



pISSN 1997-3438
eISSN 1997-3446
Indexed in
Index Pakistan (IP/016)
WHO Index Medicus (IMEMR)
EMBASE
EBSCO
Clavirate
IMEMR
Asian Digital Library (ADL)
Elsevier
Pakmedinet
NETMEDICS
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QUARTERLY

JOURNAL OF MEDICAL SCIENCES PESHAWAR - PAKISTAN

Recognized by Higher Education Commission of Pakistan

J Med Sci 2026 April - June;34(2)

KHYBER MEDICAL COLLEGE, PESHAWAR - PAKISTAN



JOURNAL OF MEDICAL SCIENCES

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Khyber Prints
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Journal of Medical Sciences (Peshawar, Print/Online) is a peer reviewed open access journal that publishes biomedical public health and educational research on quarterly basis.

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Journal of Medical Sciences is published on controlled circulation basis and distributed among the faculty of all national medical colleges, main libraries throughout the province, Pakistan Medical Research Council, PMDC, HEC and Tertiary Referral Centers.

The publisher and the members of the Editorial Board can not be held responsible for errors or for any consequences arising from the use of information contained in this journal.

Journal of Medical Sciences is published quarterly, composed and printed at Khyber Printers, Peshawar KP, Pakistan.

Annual Subscription

Pakistan: Rs. 5000/-

Overseas: US \$ 500/-

Printed at:

Khyber Prints

E-mail: khyberprints@gmail.com

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INVERTING THE EVIDENCE PYRAMID: THE THREATS OF UNREGULATED META-ANALYSES AND PREDATORY PUBLISHING BY UNDERGRADUATE STUDENTS

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This article may be cited as: Ahmed F. Inverting The Evidence Pyramid: The Threats Of Unregulated Meta-Analyses And Predatory Publishing By Undergraduate Students. J Med Sci 2026 April - June;34(2):63-65

INTRODUCTION

THE IVORY TOWER BUILT ON SAND

Walk down the historic corridors of Khyber Medical College (KMC) on any afternoon, and you will witness a profound shift in the conversations among our MBBS students. A decade ago, undergraduate research was largely confined to cross-sectional descriptive studies or basic knowledge-attitude-practice (KAP) surveys. Today, the ambition is vastly different. Driven by fierce global competition and residency match prerequisites, students from across Khyber Pakhtunkhwa (KP) are bypassing local clinical research altogether. Instead, armed with laptops, institutional internet access, and a rudimentary, self-taught understanding of statistical software, they have set their sights on the peak of the traditional Evidence-Based Medicine (EBM) hierarchy: the systematic review and meta-analysis.

In theory, this surge of academic enthusiasm should be celebrated as a victory for undergraduate medical research in Pakistan. In practice, however, it represents an alarming, unmonitored epidemic in academic publishing. It is not the case that these young, ambitious minds are attempting high-level syntheses and scientific curiosity; rather, the existential threat to modern medical literature lies in the global scientific community's willingness to publish these unguided, structurally flawed manuscripts.

Open-access journals across the globe have lowered barriers for fundamentally untrained undergraduate student groups working without robust, qualified academic mentorship. These predatory journals are actively undermining the scientific enterprise. In doing so, they risk permanently destabilizing the foundational EBM pyramid, reducing what should be our most secure evidence into our most unreliable noise.

THE VIEW FROM PESHAWAR: A DANGEROUS INSTITUTIONAL TREND

To fully grasp the scale of this phenomenon, we must examine our own institutional landscape at Khyber Medical College. An internal review of undergraduate research submissions and independent student publications over the last three academic cycles reveals an astonishing trend. Of 142 research papers published or submitted to open-access portals by KMC students and recent MBBS graduates from KP between 2023 and 2026, an unprecedented 41% were classified as systematic reviews or meta-analyses (Table 1). On the surface, this might appear to be an academic triumph for a regional institution in Pakistan. Yet a closer look at the methodology behind these figures tells a profoundly troubling story.

Of these student-led meta-analyses, fewer than 15% listed a senior faculty member or an established, published clinical researcher as a corresponding or active contributing author. Instead, the typical authorship line consists of three to five undergraduate students, occasionally joined by a junior medical officer or house officer acting as the technical facilitator. More critically, an audit of the methodologies employed revealed that over 80% of these published papers failed to register their protocols in international databases such as PROSPERO. These lacked a validated risk-of-bias assessment (such as the Cochrane Risk of Bias tool), and relied entirely on free, open-source online software packages without the guidance of a qualified biostatistician and researcher.

The human element of this crisis is deeply concerning. These students are not mischievous actors; they are trapped in a system that rewards volume over validity.¹ In interviews with KMC undergraduates, the driving motivations become clear: 'We need PubMed-indexed publications to stand a chance at matching for foreign residencies, and our own ethical boards take six months just to approve an observational study,' a final-year student confessed. Another remarked, 'Why spend months

Table No 1: Chronological surge and specific thematic distribution of undergraduate systematic reviews and meta-analyses (SR-MAs) across Khyber Pakhtunkhwa (2021–2026). Percentages reflect the proportion of SRMAs out of total student publications for that academic year

Year	SRMA Volume (% of Total Publications)	Specific Review / Meta-Analysis Focus Areas	Primary Publishing Outlets / Open-Access Portals
2021	2 (11%)	Basic efficacy of repurposed therapies during local health crises.	Khyber Medical University Journal, Local Repository Streams
2022	4 (16%)	Efficacy of global online e-learning modalities vs traditional medical rounds.	BMC Medical Education, Global Student Open Portals
2023	9 (29%)	Prevalence patterns of mental health stressors among South Asian medical students.	Cureus Open Access, Pakistan Medical Students Research Journal
2024	16 (41%)	Global surgical technique comparative outcomes; diagnostic accuracy of basic radiology AI.	Cureus, PLOS ONE, RMI Journal of Medical Students
2025	22 (45%)	Therapeutic interventions in cardiovascular medicine; large-scale epidemiological trends.	Cureus International, MDPI Healthcare, Frontiers Journals
2026*	26 (45%)	Artificial intelligence diagnostic models in low-resource settings; digital health interventions.	Cureus Network, Regional Student-led Publication Directories

tracking down non-compliant patients in the overstretched wards of Khyber Teaching Hospital when we can download twenty data sheets from our hostel rooms and write a meta-analysis in a week?’

THE EDITORIAL CRISIS: SYSTEMIC FAILURE OF GLOBAL PEER REVIEW OR SOMETHING ELSE

The structural cracks in undergraduate research are entirely predictable, but the global peer-review system’s compliance is not. Systematic reviews and meta-analyses were traditionally regarded as the definitive authorities of clinical truth because they require an extraordinary level of expertise. Conducting a valid meta-analysis demands not only absolute mastery of complex statistical modeling (such as random-effects models, heterogeneity assessments, and publication bias metrics) but also deep, years-long clinical familiarity with the subject matter to identify subtle confounders and clinical heterogeneity across primary trials.²

When an undergraduate group attempts this without experienced supervision, the resulting manuscript is inevitably plagued by fatal flaws: inappropriate pooling of clinical trials, misinterpretation of secondary outcomes, and a failure to recognize systematic bias in the primary literature.³ Yet these papers are being accepted and published at an unprecedented rate. Driven by commercial open-access publishing models that thrive on high article processing charges (APCs) and rapid turnover, many international journals have effectively compromised their peer-review mechanisms. Editorial boards frequently assign these highly specialized manuscripts to generalist reviewers who lack the statistical or clinical acumen to spot structural defects. Consequently, a deeply flawed, student-authored meta-analysis is granted the same digital object identifier (DOI) and indexation status as a rigorous, “years-in-the-making” review from an elite academic

group.

INVERTING THE EBM PYRAMID

The immediate casualty of this editorial negligence is the integrity of Evidence-Based Medicine. The EBM pyramid has a specific architecture: individual case reports and expert opinions form the broad base; observational studies occupy the middle; randomized controlled trials (RCTs) constitute the upper tier; and systematic reviews sit at the apex as the gold standard for clinical guidance.⁴ This hierarchy assumes that the quality of synthesis at the top filters and refines the evidence below.

When the scientific record is flooded with hundreds of unguided, poorly synthesized undergraduate meta-analyses, this pyramid is violently inverted. Methodological flaws at the apex contaminate the entire structure. Because systematic reviews are heavily weighted by algorithmic search tools, clinical aggregators, and artificial intelligence diagnostic models, these flawed student papers are already beginning to pollute global clinical recommendations. A weak, improperly pooled meta-analysis can erroneously conclude that a therapeutic intervention is safe or effective, directly contradicting the very RCTs it purports to synthesize. When the strongest tier of evidence is structurally weaker than the raw data it rests upon, the foundation of modern medical decision-making begins to collapse.⁵

A PATH FORWARD: INSTITUTIONAL AND EDITORIAL GUARDIANSHIP

Arresting this slide toward scientific degradation requires immediate, decisive intervention from both local institutions, such as Khyber Medical College, and editorial bodies, such as the Journal of Medical Sciences. We must move from an era of permissive student publishing to one of strict, protective academic guardianship. First, institu-

tional policy must require that no undergraduate medical student may submit a systematic review or meta-analysis to any journal without a verified, named faculty mentor with a documented publication record in that field. KMC and similar regional institutions must establish dedicated Undergraduate Research Committees to review the methodological soundness of student protocols before they are registered internationally. Moreover, the Ethical review committees and boards must act now and make the ethical approval certificate a mandatory component before initiating a systematic review or a meta-analysis.

Second, medical journals, particularly those with in developing healthcare ecosystems, must enforce strict gatekeeping. At JMS, we are introducing rigorous mandatory checklists for all systematic review submissions, requiring explicit proof of pre-registration (e.g., PROSPERO), detailed data-sharing files, and a formal sign-off from an independent biostatistician. Furthermore, we must actively educate our students that a beautifully executed, honest, and localized cross-sectional study addressing a unique healthcare challenge in KP is infinitely more valuable to the global medical community than a flawed, unguided meta-analysis on a global disease that they have never personally treated in a clinical setting.⁶

The ambition of our undergraduate medical students is one of Khyber Pakhtunkhwa's greatest untapped scientific resources. By restoring rigor, demanding absolute mentorship, and holding the global peer-review process to its sacred obligations, we can ensure that our students contribute to the elevation of medical science—rather than the erosion of its most vital foundations.

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EFFICACY OF MINI-PERCUTANEOUS NEPHROLITHOTOMY (MINI-PCNL) FOR RENAL STONES IN CHILDREN

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ABSTRACT

OBJECTIVE: This study aimed to determine whether mini-percutaneous nephrolithotomy is effective for treating lower-pole renal stones in children.

MATERIALS AND METHODS: This descriptive case series study was conducted at the Department of Urology, Khyber Teaching Hospital, Peshawar, from July 2021 to January 2022 (following approval of the study protocol by the Institutional Ethical Review Committee) and included 148 pediatric patients with a single lower-pole renal stone measuring 1.5 to 2 cm. Patients with prior renal surgery, multiple lower-pole renal stones, renal nephropathies, or anatomical abnormalities of the upper and lower renal systems were excluded. A pediatric urologist performed mini-PCNL on each patient in the prone position under general anesthesia. After injecting contrast (Urograffin) into the ureteric catheter, the renal tract was visualized using a fluoroscope.

RESULTS: The mean age and SD in this study were 9.75 ± 3.075 . The baseline stone size mean and SD were 1.65 ± 0.17 . Of the patients, 81 (54.7%) were younger than 10 years old, and 67 (45.3%) were older than 10 years. There were 45 female patients (30.4%) and 103 male patients (69.6%). According to rates and percentages indicating the effectiveness of mini-percutaneous nephrolithotomy in treating pediatric lower pole renal stones, 113 patients (76.4%) had their stones removed.

CONCLUSION: Based on its stone clearance rate and the absence of major complications, this study demonstrates that mini-PCNL is a safe and effective treatment for lower-pole renal stones in children.

KEY WORDS: Children, Percutaneous Nephrolithotomy, and Renal Stone

This article may be cited as: Ahmad T, Ali M, Muhammad S, Ali S, Ullah I, Ullah E. Efficacy Of Mini-Percutaneous Nephrolithotomy (Mini-Pcni) For Renal Stones In Children. J Med Sci 2026 April - June;34(2):66-69

INTRODUCTION

Renal stones are among the most prevalent illnesses in Pakistan and are associated with higher rates of morbidity, mortality, and societal economic burden.¹⁻³ Treatment options for kidney stone disease include open surgery, laparoscopic procedures, extracorporeal shock-wave lithotripsy, ureteroscopy, percutaneous nephrolithotomy, pharmaceutical treatments, and conservative measures.⁴ The majority of patients with renal stones now receive extracorporeal shockwave lithotripsy (ESWL), which has revolutionized the treatment of renal calculi.⁵ While the role of lower-pole anatomy in treatment remains debated, stone size appears to be a crucial predictor of ESWL outcomes.⁶⁻⁸ Following ESWL, stone-free rates in the lower pole have been reported at 60%; however, some studies indicate that stone clearance can reach 91.1%.⁹

The use of percutaneous nephrolithotomy (PCNL) as the primary therapeutic option for lower calyx calculi is growing. In skilled hands, it has a high success rate and few complications. Reports of PCNL's effectiveness in clearing stones range from 74.8% to 92.8%. PCNL yields higher stone-free rates for lower-pole renal calculi but is associated with more complications and longer hospital stays.¹⁰

The most recent guidelines from the European Association of Urology (EAU) state that PCNL should be the preferred treatment for both large renal calculi (>20 mm) and smaller stones (10–20 mm) in the lower pole when four variables make ESWL unfavorable. There have been reports of excellent stone-free rates (SFR) ranging from 76% to 98% after PCNL. PCNL remains a challenging surgical procedure and can have serious side effects that may reduce its effectiveness.^{11, 12} Lower-pole renal stones are treated with PCNL. There are no clear guidelines in our setting regarding which procedure to perform for a given patient, and when we reviewed the literature, we found that success rates for the two procedures varied. As a result, patients undergo various procedures on a regular basis, which increases their morbidity, anxiety, and financial stress. My study compares the efficacy and complications of PCNL for lower-pole renal stones measuring 1.5 to 2 cm. If our results show that PCNL is more

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Date Received: 16/12/2025

Date Revised: 25/06/2026

Date Accepted: 26/06/2026

effective than ESWL, we will recommend further research before endorsing it as the first-line treatment for lower-pole stones of this size.

MATERIALS AND METHODS

We conducted this documentary review of data in the Department of Urology, Khyber Teaching Hospital, Peshawar, from July 2021 to January 2022, after approval of the study protocol from the Institutional Ethical Review Committee Approval No. 558/DME/KMC, dated 08/04/2025 by collected and analyzing the record of 148 pediatric patients (ages 1–14) who had a single lower pole renal stone measuring 1.5–2 cm. Individuals with a history of renal surgery, multiple lower-pole renal stones, renal nephropathies, and upper and lower renal system anatomical anomalies were not included. With an efficacy rate of 74.8% for PCNL, the sample size was determined using the WHO sample size calculator with a 95% confidence interval.¹⁰

Every patient's history, physical examination, and a standard series of tests were recorded on a pro forma. Children went through Mini-PCNL while they were in the prone position and underwent general anesthesia. After infusing contrast (urografin) through the ureteric catheter, the renal tract was visualized on fluoroscopy. An 18 Fr Amplatz sheath was inserted into the tract to obtain the final access after the tract had been percutaneously accessed and dilated with metallic Alken dilators up to 18 Fr. Swiss Pneumatic Lithoclast performed lithotripsy, and a rigid pediatric nephroscope measuring 16 Fr was used in each case to visualize and remove stones. To ascertain the stone clearance and any remaining fragments, fluoroscopic images were taken. A 14 Fr 60 nephrostomy tube and a double J stent (DJS) were inserted at the conclusion of the procedure. After 24 to 48 hours, the nephrostomy tube was removed, and four weeks later, the DJS was removed. All patients received normal doses of antibiotics and analgesics for the first 24 hours after surgery. On the second postoperative day, the patients were discharged. A follow-up visit was recommended for all patients two weeks after surgery, and the effectiveness of the intervention was assessed by evaluating ultrasound results for stone-free status. A single skilled CPSP radiology fellow performed all radiological procedures. A pre-made pro forma contained all the previously listed data, including name, age, gender, and address. To control for confounders and bias in the study outcomes, strict exclusion criteria were applied.

SPSS-23 was used to analyze the data. For quantitative characteristics such as age and baseline stone size, the mean + SD was computed. For categorical factors such as gender and efficacy, frequencies and percentages were computed. A P-value of less than 0.05 was considered significant.

RESULTS

The mean age and standard deviation were 9.75 ± 3.075 years. The baseline stone size mean and SD were

1.65 ± 0.17 cm. Of the patients, 81 (54.7%) were younger than 10 years, and 67 (45.3%) were older than 10 years (Table I). There were 45 female patients (30.4%) and 103 male patients (69.6%). See Table II for details. According to efficacy frequencies and percentages, 113 individuals (76.4%) had their stones removed (Table III).

Table No 1: Distribution of patients according to age (n=148)

Age (years)	No. of Patients	%age
≤10	81	54.70
>10	67	45.30
Total	148	100.0

Table No 2: Distribution of patients according to gender (n=148)

Gender	No. of Patients	%age
Male	103	69.60
Female	45	30.40
Total	148	100.0

Table No 3: Efficacy of mini PCNL for renal stones in children (n=148)

Efficacy	No. of Patients	%age
Yes	113	76.40
No	35	23.60
Total	148	100.0

DISCUSSION

A 4.85 F all-seeing needle is used to perform Micro-PCNL, also known as Microperc, a recently described minimally invasive PCNL approach. The latter has a three-way connector that allows the insertion of a 272 μ m laser fiber, a 0.9- or 0.6-mm-diameter micro-optic, and a saline irrigation tube. This modified needle has an outside diameter of 1.6 mm (4.85 F). Fifteen adults were the first to try this novel technology. The average stone size and operating time were 30.4 mm and 101.4 minutes, respectively. Eleven individuals achieved total stone clearance after surgery. This approach has since been used to treat kidney stones in children. Renal stones are a prevalent illness in Pakistan. Renal stones are linked to increased morbidity, mortality, and societal economic burden.^{2,3} Numerous techniques, including open surgery, laparoscopic, extracorporeal shockwave lithotripsy, and ureteroscopy, are used to treat kidney stone illnesses. Medical interventions, conservative measures, and percutaneous nephrolithotomy.⁴

Men are more likely than women to develop stones, and the types of stones vary slightly between the sexes. The reported frequencies of stone types in children differ slightly from those in adults, but the effects are roughly equivalent for both sexes.¹³ According to the National Health and Nutrition Examination Surveys, periodic surveys of the US population, the prevalence of stones has been rising in both sexes over the past 30 years.¹⁴ Nearly

12% of white men and 6% of white women reported having had a kidney stone in the seventh decade, according to the most recent poll; the rate among African Americans is less than half that of Caucasians, but it has been rising.¹⁵

The majority of patients with kidney stones now undergo extracorporeal shockwave lithotripsy (ESWL), which has revolutionized the treatment of renal calculi.⁵ While the lower pole's anatomical features are debated in terms of therapy, stone size appears to be a crucial factor in predicting the outcome of ESWL.⁶⁻⁸ Following ESWL, lower pole stone-free rates have been reported to be 60%, but other studies have reported stone clearance of up to 91.1%, which is nearly consistent with our results, which showed that 113 patients (76.4%) had stone removal.^{9, 10}

The use of percutaneous nephrolithotomy (PCNL) as the primary treatment for lower calyx calculi is increasing. In skilled hands, it has a high success rate and few complications. According to reports, PCNL can remove stones in 74.8% to 92.8% of cases.¹⁰ This range is nearly consistent with the results of this investigation, which showed that 113 individuals (76.4%) had their stones removed.

PCNL has a higher stone-free rate for lower-pole renal calculi, but it also carries a higher complication rate and longer hospital stays. When ESWL is contraindicated, PCNL is recommended as the preferred treatment for large renal calculi (>20 mm) and for smaller stones (10–20 mm) of the lower renal pole, per the most recent European Association of Urology (EAU) guidelines.³ There have been reports of excellent stone-free rates (SFR) ranging from 76% to 98% after PCNL, which is nearly consistent with the results of this investigation, which showed that 113 individuals (76.4%) had their stones cleared.⁴

Wang et al. reported findings from 247 renal units in 234 patients younger than 3 years who underwent mini-PCNL.¹⁶ Each procedure used a single tract, comprising 245 14 F tracts, 1 16 F tract, and 1 12 F tract. Stone burden was 1–2 cm² in 191 instances, >2 cm² in 30 cases, and <1 cm² in 26 cases. Operating time ranged from 21 to 62 minutes, with a mean of 32.5 minutes. According to the report, the complete stone-free rate was 240 renal units (97.2%). The results of this investigation are discordant with those of another mini-PCNL study, which found SFR rates of 90.8% in stone burden < 20 mm and 76.3% in stone burden > 20 mm.¹⁷

The mean age of the 60 patients in the study was 12.90±3.16 years, with 19 (31.7%) under age 10 and 41 (68.0%) aged 11 to 18 years. Of the 60 patients, 16 (26.7%) were female and 44 (73.3%) were male. In pediatric patients with renal stones, stone clearance occurred in 56 (93.33%) and postoperative hematuria in 4 (6.66%) after micro PCNL.¹⁸ Similar results were achieved in a recent study conducted at the Hayat Abad Medical Complex in Peshawar.¹⁹ The current study's stone-free rate (SFR) was 76.40%, lower than the 80.6% reported in the Baydilli et al. study.²⁰ Our SFR is similar to the results reported in a study by Ahmad et al.²¹ Another study reported 94.5% SFR, which was significantly greater than our study.²²

There is currently little information available on cost-benefit analysis and patient-centered outcomes, both of which require attention in light of current treatment alternatives. Lastly, there is disagreement over how to assess outcomes, particularly for Mini-PCNL, which complicates comparisons between treatment approaches. A classification scheme for Mini-PCNL was published by Somani et al.²³ If the results meet a predetermined standard, the development of future care pathways will undoubtedly benefit.

