ISSN (Online) 2790-3451
ISSN (Print) 2790-3443

THE UNIVERSITY OF LAHORE | University College of Medicine & Dentistry

JOURNAL OF UNIVERSITY COLLEGE OF MEDICINE & DENTISTRY

An Official Publication of
The University of Lahore, Pakistan

https://journals.uol.edu.pk/jucmd editor.jucmd@journals.uol.edu.pk

Volume 5 issue 1 Jan to June 2026

JUCMD

Biannual | Open Access | Peer-Reviewed | Indexed in DOAJ & Crossref

Publisher Address: University of Lahore, Defence Road Campus, Lahore, Pakistan.

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Journal of University College of Medicine & Dentistry

Editorial

Strengthening Continuing Professional Development Literacy to Advance Pakistan's Health Workforce

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Submission: 15th November, 2025
Acceptance: 8th December, 2025

doi:10.51846/jucmd.v5i1.4847.

Cite this article as:

Sherman L. Strengthening continuing professional development literacy to advance Pakistan's health workforce. *J Univ Coll Med Dent.* 2026;5(1):1-2.

Continuing Professional Development (CPD) has become a defining component of modern healthcare systems, but in many low- and middle-income countries (LMICs), including Pakistan, CPD remains uneven, inconsistently regulated, and often limited to single-profession educational events. As clinical practice grows more complex and team-based, the need to strengthen CPD literacy, advocacy, and system-level capacity has never been greater. CPD is no longer an exercise in attendance nor can it be judged on satisfaction using a satisfaction scale. It is a structured, deliberate process that helps clinicians identify what they need to learn, engage in outcomes-oriented activities, and apply those gains to improve performance and patient care. Most importantly, the individuals teaching in CPD activities must be adequately prepared and equipped for this responsibility.

Globally, CPD systems have evolved from passive, credit-accumulation models toward structured, outcomes-focused approaches. The conceptual framework developed by Moore et al (2018) provides a comprehensive roadmap for planning, delivering, and assessing CPD for both single professions and interprofessional teams.[1] It emphasises learning that progresses meaningfully from knowledge acquisition to competence, performance, and measurable outcomes. This reflects a growing recognition that CPD must connect to real-world improvements and align with system needs, especially in contexts where team-based care is essential.

The recently published World Federation for Medical Education (WFME) Standards for Continuing Professional Development 2024, reinforce this direction.[2] These standards outline four stages of CPD: identify, decide, learn, and record/apply. They call for CPD systems that promote relevance, quality assurance, professional autonomy, and patient-centered practice. The emphasis on institutional accountability and interprofessional collaboration aligns particularly well with the needs of Pakistan and other LMIC health systems.

An instructive example of how interprofessional CPD can be formalised at the system level comes from the United States, where Joint Accreditation for Interprofessional Continuing Education (IPCE) has created a unified pathway for accrediting CPD designed by and for the healthcare team, and the providers that demonstrate proficiency in developing learning activities where learners from different healthcare professions are given the opportunity to learn from, with, and about each other. This model recognises that the most effective learning occurs when professionals train together for the work they do together, and it demonstrates how structural mechanisms can reinforce collaboration, standards, and shared accountability.[12]

Pakistan has made gradual progress in recognising the importance of CPD, but multiple studies show that much work remains. A 2023 national survey reported moderate awareness of CME/CPD requirements but highlighted persistent barriers, including the absence of a dedicated regulatory body, cost constraints, doubts about the credibility of certain activities, and limited alignment with clinical needs.[3] These gaps hinder the development of a cohesive, high-impact CPD environment.

For allied health professionals, who are essential members of the care team, the challenges are even more pronounced. A recent Delphi study proposed Pakistan's first set of CPD standards for allied healthcare professionals, identifying interprofessional education (IPE), professionalism, leadership and assessment as key domains.[4] Respondents cited limited institutional support, insufficient protected learning time, and a lack of consistent evaluation frameworks, all of which impede both participation and quality.

Research from Pakistan also suggests that readiness for interprofessional learning is low. One study found that undergraduate students across Balochistan scored poorly on established IPE readiness scales in the undergraduate setting, reflecting limited understanding of team roles and shared learning.[5] Without early exposure to teamwork principles, graduates enter practice less prepared to engage in interprofessional CPD once they are in practice.

These findings mirror the results of a broader global series of mixed-methods assessments of CME/CPD systems that we conducted across China, Latin America, Europe, the Middle East and North Africa, and East and Southeast Asia.[6–11] Collectively, these studies show wide variability in the maturity, governance and independence of CPD systems, yet a consistent call for clearer standards, stronger interprofessional engagement, outcomes-focused design, and system-level leadership.

CPD literacy extends far beyond participation. It includes the ability to recognise meaningful learning needs; differentiate between high-value and low-value activities; understand how education links to competence, performance, and outcomes; and engage in team-based learning aligned with real clinical pathways. It also includes the ability to advocate for stronger systems, better resources, and clearer policies.

When CPD literacy is weak, CPD becomes a formality. When it is strong, CPD becomes a mechanism for system improvement, quality assurance, and better patient outcomes. For LMICs, where needs are high and resources limited, CPD literacy directly influences the return on investment. Emerging research is exploring the relationship between preparedness of CPD educators and measurable improvements in patient care, a connection that has profound implications for health systems globally. Although profession-specific CPD remains important, team-based CPD is increasingly essential. Healthcare today is delivered by interconnected teams, and education must reflect that reality. The Moore et al. framework explicitly supports CPD designed for both single professions and teams.[1] Pakistan's allied health CPD standards similarly emphasise interprofessional education as a foundational element.[4]

Interprofessional CPD improves communication, strengthens care coordination, and enhances shared decision-making. It also aligns with WHO workforce priorities and the Sustainable Development Goals, particularly SDG 3 on ensuring healthy lives and promoting well-being for all at all ages.[13]

To build stronger CPD systems and improve CPD literacy, several steps are essential:

1. Develop national and provincial CPD policies aligned with WFME 2024 standards.[2]

2. Establish regulatory clarity to ensure consistent expectations across professions.

3. Design CPD programmes collaboratively, ensuring learning occurs within, and across, teams.

4. Use outcomes-based frameworks such as the Moore et al. model to guide planning and evaluation.[1]

5. Invest in faculty development so educators can design and deliver high-impact CPD.

6. Strengthen institutional infrastructure by protecting learning time, ensuring access to evaluation tools, and leveraging technology.

