance in lipid metabolism, inflammatory response, and genetic predisposition [6]. In an ocular context, *Malassezia* organisms have also been isolated from eyelid margins and meibomian gland secretions, which supports the concept that similar pathological mechanisms may also affect ocular tissues [7]. Chronic inflammation in these areas may lead to hyperkeratinization and blockage of gland orifices, eventually causing impairment of meibomian gland function and tear film instability. Apart from mechanical blockage, inflammatory mediators produced in SD may further worsen the ocular surface condition. These mediators contribute to epithelial injury, increased tear osmolarity, and subtle corneal surface changes, even when clinical signs are not very prominent [8]. Amitay-Laish *et al.* studied meibomian gland morphology using meibography and reported significantly more gland dropout with reduced tear breakup time (TBUT) in SD patients as compared to healthy controls [9]. Their findings suggest that ocular involvement is not incidental but part of the disease process. Similarly, Sampogna *et al.* observed higher eyelid margin scores, increased fluorescein staining, and more ocular surface damage in SD patients compared to those dry eye patients who do not have SD [10]. These observations further support that SD-related ocular changes are an extension of the same inflammatory process affecting both skin and ocular adnexa. At the mechanistic level, the inflammatory cascade in SD is thought to occur due to an imbalance between commensal and pathogenic microbes, particularly *Malassezia furfur*. These organisms produce lipase enzymes, which modify sebaceous secretions and generate pro-inflammatory fatty acids, leading to local irritation [11]. In the periocular region, this irritation may extend towards eyelid structures. Histopathological examination typically shows parakeratosis, follicular plugging, and infiltration of lymphocytes and macrophages, which confirms the inflammatory nature of the disease [12]. When this process involves ocular adnexa, the meibomian glands become functionally impaired. This results in reduced lipid

secretion, increased tear evaporation, and destabilization of the tear film [13]. Clinically, patients with facial SD may present with eyelid redness, crusting, lash debris, and fine telangiectasia resembling features of anterior or posterior blepharitis. With longer disease duration, conjunctival congestion, punctate epithelial erosions, and occasionally corneal involvement may also be seen [14]. Although these ocular changes are usually mild to moderate, they should not be ignored. Symptoms may persist and can significantly affect patient comfort and visual quality. In some cases, especially when the disease is prolonged, secondary bacterial infection may occur, further worsening inflammation and tissue damage. Despite increasing recognition of this association, there is still limited data describing the complete pattern of ocular involvement in SD, particularly in South Asian populations. Regional factors such as environment, skin phototype, and treatment practices may influence disease presentation and outcome. Most of the available literature mainly focuses on cutaneous features, while detailed ophthalmic evaluation and tear film assessment are relatively less studied [15]. Alofi *et al.* in a recent review, reported that ocular involvement in SD ranges between 10% to 40%, which is quite a wide variation. This difference is likely due to heterogeneity in study populations and diagnostic methods [12]. The authors also emphasized that collaboration between dermatologists and ophthalmologists is important for early detection and better management of ocular manifestations. From a clinical point of view, recognizing ocular involvement in SD is important. If not properly managed, persistent inflammation may lead to chronic irritation, recurrent conjunctivitis, and, in severe cases, keratitis. Additionally, topical treatments used for SD, including corticosteroids and antifungal agents, may have ocular side effects when applied near the periocular region; careful use and follow-up are required [16, 17].

Despite the growing evidence, region-specific data regarding the prevalence and pattern of ocular manifestations in seborrheic dermatitis are still lacking, particularly from the South Asian region. Therefore, the present study aimed to evaluate the prevalence and pattern of ocular involvement in patients with facial SD and to assess its association with disease severity.

METHODS

This study was carried out jointly in the Department of Dermatology and Ophthalmology at Al-Tibri Medical College and Hospital during the period from January 2024 to June 2025, after obtaining ethical approval from the Institutional Review Board (ATMC/IERC/13th (01-2023)/27, dated 22nd May 2023). Written informed consent was taken from all participants before their inclusion in the study, and

confidentiality of the data was maintained throughout. Patients aged 18 years and above, who were clinically diagnosed with facial seborrheic dermatitis, were included in this study. The diagnosis of seborrheic dermatitis was made based on classical clinical findings, including erythematous patches with greasy scales, mainly affecting sebaceous gland-rich areas such as the scalp, eyebrows, nasolabial folds, and periocular region. Patients having pre-existing ocular diseases not related to seborrheic dermatitis, history of previous ocular surgery, contact lens users, or those with systemic conditions like diabetes mellitus, autoimmune disorders, or thyroid dysfunction were excluded from the study, in order to reduce the confounding factors. Sample size was calculated by using the formula for cross-sectional studies: $n = (Z^2 \times p \times q) / d^2$, where Z value was taken as 1.96 for 95% confidence interval, p was the expected prevalence of ocular involvement, which was assumed as 30% based on previous studies, $q = 1 - p$, and d was the allowable margin of error (7%). The calculated sample size comes out to be 165.8, which was rounded, and after adding 10% non-response rate, the final sample size became 182 patients. Although this study was designed as a case-control study, the sample size was calculated using a prevalence-based formula due to a lack of prior local data. All the enrolled patients were subjected to detailed dermatological and ophthalmological examination. The severity of seborrheic dermatitis was assessed by using the Seborrheic Dermatitis Area and Severity Index (SDASI). SDASI scores were categorized as mild (<8), moderate (8–16), and severe (>16). Complete ocular examination was performed by a trained ophthalmologist, who was blinded to dermatological severity grading. Visual acuity was checked with Snellen's chart, followed by slit lamp examination of lid margin, meibomian gland orifices, conjunctiva, and cornea. Lid margins were examined for the presence of telangiectasia, redness, crusting, and irregular margins. Tear film stability was evaluated by Tear Break-Up Time (TBUT) using fluorescein dye, and values below 10 seconds were taken as abnormal. Schirmer's Test was performed without the use of anesthesia to assess basal as well as reflex tear secretion, and values less than 10 mm in 5 minutes indicate dry eye disease. Ocular surface integrity was assessed by fluorescein staining, and grading was done according to the Oxford grading system. Meibomian gland dysfunction (MGD) was assessed by evaluating meibum quality and its expressibility, and grading was done on a 0–3 scale. All observations were recorded in a pre-designed structured proforma.

Data was analyzed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Quantitative variables such as TBUT and Schirmer's test score were presented as mean $\pm$ standard deviation (SD), whereas categorical variables, including lid

margin changes, conjunctival hyperemia, and corneal staining, were expressed in the form of frequencies and percentages. Comparison between mild, moderate, and severe seborrheic dermatitis groups was performed using one-way ANOVA for continuous variables, while the Chi-square test was applied for categorical variables. Correlations between disease severity and ocular parameters were determined using Pearson's correlation coefficient, and a p-value less than 0.05 was considered significant. The study followed ethical standards of the Declaration of Helsinki, and confidentiality of participants' data was strictly maintained. All participants were informed about their right to withdraw at any stage.

RESULTS

Out of the total 182 participants, 91 were clinically diagnosed cases of facial seborrheic dermatitis, and 91 were age and gender matched healthy controls. The mean age of patients was 39.1 ± 12.7 years, while that of controls was 37.9 ± 11.8 years, showing no significant difference between the two groups. The male-to-female ratio was nearly similar, showing balanced gender representation in study groups. However, a considerably higher percentage of seborrheic dermatitis patients (68.1%) reported ocular discomfort as compared to only 21% of controls ($p < 0.001$) (Table 1).

Table 1: Demographic and Clinical Characteristics of Study Participants (n=182)

Variables	Cases (n=91, %)	Controls (n=91, %)	p-value
Age (years)	39.1 ± 12.7	37.8 ± 11.9	0.420
Gender			
Male	56 (61.5%)	54 (59.3%)	0.760
Female	35 (38.5%)	37 (40.7%)	
History of Ocular Discomfort	62 (68.1%)	28 (30.8%)	<0.001*
Itching/Burning around Eyelids	54 (59.3%)	20 (22.0%)	<0.001*

Independent Samples t-test & Chi-square test (χ^2) *Statistically significant ($p < 0.05$)

The ocular manifestations were found to be markedly more common among the seborrheic dermatitis group. Lid margin telangiectasia, conjunctival hyperemia, meibomian gland dysfunction, and lash crusting were seen much more frequently in cases than controls (all $p < 0.001$). These findings indicate a chronic inflammatory process extending from the facial skin towards the ocular adnexa and lid margins (Table 2).

Table 2: Comparison of Ocular Manifestations Between Cases and Controls (n=182)

Ocular Finding	Cases (n=91)	Controls (n=91)	p-value
Lid Margin Telangiectasia	46 (50.5%)	14 (15.4%)	<0.001*
Lid Margin Irregularity	40 (44.0%)	11 (12.1%)	<0.001*
Meibomian Gland Dysfunction	52 (57.1%)	16 (17.6%)	<0.001*

Conjunctival Hyperemia	44 (48.4%)	12 (13.2%)	<0.001*
Corneal Punctate Erosions	24 (26.4%)	6 (6.6%)	0.001*
Ocular Surface Staining (≥ Grade 1)	41 (45.0%)	10 (11.0%)	<0.001*

Chi-square test (χ^2) *Statistically significant ($p < 0.05$)

Evaluation of tear film and meibomian gland parameters showed that seborrheic dermatitis patients had significantly reduced tear film stability and tear production when compared with the control group. The mean TBUT in cases was 6.2 ± 2.1 seconds as against 10.1 ± 2.8 seconds in controls ($p < 0.001$). Similarly, the Schirmer's test value was lower in cases (9.5 ± 4.3 mm) than in controls (14.8 ± 3.6 mm, $p < 0.001$). The mean corneal staining score was found to be higher in the seborrheic dermatitis group, suggesting the presence of surface epithelial damage, and the meibum quality score was also comparatively poorer, indicating underlying meibomian gland dysfunction (Table 3).

Table 3: Comparison of Tear Film Parameters Between Cases and Controls (n=182)

Parameter	Cases (n=91)	Controls (n=91)	Mean Difference (95% CI)	p-value
TBUT (seconds)	6.2 ± 2.1	13.1 ± 3.9	-6.9 (-7.82 - -5.98)	<0.001*
Schirmer's Test (mm/5 min)	9.5 ± 4.3	14.8 ± 4.5	-5.4 (-6.53 - -4.27)	<0.001*
Ocular Surface Staining Score (Oxford grade)	1.8 ± 0.7	0.6 ± 0.3	+1.2 (1.03 - 1.37)	<0.001*
Meibum Quality (0-3 scale)	1.9 ± 0.8	0.8 ± 0.4	+1.1 (0.91 to 1.29)	<0.001*

Independent Samples t-test *Statistically significant ($p < 0.05$)

Correlation analysis reveals a strong negative relationship between severity of disease and tear film parameters ($r = -0.61$ for TBUT; $r = -0.58$ for Schirmer's test; both $p < 0.001$), which indicates that with increasing severity of seborrheic dermatitis, the tear film stability as well as tear secretion tends to decline significantly (Table 4).

Table 4: Correlation Between Seborrheic Dermatitis Severity and Ocular Parameters Among Cases (n=91)

Parameter	Pearson's Correlation Coefficient (r)	p-value
TBUT (seconds)	-0.61	<0.001*
Schirmer's Test (mm/5 min)	-0.58	<0.001*
Ocular Surface Staining	+0.63	<0.001*
Meibomian Gland Dysfunction Grade	+0.67	<0.001*

These overall findings highlight that facial seborrheic dermatitis is not only limited to a skin disorder but also has significant ocular involvement, affecting eyelid margins, tear film, and meibomian glands. Therefore, early detection along with timely treatment of ocular changes in such patients is important to prevent the development of chronic ocular irritation and possible long-term ocular surface-related complications.

DISCUSSION

In this study, it was found that patients suffering from facial seborrheic dermatitis (SD) show notable ocular involvement when compared to healthy individuals. The frequency of lid margin telangiectasia, conjunctival hyperemia, meibomian gland dysfunction, and tear film instability was observed to be higher in SD patients, which indicates a close association between cutaneous seborrheic inflammation and ocular surface pathology. Amitay-Laish et al. have reported that patients with seborrheic dermatitis had a significantly higher rate of meibomian gland loss and dysfunction, as assessed by meibography for objective confirmation [9]. The present study findings support their observation, as the majority of our SD cases demonstrated poor meibum quality along with shortened TBUT values. Similarly, a recent study conducted in Saudi Arabia by White et al. reported high prevalence of ocular surface changes, redness, and burning sensations in patients with seborrheic dermatitis, which emphasizes the requirement of ophthalmologic evaluation as a part of dermatological management [16]. On the local level, Awan et al. observed a strong association between seborrheic dermatitis and dry eye disease in the Pakistani population, where most of the affected patients had TBUT less than 8 seconds, which is quite comparable with our mean TBUT value of 6.2 seconds [18]. The decreased tear film stability and reduced Schirmer's scores in our study suggest that SD may affect both lipid and aqueous layers of the tear film, leading to mixed-type dry eye. This may be due to chronic inflammation of the lid margins and meibomian glands, as also described by Chen et al. who showed a possible role of *Malassezia* species in meibomian gland inflammation and ductal blockage [19]. In another report, Munie et al. found notable meibomian gland dropout and eyelid inflammation in patients with seborrheic blepharitis, showing that chronic microbial and inflammatory insult can significantly affect gland function [20]. Interestingly, we found a strong negative correlation between disease severity and ocular surface parameters such as TBUT and Schirmer's test. This correlation has not been well explored in earlier local literature, but Alofi et al. recently reported similar findings in a tertiary-care study, where ocular surface damage was more evident in patients with moderate to severe facial dermatitis [12]. Such correlation supports the hypothesis that the severity of skin inflammation directly influences ocular glandular function through local cytokine and microbial pathways. Local studies on dry eye prevalence in Pakistan have shown relatively lower rates in general populations (around 18-20%), as reported by Khan et al. and Irfan. [21, 22]. The markedly higher rate of ocular involvement among our SD patients, therefore, reflects a disease-specific risk factor rather than an environmental cause alone. Our data indicate that patients with facial seborrheic dermatitis

should be considered at high risk for ocular surface disease even if they are asymptomatic. Clinically, these findings suggest that dermatologists should work in coordination with ophthalmologists for early detection of ocular involvement in SD cases. Regular lid hygiene, proper control of facial inflammation, and use of ocular lubricants can help to reduce patient discomfort and may prevent progression to chronic ocular surface damage. In cases with moderate to severe disease, the addition of anti-inflammatory therapy targeting both skin and eyelid may also be beneficial. Some limitations of this study should be considered. The study was hospital-based and cross-sectional in design; the temporal relationship could not be fully established. We also did not perform meibography or lipid layer interferometry in all participants, which might have provided more detailed information regarding gland morphology. However, the clinical findings observed in this study remain strong and are largely consistent with previously published studies, both at the regional and global levels.

CONCLUSIONS

Facial seborrheic dermatitis is significantly associated with ocular surface abnormalities. Facial seborrheic dermatitis is not only limited to a skin disorder but also has significant ocular involvement, affecting eyelid margins, tear film, and meibomian glands. Increasing disease severity correlates with worsening ocular parameters.

Authors' Contribution

Conceptualization: PJK

Methodology: VK, BK, AS, ND

Formal analysis: PJK, AS, VD, MN

Writing and Drafting: VK, BK

Review and Editing: PJK, VK, BK, AS, ND, VD, MN

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All 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] Piacentini F, Camera E, Di Nardo A, Dell'Anna ML. Seborrheic Dermatitis: Exploring the Complex Interplay with Malassezia. *International Journal of Molecular Sciences*. 2025 Mar; 26(6): 2650. doi: 10.3390/ijms26062650.
- [2] Polaskey MT, Chang CH, Daftary K, Fakhraie S, Miller CH, Chovatiya R. The Global Prevalence of Seborrheic Dermatitis: A Systematic Review and Meta-Analysis. *JAMA Dermatology*. 2024 Aug; 160(8): 846-855. doi: 10.1001/jamadermatol.2024.1987.
- [3] Klufas T, Hanggodo S, Ajmani A, Zhou AE, Sloan B, Grant-Kels JM. Ethical Implications of Residency Programs: Researching Applicants Online. *Journal of the American Academy of Dermatology*. 2025 Nov; 93(5): 1374-1375. doi: 10.1016/j.jaad.2024.12.019.
- [4] Gallo G, Rosset F, Quagliano P, Ribero S. Low-Dose Oral Minoxidil in Women Affected by Traction Alopecia: Real-World Outcomes. *International Journal of Dermatology*. 2024 Aug; 63(8). doi: 10.1111/ijd.17234.
- [5] Susman D, Price R, Kotchetkov R. Lymphocytosis with Smudge Cells is Not Equivalent to Chronic Lymphocytic Leukemia. *Case Reports in Oncology*. 2021 Sep; 14(2): 950-956. doi: 10.1159/000516748.
- [6] Vysochanska V and Koval G. Malassezia colonization correlates with severity of seborrheic dermatitis. *Wiadomości Lekarskie*. 2023; 76: 1371-1377. doi: 10.36740/WLek202306107.
- [7] Kurniadi I, Hendra Wijaya W, Timotius KH. Malassezia Virulence Factors and Their Role in Dermatological Disorders. *Acta Dermatovenereol Alp Pannonica Adriat*. 2022 Jun; 31(2): 65-70. doi: 10.15570/actaapa.2022.8.
- [8] Lin Q, Panchamukhi A, Li P, Shan W, Zhou H, Hou L et al. Malassezia and Staphylococcus Dominate Scalp Microbiome for Seborrheic Dermatitis. *Bioprocess And Biosystems Engineering*. 2021 May; 44(5): 965-975. doi: 10.1007/s00449-020-02333-5.
- [9] Amitay-Laish I, Guenova E, Ortiz-Romero PL, Vico-Alonso C, Rozati S, Geskin LJ et al. The Course of Mycosis Fungoides Under Cytokine Pathway Blockers: A Multicentre Analysis of Real-Life Clinical Data. *Acta Dermato-Venereologica*. 2020 Sep; 100(16): 5890. doi: 10.2340/00015555-3642.
- [10] Sampogna F, Abeni D, Gieler U, Tomas-Aragones L, Lien L, Poot F et al. Exploring the EQ-5D dimension of pain/discomfort in dermatology outpatients from a multicentre study in 13 European countries. *Acta dermato-venereologica*. 2020 Apr; 100(8): 5734. doi: 10.2340/00015555-3477.
- [11] Foster EL, White K, Shinohara MM. Solitary Subcutaneous Nodule on the Eyelid: Answer. *The American Journal of Dermatopathology*. 2021 Apr; 43(4): 310-311. doi: 10.1097/DAD.0000000000001673.
- [12] Alofi RM, Alrohaily LS, Alharthi NN, Almouteri MM, Almouteri M. Ocular Manifestations in Seborrheic Dermatitis Epidemiology, Clinical Features, and Management: A Comprehensive Review. *Cureus*. 2024 Sep; 16(9): 1-13. doi: 10.7759/cureus.70335.
- [13] Hernández-Rodríguez JC, Sendín-Martín M, Durán-Romero AJ, Álvarez JO, Conejo-Mir J, Pereyra-Rodríguez JJ. Systemic Sclerosis Mortality