CONCLUSION

Given its stone clearance rate and the absence of major complications, this study showed that mini-PCNL is a safe and effective treatment for lower-pole renal stones in children. Therefore, we recommend that mini-PCNL be used as a first-line treatment for lower-pole renal stones in children.

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CONFLICT OF INTEREST: Authors declare no conflict of interest

GRANT SUPPORT AND FINANCIAL DISCLOSURE: NIL

Authors Contribution:

Following authors have made substantial contributions to the manuscript as under

Authors	Conceived & designed the analysis	Collected the data	Contributed data or analysis tools	Performed the analysis	Wrote the paper	Other contribution
Ahmad T	✓	✓	✗	✗	✓	✗
Ali M	✓	✗	✓	✓	✓	✗
Muhammad S	✓	✓	✗	✗	✗	✓
Ali S	✓	✗	✓	✓	✓	✗
Ullah I	✓	✓	✗	✗	✗	✓
Ullah E	✓	✗	✓	✓	✓	✗

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Ethical Approval:

This Manuscript was approved by the Ethical Review Board of Khyber Teaching Hospital, Peshawar. Vide No.565/IREB/KTH, Dated 18/04/2025



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UNVEILING THE INVISIBLE SCARS: THE PSYCHOSOCIAL EFFECTS OF BULLYING IN UNDERGRADUATE STUDENTS OF A UNIVERSITY OF PESHAWAR, PAKISTAN

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ABSTRACT

Objective: To assess the prevalence of bullying victimization and its psychosocial correlates among undergraduate students at the University of Peshawar.

Materials and methods: This cross-sectional descriptive study was conducted among undergraduate students at the University of Peshawar from January 2023 to June 2024. Data were collected using Olweus and Rosenberg's scale. Responses from 358 students were obtained. Data were analyzed using the Statistical Package for the Social Sciences (SPSS v.20.0).

Results: Of the 358 respondents, 232 (64.8%) had been victims of bullying. Of these, 66.8% were female. A total of 30.2% of respondents reported being bullied in childhood, 24.1% in adolescence, and 42.2% in adulthood. Verbal bullying was the most common form, reported by 64.5% of respondents, followed by physical bullying (19.4%) and cyberbullying (12.9%). A significant association between gender and type of bullying was found ($P = .006$). Bullying was associated with Anger in 20.6% of respondents, Sadness in 20%, Anxiety in 16.4%, Shame in 14.2%, Depression in 13.6%, and Fear in 13.3%. A total of 75.4% of students reported adverse social experiences related to bullying victimization; among these, 13.1% had trouble making new friends, 25.4% felt lonely, and 36.9% avoided social interaction. Among the 232 respondents with bullying victimization, the mean Rosenberg Scale score was 18.50 ± 6.23 . By category, 17.7% had low self-esteem, 77.6% had normal self-esteem, and 4.7% had high self-esteem.

Conclusion: Bullying victimization, particularly verbal bullying, was highly prevalent among undergraduate students at the University of Peshawar and was associated with adverse psychological and social outcomes reported by participants.

Keywords: Bullying, verbal bullying, psychological effects, social effects

This article may be cited as: Hayat N, Usman A, Arsalan M, Saif K, Ahmad SM, et al. Unveiling The Invisible Scars: The Psychosocial Effects Of Bullying In Undergraduate Students Of A University Of Peshawar, Pakistan. J Med Sci 2026 April - June;34(2):70-74

INTRODUCTION

Bullying is defined as repeatedly exposing a victim to physical, mental, or verbal abuse by another person. The perpetrator, or bully, can be an individual or a group. Acts of bullying include the use of physical force, such as hitting, kicking, or punching, as well as verbally insulting the victim by taunting or calling names. ¹ Nowadays, cyberbullying is also a major form of bullying victimization. ² A study found that the prevalence of traditional bullying

victimization was about 36%, while that of cyberbullying was 15%. ³ Studies have shown that youth with certain physical features, such as obesity or obvious disability, are more likely to be bullied. ⁴ Bullying is a very common phenomenon in schools, colleges, and universities, and is experienced by people of all races, cultures, and ethnicities at some point in their lives. ^{5,6} It is therefore considered an important global public health issue. ⁷ Several studies have shown that the majority of US youth experienced bullying in middle school. According to a study, 35% of youth have experienced recurrent bullying. Similarly, another survey of 3530 students from the West Coast region of the United States found that 22% of students reported being involved in bullying either as a victim or a bully. ⁸

Many studies have concluded that the African region has the highest prevalence of bullying among adolescents (47.36%). ⁹ Middle school students in low- and middle-income countries have an average peer victimiza-

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Date Received: 31/12/2025

Date Revised: 25/06/2026

Date Accepted: 26/06/2026

tion rate of 34.2%, with rates of 44.2% in Jordan, 33.6% in Lebanon, 31.9% in Morocco, 39.1% in Oman, and 20.9% in the United Arab Emirates.¹⁰

Several studies have also been conducted in Pakistan to assess the prevalence of bullying. For example, in a study of 4676 Pakistani students, 41% reported being bullied.¹¹ Another study conducted in Nawabshah City, Pakistan, found that 94% of boys and 85% of girls had been victims of bullying.¹²

Bullying is associated with long-term effects on mental as well as physical health.¹³ People who have been bullied are at a greater risk of experiencing depression, anxiety, social isolation, and having suicidal thoughts.¹⁴ A study conducted by Hawker and Boulton revealed a strong link between bullying victimization and loneliness, depression, and a reduction in the level of self-esteem.¹⁵ According to another study, children who had been bullied at school had double the chance of developing depression than those who had not been bullied.¹⁶

Numerous studies have examined the prevalence and psychosocial outcomes of bullying among students globally. However, very few studies have explored the prevalence and impact of bullying among university students in Pakistan, especially in Peshawar. Therefore, the aim of this study was to determine the prevalence of bullying victimization and to examine its psychosocial correlates among undergraduate students at the University of Peshawar.

MATERIALS AND METHODS

This cross-sectional descriptive study was conducted among undergraduate students at the University of Peshawar from January 2023 to June 2024. Sample size was calculated using Open Epi online software with the following values: confidence level = 95% and anticipated frequency (p) = 59.1%.¹⁷ The calculated sample size was rounded to 400. Students aged 18 to 26 years enrolled in undergraduate bachelor's programs at the University of Peshawar were eligible for inclusion. Data were collected using a nonprobability, voluntary-response sampling approach. Eligible undergraduate students were invited to participate by completing a self-administered questionnaire, which they returned anonymously after obtaining approval from the Ethical Board, using a validated instrument adapted from Olweus and the Rosenberg scale.¹⁸

¹⁹ Informed verbal consent was obtained, and the questionnaires, along with sealed envelopes, were distributed to volunteer students. A collection box was placed in the administrative block for a week, and then the sealed envelopes were collected. A total of 358 completed responses were analyzed. The frequency of bullying victimization was estimated. Various factors, such as socioeconomic background, support from parents and friends, psychological responses to bullying, effects on social life, and self-esteem, were also taken into account. The data were analyzed using the Statistical Package for the Social Sciences (SPSS v.20.0).

RESULTS

The calculated sample size was 400; however, some questionnaires were not returned, and others were incompletely filled out, so they were excluded. The adjusted sample size was 358. Of these 358 respondents, 232 (64.8%) students had been victims of bullying. Of these, 155 (66.8%) were female students, and 77 (33.2%) were male students. A total of 70 (30.2%) of the respondents reported being bullied in childhood, 56 (24.1%) in adolescence, and 98 (42.2%) in adulthood. Among respondents, bullying lasted a few weeks for 77 (33.2%), from several months to a year for 38 (16.4%), and several years for 38 (16.4%). Verbal bullying was the most common form, reported by 160 (64.5%), followed by physical bullying by 48 (19.4%), cyberbullying by 32 (12.9%), and other forms of bullying (by parents, siblings, and relatives) by 8 (3.2%), the least common among respondents (Fig. 1).

In Table 1, the chi-square test of association revealed a significant association ($P = 0.006$) between gender and the type of bullying experienced (The Chi-square statistic is significant at the .05 level).

Among the respondents, 20 (8.6%) had a poor socioeconomic background, 131 (56.5%) had a satisfactory socioeconomic background, and 81 (34.9%) had a good socioeconomic background. The chi-square test of association did not reveal a significant association between socioeconomic status and the pattern of bullying experienced by respondents ($P > .05$). A total of 178 (76.7%) respondents received help and support from family, friends, and teachers, while 54 (23.3%) did not receive any help.

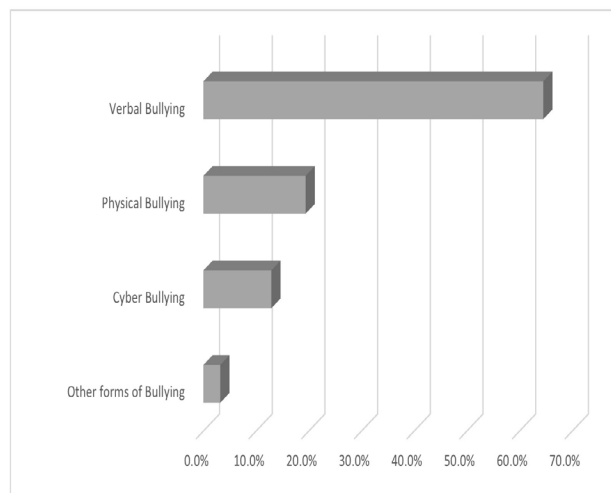
The majority of students reported more than one psychological effect associated with bullying. Anger was reported by 68 (20.6%) respondents, and sadness by 66

Table No 1: Gender differences in types of Bullying

Types of Bullying	Gender of the Participant				Pearson	Chi-Square Test
	male		female			
	Frequency	N %	Frequency	N %	Chi-square Sig.	14.639 .006*
Physical Bullying	25	32.5%	23	14.8%		
Verbal Bullying	46	59.7%	114	73.5%		
Cyber Bullying	10	13.0%	22	14.2%		
Other types of bullying	2	2.6%	6	3.9%		

Table No 2: Psychological Response to Bullying

Effects Of Bullying	Responses	
	N	Percent
Anger	68	20.6%
Sadness	66	20.0%
Anxiety	54	16.4%
Shame	47	14.2%
Depression	45	13.6%
Fear	44	13.3%
Others	6	1.8%
Total	330	%100.0
p-value		0.002

**Fig 1: Percentage of various types of bullying**

(20%), making these the most common psychological effects (Table 1). The chi-square test of association revealed a significant association between the type of bullying experienced and the psychological effects in respondents ($P = .002$).

A total of 170 (75.4%) students reported social difficulties associated with bullying victimization; among these, 33 (13.1%) had lost friends or had trouble making new friends, 64 (25.4%) felt isolated and lonely, and 93 (36.9%) avoided social interaction. A total of 62 (24.6%) reported no difficulties related to bullying victimization. Among the 232 respondents who experienced bullying victimization, the mean Rosenberg Scale Score was 18.50 ± 6.23 . Based on Rosenberg Scale Categories, 41 (17.7%) scored in the range of 0-15 on the Rosenberg Self-Esteem Scale, which indicates low self-esteem; 180 (77.6%) scored in the normal range; and 11 (4.7%) scored in the high self-esteem range.

DISCUSSION

The results of this study provide important insights into the frequency, types, and psychological correlates of bullying victimization among undergraduate students. The

majority of the adolescents in the survey reported having experienced bullying victimization, indicating a worrying frequency (64.8%) of bullying among them. The frequency is very high compared to the previous studies conducted in the US, the Middle East, and African countries. The comparatively higher prevalence observed in our study may reflect differences in contextual and cultural factors, but also may be partly explained by methodological differences. Unlike studies that assess bullying within a specific recent period or a single development stage, our study captured self-reported bullying experiences across childhood, adolescence, and adulthood. This broader recall window may have increased the probability of identifying participants with any history of bullying victimization and may also have introduced recall bias. In opposition to previous studies that have consistently shown a higher prevalence of bullying among males than females, our findings indicate a reverse trend, with females experiencing higher rates of bullying.²⁰ This difference may be due to various factors, including differences in sample populations, data collection methods, or cultural contexts.

Consistent with previous research, verbal bullying emerged as the most common form (64.5%), followed by physical (19.4%) and cyberbullying (12.9%). Similarly, the findings of this study are consistent with previous literature reporting an association between bullying victimization and adverse psychological experiences among students.²¹ It is interesting to note that our study indicates that socioeconomic status does not significantly correlate with the pattern of bullying experienced or its impact on social life. This contrasts with previous research, which suggests that individuals from lower socioeconomic backgrounds are more frequently subjected to bullying, thereby highlighting socioeconomic disparities in bullying prevalence.²² This difference may be due to the study setting, which is in a developing country.

The self-esteem analysis using the Rosenberg Self-Esteem Scale revealed an intriguing finding. The majority of respondents fell within the normal range. This contrasts with previous studies that typically show lower self-esteem among victims. Several explanations could account for this discrepancy. One possibility is the self-report nature of our study, which may have led participants to overestimate their self-esteem. Additionally, effective coping mechanisms or supportive behaviors may have influenced how participants reported their self-esteem and bullying victimization.²³ The findings may also be understood in relation to the cultural and institutional context of Pakistani Universities.²⁴ In such settings, interpersonal relationships are often shaped by strong social hierarchies, peer group dynamics, and gender norms, which may influence both the experience and reporting of bullying victimization.²⁵ Female students may be more likely to report verbal and relational forms of bullying, whereas male students may underreport such experiences because of social expectations related to masculinity and emotional restraint.^{24,25} In addition, concerns about stigma, reputation,

and social judgment may discourage students from openly discussing bullying or its psychological correlates.²³ Institutional factors may also be relevant, as many universities in low-resource settings have limited formal mechanisms for reporting bullying, addressing peer victimization, or providing accessible psychological support to affected students.^{24,26} The higher proportion of female participants reporting bullying victimization in our study may reflect context-specific social and gender dynamics rather than a simple difference in exposure alone.²⁵ It is possible that female students are more likely to recognize and report verbal, relational, or emotionally distressing experiences as bullying, whereas male students may normalize similar experiences or be less willing to disclose them. This interpretation should be considered cautiously, but it may partially explain why our findings differ from studies reporting higher bullying prevalence among males.^{24, 26}

Because of the cross-sectional design, temporal relationships and causality cannot be established. The observed psychological and social outcomes should therefore be interpreted as associations reported by participants rather than as consequences directly attributable to bullying victimization. In addition, the use of a non-probability, voluntary-response sampling approach may limit the generalizability of the findings. Students who chose to participate may differ from those who did not respond, introducing the possibility of self-selection and non-response bias. Because bullying experiences were self-reported across multiple life stages, the study is also subject to recall bias. Participants may have remembered or interpreted experiences from childhood, adolescence, and adulthood differently, which may have influenced the reported prevalence.

CONCLUSION

Bullying is notably prevalent among undergraduate students at the University of Peshawar, with verbal bullying the most commonly reported type. Bullying victimization was associated with adverse psychological responses and social difficulties reported by participants. These findings highlight the need for further analytical and longitudinal research to better understand the temporal relationship between bullying victimization and psychological well-being and to inform support strategies for affected students.

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CONFLICT OF INTEREST: Authors declare no conflict of interest

GRANT SUPPORT AND FINANCIAL DISCLOSURE: NIL

Authors Contribution:

Following authors have made substantial contributions to the manuscript as under

Authors	Conceived & designed the analysis	Collected the data	Contributed data or analysis tools	Performed the analysis	Wrote the paper	Other contribution
Hayat N	✓	✓	✗	✗	✓	✗
Usman A	✓	✗	✓	✓	✓	✗
Arsalan M	✓	✓	✗	✗	✗	✓
Saif K	✓	✗	✓	✓	✓	✗
Ahmad SM	✓	✓	✗	✗	✗	✓
Kashif M	✓	✗	✓	✓	✓	✗
Sanan A	✓	✗	✓	✓	✓	✗
Muiz A	✓	✓	✗	✗	✗	✓
Ali F	✓	✗	✓	✓	✓	✗
Ahmad IB	✓	✓	✗	✗	✗	✓

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethical Approval:

This Manuscript was approved by the Ethical Review Board of Khyber Medical College, Peshawar. Vide No. 57/DME/KMC, Dated 30/01/2024.



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THE ASSOCIATION OF VITAMIN D DEFICIENCY IN POLYCYSTIC OVARIAN SYNDROME

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ABSTRACT

Objective: To determine the association of vitamin D deficiency in patients with polycystic ovarian syndrome (PCOS).

Material & Methods: A case-control study was conducted on forty-eight patients, twenty-four cases and twenty-four controls, at the Department of Obstetrics and Gynecology at Lady Reading Hospital, Peshawar, Pakistan, from June 2024 to November 2024. Vitamin D deficiency was assessed in patients with PCOS and in controls. Pregnant patients and those already diagnosed with vitamin D deficiency were excluded from the study. 25 OH D3 levels were measured in both groups, and patients with vitamin D deficiency were classified as positive if vitamin D levels were < 20 ng/mL. A Chi-square test and Pearson Correlation Coefficient were used to assess the association between the two categories.

Results: The mean age of cases was 29.88 ± 6.58 years, while the mean age of controls was 30.54 ± 6.13 years ($P=0.71$). The mean BMI of cases was 27.16 ± 2.60 kg/m² while that of controls was 25.40 ± 2.70 kg/m²; cases had a notably higher BMI than controls ($P=0.02$). Cases had a higher frequency of vitamin D deficiency (54.2%) than controls (20.8%; $p=0.01$). The mean vitamin D concentrations were lower in cases than in controls (24.82 ± 8.59 ng/mL vs 29.54 ± 7.91 ng/mL), with a trend toward significance ($p=0.054$). However, the frequency of vitamin D deficiency was significantly higher in cases than in controls (54.2% vs 20.8%; $p=0.017$). Vitamin D concentrations were negatively associated with age and BMI in both cases and controls.

Conclusion: Mean vitamin D levels trended lower in PCOS patients; vitamin D deficiency was significantly higher in the PCOS group, and levels were negatively associated with age and BMI in both groups.

Keywords: Vitamin D Deficiency, Obesity, Polycystic ovarian syndrome

This article may be cited as: Sabir SA, Sultan S. The Association Of Vitamin D Deficiency In Polycystic Ovarian Syndrome. J Med Sci 2026 April - June;34(2):75-80

INTRODUCTION

Polycystic ovarian syndrome (PCOS) is a multifaceted condition characterized by hormonal imbalances that result in irregular menstrual cycles and the presence of cysts on one or both ovaries.^{1, 2} PCOS affects women throughout their reproductive years.³ This syndrome is associated with several health complications, including cardiovascular conditions, infertility, obesity, and insulin resistance.^{4, 5}

A study conducted in Pakistan on 153 participants found PCOS in 33.3% of cases.⁶ Another study conducted in Pakistan showed that obesity, abdominal hair develop-

ment, irregular periods, cramps, and hormonal acne are related to PCOS.⁷ Approximately 50% of the participants were found to have symptoms associated with PCOS. This study reported that 46.5% of the participants indicated their awareness of the hereditary nature of PCOS, and overall, 28.5% of females were found to have a familial predisposition to PCOS.

Insufficient levels of vitamin D lead to calcium instability among women affected with PCOS, which is related to irregular cycles of menstruation and fertility problems.^{8, 9} Research has established a link between metabolic changes in PCOS and variations in VDR genes.¹⁰ Insulin resistance and vitamin D are tightly associated, representing a prominent feature of the PCOS phenotype.¹¹ In conjunction with insulin resistance, Women with PCOS who suffer from deficient vitamin D levels also experience cardiovascular issues.¹²

There exists a multidimensional and delicate relationship between Vitamin D3 and PCOS. Vitamin D significantly enhances glucose metabolism by augmenting

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Date Received: 18/01/2026

Date Revised: 25/06/2026

Date Accepted: 26/06/2026

insulin secretion, promoting insulin receptor expression, and mitigating the effects of Cytokines that promote inflammation. Vitamin D's effect on insulin resistance may explain how it helps with PCOS-related metabolic and reproductive problems.¹² A complete analysis, including many elements, is necessary to comprehend the levels of Vitamin D among women affected with and without having PCOS. At the very start, it is necessary to clarify the processes that govern Vitamin D metabolism and its interactions with hormonal pathways in the context of PCOS. Furthermore, examining the impact of vitamin D concentrations on key metabolic markers, lipid profiles, insulin resistance, and inflammatory markers can yield significant insights into the clinical importance of Vitamin D in the treatment of PCOS.

This study aims to investigate the association between vitamin D deficiency and PCOS among patients, raise awareness among health workers, and provide local-level data on this topic, thereby improving the management of PCOS-related symptoms.

MATERIAL AND METHODS

A comparative cross-sectional study was conducted with two groups, in which women with PCOS were assigned to the case group and healthy women to the control group. Subjects were recruited from the Department of Obstetrics and Gynecology at Lady Reading Hospital, Peshawar, Pakistan, from June 2024 to November 2024, after obtaining ethical approval from the hospital and patient consent. In both cases and controls, subjects were aged 18 to 40 years. Sample size was determined using OpenEPI, with a previous frequency of vitamin D deficiency of 56.3% in cases and 56.3.7% in controls, a test power of 80%, and a 95% confidence interval.

Twenty-four patients in each group were allocated.¹³ We used a nonprobability sampling technique. Patients with 12 or more follicles on ultrasonography, measuring 4-9 mm, were labeled as cases. Pregnant patients and those already on vitamin D were not included. We collected blood samples from all subjects and sent them to the hospital laboratory to determine vitamin D concentrations using the CLIA (Chemiluminescent Immunoassay) method.

Vitamin D deficiency was labeled positive if vitamin D levels were < 20 ng/mL. PCOS was diagnosed in all patients using the Rotterdam Criteria, which require at least two of the following three features: irregular or absent ovu-

lation, clinical or biochemical evidence of high androgens, and polycystic morphology on ultrasound. Diabetes was labeled yes if HbA1c was > 6.5%; hypertension was labeled yes if systolic BP was $\geq$ 140 mmHg and diastolic BP was $\geq$ 90 mmHg. Hirsutism was assessed according to the Ferriman-Gallwey scoring system; a score of less than 8 was considered normal, mild to moderate if 8 to 15, and severe if greater than 15.¹⁴

All data were recorded on a pre-designed proforma. Data analysis was performed using SPSS 23. For qualitative associations, the Chi-square test was used; for associations between qualitative and quantitative variables, the t-test was used; and Pearson's correlation coefficient was used to assess correlations between quantitative variables. We considered P significant at 0.05.