7. Promote advocacy and awareness, building a national conversation around the role and value of CPD literacy.

The call for better, stronger and more impactful CPD is both a local and global imperative. Pakistan has the opportunity to build modern, team-oriented CPD systems that support high-quality care while aligning with international standards. By strengthening CPD literacy and promoting advocacy across professions and institutions, the country can accelerate progress toward a more competent, collaborative, and resilient health workforce.

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Journal of University College of Medicine & Dentistry

Editorial

The Essential Role of Human Oversight in the Era of AI-Enabled Medical Assessment

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Submission: 1st November 2025
Revision: 10th December, 2025
Acceptance: 25th December, 2025

DOI: https://doi.org/10.51846/jucmd.v5i1.4842

Cite this article as:

Sethi A, Hidayat M. Human oversight in an algorithmic era: preserving integrity in medical assessment. J Univ Coll Med Dent.2026;5(1):4-5.

Every medical educator recognizes the importance of assessment in health professions education.[1] A decision made in an examination room or an OSCE station can determine whether a learner progresses, repeats a year, or leaves the profession altogether. Such judgments are rarely based on scores alone. These decisions are shaped by the context, training of assessors, students' competence, response to uncertainty, professionalism, and performance in ambiguous situations. In medicine, assessment is therefore not merely a technical exercise; it is a moral responsibility with direct implications for patient safety and public trust.[1,2]

Across health professions education, AI systems are increasingly being advocated and used to generate assessment items, score written responses, detect plagiarism, and predict learner performance.[3] While their appeal is understandable, particularly in an era of expanding student numbers, faculty workload, and demands for standardization, the central question confronting medical education is not whether AI can assist assessment, but whether it should be allowed to influence judgments that carry profound professional and ethical consequences.[4]

AI systems excel at identifying patterns and reproducing statistical regularities from large datasets. However, apparent competence should not be mistaken for understanding. The classic example of *Clever Hans*, the horse that appeared to perform arithmetic while merely responding to subtle human cues, illustrates how convincing performance can mask shallow cognition.[5] Similarly, the concept of the *stochastic parrot* highlights how large language models generate fluent responses by predicting sequences rather than by reasoning or comprehension.[6] In assessment, this distinction matters deeply. Algorithms may score correctness, but they cannot interpret intent; they may analyse observable behaviour, but they cannot authentically discern empathy, integrity, or moral judgment, which are the core attributes that define a competent doctor.[2]

These limitations become particularly evident when assessment is viewed through Miller's Pyramid of Clinical Competence. AI may reasonably support assessments at the *Knows* and *Knows How* levels, such as factual recall or structured problem-solving. At the *Shows How* and *Does* levels, however, competence is demonstrated through performance, interaction, and professional conduct in real or simulated contexts. Here, assessment is inherently relational and value-laden. Reducing such judgments to algorithmic outputs risks oversimplifying complex human behaviour and misclassifying competence in ways that may be educationally and ethically harmful.[7]

AI undoubtedly has the potential to enhance assessment by improving efficiency and consistency.[8] AI automated assessment can reduce personal bias, make marking more consistent, and save time, especially when large numbers of students are assessed. Research also shows that AI-based scoring can be useful for structured assessments and can help spot differences in scoring.[8] However, growing evidence also highlights important shortcomings. Studies comparing AI and human evaluators in OSCEs have reported disagreement in scoring, limited sensitivity to nuanced communication skills, and difficulty interpreting contextual or culturally embedded expressions of professionalism.[8]

Rather than eliminating bias, inadequately contextualized AI systems may simply reproduce it in less visible ways. These concerns are especially salient in Global South contexts. Most AI systems are trained predominantly on datasets derived from the Global North, reflecting specific linguistic norms, cultural expectations, and professional behaviours. Learners from different cultural, linguistic, or religious backgrounds, including those in many Muslim-majority societies, may show

empathy, respect, or reasoning in ways that these systems do not easily recognize as standard. Without careful attention to how training data are generated and whose behaviours are represented, AI-based assessment risks disadvantaging those who do not conform to dominant cultural templates.[9]

Some early efforts have tested the use of AI to analyse video-recorded patient interactions in order to assess communication skills and empathy.[10] Although these methods are interesting, they raise important concerns. Can empathy truly be judged using visible behaviour alone? Who decides the rules used by the algorithm? What should be done when the judgment of a human assessor differs from that of a machine? Until clear evidence and transparent standards are available, such tools should be used with caution, only as support and not as the basis for final decisions.[4]

The responsible integration of AI into medical assessment, therefore, requires clear governance and layered accountability. Regulatory bodies and universities should lead by establishing guidelines that define acceptable and unacceptable uses of AI, particularly for high-stakes decisions. Universities must translate these principles into institutional policies that ensure transparency, auditability, and data protection. Academic leaders bear responsibility for resourcing faculty development and ensuring the integrity of assessment. Educators and assessors, ultimately, must retain authority, adopting a human-in-the-loop approach in which AI supports but never replaces professional judgment.[11]

In medicine, judgment requires experience, compassion informed by context, and accountability grounded in professional responsibility, all the features that algorithms may not possess.[12] The challenge before us is not whether AI should be used, but where its authority must end. As medical educators, we are now confronted with the question: While technology offers certainty without understanding, are we prepared to surrender assessment to AI without being accountable for the decisions that shape our learners, our patients, and our profession?