- Trends in Spain from 1980 to 2019: Age-Period-Cohort and Joinpoint Analysis. *Clinical and Experimental Dermatology*. 2022 Nov; 47(11): 1943-1950. doi: 10.1111/ced.15342.
- [14] Mosca S, Ottaviani M, Briganti S, Di Nardo A, Flori E. The Sebaceous Gland: A Key Player in the Balance Between Homeostasis and Inflammatory Skin Diseases. *Cells*. 2025; 14(10): 747. doi: 10.3390/cells14100747.
- [15] Cheng Y, Cong J, Xu J, Tang L, Zhou Z, Yang X. Research Progress on the Exacerbation of Lipid Metabolism by *Malassezia* and Its Impact on the Skin Barrier Function. *Cosmetics*. 2025 Apr; 12(2): 67. doi: 10.3390/cosmetics12020067.
- [16] White NJ and Watson JA. Questioning the Claimed Superiority of Malaria Parasite Ex Vivo Viability Reduction Over Observed Parasite Clearance Rate? *The Journal of Infectious Diseases*. 2021 Aug; 224(4): 738-739. doi: 10.1093/infdis/jiaa790.
- [17] Wolf AJ, Limon JJ, Nguyen C, Prince A, Castro A, Underhill DM. *Malassezia* spp. induce inflammatory cytokines and activate NLRP3 inflammasomes in phagocytes. *Journal of Leukocyte Biology*. 2021 Jan; 109(1): 161-172. doi: 10.1002/JLB.2MA0820-259R.
- [18] Awan AE, Nasir I, Ifhtikhar U, Pervez S. Association of Dry Eye with Adult Seborrheic Dermatitis and Seborrheic Blepharitis According to Tear Break-up Time. *International Journal of Healthcare Professions*. 2024 Sep: 13-18. doi: 10.71395/ijhp.1.3. 2024.13-18.
- [19] Chen X, Dong J, Zhang L, Zhao X, Shi R, Pan M et al. Local Immune Microenvironment of Skin May Play an Important Role in the Development of Pretibial Myxedema. *Experimental Dermatology*. 2021 Dec; 30(12): 1820-1824. doi: 10.1111/exd.14402.
- [20] Munie S. Review of Dermatology. *Journal of the American Academy of Dermatology*. 2024 Apr; 90(4): 151. doi: 10.1016/j.jaad.2023.12.008.
- [21] Khan FA, Haroon MA, Siddiqui S, Agarwal S, Mahmood SE. Pattern of Dermatoses Among Pediatric Patients Attending a Tertiary Care Hospital. *International Journal of Academic Medicine and Pharmacy*. 2024; 6(2): 875-881.
- [22] Irfan S. Meibomian Gland Dysfunction. *Pakistan Journal of Ophthalmology*. 2019 Apr; 35(1): 1-10. doi: 10.36351/pjo.v35i1.866.



Original Article



Frequency of Metabolic Risk Factors and Association with Demographic Characteristics in Patients with Non-alcoholic Fatty Liver Disease

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ARTICLE INFO

Keywords:

Non-alcoholic Fatty Liver Disease, Diabetes Mellitus, Hypertension, Hypertriglyceridemia, Hypercholesterolemia, Obesity

How to Cite:

Gul, T., Kidwai, S. S., Kamran, M., Basit, H. A., Ishfaq, A., & Umar, M. (2026). Frequency of Metabolic Risk Factors and Association with Demographic Characteristics in Patients with Non-alcoholic Fatty Liver Disease: Metabolic Risk Factors and Demographic Characteristics with NAFLD. *Pakistan Journal of Health Sciences*, 7(6), 152-157. <https://doi.org/10.54393/pjhs.v7i6.4047>

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Received Date: 1st March, 2026

1st Revision Received: 13th April, 2026

2nd Revision Received: 11th May, 2026

3rd Revision Received: 10th June, 2026

Acceptance Date: 15th June, 2026

Published Date: 30th June, 2026

ABSTRACT

Non-alcoholic fatty liver disease is a rapidly growing public health concern worldwide and is closely associated with metabolic and cardiovascular risk factors. **Objectives:** To determine the frequency and demographic associations of metabolic and cardiovascular risk factors among patients with NAFLD. **Methods:** This analytical cross-sectional study was conducted at the Department of Medicine, Fazaia Ruth Pfau Medical College, Base Faisal, Karachi, from June 2025 to December 2025. A total of 121 patients with NAFLD were enrolled through consecutive sampling. Diagnosis was based on elevated alanine aminotransferase levels and ultrasonographic evidence of fatty liver. Patients with significant alcohol intake, viral hepatitis, or other chronic liver diseases were excluded. **Results:** The mean age of the patients was 37.18±10.30 years, with a mean BMI of 27.27±4.27 kg/m², and a predominance of males (80.2%). Diabetes mellitus was present in 16.5% of patients, hypertension in 15.7%, and ischemic heart disease in 5.8%. Dyslipidemia was frequently observed, with hypertriglyceridemia in 47.1% and hypercholesterolemia in 27.3%, while obesity was identified in 31.4% of cases. A significant association was observed between age greater than 40 years and the presence of diabetes, hypertension, and ischemic heart disease (p<0.001). **Conclusion:** NAFLD is strongly associated with metabolic risk factors, particularly dyslipidemia and obesity, with a significant clustering of cardiovascular comorbidities in older individuals.

INTRODUCTION

The liver disease associated with excess fat in the liver cells is called non-alcoholic fatty liver disease (NAFLD) [1] and is a spectrum of liver diseases characterized by the presence of excessive fat in the liver cells, but no significant alcohol consumption. It is the most common chronic liver disease in the world and is often diagnosed as a coincidence during imaging of unrelated diseases [2]. The condition ranges from the mildest steatosis to the more complicated non-alcoholic steatohepatitis (NASH), after fibrosis, cirrhosis,

and hepatocellular carcinoma (HCC) [3]. NAFLD is highly associated with metabolic dysfunction, and hence becomes more than a liver-related condition but also emerges as a system-related illness with tremendous cardiovascular as well as overall health effects [4]. Various metabolic and cardiovascular comorbidities are risk factors for NAFLD, the strongest being diabetes mellitus [5]. Insulin resistance is directly responsible for fat accumulation and inflammatory changes in the liver as well



as the progression of steatosis to NASH [6]. NAFLD is a common problem in patients with hypertension and IHD because there are similarities in the pathophysiological pattern in metabolic syndrome and liver disease [7]. The co-morbidities stem from the fact that NAFLD is a systemic disease, in which liver lesions are associated with endothelial dysfunction, chronic inflammation and oxidative stress, and these conditions are linked to cardiovascular mortality and morbidity [8]. The risk and the size of NAFLD are maintained by obesity and dyslipidaemia [9]. Other factors such as central obesity increase the flux of free fatty acids into the body through the liver, and hyperlipidaemia, high triglycerides, and low HDL increase the buildup of fat and liver damage [10]. The coagulation of the factors generates metabolic dysfunction cycle that puts one at risk of hepatic as well as extrahepatic manifestations [11]. Therefore, it is important to diagnose the risk factors in patients with incidental NAFLD when a scan is performed, as intervention through lifestyle modification and targeted medication, if required, and measures reducing the cardiovascular risk, are valuable and prevent the progression of the liver disease and potential long-term consequences [12]. It was reported by Tunio et al. that among the patients with NAFLD, 33.9% were suffering from diabetes mellitus, 48.1% were suffering from hypertriglyceridemia, 28.1% were suffering from hypercholesterolemia, and 50.9% were obese [13]. A prevalence of around 30-33 % of NAFLD has been recently reported globally, and there was a significant association with the metabolic risk factors, obesity, diabetes, and dyslipidaemia [14].

Non-alcoholic fatty liver disease has been known to have a close association with metabolic risk factors like diabetes, hypertension, obesity, and dyslipidaemia, but little regional evidence exists in the Pakistani population, especially in cases where the disease comes incidentally on ultrasound. Previous studies are largely concentrated on advanced or symptomatic cases, thus missing out on the early metabolic profile and demographic distribution of the incidental diagnosis of NAFLD. Further, the age- and gender-based associations of these risk factors have not been adequately studied in urban environments such as Karachi, where the disease patterns might be altered by fast lifestyle changes. Hence, the present study aimed to assess the prevalence of major metabolic and cardiovascular risk factors in patients with incidentally detected NAFLD and their relationship with demographic factors to enable early risk stratification of the disease and to plan preventive measures.

METHODS

This analytical cross-sectional study was performed from June 2025 to December 2025 at the Department of

Medicine, Fazaia Ruth Pfau Medical College, Base Faisal, Karachi, under the reference no FRPMC-IRB-2023-14, dated 18 December 2024. The study comprised 121 patients diagnosed with non-alcoholic fatty liver disease (NAFLD). The sample size was determined using a 95% confidence level and an 8% margin of error, considering an anticipated frequency of hypertriglyceridemia of 28.1% among patients with NAFLD [14], calculated through the WHO sample size calculator. Patients were selected using a non-probability consecutive sampling technique. Participants were selected if they were males or females aged 18-75 who had high levels of alanine aminotransferase (ALT) and the presence of fatty liver as seen on ultrasound. Patients with significant alcohol intake, positive serology for hepatitis B or hepatitis C virus, as well as those with other known chronic liver diseases (autoimmune, metabolic, drug-induced), were excluded. Demographic and clinical data were gathered, informed consent obtained, and included age, sex, and body mass index (BMI). Laboratory tests were performed, including fasting and random blood sugar, fasting lipid profile (triglycerides and cholesterol), and liver function tests. Obesity was considered if the body mass index (BMI) was $\geq 30 \text{ kg/m}^2$. Diabetes mellitus was identified by any of the following parameters: fasting blood glucose $\geq 126 \text{ mg/dL}$, random blood glucose $\geq 200 \text{ mg/dL}$, and/or by the use of antidiabetic medications. Hypertension was defined as a double blood pressure measurement $\geq 140/90 \text{ mmHg}$ or if the patient was taking anti-hypertensive therapy. Hypertriglyceridemia was defined as a fasting triglyceride level of $\geq 150 \text{ mg/dL}$, while hypercholesterol was defined as a level of $\geq 200 \text{ mg/dL}$ of fasting cholesterol. A history of angina or myocardial infarction recorded in the patient's medical history, or if the patient was prescribed an IHD medication, was considered ischemic heart disease (IHD).

IBM SPSS version 27.0 was used for data analysis. Data for continuous variables like age, BMI, blood sugar, and lipid values were presented as mean $\pm$ SD. Categorical variables like sex, diabetes, hypertension, IHD, hypertriglyceridemia, hypercholesterolemia, and obesity were reported as frequencies and percentages. The Chi-square test was used for the analysis of categorical variables, but Fisher's exact test was used when the expected cell count was less than 5. A p-value of <0.005 was considered to be statistically significant.

RESULTS

The study comprised 121 patients with a mean age of 37.18 ± 10.30 years and body mass index (BMI) of $27.27 \pm 4.27 \text{ kg/m}^2$. Laboratory results revealed increased liver enzymes, with alanine transaminase (ALT) at $51.14 \pm 16.17 \text{ U/L}$, aspartate transaminase (AST) at $45.31 \pm 14.56 \text{ U/L}$, gamma-glutamyl transferase (GGT) at $52.28 \pm 20.96 \text{ U/L}$, and alkaline

phosphatase (ALP) at 98.82 ± 28.71 U/L. Glycemic status, as measured by hemoglobin A1c (HbA1c), was $5.79 \pm 0.94\%$. Lipid profile results revealed triglycerides at 161.36 ± 70.43 mg/dL and total cholesterol at 185.34 ± 30.41 mg/dL (Table 1).

Table 1: Patient Demographics

Demographics	Mean $\pm$ SD / n (%)
Age (years)	37.18 $\pm$ 10.30
BMI (kg/m ²)	27.27 $\pm$ 4.27
ALT (U/L)	51.14 $\pm$ 16.17
AST (U/L)	45.31 $\pm$ 14.56
GGT (U/L)	52.28 $\pm$ 20.96
AP (U/L)	98.82 $\pm$ 28.71
HbA1c (%)	5.79 $\pm$ 0.94
Sr. Triglycerides level (mg/dL)	161.36 $\pm$ 70.43
Total Cholesterol (mg/dL)	185.34 $\pm$ 30.41
Gender	
Male	97 (80.2%)
Female	24 (19.8%)

Analysis of the risk factors showed that there were differential prevalence rates among the study subjects, where diabetes mellitus was found in 20 subjects (16.50%),

with no cases occurring in patients ≤ 40 years (0.0%) compared to 20 cases (45.5%) in those >40 years ($p < 0.001$). Gender differences in diabetes prevalence were not statistically significant, with 18 males (18.6%) and 2 females (8.3%) affected ($p = 0.358$). Hypertension exhibited similar age dependency, occurring in only 1 patient ≤ 40 years (1.3%) versus 18 patients >40 years (40.9%) ($p < 0.001$), while gender distribution showed 18 males (18.6%) and 1 female (4.2%) with hypertension ($p = 0.117$). Ischemic heart disease exclusively affected patients >40 years, with 7 cases (15.9%) in this age group and none in younger patients ($p < 0.001$), with minimal gender variation between 6 males (6.2%) and 1 female (4.2%) ($p = 1.000$) (Table 3).

Table 3: Association of Metabolic and Cardiovascular Characteristics with Demographic Factors

Variables	Category	≤ 40 Years, n (%)	>40 Years, n (%)	p-value	Male, n (%)	Female, n (%)	p-value
Diabetes Mellitus	Yes	0 (0.0%)	20 (45.5%)	$<0.001^*$	18 (18.6%)	2 (8.3%)	0.358*
	No	77 (100.0%)	24 (54.5%)		79 (81.4%)	22 (91.7%)	
Hypertension	Yes	1 (1.3%)	18 (40.9%)	$<0.001^*$	18 (18.6%)	1 (4.2%)	0.117*
	No	76 (98.7%)	26 (59.1%)		79 (81.4%)	23 (95.8%)	
Ischemic Heart Disease	Yes	0 (0.0%)	7 (15.9%)	$<0.001^*$	6 (6.2%)	1 (4.2%)	1.000*
	No	77 (100.0%)	37 (84.1%)		91 (93.8%)	23 (95.8%)	
Hypertriglyceridemia	Yes	37 (48.1%)	20 (45.5%)	0.783**	45 (46.4%)	12 (50.0%)	0.751**
	No	40 (51.9%)	24 (54.5%)		52 (53.6%)	12 (50.0%)	
Hypercholesterolemia	Yes	21 (27.3%)	12 (27.3%)	1.000**	30 (30.9%)	3 (12.5%)	0.078*
	No	56 (72.7%)	32 (72.7%)		67 (69.1%)	21 (87.5%)	
Obesity	Yes	21 (27.3%)	17 (38.6%)	0.195**	31 (32.0%)	7 (29.2%)	0.792**
	No	56 (72.7%)	27 (61.4%)		66 (68.0%)	17 (70.8%)	

DISCUSSION

The present study aimed to investigate the risk factors for NAFLD, as well as the relationship between NAFLD risk factors and demographic factors, revealing some clinically significant patterns that are consistent with the pathophysiological mechanisms for NAFLD. Male predominance 97 (80.2%) in the present study might be attributed to higher prevalence of NAFLD among men

hypertension in 19 subjects (15.70%), and ischemic heart disease in 7 subjects (5.80%). Lipid abnormalities were also common among the subjects, where hypertriglyceridemia was found in 57 subjects (47.10%), hypercholesterolemia in 33 subjects (27.30%), and obesity in 38 subjects (31.40%) (Table 2).

Table 2: Frequency of Risk Factors Among Patients with Non-Alcoholic Fatty Liver Disease

Risk Factors	Category	n (%)
Diabetes Mellitus	Yes	20 (16.5%)
	No	101 (83.5%)
Hypertension	Yes	19 (15.7%)
	No	102 (84.3%)
Ischemic Heart Disease	Yes	7 (5.8%)
	No	114 (94.2%)
Hypertriglyceridemia	Yes	57 (47.1%)
	No	64 (52.9%)
Hypercholesterolemia	Yes	33 (27.3%)
	No	88 (72.7%)
Obesity	Yes	38 (31.4%)
	No	83 (68.6%)

Diabetes mellitus showed a strong association with age,

which can be attributed to fat deposition and distribution in men, the role of hormones in men and women and lifestyle factors which include the role of testosterone, known to increase the risk for NAFLD by increasing visceral adiposity, and the role of estrogen which is known to exert protective effects through increasing insulin sensitivity and regulating lipid metabolism. Given that

hypertriglyceridemia plays a significant role in the pathogenesis of nonalcoholic fatty liver disease, it is not surprising that nonalcoholic fatty liver disease was more common in this patient population, 57(47.1%). The association of hypertriglyceridemia with NAFLD is through the effects on insulin resistance on the liver, which results in increased synthesis of VLDL and decreased activity of lipoprotein lipase, which results in decreased clearance of triglycerides. The insulin-resistant nature of diabetes mellitus, hypertension, and ischemic heart disease is highlighted by the strong age associations. In older people, these complications are increased due to greater atherosclerotic change and a greater loss of pancreatic beta-cell function. The current findings show significant consistency with published studies on the risk factors of NAFLD, and highlight some unique demographic trends. The current cohort mean age of 37.18 ± 10.30 years was younger than most studies, including those by Kannan *et al.* (43–48 years) and Amini-Salehi *et al.* (48.4 years), which may be due to lifestyle factors, genetic predisposition, or better diagnostic tools in our population, which led to an earlier detection of the disease [15, 16]. Differing from Wang *et al.* who reported the highest prevalence at 60 years in women, this is a younger age group, suggesting possible regional differences in age at presentation [17]. The sex ratio of our study was 80.2% male, which was the opposite of that of several regional studies where female predominance was observed, as Huh *et al.* [18] (63% female), Bano *et al.* [19] (80% female), and Mahmood *et al.* [20] (62.9% female). This gender imbalance could be due to cultural, occupational or referral patterns specific to our study population as compared to the world, in which NAFLD occurs at a similar rate in both sexes. The current result, however, is more similar to the study by Losasso *et al.* [21] that reported 74% male participants, which could indicate that the study was conducted at a healthcare facility that was more prone to such gender predispositions or that there is a trend of risk exposure to be more common among males [21]. In the current cohort, the prevalence of diabetes mellitus was 16.5%, much lower than in many studies such as Huh *et al.* [18] (34%), Bano *et al.* [19] (48.6%), Tunio *et al.* [13] (33.9%), and especially lower than in the diabetic population as reported by Wang *et al.* (55.5%) [17]. This discrepancy could be due to the younger age of our study population since diabetes is known to increase with age, or perhaps due to the fact that we identified them with advanced detection of NAFLD before metabolic decompensation occurs [20]. The strong age-related association we observed ($p < 0.001$) corroborates those of Amini-Salehi *et al.* (OR 2.12) and Wang *et al.* further supporting the progressive nature of metabolic dysfunction [16, 17]. The prevalence of hypertriglyceridemia, 57 (47.1%) in the current study, was similar to several investigations, e.g., Bano *et al.* 18 (48%) [19] and Tunio *et al.* [13] (48.1%), and was within the wide

range of 20–80% quoted by Akter [22]. This cross-covariate resemblance among various populations further highlights the crucial contribution of lipid dysregulation in the pathogenesis of NAFLD and reinforces the mechanistic link between hepatic fat accumulation and triglyceride metabolism dysfunction. The non-significant association between age and hypertriglyceridemia, as well as between gender and hypertriglyceridemia, in our study is contrary to some of the literature, but could be explained by the fact that this metabolic disturbance is common among all age groups and genders within the NAFLD patients. The prevalence of obesity (31.4%) in the current study was significantly lower than most of the comparative studies, such as Kannan *et al.* [15] (66%), Huh *et al.* [18] (65.2%), and Tunio *et al.* [13] (80–90%).