RESULTS

Forty-eight women were selected for this study; twenty-four were allocated to the case group (PCOS), and twenty-four to the control group. The mean age of cases was 29.88 ± 6.58 years, while the mean age of controls was 30.54 ± 6.13 years ($P = 0.71$).

Table 1 presents the categorical demographic details of cases and controls. HbA1c levels were above 6.5% in 16 (66.7%) cases, compared with 7 (29.2%) controls ($P = 0.009$). Hypertension was more prevalent in cases (11; 45.8%) than in controls (4; $P=0.02$). Figure 1 compares vitamin D levels between cases and controls. Cases had lower mean vitamin D levels than controls; however, this difference did not reach statistical significance ($p=0.054$), though it showed a trend toward significance.

Figure 2 compares BMI between cases and controls using an independent t-test; cases had a significantly higher BMI than controls ($p=0.026$). The comparison of vitamin D deficiency between cases and controls using the Chi-Square test is shown in Table 2. Cases had a significantly higher frequency of vitamin D deficiency than controls ($P=0.01$). Pearson's correlation coefficient was used to examine the relationship between vitamin D levels and continuous variables (age and BMI).

As shown in Table 3, vitamin D levels demonstrated a significant negative correlation with age in both cases and controls. Similarly, a significant negative association was found between vitamin D levels and BMI in both cases and controls. Table 4 presents the distribution of vitamin D levels between cases and controls.

Table No 1: Demographics of patients with cases and controls

Demographics		Groups				P value
		Cases		Controls		
		N	%	N	%	
Marital status	Married	17	70.8%	15	62.5%	0.54
	Unmarried	7	29.2%	9	37.5%	
Monthly income (PKR/ Month)	Monthly income < 50000	6	25.0%	4	16.7%	0.73
	Monthly income 50000 to 80000	16	66.7%	17	70.8%	
	Monthly income > 80000	2	8.3%	3	12.5%	
HbA1c	≤ 6.5%	8	33.3%	17	70.8%	0.009
	> 6.5%	16	66.7%	7	29.2%	
Hypertension	Yes	11	45.8%	4	16.7%	0.02
	No	13	54.2%	20	83.3%	
Hirsutism	Normal	4	16.7%	17	70.8%	0.0001
	Mild	15	62.5%	7	29.2%	
	Moderate to severe	5	20.8%	0	0.0%	
BMI distribution	Normal	6	25.0%	14	58.3%	0.05
	Overweight	13	54.2%	8	33.3%	
	Obese	5	20.8%	2	8.3%	

Table No 2: Comparison of Vitamin D Deficiency between cases and controls

		Vitamin D deficiency		Total	p value
		Yes	No		
Groups	Cases	13	11	24	0.017
		54.2%	45.8%	100.0%	
	Controls	5	19	24	
		20.8%	79.2%	100.0%	
		Total		18	
		37.5%	62.5%	100.0%	

Table No 3: Secondary analysis of vitamin D levels with age and BMI

Age (Years)		
Correlation	P value	Pearson'(r)
Cases	0.004	-0.56
Controls	0.01	-0.47
BMI (Kg/m2)		
Cases	0.002	-0.58
Controls	0.01	-0.47

Table No 4: Comparison of different Vitamin levels between cases and controls

		Groups				p value
		Controls		Cases		
		n	%	n	%	0.059
Vitamin D levels	Deficient	5	22.7%	13	56.5%	
	Insufficient	7	31.8%	3	13.0%	
	Sufficient	10	45.5%	7	30.4%	

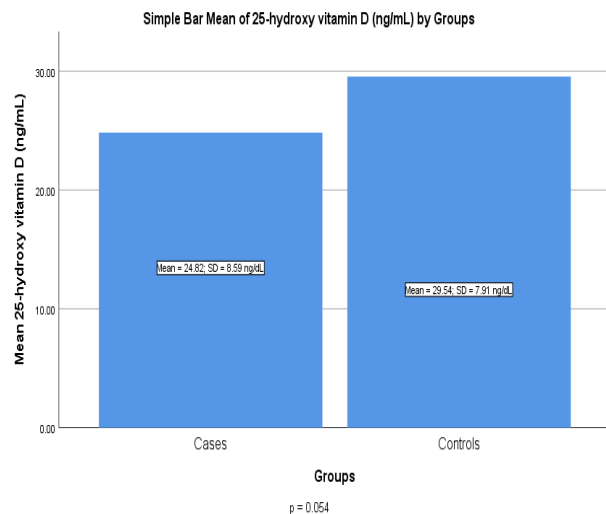


Fig 1: Comparison of Vitamin D levels in cases and controls using an independent-samples t-test

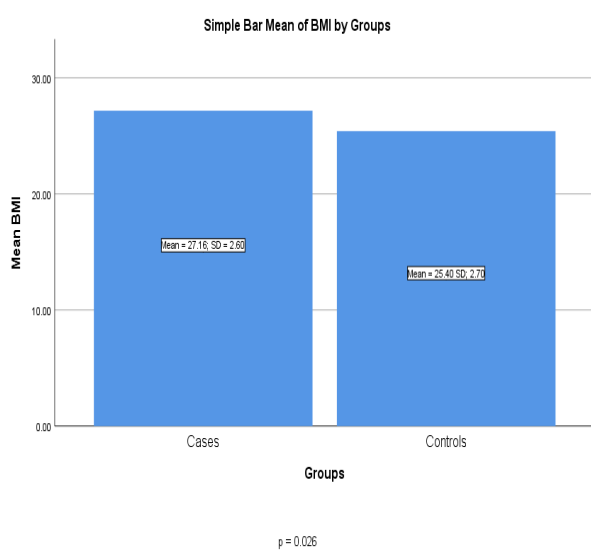


Fig 2: Comparison of BMI in cases and controls using an independent-samples t-test

DISCUSSION

This study was conducted on 48 women, of whom 24 had PCOS, and 24 were healthy controls. Neither group showed a notable difference in mean age, monthly income, or marital status.

Despite extensive research on PCOS and vitamin D, a notable gap remains in the literature regarding the independent contributions of PCOS and obesity-related mechanisms to vitamin D deficiency.

Many previous studies have reported an association between PCOS and low vitamin D levels without adequately controlling for BMI, potentially overestimating the

direct effect of PCOS.

Furthermore, most existing studies have been conducted in Western populations, with limited data from South Asian settings, where dietary patterns, sunlight exposure, and genetic factors may differ significantly. The role of age as a modifier of the PCOS-vitamin D relationship has also been insufficiently explored.

Various investigations have observed a higher occurrence rate of Vitamin D deficiency among women with PCOS.^{9, 10} Our results showed similar findings: 54.2% of PCOS cases had low vitamin D levels, compared with only 20.8% of healthy controls. In the current study, the difference showed a trend toward significance. Supporting our findings, a Pakistani study reported similar observations and concluded that women with PCOS had higher rates of vitamin D deficiency than women without PCOS.¹⁵ A study conducted in India reported that the majority of women with PCOS had vitamin D deficiency or insufficiency when compared to healthy controls; a total of 56.3% of PCOS patients had vitamin D deficiency, while 35.4% had vitamin D insufficiency.¹³

Insulin resistance is common in patients with PCOS and is strongly linked to vitamin D deficiency.¹⁶ In our study, the case group had a higher prevalence of diabetes than the controls. The aforementioned Pakistani study reported similar findings, noting that patients with PCOS had higher glucose levels than controls.¹⁵ Studies suggest that vitamin D supplementation can help control insulin resistance in patients with PCOS.^{17, 18}

One of the findings of our study was a negative correlation between vitamin D levels and increasing BMI. It has been hypothesized that being overweight could be associated with insufficient vitamin D intake.¹⁹ Researchers found that serum 25(OH)D levels were lower in people with a higher body fat percentage. This has been attributed to adipose tissue sequestering fat-soluble vitamin D. Research has demonstrated a significant negative association between low vitamin D levels, increased fat mass, and the likelihood of future weight gain. This correlation has been consistently demonstrated.^{20, 21} Similar to our findings, the aforementioned Indian study reported a negative correlation between low vitamin D levels and high BMI.¹³ A study conducted in Pakistan reported similar findings, showing an association between obesity and vitamin D deficiency.²² Another important finding of our study was the negative association between low vitamin

D levels and increasing age. The aforementioned Indian study also reported similar findings, showing a negative correlation between low vitamin D levels and advancing age.¹³

Several limitations of this study should be acknowledged. The small sample size limited statistical power and precluded robust multivariable adjustment for confounders such as BMI, sunlight exposure, dietary vitamin D intake, and seasonal variation. With only 18 vitamin D deficiency events, the study violated the recommended events-per-variable ratio for logistic regression. As a single-center study, it limits the generalizability of our findings to other populations. We also did not assess biochemical hyperandrogenism, body fat percentage, or parathyroid hormone levels, which may have provided further insights. Despite these limitations, our findings provide valuable preliminary data on the PCOS-vitamin D relationship in a Pakistani population and highlight the need for larger, multi-center prospective studies with comprehensive covariate adjustment.

CONCLUSION

While mean vitamin D levels showed only a trend toward lower levels in PCOS patients, the proportion of patients with vitamin D deficiency was significantly higher in the PCOS group. Further interventional studies are required to determine whether vitamin D supplementation has a therapeutic role in improving metabolic outcomes in patients with PCOS, particularly those with higher BMI.

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CONFLICT OF INTEREST: Authors declare no conflict of interest

GRANT SUPPORT AND FINANCIAL DISCLOSURE: NIL

Authors Contribution:

Following authors have made substantial contributions to the manuscript as under

Authors	Conceived & designed the analysis	Collected the data	Contributed data or analysis tools	Performed the analysis	Wrote the paper	Other contribution
Sabir SA	✓	✓	✗	✗	✓	✗
Sultan S	✓	✗	✓	✓	✓	✗

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethical Approval:

**This Manuscript was approved by the IRB of Lady Reading Hospital, Peshawar. Vide No. 128/IRB/LRH/MTI.
Dated 02/05/2024**



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ADHERENCE TO ANTIHYPERTENSIVE MEDICATION AMONG PATIENTS WITH HYPERTENSION IN PESHAWAR, PAKISTAN: A CROSS-SECTIONAL STUDY

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ABSTRACT

Objective: To assess the adherence to antihypertensive therapy and its associated sociodemographic factors among hypertensive patients attending public sector tertiary care hospitals in Peshawar.

Materials and Methods: A cross-sectional descriptive study was conducted from May to November 2024 using the Hill-Bone Compliance to High Blood Pressure Therapy Scale (CHBPTS). A sample of 390 was collected through consecutive sampling from three public-sector tertiary care hospitals in Peshawar. Data were analyzed using SPSS version 25. Continuous outcomes were compared using the Mann-Whitney U test and the Kruskal-Wallis test, with Dunn-Bonferroni post hoc tests for significant pairwise comparisons. Spearman's rank correlation coefficient was used to assess correlations between variables.

Results: The study included participants with a mean age of 54.0 ± 10.3 years, of whom 39.2% were men and 60.8% were women. The mean overall adherence score on the Hill-Bone Compliance to High Blood Pressure Therapy Scale (Hill-Bone CHBPTS) was 27.27 ± 6.8 . The mean subscale scores were 17.52 ± 4.98 for medication-taking, 5.03 ± 1.38 for reduced sodium intake, and 4.70 ± 1.38 for appointment-keeping. According to the Hill-Bone CHBPTS scoring criteria, 44.6% of participants were adherent to antihypertensive treatment.

Conclusion: The study results showed that adherence to antihypertensive treatment requires attention to better control of hypertension in our local context. Sociodemographic factors play an important role in adherence to antihypertensive treatment.

Keywords: Hill Bone Compliance Scale, Hypertension, adherence.

This article may be cited as: Ghayur US, Aliya B, Syed S, Ghani MA, Azam M, Rafi S. Adherence To Antihypertensive Medication Among Patients With Hypertension In Peshawar, Pakistan: A Cross-Sectional Study. J Med Sci 2026 April - June;34(2):81-86

INTRODUCTION

Hypertension has been defined as “a progressive cardiovascular syndrome due to multiple etiologies that results in physical & operational changes to the heart and vascular systems.”¹ Hypertension has emerged as a global epidemic affecting nearly 1.4 billion individuals worldwide and is responsible for 57 million disability adjusted life years, which accounts 3.7% of the total disability adjusted life years.² The prevalence of hypertension in Pakistan is approximately 18% in individuals above 15 years, with higher rates in urban areas and in females rather than men. It is a highly common condition in Pakistan, impact-

ing about 18% of individuals aged 15 years and older, so every fourth person in Pakistan is suffering from hypertension.³ As hypertension is a chronic condition that requires lifelong adherence to treatment.

The control of Hypertension is considered to be inadequate in most Asian countries. Literature shows that developed countries have a higher percentage of patients with controlled hypertension as compared to developing nations like Pakistan, where the control rate is 6%.^{4, 5} Additionally, it is increasingly among the most frequent reasons for hospital visits in our setting, but still, adherence towards antihypertensive treatment remains a key challenge to achieve optimal blood pressure control and reduce complications.⁶

Adherence can be defined as the extent to which patients follow medical instructions given by physicians.^{6, 7} In addition to treatment, several daily lifestyle modifications are crucial for disease control & management.⁸ In addition, a variety of other factors, including patient-related characteristics, treatment regimens, socioeconomic status, and patients' awareness levels, also influence ad-

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Date Received: 10/02/2026

Date Revised: 25/06/2026

Date Accepted: 26/06/2026

herence to the treatment regimen.⁹

Studies have shown that adherence rates can vary widely across different populations, with compliance reported to range from approximately 33% to 86%.^{10, 11} Therapeutic adherence towards anti-hypertensive treatment remains a substantial challenge in our society. Hypertension remains a critical public health challenge globally, with effective treatment largely dependent on patient adherence to prescribed therapeutic regimens. However, adherence rates vary widely, influenced by psychosocial, economic, and health system factors.¹² Non-adherence contributes significantly to poor blood pressure control and increased cardiovascular risk. Understanding factors influencing compliance using validated scales enables targeted interventions to improve health outcomes.¹³

This study aimed to assess the role of sociodemographic factors towards adherence to antihypertensive treatment in our local context, thus to design interventions to improve the management of hypertension and patient care outcomes.

MATERIALS AND METHODS

A cross-sectional study was conducted from May to November 2024 in three public-sector tertiary care hospitals: Lady Reading Teaching Hospital, Khyber Teaching Hospital & Hayatabad Medical Complex, in the district of Peshawar, Pakistan. A sample size of 390 participants was calculated using the prevalence formula, with an estimated good adherence of 50% (Desired precision of 0.05 at a 95% confidence level). Participants were selected through a consecutive sampling method.¹⁴

Inclusion criteria were individuals aged 35 years or older with a documented diagnosis of hypertension for at least 12 months, as confirmed by medical records and physician notes. The hypertensive patients with comorbidities and having psychiatric issues were excluded. The tool for data collection used in our study was a standardized Hill-Bone Compliance to High Blood Pressure Therapy Scale (Hill-Bone CHBPTS) with high internal consistency and reliability of Cronbach's alpha value (0.84).¹⁵ As per the literature, adherence is defined as the extent to which an individual's behavior, including medication-taking, dietary practices, and lifestyle modifications, corresponds to the recommendations provided by a healthcare professional.¹⁶

Hill-Bone CHBPT is a widely used, validated 14-item tool that helps identify specific behavioral barriers to controlling blood pressure through self-reporting by hypertensive patients. It assesses patient adherence to antihypertensive medication across three behavioral domains, including:

Medication Adherence (9 items) tracks behaviors that lead to forgetting, missing, or running out of medi-

cines.

Reduced Salt Intake (3 items) assesses dietary habits focusing on salt intake in their daily life.

Appointment keeping (2 items) reflects the patient's consistency in attending follow-up visits with physicians.

Each item is scored on a 4-point Likert scale. The minimum overall score for the Hill-Bone CHBPTS is 14, and the maximum is 56. The maximum scores for the medication adherence, sodium intake, and appointment-keeping subscales are 36, 12, and 8, respectively. Adherence was operationally defined as the sample mean score on the Hill-Bone CHBPTS. Study participants scoring below the mean were categorized as adherent, while those with scores equal to or exceeding the mean were classified as non-adherent. Because there is no universal cutoff, many studies use the group mean or a specific threshold (such as a score of 50% in certain adapted versions) to categorize patients as "adherent" or "non-adherent".

Ethical approval was obtained from the Rehman Medical Institute (Letter No: RMI/RMI-RMC/Article Approval/122), and administrative permissions were acquired from Khyber Teaching Hospital, Lady Reading Hospital, and Hayatabad Medical Complex, Peshawar. Data were collected through interviews with patients using the validated CHBPT questionnaire.

Data analysis was conducted using SPSS version 25. A comparison between 2 groups was performed using the Mann-Whitney test, and a comparison between 3 or more groups was performed using the Kruskal-Wallis test. When a statistically significant difference was detected, a post hoc analysis was performed using the Dunn test to identify significant differences among groups. Spearman's rank correlation coefficient was used to assess correlations between variables. For independent influences of relevant variables, multivariate analysis of the numerical variable was performed using linear regression. The results are presented as standardized beta coefficients from a regression model, with 95% CIs; values with P-values < 0.05 are considered statistically significant.

RESULTS

The outcomes of our study are described in two sections.

1. DEMOGRAPHIC SECTION

The demographic data of the study participants were summarized as shown in Table 1:

The overall adherence score for hypertension treatment among the study participants was 27.2745 ± 6.83 , indicating moderate adherence according to the criteria outlined in the methodology section. The results for the three

subscales of the Hill-Bone Compliance to High Blood Pressure Therapy Scale (CHBPTS) are shown in Table 2:

Medication-taking had the highest mean adherence score (17.52 ± 4.98), followed by reduced salt intake (5.03 ± 1.38) and appointment-keeping (4.70 ± 1.38). The overall mean adherence score was 27.27 ± 6.83 , indicating moderate adherence among participants.

Note: P values were calculated using the Mann-Whitney U test for comparing between two groups, and the Kruskal-Wallis H test was used for comparisons among three or more groups. Pairwise comparisons were performed using Dunn's post hoc test.

MULTIVARIATE ANALYSIS OF MEDICATION TAKING SUBSCALE

The analysis showed that individuals who were single, divorced, or widowed had significantly lower adherence scores ($\beta = -1.024$, $p = 0.019$). Similarly, participants who were employed or self-employed showed a modest but significant decrease in adherence ($\beta = -0.44$, $p = 0.047$). The regression model explained 22.3% of the variance in the medication-taking subscale ($R^2 = 0.223$), indicating moderate explanatory power.

MULTIVARIATE ANALYSIS OF REDUCED SALT INTAKE SUBSCALE

No independent variable reached statistical significance. However, urban residence ($p = 0.079$), employment ($p = 0.068$), and income level ($p = 0.074$) were marginally associated. The model accounted for 12.0% of the variation in reduced salt intake scores ($R^2 = 0.120$).

MULTIVARIATE ANALYSIS OF APPOINTMENT KEEPING SUBSCALE

Two factors were significantly associated with the outcome. Lower educational attainment (primary or no formal education) was significantly associated ($p = 0.013$). In addition, a duration since diagnosis of 1–10 years was associated with a 0.275-point increase in the score ($\beta = 0.275$, $p = 0.022$). The model explained 17.8% of the variance in the outcome ($R^2 = 0.178$), indicating modest explanatory power.

DISCUSSION

Our study results revealed that 44.6% of the participants demonstrated good adherence to antihypertensive treatment, whereas 55.7% exhibited poor adherence. The study participants exhibited the lowest adherence to appointment-keeping, while relatively better adherence was observed for medication-taking.