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Journal of University College of Medicine & Dentistry

Original Article

Dietary Counseling and Nutritional Monitoring for Cancer Cachexia in Breast Cancer: A Randomized Controlled Trial

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Submission: 17th July, 2025
First revision: 8th September, 2025
Second revision: 11th December, 2025
Third revision: 25th December, 2025
Acceptance: 10th January, 2026

DOI: https://doi.org/10.51846/jucmd.v5i1.4341

Cite this article as:

1. Maria R, Saba A, Jamshed J. Dietary counseling and nutritional monitoring for cancer cachexia in breast cancer: a randomized controlled trial. J Univ Coll Med Dent. 2026;5(1): 6-13.

Abstract

Objective: To assess the effectiveness of personalized dietary counseling and regular nutritional monitoring in improving cancer-related cachexia among women with breast cancer, using the validated Mini-Cancer Cachexia Score (Mini-CASCO).

Methodology: A parallel, single phase, two-arm interventional study was conducted at Fauji Foundation Hospital, Rawalpindi from June to December 2024. A total of 134 participants were randomized in a 1:1 ratio using block stratified allocation to either an intervention group (n=67), which received standard oncologic care supplemented with individualized dietary counseling and nutritional monitoring every 15–21 days, or a control group (n=67), which received standard care alone. The magnitude and severity of cachexia was assessed at baseline and 6 months using Mini-CASCO across five domains including body composition, inflammatory-metabolic profile, physical performance, appetite, and quality of life (QOL).

Results: Of 134 participants enrolled, 130 (97%) completed follow-up. After 6 months, the intervention group demonstrated a significant reduction in overall Mini-CASCO score ($\Delta=-14.4 \pm 5.1$; $p<0.01$; Cohen's $d=2.0$), whereas the control group showed only a small decrease ($\Delta=-2.6 \pm 4.9$; $p=0.03$). Between-group analyses demonstrated significant improvements attributable to the intervention across all Mini-CASCO domains, including body weight/composition ($\Delta=-5.2 \pm 2.6$), inflammatory–metabolic profile ($\Delta=-2.5 \pm 1.5$), physical performance ($\Delta=-1.8 \pm 1.1$), appetite/anorexia ($\Delta=-1.9 \pm 1.0$), and quality of life ($\Delta=-1.0 \pm 0.7$) (all $p<0.001$). The overall effect size was large (partial $\eta^2=0.38$), indicating strong clinical relevance.

Conclusion: Incorporating structured dietary counseling and nutritional monitoring into routine oncology care significantly attenuates cachexia and enhances functional, metabolic, and psychosocial outcomes in women with breast cancer. Mini-CASCO functioned effectively as an outcome tool for monitoring therapeutic response, supporting nutrition-sensitive strategies within cancer care pathways.

Keywords: Breast cancer, Cancer cachexia, Dietary counseling, Nutritional monitoring, Mini-CASCO, Randomized controlled trial.

Introduction

Cancer remains a major global health issue, with approximately 20 million new cases and 9.7 million cancer-related deaths reported in 2022.[1] By 2050, the global incidence of cancer is projected to increase by 77%, with low income countries accounting for nearly 70% of cancer-related morbidity and mortality due to limited access to early detection, advanced cancer therapies, and supportive care.[1] Among women, breast cancer is the most commonly diagnosed malignancy, with an estimated 2.3 million new cases and approximately 670,000 deaths recorded globally in 2022.[2] In LMICs, including Pakistan, breast cancer remains a major public health challenge due to late stage presentation and limited access to specialized oncology services. In Pakistan, about one in nine female is expected to develop breast cancer during her lifetime-the highest rate in Asia.[3] As a result, a significant number of patients present with late-stage disease which usually requires systemic chemotherapy. While chemotherapy is important for cancer control, it is also a major cause of cancer cachexia. This bidirectional relationship between cachexia and chemotherapy contributes to decline physical functional and poor treatment compliance.[4,5] Addressing cancer cachexia is therefore important for improving treatment outcomes and overall QOL in female oncology patients, especially in LMICs such as Pakistan.

Cachexia is a complex and multi-factorial metabolic syndrome including involuntary loss of weight, systemic inflammation, progressive loss of physical performance, and depletion of skeletal muscle mass. More than 80% of patients with advanced cancer are usually affected by cachexia and it is associated with 20% of cancer-related deaths.[6] Unlike starvation, cancer cachexia persists despite proper intake of calories, driven by neurohormonal and inflammatory dysregulation.[7] Argilés et al. (2011) formulated the CAchexia SCOre (CASCO) to support clinical assessment

and management of cancer-associated cachexia. It is a multi-dimensional scoring system used to assess five key domains including body weight and composition (BWC), inflammatory, metabolic or immunological disturbances (IMD), physical performance (PHP), anorexia (ANO), and quality of life (QOL) relevant to cachexia. Its simplified version which is also known as the Mini-CASCO retains high internal validity (r=0.96) while providing practicality for use in daily cancer care and RCTs.[8,9] Although evidence from HICs supports the use of nutritional interventions in cachexia, few comprehensive studies have been carried out in LMICs.[9-11] A study from India indicated improved body weight and appetite among female oncology patients as a result of culturally adapted dietary counseling.[12] However, no study in Pakistan has determined the impact of personalized dietary counseling and regular nutritional monitoring using the validated Mini-CASCO assessment tool among female breast cancer patients receiving chemotherapy. This gap underscores an urgent need for evidence-based resource-sensitive interventions in LMICs aligning with global frameworks, including the WHO Global Breast Cancer Initiative and Sustainable Development Goal (SDG) of good health and well-being which advocates integrated supportive cancer care to reduce cancer causing morbidity and mortality.