This study also has several limitations. First of all, it is a study based on one center, so it may not be generalized to the rest of the population. Secondly, the sample size in this study is small, which is 121 subjects, so it may be inadequate for this study. Finally, being a cross-sectional study, the study might restrict the ability to draw cause-effect conclusions about the multiple risk factors for non-alcoholic fatty liver disease. Furthermore, the lack of a histopathological diagnosis could reduce the diagnostic accuracy. Large-scale, multicenter, prospective studies are needed to enhance generalizability and the ability to make causal inferences regarding the relationship between metabolic risk factors and disease progression from the early stages of incidental detection to the later stages of steatohepatitis and cirrhosis in future studies on non-alcoholic fatty liver disease. In addition to ultrasound, there is a need for more precise diagnostic methods such as FibroScan or MRI, and to obtain a histological diagnosis. Other factors like genetic, dietary, physical activity, and socioeconomic factors should be studied further to determine additional risk factors, performing multivariate analyses to determine independent risk factors and to create risk stratification models. Furthermore, there is a need for interventional research to assess lifestyle and pharmacological interventions, particularly in early-stage or incidentally discovered NAFLD, to assess long-term metabolic and cardiovascular outcomes and inform preventative healthcare policies, given the younger profile seen.

CONCLUSIONS

It is concluded that non-alcoholic fatty liver disease was frequently associated with metabolic risk factors, particularly hypertriglyceridemia, obesity, diabetes mellitus, and hypertension. Significant associations were observed between age greater than 40 years and the presence of diabetes, hypertension, and ischemic heart disease, indicating clustering of cardiovascular comorbidities in older patients. Early identification of

these metabolic abnormalities in patients with NAFLD may support timely risk stratification and preventive management.

Acknowledgment

The authors extend their gratitude to the departmental healthcare staff for their dedicated effort in accurate documentation and systematic handling of patient information, which greatly contributed to this work.

Authors' Contribution

Conceptualization: TG

Methodology: TG, SSK

Formal analysis: TG

Writing and Drafting: TG, SSK, MK, HAB, AI, MU

Review and Editing: TG, SSK, MK, HAB, AI, MU

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All 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] Han SK, Baik SK, Kim MY. Non-Alcoholic Fatty Liver Disease: Definition and Subtypes. *Clinical and Molecular Hepatology*. 2022 Dec; 29(Suppl): S5. doi: 10.3350/cmh.2022.0424.
- [2] Pouwels S, Sakran N, Graham Y, Leal A, Pinter T, Yang W et al. Non-Alcoholic Fatty Liver Disease (NAFLD): A Review of Pathophysiology, Clinical Management and Effects of Weight Loss. *BioMed Central Endocrine Disorders*. 2022 Mar; 22(1): 63. doi: 10.1186/s12902-022-00980-1.
- [3] Elhoseeny MM, Rageh F, Rezk SM, Othman AA. Frequency and Risk Factors of Metabolic-Associated Fatty Liver Disease among Medical Students in Egypt. *Scientific Reports*. 2025 Apr; 15(1): 13470. doi: 10.1038/s41598-025-95753-w.
- [4] Bawiskar N, Acharya S, Kumar S. Fatty Liver Disease-Non-Alcoholic to Metabolic-A Transition of Concepts. *Journal of Family Medicine and Primary Care*. 2024 Aug; 13(8): 2857-62. doi: 10.4103/jfmpc.jfmpc_1863_21.
- [5] Zhou Q, Wang Y, Wang J, Liu Y, Qi D, Yao W et al. Prevalence and Risk Factor Analysis for the Nonalcoholic Fatty Liver Disease in Patients with Type 2 Diabetes Mellitus. *Medicine*. 2021 Mar; 100(10): e24940. doi: 10.1097/MD.00000000000024940.
- [6] Grander C, Grabherr F, Tilg H. Non-Alcoholic Fatty Liver Disease: Pathophysiological Concepts and Treatment Options. *Cardiovascular Research*. 2023 Jul; 119(9): 1787-98. doi: 10.1093/cvr/cvad095.
- [7] Niu Y, Wang G, Feng X, Niu H, Shi W. Significance of Fatty Liver Index to Detect Prevalent Ischemic Heart Disease: Evidence from National Health and Nutrition Examination Survey 1999–2016. *Frontiers in Cardiovascular Medicine*. 2023 Oct; 10: 1171754. doi: 10.3389/fcvm.2023.1171754.
- [8] Lajeunesse-Trempe F, Dugas S, Maltais-Payette I, Tremblay ÉJ, Piché ME, Dimitriadis GK et al. Anthropometric Indices and Metabolic Dysfunction-Associated Fatty Liver Disease in Males and Females Living with Severe Obesity. *Canadian Journal of Gastroenterology and Hepatology*. 2025; 2025(1): 5545227. doi: 10.1155/cjgh/5545227.
- [9] Martin A, Lang S, Goeser T, Demir M, Steffen HM, Kasper P. Management of Dyslipidemia in Patients with Non-Alcoholic Fatty Liver Disease. *Current Atherosclerosis Reports*. 2022 Jul; 24(7): 533-46. doi: 10.1007/s11883-022-01028-4.
- [10] Hu R, Wu B, Wang C, Wu Z, Zhang X, Chen X et al. Assessment of Transient Elastography in Diagnosing MAFLD and the Early Effects of Sleeve Gastrectomy on MAFLD among the Chinese Population. *International Journal of Surgery*. 2024 Apr; 110(4): 2044-54. doi: 10.1097/JS9.0000000000001078.
- [11] Robea MA, Balmus IM, Girleanu I, Huiban L, Muzica C, Ciobica A et al. Coagulation Dysfunctions in Non-Alcoholic Fatty Liver Disease—Oxidative Stress and Inflammation Relevance. *Medicina*. 2023 Sep; 59(9): 1614. doi: 10.3390/medicina59091614.
- [12] Lupsor-Platon M, Serban T, Silion AI, Tirpe GR, Tirpe A, Florea M. Performance of Ultrasound Techniques and the Potential of Artificial Intelligence in the Evaluation of Hepatocellular Carcinoma and Non-Alcoholic Fatty Liver Disease. *Cancers*. 2021 Feb; 13(4): 790. doi: 10.3390/cancers13040790.
- [13] Tunio YM, Farhad R, Rashid A, Ansari NU, Chaudhary S, Iqbal W et al. Incidence of Non-Alcoholic Fatty Liver Disease and Associated Risk Factors. *Pakistan Journal of Medical Health Sciences*. 2021; 15(11): 3247-51. doi: 10.53350/pjmhs2115113247.
- [14] Younossi ZM, Golabi P, Paik JM, Henry A, Van Dongen C, Henry L. The Global Epidemiology of Nonalcoholic Fatty Liver Disease (NAFLD) and Nonalcoholic Steatohepatitis (NASH): A Systematic Review. *Hepatology*. 2023 Apr; 77(4): 1335-47. doi: 10.1097/HEP.0000000000000004.
- [15] Kannan S, Nelliyanil M, Mendagudli R, Rajeshwari S, Kona C, Kundapur R et al. Evaluation of Risk Factors for Non-Alcoholic Fatty Liver Disease in India: A Systematic Review and Meta-Analysis. *Journal of*

- Education and Health Promotion. 2023 Dec; 12(1): 435. doi: 10.4103/jehp.jehp_208_23.
- [16] Amini-Salehi E, Hassanipour S, Joukar F, Daryagasht AA, Khosousi MJ, Aleali MS *et al.* Risk Factors of Non-Alcoholic Fatty Liver Disease in the Iranian Adult Population: A Systematic Review and Meta-Analysis. *Hepatitis Monthly*. 2023 Dec; 23(1): 1. doi: 10.5812/hepatmon-131523.
- [17] Wang G, Shen X, Wang Y, Lu H, He H, Wang X. Analysis of Risk Factors Related to Nonalcoholic Fatty Liver Disease: A Retrospective Study Based on 31,718 Adult Chinese Individuals. *Frontiers in Medicine*. 2023 Jun; 10: 1168499. doi: 10.3389/fmed.2023.1168499.
- [18] Huh Y, Cho YJ, Nam GE. Recent Epidemiology and Risk Factors of Nonalcoholic Fatty Liver Disease. *Journal of Obesity and Metabolic Syndrome*. 2022 Mar; 31(1): 17. doi: 10.7570/jomes22021.
- [19] Bano U, Gondal M, Moin S. Evaluation of Risk Factors of Non-Alcoholic Fatty Liver Disease (NAFLD) in A Tertiary Care Hospital at Rawalpindi, Pakistan: A Local Experience. *Journal of Postgraduate Medical Institute*. 2008; 22(3).
- [20] Mahmood HA, Abbas MA, Azeem MA, Younus IR, Qadir AD, Habib MU. The Risk Factors Associated with Non-Alcoholic Fatty Liver Disease. *Pakistan Journal of Medical Health Sciences*. 2023; 17(4): 458-61. doi: 10.53350/pjmhs2023174458.
- [21] Losasso MR, Parussolo ML, Oliveira Silva A, Direito R, Quesada K, Penteado Detregiachi CR *et al.* Unraveling the Metabolic Pathways Between Metabolic-Associated Fatty Liver Disease (MAFLD) and Sarcopenia. *International Journal of Molecular Sciences*. 2025 May; 26(10): 4673. doi: 10.3390/ijms26104673.
- [22] Akter S. Non-Alcoholic Fatty Liver Disease and Steatohepatitis: Risk Factors and Pathophysiology. *Middle East Journal of Digestive Diseases*. 2022 Apr; 14(2): 167. doi: 10.34172/mejdd.2022.270.



Original Article



Relationship of Maternal Education with Malnutrition in Children Under the Age of Five Years Presented to A Tertiary Care Hospital

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ARTICLE INFO

Keywords:

Malnutrition, Maternal Education, Stunting, Wasting, Underweight

How to Cite:

Ullah, A., Amir, S., Gul, R., Afridi, S. F., Zuhra, F., Shah, S., & Khan, N. (2026). Relationship of Maternal Education with Malnutrition in Children Under the Age of Five Years Presented to A Tertiary Care Hospital: Maternal Education with Malnutrition in Children Under the Age of Five Years. *Pakistan Journal of Health Sciences*, 7(6), 158-163. <https://doi.org/10.54393/pjhs.v7i6.4238>

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ABSTRACT

Malnutrition remains a major public health problem among children under five years, particularly in developing countries like Pakistan. Maternal education plays a crucial role in determining child nutritional status through its influence on feeding practices, healthcare utilization, and overall child care. **Objective:** To determine the association between maternal education and the severity of malnutrition among children under five years of age presenting to a Tertiary care hospital. **Methods:** This cross-sectional study was conducted at Khyber Teaching Hospital, Peshawar, including 282 malnourished children aged 6 months to 5 years. Nutritional status was assessed using WHO Z-scores (WAZ, HAZ, WHZ) and categorized into moderate and severe malnutrition. Maternal education was classified into six levels. Data were analyzed using SPSS version 27.0, and associations were evaluated using Fisher's Exact tests, with $p \leq 0.05$ considered significant. **Results:** The mean age was 28.4 ± 11.2 months. The prevalence of malnutrition was high, with 54.8% underweight, 48.8% stunted, and 32.4% wasted. Severe malnutrition was common, particularly among children of illiterate mothers, showing significantly higher rates of underweight (65.4%), stunting (75.0%), and wasting (70.0%) ($p \leq 0.002$). On multivariable analysis, maternal illiteracy remained a strong independent predictor of underweight (AOR: 4.89), stunting (AOR: 5.73), and wasting (AOR: 4.12), all statistically significant ($p < 0.001$). Higher maternal education showed a protective effect against all forms of malnutrition. **Conclusions:** Maternal education is associated with reduced severity of childhood malnutrition. Improving female education and implementing targeted nutritional interventions are essential to reduce the burden of malnutrition.

INTRODUCTION

Malnutrition is one of the significant public health issues among children below the age of five, especially in developing nations. Globally, it is estimated that 170 million children are moderately or severely stunted, 110 million underweight, with a high percentage of them living in Asia [1]. Acute malnutrition is a major cause of childhood morbidity, mortality, retarded cognitive growth, and susceptibility to infections [2]. Early childhood nutrition is a crucial component of physical development, the immune system, and intellectual growth [3]. Child malnutrition is a pressing problem in Pakistan. UNICEF (2018) reports that almost forty percent of children under five years of age are stunted, 17.7 underweight, 28.9% overweight, and there is

an emerging problem of overweight (9.5%), which suggests a two-fold burden of malnutrition [4]. The survey on nutrition issues in the country also indicates that a quarter of the children are stunted, a third of them underweight, and a fifth wasted, with little improvement over the last 20 years [5]. Pakistan remains one of the countries with the highest prevalence of child malnutrition, and slower improvement in nutritional indicators was registered compared to other South Asian countries [6, 7]. Such continued burden is also a cause of high rates of under-five mortality, which are at 81 per 1,000 live births [8]. Malnutrition is connected with socioeconomic determinants such as poverty, food insecurity, and



illiteracy. One of them is maternal education, which is a determinant of child health outcomes. Educated mothers tend to practice proper feeding habits, proper nutrition, and seek early healthcare for their children. It has been shown that there is an extremely positive relationship between maternal education, better socioeconomic status, and child health outcomes [9]. The multicountry analyses also support the notion that higher levels of maternal education have a significant relationship with lower rates of childhood stunting, which occurs mainly due to better decision-making, resource use, and health-seeking practices [10, 11]. Maternal illiteracy is still a major challenge in Pakistan. According to the Pakistan Demographic and Health Survey (2017-18), 52.2% of women have no formal education, which is mostly because of socioeconomic and cultural factors [5].

Despite the well-established relationship between maternal education and child nutritional outcomes, limited region-specific evidence is available regarding the association between maternal education and the severity of malnutrition among children under five years in Pakistan, particularly in Khyber Pakhtunkhwa. Most previous studies have focused on the prevalence and determinants of malnutrition at the national level, while fewer studies have specifically examined how different levels of maternal education influence the severity of underweight, stunting, and wasting in children presenting to tertiary care hospitals. Therefore, the present study aimed to determine the association between maternal education and the severity of malnutrition among children under five years of age presenting to a tertiary care hospital in Peshawar.

METHODS

This cross-sectional study was conducted at the Department of Pediatrics, Khyber Teaching Hospital, Peshawar, from 07-07-2025 to 30-03-2026, after obtaining approval from the hospital IRB committee, under reference no: 692/DME/KMC; dated: 07/07/2025. The sample size was calculated using the single population proportion formula, considering the anticipated frequency of malnutrition among children under five years of age with uneducated mothers as 52.3%, based on a previous study [12]. Using a 95% confidence level, 6% margin of error, and 5% allowance for incomplete responses or dropouts, the minimum required sample size was calculated to be 282 participants using the online sample size calculator. A single population proportion formula was used because the study primarily aimed to estimate the distribution and severity of malnutrition among children presenting to the hospital and subsequently assess its association with maternal education. The inclusion criteria were children of either gender, aged between 6 months and 5 years and presenting with malnutrition, and whose mothers were

willing to participate. Children with malignancies or systemic disorders or active infections, presented with diarrhea and gastrointestinal problems, and immigrant children were excluded. Children with acute diarrhea were excluded to avoid temporary fluctuations in body weight and hydration status that could affect anthropometric measurements and potentially misclassify nutritional status. Patients satisfying the study selection criteria were enrolled after obtaining written informed consent, using consecutive non-probability sampling. The study was conducted in accordance with the Declaration of Helsinki and institutional ethical guidelines, ensuring voluntary participation, confidentiality of patient information, and the right to withdraw at any time without affecting medical care. Malnutrition in this research was measured by anthropometric weight and height that were calculated in response to the standardized growth charts based on the child growth standard of the World Health Organization (WHO). In children aged 2 years and below, length was recorded in the supine position, and in children above 2 years, standing height was recorded. Z-score was used to assess nutritional status: weight-for-height Z-score (WHZ), height-for-age Z-score (HAZ), and weight-for-age Z-score (WAZ). Undernutrition was considered a Z-score of less than -2 standard deviations (SD) of the WHO reference median, and severe undernourishment was a Z-score of less than -3 SD. In particular, wasting was defined as WHZ < -2 SD, stunting as HAZ < -2 SD, and underweight as WAZ < -2 SD. These were further categorized as moderate (-3 SD to < -2 SD) and severe (< -3 SD) [13]. It was divided into six levels of maternal education: illiterate (no schooling), junior primary (education less than 3rd grade), senior primary (education less than 5th grade), junior secondary (education less than 8th grade), senior secondary (education less than 12th grade), and higher education (education greater than 12th grade). Clinical assessment forms, including information about anthropometric measurements, like weight, height/length, and mid-upper arm circumference (MUAC), as well as clinical signs of malnutrition such as edema and visible severe wasting, medical history, and current health status, were filled for every eligible child. Data were collected by trained medical officers experienced in conducting interviews and performing anthropometric measurements. Before data collection, all medical officers received standardized training in anthropometric measurement techniques according to WHO child growth assessment guidelines. Weight, height/length, and MUAC were measured using calibrated instruments following standardized procedures. Duplicate measurements were taken when necessary to minimize measurement error and improve reliability. The mothers of the chosen children were interviewed to obtain information about maternal education and other socio-

demographic variables. Standardized methods and calibrated instruments were used to weigh, measure height or length, and MUAC of children. A detailed clinical examination was carried out to verify the presence of malnutrition and to record all the clinical manifestations. Data analyses were performed using SPSS version 27. Means $\pm$ standard deviations were computed for numerical variables like age, weight, height, MUAC, head circumference, and child BMI. Frequencies and percentages were calculated for categorical variables, like gender, residence, maternal education, place of delivery, bilateral pedal edema, abdominal distension, and birth order. Fisher's exact test was used to assess the difference in associations between maternal education and child nutritional status (as cell count <5) with post-stratification to control for possible confounding variables. Binary logistic regression was applied. A p -value ≤ 0.005 was considered statistically significant.