The literature shows that several studies using different adherence tools, including the Hill-Bone CHBPTS, have reported challenges with adherence among hyper-

Table No 1: Demographic data of the Hypertensive Patients

Variables	Mean (SD)	Median (quartile)
Age	54.03(10.3)	55(45–62)
Features	n	%
Gender		
Male	153	39.2
Female	237	60.8
Residence		
Rural	242	62.1
Urban	148	37.9
Living Arrangements		
Living alone	52	13.3
Living with family	338	86.7
Marital status		
Single	10	2.6
Married	321	82.3
Divorced	19	4.9
Widowed	40	10.3
Education		
None	169	43.3
primary	109	27.9
Secondary	64	16.4
Tertiary	48	12.3
Occupation		
Employed	88	22.6
Self employed	77	19.7
Unemployed	209	53.6
Retired with pension	16	4.1
Income		
Below 20,000 Rs	121	31.0
20,000-50,000 Rs	151	38.7
50,000-100,000 Rs	98	25.1
Above 100,000 Rs	20	5.1
Medication		
Less than 2 drugs	288	74.1
3 drugs or more	102	25.9
Duration of Disease		
1-5 Years	180	46.2
6-10 years	143	36.7
11-15 years	56	14.4
More than 15 years	11	2.8

Table No 2: Hill-Bone CHBPTS - Adherence Scores

Total Score	Mean Adherence Score $\pm$ SD
Reduced sodium intake	5.03 ± 1.38
Appointment keeping	4.70 ± 1.38
Medication taking	17.52 ± 4.98
Overall Adherence Score	27.27 ± 6.8

Table No 3: Comparison of adherence scores

Male	26 (22-30)	5 (4-6)	4 (3-5)	17 (14-20)
Female	26 (23-29)	5 (4-6)	4 (4-5)	17 (14-19)
P-value*	0.533	0.156	0.563	0.640
Residence				
Rural	26 (21-29)	5 (3-6)	4 (4-5)	16 (13-19)
Urban	27 (24-31)	5 (4-6)	4 (4-5)	18 (14-21)
P-value*	0.006	0.077	0.111	0.013
Living				
Living Alone	27 (24-31)	5 (3-6)	5 (4-5)	18 (15-21)
Living with Family	26 (22-29)	5 (4-6)	4 (3-5)	17 (14-19)
P-value*	0.037	0.515	0.049	0.073
Marital Status				
Married (A)	26 (22-29)	5 (4-6)	4 (4-5)	16 (13-19)
Single or Divorced (B)	32 (28-35)	5 (4-8)	5 (4-5)	22 (20-23)
Widowed (C)	27 (23-29)	4 (3-6)	4 (4-5)	18 (14-19)
P-value*	0.004	0.601	0.941	0.000
Post hoc**	B>A,C	A,B>C	B>AC	B>AC
Education				
Primary or None (A)	26 (23-29)	5 (4-6)	4 (4-5)	18 (14-20)
Secondary (B)	27 (25-32)	5 (4-6)	4 (4-6)	17 (15-20)
Tertiary (C)	27 (23-31)	5 (4-6)	4 (3-5)	18 (14-20)
P-value*	0.004	0.044	0.049	0.022
Post hoc**	C>A	-	-	AC>B
Employment				
Employed or Self employed (A)	27 (22-32)	5 (4-6)	4 (4-6)	17 (14-21)
Unemployed (B)	25 (21-29)	5 (3-6)	4 (4-5)	16 (13-19)
Retired with pension (C)	28 (25-30)	6 (5-7)	5 (4-6)	16 (15-20)
P-value*	0.049	0.027	0.353	0.047
Post hoc**	C>A	C>A	C>A	A>C
Income				
Below 20,000 Rs (A)	27 (22-30)	5 (4-5)	5 (4-6)	18 (13-20)
20,000-50,000 Rs (B)	26 (22-29)	5 (3-6)	4 (4-5)	17 (14-20)
50,000-100,000 Rs (C)	26 (21-29)	5 (4-6)	4 (3-5)	16 (14-19)
above 100,000 Rs (D)	26 (21-31)	6 (5-6)	4 (3-5)	16 (12-19)
P-value*	0.732	0.015	0.011	0.568
Post hoc**	A>D	D>A	A>D	A>D
Duration of Disease				
1-5 Years (A)	25 (21-28)	5 (3-6)	4 (3-5)	16 (13-18)
6-10 years (B)	27 (23-31)	5 (4-6)	4 (4-5)	18 (14-21)
11-15 years (C)	28 (25-32)	4 (3-6)	4 (4-6)	18 (15-21)
More than 15 years (D)	24 (19-28)	5 (4-6)	5 (4-6)	16 (10-17)
P-value*	0.000	0.451	0.073	0.000
Post hoc**	C> A,B,D	A>C	D>A	B,C>A,D

Note: P values were calculated using the Mann-Whitney U test for comparing between two groups, and the Kruskal-Wallis H test was used for comparisons among three or more groups. Pairwise comparisons were performed using Dunn's post hoc test.

tensive patients in developing countries. A study conducted at a tertiary care hospital in Quetta, Pakistan, found that 83.4% had imperfect adherence, while 16.2% had perfect adherence. Several demographic factors, such as gender, age, marital status, and income, showed a strong correlation with adherence to antihypertensive treatment in this study.¹⁷ Another study reported that only 55.9% of the study population adhered to antihypertensive treatment in the Middle East.¹⁸ Similarly, about 53.4% were found adherent to antihypertensive treatment in a study conducted in Malaysia. Female patients were found to show more compliance towards antihypertensive treatment. The multi-drug prescription to hypertensive patients and increased daily dose frequency are the main predictors of non-compliance towards hypertensive treatment.¹⁹ A study conducted in Primary health care centers in Saudi Arabia showed overall good compliance but highlighted patterns of intentional non-adherence and frequent running out of medicines as the main factors contributing to non-adherence.²⁰ In a study conducted in Dhaka, Bangladesh, revealed that 54.83% of study participants had shown good medication adherence. The most frequent predictors for irregular medication use were forgetfulness (20.29%), followed by work-related commitments (7.71%). Among sociodemographic associations, medication adherence was notably higher among married patients than unmarried participants, consistent with our study results.²¹ A study conducted in rural India reported that 46% of patients had high adherence to their medication, 41.3% had moderate adherence, and 12.7% showed low adherence. The main challenges linked to poor adherence were being asymptomatic at the time of diagnosis, poor knowledge of hypertension complications, and obtaining medication from government pharmacies.²² Our study showed that sociodemographic factors, specifically urban residency, tertiary education, and participants with a longer duration of diagnosis, exhibited better overall adherence, but there is no statistically significant difference in the adherence levels between males and females whereas a study conducted in Nigeria stated a gender difference towards adherence patterns in their population, with males exhibiting better adherence than females.²²

This study has a few limitations, such as selection bias due to the convenience sampling method and recall bias, as we rely on patient self-reported information, which limits the generalizability of the study findings. Further research in a wider community is recommended to address this important public health issue.

CONCLUSION

The study results showed that adherence to antihypertensive treatment requires attention to improve hypertension control in our local context. This study underscores the need for targeted, context-specific interventions, particularly those focused on socially vulnerable

groups and individuals with lower educational levels, to enhance adherence and improve health outcomes.

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CONFLICT OF INTEREST: Authors declare no conflict of interest

GRANT SUPPORT AND FINANCIAL DISCLOSURE: NIL

Authors Contribution:

Following authors have made substantial contributions to the manuscript as under

Authors	Conceived & designed the analysis	Collected the data	Contributed data or analysis tools	Performed the analysis	Wrote the paper	Other contribution
Ghayur US	✓	✓	✓	✓	✓	✗
Aliya B	✓	✗	✓	✓	✓	✗
Syed S	✓	✓	✗	✗	✓	✓
Ghani MA	✓	✗	✓	✓	✓	✗
Azam M	✓	✓	✗	✗	✗	✓
Rafi S	✓	✗	✓	✓	✓	✗

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethical Approval:

This Manuscript was approved by the Ethical Review Board of Rehman Medical College, Peshawar. Vide No. RMI/RMI-REC/ Article Approval/122. Dated 07, 04, 2024.



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THE ROLE OF AI ASSISTANCE IN CONVENTIONAL KARYOTYPING: ENHANCEMENTS, LIMITATIONS, AND THE CONTINUING NEED FOR HUMAN EXPERTISE

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ABSTRACT

Objectives: This study aimed to assess the performance, efficiency, and limitations of AI-assisted karyotyping using Applied Spectral Imaging (ASI) software and to highlight the importance of expert cytogeneticist involvement to ensure that the diagnosis is accurate, reliable, and properly interpreted in light of clinical history and laboratory findings.

Material & Methods: A comparative observational study was conducted at Islamabad Diagnostic Center from October 2025 to December 2025. A total of 2,305 chromosomes were analyzed using ASI AI-based karyotyping software. Each AI-generated karyogram was reviewed by two cytogeneticists. Parameters evaluated in this study included chromosome count accuracy, overlap detection, segmentation errors requiring joining or separation, and the correctness of chromosome placement. The time required for AI-assisted analysis was compared with that of conventional manual karyotyping.

Results: The AI software detected a mean of 49.34 ± 2.63 chromosomes per metaphase, indicating a tendency toward over-segmentation. Chromosomal overlap was observed in 2.30% of cases. Manual joining and separation of chromosome segments were required in 7.50% and 4.59% of chromosomes, respectively. Correct placement without human intervention was achieved in 82.93% of chromosomes. AI-assisted analysis, including manual verification, required approximately 2 minutes per metaphase, compared with 10–15 minutes for manual karyotyping.

Conclusion: AI-assisted karyotyping improves efficiency and reduces turnaround time. Expert review remains essential for resolving errors and interpreting complex patterns. A combined AI–human approach provides the most reliable framework for accurate cytogenetic interpretation.

Keywords (MeSH): Artificial Intelligence, Karyotyping, Cytogenetics, Chromosomal abnormalities

This article may be cited as: Rehan GE, Khan AA, Uppal R, Malik HS. The Role Of Ai Assistance In Conventional Karyotyping: Enhancements, Limitations, And The Continuing Need For Human Expertise. J Med Sci 2026 April - June;34(2):87-92

INTRODUCTION

Examination of metaphase chromosomes under a light microscope using Giemsa banding (G-banding) is a time-tested cytogenetic technique. This method detects microscopic chromosomal anomalies, including aneuploidies, translocations, inversions, deletions, and duplications. Despite the introduction of numerous molecular techniques and advanced methodologies, conventional karyotyping remains indispensable. This is due to its ability to assess abnormalities at the whole-chromosome level by an expert.^{1,2} However, this technique is time-consuming, mainly performed manually, and highly dependent on the capabilities and experience of cytogeneticists, leading

to subjective differences in interpretation and prolonged turnaround time.^{3,4} In recent years, software-assisted image analysis and digital microscopy have been developed to reduce these limitations. These approaches improve chromosome segmentation, capture metaphases, and generate ideograms.^{5,6} Artificial Intelligence is emerging as a rapidly evolving component that aids in multiple steps, ultimately leading to markedly reduced analysis time and increased consistency.^{7,8}

Applied Spectral Imaging (ASI) software provides an AI-augmented karyotyping tool. It helps analyze metaphase spreads and align chromosomes in under 2 minutes, compared with the 10–15 minutes typically required for manual analysis.⁹ Additionally, data is saved as comprehensive, high-resolution images, which are incorporated into the final report and can be retrieved later if required.

Despite these qualities, AI-driven platforms face several limitations. Expert examination of metaphases and manual correction are required to confirm low-quality metaphase images, metaphases with overlapping or

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Date Received: 13/03/2026

Date Revised: 25/06/2026

Date Accepted: 26/06/2026

closely spaced chromosomes that the software fails to separate, complex structural rearrangements and abnormalities, and marker chromosomes. Also, the software lacks interpretive results and integration with clinical context, which are provided and verified by cytogeneticists.¹⁰

This emerging situation spotlights the requirement for a hybrid diagnostic model in conventional cytogenetics. The introduction of AI-assisted software in this field markedly affects work speed, but the role of human expertise is irreplaceable. This article examines the role of AI in conventional karyotyping, its benefits and limitations, and emphasizes the need for expert cytogeneticist interpretation to achieve accurate results and diagnoses.

The objective of this study was to assess the strength of software in the correct placement of chromosomes according to ICSN guidelines and the level of human mediation required for correct diagnosis and ultimately authentic reporting.

MATERIAL AND METHODS

This observational study was conducted at the Department of Cytogenetics, Islamabad Diagnostic Center (IDC), Islamabad, from October to December 2025. The study aimed to evaluate the efficiency and accuracy of AI-assisted karyotyping using ASI software (Applied Spectral Imaging, CA, USA) compared with traditional manual karyotyping performed by experienced cytogeneticists.

Following approval from the institutional ethical review board, cytogenetic samples received for evaluation were included based on clinical indications, including suspicion of Down syndrome, Edwards syndrome, Patau syndrome, and other aneuploidies; developmental delay; disorders of sex development (DSD) (including suspected Klinefelter syndrome, Swyer syndrome, MRKH syndrome, gender dysphoria, congenital adrenal hyperplasia, and Turner syndrome); recurrent fetal loss (RFL); preimplantation genetic testing for in vitro fertilization (IVF); acute leukemias; myeloid neoplasms such as chronic myeloid leukemia; and other suspected chromosomal abnormalities. All samples were processed in accordance with standardized cytogenetic laboratory protocols to ensure consistency and reliability.

Conventional karyotyping was performed on peripheral blood lymphocyte cultures, followed by cell harvesting, hypotonic treatment, fixation, and slide preparation. G-banding was used to obtain well-defined chromosomal banding patterns. Slides were pre-screened for quality assurance to ensure optimal metaphase spreads, minimal overlap, and sufficient band resolution before detailed analysis. Only high-quality metaphases meeting established criteria were included in the study to minimize analytical bias.

A total of 2,305 chromosomes from 50 metaphases

were selected for analysis. The GenASIs BandView module of the ASI software, an AI-based image analysis platform, was used to automate chromosome detection, segmentation, and preliminary classification for each metaphase. The software's results were then reviewed and validated by expert cytogeneticists to assess concordance with the actual findings, identify any discrepancies, and ensure diagnostic accuracy.

Two experienced cytogeneticists independently reviewed the chromosomal assessments generated by the software. For each metaphase, they carefully examined several parameters, including the number of chromosomes correctly aligned in the initial automated run, the presence of overlapping chromosomes, and instances in which chromosome segments required joining due to improper splitting. They also assessed instances in which chromosomes needed to be separated, as well as the software's overall accuracy in classifying and placing chromosomes.

All observations were recorded using a standardized checklist, and mean $\pm$ standard deviation (SD) values were calculated for each metaphase. To minimize interobserver variation, both cytogeneticists discussed discrepancies in their evaluations and reached consensus. This step helped ensure consistency and strengthened the reliability of the findings. In addition, occasional cross-checks of previously reviewed slides were conducted to maintain uniformity throughout the analysis.

For statistical evaluation, descriptive statistics were used to summarize the data. Means, standard deviations, and percentages were calculated for each parameter across all metaphases. Data were entered and analyzed using SPSS version 26.0. Continuous variables are presented as mean $\pm$ SD with 95% confidence intervals (CIs), and categorical data are reported as frequencies and percentages, with 95% CIs.

RESULTS

In our study, a total of 2,305 chromosomes from 50 metaphase spreads were evaluated. To assess the performance of the ASI (Applied Spectral Imaging) AI-based karyotyping software, the software was evaluated (Figure 1). The key performance indicators included accurate assessment of chromosome counts, detection of overlapping chromosomes, correction of segmentation needed in metaphases, appropriate placement of chromosomes, and time-saving effectiveness for the expert. Hence, its role is to reduce turnaround time and enable early report generation.

In the study, the software automatically identified, on average, 49.34 ± 2.63 chromosomes per metaphase. This indicates a trend toward over-segmentation of chromosomes, particularly in metaphases with suboptimal band resolution, overlapping chromosomes, and closely

spaced chromosomes, ultimately resulting in the splitting of chromosomes into two or more segments. This required manual intervention for correct placement (Figure 2).

Chromosome overlap was observed in 2.30% of chromosomes across the metaphases considered. Manual intervention by expert cytogeneticists was required to resolve overlaps and ensure accurate interpretation and correct placement. Chromosomes requiring manual joining of fragmented segments numbered 3.45 ± 1.84 per metaphase. On the other hand, almost 4.59% of chromosomes (mean: 2.11 ± 1.54) needed manual separation.

AI-based technology mistakenly joined the neighboring chromosomes into a single structure and ultimately placed them in the wrong position. (Figure 3)

On average, in the AI analysis, the number of chromosomes that were incorrectly placed and ultimately required intervention and human correction was 7.85 ± 2.37 per metaphase, corresponding to 17.07%. This shows that 82.93% of all the chromosomes in the considered metaphases were placed appropriately and required no adjustments by the relevant expert.

One of the most effective benefits of ASI software was the marked reduction in required analysis time. In contrast to the 10–15 minutes required for manual karyotyping, AI-assisted karyotyping required only an average of 2 minutes per metaphase. This time included the necessary manual intervention by an expert cytogeneticist. More than an 80% improvement in time savings was observed



Fig 1: Representative G-banded metaphase spread, which is obtained from cultured peripheral blood lymphocytes (x1000, oil immersion)

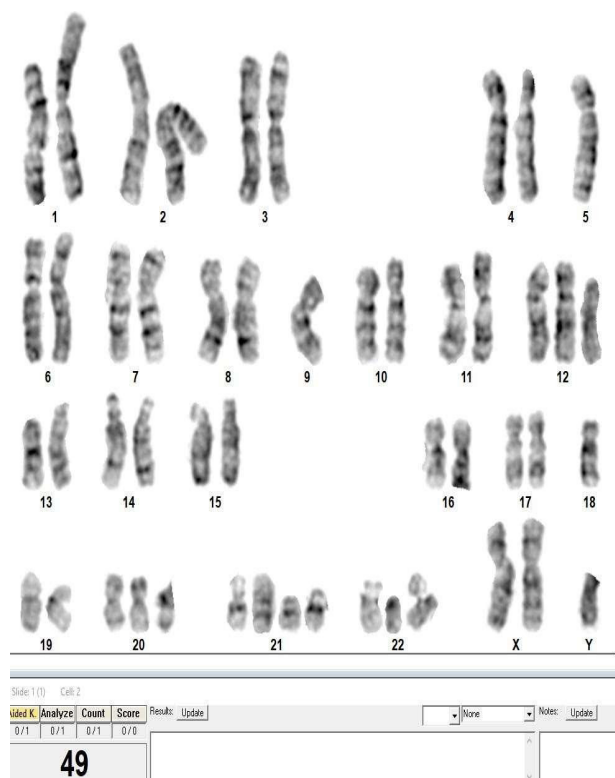


Fig 2: An initial automated karyotype output generated from a metaphase, analyzed by AI-based software, and showing an extra number. This is the unrefined chromosome detection prior to manual rearrangement performed by an expert.

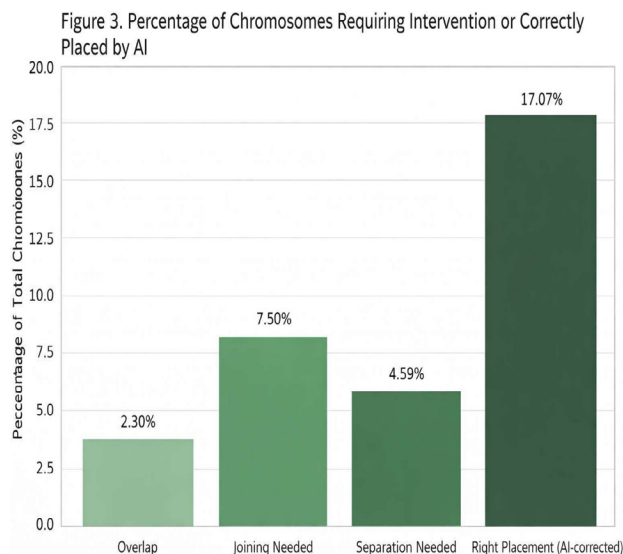


Fig 3: Percentage of Chromosomes requiring intervention or correctly placed by AI

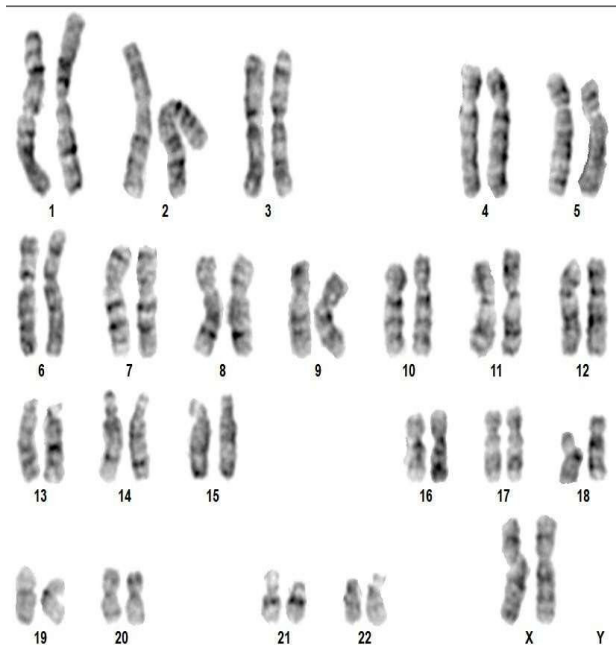


Fig 4: Karyogram showing karyotype of 46, XX. Manual correction of chromosome placement done according to ISCN guidelines

in our study, which significantly affects workflow optimization in high-volume cytogenetics laboratories. In addition, digital data storage, its incorporation into final report generation, and retrieval are strengths of the software. All these factors make the analysis robust and up to the mark. Hence, it positively affects diagnosis and the desired treatment strategy for patients (Figure 4).

DISCUSSION

The use of Artificial Intelligence (AI) in conventional karyotyping has shown very favorable outcomes, particularly in optimizing processes, improving operational efficiency, and reducing manual workload compared with previous cytogenetic techniques. In this study, experts evaluated ASI (Applied Spectral Imaging) software and analyzed a total of 2,305 chromosomes across 50 metaphase spreads.

It was observed that ASI software tends to over-segment, with an average chromosome count of 49.34 ± 2.63 per metaphase. This is above the standard chromosome number, indicating that chromosomes were occasionally split into two or more fragments. This kind of issue has been reported in a few studies that evaluated AI-based chromosome segmentation. It was noted that suboptimal banding quality, artifacts, closely spaced centromeres on chromosomes, and chromosomal crossing over may mislead the software's detection capabilities.^{5, 6, 8} However, 2.30% of the chromosomes required manual correction and placement by an expert due to overlap. This finding concurs with studies by Zhou et al. and Chen et al., which showed that even advanced segmentation

models still require expert input when dealing with tightly clustered metaphase spreads or chromosomal overlap.^{6, 9}

Consistent with earlier studies, our results also confirm that AI-based karyotyping systems still require expert manual correction, particularly for fragmented, overlapped, and fused chromosomes.^{10, 11} The observed similarity points to a shared constraint in automated systems, underscoring their limited capacity to distinguish chromosomal continuity from close physical alignment.

A key strength of the ASI software platform was its ability to automatically position 82.93% of the chromosomes in their appropriate locations. This indicates that when image acquisition is high quality, AI-based systems can organize the majority of chromosomal elements. Comparable performance trends have been reported in evaluations of GenASIs and MetaSystems software. These automated karyotyping methods demonstrated high accuracy.^{12, 13}

Nevertheless, 17.07% of the chromosomes still required correction by trained professionals. This finding emphasizes that automated analysis can't be a substitute; it's supportive. Expert assessment remains essential, particularly when interpreting complex structural rearrangements or cases of numerical mosaicism, where algorithmic detection may struggle to identify subtle variations.