Therefore, this RCT was conducted to determine the impact of personalized dietary counseling sessions, alongside regular nutritional monitoring, on severity of cachexia in female oncology patients, as measured by the validated Mini-CASCO scoring system, at a major tertiary care center in Rawalpindi, Pakistan. Patients who were receiving the intervention would show high level of improvements in cachexia associated outcomes including BWC, systemic inflammation, PHP, appetite, and QOL as compared to those who were receiving standard oncology care only. Findings from this study may inform nutrition-specific measures for routine integration into oncology care in resource-constrained settings such as Pakistan.

Methodology

This was a prospective, parallel-group, two-arm, single-phase RCT designed to determine the impact of personalized dietary counseling combined with regular nutritional monitoring on cachexia severity in women with breast cancer, compared with standard oncological care alone. The severity of cancer cachexia was objectively measured using the validated Mini-CASCO scoring system which involves five key domains including BWC, inflammatory, metabolic or immune status, PHP, ANO, and QOL.

The study was conducted at the Department of Medical Oncology, Fauji Foundation Hospital (FFH), a tertiary care oncology center in Rawalpindi, Pakistan, with participant enrollment from March to July 2024 and a six months follow-up period. Ethical approval was sought from the Intuitional Review Board of FFH (794/RC/FFH/RWP). Both written and verbal informed consent was obtained from all participants prior to enrollment. The study was prospectively registered at ClinicalTrials.gov (NCT07112482).

The sample size for this study was estimated using G*Power software, assuming a moderate effect size (Cohen's d=0.5), a 95% confidence level and about 80% power. The calculation was based on an independent sample t-test comparing between-group differences in Mini-CASCO total score change at 6-month follow-up, which represents the primary endpoint of the trial. About 64 participants per group were required. The assumed effect size (Cohen's d=0.5) reflects a conservative, moderate treatment effect commonly used in behavioral and nutritional oncology interventions, particularly in the absence of robust local pilot data. This estimate is consistent with prior randomized trials evaluating nutritional or multimodal cachexia interventions that have reported small-to-moderate effect sizes for functional and composite cachexia outcomes. To account for potential attrition (10%), 140 patients were initially screened.

Participants were randomized (1:1) employing a computer-generated, block-stratified algorithm (block size=4), stratified by disease stage (locally advanced vs metastatic) and baseline Mini-CASCO severity (moderate vs severe). Allocation concealment was ensured via sequentially numbered, sealed, opaque envelopes. Participant enrollment was conducted by the principal investigator, with group assignment occurring after baseline assessment. The blinding of participants and intervention providers was not feasible because the intervention was behavioral and counseling-based. Outcome assessors responsible for Mini-CASCO scoring, laboratory measurements, and physical performance assessments were blinded to group allocation. Additionally, biostatistician conducting the statistical analyses was blinded until completion of the primary analysis, hence reducing detection and analysis bias.

Participants in the intervention group received personalized dietary counseling and regular nutritional monitoring in addition to standard oncological care for duration of 6 months. The follow-up period was chosen based on past literature showing that clinically relevant improvements in cancer cachexia usually require at a minimum 3 to 6 months.[13] The study object was a structured, personalized nutritional counseling program, implemented as a complex behavioral intervention targeting adequacy of energy-protein consumption, symptom-associated nutritional barriers, and compliance with evidence-based cachexia dietary recommendations. Comprehensive dietary plans were recommended for each patient, targeting an energy intake of about 25 to 30 kcal/kg per day and protein consumption of 1.2 to 1.5 g/kg/ per day were adjusted for the clinical status of patients, dietary tolerance, side effects of treatment, and individual choices or preferences.

Counseling sessions were delivered by certified clinical dietitians with experience in oncology nutrition, rather than by physicians or nursing staff, to ensure both feasibility and cost-effectiveness of implementation. Sessions were held every 15-21 days and lasted approximately 25–30 minutes, representing dietitian time per appointment. The dietary sessions involved key nutrition barriers such as symptom-associated eating difficulties, food aversion, texture modification, and measures taken to incorporate energy- and protein-dense foods. Dietary adherence was assessed using goal adherence checklists and structured food records. No additional nursing consultation or physician time was required beyond standard oncological care. Moreover, patients were advised to engage in light physical activities, such as stretching or walking according to their tolerance levels. Psychosocial support was offered by a certified psychologist to improve anorexia, fatigue and

emotional distress. Adherence was defined as attending at least 75% of scheduled meeting or sessions 80% or more of the personalized nutrition goals. To reduce attrition, patients who missed appointments were followed up during their next chemotherapy cycle and provided a rescheduled nutrition session.

The primary outcome was change (Δ) in cachexia severity, measured using validated Mini-CASCO assessment tool at enrollment and after six months. The Mini-CASCO tool comprises five domains including BWC, IMD, PHP, ANO, and QOL, each contributing to the overall cachexia score. Domain scores were calculated according to the original Mini-CASCO framework and aggregated into a weighted total score across domains. Data management involved de-identified study codes, double data entry, and multiple imputations for missing values, following standard Mini-CASCO analytic recommendations.

The data was analysed using Statistical Programme of Social Sciences (SPSS) version 25.0. Categorical variables were presented as frequencies and percentages while continuous variables as means and standard deviations (SD). Comparison of baseline characteristics between intervention and control groups was conducted using chi-square tests for categorical variables and independent t-tests for continuous variables. Primary analyses of Mini-CASCO total and domain scores over time were conducted using repeated-measures ANCOVA, adjusting for baseline values. Effect sizes were measured employing Cohen's d for within-group changes and partial eta squared value (η^2) for between-group comparisons. P-values < 0.05 were considered as statistically significant.