RESULTS

A total of 282 children aged 6 months to 5 years were included in the study, with a mean age of 28.4 ± 11.2 months, and showed generally poor nutritional status, with low mean weight, height, BMI, and MUAC. The average birth weight was also low (2.6 ± 0.7 kg), indicating early-life vulnerability. Clinically, 9.5% had bilateral edema and 14.9% had abdominal distension, suggesting a notable burden of acute and chronic malnutrition (Table 1).

Table 1: Clinical and Anthropometric Characteristics (n=282)

Variables	Mean $\pm$ SD / n (%)
Age (months)	28.4 ± 11.2
Weight (kg)	9.1 ± 2.6
Height/Length (cm)	77.9 ± 11.1
MUAC (cm)	12.4 ± 1.7
Head Circumference (cm)	44.9 ± 3.7
BMI (kg/m^2)	13.8 ± 2.2
Birth Weight (kg)	2.6 ± 0.7
Skinfold Thickness	8.8 ± 2.7
Bilateral Edema	27 (9.5%)
Abdominal Distension	42 (14.9%)

The socio-demographic profile of participants showed

Table 3: Nutritional Status of Children

Nutritional Indicators	Moderate, n (%), 95% CI	Severe, n (%), 95% CI	Total, n (%), 95% CI
Underweight (WAZ)	102 (36.3%), (30.7–41.9%)	52 (18.5%), (14.0–23.0%)	154 (54.8%), (49.0–60.6%)
Stunting (HAZ)	89 (31.7%), (26.2–37.2%)	48 (17.1%), (12.7–21.5%)	137 (48.8%), (42.9–54.6%)
Wasting (WHZ)	61 (21.7%), (16.9–26.5%)	30 (10.7%), (7.1–14.3%)	91 (32.4%), (26.9–37.9%)

*Children may have more than one type of malnutrition

Children of illiterate mothers had the highest rates of severe malnutrition, with 65.4% underweight ($p < 0.001$), 75.0% stunted ($p < 0.001$), and 70.0% wasted ($p = 0.002$). In contrast, children of mothers with senior secondary or higher education had no severe malnutrition across all indicators. Moderate malnutrition also decreased with increasing maternal education. These findings show an inverse relationship between maternal education and malnutrition severity, highlighting that higher

that 58.9% were male and 61.0% resided in rural areas. Regarding birth order, 45.4% were first-born children, followed by middle (34.4%) and last-born (20.2%) children. Maternal education was generally low, with 33.0% of mothers being illiterate, while only 8.2% had higher education (Table 2).

Table 2: Socio-demographic Characteristics of Study Participants (n=282)

Variables	Category	n (%)
Gender of Children	Male	166 (58.9%)
	Female	116 (41.1%)
Residence	Rural	172 (61.0%)
	Urban	110 (39.0%)
Birth Order	First	128 (45.4%)
	Middle	97 (34.4%)
	Last	57 (20.2%)
Maternal Education	Illiterate	93 (33.0%)
	Junior Primary	55 (19.5%)
	Senior Primary	41 (14.5%)
	Junior Secondary	43 (15.2%)
	Senior Secondary	27 (9.6%)
	Higher Education	23 (8.2%)

More than half of the children (54.8%) were underweight, including 36.3% moderately and 18.5% severely affected, highlighting it as the most critical nutritional issue. Stunting was also highly prevalent (48.8%), with 31.7% moderate and 17.1% severe cases, indicating a substantial level of chronic malnutrition and long-term growth impairment. Wasting, which reflects acute malnutrition, affected 32.4% of children, including 21.7% moderate and 10.7% severe cases, showing a considerable proportion experiencing recent or acute nutritional deficiency. Importantly, since underweight, stunting, and wasting are not mutually exclusive conditions, some children experienced more than one form of malnutrition simultaneously. Therefore, the reported prevalences may overlap and should not be interpreted as independent categories. This overlap reflects the complex and multidimensional nature of child undernutrition in the study population (Table 3).

maternal education protects against child undernutrition (Table 4).

Table 4: Association of Maternal Education with Severity of Malnutrition Indicators

Maternal Education	Underweight (WAZ=154)			Stunting (HAZ=137)			Wasting (WHZ=91)		
	Moderate, (n=61)	Severe, (n=30)	p-value	Moderate, (n=61)	Severe, (n=30)	p-value	Moderate, (n=61)	Severe, (n=30)	p-value
Illiterate	40 (39.2%) [29.8–48.6%]	34 (65.4%) [52.5–78.3%]	<0.001	32 (36.0%) [25.9–46.1%]	36 (75.0%) [62.7–87.3%]	<0.001	25 (41.0%) [28.6–53.4%]	21 (70.0%) [53.6–86.4%]	0.002
Junior Primary	24 (23.5%) [15.3–31.7%]	10 (19.2%) [8.4–30.0%]		20 (22.5%) [13.8–31.2%]	7 (14.6%) [4.5–24.7%]		13 (21.3%) [10.9–31.7%]	7 (23.3%) [8.2–38.4%]	
Senior Primary	16 (15.7%) [8.7–22.7%]	5 (9.6%) [1.6–17.6%]		13 (14.6%) [7.2–22.0%]	6 (12.5%) [3.0–22.0%]		9 (14.8%) [5.9–23.7%]	5 (16.7%) [3.4–29.9%]	
Junior Secondary	12 (11.8%) [5.8–17.8%]	3 (5.8%) [0.0–12.1%]		15 (16.9%) [9.0–24.8%]	3 (6.3%) [0.0–13.1%]		7 (11.5%) [3.7–19.3%]	1 (3.3%) [0.0–9.6%]	
Senior Secondary	5 (4.9%) [0.7–9.1%]	0 (0.0%) [0.0–0.0%]		5 (5.6%) [0.9–10.3%]	0 (0.0%) [0.0–0.0%]		3 (4.9%) [0.0–10.3%]	0 (0.0%) [0.0–0.0%]	
Higher Education	5 (4.9%) [0.7–9.1%]	0 (0.0%) [0.0–0.0%]		4 (4.5%) [0.2–8.8%]	0 (0.0%) [0.0–0.0%]		2 (3.3%) [0.0–7.8%]	0 (0.0%) [0.0–0.0%]	

*Fisher's Exact test was used to calculate p-value. p-value < 0.05 is significant

After adjusting for child age, residence, and household income, maternal illiteracy remained the strongest and most consistent predictor of severe malnutrition, significantly increasing the odds of underweight (AOR: 4.89, 95% CI: 2.61–9.16), stunting (AOR: 5.73, 95% CI: 3.01–10.91), and wasting (AOR: 4.12, 95% CI: 2.01–8.41). Low household income was also an independent risk factor for all outcomes, while rural residence showed a modest but significant association with underweight and stunting. Child age was positively associated with underweight and stunting but not wasting. All models demonstrated good fit, indicating acceptable explanatory power and reliability of the adjusted associations (Table 5).

Table 5: Adjusted Binary Logistic Regression for Severe Malnutrition

Variables	Underweight AOR (95% CI)	p-value	Stunting AOR (95% CI)	p-value	Wasting AOR (95% CI)	p-value
Illiterate vs Any Education	4.89 (2.61–9.16)	<0.001	5.73 (3.01–10.91)	<0.001	4.12 (2.01–8.41)	<0.001
Rural vs Urban	1.68 (1.05–2.69)	0.031	1.61 (1.03–2.53)	0.037	1.49 (0.94–2.37)	0.090
Child Age (Months)	1.03 (1.01–1.05)	0.018	1.07 (1.04–1.11)	<0.001	0.99 (0.96–1.02)	0.410
Household Income (Low vs High)	2.74 (1.66–4.51)	<0.001	2.31 (1.38–3.87)	0.001	2.19 (1.21–3.96)	0.009

Underweight model (Nagelkerke $R^2 = 0.36$, Hosmer–Lemeshow $p = 0.640$), Stunting model ($R^2 = 0.43$, $p = 0.720$), and Wasting model ($R^2 = 0.27$, $p = 0.550$)

DISCUSSION

The present study revealed a high prevalence of malnutrition among children under 5 years of age, with underweight, stunting, and wasting being prevalent. The severity and complexity of malnutrition in this hospital-based population seem to be higher than in community-based populations, which may be because tertiary care centers receive more complicated and severe cases. This suggests that children admitted to the hospital are more severely malnourished, as seen in previous studies [14]. The demographic profile revealed that most affected children were in early childhood, especially below 2 years of age, known to be a very susceptible age for growth faltering. This is attributed to the increased nutritional demands, poor complementary feeding, and increased vulnerability to infections during this period of development [15, 16]. A gender difference was also noted for malnourished cases, with a higher proportion of males, which has also been seen in other studies [17, 18]. This could be attributed to biological susceptibility and also to potential gender differences in child care practices. The

higher proportion of children in this study living in a rural area reflects the ongoing association between malnutrition and disadvantaged circumstances. Living in a rural area is often linked to food insecurity, poor sanitation, and limited access to healthcare, all of which have a detrimental impact on children's nutrition status [17, 19]. The presence of both acute and chronic malnutrition was also suggested by clinical symptoms including bilateral oedema and abdominal distention, which occurred in a substantial number of children, indicating the severity of the disease at a late stage [15, 17]. A crucial result of this study was that there was a negative relationship between the level of education of the mother and the degree of malnutrition observed. Across all indicators, children of illiterate mothers were the most undernourished, and children of highly educated mothers were never severely undernourished. This gradient was similar at all levels of education and indicates that maternal education has a protective effect. Low level of maternal education has been linked in previous studies with high risk of

undernutrition, which was found to stem from poor feeding practices, insufficient health awareness, and delayed health-seeking behaviour [18-20]. Maternal illiteracy was the most consistent predictor of severe malnutrition, even after accounting for other factors, suggesting that it is a factor other than socioeconomic conditions alone. Household income and rural living, however, were also important determinants and confirmed that malnourishment of children is a multifactorial problem, and these factors are educational and economic disadvantage [21-23]. The results indicate that maternal education has an interaction effect on other socioeconomic factors that determine nutritional outcomes of the child. Being younger than age 5 was significantly associated with underweight and stunting, suggesting that the deficits are cumulative with age, especially when dietary intake is suboptimal and repeated infections occur. This reinforces the notion that chronic malnutrition is a process and not an event [15, 16]. The study only concentrated on maternal education, but a number of other factors affect the nutritional status of children, such as feeding practices, infection history, maternal health, and household food insecurity. All this would likely combine with variations in maternal education and socioeconomic status to shape the nutrition of children in this context [20, 21].

This study has certain limitations. Since this was a single-centre, hospital-based, cross-sectional study, the results may be representative only of the hospital systems where the study was conducted; not generalizable to the broader population; and may not infer a cause-and-effect relationship. Furthermore, key variables like maternal diet, breastfeeding and maternal nutritional status were not adequately evaluated and could have affected the reported associations. There was probably underestimation of wasting, as children with acute diarrhoea were excluded from analysis, and the results may be limited to children without acute diarrhoea. Longitudinal studies of nutrition status in large, community-based populations should be conducted in the future to further demonstrate causation and track long-term trends in nutrition status. Detailed behavioural, dietary and maternal health variables should also be added to further studies in order to gain a more complete understanding of the determinants of childhood malnutrition in similar settings.

CONCLUSIONS

This study illustrates that children under 5 years of age are severely under-nourished and there is a significant level of wasting, under-weight and stunting, often co-occurring. Maternal education level was one of the factors identified as affecting the nutritional status of the children, with a higher degree of malnutrition seen in the children of illiterate mothers and a better nutritional status in cases of educated mothers. Improving the health outcomes of

children requires improvement in the education of women, in targeted nutrition awareness-raising activities, and in poverty reduction policies. Combined interventions that tackle the educational and socio-economic determinants of childhood malnutrition should be given specific consideration by policymakers to be effective in reducing the burden of childhood malnutrition in similar settings.

Authors' Contribution

Conceptualization: SA

Methodology: AU, SA, FZ, NK

Formal analysis: SA, RG

Writing and Drafting: AU, SA, SFA, MI, SS

Review and Editing: AU, SA, RG, SFA, FZ, SS, NK

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All 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] Stevens GA, Finucane MM, Paciorek CJ, Flaxman SR, White RA, Donner AJ *et al.* Trends in Mild, Moderate, and Severe Stunting and Underweight, and Progress Towards MDG 1 in 141 Developing Countries: A Systematic Analysis of Population Representative Data. *The Lancet*. 2012 Sep; 380(9844): 824-34. doi: 10.1016/S0140-6736(12)60647-3.
- [2] Wali N, Agho K, Renzaho AM. Past Drivers of and Priorities for Child Undernutrition in South Asia: A Mixed Methods Systematic Review Protocol. *Systematic Reviews*. 2019 Jul; 8(1): 189. doi: 10.1186/s13643-019-1112-7.
- [3] Ali SS, Karim N, Billoo AG, Haider SS. Association of Literacy of Mothers with Malnutrition among Children Under Three Years of Age in Rural Area of District Malir, Karachi. *Children*. 2005; 9(10).
- [4] Hussain S, Naveed M, Sharif MA, Tahir A, Raza HM. Impact of the Mamta UNICEF: A Fortified Food Nutrition Program on Childhood Malnutrition During Pregnancy in Pakistan. *Cureus*. 2025 Apr; 17(4). doi: 10.7759/cureus.81820.
- [5] Ali H, Ali A, Begum F. Utilization of Family Planning Methods among Currently Married Women in Pakistan: Insight from Pakistan Demographic and Health Survey 2017-2018. *Health Care for Women International*. 2024 Jan; 45(1): 129-43. doi: 10.1080/07399332.2021.1902527.
- [6] Ali A. Current Status Of Malnutrition and Stunting in Pakistani Children: What Needs to Be Done?. *Journal*

- of the American College of Nutrition. 2021 Feb; 40(2): 180-92. doi: 10.1080/07315724.2020.1750504.
- [7] Pal A, Manna S, Dalui R, Mukhopadhyay R, Dhara PC. Undernutrition and Associated Factors among Children Aged 5-10 Years in West Bengal, India: A Community-Based Cross-Sectional Study. *Egyptian Pediatric Association Gazette*. 2021 Dec; 69(1): 40. doi: 10.1186/s43054-021-00087-7.
- [8] Khaliq A, Wraith D, Miller Y, Nambiar-Mann S. Prevalence, Trends, and Socioeconomic Determinants of Coexisting Forms of Malnutrition Amongst Children Under Five Years of Age in Pakistan. *Nutrients*. 2021 Dec; 13(12): 4566. doi: 10.3390/nu13124566.
- [9] Boah M, Azupogo F, Amporfro DA, Abada LA. The Epidemiology of Undernutrition and Its Determinants in Children Under Five Years in Ghana. *PLOS ONE*. 2019 Jul; 14(7): e0219665. doi: 10.1371/journal.pone.0219665.
- [10] Adedokun ST and Yaya S. Factors Associated with Adverse Nutritional Status of Children in Sub-Saharan Africa: Evidence from the Demographic And Health Surveys from 31 Countries. *Maternal and Child Nutrition*. 2021 Jul; 17(3): e13198. doi: 10.1111/mcn.13198.
- [11] Keats EC, Das JK, Salam RA, Lassi ZS, Imdad A, Black RE et al. Effective Interventions to Address Maternal and Child Malnutrition: An Update of the Evidence. *The Lancet Child and Adolescent Health*. 2021 May; 5(5): 367-84. doi: 10.1016/S2352-4642(20)30274-1.
- [12] Khan S, Zaheer S, Safdar NF. Determinants of Stunting, Underweight and Wasting among Children < 5 Years of Age: Evidence from 2012-2013 Pakistan Demographic and Health Survey. *BioMC Public Health*. 2019 Apr; 19(1): 358. doi: 10.1186/s12889-019-6688-2.
- [13] Mansukoski L, Qamar H, Perumal N, Aimone A, Bassani DG, Roth DE. Growth Delay: An Alternative Measure of Population Health Based on Child Height Distributions. *Annals of Human Biology*. 2022 Feb; 49(2): 100-8. doi: 10.1080/03014460.2022.2091794.
- [14] Siddiqua M, Zubair A, Kamal A, Ijaz M, Abushal T. Prevalence and Associated Factors of Stunting, Wasting and Underweight of Children Below Five Using Quintile Regression Analysis (PDHS 2017-2018). *Scientific Reports*. 2022 Nov; 12(1): 20326. doi: 10.1038/s41598-022-24063-2.
- [15] Bavurhe RF, Ahmad B, Naaz F, Oduoye MO, Rugendabanga E, Nkundakozera M et al. Epidemiology and Clinical Characteristics of Acute Malnutrition Among Under-5 Children Attending A Rural Hospital in the Democratic Republic of Congo: A Cross-Sectional Study. *Annals of Medicine and Surgery*. 2024 Aug; 86(8): 4402-9. doi: 10.1097/MS9.0000000000002264.
- [16] Chama GC, Siame L, Kapoma C, Hamooya BM, Masenga SK. Severe Acute Malnutrition among Children Under the Age of 5 Years. *PLoS One*. 2024 Aug; 19(8): e0309122. doi: 10.1371/journal.pone.0309122.
- [17] Kahinda JS, Mucaïl-a-Mucaïl T, Kabimbi MM, Kafutshi DM, Ilonda RL, Lukomba DK et al. Sociodemographic, Clinical, and Outcome Profile of Children Under 5 Years of Age Hospitalized for Severe Acute Malnutrition at Sendwe Hospital in Lubumbashi. *Revue de l'Infirmier Congolais*. 2021 Jul; 5(2): 8-14. doi: 10.62126/zqrx.2021522.
- [18] Soofi SB, Khan A, Kureishy S, Hussain I, Habib MA, Umer M et al. Determinants of Stunting among Children Under Five in Pakistan. *Nutrients*. 2023 Aug; 15(15): 3480. doi: 10.3390/nu15153480.
- [19] Singha A, Sinha SK, Khan MA, Mazumder P. Clinical Profile and Outcome of Severe Acute Malnutrition Patients Admitted in a Secondary Level Hospital of Bangladesh. *Scholars Journal of Applied Medical Sciences*. 2024 Jun; 12: 741-5. doi: 10.36347/sjams.2024.v12i06.006.
- [20] Siddiqua M, Shah GH, Mayo-Gamble TL, Zubair A. Determinants of Child Stunting, Wasting, and Underweight: Evidence from 2017 to 2018 Pakistan Demographic and Health Survey. *Journal of Nutrition and Metabolism*. 2023; 2023(1): 2845133. doi: 10.1155/2023/2845133.
- [21] Umar Farooq M, Majeed Nadeem A, Ali F. The Impact of Parents' Education on Child Health from the Perspective of Demographic and Health Survey. *European Online Journal of Natural and Social Sciences*. 2019 Mar; 8(1): 158.
- [22] Marsianah J, Adhani R, Nugroho A, Husaini H, Ilmi B. Relationship of Mother's Characteristics and Nutritional Status in Children in Indonesia. *Jurnal Berkala Kesehatan*. 2022; 8(1): 68-75. doi: 10.20527/jbk.v8i1.11131.
- [23] Berrouyne M and Hami H. Individual and Contextual Factors of Malnutrition in Moroccan Children Under Five. *Bangladesh Journal of Multidisciplinary Scientific Research*. 2024; 9(2): 19-29. doi: 10.46281/bjmsr.v9i2.2221.