Importantly, AI-assisted analysis substantially reduced processing time. The average evaluation time per metaphase was approximately two minutes with an automated support system, whereas conventional manual assessment typically required 10 to 15 minutes. This represents a five- to sevenfold improvement in turnaround time. These benefits align with previous studies that identify time reduction as a primary advantage of AI integration in cytogenetics.^{11, 12, 14} Faster processing is especially beneficial when prompt diagnostic reporting directly influences patient management decisions.^{4, 10, 16}

Additionally, AI systems offer advantages in digital infrastructure. Their platform-based capabilities for remote case review, long-term storage of metaphases and finalized karyotype images, and systematic data archiving are worth noting. These capabilities enhance traceability and enable retrospective analysis.^{14, 19, 20}

Despite these benefits, current AI technologies are not without constraints. Automated algorithms may encounter difficulties when analyzing abnormal karyotypes, suboptimal banding patterns, or complex structural abnormalities, where image variability and chromosomal distortion can compromise accuracy.¹⁷ Moreover, while software may aid in chromosomal identification and image arrangement, it lacks the capability to correlate these findings with clinical context and to provide interpretive judgment related to patients' diagnosis and ultimately treatment strategy. This is done by human experts using

their knowledge and clinical expertise.¹⁸

Therefore, the integration of AI in cytogenetics should be viewed as a complementary approach, with the role of cytogeneticists indispensable for validating results, resolving ambiguous findings, and ensuring that interpretations are clinically meaningful. This collaborative model will not only enhance diagnostic accuracy but also support the effective and safe implementation of AI technologies in routine cytogenetic practice. In addition, recent advancements highlight that although AI-assisted karyotyping significantly improves efficiency and reproducibility and reduces turnaround time, its performance remains highly dependent on the diversity of training datasets and the quality of the advancements.²⁴

Importantly, our findings emphasize a hybrid approach that combines the speed and standardization of AI with expert human review as the gold standard for clinically relevant diagnoses and final case interpretation.

As molecular genetics and sequencing techniques continue to evolve, AI-assisted karyotyping will likely serve as a bridging technology, improving conventional cytogenetic workflows while integrating them with other modern genomic tools. Ultimately, this will improve patient health-care in a robust manner.²¹ Also, future improvements include enhanced machine learning algorithms through training and the introduction of learning models based on user feedback.^{22,23}

CONCLUSION

This study concludes that the ASI Artificial Intelligence-assisted karyotyping system significantly streamlines conventional chromosome analysis by reducing the time required for metaphase interpretation. With most chromosomes correctly placed without manual correction, the software proves highly effective for the cytogenetic workflow. However, shortcomings such as over-segmentation, inability to resolve complex overlaps, and the need for manual correction highlight the indispensable role of expert cytogeneticists. Despite being an advanced technique, AI-assisted karyotyping still lacks the understanding required to interpret structurally complex or clinically subtle abnormalities.

Thus, the most suitable model combines the computational strength of AI platforms with the interpretive acumen of trained human professionals. With continued development, AI has the potential to enhance the efficiency and accuracy of cytogenetic diagnostics, thereby improving patient management.

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CONFLICT OF INTEREST: Authors declare no conflict of interest

GRANT SUPPORT AND FINANCIAL DISCLOSURE: NIL

Authors Contribution:

Following authors have made substantial contributions to the manuscript as under

Authors	Conceived & designed the analysis	Collected the data	Contributed data or analysis tools	Performed the analysis	Wrote the paper	Other contribution
Rehan GE	✓	✓	✗	✗	✓	✗
Khan AA	✓	✗	✓	✓	✓	✗
Uppal R	✓	✓	✗	✗	✗	✓
Malik HS	✓	✗	✓	✓	✓	✗

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethical Approval:

This Manuscript was approved by the Ethical Review Board of Islamabad Diagnostic Center (IDC), Islamabad, Pakistan.

Dated: 10 27 2025



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THE IMPACT OF TRANEXAMIC ACID ON HEMATOMA AND SEROMA FORMATION IN BREAST CONSERVATION SURGERY

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ABSTRACT

Objective: This study was conducted to evaluate the effect of perioperative tranexamic acid on postoperative hematoma and subsequent seroma formation in patients undergoing breast-conserving surgery (BCS).

Methods: This quasi-experimental study was conducted at the Breast Unit, Khyber Teaching Hospital, Peshawar. Sixty-two patients undergoing BCS with axillary dissection were included and equally divided into two groups (n=31 each). In the intervention group, tranexamic acid (TXA) at 1 g, diluted in 100 mL of saline, was administered intravenously at wound closure, whereas no TXA was given in the control group. Patients were monitored for hematoma formation, seroma, drain output, duration of drainage, and any other postoperative complications.

Results: Hematoma occurred in 3 patients (9.7%) in the TXA group and 6 patients (19.4%) in the control group. Seroma formation was observed in 1 patient (3.2%) in the TXA group, while 2 patients (6.5%) in the controls. Neither of these differences was statistically significant. The mean drain output was comparable between the two groups (i.e., 92.1 ± 43.5 ml vs. 95.9 ± 40.5 ml; $p=0.73$). However, drain removal occurred earlier in the TXA group (4.7 days vs. 6.2 days). No thromboembolic events were reported.

Conclusion: Peri-operative Tranexamic Acid appears safe and may reduce postoperative bleeding and shorten drainage duration, although larger randomized trials are needed to strengthen the results of this study.

Keywords: Tranexamic acid, Breast-conserving surgery, Hematoma, Seroma, Drain output, Breast cancer surgery

This article may be cited as: Wahid A, Ali IS, Saeed F, Ahmad Z, Jehanzeb A, et al. The Impact Of Tranexamic Acid On Hematoma And Seroma Formation In Breast Conservation Surgery. J Med Sci 2026 April - June;34(2):93-97

INTRODUCTION

The management of breast cancer has evolved over the years from surgery as the stand-alone modality to an evidence-based, multidisciplinary specialty approach.^{1, 2} While radical and modified radical procedures have been gradually de-escalated to oncoplastic breast-conserving surgery in many patients, postoperative complications remain.

Postoperative complications after breast surgery include hematoma, seroma, wound infection, dehiscence, and flap necrosis. After breast cancer surgery, the rate of hematoma formation ranges from 1-5%, while that of seroma varies between 2.5-85%.³ Seroma formation remains an unforeseeable sequela rather than a complication, resulting in additional treatment, a prolonged hospital stay, and a delay in the commencement of adjuvant treatment.⁴

The use of Tranexamic acid (TXA) to reduce intra- and postoperative bleeding and seroma formation has been widely practiced across a broad spectrum of surgical procedures.^{4, 5} Its use has even been explored in cardiothoracic surgery, where it has been associated with decreased blood loss during open-heart surgery. With the increasing trend of day surgery, more and more disciplines are encouraging its use.⁶ The use of Tranexamic acid to reduce hematoma and seroma formation has recently been studied in breast surgeries with mixed results, with some showing a significant decrease in hematoma and seroma formation while other studies didn't show any benefit at all.⁷ Plastic surgical procedures, on the other hand, have shown promising results, attracting significant attention from plastic surgeons. Knowledge of Tranexamic acid use in our population and data on its impact in breast surgery are even more limited; therefore, this study is planned to determine the impact of Tranexamic acid in breast-conserving surgeries, which could lead to the establishment of local protocols for the prevention of hematoma and seroma formation.

MATERIALS AND METHODS

This quasi-experimental study was conducted at the Breast Unit, Department of Surgery, Khyber Teaching Hospital, Peshawar, Pakistan, over six months (from 22nd

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Date Received: 17/05/2026

Date Revised: 25/06/2026

Date Accepted: 26/06/2026

March to 21st September 2025).

The sample size was determined using the WHO sample size calculator to be 31 patients per group, based on a 95% confidence interval and 80% power, with hematoma frequencies of 7.3% and 12.9% in those given TXA, as reported in a recent meta-analysis using a consecutive non-probability sampling technique.

Patients aged over 20 years with invasive breast cancer undergoing breast-conserving surgery, either upfront or after neoadjuvant chemotherapy, with axillary lymph node dissection, were included in the study. Patients undergoing mastectomy, those who had previous breast surgery of any type, patients with known bleeding disorders, and those with a documented history of allergy to tranexamic acid were excluded.

The study was conducted after obtaining approval from the institution's ethics and research board. All eligible patients were admitted, and routine baseline investigations were performed. After the purpose of the study was explained, written informed consent was obtained for participation. Randomization was performed using the lottery method to assign patients to two groups.

Patients were kept "Nil Per Oral" for 6 hours prior to surgery. In the intervention group, 1 g of tranexamic acid, diluted in 100 mL of normal saline, was administered intravenously over 20 minutes during wound closure. The control group did not receive tranexamic acid. Postoperatively, patients were monitored for hematoma formation, daily drain output, and other complications, with follow-up visits scheduled at 7, 14, and 21 days in the outpatient department.

Drains were removed when the output was less than 25 mL in 24 hours. Data were analyzed using SPSS version 28.0. Mean and standard deviation were calculated for quantitative variables, including age, tumor size, and drain output, while frequencies and percentages were calculated for qualitative variables, including receipt of neoadjuvant chemotherapy, menstrual status, and seroma formation in both groups. These variables were compared between the groups using a t-test for the former and

a chi-square test for the latter, with a p-value of less than 0.05 considered statistically significant.

RESULTS

A total of 62 patients were included in this study, equally divided into two groups. One group received tranexamic acid at the time of surgical closure, and the second group did not receive tranexamic acid (control). The mean age was 48.7 ± 10.2 years in the tranexamic acid group and 49.5 ± 11 years in the control group. Most patients were premenopausal in both groups, and the majority had T2-stage disease at the time of surgery. Twenty patients in the tranexamic acid group and 18 in the control group had received neoadjuvant chemotherapy. Baseline demographics and tumor characteristics were statistically similar between the two groups, as shown in Table 1.

Post-operative hematoma formation occurred in 3 patients receiving Tranexamic acid, while 6 patients in the control group had hematoma postoperatively, as depicted in chart I. Post-operative seroma formation was observed in 1 patient receiving Tranexamic acid and in 2 patients in the control group, with a p-value of 1% (not significant), as shown in Table 2.

The mean postoperative drain output was 92.1 ± 43.5 mL in the tranexamic acid group and 95.9 ± 40.5 mL in the control group. However, this difference was not statistically significant ($p = 0.73$). In the study, 2 patients had their drains removed on the first postoperative day because the drains contained only 30 mL of blood, and 1 patient had the drain inadvertently removed in the evening after surgery, as shown in Table 3.

The mean drain output was slightly lower in the tranexamic acid group than in the control group; however, the difference was not statistically significant ($p=0.732$). In the tranexamic acid group, the mean time to drain removal was 4.7 days, compared with 6.2 days in the control group. Tranexamic acid didn't affect the rate of complications in either group. No thromboembolic events were observed in either group. The frequency of wound infection was also comparable between the two groups.

Table No 1: Baseline Demographic and Clinical Characteristics of the Study Population (n = 62)

Variable		Tranexamic acid group	Control group
Age	Mean +/- SD	48.7 +/- 10.2	49.5 +/- 11
	Range	35-67	36-68
Menopausal Status	Premenopausal	19 (61.3%)	18 (58.1%)
	Postmenopausal	12 (38.7%)	13 (41.9%)
Tumor size (mm)	Mean +/- SD	26.1 +/- 6.4	26.7 +/- 6.8
	T1	9 (29%)	8 (25.8%)
	T2	22 (71%)	23 (74.2%)
Neo Adjuvant chemotherapy	Yes	20 (64.5%)	18 (58.1%)
	No	11 (35.5%)	13 (41.9%)

Table No 2: Effect of Tranexamic acid on Seroma formation

	Seroma Formation		
	YES	NO	
TXA Group	1 (3.2%)	30 (96.8%)	p = 1.00 (Not significant)
Control Group	2 (6.5%)	29 (93.5%)	

Table No 3: Effect of Tranexamic Acid on Drain Output

Drain Output	TXA group	Control group	p-value
Mean drain output +/- SD, ml	85.3 +/- 43.5	95.9 +/- 40.5	0.732
Mean duration of drain placement, days	4.7	6.2	0.685

DISCUSSION

This study aimed to assess the efficacy of tranexamic acid in reducing hematoma and seroma formation in patients undergoing breast-conserving surgery with axillary dissection. Although no statistically significant difference was observed between the two groups in hematoma and seroma formation, several clinically relevant trends were noted, including a lower incidence of hematoma and earlier drain removal in patients receiving tranexamic acid. The lack of statistical significance is likely due to a small sample size rather than the absence of a clinical effect.

TXA has many beneficial properties, including reducing bleeding, transfusion requirements, hematoma formation, and the duration of drain use.¹⁰ Its anti-inflammatory effect has also been demonstrated in several studies.^{11,12} Its effectiveness has been widely studied in cardiac, obstetric, orthopedic, and trauma settings, with many trials reporting its long-term benefits and potential risks.¹³

Our findings are consistent with previously published studies that report mixed outcomes regarding TXA use in breast surgery. Buheiri et al. conducted a meta-analysis of tranexamic acid use in breast cancer surgery and concluded that both topical and IV tranexamic acid use in breast surgery leads to a decreased rate of hematoma and seroma formation, with no impact on infection rate or thromboembolic events.¹⁴ Liechti et al. also reported a reduction in hematoma and seroma formation after perioperative intravenous administration of tranexamic acid in breast-conserving and free-flap surgery, with a mean difference of 132 mL in drain output.¹⁵

Fung et al. conducted a meta-analysis examining the use of tranexamic acid in patients undergoing mastectomy with or without breast reconstruction, assessing outcomes including hematoma formation, seroma formation, infection, drain output, and drain duration. They reported a 60% decrease in hematoma formation with tranexamic acid use, and drain duration was only 1.2 days, with no impact on seroma formation or surgical site infection.¹⁶ In contrast, Yao et al. found no effect on hematoma formation when assessing the role of tranexamic acid in breast reduction mammoplasties.¹⁷ Similarly, Weissler et

al. did not observe a significant reduction in hematoma or seroma formation after perioperative tranexamic acid administration.¹⁸ As in our observations, these studies have failed to demonstrate statistically significant benefits, often attributing this to small sample sizes or heterogeneity in TXA administration methods.

In our study, Post-operative hematoma formation was observed in 3 patients (9.7%) in the Tranexamic acid (TXA) group compared to 6 patients (19.4%) in the control group. Although this difference was not statistically significant, patients who did not receive TXA had nearly a two-fold higher incidence of hematoma, suggesting peri-operative tranexamic acid may be associated with a clinically meaningful decrease in bleeding complications. Hematoma formation after breast-conserving surgery can result in patient discomfort, wound tension, increased risk of infection, need for re-intervention, and potential delay in adjuvant therapy. The lack of statistical significance is likely related to the relatively small sample size rather than the absence of a therapeutic effect. These findings are in accordance with previously published literature demonstrating a reduction in postoperative bleeding complications with TXA use in breast and plastic surgical procedures.^{19, 20, 21}

Postoperative seroma formation was observed in 1 patient (3.2%) in the tranexamic acid (TXA) group, compared with 2 patients (6.5%) in the control group. Although the incidence was lower in the TXA group, the difference was not statistically significant. The overall seroma rate in both groups was low, which may have limited the ability to detect a meaningful statistical difference. Compared with hematoma, which primarily reflects bleeding, seroma formation primarily results from lymphatic disruption, dead space, and the inflammatory response after axillary dissection.^{22, 23} Larger studies with greater statistical power are required to clarify whether TXA plays a significant role in reducing seroma formation after breast-conserving surgery.

The average time to drain removal was shorter in the Tranexamic acid (TXA) group (4.7 days) than in the control group (6.2 days), suggesting a potential clinical benefit of TXA administration. Although mean drain output

did not differ significantly between the two groups, earlier drain removal in the TXA group may reflect improved hemostasis and reduced postoperative oozing. Prolonged drain placement is associated with increased patient discomfort, a higher risk of ascending infection, delayed mobilization, and an extended hospital stay.^{24, 25} Therefore, even a modest reduction in drain duration can translate into meaningful improvements in postoperative recovery and patient satisfaction.

No increase in wound infection, flap-related complications, or other adverse surgical outcomes was observed with TXA administration. Importantly, no thromboembolic events were reported in either group, reinforcing the safety profile of peri-operative TXA in breast-conserving surgery.

This study has several limitations. The relatively small sample size may have reduced statistical power to detect significant differences between groups. As a single-center, quasi-experimental study, it may not be broadly applicable to other populations or surgical settings. Additionally, variations in TXA administration methods and the short follow-up period may have affected the assessment of postoperative outcomes. Larger, multicenter randomized controlled trials are needed to validate these findings and establish standardized protocols.

CONCLUSION

Peri-operative administration of tranexamic acid in patients undergoing breast-conserving surgery with axillary dissection appears to be safe and may offer clinically meaningful benefits. Although the reductions in hematoma and seroma formation did not reach statistical significance in this study, a lower incidence of hematoma and earlier drain removal were observed in the TXA group. Importantly, no increase in wound complications or thromboembolic events was noted, reinforcing its favorable safety profile.

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CONFLICT OF INTEREST: Authors declare no conflict of interest

GRANT SUPPORT AND FINANCIAL DISCLOSURE: NIL

Authors Contribution:

Following authors have made substantial contributions to the manuscript as under

Authors	Conceived & designed the analysis	Collected the data	Contributed data or analysis tools	Performed the analysis	Wrote the paper	Other contribution
Wahid A	✓	✓	✗	✗	✓	✗
Ali IS	✓	✗	✓	✓	✓	✗
Saeed F	✓	✓	✗	✗	✗	✓
Ahmad Z	✓	✗	✓	✓	✓	✗
Jehanzeb A	✓	✓	✗	✗	✗	✓
Afridi A	✓	✗	✓	✓	✓	✗
Khan MM	✓	✗	✓	✓	✓	✗

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethical Approval:

This Manuscript was approved by the Ethical Review Board of Khyber Teaching Hospital, Peshawar. Vide No. 273/DME/KMC.

Dated: 21 03 2025



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FUNCTIONAL OUTCOME OF ACROMIOCLAVICULAR JOINT RECONSTRUCTION USING SINGLE ENDOBUTTON

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ABSTRACT

Objective: To determine the functional outcome of acromioclavicular joint reconstruction using the single Endobutton technique in patients with Rockwood type III-VI AC joint dislocations.

Materials & Methods: The study was a quasi-experimental study carried out at MTI, Khyber Teaching Hospital, Peshawar, from April 2025 to March 2026. The nonprobability consecutive sampling was used and 117 patients were included. The mean age of the patients was 20-60 years, and the Rockwood types of the AC joints were III to VI. Open reduction and coracoclavicular reconstruction with a single Endobutton and TightRope fixation were performed in all patients. The Constant-Murley score was used to evaluate functional outcomes preoperatively and at 6 and 12 weeks postoperatively. Data were analyzed using SPSS version 26 and a repeated measure analysis was used to compare the outcomes over time.

Results: The mean Constant-Murley score improved significantly from 38.4 ± 6.7 preoperatively to 64.7 ± 7.2 at 6 weeks and 87.3 ± 5.5 at 12 weeks ($p < 0.001$). The improvements were uniform in all subgroups, with slightly better results in the younger and lower Rockwood grade subgroups. The radiographic results demonstrated a sustained reduction in 93% of patients, with few complications and no hardware failures or neurovascular injury.

Conclusion: Single Endobutton fixation provides significant early functional improvement, with a high rate of maintained reduction and a low complication rate. It is cost-effective and less complex and reliable than other methods in the management of Rockwood type III-VI AC joint dislocation. Further long-term comparative studies are recommended.

Keywords: Acromioclavicular joint, Coracoclavicular ligament, Endobutton, Rockwood classification, Shoulder reconstruction

This article may be cited as: Ullah U, Ali A, Ullah R, Rehman IU, Ahmad A, Shah SDA. Functional Outcome Of Acromioclavicular Joint Reconstruction Using Single Endobutton. J Med Sci 2026 April - June;34(2):98-103

INTRODUCTION

Acromioclavicular (AC) joint injury is the most frequent shoulder injury and can occur as a direct blow to the lateral shoulder or after high impact trauma like a fall or road traffic accident, especially in young, active people. The available data suggest that AC joint dislocations represent about 9-12% of all shoulder injuries, most of the time in males, and mostly in people who play contact sports or work by manual work.¹

The AC joint is stabilized by two ligaments: the acromioclavicular (AC) and coracoclavicular (CC). The lateral conoid and trapezoid ligaments and the capsular ligament that extends horizontally are part of the AC joint

that are torn in high grade injuries.

In high-grade (Rockwood types IV-VI) dislocations, surgery is most commonly recommended due to increased instability and functional loss associated with complete ligamentous rupture, while type III injuries remain controversial regarding surgical management.²

The surgical techniques used to reconstruct the AC joint have improved significantly in the past decade to restore both vertical and horizontal stability with minimal morbidity. Anatomical reconstruction of the CC ligament complex is supported by biomechanical and clinical studies, and has outperformed non-anatomical fixation methods with modern devices like cortical button systems and suture-button constructs which provide strong fixation and early functional recovery.²

The Endobutton technique, among these, has gained popularity as a reliable approach that approximates native ligament biomechanics with minimally invasive, tensioned fixation between the clavicle and the coracoid process.³ Recent clinical studies show that Endobutton-based reconstructions, whether single- or double-button designs, result in significant improve-

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Date Received: 13/04/2026

Date Revised: 26/06/2026

Date Accepted: 26/06/2026

ments in validated shoulder scores, including Constant and DASH metrics, and that the procedures maintain reduction well with early return of motion.⁴

Despite promising functional results with suspensory fixation systems like the Endobutton, challenges remain in achieving good long-term outcomes and reducing complications. Postoperative loss of reduction and hardware-related complications remain concerns. Recent large cohort studies suggest that about 25% of AC joint reconstructions with button-based fixation systems experience loss of reduction, and this loss correlates with inferior clinical outcomes, including lower Constant scores and greater pain at follow-up, especially when technical issues such as tunnel malposition or premature weight-bearing occur.⁵

Other research shows that while the short-term complication rate after AC joint surgery is generally low, patient comorbidities and procedural factors can significantly impact adverse events.⁶ Additionally, complications such as tunnel widening, ongoing loss of reduction, distal clavicular osteolysis, and persistent pain have been observed after combined CC-AC stabilization procedures, illustrating that even methods meant to tackle both vertical and horizontal instability can still lead to negative radiographic and clinical outcomes.⁷

While studies continue to compare isolated coracoclavicular reconstruction to combined CC and AC ligament repair, the results are mixed regarding whether adding AC ligament repair reliably enhances outcomes beyond CC fixation alone.