Results

A total of 140 patients were screened, of whom 134 met eligibility criteria and were randomized equally to the intervention group and control group (n = 67 per group). Following attrition (two participants from each group), 130 participants completed the six-month study period (n = 65 per group). Baseline characteristics of patients were comparable between intervention and control groups (Table 1). There were no statistically significant differences observed in age of participants, body composition, biochemical markers, energy intake, functional status, or Mini-CASCO total scores ($p>0.05$ for all variables), indicating effective randomization and group comparability. The CONSORT flow diagram (Figure 1) details participant enrollment, allocation, follow-up, and analysis. Table 1 further demonstrates that the groups were balanced at baseline, prior to initiation of dietary counseling and nutritional monitoring, supporting the validity of the randomization procedure.

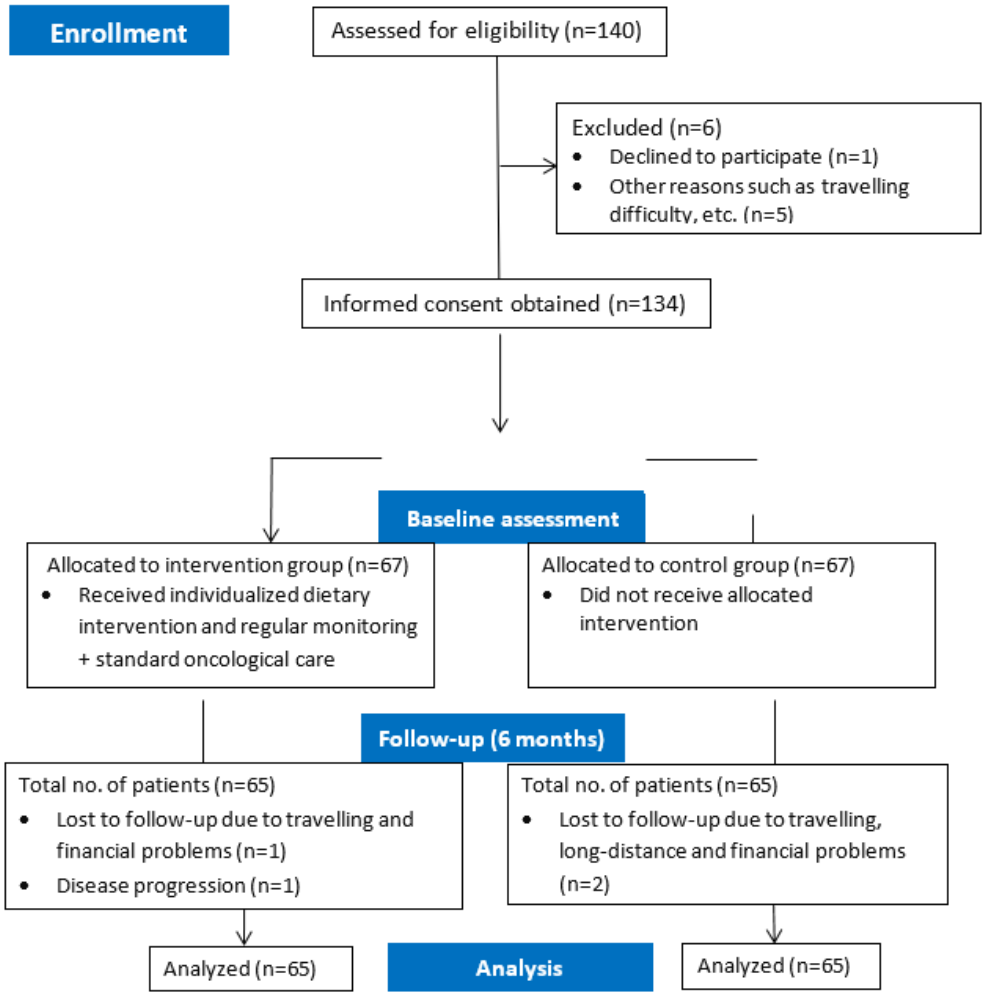

Figure 1. Study Consort diagram

Table 1: Baseline Characteristics of the Study Participants

Variable	Intervention group (n = 65)	Control group (n = 65)	p-value
	Mean ± SD	Mean ± SD	
Age at enrollment (in years)	48.7 ± 8.1	47.9 ± 7.6	0.51
Hb (g/dL)	10.7 ± 1.2	10.9 ± 1.1	0.38
Weight loss (% of usual body weight)	8.4 ± 2.6	8.2 ± 2.9	0.66
Lean body mass (kg)	34.8 ± 3.9	35.1 ± 4.4	0.53
CRP (mg/L)	18.1 ± 6.7	17.7 ± 5.9	0.48
Albumin (g/dL)	3.3 ± 0.4	3.2 ± 0.5	0.36
Total lymphocyte count (cells/mm³)	1280 ± 320	1245 ± 290	0.43
Daily energy intake (kcal/day)	1375 ± 210	1405 ± 195	0.27
ECOG performance status (median, IQR)	2 (1–2)	2 (1–2)	0.88
Physical performance score (PHP, 0-15)	9.4 ± 2.1	9.6 ± 2.3	0.61
Appetite Score (SNAQ, 4–20)	11.2 ± 2.7	11.5 ± 2.3	0.47
Quality of life score (EORTC, 0–100)	58.7 ± 9.4	57.3 ± 10.2	0.39
Total Mini-CASCO score (0–100)	32.4 ± 6.8	33.1 ± 6.5	0.51

Continuous variables were compared using independent-samples t-tests, while ECOG performance status was compared via the Mann–Whitney U test.