Systematic Review


Anatomical Variations of the Circle of Willis and Their Clinical Significance: A Systematic Review

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ARTICLE INFO

Keywords:

Circle of Willis, Anatomical Variation, Collateral Circulation, Ischemic Stroke, Intracranial Aneurysm, Magnetic Resonance Angiography, Computed Tomography Angiography

How to Cite:

Ansari, H., Qayyum, M. A., Waheed, S. A., Bibi, H., Nawaz, A., & Ansar, T. (2026). Anatomical Variations of the Circle of Willis and Their Clinical Significance: A Systematic Review: Anatomical Variations of the Circle of Willis and Their Clinical Significance. *Pakistan Journal of Health Sciences*, 7(6), 164-171. <https://doi.org/10.54393/pjhs.v7i6.3889>

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Received Date: 26th January, 2026

1st Revision Received: 2nd March, 2026

Acceptance Date: 16th March, 2026

Published Date: 30th June, 2026

ABSTRACT

The Circle of Willis (CoW) is the principal intracranial collateral network connecting the anterior and posterior cerebral circulations. Anatomical variations of the CoW are common and may influence cerebral hemodynamics, collateral capacity, ischemic stroke outcomes, and aneurysm development. However, contemporary imaging-based evidence regarding their clinical significance has not been systematically synthesized. **Objectives:** To systematically review recent human imaging studies (2020–2025) evaluating anatomical variations of the Circle of Willis and their reported clinical associations. **Methods:** A systematic search of PubMed, Scopus, and the Cochrane Library was conducted following PRISMA 2020 guidelines. Original human studies assessing CoW anatomy using computed tomography angiography (CTA), magnetic resonance angiography (MRA), or conventional angiography were included. Data extracted included study design, population characteristics, imaging modality, prevalence of major variants, and clinical associations. Risk of bias was assessed using a qualitative domain-based approach. Due to methodological heterogeneity, findings were synthesized narratively. **Results:** Eighteen imaging-based studies were included. Incomplete CoW configurations and posterior communicating artery hypoplasia/aplasia were the most frequently reported variants, with incomplete configurations reported in 30–70% of participants. Several studies demonstrated associations between incomplete configurations and poorer ischemic stroke outcomes, vulnerable intracranial plaque features, and increased odds of intracranial aneurysm. Fetal-type posterior cerebral artery and A1 segment asymmetry were linked to distinct hemorrhagic and aneurysmal patterns. **Conclusions:** Anatomical variations of the Circle of Willis are highly prevalent and clinically relevant. Standardized reporting of CoW configuration may enhance cerebrovascular risk stratification and inform neurovascular decision-making.

INTRODUCTION

The Circle of Willis (CoW) is a polygonal arterial network located at the base of the brain that enables collateral circulation between the anterior and posterior cerebral circulations. This anatomical structure plays a critical role in maintaining cerebral perfusion during proximal arterial stenosis or occlusion [1]. Although traditionally described as a symmetrical and complete arterial ring, a complete Circle of Willis is found only in a minority of individuals,

while segmental hypoplasia, aplasia, and asymmetry are common in both normal and diseased populations [2]. The physiological and clinical relevance of these anatomical variations is increasingly recognized. The presence or absence of communicating arteries influences collateral capacity, determines redistribution of cerebral blood flow, and may alter tissue vulnerability during acute ischemic events [3]. Experimental and clinical studies suggest that

incomplete configurations may limit compensatory flow during large-vessel occlusion, contributing to larger infarct volumes and poorer functional outcomes. Conversely, well-developed communication pathways may provide protective collateral channels that preserve perfusion in critical regions [4]. Beyond ischemic stroke, variations in the Circle of Willis have also been implicated in the pathogenesis of intracranial aneurysms and hemorrhagic stroke. Asymmetries that alter flow dynamics, such as anterior cerebral artery A1 segment asymmetry or fetal-type posterior cerebral artery, may create focal hemodynamic stress at arterial bifurcations and perforator origins [5]. These altered flow states have been proposed as contributing factors in aneurysm formation, aneurysm progression, and specific hemorrhagic phenotypes involving deep or posterior circulation territories [6].

Although imaging-based studies evaluating Circle of Willis variations have increased substantially in recent years, the available evidence remains heterogeneous in terms of study design, imaging modality, operational definitions of anatomical variants, and reporting of clinical outcomes. Most studies are single-center and referral-based, limiting generalizability. Furthermore, despite advances in computed tomography angiography (CTA) and high-resolution magnetic resonance angiography (MRA) that have enhanced visualization of intracranial arterial anatomy, a contemporary synthesis of recent evidence is lacking. Therefore, this systematic review was conducted to synthesize recent human imaging studies (2020–2025) evaluating anatomical variations of the Circle of Willis and their clinical significance. This review aims to summarize the prevalence of major CoW variants and examine their reported associations with ischemic stroke outcomes, intracranial aneurysms, and hemorrhagic cerebrovascular disease.

METHODS

This systematic review aimed to assess anatomical variations of the Circle of Willis (CoW) and their clinical implications in human populations. The review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. The methodological framework, including objectives, eligibility criteria, search strategy, and data synthesis approach, was predefined before conducting the review to enhance transparency and reproducibility. Although a structured protocol was developed a priori, it was not prospectively registered in an international database (e.g., PROSPERO), which is acknowledged as a limitation. An electronic literature search was conducted in three major databases: PubMed, Scopus, and the Cochrane Library. The search included studies published between January 2020 and December

2025. Both controlled vocabulary and free-text terms were used to maximize search sensitivity. The primary PubMed search strategy was: ("Circle of Willis" OR "cerebral arterial circle") AND (variation OR variant OR anomaly OR hypoplasia OR aplasia OR "incomplete circle") AND (angiography OR "computed tomography angiography" OR CTA OR "magnetic resonance angiography" OR MRA). Equivalent search strategies were adapted for Scopus and the Cochrane Library. In addition, the reference lists of all included studies were manually screened to identify any potentially eligible articles not captured in the electronic search. Studies were selected based on predefined inclusion and exclusion criteria. Eligible studies were original human research published between 2020 and 2025 that evaluated anatomical variations of the Circle of Willis using imaging modalities such as computed tomography angiography (CTA), magnetic resonance angiography (MRA), or conventional angiography. Studies were required to report either the prevalence of CoW variants or their clinical associations with cerebrovascular outcomes. Animal studies, case reports, narrative reviews, systematic reviews, meta-analyses, pilot studies, conference abstracts without full text, and studies that did not report Circle of Willis configuration were excluded. All identified records were imported into reference management software, and duplicates were removed before screening. Titles and abstracts were independently screened by two reviewers according to predefined eligibility criteria. Full-text articles of potentially relevant studies were subsequently retrieved and independently assessed for eligibility by the same two reviewers. Disagreements at any stage were resolved through discussion and consensus. Formal inter-rater agreement statistics (e.g., kappa coefficient) were not calculated, which is acknowledged as a methodological limitation. The study selection process followed the PRISMA 2020 framework. A total of 515 records were identified through database searching. After the removal of records before screening, 350 records underwent title and abstract screening. Fifty-three full-text articles were assessed for eligibility, and 18 studies were ultimately included in the qualitative synthesis. Flow diagram illustrating the identification, screening, eligibility assessment, and inclusion of studies in this systematic review. A total of 515 records were identified from PubMed (n=210), Scopus (n=185), and Cochrane Library (n=120). After removal of 165 records before screening (duplicates and other exclusions), 350 records were screened. Out of these, 285 were excluded at the title and abstract level. Sixty-five full-text reports were sought for retrieval, of which 12 were not retrieved. Fifty-three full-text articles were assessed for eligibility, and 35 were excluded based on predefined criteria. Ultimately, 18 studies were included in the qualitative synthesis (Figure 1).

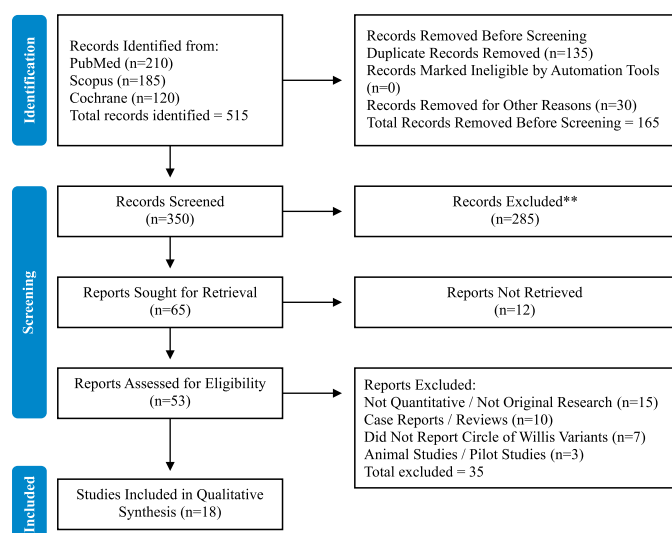


Figure 1: Study Selection Process

Data extraction was performed using a standardized data extraction form. Extracted variables included first author and year of publication, study design, sample size, characteristics of the study population, imaging modality and protocol, definitions of anatomical variants, prevalence of major CoW variants, reported clinical associations, and effect estimates such as odds ratios where available. Data extraction was conducted independently by two reviewers, and discrepancies were resolved through consensus to ensure data accuracy and completeness. Standardized definitions of “incomplete Circle of Willis” and “hypoplasia” were not uniformly applied

across included studies. Diameter thresholds used to define hypoplasia and criteria for completeness varied between studies, contributing to methodological heterogeneity. This variability was documented during data extraction and considered during qualitative synthesis. Risk of bias was assessed using a qualitative domain-based approach tailored to observational imaging studies. Three principal domains were evaluated: selection bias (population representativeness), measurement bias (imaging protocol standardization and clarity of variant definitions), and control of confounding (use of multivariable or adjusted analyses when reporting associations). Formal risk-of-bias tools designed for randomized controlled trials were not applicable because the majority of included studies were cross-sectional or observational imaging studies. Each study was categorized as having low, moderate, or low-moderate overall risk of bias. Due to substantial heterogeneity in study design, imaging modalities, operational definitions of anatomical variants, outcome measures, and population characteristics, a quantitative meta-analysis was not performed. The decision to refrain from pooled statistical synthesis was based on methodological variability that precluded meaningful statistical aggregation. Instead, prevalence ranges and reported associations were summarized descriptively. A structured qualitative narrative synthesis was conducted to compare patterns of anatomical variation and reported clinical associations across studies.

RESULTS

A total of 18 original human imaging studies published between 2020 and 2025 were included in the qualitative synthesis. Across studies, Circle of Willis (CoW) anatomy was assessed predominantly using CTA and MRA in symptomatic, referral-based, or population cohorts. The study summarizes the characteristics of the 18 included studies (2020–2025), including design, population, imaging modality, reported variants, and clinical relevance. Most studies were cross-sectional or observational and mainly included symptomatic or referred cerebrovascular populations, with sample sizes ranging from 85 to >1,000 participants. CTA and MRA were the most frequently used modalities, reflecting modern imaging-based evaluation of CoW variants (Table 1).

Table 1: Characteristics of Included Studies (2020–2025) on Anatomical Variations of the Circle of Willis and Their Clinical Significance

Sr. No.	References	Design / Population	Modality	Key CoW Findings	Clinical Significance Reported
1	[7]	Cross-sectional; suspected cerebrovascular pathology (n=95)	CTA	Variants in 55%; PCoA hypoplasia common; fetal PCA present	Variants noted as important for aneurysm/vascular planning
2	[8]	Retrospective; symptomatic patients (n=231)	3T MRA	PCoA hypoplasia and fetal-type PCA documented	Highlights the prognostic/diagnostic relevance of posterior variants
3	[9]	Large observational; ischemic stroke vs controls (>1000 stroke)	Imaging-based CoW assessment	Higher variant prevalence in the stroke cohort	Examined severity/in-hospital prognosis associations
4	[10]	Cross-sectional; CTA dataset (n=255)	CTA	CoW variants characterized alongside stenosis patterns	Linked variants with cerebral/cervical stenosis patterns (plus automated analysis)
5	[11]	Cross-sectional; children vs adults	MRA	CoW morphometric differences by age group	Developmental anatomy implications for flow/collateral interpretation
6	[12]	Cross-sectional; suspected cerebrovascular disease (n=102)	64-MSCT angiography	Anterior and posterior pattern classifications: ACoA/PCoA aplasia/hypoplasia patterns	Relevance for endovascular planning in their cohort

7	[13]	Cross-sectional; large clinical sample (n=867)	MRA	Detailed variant prevalence; incomplete CoW frequent	Collateral-pathway implications emphasized
8	[14]	Observational; stroke patients	Imaging-based CoW completeness	Incomplete CoW common (1/3)	An incomplete CoW is associated with worse functional outcome (adjusted)
9	[15]	Cross-sectional; clinical referrals (n=264)	MRA	Variation frequencies reported	Emphasized clinical importance for neurovascular procedures
10	[16]	Prospective cross-sectional; tertiary MRA cohort (n=152)	MRA	Complete CoW 24%; posterior variants common (PCoA aplasia)	Links discussed with future cerebrovascular risk and demographics
11	[17]	Observational association; ICAS/AIS focus	Vascular imaging	Incomplete CoW phenotypes categorized	Incomplete CoW associated with vulnerable plaque features and AIS
12	[18]	Population study (Tromsø)	Imaging-based CoW variants	Incomplete CoW variants defined	An incomplete CoW is associated with higher odds of intracranial aneurysm
13	[19]	Observational; anterior circulation ischemic stroke	CoW communicating artery presence	Presence/absence of communicating arteries assessed	Communicating arteries associated with higher functional recovery rates
14	[20]	Retrospective; cerebral angiography/MRA images (n=85)	Angiography/MRA	Age/sex differences in completeness and vessel diameters	Highlights demographic influences relevant to interpretation/planning
15	[21]	Observational; hypertensive thalamic hemorrhage	Imaging-defined fetal PCA	Fetal-type PCA presence assessed	Reported association between fetal PCA and hemorrhage-related phenotype
16	[22]	Cross-sectional; archived CT brain images (n=200)	CT-based vascular assessment	Posterior/anterior communicating segment variants	Emphasized implications for cerebrovascular risk/interpretation
17	[23]	Retrospective cross-sectional (n=384)	3T MRA	Patterns and prevalence of CoW variants	Clinical relevance framed around cerebrovascular health
18	[24]	Association study; aneurysm vs control	CTA	A1 dysplasia/variation analyzed	A1 variation associated with MCA aneurysm occurrence/rupture indicators

The results summarize the most frequently reported CoW variants and the clinical associations described across included studies. The most commonly reported variants were posterior communicating artery (PCoA) hypoplasia/aplasia and incomplete Circle of Willis configurations. Across studies, incomplete configurations were reported in approximately 30–70% of participants, depending on the study population and operational definitions. Several studies reported associations between incomplete configurations and poorer ischemic stroke outcomes, vulnerable intracranial plaque features, or increased odds of intracranial aneurysm (Table 2).

Table 2: Major Patterns of Circle of Willis Variations and Their Reported Clinical Associations in Included Studies

Variant / Configuration	References	Typical Prevalence / Description	Main Clinical Associations Reported
Posterior communicating artery (PCoA) hypoplasia/aplasia	[16, 22]	Most frequent posterior variant; often unilateral or bilateral	Reduced collateral capacity; relevance for stroke prognosis and endovascular planning
Incomplete Circle of Willis (any segment absent/hypoplastic)	[13, 17]	Reported in 30–70%, depending on the definition and population	Worse functional outcome after stroke; higher odds of intracranial aneurysm; vulnerable plaque features
Fetal-type posterior cerebral artery (fetal PCA)	[7, 8]	Present in a substantial minority; usually unilateral	Associated with hemorrhagic phenotype; important for posterior circulation flow patterns
Anterior cerebral artery A1 segment asymmetry/dysplasia	[17, 24]	Variable frequency; often unilateral	Associated with the middle cerebral artery aneurysm occurrence and altered flow distribution
Absence or hypoplasia of the anterior communicating artery (ACoA)	[12, 13]	Less frequent than PCoA variants	Impaired anterior collateral circulation; relevance for procedural planning
Age-related morphological differences	[11, 20]	Children show different calibers and configurations than adults	Developmental and demographic influence on collateral interpretation
Presence of complete communicating pathways	[19]	Minority of patients with a fully complete Circle of Willis	Higher rates of functional recovery after anterior circulation stroke

The study outlines the methodological distribution of included studies by imaging modality, study design, and study population. MRA was the most frequently used modality, particularly in prevalence-focused studies, whereas CTA was more commonly used in studies examining acute stroke and aneurysm-related outcomes. Cross-sectional designs predominated, while a smaller subset of studies assessed clinical associations with stroke outcomes, aneurysm presence, or hemorrhagic phenotypes (Table 3).

Table 3: Distribution of Imaging Modalities, Study Designs, and Study Populations in Included Studies(2020–2025)

Category	Subgroup	References	Key Observations
Imaging Modality	Computed tomography angiography (CTA / CT-based)	[7, 22]	CTA was mainly used in acute stroke and aneurysm-focused studies, allowing detailed segmental assessment
	Magnetic resonance angiography (MRA)	[8, 11]	MRA was the most frequently used modality, particularly in prevalence and population-based studies
	Mixed/conventional angiography	[20]	Used for detailed morphometric and anatomical evaluation
Study Design	Cross-sectional prevalence studies	[7, 15]	Predominant design: focused on describing frequency and patterns of Circle of Willis variants
	Observational association studies	[18, 19]	Explored associations with stroke outcome, aneurysm risk, plaque vulnerability, and hemorrhagic phenotypes
	Prospective imaging cohort	[16]	Provided standardized imaging protocol and demographic analysis
Study Population	Symptomatic cerebrovascular patients	[23, 24]	Majority of studies involved clinically relevant stroke or vascular disease populations
	General / referred imaging population	[15, 16]	Used primarily for prevalence estimates of Circle of Willis variants
	Pediatric/developmental population	[11]	Only study specifically addressing developmental differences

The results present the domain-based qualitative risk-of-bias assessment across the included studies. Most studies were judged to have a moderate overall risk of bias, primarily due to referral-based sampling and limited population representativeness. Measurement bias was generally low in studies using standardized CTA or high-field MRA protocols, whereas confounding control varied across association studies depending on whether multivariable adjustment was performed (Table 4).