In this context, it is crucial that a careful assessment be conducted of the functional outcomes of specific reconstructive techniques, such as the single Endobutton construct, using standardized measures at specified follow-up intervals to determine their efficacy. This will ultimately help to understand which methods should be used and improved for AC joint reconstruction. This study aims to assess functional outcomes in patients undergoing AC joint reconstruction using the single Endobutton technique. Results will provide valuable information on the technique's effectiveness based on local experience.

MATERIALS AND METHODS

After obtaining ethical approval, this quasi-experimental study was carried out in Orthopedic Department of Khyber Teaching Hospital in Peshawar, Pakistan from April 2025 to March 2026. Consecutive patients with acute AC joint dislocations of Rockwood types III through VI were included using nonprobability sampling.

The sample size of 117 patients was calculated a priori using the WHO sample size calculator. The calculation was based on an expected proportion of 12.5% for an adequate functional outcome, a 7% margin of error, and a 95% confidence interval. This ensured sufficient power to detect significant differences in func-

tional scores between follow-up intervals.

Patients aged 20 to 60 years who presented within two weeks of injury were included. Patients with open wounds, poor local skin conditions, polytrauma or any other comorbidities were excluded to minimize confounding factors that may influence postoperative recovery and functional assessment.

Patients eligible for the study provided written informed consent. Baseline demographics and clinical details, including age, gender, BMI, injury laterality, Rockwood classification, and the time from injury to surgery, were obtained. To confirm the diagnosis and measure CC distance, bilateral anteroposterior and Zanca view radiographs were obtained preoperatively.

All patients were positioned in a beach-chair under general anesthesia and underwent open reduction of the AC joint, followed by anatomical reconstruction of the CC ligaments using a single Endobutton construct with Tight-Rope suture fixation. A standardized surgical technique was used, involving drilling a clavicular tunnel to match the natural locations of the conoid and trapezoid ligament insertions. A TightRope was passed around the coracoid process and through the clavicular tunnels, followed by reduction to restore normal alignment, and then secured with a single Endobutton.

Reduction and proper placement of the implant were confirmed using intraoperative imaging. All patients received a standard postoperative rehabilitation program, which consisted of four weeks of sling immobilization followed by gradual physiotherapy emphasizing range of motion and strengthening exercises. This method was similar to that used in recent reconstruction studies in which functional outcome was evaluated at 6 and 12 weeks.

Constant-Murley Score was used as a validated functional outcome tool performed preoperatively and at 6 and 12 weeks postoperatively. Pain, activities of daily living, range of motion, and strength were documented. This follow-up schedule was based on prior studies showing significant improvements in functional scores and radiographic stability within similar early time frames. It established a reliable period for evaluating short-term recovery and reducing follow-up loss.

To assess maintenance of reduction and hardware integrity, we obtained a radiograph at each visit. All outcome assessments were performed by independent clinicians blinded to preoperative data. Statistical analysis was performed using SPSS version 26. Continuous variables were expressed as mean $\pm$ standard deviation or as median with interquartile range, depending on distribution.

Distribution was assessed with the Shapiro-Wilk test. Cat-egorical variables were presented as frequencies and per-cent-ages. Stratified analysis was conducted by age, gen-der, body mass index, Rockwood grade, and duration of injury. We used the chi-square test or Fisher's exact test, as appropriate. A p-value ≤ 0.05 was considered statis-tically significant.

This methodology enabled a thorough evaluation of functional recovery after a single Endobut-ton reconstruction. It also provided a comparison with the current literature on AC joint stabilization techniques and contributed to evidence-based rec-ommendations for clinical practice.

RESULTS

All 117 patients were followed up after surgery at six weeks and twelve weeks. The group included 83 males (71%) and 34 females (29%), with a mean age of 35.6 ± 9.2 years.

The most common cause of injury was road traffic accident (59%), followed by sports-related trauma (27%) and falls (14%). There was a significant functional limita-tion before surgery with a mean Constant Murley Score of 38.4 ± 6.7 .

At 12 weeks, 12% noted further improvement with a mean Constant score of 87.3 ± 5.5 . The difference be-tween the Constant scores at the three points was statis-tically significant as verified by re-peated-measures anal-ysis of variance ($p < 0.001$). Please see Figures 1 and 2.

Improvements were found to be consistent across subgroups with stratified analysis. The mean Constant scores in the age group 40 years or less were higher than those for 40 years or more at each post-operative visit, but both groups had statistically significant improvement ($p < 0.001$).

At six weeks postoperatively, there was a no-tice-able improvement in shoulder function, with a mean

Table No 1: Constant–Murley Score Stratified by Patient Subgroups

Subgroup	Subgroup	Preop Mean $\pm$ SD	6 wk Mean $\pm$ SD	12 wk Mean $\pm$ SD
Age	≤ 40 years	36.8 ± 6.3	66.1 ± 6.9	89.1 ± 4.8
	> 40 years	41.2 ± 7.0	61.9 ± 7.1	85.7 ± 5.8
Gender	Male	38.2 ± 6.5	64.3 ± 7.0	87.1 ± 5.2
	Female	38.9 ± 7.1	65.7 ± 7.7	87.9 ± 6.3
Rockwood Grade	III	37.1 ± 6.8	65.5 ± 7.1	89.1 ± 4.8
	IV – VI	40.5 ± 6.4	63.9 ± 7.3	85.7 ± 5.8

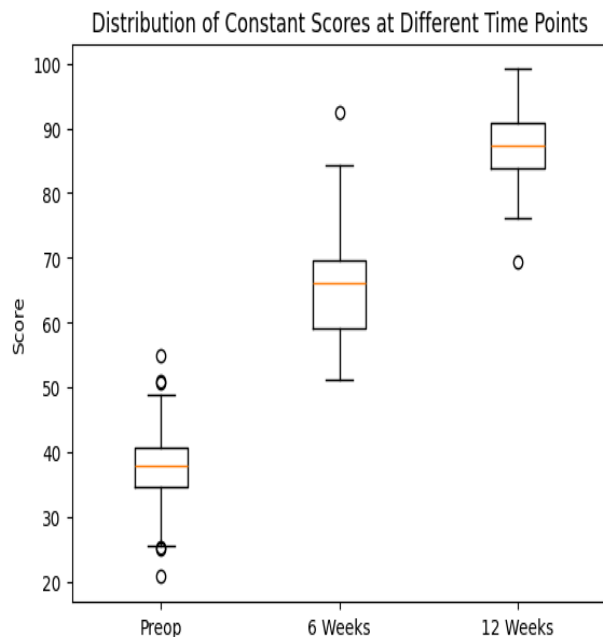


Fig 1: Boxplot illustrating the distribution and variability of Constant-Murley scores at pre-operative, 6-week, and 12-week time points

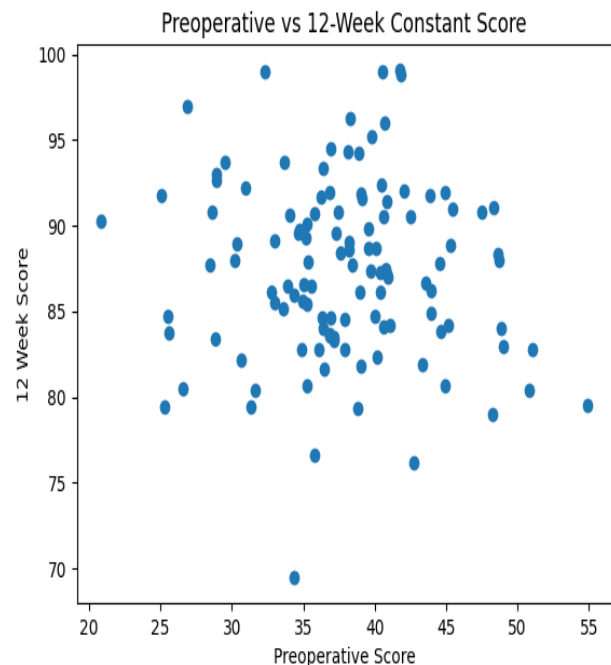


Fig 2: Scatter plot showing the relationship between preoperative and 12-week Constant-Murley scores

Constant score of 64.7 ± 7.2 .

Similarly, no notable differences in score improvement were observed between genders. Rockwood grade III injuries had slightly higher scores at 12 weeks than grades IV-VI (mean 89.1 ± 4.8 vs. 85.7 ± 5.8 , $p = 0.03$), but both groups demonstrated significant functional recovery (Table 1). Radiographic assessment revealed that 93% of patients maintained joint reduction at 12 weeks. 7% showed minor, asymptomatic widening of the coraco-clavicular interval without functional problems. No instances of hardware migration or serious neurovascular complications were noted.

DISCUSSION

The current study demonstrates significant, progressive improvements in functional outcomes after acromioclavicular joint reconstruction with the single Endobutton technique. The mean Constant-Murley score improved significantly from the preoperative period to 6 weeks and further to 12 weeks postoperatively, indicating marked early functional recovery. These results suggest that this technique effectively restores shoulder function within a relatively short follow-up period.

Improvements remain consistent across demographic and injury-related groups. Younger patients and those with low-grade injuries showed relatively greater improvement. The reliability and safety of this approach for high-grade AC joint dislocations are further supported by the high rate of maintained reduction and low complication rates.

The findings of this study are consistent with several recent studies on suspensory fixation for AC joint reconstruction. Gad et al. (2024) reported a significant improvement in the Constant score, from 45.3 preoperatively to 92.3 at the final follow-up.⁹

The current study shows similar results. Other studies have likewise shown that Endobutton constructs provide better functional outcomes, stable anatomical reduction, and significantly improved Constant scores.^{3,10}

A retrospective study from 2025 confirmed that Endobutton-based reconstruction is reliable for restoring shoulder function and achieving high patient satisfaction.¹¹ Collectively, these studies indicate that the suspensory fixation system is highly effective in achieving early and midterm functional results, which align with the observations of the current study.

Moreover, the improvement in Constant-Murley Scores observed in this study aligns with the literature on AC joint reconstruction techniques. Both graft-based and button-based reconstruction studies report significant gains in functional scores, often reaching excellent levels during follow-up.¹²

The biomechanical benefits of the Endobutton construct, including stable coracoclavicular fixation and restoration of vertical stability, are key contributors to these outcomes.¹³ However, despite positive functional results, loss of reduction and tunnel-related problems remain major concerns. Loss of

reduction rates of up to 25% have been reported in some studies, underscoring the importance of surgical accuracy and rehab protocols.^{5,14}

In comparison, the low complication rate in this study further highlights the effectiveness of the single Endobutton technique when performed with appropriate methods and patient selection. The findings of this

study underscore the clinical significance of the single Endobutton technique as a reliable approach to high-grade acromioclavicular joint dislocations. The significant improvement in functional results, along with a high rate of maintained reduction and few complications, makes a strong case for its use as a practical alternative to more complex methods.

The single Endobutton technique offers advantages such as reduced operative time, lower costs, and lower surgical morbidity compared with double Endobutton or graft-based techniques, which are especially important in resource-limited settings. Recent studies have also shown that suspensory fixation systems provide stable anatomical reconstruction, excellent functional recovery, and support early rehabilitation.¹⁰

Furthermore, evidence suggests that surgical technique and proper patient selection are more critical for outcomes than the complexity of the constructs, supporting the effectiveness of simpler fixation methods such as the single Endobutton technique.⁵

The debate over whether to use a single or double Endobutton continues. Double Endobutton techniques offer greater biomechanical stability and restore the ligament's natural anatomy, with studies reporting excellent radiologic and functional results.^{3,15}

Other studies, however, show that this extra complexity does not always benefit clinical results and may even raise technical requirements and the risk of implant-related complications.¹⁶ In contrast, single Endobutton fixation provides comparable functional results, with reduced surgical complexity, shorter operating time and lower costs.¹⁷

These findings suggest that a single, well-placed suspensory construct is often sufficient to restore functional stability. This is also reflected in the outcomes of the current study.

Complications after Endobutton fixation are still a concern. Loss of reduction is the most frequently reported issue, occurring in about 12-28% of cases in recent studies.⁵ This complication is mainly because of technical factors like tunnel malposition and early loading postoperatively, rather than patient-related factors.

Other complications may include infection, failure of implant, and fracture of the clavicle and coracoid, although these occur less frequently.¹⁸ Nonetheless, the present study reports a low incidence of complication rate and a high proportion of maintained reduction. This emphasizes the necessity of standardized surgical technique and post-op rehabilitation for successful re-

sults.

The strength of this study lies in its larger sample size, standardized surgical technique, and regularly scheduled, pre-determined follow-up intervals, which together provide a more reliable evaluation of functional outcomes. Nonetheless, several shortcomings must be considered. Assessment of long-term stability and late complications, which have received increasing attention in recent literature, cannot be performed due to the short follow-up period.¹⁸

Additionally, the study's single-center design and lack of a control group make the findings less generalizable. The absence of detailed radiological correlation precludes a thorough assessment of anatomical outcomes. Even with these limitations, the study provides significant clinical evidence supporting the effectiveness of the single Endobutton technique.

CONCLUSION

To summarize, acromioclavicular joint reconstruction using the single Endobutton technique demonstrated significant improvements in functional outcomes, including higher Constant-Murley scores and a high rate of maintained reduction.

The results of the current study are consistent with the available literature, which indicates that Endobutton-based reconstruction provides adequate restoration of joint stability and improved shoulder function. This technique offers biomechanical effectiveness and surgical simplicity, making it a cost-effective choice for high-grade AC joint dislocations. Further comparative studies with extended follow-up are recommended to validate these findings and establish definitive treatment guidelines.

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CONFLICT OF INTEREST: Authors declare no conflict of interest

GRANT SUPPORT AND FINANCIAL DISCLOSURE: NIL

Authors Contribution:

Following authors have made substantial contributions to the manuscript as under

Authors	Conceived & designed the analysis	Collected the data	Contributed data or analysis tools	Performed the analysis	Wrote the paper	Other contribution
Ullah U	✓	✓	✓	✓	✓	✓
Ali A	✓	✗	✓	✓	✓	✗
Ullah R	✓	✓	✗	✗	✗	✓
Rehman IU	✓	✗	✓	✓	✓	✗
Ahmad A	✓	✓	✗	✗	✗	✓
Shah SDA	✓	✗	✓	✓	✓	✗

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethical Approval:

This Manuscript was approved by the Ethical Review Board of Khyber Teaching Hospital, Peshawar. Vide No. 379/DME/KMC.

Dated: 25 04 2025



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FACTORS CONTRIBUTING TO EXAMINATION ANXIETY AND THEIR ASSOCIATION WITH GENDER AMONG UNDERGRADUATE MEDICAL AND DENTAL STUDENTS: A CROSS-SECTIONAL STUDY AT A PUBLIC SECTOR UNIVERSITY IN KARACHI, PAKISTAN

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ABSTRACT

Objectives: To evaluate the factors contributing to examination anxiety among undergraduate medical and dental students at Sindh Medical College (SMC) and Sindh Institute of Oral and Health Sciences (SIOHS), Jinnah Sindh Medical University (JSMU), and to determine their association with gender.

Materials & Methods: A cross-sectional study was conducted at SMC and SIOHS, JSMU, over a period of 3 months, after approval from the Institutional Review Board (reference no. JSMU/IRB/2025/1070). Data were collected using a modified, structured, pretested, and validated questionnaire and analyzed using IBM SPSS 27. The overall response rate was 90.7%. Descriptive analysis was used for categorical variables. A chi-square test was used to evaluate the association between factors contributing to examination anxiety and gender. A P value of less than 0.05 was considered statistically significant.

Results: A total of 322 participants responded, of whom 207 were female and 115 were male. Factors associated with gender included sufficient time for exam preparation ($p=0.022$), staying up overnight before the exam ($p=0.006$), dietary habits during exams ($p=0.041$), difficulty understanding medical/dental terminology ($p=0.008$), insufficient time for revision ($p=0.001$), limited library resources ($p=0.046$), and difficulty understanding lectures in English ($p=0.03$).

Conclusion: Examination anxiety among medical and dental students is influenced by many factors. Addressing these factors through supportive strategies and targeted interventions may improve student well-being, performance, and academic experience.

Keywords: Test Anxiety, Medical Students, Dental Students

This article may be cited as: Shah H, Urooj I, Muqri IA, Mubasher A, Kanwal K, Ayoub D. Factors Contributing To Examination Anxiety And Their Association With Gender Among Undergraduate Medical And Dental Students: A Cross-Sectional Study At A Public Sector University In Karachi, Pakistan. J Med Sci 2026 April - June;34(2):104-109

INTRODUCTION

Examination anxiety refers to a state of psychological distress experienced before or during examinations, characterized by physical, cognitive, emotional, and behavioral symptoms such as tachycardia, insomnia, headaches, negative thoughts, social withdrawal, and impaired concentration.^{1,2} Previous studies reveal the prevalence of

medical students experiencing some level of exam-related anxiety to be 33.33%.³

Medical education requires extensive training, which includes study, research, learning, and evaluation. Unlike students in other fields, medical students are required to memorize extensive information and are rigorously tested, which affects their cognitive status.^{4,5} Studies have shown that many medical students lack adequate awareness of effective examination-preparation techniques and anxiety-management strategies. Even among those who are aware of such approaches, implementation during examinations remains limited.⁶

Examinations are overwhelming for students, but they should motivate them to become qualified doctors and to test their ability to pursue medicine.^{7,8} Some studies suggest that extensive course content, ineffective study methods, and complex examination formats, such

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Date Received: 13/04/2026

Date Revised: 26/06/2026

Date Accepted: 26/06/2026

as the Objective Structured Clinical Examination (OSCE), may contribute to anxiety among medical students.⁹

There are four main domains of exam anxiety, including life challenges, lack of academic resources, mental well-being, and learning patterns.¹⁰ Experts have indicated that lifestyle-related issues such as poor sleep quality, inadequate physical activity, lack of appetite, and poor time management are also linked to exam anxiety.¹¹ Additional factors include the burden of the curriculum, lack of support, poor self-confidence, inability to self-study, and overly critical self-standards.¹² Addressing these factors can reduce students' anxiety levels, improve their academic performance, and ultimately improve the quality of patient care they provide in clinical practice.¹³

While a certain level of anxiety is normal, it is crucial to remain mentally and physically alert to stay motivated during exams.¹⁴ However, extreme anxiety, such as negative thoughts about exams, can inhibit a student's ability to manage nervous responses during exams.¹⁵ Studies show that students with high exam anxiety have lower grades than those with low exam anxiety.¹⁶ According to Putwain et al. (2023), the fear of failing to meet one's own and others' expectations creates a sense of inadequacy and anxiety.¹⁷

While exams are essential in medical and dental education, students often face stressors such as limited clinical exposure and the transition to online learning, which may contribute to increased anxiety.¹⁸ The underlying factors contributing to examination anxiety remain unclear, as previous studies have been unable to identify them. To address this knowledge gap, especially within the local context where limited research exists, a cross-sectional study was conducted to evaluate the factors contributing to examination anxiety among undergraduate medical and dental students of Sindh Medical College (SMC) and Sindh Institute of Oral and Health Sciences (SIOHS), Jinnah Sindh Medical University (JSMU), and to determine their association with gender. The insights gained from this study would help students in managing examination anxiety, ultimately improving their overall learning experience.

MATERIALS AND METHODS

A cross-sectional study was conducted at SMC and SIOHS, JSMU, over period of 3 months, from October 2025 to December 2025, after receiving approval from its Institutional Review Board (reference no. JSMU/IRB/2025/1070). It involved undergraduate medical and dental students from all five academic years of MBBS and all four academic years of BDS. Only participants who provided verbal and written consent were included. Participants were reassured that their responses would remain anonymous and confidential.

Medical and dental house officers, residents, and postgraduate students of JSMU were excluded because

they were not a part of the undergraduate examination system. The entire teaching and non-teaching medical and dental faculty were excluded from the study because they do not undergo academic examinations.

The determination of the sample size for this study used a nonprobability convenience sampling technique. The total target population of SMC and SIOHS at JSMU was 1950. To calculate the sample size, the prevalence among medical and dental students was estimated at 50%, with a 5% margin of error and a 95% confidence level.⁶ A minimum sample size of 322 participants was calculated using OpenEpi.

Data were collected using a modified structured, pre-tested questionnaire adapted from a previously validated study tool.¹⁵ The questionnaire consisted of two parts. The first part presented demographic data on the study participants, including age, gender, year of study, socio-economic status, and marital status. The second section consisted of 19 closed-ended items rated on a five-point Likert scale and assessed factors associated with examination anxiety.¹⁵ The questionnaire was pilot tested on 10% of the study population (approximately 35 participants) to check the clarity, reliability, and validity of questions. Cronbach's alpha was computed, where a threshold of $\alpha \geq 0.70$ was considered acceptable. Feedback from the pilot study was collected to refine the tool. Data from the pilot study were not included in the final analysis.

Data were entered and analyzed using the Statistical Package for the Social Sciences (SPSS) version 27. Descriptive statistics summarized categorical variables as frequencies and percentages. A chi-square test was used to assess the association between factors contributing to examination anxiety and gender. A P value less than 0.05 was considered statistically significant.¹⁵

RESULTS

A total of 322 participants responded. About 281 were medical students, and 41 were dental students. The mean age of the participants was 21.3 (SD = 1.6). About 64.3% (n=207) were female students, while 35.7% (n=115) were male students. Table 1 shows the demographic data of the study participants. Table 2 presents the distribution of participants by gender and the factors contributing to exam anxiety. Most female (60.4%) and male (52.2%) participants reported having an extensive course. A similar proportion of male (35.7%) and female (35.3%) students found it difficult to manage time for self-study. Nearly half of the female (47.8%) and male (44.3%) participants reported understanding English without any difficulty. The majority of females (56.5%) and males (52.2%) agreed that they knew their exam pattern. Many male (44.3%) and female (42.5%) students also reported that their studies were affected by digital distractions.