After six months, participants in the intervention group showed clinically and statistically significant improvements across all Mini-CASCO domains as compared to the control group (Table 2). The overall Mini-CASCO score, a validated multidimensional measure of cachexia severity, decreased in the intervention group from 32.4 ± 6.8 at baseline to 18.0 ± 5.9 at six months, corresponding to a mean change of -14.4 ± 5.1 ($p < 0.01$) and a large between-group effect size (Cohen's $d = 2.0$). In contrast, the control group exhibited a modest reduction in Mini-CASCO score, from 33.1 ± 6.5 to 30.5 ± 6.8 ($\Delta = -2.6 \pm 4.9$, $p = 0.03$), with a large within-group effect size ($\eta^2 = 0.38$), underscoring the substantial impact of the intervention.

Discussion

This RCT evaluated the impact of personalized dietary counseling sessions combined with regular nutritional monitoring on cancer-related cachexia among female oncology patients, using the multi-dimensional, validated Mini-CASCO assessment tool. The study was carried out as a multi-component strategy, integrating structured dietary counseling sessions and regular nutritional monitoring, psycho-social support, and guidance on light physical activity, according to contemporary recommendations for multi-dimensional assessment of cancer cachexia. Embedding personalized dietary counseling and nutritional monitoring into routine cancer care is grounded in the complex and multifactorial pathophysiology of cachexia, which involves systemic inflammation, ANO, physical debilitation, and metabolic dysregulation. Unlike other conventional strategies that focus mainly on weight loss, the Mini-CASCO scoring system provides a comprehensive evaluation across multiple domains related to cancer cachexia.[14] This study was designated to assess whether a structured, patient-centered nutrition intervention could significantly influence cachexia trajectories by not only improving body weight,

Table 2: Mini-CASCO Scores at Baseline and 6 Months Post-Intervention

Domain	Group	Baseline	6 Months	Δ in score	p-value
		Mean ± SD	Mean ± SD	Mean ± SD	
BWC (Weight loss, Lean body mass)	Intervention	13.4 ± 3.2	8.2 ± 2.8	–5.2 ± 2.6	< 0.001
	Control	13.6 ± 3.5	12.9 ± 3.7	–0.7 ± 2.9	0.12
IMD (CRP, Albumin, TLC)	Intervention	6.6 ± 2.1	4.1 ± 1.8	–2.5 ± 1.5	< 0.001
	Control	6.8 ± 2.0	6.5 ± 2.3	–0.3 ± 1.8	0.31
PHP (ECOG score)	Intervention	4.9 ± 1.5	3.1 ± 1.2	–1.8 ± 1.1	< 0.001
	Control	5.1 ± 1.6	5.0 ± 1.7	–0.1 ± 1.3	0.76
ANO (SNAQ score)	Intervention	4.9 ± 1.4	3.0 ± 1.1	–1.9 ± 1.0	< 0.001
	Control	5.1 ± 1.3	4.8 ± 1.5	–0.3 ± 1.2	0.44
QOL (EORTC QOL score)	Intervention	2.6 ± 1.2	1.6 ± 1.0	–1.0 ± 0.7	< 0.01
	Control	2.5 ± 1.3	2.3 ± 1.4	–0.2 ± 1.1	0.39
Total Mini-CASCO score	Intervention	32.4 ± 6.8	18.0 ± 5.9	–14.4 ± 5.1	< 0.001
	Control	33.1 ± 6.5	30.5 ± 6.8	–2.6 ± 4.9	0.03

P-values represent within-group comparisons from baseline to 6 months, analyzed using repeated-measures ANCOVA adjusted for baseline values. Δ is change in scores from baseline to 6 months.

but also enhancing muscle preservation, appetite, PHP, and overall QOL.

The findings revealed that personalized dietary sessions with regular nutritional monitoring significantly improved cachexia outcomes. However, given the multi-dimensional and integrated nature of the study, reported benefits should be interpreted as the synergistic and cumulative effect of dietary sessions, nutritional monitoring, psychosocial support, and guidance on light physical activity, rather than being attributed to dietary counseling alone. After six months, participants in the intervention group showed significant improvements across all Mini-CASCO domains, along with a significant decline in the overall Mini-CASCO score, indicating a positive impact of the nutrition intervention. On the other hand, the control group receiving routine oncologic care showed only a modest change in overall Mini-CASCO scores highlighting the limited impact of routine cancer care in improving complex and multidimensional nature of cachexia. This finding is in comparison with recent evidence from a multimodal intervention among patients with advanced lung cancer, which demonstrated that combined nutritional and physical measures significantly improved functional outcomes.[15] This nutrition intervention addressed this important public health issue by implementing personalized dietary counseling and regular nutritional monitoring, which resulted in improved treatment compliance and treatment outcomes.

In the BWC domain, weight and lean body mass changes demonstrated significant improvements in the intervention group, reflecting preservation of both skeletal muscle and overall body weight. Bye et al. (2020) also noted that timely nutrition support significantly reduced muscle wasting for BWC outcomes.[16] Similarly, van der Werf et al. (2020) reported that nutrition intervention when combined with encouragement of physical activity resulted in reduced loss of muscle mass during chemotherapy.[17] In our study, participants in the control group demonstrated a slight decline (-0.7 scores) in this domain, whereas those received dietary counseling and regular nutritional monitoring showed significant benefits, highlighting the significance of nutritional support in improving metabolic decline. Clinically, maintaining body weight and lean body mass is associated with increased treatment compliance and improved survival outcomes.[18] These findings emphasize the need for early dietary assessment and timely referral to nutrition services, especially for female oncology patients who may present with reduced baseline reserves and increased susceptibility to sarcopenia.