Table 4: Risk of Bias Assessment of Included Studies Using a Domain-Based Qualitative Approach

References	Selection Bias (Population Representativeness)	Measurement Bias (Imaging and Definitions)	Confounding Control	Overall Risk of Bias
[7]	Moderate (single-center, symptomatic cohort)	Low (standard CTA protocol)	Not applicable	Moderate
[8]	Moderate (referred clinical population)	Low (3T MRA, clear definitions)	Not applicable	Moderate
[9]	Moderate	Low	Moderate (adjusted analyses)	Moderate
[10]	Moderate	Low	Low (multivariable + automated model)	Low-Moderate
[11]	Low (healthy controls included)	Low	Not applicable	Low
[12]	Moderate	Moderate (mixed CT definitions)	Not applicable	Moderate
[13]	Moderate	Low (standard MRA protocol)	Not applicable	Moderate
[14]	Moderate	Low	Low (multivariable outcome model)	Low-Moderate
[15]	Moderate	Moderate	Not applicable	Moderate
[16]	Moderate	Low	Not applicable	Moderate
[17]	Moderate	Low	Low (adjusted plaque analysis)	Low-Moderate
[18]	Low (population-based cohort)	Low	Low (multivariable model)	Low
[19]	Moderate	Low	Low (adjusted functional outcome model)	Low-Moderate
[20]	Moderate	Low	Not applicable	Moderate
[21]	Moderate	Low	Low (adjusted hemorrhage model)	Low-Moderate
[22]	Moderate	Moderate	Not applicable	Moderate
[23]	Moderate	Low	Not applicable	Moderate
[24]	Moderate	Low	Low (case-control adjustment)	Low-Moderate

DISCUSSION

The present systematic review synthesizes contemporary imaging-based evidence (2020–2025) regarding anatomical variations of the Circle of Willis (CoW) and their clinical relevance. Across included studies, incomplete CoW configurations and posterior communicating artery (PCoA) hypoplasia/aplasia emerged as the most frequently reported variants, whereas a fully complete arterial circle was consistently observed in a minority of individuals. This finding is consistent with recent large imaging cohorts

demonstrating that incomplete configurations represent the predominant anatomical pattern in adult populations [25, 26]. Beyond prevalence, this review demonstrates that CoW configuration has meaningful implications for collateral flow and ischemic vulnerability. Incomplete configurations and absent communicating segments may limit compensatory redistribution of blood flow during large-vessel occlusion, potentially contributing to larger infarct volumes and poorer functional recovery. Recent

systematic and imaging-based studies have similarly reported that preserved collateral anatomy is associated with improved functional outcomes after ischemic stroke [27]. These findings support the hypothesis that structural collateral anatomy directly influences hemodynamic resilience in acute ischemic events. In the context of mechanical thrombectomy, preserved communicating pathways may enhance procedural efficacy by maintaining perfusion to distal territories, as suggested by contemporary endovascular outcome studies [28]. The relationship between CoW variants and intracranial aneurysm formation is also highlighted in this synthesis. Anterior cerebral artery (A1) segment asymmetry appears to alter flow dominance within the anterior communicating complex, potentially increasing focal wall shear stress and aneurysm susceptibility. Hemodynamic modeling studies have demonstrated that altered flow patterns within asymmetric anterior circulation segments may predispose to aneurysm development [29]. Similarly, clinical imaging studies have reported associations between anterior circulation dominance and aneurysm characteristics [30]. These findings suggest that CoW morphology may influence aneurysm biology through flow redistribution rather than acting as a purely incidental anatomical variant. Posterior circulation variants, particularly fetal-type posterior cerebral artery (fetal PCA), were also associated with distinct clinical phenotypes. Fetal PCA shifts perfusion dependency toward the internal carotid system, which may modify posterior circulation hemodynamics. Recent studies have reported associations between fetal PCA configuration and specific hemorrhagic or posterior circulation stroke patterns [31, 32]. Although the exact causal mechanisms remain incompletely defined, consistent associations across imaging cohorts indicate potential prognostic relevance. Age- and sex-related morphological differences were observed in selected studies. Developmental variation in CoW anatomy suggests that collateral capacity may not be static across the lifespan. Population-based anatomical studies have demonstrated that vessel caliber and completeness vary with age and sex [33, 34]. Pediatric and adult configurations differ in vessel morphology, which may partly explain heterogeneity in cerebrovascular risk profiles. Importantly, methodological heterogeneity across studies must be considered when interpreting prevalence ranges. Operational definitions of "incomplete CoW" and "hypoplasia" varied substantially, and imaging modality (CTA vs. MRA) may influence detection rates of small-caliber segments. Prior imaging comparison studies have shown imperfect agreement between modalities in detecting small communicating arteries [35]. Such variability limits direct quantitative comparison across cohorts and underscores the need for standardized

definitions.

This review has several limitations. First, the majority of included studies were single-center and referral-based, raising the possibility of spectrum bias and limiting generalizability to broader populations. Second, heterogeneity in imaging protocols and variant definitions precluded quantitative meta-analysis and limited pooled prevalence estimation. Third, formal inter-rater agreement statistics were not calculated during screening, and standardized risk-of-bias tools specific to observational imaging studies are lacking. Fourth, because most included studies were cross-sectional, causal inference between anatomical configuration and clinical outcomes remains limited. Future research should prioritize large-scale, multicenter population-based studies using harmonized definitions of CoW completeness and hypoplasia. Standardized imaging acquisition protocols and consensus-based reporting frameworks would improve comparability across studies. Prospective longitudinal designs are needed to clarify causal relationships between CoW morphology and cerebrovascular outcomes. Furthermore, integration of computational flow modeling with clinical outcome data may provide mechanistic insight into how specific configurations influence hemodynamic stress and stroke vulnerability.

CONCLUSIONS

This systematic review demonstrates that anatomical variations of the Circle of Willis, particularly incomplete configurations and posterior communicating artery hypoplasia or aplasia, are common findings in contemporary imaging cohorts. Evidence suggests that these variants are associated with altered collateral capacity, ischemic stroke outcomes, aneurysm susceptibility, and distinct hemorrhagic phenotypes. Standardized and routine reporting of CoW configuration in neurovascular imaging may enhance risk stratification, inform procedural planning, and improve individualized clinical decision-making. Future harmonized, population-based, and longitudinal investigations are required to refine prognostic models and clarify the mechanistic pathways linking vascular anatomy with cerebrovascular disease.

Authors' Contribution

Conceptualization: HA

Methodology: MAQ, SAW, AN, TA

Formal analysis: SAW, AN, TA

Writing and Drafting: HA, MAQ, HB, AN, TA

Review and Editing: HA, MAQ, SAW, HB, AN, TA

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All 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] Kashtiara A, Beldé S, Menovsky T, Morales EV. Anatomical Variations and Anomalies of the Anterior Communicating Artery Complex. *World Neurosurgery*. 2024 Mar; 183: e218-27. doi: 10.1016/j.wneu.2023.12.060.
- [2] Bulcha G, Bekele A, Muche A. Preliminary Study of Morphological Variability in the Circle of Willis and Its Clinical Significance in Ethiopia: A Cadaveric Study. *Ethiopian Journal of Health Sciences*. 2025 Jun; 35(3). doi: 10.4314/ejhs.v35i3.6.
- [3] Negatie HM, Kebede MA, Abate AD, Admassie SH, Worku AB, Ahmed HT et al. Association of Circle of Willis Variants with Stroke and Aneurysm: Insights from a Tertiary Hospital in Ethiopia. *BioMed Central Neurology*. 2025 Feb; 25(1): 73. doi: 10.1186/s12883-025-04082-y.
- [4] Tritsch T, Shoja MM, Schleffer A, Tubbs RS. Examining Atherosclerosis Patterns in the Circle of Willis: A Case Study of Duplicated Anterior Communicating Artery. *Cureus*. 2024 Jan; 16(1). doi: 10.7759/cureus.53321.
- [5] Karahan M, Kocabeyoglu SS, Kervan U, Sert DE, Aygun E, Tola M et al. Effects of Continuous-Flow Left Ventricular Assist Devices on Cerebral Hemodynamics. *Artificial Organs*. 2020 May; 44(5): 457-64. doi: 10.1111/aor.13616.
- [6] Berghout BP, Soyupak RF, Ikram MK, Bos D. Variations in Intracranial Arterial Anatomy of the Circle of Willis and Their Association with Arteriosclerosis in Patients with Ischemic Cerebrovascular Disease. *International Journal of Stroke*. 2025 Aug; 20(7): 843-51. doi: 10.1177/17474930251322678.
- [7] Dhakal P, Kayastha P, Paudel S, Suwal S, Sharma MR, Ghimire RK. Anatomical Variations in Circle of Willis in Patients Undergoing CT Cerebral Angiography in a Tertiary Hospital in Nepal: A Descriptive Cross-Sectional Study. *Journal of the Nepal Medical Association*. 2020 Dec; 58(232): 1065. doi: 10.31729/jnma.5893.
- [8] Bhanu SP, Pentyala S, Sankar DK. Incidence of Hypoplastic Posterior Communicating Artery and Fetal Posterior Cerebral Artery in Andhra Population of India: A Retrospective 3-Tesla Magnetic Resonance Angiographic Study. *Anatomy and Cell Biology*. 2020 Sep; 53(3): 272-8. doi: 10.5115/acb.20.066.
- [9] De Caro J, Ciacciarelli A, Tessitore A, Buonomo O, Calzoni A, Francalanza I et al. Variants of the Circle of Willis in Ischemic Stroke Patients. *Journal of Neurology*. 2021 Oct; 268(10): 3799-807. doi: 10.1007/s00415-021-10454-4.
- [10] Hou J, Gao MY, Pan AZ, Wang QD, Liu B, Jin YB et al. Relationship Between Circle of Willis Variations and Cerebral or Cervical Arteries Stenosis Investigated by Computer Tomography Angiography and a Multitask Convolutional Neural Network. *Journal of Healthcare Engineering*. 2021; 2021(1): 6024352. doi: 10.1155/2021/6024352.
- [11] Guilliams KP, Gupta N, Srinivasan S, Binkley MM, Ying C, Couture L et al. MR Imaging Differences in the Circle of Willis Between Healthy Children and Adults. *American Journal of Neuroradiology*. 2021 Nov; 42(11): 2062-9. doi: 10.3174/ajnr.A7290.
- [12] Hoang TM, Huynh TV, Ly AV, Pham MV. The Variations in the Circle of Willis on 64-Multislice Spiral Computed Tomography. *Trends in Medical Sciences*. 2022; 2(3): e128729. doi: 10.5812/tms-128729.
- [13] Kızılöz V, Kantarcı M, Kahraman Ş. Evaluation of Circle of Willis Variants Using Magnetic Resonance Angiography. *Scientific Reports*. 2022 Oct 20; 12(1): 17611. doi: 10.1038/s41598-022-21833-w.
- [14] Lin E, Kamel H, Gupta A, RoyChoudhury A, Girgis P, Glodzik L. Incomplete Circle of Willis Variants and Stroke Outcome. *European Journal of Radiology*. 2022 Aug; 153: 110383. doi: 10.1016/j.ejrad.2022.110383.
- [15] Kaul NV, Pandey VD, Dixit VP, Gupta V, Rastogi R, Shukla S. A Comprehensive Study of Magnetic Resonance Angiography of Circle of Willis in Population of Western Uttar Pradesh. *International Journal of Health Sciences*. 2022; 6(S6): 6764-74. doi: 10.53730/ijhs.v6nS6.11304.
- [16] Diljohn J, Rampersad F, Maharaj P, Parmesar K. Anatomical Variations in the Circle of Willis on Magnetic Resonance Angiography in a South Trinidad Population. *British Journal of Radiology: Open*. 2024 Jan; 6(1): tzad002. doi: 10.1093/bjro/tzad002.
- [17] Wang H, Shen L, Zhao C, Liu S, Wu G, Wang H et al. The Incomplete Circle of Willis Is Associated with Vulnerable Intracranial Plaque Features and Acute Ischemic Stroke. *Journal of Cardiovascular Magnetic Resonance*. 2023 Feb; 25(1): 23. doi: 10.1186/s12968-023-00931-2.
- [18] Hindenes LB, Ingebrigtsen T, Isaksen JG, Håberg AK, Johnsen LH, Herder M et al. Anatomical Variations in the Circle of Willis Are Associated with Increased

- Odds of Intracranial Aneurysms: The Tromsø Study. *Journal of the Neurological Sciences*. 2023 Sep; 452: 120740. doi: 10.1016/j.jns.2023.120740.
- [19] Sablić S, Dolić K, Kraljević I, Budimir Mršić D, Čičmir-Vestić M, Benzon B et al. The Presence of Communicating Arteries in the Circle of Willis Is Associated with a Higher Rate of Functional Recovery After Anterior Circulation Ischemic Stroke. *Biomedicines*. 2023 Nov; 11(11): 3008. doi: 10.3390/biomedicines11113008.
- [20] Alharbi Y and Al Saffar RA. Anatomical Study of Variations in the Configurations of the Circle of Willis in Relation to Age, Sex, and Diameters of the Components. *Anatomy and Cell Biology*. 2024 Dec; 57(4): 579-91. doi: 10.5115/acb.24.020.
- [21] Pu T, Zhong X, Jiang G, Wu Z, He S, Long Y et al. Association Between the Fetal-Type Posterior Cerebral Artery and Hypertensive Thalamic Hemorrhage. *Brain and Behavior*. 2024 Nov; 14(11): e70147. doi: 10.1002/brb3.70147.
- [22] Zaki SM, Shaaban MH, Abd Al Galeel WA, El Husseiny AA. Configuration of the Circle of Willis and Its Two Parts among Egyptian: A Magnetic Resonance Angiographic Study. *Folia Morphologica*. 2019; 78(4): 703-9. doi: 10.5603/FM.a2019.0015.
- [23] Thapa S, Desai R, Basnet J, Thapa S. Prevalence and Patterns of Circle of Willis Variants in Civil Service Hospital: A Retrospective Cross-Sectional Study Using 3 Tesla Magnetic Resonance Angiography. *Journal of the Nepal Medical Association*. 2025 Jun; 63(286). doi: 10.31729/jnma.9057.
- [24] Li X, Yue X, Xie Z, Nie L, Huang G, Peng Y et al. Association of Middle Cerebral Artery Aneurysms and Variation of the A1 Segment. *Plos One*. 2025 Mar; 20(3): e0319500. doi: 10.1371/journal.pone.0319500.
- [25] Jiao S, Zhi J, Li M, Chen L, Gong Z, Ma H et al. Superior Circle of Willis Configuration in Oldest-Old Patients with First-Ever Ischemic Stroke: A Retrospective Clinical-Radiological Study on Its Association with Delayed Onset and Enhanced Female Prominence. *BioMed Central Neurology*. 2025 Oct; 25(1): 443. doi: 10.1186/s12883-025-04456-2.
- [26] Barakoti A, Regmi S, Khadka H. Anatomical Variation of Circle of Willis in Computed Tomographic Angiography Study. *Journal of Gandaki Medical College-Nepal*. 2025 Jun; 18(1): 14-20. doi: 10.3126/jgmc-n.v18i1.73298.
- [27] Širvinskis A, Lengvenis G, Ledas G, Mosenko V, Lukoševičius S. Circle of Willis Configuration and Thrombus Localization Impact on Ischemic Stroke Patient Outcomes: A Systematic Review. *Medicina*. 2023 Dec; 59(12): 2115. doi: 10.3390/medicina59122115.
- [28] Renieri L, Valente I, Dmytriw AA, Puri AS, Singh J, Nappini S et al. Mechanical Thrombectomy Beyond the Circle of Willis: Efficacy and Safety of Different Techniques for M2 Occlusions. *Journal of Neuro-Interventional Surgery*. 2022 Jun; 14(6): 546-50. doi: 10.1136/neurintsurg-2021-017425.
- [29] Shen Y, Molenberg R, Bokkers RP, Wei Y, Uyttenboogaart M, van Dijk JM. The Role of Hemodynamics Through the Circle of Willis in the Development of Intracranial Aneurysm: A Systematic Review of Numerical Models. *Journal of Personalized Medicine*. 2022 Jun; 12(6): 1008. doi: 10.3390/jpm12061008.
- [30] Zhong W, Du Y, Guo Q, Tan X, Li T, Chen C et al. The Clinical and Morphologic Features Related to Aneurysm Wall Enhancement and Enhancement Pattern in Patients with Anterior Circulation Aneurysms. *World Neurosurgery*. 2020 Feb; 134: e649-56. doi: 10.1016/j.wneu.2019.10.156.
- [31] Davidoiu AM, Mincă DI, Rusu MC, Hostiuc S, Toader C. The Fetal Type of Posterior Cerebral Artery. *Medicina*. 2023 Jan; 59(2): 231. doi: 10.3390/medicina59020231.
- [32] Salerno A, Strambo D, Nannoni S, Dunet V, Michel P. Patterns of Ischemic Posterior Circulation Strokes: A Clinical, Anatomical, and Radiological Review. *International Journal of Stroke*. 2022 Aug; 17(7): 714-22. doi: 10.1177/17474930211046758.
- [33] Wijesinghe P, Steinbusch HW, Shankar SK, Yasha TC, De Silva KR. Circle of Willis Abnormalities and Their Clinical Importance in Ageing Brains: A Cadaveric Anatomical and Pathological Study. *Journal of Chemical Neuroanatomy*. 2020 Jul; 106: 101772. doi: 10.1016/j.jchemneu.2020.101772.
- [34] Sonare S and Nikam P. A Cross-Sectional Study on the Variations of the Circle of Willis in Human Cadavers and Its Clinical Significance. *European Journal of Cardiovascular Medicine*. 2025 May; 15: 574-8.
- [35] Li J, Wang J, Wei XE, Zhao YW, Wang F, Li YH. Examination of Structural Variations of the Circle of Willis by 3D Time-of-Flight Magnetic Resonance Angiography. *Frontiers in Neuroscience*. 2020 Feb; 14: 71. doi: 10.3389/fnins.2020.00071.


Systematic Review


Sleep Deprivation and Its Effects on Cognitive and Neurophysiological Functions: A Systematic Review

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ARTICLE INFO

Keywords:

Sleep Deprivation, Cognition, Electroencephalography, Event-Related Potentials, Functional MRI, Vigilant Attention

How to Cite:

Mehwish, R., Riaz, A., Ajmal, A., Hameed, S., Baig, I. M., & Samad, A. (2026). Sleep Deprivation and Its Effects on Cognitive and Neurophysiological Functions: A Systematic Review: Sleep Deprivation and Its Effects on Cognitive and Neurophysiological Functions. *Pakistan Journal of Health Sciences*, 7(6), 172-181. <https://doi.org/10.54393/pjhs.v7i6.3890>

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Received Date: 26th January, 2026

1st Revision Received: 5th March, 2026

Acceptance Date: 16th March, 2026

Published Date: 30th June, 2026

ABSTRACT

Sleep deprivation is common among students, healthcare workers, and shift-based occupations and is associated with impaired cognition and altered brain function. Modern electrophysiological and neuroimaging methods (EEG/ERP and functional neuroimaging) help explain neurophysiological mechanisms underlying sleep-loss-related cognitive impairment.

Objectives: To systematically evaluate the effects of sleep deprivation on cognitive outcomes and neurophysiological measures in human participants. **Methods:** This systematic review followed PRISMA 2020 guidelines. PubMed, Scopus, and the Cochrane Library were searched for studies published from January 2021 to December 2025. Eligible studies were original quantitative human research reporting at least one cognitive outcome (e.g., attention, working memory, executive function, reaction time) and one neurophysiological measure (EEG, ERP, fMRI, fNIRS, or multimodal) using total or partial sleep deprivation. Risk of bias was assessed using RoB 2 and the NIH Quality Assessment Tool. Due to heterogeneity, findings were synthesized narratively. **Results:** Sixteen studies were included. Sleep deprivation consistently impaired vigilant attention and reaction time (increased PVT lapses and slower responses). Executive control and cognitive flexibility were frequently reduced, whereas working memory effects were task- and load-dependent. Neurophysiological changes included altered EEG activity, modulation of ERP components (P300, N2, CNV), and disrupted connectivity in frontoparietal and default mode networks. **Conclusions:** Sleep deprivation produces reproducible attention and executive deficits, accompanied by parallel neurophysiological alterations, underscoring the critical role of sleep in performance and safety.