More females (29.5%) than males reported having unhealthy eating habits during their exams. Several male participants (27.1%) disagreed that the institute provided enough time for exams. The majority of female (71.5%) and male (62.6%) students reported that their institution had limited library resources. Nearly half of female (46.4%) and male (40%) students reported that they never found it difficult to understand lectures delivered in English rather than Urdu.

The last column of Table 2 shows the association between factors contributing to exam anxiety and gender. Factors that showed significant associations with gender included sufficient time for exam preparation from the institute ($p=0.022$), staying up all night before the exam ($p=0.006$), dietary habits during exams ($p=0.041$), difficulty understanding medical and dental terminology ($p=0.008$), insufficient time for revision ($p=0.001$), limited library resources at the institute ($p=0.046$), and difficulty understanding English lectures ($p=0.03$).

DISCUSSION

Several factors have been linked to examination anxiety, including low confidence, poor time management, stress, overnight revision, fear of failure, insufficient preparation time, a curriculum designed in a foreign language, high parental expectations, poor study habits, and a heavy academic workload.^{2, 13, 15}

In this study, more than half of the participants agreed to having an extensive course load, which has been found to be a factor associated with examination anxiety among medical students in various studies. An expansive curriculum covered in a short time may contribute to examination anxiety among students, leading to poor academic performance.^{2,15}

Consistent with the findings of Simran et al., the majority of students in this study (37.9%) reported having insufficient time for revision. More males reported having sufficient time for preparation than females, which is consistent with other studies showing that insufficient preparation time is linked to examination anxiety among females.¹³

A significant percentage of participants in this study reported that limited library space affected their studies, a concern more commonly associated with female participants. This finding is significant because studying in libraries was positively associated with better academic performance in a study conducted in Peshawar.^{19, 20}

Participants showed mixed responses when asked about the allocated time for completing exams. More males than females disagreed that they had sufficient time to complete their exams. Although evidence within the literature is limited, studies have linked poor time management during exams to higher exam anxiety.²

Table No 1: DEMOGRAPHIC DATA OF STUDY PARTICIPANTS

VARIABLES	FREQUENCIES (%)
Age	
Mean (SD)	21.3 (1.6)
Gender	
Male	115 (35.7)
Female	207 (64.3)
Marital status	
Single	316 (98.1)
Married	6 (1.9)
Institute	
SMC	281 (87.3)
SIOHS	41 (12.7)
Academic year	
1st year	57 (17.7)
2nd year	69 (21.4)
3rd year	69 (21.4)
4th year	62 (19.3)
5th year	65 (20.2)
Mother's education	
Uneducated	15 (4.7)
Primary	15 (4.7)
Secondary	22 (6.8)
Higher Secondary	70 (21.7)
Bachelors	129 (40.1)
Master	66 (20.5)
PHD	5 (1.6)
Mother's occupation	
Non-working	252 (78.3)
Working	70 (21.7)
Father's education	
Uneducated	3 (0.9)
Primary	9 (2.8)
Secondary	15 (4.7)
Higher Secondary	60 (18.6)
Bachelors	117 (36.3)
Master	107 (33.2)
PHD	11 (3.4)
Family income per month	
Mean (SD)	143462.7 (134709.1)
Family size	
Mean (SD)	5.8 (2.0)
Living area	
Urban	306 (95.0)
Rural	16 (5.0)

Table No 2:FACTORS CONTRIBUTING TO EXAMINATION ANXIETY AND THEIR ASSOCIATION WITH GENDER

Factors	Gender (%)	Strongly agree	Agree	Neutral	Disagree	Strongly disagree	P-value
Do you think your academic course is very extensive?	Male	60 (52.2)	35 (30.4)	16 (13.9)	4 (3.5)	0 (0.0)	0.286
	Female	125 (60.4)	58 (20.0)	15 (7.2)	8 (3.9)	1 (0.5)	
Do you have sufficient time for revision before the exam?	Male	7 (6.1)	21 (18.3)	25 (21.7)	38 (33.0)	24 (28.9)	0.001*
	Female	0 (0.0)	25 (12.1)	39 (18.8)	84 (40.6)	59 (28.5)	
Do you find it easy to manage your time for self-study?	Male	6 (5.2)	21 (18.3)	29 (25.2)	41 (35.7)	18 (15.7)	0.091
	Female	3(1.4)	24 (11.6)	63 (30.4)	73 (35.3)	44 (21.3)	
Do you feel pressured by your parents' expectations?	Male	15 (13.0)	21 (18.3)	33 (28.7)	30 (26.1)	16 (13.9)	0.525
	Female	20 (9.7)	42 (20.3)	50 (24.2)	53 (25.6)	42 (20.0)	
Do you easily recall and review lessons before exams?	Male	4 (3.5)	38 (33.0)	28 (24.3)	33 (28.7)	12 (10.4)	0.075
	Female	3(1.4)	43 (20.8)	69 (33.3)	64 (30.9)	28 (13.5)	
Do you often worry about failing exams?	Male	24(20.9)	34 (29.6)	24 (20.9)	20 (17.4)	13(11.3)	0.059
	Female	72 (34.8)	49 (23.7)	44 (21.3)	30 (14.5)	12 (5.8)	
Do you find it difficult to understand the course in English?	Male	4 (3.5)	11 (9.6)	13 (11.3)	36 (31.3)	51 (44.3)	0.131
	Female	5 (2.4)	6 (2.9)	28 (13.5)	69 (33.3)	99(47.8)	
Do you know about the pattern of exams?	Male	20 (17.4)	60 (52.2)	19 (16.5)	12 (10.4)	4 (3.5)	0.233
	Female	37 (17.9)	117 (56.5)	36 (17.4)	8 (3.9)	9 (4.3)	
Do you often stay up all night before an exam?	Male	25 (21.7)	35 (30.4)	11 (9.6)	24 (20.9)	20 (17.4)	0.006*
	Female	70 (33.8)	48 (23.2)	38 (18.4)	32 (15.5)	19 (9.2)	
Do digital distractions (e.g. social media, mobile, etc.) interfere with your studies?	Male	51 (44.3)	36 (31.3)	18 (15.7)	7 (6.1)	3 (2.6)	0.958
	Female	88 (42.5)	70 (33.8)	35 (16.9)	10 (4.8)	4 (1.9)	
Do you maintain a healthy diet during exams?	Male	11 (9.6)	31 (27.0)	37 (32.2)	25 (21.7)	11 (9.6)	0.04 *
	Female	9 (4.3)	46 (22.2)	54 (26.1)	61 (29.5)	37 (17.9)	
Do you feel pressure to get higher marks from top students?	Male	15 (13.0)	32 (27.8)	29 (25.2)	25 (21.7)	14 (12.2)	0.588
	Female	37 (33.4)	62 (30.0)	53 (25.6)	38 (18.4)	17 (8.2)	
Do you find it difficult to understand medical/dental terminology?	Male	6 (5.2)	24 (20.9)	21 (18.3)	36 (31.3)	28 (24.3)	0.00 *
	Female	10 (4.8)	24 (11.6)	71 (34.3)	69 (33.3)	33 (15.9)	
Does the institute provide you with sufficient time to complete your exams?	Male	13 (11.3)	24 (20.9)	30 (26.1)	31 (27.0)	17 (14.8)	
	Female	21 (10.1)	56 (27.1)	38 (18.4)	36 (17.4)	56(27.1)	0.022*
Do you rely on rote memorization instead of understanding concepts?	Male	11 (9.6)	21 (18.3)	25 (21.7)	38 (33.0)	20 (17.4)	
	Female	10 (4.8)	26 (12.6)	66 (31.9)	65 (31.4)	40 (19.3)	0.131
Do you feel that limited library space or study resources at your institute affects your exam preparation?	Male	72 (62.6)	20 (17.4)	9 (7.8)	7 (6.1)	7 (6.1)	
	Female	148 (71.5)	34 (16.4)	17 (8.2)	6 (2.9)	2 (1.0)	0.046*
Does living in a joint family environment make it difficult for you to study for exams?	Male	15 (13.0)	25 (21.4)	32 (27.8)	22 (19.1)	21 (18.3)	
	Female	40 (19.3)	35 (16.9)	78 (37.7)	24 (11.6)	30 (14.5)	0.08
Do you feel pressure to perform well in exams because of financial sacrifices made by your parents?	Male	21 (18.3)	28 (24.3)	37 (32.2)	20 (17.4)	9 (7.8)	
	Female	33 (15.9)	47 (22.7)	72 (34.8)	31 (15.0)	24 (11.6)	0.778
Do you face difficulty in understanding lecture material when it is delivered in English rather than Urdu?	Male	10 (8.7)	4 (3.5)	25 (21.7)	30 (26.1)	46 (40.0)	
	Female	4 (1.9)	12 (5.8)	34 (16.4)	61 (29.5)	96 (46.4)	0.03*

*Statically significant

Fear of failing in exams was also associated with exam anxiety in this study, a factor commonly reported among Greek medical students.^{1, 16}

Most participants in the present study did not find lectures in English challenging, despite it not being their

native language. This contradicts other studies in which a curriculum taught in a foreign language was associated with exam anxiety among students.²¹ Participants, mostly female, reported no difficulties understanding medical or dental terminology. The results of the present study

showed that fewer students felt pressured by their family's expectations, a finding that contradicts the study by Wadi et al., which reported that most medical students felt pressured by high family expectations, thereby negatively impacting their anxiety levels.⁹

This study also demonstrated that most participants stayed awake the day before the exam to prepare, consistent with a previous study reporting that 41% of medical students studied late at night during exams.²²

About 43.2% of participants in this study acknowledged that digital distractions interfered with their studies, a finding supported by Al-Sahman et al., who reported that 56% of students were preoccupied by distractions during study sessions.¹⁵

Poor dietary habits were found to be linked with anxiety and depression among students.²³ This study showed that females were more frequently unable to maintain a healthy diet during the exam period.

The cross-sectional design of this study limits the ability to establish causal relationships. Furthermore, data were collected via self-report questionnaires, which may be subject to recall bias. Third, the study was conducted among a limited population, which limits the generalizability of the findings to students at other institutions or in other regions.

CONCLUSION

Examination anxiety is common among medical and dental students and is influenced by many factors. Addressing these factors through supportive strategies and targeted interventions may improve student well-being, performance, and overall academic experience.

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CONFLICT OF INTEREST: Authors declare no conflict of interest

GRANT SUPPORT AND FINANCIAL DISCLOSURE: NIL

Authors Contribution:

Following authors have made substantial contributions to the manuscript as under

Authors	Conceived & designed the analysis	Collected the data	Contributed data or analysis tools	Performed the analysis	Wrote the paper	Other contribution
Shah H	✓	✓	✗	✗	✓	✗
Urooj I	✓	✗	✓	✓	✓	✗
Muqri IA	✓	✓	✗	✗	✗	✓
Mubasher A	✓	✗	✓	✓	✓	✗
Kanwal K	✓	✓	✗	✗	✗	✓
Ayoub D	✓	✗	✓	✓	✓	✗

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethical Approval:

**This Manuscript was approved by the Ethical Review
Board of Jinnah Sindh Medical University. Vide No. JSMU/
IRB/2025/1070. Dated: 22 10 2025**



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PSYCHOLOGICAL AND SOCIAL IMPACT ON THE LIVES OF VESICOVAGINAL FISTULA PATIENTS PRE- AND POST-SURGICAL REPAIR

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ABSTRACT

Objective: This study evaluated the psychological and social changes in patients undergoing surgical repair for VVF.

Materials & Methods: A cross-sectional study was conducted in the Department of Urology at Khyber Teaching Hospital, Peshawar, from May 2019 to September 2024. Seventy patients with confirmed VVF were enrolled. Diagnosis was established by cystoscopy and vaginoscopy. Surgical repair was performed 4–6 weeks after onset, followed by three days of hospitalization and regular follow-up. Psychological and social outcomes were assessed using validated tools and the Patient Global Impression of Improvement (PGI-I) scale at three months.

Results: The mean age of participants was 40.6 ± 10.2 years; 78.9% were multiparous. The mean fistula size was 11.5 ± 4.5 mm, with supratrigonal fistulas more common (60.6%). Hysterectomy was the leading cause (46.5%), followed by cesarean section (29.6%) and difficult labor (16.9%). The overall closure success rate was 90.1%, with higher rates in smaller fistulas ($p = 0.02$). Patients with failed repairs had longer hospital stays (5.1 ± 0.7 vs. 3.7 ± 0.7 days, $p < 0.001$). Minor complications occurred in 14.2% of cases. Psychological distress decreased significantly after surgery; persistent incontinence was associated with higher PTSD and depression. Over 90% reported symptom improvement (PGI-I < 3).

Conclusion: Early surgical repair of VVF yields high closure rates and substantial psychological and social recovery. Comprehensive care, including psychosocial support, is essential for optimal reintegration and quality of life.

Keywords: Vesicovaginal fistula (VVF), surgical repair, psychological impact, social reintegration, quality of life.

This article may be cited as: Masood I, Ullah H, Ali M, Anees M, Sabir M, Ali A. Psychological And Social Impact On The Lives Of Vesicovaginal Fistula Patients Pre- And Post-Surgical Repair. J Med Sci 2026 April - June;34(2):110-115

INTRODUCTION

Vesicovaginal fistula (VVF) is a serious medical condition caused by an abnormal passage between the bladder and vagina. It leads to constant urine leakage.¹ The condition causes not only remarkable physical discomfort by means of a wet feeling, odor, and predisposing the self to irritation, but also fundamentally damages patients' mental health, social relationships, and sex life. The psychological and social consequences of VVF are well established, with patients often experiencing social isolation, stigma, marital discord, depression, and reduced quality of life.⁶⁻⁹ These challenges emphasize the pressing need for a management strategy that addresses both the physical and psychosocial aspects of this condition.

In this study, psychological impact refers to the emotional and mental health consequences of VVF, including depression, post-traumatic stress symptoms, and psychological distress. Social impact refers to the effects of the condition on interpersonal relationships, marital life, social participation, stigma, isolation, and reintegration into the community. Assessing both domains provides a comprehensive understanding of the burden of VVF before and after surgical repair. The causes of VVF are significantly different between developed and developing countries. In high-income nations, the condition is primarily associated with gynecological or pelvic surgeries, radiotherapy, and malignancies.² In contrast, in low-resource settings, obstructed labor is the leading cause of VVF. Prolonged labor with an obstructed fetal head can cause ischemic injury to the tissue, resulting in the formation of a fistula. The incidence of VVF in developed countries ranges from 0.3% to 2.0%, whereas in regions such as South Asia and Africa, the prevalence can reach up to 4.09 cases per 1,000 deliveries.^{3,6} Factors such as early marriage, poverty, low literacy rates, malnutrition, and lack of access to antenatal and emergency obstetric care all contribute to making the problem worse in these areas.⁷ These dis-

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Date Received: 16/01/2026

Date Revised: 28/06/2026

Date Accepted: 29/06/2026

crepancies strongly suggest that in both medical and economic terms, VVF must thus be confronted. Hysterectomy, whether cesarean or simple, is the most common surgical procedure associated with VVF (63%-91% of cases).⁴ Unintended injuries to the urinary system during electro-coagulation treatment are also a significant cause, constituting 70% of such injuries diagnosed after surgery.⁵ Various surgical techniques, including transabdominal, transvaginal, laparoscopic, and robotic approaches, have been used to repair VVF.⁸

However, no consensus has been reached on the optimal timing of surgical intervention. Even though the literature presents various opinions, most recommend waiting 3 months after a fistula is created for the inflammation to subside. But this delay only increases the psychological and social burden on patients.⁸ VVF has long-term effects in both psychological and physical terms. Research has shown that early surgical intervention can significantly improve patients' quality of life and psychological well-being.^{14,16} For example, research conducted in Ethiopia found a substantial drop in psychological distress among fistula patients two weeks after surgery.¹⁷ Nevertheless, there are no published quantitative studies specifically examining the psychological and social issues that patients face when they return home, where they may encounter obstacles and hardships of a different nature.¹⁵ This gap in the research indicates that the long-term psychosocial impact of VVF and the effect of early surgery need further scrutiny.

The focus of the research is to evaluate whether early surgery can help resolve VVF arising from benign gynecologic procedures, and to explore how this treatment affects patients' quality of life psychologically and socially. Using a pre/post design, we aimed to measure changes in psychiatric symptoms and social consequences of bladder repair before treatment until 3 months after discharge from the hospital. The study will fill these knowledge gaps, adding to the already substantial body of data supporting early surgical intervention and supportive care for VVF sufferers. Such findings could be used to shape clinical practice and thus impact those who suffer from the condition.

MATERIALS AND METHODS

We conducted a cross-sectional study in the Department of Urology at Khyber Teaching Hospital, Peshawar, from May 2019 to September 2024. The study included 70 women aged 20–60 years with vesicovaginal fistula (VVF) secondary to benign gynecological surgeries, including abdominal or vaginal hysterectomy, cesarean section, myomectomy, and pelvic organ prolapse surgery. Patients with fistulas related to malignancy, radiotherapy,

diabetes mellitus (fasting blood glucose >126 mg/dL), immunosuppressive conditions (e.g., HIV or genitourinary tuberculosis), or other fistula types (e.g., ureterovaginal or rectovaginal fistulas) were excluded.

Ethical approval was granted by the hospital's research committee. Participants were briefed on the study and its benefits, and written informed consent was obtained from each participant. Patients were recruited through the outpatient department (OPD) and underwent comprehensive clinical assessments, including a medical history, physical examination, and relevant preoperative tests.

Data Collection and Analysis: Clinical and demographic data were prospectively collected by the treating research team using a structured data collection form at admission, surgery, and follow-up visits. Psychological questionnaires were administered preoperatively and repeated at the three-month follow-up. All collected data were entered into SPSS version 20 after verification for completeness and accuracy, prior to statistical analysis. Quantitative variables (age, fistula size, etc.) were presented as mean and standard deviation, and categorical variables (parity, fistula location, etc.) were expressed as frequency and percentage. Comparisons were performed using the chi-square test and Student's t-test; a two-tailed p-value of ≤ 0.05 was considered significant.

To confirm the previous diagnosis, assess the fistula's position and size in relation to the ureteral orifices, and exclude any associated ureteral damage, cystoscopy and vaginoscopy were performed. For further analysis, computer tomography urography (CTU) was done. The surgical reconstruction was performed by a consultant urologist with over five years' experience, using the suprapubic approach described by O'Connor et al.⁹ The surgeries were performed four to six weeks after the onset of the fistula to allow time for the tissue to heal.

Patients remained in the ward for 3 days after surgery and were discharged on the 4th day if stable. A 16 Fr Foley urethral catheter was kept in place for continuous bladder drainage after surgery. On the 14th postoperative day, a retrograde cystogram was performed to confirm successful fistula closure and to exclude urinary leakage before catheter removal. The catheter was removed only after a satisfactory cystogram showed no contrast extravasation. Double-J ureteric stents were selectively placed in patients with fistulas near the ureteric orifices or when ureteric identification or protection was required during reconstruction. The DJ stents were removed via a flexible cystoscope after approximately four weeks. Patients were reassessed three months later to evaluate symptom resolution, stress incontinence, urgency, and complications such as urinary tract infections.

Outcome Measures: Success was defined as anatomical closure of the fistula or the absence of continuous urinary leakage, with symptom resolution. Psychological and social outcomes were assessed using validated tools: the Center for Epidemiologic Studies Depression Scale (CES-D; $\alpha = 0.85$) for depression.¹⁷ the PTSD Checklist-Civilian Version (PCL-C; $\alpha = .83$) for PTSD, and the Bradford Somatic Inventory (BSI; $\alpha = 0.94$) for somatic symptoms.^{18, 21} Avoidant coping was measured using three items from the Brief COPE, which has been validated in obstetric fistula patients.^{19, 22} Patients' perceptions of cure and leakage severity were assessed using a 5-point scale adapted from Browning and Member.¹³ All psychological assessment instruments were administered according to their published guidelines and standardized scoring procedures. These validated tools have been widely used in clinical research, including studies involving women with vesicovaginal fistula.

RESULTS

1. Demographic and Clinical Characteristics

The mean age of study participants was 40.6 years (SD $\pm$ 10.2), with a total of 70 subjects. Most participants were multiparous (78.9%), and the mean fistula size was 11.5 mm (SD $\pm$ 4.5).

Supratrigonal fistulas were more prevalent at 60.6%, surpassing trigonal fistulas at 38%. The most common cause of VVF was hysterectomy, including cesarean and simple hysterectomy, at 46.5%, followed by cesarean section at 29.6% and difficult labor at 16.9%. The mean operative time was 125.3 minutes (SD $\pm$ 10.7), and the mean length of stay was 3.8 days (SD $\pm$ 0.8).

2. Success Rate and Factors Influencing Repair

Overall, fistula closure operations were successful in 90.1% of cases. Of the patients studied, 64 were symptom-free. Success rates were higher for smaller fistulas (5-10 cm) than for larger ones (11-20 cm) ($p = 0.02$). The location of the appendix fistula, the stage of pregnancy, and the timing of surgery did not substantially affect repair success. Those with failed repairs remained in the hospital longer (5.1 ± 0.7 days) than those with successful repairs (3.7 ± 0.7 days), $p < 0.001$.

3. Postoperative Complications

Minor complications of patients monitored reached 14.2%. These included wound infection (2.9%), urinary tract infections requiring antibiotic therapy (7.1%), and hematuria requiring bladder irrigation (4.3%). There were no cases of life-threatening complications reported.

4. Patient-Reported Outcomes

After 3 months of follow-up, 90% of patients showed improvement in symptoms, with the Patient Glob-

al Impressions of Improvement (PGI-I) score below 3. In detail, 50% of the population reported being "very much better," and 40% were "much better," but 4.2% were unchanged and primarily returned to having strong urinary urges along with incontinence.