The IMD domain including key nutritional and inflammatory markers such as CRP, TLC and albumin indicated improvement in the intervention group, showing a significant reduction in systemic inflammation and improvement of nutritional status. On contrary, the control group indicated no significant change, highlighting the lack of passive nutrition advice in improving the inflammatory and metabolic components of cachexia. These findings align with numerous other studies indicating the dietary and immunomodulatory benefits of targeted nutritional interventions. For instance, Amiri et al. (2024) carried out a meta-analysis examining omega-3 polyunsaturated fatty acids in gastrointestinal oncology patients and found significant decline in CRP while albumin level was stable. In our study, mechanistic interpretation is limited to the nutritional and inflammatory biomarkers directly measured (CRP, hemoglobin, albumin, and TLC), and extrapolation to unexamined molecular pathways or cytokines should be considered hypothesis-generating rather than confirmatory. The mechanistic basis for these effects lies in the anti-inflammatory and anabolic properties of nutrients for instance omega-3 fatty acids, antioxidants, and protein-rich formulations, all of which were integral components of our dietary plans.[19] The observed changes in CRP and albumin are clinically relevant, given their established crucial role as early biomarkers of progression of cancer cachexia and predictors of morbidity and mortality in cancer patients. These findings highlight incorporation of

regular nutritional monitoring and inflammatory assessments into clinical guidelines for management of cancer-related cachexia, enabling timely identification and optimization of metabolic status of the patients.

The PHP domain, reflecting physical performance as measured by the ECOG performance status, improved significantly in the intervention group ($\Delta = -1.8 \pm 1.1$; $p < 0.001$). Physical performance was assessed using ECOG, a validated clinician-rated functional scale; however, objective measures such as gait speed, handgrip strength, or accelerometer were not included and may provide greater sensitivity for detecting functional changes in future studies. This finding is supported by a recent multimodal RCT in advanced lung cancer patients, where combined nutritional supplementation and regular exercise were significantly related to improvements in functional capacity, muscle mass, and quality of life.[20] The finding highlights that nutritional support must be accompanied by structured guidance, appetite optimization, and energy balance strategies to be effective. The observed correlation between enhanced energy intake and preserved physical function emphasizes the essential role of comprehensive functional assessments within cachexia management protocols. Accordingly, we recommend integrating dietary support with objective mobility tracking to monitor performance and preempt sarcopenia through early, individualized adjustments.

In the ANO domain, patients receiving dietary counseling showed a significant improvement in appetite scores ($\Delta = -1.9 \pm 1.0$; $p < 0.001$), while the appetite of control group remained stable. Appetite loss in cancer patients is multifactorial, driven by both disease-related metabolic changes and the adverse effects of cancer treatments. Our study supported patients through small, frequent meals, preference-based diet planning, and psycho-nutritional counseling. These findings are aligned with an Indian study, where an intervention combining dietary counseling and daily IAtta chapatis led to significant improvements in appetite and reduced fatigue over six months in female cancer patients under palliative care.[21] This culturally adapted, natural supplement and enriched chapati highlights the importance of sensory and cultural acceptability in nutritional interventions. Because appetite loss often results in cachexia, strategies that successfully enhance appetite may improve dietary intake, functional strength, and psychological well-being.[20] Future interventions should therefore incorporate behavioral strategies such as meal frequency adjustments, cultural preferences, and psychoeducation alongside dietary modifications to address anorexia effectively.

The QOL domain demonstrated a significant decline in the intervention group compared with a slight change in the control group highlighting the significance of a holistic cancer care approach. Wang et al. (2025) also reported that advanced stage oncology patients receiving integrated palliative care including nutritional counseling, psychological support, and symptom management indicated significantly improved QOL scores using the EORTC scale, particularly in social functioning and fatigue domains.[22] Patients in our study also reported improved emotional well-being and better treatment compliance and tolerance. This reinforces the significance of integrating nutritional measures within routine cancer care, rather than treating them as ancillary.

The overall Mini-CASCO score declined significantly in the intervention group from baseline and after 6 months, indicating clinically significant improvement. On the other hand, the control group experienced only a slight change, highlighting the lack of standard oncology care in improving cancer cachexia. These findings are in line with a RCT from South Korea reporting that a multi-modal intervention incorporating nutrition counseling, physical activity, anti-inflammatory agents, and psycho-social support significantly improved lean body mass and QOL compared to conventional oncology care.[23] The Mini-CASCO scoring system should be incorporated into oncology and palliative care settings for assessing both baseline cancer cachexia severity and monitoring of response to multi-modal interventions.[7] To improve treatment outcomes, clinical care pathways must include protocols for implementing nutritional assessment, dietary counseling, and regular monitoring, anchored by validated assessment tools like Mini-CASCO.

Overall, this study provides strong evidence that a personalized dietary intervention, combined with regular nutritional monitoring, significantly improved the progression of cancer cachexia. These findings should be taken as evidence supporting multi-disciplinary and integrated cancer care pathways rather than only nutritional strategies. The intervention yielded significant improvements across all Mini-CASCO domains compromising body weight, appetite, systemic inflammation, PHP, and QOL highlighting the multifactorial nature of cachexia and the need for integrated management. These findings advocate for the incorporation of structured, nutrition-specific care pathways within standard cancer care to improve patient outcomes and support comprehensive cancer care.