INTRODUCTION

Sleep plays a crucial role in optimal cognitive functioning and stable neurophysiological processes. Partial sleep restriction and acute total sleep deprivation are increasingly common in modern educational and professional environments, particularly among students, healthcare workers, and individuals engaged in shift-based occupations [1]. Even short-term sleep deprivation can negatively affect several cognitive domains, including attention, reaction time, working memory, and executive control, which in turn may influence learning ability, clinical

decision-making, and safety-sensitive performance [2, 3]. The cognitive effects of sleep deprivation are not uniform across domains. Vigilant attention and sustained performance, often measured using the Psychomotor Vigilance Test (PVT) appear to be particularly vulnerable to sleep loss and are typically characterized by slower reaction times and increased attentional lapses [4]. Executive functions such as inhibitory control, proactive and reactive control, and cognitive flexibility may also deteriorate, especially during prolonged sleep deprivation

or in situations requiring strong top-down cognitive regulation [5]. In contrast, some studies have reported relative preservation of certain working-memory outcomes under specific sleep restriction paradigms, suggesting that vulnerability to sleep loss may depend on task characteristics and cognitive load rather than representing a uniform impairment across all cognitive domains [6, 7]. A growing body of neurophysiological research has demonstrated that sleep deprivation is associated with measurable alterations in brain activity. Electroencephalography (EEG) studies have identified changes in resting-state aperiodic activity and functional network organization, which may reflect disrupted arousal regulation and reduced cortical efficiency [8]. Event-related potential (ERP) research has also shown modulation of attention- and control-related components, including P300, N2, and contingent negative variation (CNV), indicating that sleep deprivation may impair information-processing capacity and preparatory cognitive control mechanisms [9]. Similarly, functional neuroimaging studies have reported altered stability and connectivity within large-scale brain networks, including reduced engagement of frontoparietal control systems and changes in default mode and thalamic network activity, which are associated with behavioral impairments and sleepiness-related declines in performance [10].

Despite the extensive literature on sleep deprivation, recent years have witnessed rapid advances in multimodal neurophysiological techniques, including EEG/ERP, functional magnetic resonance imaging (fMRI), and functional near-infrared spectroscopy (fNIRS), as well as network-based analytical approaches. These developments have provided new insights into attentional lapses as complex neurovascular and physiological processes. However, considerable variability in sleep deprivation paradigms, cognitive assessment tasks, and outcome reporting continues to pose challenges for synthesizing findings and translating them into clear educational and clinical implications. Therefore, this systematic review was conducted to evaluate contemporary human evidence published between 2021 and 2025 on the effects of sleep deprivation on cognitive outcomes and neurophysiological measures. By integrating findings from behavioral assessments and brain-based modalities, this study aims to identify the cognitive domains most consistently affected by sleep loss, characterize reproducible neurophysiological signatures, and highlight implications for performance, safety, and future research.

METHODS

The systematic review was conducted to assess the impact of sleep deprivation on cognitive and neurophysiological

functions in human participants. It was reported and structured in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. A predefined review protocol was followed throughout the review process, including literature searching, study selection, data extraction, and synthesis. An electronic literature search was conducted in three major databases: PubMed, Scopus, and the Cochrane Library. Although the search was conducted in three major biomedical databases (PubMed, Scopus, and Cochrane Library), manual screening of reference lists was also performed to identify additional relevant studies. The search included studies published between January 2021 and December 2025, and the final search was performed in December 2025. The search strategy combined controlled vocabulary terms and free-text keywords related to sleep deprivation, cognitive performance, and neurophysiological outcomes. The following Boolean strategy was applied with database-specific adaptations: ("sleep deprivation" OR "total sleep deprivation" OR "partial sleep restriction" OR "sleep loss") AND ("cognitive function" OR "attention" OR "working memory" OR "executive function" OR "reaction time") AND ("EEG" OR "ERP" OR "fMRI" OR "functional connectivity" OR "neurophysiology" OR "brain network"). In addition, reference lists of eligible studies were manually screened to identify any further relevant articles. Inclusion criteria comprised original quantitative human studies published between 2021 and 2025, employing experimental, within-subject, or longitudinal designs that investigated acute total sleep deprivation and/or partial sleep restriction (including time-in-bed restriction). Eligible studies were required to report at least one cognitive outcome (e.g., attention/vigilance, working memory, executive function/cognitive control, processing speed, reaction time, or accuracy/errors) and at least one neurophysiological outcome (EEG, ERP, fMRI, fNIRS, or multimodal measures). Cognitive outcomes were categorized into standardized domains, including vigilant attention, working memory, executive function/cognitive control, processing speed, reaction time, and accuracy, based on established neuropsychological classifications to ensure consistency across studies. Exclusion criteria included review articles, meta-analyses, case reports, conference abstracts, studies focused solely on clinical sleep disorders without an experimental sleep-loss paradigm, and non-human (animal or in vitro) studies. All records retrieved from databases were exported to reference management software, and duplicates were removed before screening. Titles and abstracts were screened to identify potentially eligible studies, followed by full-text assessment using the prespecified inclusion and exclusion criteria. Any disagreements during screening or eligibility assessment were resolved through discussion

and consensus. The study selection process, including the number of records identified, screened, excluded, and included, is summarized in the PRISMA 2020 flow diagram. The study shows the identification of 473 records from electronic databases, removal of duplicates and ineligible records, screening of titles and abstracts, full-text eligibility assessment, and final inclusion of 16 studies in the qualitative synthesis (Figure 1).

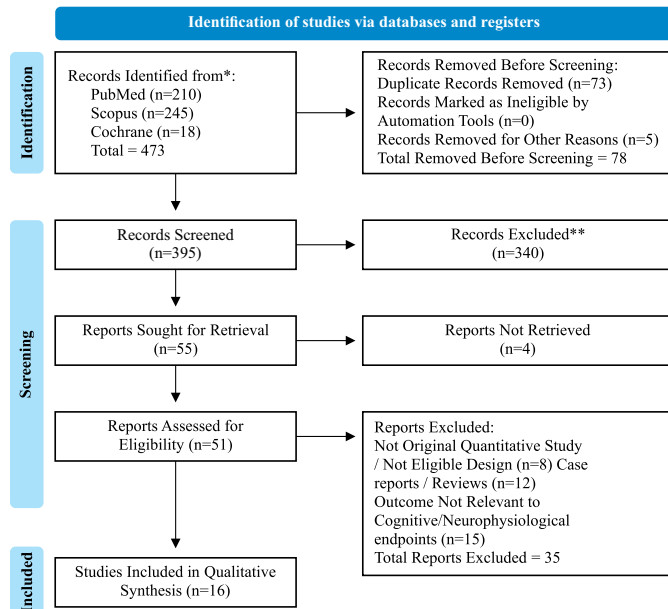


Figure 1: Study Selection Process for the Systematic Review of Sleep Deprivation and Cognitive and Neurophysiological Outcomes

Data were extracted using a standardized form that captured study design, sample characteristics, sleep deprivation protocol, cognitive domains assessed, neurophysiological modality, and key findings. Variability in sleep deprivation paradigms (e.g., total sleep deprivation, partial sleep restriction, and time-in-bed restriction protocols) was considered during narrative synthesis by examining the consistency and direction of reported outcomes across studies. Methodological quality was assessed using the Cochrane Risk of Bias 2 (RoB-2) tool for randomized and within-subject experimental studies and the NIH Quality Assessment Tool for non-randomized/observational designs. Given substantial clinical and methodological heterogeneity across the included studies (including variation in sleep-loss paradigms, cognitive tasks, neurophysiological techniques, and outcome reporting), a meta-analysis was not performed. Instead, results were synthesized using a structured narrative approach, emphasizing consistency in direction and patterns of effects across cognitive domains and neurophysiological measures. Because individual participant data were not available across studies, associations between neurophysiological alterations and behavioral impairments were interpreted descriptively based on study-level findings. A formal sensitivity analysis was not performed because the review employed qualitative narrative synthesis; however, methodological quality assessment using validated risk-of-bias tools was incorporated when interpreting the strength of evidence.

RESULTS

A total of 16 studies published between 2021 and 2025 were included in the final qualitative synthesis. Most studies employed experimental or within-subject designs and were conducted in healthy adult or adolescent populations. Sleep deprivation protocols included acute total sleep deprivation (24–36 hours), partial sleep restriction, or time-in-bed manipulation. Across studies, cognitive domains such as vigilant attention, executive function, working memory, reaction time, and processing speed were evaluated alongside neurophysiological measures including EEG, ERP, fMRI, and fNIRS. The results summarize the characteristics of the included studies examining the cognitive and neurophysiological effects of sleep deprivation. Most studies used experimental or within-subject designs, allowing within-participant comparison of sleep-deprived and rested states. The majority of studies implemented acute total sleep deprivation protocols ranging from overnight deprivation to 36 hours of wakefulness, although some studies also investigated partial sleep restriction or time-in-bed manipulation. Cognitive outcomes frequently assessed included vigilant attention, inhibitory control, working memory, and cognitive flexibility, while neurophysiological measures primarily involved EEG, ERP, resting-state fMRI, or fNIRS-based hemodynamic responses. Across studies, sleep deprivation was consistently associated with impaired attention and executive performance, as well as measurable alterations in neural activity and brain network organization (Table 1).

Table 1: Characteristics of Included Studies (2021–2025) on Sleep Deprivation and Cognitive + Neurophysiological Outcomes

References	Design/Sample	Sleep Deprivation Exposure	Cognitive Outcomes Assessed	Neurophysiological Outcomes	Key Result (Direction)
[11]	Experimental; healthy adults	Total sleep deprivation and partial sleep restriction	Inhibitory control + vigilant attention	(Neurocognitive task-based outcomes)	Vigilant attention impairment partly explained inhibitory-control deficits after sleep loss.
[12]	Experimental; healthy participants	Acute SD	Vigilant attention	Baseline brain activity changes	SD altered baseline brain activity and worsened vigilant-attention performance.

[13]	Within-subject; 24 healthy women	24 h SD	Digit symbol, digit span, TMT, complex figure	Resting-state fMRI (functional stability metrics)	SD changed the stability of functional architecture and was related to poorer neurocognitive scores.
[14]	Observational/ experimental; adults	Sleep deprivation (SD) exposure	Vigilance / sleepiness- related performance	Resting-state networks (DMN/FPN/thalamus activity patterns)	SD is associated with ↑ DMN/ thalamus activity and ↓ FPN activity, correlating with sleepiness.
[15]	Experimental; adults	Total SD	Working memory under different cognitive loads	ERP	Cognitive load moderated SD effects on working memory; ERP markers shifted with SD.
[16]	Multisite; healthy young adults	Total SD with recovery	Global cognitive state (brain-age prediction)	Neuroimaging-based brain-age metrics	SD increased “brain age” prediction reversibly after recovery.
[17]	Experimental (fNIRS); adults	Acute SD	Executive/cognitive task performance	fNIRS hemodynamic response in PFC	SD altered prefrontal hemodynamic responses, consistent with reduced executive efficiency.
[18]	Experimental; adults	Sleep deprivation	Situational cognitive impairment	“Brain vital signs” (ERP-based monitoring approach)	Brain vital-sign monitoring detected SD-related cognitive impairment in a situational paradigm.
[19]	Experimental; n=13	Extended wakefulness / SD protocol	Psychomotor Vigilance Test (PVT)	EEG functional networks (graph metrics)	EEG network properties at baseline related to vulnerability/ resilience on PVT under SD.
[20]	Experimental	Total SD	Self-reported vigilance / alertness-linked outcomes	Resting EEG (aperiodic parameters; alpha bandwidth)	SD increased aperiodic offsets (notably occipital) and related to reduced vigilance.
[10]	Dose-response, semi-longitudinal; adolescents/young adults	Time-in-bed restriction (7 vs 8.5 vs 10 h for 4 nights)	Attention control, cognitive flexibility, PVT, working memory	(Behavioral emphasis)	Restriction to 7 h impaired attention control & flexibility; PVT worsened dose- dependently; WM relatively spared.
[21]	Experimental; adolescents/young adults	24 h SD	Cognitive flexibility tasks	Neuroelectrophysiology (ERP/EEG measures)	SD impaired cognitive flexibility with measurable neuroelectrophysiological alterations.
[22]	Experimental: young vs older groups	Partial SD	Emotional/cognitive performance indices	fMRI/network dynamics (energy landscape)	Partial SD altered brain-state switching/dynamics; age-related differences reported.
[23]	Within-subject; 60 healthy males	36 h acute SD	PVT, sleepiness (ESS), mood (POMS)	Resting-state fMRI (visual-network FC)	SD disrupted FC in visual-related circuits; changes correlated with slower PVT and worse sleepiness/ mood.
[24]	Within-subject; n=33	36 h SD	AX-CPT (proactive vs reactive control), RT/errors	ERP (P3, CNV, N2)	SD impaired both proactive/ reactive control; ERP indices showed altered control dynamics under SD.
[25]	Within-subject; n=26	Overnight total SD	Attentional failures during PVT	Fast fMRI-EEG + pupil + CSF flow	Attentional lapses after SD aligned with coupled brain-body dynamics, including neurovascular and CSF-flow pulsations.

The study presents the direction of cognitive outcomes across studies following sleep deprivation. The most consistently reported deficit was impaired vigilant attention, commonly measured using the Psychomotor Vigilance Test (PVT), which demonstrated increased lapses and slower reaction times in multiple studies. Executive function and cognitive control, including inhibitory control and cognitive flexibility, were also frequently affected. In contrast, working memory findings were less consistent, with several studies showing task-dependent or load-dependent impairment while others reported minimal change. Overall, sleep deprivation was associated with slower processing speed, prolonged reaction time, and increased error rates, reflecting reduced cognitive efficiency and performance stability (Table 2).

Table 2: Cognitive Outcomes Affected by Sleep Deprivation(Study-Wise Direction of Effect)

References	Attention/Vigilance	Working Memory	Executive Function / Cognitive Control	Processing Speed	Reaction Time	Accuracy/Errors
[11]	↓ (PVT)	↓ (Go/No-Go inhibition)	—	—	↓ (PVT + Go RT slower)	↓ (↑ omission errors Go/No-Go)
[12]	↓ (PVT)	—	—	—	↓ (PVT RT)	↓ (PVT lapses/poorer performance)
[13]	↓	↓	↓	↓	↓	↓
[14]	↓ (sleepiness-linked performance reported)	—	—	—	—	—
[15]	—	↓ (N-back; load-dependent)	—	—	—	↓ (worse WM performance)
[16]	—	—	—	—	—	—
[17]	↓	↓	↓ (executive/interference resolution)	—	↓	↓
[18]	↓ (attention indexed via P300 "brain vital signs")	—	↓ (processing-related ERP indices)	—	—	—
[19]	↓ (PVT lapses)	—	—	—	↓ (PVT RT)	↓ (PVT lapses/poorer PVT)
[20]	↓ (self-reported vigilance/alertness)	—	—	—	—	—
[21]	—	—	↓ (cognitive flexibility)	—	↓	↓
[22]	—	—	—	—	—	— (emotional performance was highlighted rather than classic domains)
[23]	↓ (PVT + sleepiness)	—	—	—	↓ (PVT)	↓ (PVT lapses/poorer performance)
[24]	—	—	↓ (proactive + reactive control)	—	↓	↓ (↑ errors; slower responses)
[25]	↓ (attentional failures during PVT)	—	—	—	↓	↓

↓ worsened/declined, ↔ no clear change/preserved, — not assessed/not reported. SD = sleep deprivation; PVT = psychomotor vigilance test; RT = reaction time; EF = executive function

The results summarize the neurophysiological alterations observed following sleep deprivation across included studies. EEG-based studies commonly reported changes in aperiodic activity, spectral dynamics, and functional network organization, suggesting disrupted cortical efficiency and arousal regulation. ERP studies demonstrated alterations in attention- and control-related components such as P300, N2, and CNV, indicating slowed stimulus evaluation and reduced cognitive control under sleep-deprived conditions. Functional neuroimaging findings showed altered connectivity and stability within large-scale brain networks, particularly the default mode network (DMN), thalamic circuits, and frontoparietal control networks. Multimodal studies integrating EEG, fMRI, pupil dynamics, and cerebrospinal fluid (CSF) flow further demonstrated that attentional lapses during sleep deprivation were associated with coordinated neurovascular and physiological fluctuations (Table 3).

Table 3: Neurophysiological Outcomes Affected by Sleep Deprivation(Study-Wise Direction of Effect)(2021–2025)

References	EEG Spectral / Aperiodic Activity	ERP (P300 / N2 / CNV / N400)	fMRI Connectivity / Stability	Neurovascular / Pupil / CSF Dynamics	Other Neurophysiology
[11]	—	—	—	—	—
[12]	—	—	—	—	Baseline brain activity altered
[13]	—	—	Altered functional stability (shift vs baseline)	—	—
[14]	—	—	↑ DMN / thalamus activity; ↓ FPN activity	—	—
[15]	—	ERP altered with SD (load-dependent change)	—	—	—
[16]	—	—	Neuroimaging "brain-age" ↑ after SD; reversible after recovery	—	—
[17]	—	—	—	—	fNIRS PFC hemodynamic response altered (task-related change)

[18]	—	ERP “brain vital signs” altered (P300/N400 indices changed)	—	—	—
[19]	EEG functional networks altered (graph metrics changed)	—	—	—	—
[20]	↑ aperiodic offset; alpha bandwidth altered	—	—	—	—
[10]	—	—	—	—	— (primarily behavioral dose-response)
[21]	EEG/ERP altered (neuroelectro-physiological changes)	ERP altered (reported)	—	—	—
[22]	—	—	Brain-state dynamics altered (energy landscape /switching)	—	—
[23]	—	—	Visual-network FC disrupted (direction: altered connectivity vs baseline)	—	—
[24]	—	P3, N2, CNV altered (control-related ERP changes)	—	—	—
[25]	EEG coupled with lapses (change reported)	—	Fast fMRI dynamics linked to lapses (change reported)	Neurovascular + pupil + CSF-flow dynamics coupled to attentional failures	—

↑ increased, ↓ decreased, ↔ no clear change, — not assessed/not reported. EEG = electroencephalography; ERP = event-related potentials; fMRI = functional MRI; FC = functional connectivity; fNIRS = functional near-infrared spectroscopy; DMN = default mode network; FPN = frontoparietal network; CNV = contingent negative variation; P3/P300 = P300 component

The findings present the risk-of-bias assessment for the included studies. Overall methodological quality was generally high, with most studies rated as having low risk of bias across major domains, including outcome measurement and handling of missing data. Some studies were classified as having “some concerns”, primarily due to limitations in participant blinding, small sample sizes, or incomplete control of potential confounding factors. Importantly, no study was classified as having a high overall risk of bias, suggesting a moderate-to-high level of confidence in the reliability of the synthesized evidence. The quality appraisal supports the robustness of the overall findings linking sleep deprivation with measurable cognitive and neurophysiological alterations (Table 40).