Table No 1: Demographic and Clinical Characteristics

Parameter	Value	95% CI
Mean Age (years)	40.6 $\pm$ 10.2	38.1 – 43.0
Parity	Primipara: 14 (19.7%)	-
	Multipara: 56 (78.9%)	-
Mean Fistula Size (mm)	11.5 $\pm$ 4.5	9.4 – 11.6
Fistula Location	Supratrigonal: 43 (60.6%)	-
	Trigonal: 27 (38%)	-
Etiology of VVF	Hysterectomy: 33 (46.5%)	-
	Cesarean Section: 21 (29.6%)	-
	Difficult Labor: 12 (16.9%)	-
Mean Operative Time (min)	125.3 $\pm$ 10.7	122.7 – 127.9
Mean Hospital Stay (days)	3.8 $\pm$ 0.8	3.6 – 4.0

Table No 2: Factors Associated with Successful Fistula Repair

Parameter	Successful Repair (n = 64)	Failed Repair (n = 6)	p-value
Fistula Size (mm)	5-10 mm: 32 (50%)	0 (0%)	0.02
	11-20 mm: 32 (50%)	6 (100%)	
Fistula Location	Supratrigonal: 38 (59.3%)	5 (83.3%)	0.3
	Trigonal: 26 (40.6%)	1 (16.7%)	
Parity	Primipara: 12 (18.7%)	2 (33.3%)	0.5
	Multipara: 52 (81.2%)	4 (66.7%)	
Operative Time (min)	124.9 $\pm$ 10.7	130 $\pm$ 11.4	0.2
Hospital Stay (days)	3.7 $\pm$ 0.7	5.1 $\pm$ 0.7	<0.001

Table No 3: Postoperative Complications

Complication	Number of Patients (%)
Wound Infection	2 (2.9%)
Urinary Tract Infection	5 (7.1%)
Hematuria	3 (4.3%)
Total	10 (14.2%)

Table No 4: Patient Global Impression of Improvement (PGI-I) Scores at 3 Months

PGI-I Score	Interpretation	Number of Patients (%)
1	Very Much Better	35 (50%)
2	Much Better	28 (40%)
3	A Little Better	4 (6%)
4	No Change	3 (4.2%)

DISCUSSION

The results of this research underscore the extreme hardships that patients with vesicovaginal fistula (VVF) face, whether physical, psychological, or social. The condition is caused by the continuous leakage of urine, which results in pain and discomfort, along with severe emotional and social repercussions, such as stigma, isolation, and marital conflict.^{1, 6-9} These findings are consistent with prior studies, which confirm that VVF repair surgery enhances patients' everyday lives and ameliorates their mental health.¹⁴⁻¹⁶ Nonetheless, the study highlights the persistent psychosocial problems that patients, especially those with chronic conditions such as incontinence or urgency, continue to endure.

The demographic profile of participants in our study, with an average age of 40.6 years and a high proportion of multiparous women (78.9%), is consistent with findings from other research conducted in comparable contexts.^{6, 7} The high incidence of supratrigonal fistula and the increased proportion of hysterectomy as a contributing factor (60.6% and 46.5%, respectively) are indicative of the surgical and obstetric pathology that exists in poor regions.^{2, 4} These results underscore the necessity for more advanced obstetric care and more intensive surgical skills to avert accidental damage to the organs during gynecological surgeries.

The overall success rate of 90.1% in our study contrasts with the literature, where success rates are reported at about 75%-95%¹⁰. The considerable success rate observed with smaller fistula repair (5-10 mm) compared with larger fistula repair (11-20 mm) ($p=0.02$) does not support the concept that fistula size is an important determinant of surgical outcomes [8]. Nonetheless, some factors, such as fistula site, parity, and operative time, did not significantly affect repair success, suggesting that surgical method and timing are more important to the outcome. The longer hospital stays among patients with failed repairs (5.1 ± 0.7 days vs 3.7 ± 0.7 days, $p < 0.001$) underscore the additional physical and financial burden these patients must shoulder.

Some complications were noted in 14.2% of pa-

tients at follow-up, including surgical site infection (2.9%), urinary tract infection (7.1%), and hematuria (4.3%). These figures align with those reported in other studies, underscoring the need for careful postoperative attention to reduce morbidity.^{11, 12} The absence of severe complications in our cohort confirms the effectiveness of the operative strategy and the operating team's skills. Nonetheless, even the slightest problems demonstrate the necessity for ongoing attention, education, and motivation from the nursing staff to support favorable recuperation.

The self-reported outcomes indicate substantial symptom improvement, with 90% of patients scoring below 3 on the PGI-I. This supports the claim that early surgical intervention is beneficial. Nevertheless, the 4.2% of patients who reported no change, most of whom had ongoing urinary urgency and incontinence, demonstrate the extent to which surgical repair fails to address certain aspects of VVF morbidity. This aligns with qualitative investigations that describe the residual psychological and social difficulties faced by fistula patients following successful repair.^{14, 15} The self-reported severity of leakage, together with psychological distress (depression and even PTSD), indicates a stark need for holistic interventions in VVF.

The timing of VVF repair remains a subject of debate. Some researchers recommend postponing surgery for three months to allow inflammation to subside. However, we believe that when infection or radiotherapy is absent, early repair within 4-6 weeks is practical and useful.^{8, 12} In addition to minimizing the duration of physical suffering, early intervention helps reduce the emotional and social impacts of prolonged urinary leakage. Nonetheless, the success of early repair depends on fundamental surgical principles, such as adequate exposure, tension-free closure, and bladder drainage.¹³

The psychosocial aspect of VVF is very much present. Patients and their families often face severe stigma, social withdrawal, and marital problems that can persist even after successful repair [6-9]. The combination of high baseline psychological distress noted in the study and the marked change following surgery underscores the need to integrate the fistula care program into mental healthcare services. Such findings are reported from a fistula repair program in Tanzania, which demonstrated the effect of psychological support and serves as a model for addressing VVF patients' mental health.²²

This study has some limitations. First, the findings may not be generalizable because of the single-center design and small sample size. Second, the three-month follow-up may not capture long-term outcomes, particular-

ly for sexual function and quality of life. Third, gaps in patients' education, knowledge of emergency obstetric care, and access to healthcare limit our ability to fully interpret the results. These limitations may be addressed in future research through multi-center studies, longer follow-up periods, and consideration of additional sociodemographic factors.

CONCLUSION

This study demonstrates that early surgical repair of vesicovaginal fistula (VVF) is feasible and effective, achieving a high closure rate (90.1%) and resulting in significant improvement in the psychological well-being and social functioning of affected women. Smaller fistulas (5–10 mm) were associated with higher repair success, whereas failed repairs were associated with longer hospital stays, highlighting the additional physical and financial burden on patients.

Although most women experienced substantial recovery following surgery, persistent urinary symptoms in a small proportion of patients continued to affect their psychosocial well-being. These findings emphasize the importance of timely surgical intervention combined with comprehensive multidisciplinary care, including psychological support, to optimize both physical and psychosocial outcomes in women with VVF.

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CONFLICT OF INTEREST: Authors declare no conflict of interest

GRANT SUPPORT AND FINANCIAL DISCLOSURE: NIL

Authors Contribution:

Following authors have made substantial contributions to the manuscript as under

Authors	Conceived & designed the analysis	Collected the data	Contributed data or analysis tools	Performed the analysis	Wrote the paper	Other contribution
Masood I	✓	✓	✗	✗	✓	✗
Ullah H	✓	✗	✓	✓	✓	✗
Ali M	✓	✓	✗	✗	✗	✓
Anees M	✓	✗	✓	✓	✓	✗
Sabir M	✓	✓	✗	✗	✗	✓
Ali A	✓	✗	✓	✓	✓	✗

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethical Approval:

This Manuscript was approved by the Ethical Review Board of Khyber Teaching Hospital, Peshawar. Vide No. 45/DME/KMC.

Dated 16/01/2025



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SUCCESSFUL SALVAGE THERAPY WITH CEFTAZIDIME-AVIBACTAM PLUS AZTREONAM FOR PAN-RESISTANT SERRATIA MARCESCENS SEPSIS IN AN INFANT: A CASE REPORT

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ABSTRACT

Invasive infections caused by pan-resistant Gram-negative pathogens pose significant therapeutic challenges in neonatal intensive care units. We report a 35-day-old male infant presenting with severe sepsis, respiratory failure, and apnea. Initial empirical antimicrobials failed. Blood culture isolated *Serratia marcescens* with pan-resistance to conventional antibiotic classes, including carbapenems, aztreonam, and ceftazidime-avibactam. Following a pediatric infectious diseases consultation, a weight-adjusted combination of intravenous ceftazidime-avibactam and aztreonam was initiated to exploit potential mechanistic synergy. The patient achieved clinical cure and hematologic recovery over a 21-day course without renal toxicity, suggesting a potential salvage option when standard choices are exhausted.

Keywords: Anti-Bacterial Agents; Drug Resistance, Multiple, Bacterial; Infant; Sepsis; *Serratia marcescens*

This article may be cited as: Ashraf MM, Ain NU, Ehsan F. Successful Salvage Therapy With Ceftazidime-Avibactam Plus Aztreonam For Pan-Resistant *Serratia Marcescens* Sepsis In An Infant: A Case Report. J Med Sci 2026 April - June;34(2):116-117

INTRODUCTION

Neonatal and infant sepsis remains a leading driver of pediatric mortality in developing countries, a burden intensified by rising antimicrobial resistance among Gram-negative bacilli.^{1,2}

Serratia marcescens is a resilient opportunistic pathogen capable of causing neonatal outbreaks and acquiring extensive drug resistance.³

When isolates are resistant to standard antimicrobial classes, clinicians have few viable single-agent options. Ceftazidime-avibactam, combined with aztreonam, has emerged as a salvage therapy for refractory Gram-negative infections, but clinical validation in young infants remains limited.^{4,5}

CASE REPORT

A 35-day-old male infant weighing 2.2 kg presented with one week of pyrexia, poor feeding, lethargy, and severe respiratory distress.

On arrival, he developed apnea and required im-

mediate bag-mask ventilation before stabilization on continuous positive airway pressure. Empirical intravenous fluids, cefotaxime, and gentamicin were started for presumed sepsis. Baseline testing revealed leukopenia ($2.8 \times 10^9/L$), thrombocytopenia ($115 \times 10^9/L$), anemia (hemoglobin 10.0 g/dL), and indirect hyperbilirubinemia. Chest radiography showed bronchopulmonary pneumonia.

Admission blood culture yielded *Serratia marcescens* with pan-resistance to cephalosporins, piperacillin-tazobactam, carbapenems, aminoglycosides, fluoroquinolones, ceftazidime-avibactam, and aztreonam.

Given the clinical decline, a pediatric infectious disease review was obtained. Intravenous ceftazidime-avibactam 90 mg every 8 hours was given concurrently with aztreonam 100 mg every 8 hours to exploit functional synergy.

Platelets reached $51 \times 10^9/L$, and hemoglobin dropped to 6.7 g/dL, requiring platelet and packed red cell transfusions. Renal metrics remained stable.

A single-bottle growth of a *Staphylococcus* species was treated as skin contamination, as the infant was improving with no other symptoms.

The infant completed 21 days of dual therapy, achieved hematologic recovery, and was discharged stable. The integrated clinical timeline is summarized in Table 1.

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Date Received: 20/05/2026

Date Revised: 25/06/2026

Date Accepted: 25/06/2026

Table No 1: Chronological Timeline and Patient Management

Phase / Dates	Key Findings	Management / Outcome
Admission (08-09 Sep 2025)	Fever, lethargy, respiratory distress, apnea; WBC $2.8 \times 10^9/L$, platelets $115 \times 10^9/L$; pneumonia on chest radiograph	CPAP support, intravenous fluids, cefotaxime plus gentamicin; blood culture sent
Culture Phase (12-13 Sep. 2025)	Pan-resistant <i>Serratia marcescens</i> isolated; platelet nadir $51 \times 10^9/L$	Infectious diseases consultation obtained; ceftazidime-avibactam plus aztreonam initiated
Supportive Phase (14-16 Sep. 2025)	Hb nadir 6.7 g/dL; repeat <i>Staphylococcus</i> culture considered contaminant	Platelet and packed red cell transfusions; salvage therapy continued
Recovery (18 Sep-04 Oct. 2025)	Clinical improvement; WBC $11.9 \times 10^9/L$, platelets $155 \times 10^9/L$, Hb 14.5 g/dL	Completed 21-day therapy; discharged stable

DISCUSSION

Management of invasive *Serratia marcescens* infection is challenging due to its environmental persistence and rapid acquisition of resistance.³

Aztreonam resists degradation by metallo-beta-lactamases, while avibactam inhibits co-produced serine beta-lactamases; together, they may restore activity despite apparent single-agent resistance.⁵

In settings without molecular testing or synergy panels, expert-guided combination therapy may be a practical bedside option.

Although limited by a single-patient design and lack of genotypic confirmation, this case supports cautious use of ceftazidime-avibactam plus aztreonam when all standard therapies fail.

CONCLUSION

A carefully dosed combination of ceftazidime-avibactam and aztreonam cured pan-resistant *Serratia marcescens* sepsis in an early infant, supporting its use as expert-guided salvage therapy when standard antimicrobial choices are exhausted.

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AUTHOR'S AGREEMENT

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ETHICAL AND EDITORIAL POLICY OF THE JOURNAL OF MEDICAL SCIENCES (JMS) - UPDATED 2024

1. PURPOSE

This document highlights JMS's mission, objectives, and editorial policy regarding the publication process by adhering to the guidelines of COPE (Committee in Publication Ethics) and ICMJE (International Committee of Medical Journals Editors). Each component of the editorial policy is explained in the next sections.

A- MISSION OF JMS

To publish relevant, scientific, and accessible material to help medical students and health professionals in their practice, teaching and learning, and career development

B- OBJECTIVES OF JMS

To publish clinical, epidemiological, public health, educational, translational, and allied sciences research to enable scientists, clinicians, and researchers to learn about developments and innovations in these disciplines

To publish high-quality descriptive and experimental research, review articles, editorials, letters to the Editors, and case reports to enhance the understanding of the scientific community regarding clinical practice and education

To provide a platform for the scientific community to promote their career development through publishing quality research

2- SCOPE

This policy applies to the authors, reviewers, and readers of the JMS inside and outside the institution.

PROCESS / POLICY DESCRIPTION

1. OPEN ACCESS

JMS is an Open-access scholarly literature source that is free of charge and often carries less restrictive copyright and licensing barriers than traditionally published works, for both the users and the au-

thors. However, it complies with well-established peer review processes and tries to maintain high publishing standards.

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The review process of JMS follows a "triage approach". Upon submission of a manuscript, either online or physical, the document undergoes a preliminary open (un-blinded) review by the Editorial team. The document is either accepted for further review, sent for revision back to the authors, or rejected at that time mentioning the reasons for rejection/declining. Further review of JMS follows a blinded approach, where the article is sent to 2 reviewers, local and international who are already registered on the JMS website. During this process, the confidentiality of the authors and reviewers is ensured. The editorial board has the authority to retract an article if a serious violation of credibility or quality of research is found any time before publication, including after acceptance or after the article is published if concerns arise about the integrity of the work. (See also the section on 'Correction and retraction of articles').

3. AUTHORSHIP

According to the ICMJE criteria, authorship is based on 4 criteria; (1) conceptualization and designing, (2) AND, data collection, (3) AND, writing and critical review, (4) AND, taking responsibility for the authenticity and integrity of all the research process. All those designated as authors should meet all these 4 criteria. The co-authors should declare their roles and contributions in the research process explicitly. Those who do not meet all 4 criteria should be ACKNOWLEDGED only. If agreement cannot be reached about who qualifies for authorship, the institution(s) where the work was performed, not the journal editor, should be asked to investigate. The journal editor should seek an explanation and signed statement of the agreement if a corresponding author requests the removal, addition, or changes in the sequence of a co-author after manuscript submission and processing mentioning the approval of all listed authors and the author concerned. The corresponding author is the one individual who takes primary responsibility

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4.4: No article in any form should contain more than 4 figures and more than 5 tables.

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The authors, peer reviewers, and editors must declare conflicts of interest about the financial aspects, academic competitions, and relationships during the writing, reviewing, and publishing of the manuscripts. This will ensure transparency in the research conduction, writing, and publication. The authors should clearly state the details of sponsors along with their roles and access to data.

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8.2: The editor should also post a new article version in the journal with details of the changes from the original version and the date(s) on which the changes were made.

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8.4: If the error is judged to be unintentional, the underlying science appears valid, and the changed version of the paper survives further review and editorial scrutiny, then retraction with republication of the changed paper, with an explanation, allows full correction of that research paper.

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Correspondence for submitting an article in JMS will be through a corresponding author. The duties of a corresponding author have already been presented in a previous section. Correspondence re-

garding debating an article is given high value and a separate page for letters to the editors has been allocated. Derogatory and demeaning letters are screened and letters that promote debates and critique are encouraged to be published. However, correspondence about the articles published in the last 1 year will be included only.

10. THE FEE SUBMISSION PROCESS

A processing and publication fee of Rs. 15,000/- (Pakistani) for local authors and \$ 250 (US) for international authors has been approved by the competent authority. The fee should be submitted as bank draft/online payment through the account (IBAN) no: PK56NBPA0388004048685170 (Branch code: 0388 / National Bank of Pakistan, University campus branch, Peshawar, Pakistan) as follows:

1. Article processing fee of 5000/- PKR at the time of submission of the article. This amount will be non-refundable.
2. Article publication fee of 10000/- PKR at the time of acceptance of article after external review. This amount will be refundable if the article is rejected for any reason.
3. For international authors, the amount of 250 US dollars will be accepted after both internal and external review. Researchers belonging to countries other than Pakistan are advised to submit the fee after the whole process of review is completed and the article is accepted for publication.
4. There will be no fee exemption in any circumstances, including members of the editorial board.

11. ROLES OF THE EDITORIAL BOARD, EDITORS, AND MEMBERS

The editorial board of JMS is following the Higher Education Commission (HEC) policy for research journals. The roles of the editorial board for JMS are mentioned below:

11.1: The roles of the Editorial Board are:

11.1.1: To offer expertise in their specialist area

11.1.2: To review submitted manuscripts

11.1.3: To advise on journal policy and scope

11.1.4: To work with the Editor to ensure ongoing development of the journal

11.1.5: To identify topics for special issues of

the journal or recommend a Conference which would promote the journal, which they might also help to organize and/or guest edit

11.1.6: To attract new and established authors and articles

11.1.7: To submit some of their own work for consideration, ensuring that they adhere to Conflict of Interest rules and stating their relationship to the journal. This is very important as the journal cannot be seen to publish only papers from members of the Editorial Board.

11.1.8: It is important that Editorial Boards have a regular communication forum with other boards of similar nature, either face to face in person (depending on their country of origin, funding availability, etc.) or as more journals are doing today, communicating by teleconference, Skype or other web platforms.

11.2: THE PATRON:

The Patron is usually the Dean of the institute, and is overall in charge of the journal, who needs to be kept informed of the decisions taken by the editorial board. The patron is the final authority to approve the decisions and policies of the editorial board.

11.3: THE CHIEF EDITOR:

11.3.1: THE CRITERIA FOR SELECTION OF CHIEF EDITOR ARE:

- i. Expertise and experience in the specialist field related to the journal
- ii. Publication record of a number of articles and /or books (usually in / related to the specialist field)
- iii. Being a reviewer for an international peer-reviewed journal
- iv. Senior research position with equivalent experience in research and scholarship
- v. Enthusiasm to undertake the Editor role
- vi. Preferably a diploma, master or doctoral degree in Education and Research
- vii. It is not necessary to fulfill all the criteria to become a chief editor.

11.3.2: THE ROLES OF CHIEF EDITOR ARE:

- i. The key role of a journal's chief editor is to promote scholarship in the specialist field associated with the journal, whilst also promoting the journal as the best journal to publish in. For any journal,

the editor will need to encourage new and established authors to submit articles and set up a reliable panel of expert reviewers. Editors are also responsible for offering feedback to reviewers when required and ensure that any feedback to authors is constructive.

- ii. An editor should also familiarize themselves with the Committee on Publication Ethics (COPE) 'Code of Conduct and Best Practice Guidelines for Journal Editors'.
- iii. Depending on how the journal is managed and how it is structured, an Editor may have to make all the decisions regarding which articles to accept or reject for publication.

11.3.3: MANAGING EDITOR:

- i. The roles of managing editor are:
- ii. To help the chief editor to achieve the above-mentioned goals
- iii. To communicate with the authors, reviewers, publishers and other agencies for smooth running of the journal
- iv. To regularly evaluate the research work
- v. To communicate with funding and regulating agencies (HEC and others) for grants and accreditations.

11.3.4: EXECUTIVE EDITOR:

- i. The roles of executive editor are:
- ii. To evaluate the research articles presented for publication
- iii. To help the editorial board in policy making
- iv. To help the editorial board in smooth publishing
- v. To communicate with reviewers and collaborate with external agencies for relevant purposes

11.3.5: SECTION EDITORS:

Section editors are allotted different responsibilities. Some of these are mentioned below:

- i. Bibliography
- ii. Proof-reading
- iii. Academic writing reviewing, grammar and spell checking
- iv. Dissemination of articles for review
- v. Contact with publishers under the supervision of

senior editorial team

- vi. Training of future reviewers, young members and other faculty members
- vii. others

11.3.6: EDITORIAL ADVISORY BOARD:

Editorial advisory board members consist of national and international senior academicians, researchers, clinicians and others to help the current editorial board in designing, implementing and evaluating policies regarding upgrading the quality of research work. These people also share best practices to help the editorial team to refine their research work.

12. POLICY REGARDING RECRUITMENT AND CONTINUATION OF EDITORIAL BOARD

The policy for recruitment and continuation of the editorial board is based on the guidelines discussed in the previous section. The chief editor, managing editor, and executive editors are recruited by the patron in-Chief. Members are then selected by them

from amongst the faculty who have an aptitude for research, and their names are endorsed by the patron. The tenure of the editorial board is decided by the Patron after 3 years whether to continue or recruit a new team or member. The editorial advisory board members are recruited for an indefinite period by the editorial team of JMS.

13. PLAGIARISM POLICY

The journal follows the plagiarism policy of the Higher Education Commission of Pakistan, and for this purpose, a plagiarism standing and review committee has been established under the chairmanship of the Chief Editor of JMS along with 4 members amongst senior faculty. The committee has been given the authority to review research papers and plagiarism complaints related to published work in the journal.

14. CONTACT INFORMATION

The office of managing editor or chief editor should be contacted anytime in working hours or can be contacted through their emails for correspondence.