Table 4: Risk of Bias Assessment of Included Studies (2021–2025)

References	Study Design	Randomization /Allocation	Blinding of Participants and Assessors	Outcome Measurement	Missing Data /Attrition	Confounding Control	Overall Risk of Bias
[11]	Experimental	Low	Some concerns	Low	Low	Low	Low risk
[12]	Experimental	Low	Some concerns	Low	Low	Low	Low risk
[13]	Within-Subject	Low	Some concerns	Low	Low	Low	Low risk
[14]	Observational/Experimental	Some concerns	High	Low	Low	Some concerns	Some concerns
[15]	Experimental	Low	Some concerns	Low	Low	Low	Low risk
[16]	Multisite Experimental	Low	Some concerns	Low	Low	Low	Low risk
[17]	Experimental (fNIRS)	Low	Some concerns	Low	Low	Low	Low risk
[18]	Experimental	Low	Some concerns	Low	Low	Low	Low risk
[19]	Experimental (Small N)	Low	Some concerns	Low	Some concerns	Low	Some concerns
[20]	Experimental	Low	Some concerns	Low	Low	Low	Low risk
[10]	Semi-Longitudinal	Some concerns	High	Low	Low	Low	Some concerns
[21]	Experimental	Low	Some concerns	Low	Low	Low	Low risk
[22]	Experimental	Low	Some concerns	Low	Low	Some concerns	Some concerns
[23]	Within-Subject	Low	Some concerns	Low	Low	Low	Low risk
[24]	Within-Subject	Low	Some concerns	Low	Low	Low	Low risk
[25]	Multimodal Experimental	Low	Some concerns	Low	Low	Low	Low risk

Risk of bias was assessed using the Cochrane Risk of Bias 2 tool for randomized and within-subject experimental studies and the NIH Quality Assessment Tool for non-randomized and observational designs. Each study was rated as having low risk of bias, some concerns, or high risk of bias based on randomization procedures, blinding, outcome measurement, handling of missing data, and control of confounding

DISCUSSION

This systematic review synthesizes recent human evidence published between 2021 and 2025, examining the cognitive and neurophysiological consequences of sleep deprivation. Overall, the findings demonstrate that sleep deprivation produces consistent impairments in several cognitive domains, particularly vigilant attention and reaction time, accompanied by measurable neurophysiological alterations. Across the included studies, deficits in vigilant attention commonly assessed using the Psychomotor Vigilance Test (PVT) were the most consistently reported behavioral outcomes. These impairments typically manifested as increased lapses, slower responses, and reduced performance accuracy during prolonged wakefulness or under cognitively demanding conditions [10, 19]. Similarly, several studies reported worsening of vigilant attention and reaction time, reflected by increased PVT lapses, slower responses, and reduced task accuracy when sleep deprivation was prolonged, or tasks were cognitively demanding [10, 11]. Similarly, several studies reported worsening of vigilant attention and reaction time, reflected by increased PVT lapses, slower responses, and reduced task accuracy when sleep deprivation was prolonged, or tasks were cognitively demanding [15, 18]. Supporting this, a recent ERP and reaction-time study demonstrated a significant delay in P300 latency accompanied by slower reaction times following sleep deprivation, highlighting the sensitivity of P300 dynamics to acute sleep loss and their association with behavioral performance [26]. Similarly, EEG studies have shown that sleep deprivation alters spectral activity and functional network organization, which may reflect decreased cortical efficiency and disruption of arousal regulation [20]. These electrophysiological findings provide plausible mechanistic explanations linking sleep loss with deficits in vigilance, cognitive flexibility, and executive control. A network-level explanation for impaired cognition following sleep deprivation is further supported by neuroimaging evidence. Several studies included in this review reported alterations in resting-state functional stability and connectivity, particularly involving decreased activity or connectivity in cognitive control systems such as the frontoparietal network and increased activity within internally directed networks such as the default mode network (DMN) and thalamic circuits [13, 14]. This pattern of reorganization is consistent with reduced top-down cognitive regulation and increased intrusion of internally directed processing during prolonged wakefulness. Such changes may contribute to attentional lapses and impaired response control. Additionally, more region-specific studies have demonstrated that acute sleep deprivation disrupts thalamocortical connectivity, which is strongly associated with declines in attentional performance [23,

27]. Dynamic connectivity analyses further suggest that cognitive impairment following sleep loss is not static but fluctuates over time, with increased transitions between unstable brain states that correspond with variations in PVT performance during extended wakefulness [28]. These findings suggest that sleep deprivation progressively destabilizes neural systems responsible for maintaining alertness and cognitive performance. The vulnerability to sleep deprivation may also vary according to age and exposure patterns. Evidence from adolescent and young adult populations suggests that sleep restriction produces dose-dependent impairments in attention control and cognitive flexibility while sometimes sparing certain working-memory tasks under low cognitive load. However, more prolonged deprivation, such as 24-hour sleep loss in adolescents, has been associated with neuroelectro-physiological alterations accompanied by reduced cognitive flexibility [21]. Comparisons between younger and older adults also indicate that partial sleep deprivation may influence brain-state dynamics differently across age groups, suggesting possible age-related differences in neural compensation or vulnerability to sleep loss [29, 30]. Together, these findings indicate that developmental stage and the duration or type of sleep deprivation (acute total deprivation versus repeated restriction) influence the magnitude and profile of cognitive impairment. Beyond cognitive performance, emerging evidence suggests that sleep deprivation may also affect emotional processing and decision-making. Experimental research has demonstrated that sleep deprivation reduces the ability to engage in cognitive reappraisal, a key strategy involved in emotional regulation, which may negatively influence real-life decision-making under conditions of sleep debt [31]. Other studies have shown that sleep deprivation can increase reward sensitivity during sequential decision-making tasks, potentially altering decision strategies even when overall accuracy remains relatively preserved [32, 33]. These findings extend the impact of sleep deprivation beyond traditional cognitive domains and highlight its potential implications for decision-making in professional environments such as healthcare, education, and other safety-sensitive occupations [34, 35]. The certainty of the evidence synthesized in this review is generally favorable, as most studies were rated as having a low risk of bias. Nevertheless, several limitations should be acknowledged. First, there was considerable heterogeneity in sleep deprivation paradigms, cognitive testing protocols, and neurophysiological methodologies, which limited the feasibility of conducting a quantitative meta-analysis and comparing effect sizes across studies. Second, many studies involved relatively small sample sizes, particularly in EEG-based network analyses, which may increase

variability and limit generalizability. Third, sleep deprivation studies often face methodological challenges related to participant blinding, and some designs cannot fully exclude expectancy effects (Table 4). Finally, the predominance of healthy volunteer populations limits the generalizability of findings to clinical populations or individuals exposed to chronic sleep disruption, such as shift workers. Despite these limitations, consistent evidence across behavioral, electrophysiological (EEG/ERP), and neuroimaging (fMRI/fNIRS) modalities supports the conclusion that sleep deprivation disrupts neural systems responsible for maintaining cognitive stability and attentional control. The convergence of findings across multiple methodologies highlights sleep deprivation as a measurable neurocognitive stressor with identifiable neural signatures. Future research should focus on standardized cognitive assessment batteries, harmonized reporting of neurophysiological outcomes, multimodal study designs, and ecologically valid settings such as healthcare shift work environments. Longitudinal studies examining recovery sleep will also be important to determine whether sleep deprivation leads to transient or persistent neurocognitive alterations.

CONCLUSIONS

Evidence from 2021–2025 demonstrates that sleep deprivation produces consistent impairments in vigilant attention, reaction time, and executive control, paralleled by reproducible neurophysiological alterations on EEG/ERP and network-level reorganization on functional neuroimaging. These findings support sleep loss as a measurable neurocognitive stressor with identifiable electrophysiological and connectivity signatures, underscoring the importance of sleep-protection strategies in students, shift workers, and safety-critical professions.

Authors' Contribution

Conceptualization: RM

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All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All 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] Khan MA and Al-Jahdali H. The Consequences of Sleep Deprivation on Cognitive Performance. *Neurosciences Journal*. 2023 Apr; 28(2): 91-9. doi: 10.17712/nsj.2023.2.20220108.
- [2] Agrawal S, Kumar V, Singh V, Singh C, Singh A. A Review on Pathophysiological Aspects of Sleep Deprivation. *CNS and Neurological Disorders-Drug Targets-CNS and Neurological Disorders*. 2023 Oct; 22(8): 1194-208. doi: 10.2174/1871527321666220512092718.
- [3] Griggs S, Harper A, Hickman Jr RL. A Systematic Review of Sleep Deprivation and Neurobehavioral Function in Young Adults. *Applied Nursing Research*. 2022 Feb; 63: 151552. doi: 10.1016/j.apnr.2021.151552.
- [4] Kiriş N. Effects of Partial Sleep Deprivation on Prefrontal Cognitive Functions in Adolescents. *Sleep and Biological Rhythms*. 2022 Oct; 20(4): 499-508. doi: 10.1007/s41105-022-00396-3.
- [5] Helakari H, Järvelä M, Väyrynen T, Tuunanen J, Piispala J, Kallio M et al. Effect of Sleep Deprivation and NREM Sleep Stage in Physiological Brain Pulsations. *Frontiers in Neuroscience*. 2023 Dec; 17: 1275184. doi: 10.3389/fnins.2023.1275184.
- [6] Magnuson JR, Kang HJ, Dalton BH, McNeil CJ. Neural Effects of Sleep Deprivation on Inhibitory Control and Emotion Processing. *Behavioural Brain Research*. 2022 May; 426: 113845. doi: 10.1016/j.bbr.2022.113845.
- [7] Kong J, Zhou L, Li X, Ren Q. Sleep Disorders Affect Cognitive Function in Adults: An Overview of Systematic Reviews and Meta-Analyses. *Sleep and Biological Rhythms*. 2023 Apr; 21(2): 133-42. doi: 10.1007/s41105-022-00439-9.
- [8] Chung Y, Wu JL, Huang WC. Effects of Prebiotics on Intestinal Physiology, Neuropsychological Function, and Exercise Capacity of Mice with Sleep Deprivation. *Food Research International*. 2023 Mar; 165: 112568. doi: 10.1016/j.foodres.2023.112568.
- [9] Davidescu D, Galea-Holhoş LB, Voiță-Mekereş F, Davidescu L. Effects of Sleep Deprivation on Learning and Memory: A Review Study. *Journal of Biochemical Technology*. 2023; 14(4-2023): 25-30. doi: 10.51847/01ztnjmk66.
- [10] Campbell IG, Kurinec CA, Zhang ZY, Cruz-Basilio A, Figueroa JG, Bottom VB et al. Sleep Restriction and Age Effects on Distinct Aspects of Cognition in Adolescents. *Sleep*. 2024 Dec; 47(12): zsae216. doi: 10.1093/sleep/zsae216.
- [11] Mao T, Dinges D, Deng Y, Zhao K, Yang Z, Lei H et al. Impaired Vigilant Attention Partly Accounts for Inhibition Control Deficits After Total Sleep

- Deprivation and Partial Sleep Restriction. *Nature and Science of Sleep*. 2021 Sep; 1545-60. doi: 10.2147/NSS.S314769.
- [12] Tramonti Fantozzi MP, Banfi T, Di Galante M, Ciuti G, Faraguna U. Sleep Deprivation-Induced Changes in Baseline Brain Activity and Vigilant Attention Performance. *Brain Sciences*. 2022 Dec; 12(12): 1690. doi: 10.3390/brainsci12121690.
- [13] Huang NX, Gao ZL, Lin JH, Lin YJ, Chen HJ. Altered Stability of Brain Functional Architecture After Sleep Deprivation: A Resting-State Functional Magnetic Resonance Imaging Study. *Frontiers in Neuroscience*. 2022 Oct; 16: 998541. doi: 10.3389/fnins.2022.998541.
- [14] Wang X, Li Y, Jiao F, Guo M, Wei S, Tian P et al. Functional Connectivity Alterations During Sleep Deprivation: Investigating Key Brain Regions and Networks. *Journal Of Integrative Neuroscience*. 2023 Nov; 22(6): 169. doi: 10.31083/j.jin2206169.
- [15] Yin Y, Chen S, Song T, Zhou Q, Shao Y. Cognitive Load Moderates the Effects of Total Sleep Deprivation on Working Memory: Evidence from Event-Related Potentials. *Brain Sciences*. 2023 Jun; 13(6): 898. doi: 10.3390/brainsci13060898.
- [16] Chu C, Holst SC, Elmenhorst EM, Foerges AL, Li C, Lange D et al. Total Sleep Deprivation Increases Brain Age Prediction Reversibly in Multisite Samples of Young Healthy Adults. *Journal of Neuroscience*. 2023 Mar; 43(12): 2168-77. doi: 10.1523/JNEUROSCI.0790-22.2023.
- [17] Ji K, Chen DY, Karunakaran KD, Biswal BB. Altered Brain Hemodynamic Response and Cognitive Function After Sleep Deprivation: A Functional Near-Infrared Spectroscopy Study. *Brain-Apparatus Communication: A Journal of Bacomics*. 2023 Dec; 2(1): 2169589. doi: 10.1080/27706710.2023.2169589.
- [18] Jones KB, Frizzell T, Fickling S, Pawlowski G, Brodie SM, Lakhani B et al. Brain Vital Sign Monitoring of Sleep Deprivation Detects Situational Cognitive Impairment. *Frontiers in Human Neuroscience*. 2024 Apr; 18: 1358551. doi: 10.3389/fnhum.2024.1358551.
- [19] Mason SL, Junges L, Woldman W, Ftouni S, Anderson C, Terry JR et al. Associating EEG Functional Networks and the Effect of Sleep Deprivation as Measured Using Psychomotor Vigilance Tests. *Scientific Reports*. 2024 Nov; 14(1): 27999. doi: 10.1038/s41598-024-78814-4.
- [20] Bai D, Hu J, Jülich S, Lei X. Impact of Sleep Deprivation on Aperiodic Activity: A Resting-State EEG Study. *Journal of Neurophysiology*. 2024 Nov; 132(5): 1577-88. doi: 10.1152/jn.00304.2024.
- [21] Zhang X, Feng S, Yang X, Peng Y, Du M, Zhang R et al. Neuroelectrophysiological Alteration Associated with Cognitive Flexibility After 24h Sleep Deprivation in Adolescents. *Consciousness and Cognition*. 2024 Sep; 124: 103734. doi: 10.1016/j.concog.2024.103734.
- [22] Wu Y, Fan L, Chen W, Su X, An S, Yao N et al. Brain Dynamics Alterations Induced by Partial Sleep Deprivation: An Energy Landscape Study. *Neuroimage*. 2025 Apr; 310: 121108. doi: 10.1016/j.neuroimage.2025.121108.
- [23] Weng X, Wen K, Guo J, Zhang P, Zhang Y, Cao Q et al. The Impact of Sleep Deprivation on the Functional Connectivity of Visual-Related Brain Regions. *Sleep Medicine*. 2025 Jan; 125: 155-67. doi: 10.1016/j.sleep.2024.11.026.
- [24] Zhang Y, He H, Miao H, Qian Y, Wu B, Chen X et al. Impact of Sleep Deprivation on Cognitive Control: Insights from the Dual Mechanisms of Control Theory. *Biological Psychology*. 2025 Sep; 109131. doi: 10.1016/j.biopsycho.2025.109131.
- [25] Yang Z, Williams SD, Beldzik E, Anakwe S, Schimmelpfennig E, Lewis LD. Attentional Failures After Sleep Deprivation Are Locked to Joint Neurovascular, Pupil and Cerebrospinal Fluid Flow Dynamics. *Nature Neuroscience*. 2025 Oct: 1-1. doi: 10.1101/2024.11.15.623271.
- [26] Ren Z, Mao X, Zhang Z, Wang W. The Impact of Sleep Deprivation on Cognitive Function in Healthy Adults: Insights from Auditory P300 and Reaction Time Analysis. *Frontiers in Neuroscience*. 2025 Apr; 19: 1559969. doi: 10.3389/fnins.2025.1559969.
- [27] Feng S, Wu Z, Zheng S, Dong L, Jia H, Ning Y. Altered Functional Connectivity of the Thalamus Subregions Associated with Impaired Attention After Sleep Deprivation. *Nature and Science of Sleep*. 2024 Dec; 1109-18. doi: 10.2147/NSS.S472323.
- [28] Xu Z, Ma C, Wang C, Guo F, Zheng M, Fang P et al. Dynamic Changes in Brain Function During Sleep Deprivation: Increased Occurrence of Non-Stationary States Indicates the Extent of Cognitive Impairment. *Neuro-Image*. 2025 Apr; 309: 121099. doi: 10.1016/j.neuroimage.2025.121099.
- [29] Agyapong-Opoku F, Agyapong-Opoku N, Agyapong B. Examining the Effects of Sleep Deprivation on Decision-Making: A Scoping Review. *Behavioral Sciences*. 2025 Jun; 15(6):823. doi: 10.3390/bs15060823.
- [30] Lima NC, Kirov R, de Almondes KM. Impairment of Executive Functions Due to Sleep Alterations: An Integrative Review on the Use of P300. *Frontiers in Neuroscience*. 2022 Jul; 16: 906492. doi: 10.3389/fnins.2022.906492.

- [31] Li ZQ, Qin Y, Cai WP, Deng SQ, Mao XF, Zhang JG et al. Sleep Deprivation Impairs Human Cognitive Reappraisal Ability: A Randomized Controlled Trial. *Nature and Science of Sleep*. 2023 Dec; 729-36. doi: 10.2147/NSS.S414962.
- [32] Lim JY, Bennett D, Drummond SP. Sleep Restriction Increases Reward Sensitivity During Sequential Updating. *SLEEPJ*. 2025 Nov: zsaf354. doi: 10.1093/sleep/zsaf354.
- [33] Sun X, Qu Z, Zhang X, Zhang Y, Zhang X, Zhao H et al. The Effects of Sleep Deprivation on Cognitive Flexibility: A Scoping Review of Outcomes and Biological Mechanisms. *Frontiers In Neuroscience*. 2025 Jul; 19: 1626309. doi: 10.3389/fnins.2025.1626309.
- [34] Kayser KC, Puig VA, Estepp JR. Predicting and Mitigating Fatigue Effects Due to Sleep Deprivation: A Review. *Frontiers in Neuroscience*. 2022 Aug; 16: 930280. doi: 10.3389/fnins.2022.930280.
- [35] Umemura GS, Furtado F, Santos FC, Gonçalves BD, Forner-Cordero A. Is Balance Control Affected by Sleep Deprivation? A Systematic Review of the Impact of Sleep on the Control of Balance. *Frontiers In Neuroscience*. 2022 May; 16: 779086. doi: 10.3389/fnins.2022.779086.