Limitations

This RCT employed a validated multimodal Mini-CASCO assessment tool alongside a comprehensive personalized dietary counseling program. Nonetheless, several limitations should be acknowledged. Dietary consumption data were self-reported, potentially resulting recall bias. Although compliance to the intervention was monitored, actual nutrient consumption was not biochemically examined, and variability in dietary consumption could not be objectively measured. The study population was limited to female oncology patients with late-stage breast cancer; therefore, the findings should not be generalized to male or to patients with other malignancies without further confirmatory studies. PHP was assessed using the ECOG tool rather than objective measures such as handgrip strength or gait speed, which may offer more comprehensive functional assessment. As this study was multi-component and composite, the independent role of specific nutrients or individual components could not be isolated. Lastly, due to the composite nature of the intervention, the independent impact of specific nutrients could not be isolated.

Conclusion

The findings indicated that integrating personalized dietary counseling sessions and regular nutritional monitoring with standard oncological care can significantly reduce the severity of cachexia in female breast cancer patients. Significant improvements were observed across all domains of the Mini-

CASCO score, including body composition, inflammatory-metabolic status, physical performance, anorexia, and quality of life. The Mini-CASCO tool indicated high clinical utility as a multidimensional and standardized instrument for assessing cachexia severity and monitoring treatment response. Its incorporation into routine oncology practice may enhance the accuracy of cachexia evaluation and support more effective, evidence-based nutritional interventions. Embedding personalized nutritional support within palliative and supportive oncology care not only improves appetite and preserves lean body mass but also contributes significantly to functional status and psychosocial well-being which are essential dimensions in the comprehensive management of cancer-associated cachexia.

Acknowledgements: We thank the Department of Medical Oncology, Fauji Foundation Hospital Rawalpindi for support in participant recruitment and clinical oversight and we also acknowledge the contributions of the clinical dietitians and the study psychologist for delivery of the intervention.

Authors' Contributions: RM made contributions to the design and conception of the intervention, data acquisition, drafting, and finally a critical revision. SA contributed to the interpretation of data, critically revised the article for important intellectual content, and approved the final version. AS contributed to data acquisition and drafting of the manuscript. JJ was responsible for data analysis and interpretation. All authors approved the final version to be published and agree to be accountable for all aspects of the work to ensure integrity and accuracy.

Conflict of Interest: None.

Data Sharing: Available upon reasonable request.

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Journal of University College of Medicine & Dentistry

Original Article

Cinemeducation for Teaching Medication Safety: A Pre-Post Assessment and Student Reflections in Pakistan

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Submission: 23rd August, 2025
First revision: 14th November, 2025
Second revision: 10th December, 2025
Acceptance: 1st January, 2026

DOI: https://10.51846jucmd.v5i1.4457.

Cite this article as:

Nasir Y, Habib S, Ali S, Anwar S. Cinemeducation for teaching medication safety: a pre–post assessment and student reflections in Pakistan. *J Univ Coll Med Dent*. 2026;5(1):14-20.

Abstract

Objective: To assess the improvement in the understanding of third year medical students about medication safety after a brief cinemeducation session.

Methodology: We conducted a single group pre and posttest educational intervention study at the Liaquat National Medical College in Karachi from July to September 2025. A total of 52 third-year undergraduate medical students participated in this study. The educational intervention consisted of a two-hour teaching session. The session included assigned pre readings, a short introductory lecture, several video clips demonstrating medication errors, group discussions, reflective writing based on the Gibbs reflection cycle. Multiple-choice questions were used before and after the course to assess students' knowledge. Post session feedback was obtained and reflections were thematically analyzed. Paired t-test was used to compare participants' overall knowledge scores before and after the test. $P < 0.05$ was considered as statistically significant. We analyzed the feedback data using descriptive statistical methods.

Results: The mean age was 60.6 ± 10.1 years, while the mean BMI was 30.6±6.27 kg/m². For the T-score, the mean was -1.023± 1.66 at the lumbar spine and -.908±1.2 at the femur. The lumbar BMD status was significantly associated with age $p = 0.001$, whereby older patients have higher proportions of osteopenia and osteoporosis. No significant associations were noted between either BMI or gender and BMD status; however, Spearman correlation demonstrated a weak negative association of age with BMD in both sites and a positive correlation with BMI, especially in the femoral neck ($r = 0.285$).

Conclusion: Cinemeducation was effective in strengthening students' understanding and attitudes related to medication safety. While knowledge gains were modest, the approach encouraged reflection, emotional engagement, and practical insight. This suggested the value of this tool as an engaging method for teaching patient safety and other longitudinal themes within the medical curriculum

Keywords: Patient safety, Cinemeducation, Curriculum, Medical Students

Introduction

The instructional potential of visual media has long been recognized; it has evolved from a source of amusement to a deliberate teaching medium.[1] The purposeful use of films, also known as "cinemeducation," in medical and allied health education has recently gained attention as an education methodology that integrates guided reflection with visual storytelling.[1] Alexander et al initially defined the term as either short films or feature length movies that capture the ethical dilemmas, clinical uncertainty, and humanistic challenges that health professionals face.[1] Students are exposed to situations that reflect empathy, compassion, and critical thinking through the use of this narrative.[1,2] Instructors select scenes from movies or television shows that relate to a particular learning objective. Before viewing the selected video, students receive a brief orientation that describes the purpose of the exercise and identifies specific issues to observe. A structured debriefing that occurs either individually or in small groups ensues. The discussion focuses on the emotional responses of the students, the narrative they create regarding the events and how they identify with "actual clinical practice.[20] Globally, the concept of cinemeducation has been applied in various disciplines such as bioethics, psychiatry, general medicine and palliative care.[2] A study at Ludwig Maximilian University of Munich showed that learning through movies facilitated longer retention of essential concepts.[3] Similarly, research conducted in Tehran reported that after reflection on movie-viewing experiences, there was an increase in medical students' empathy and understanding of the whole person.[4] Another study carried out amongst clinical year MBBS students in Pakistan demonstrated high satisfaction and support for the integration of cinemeducation as a teaching methodology into the curriculum.[5]

The World Health Organization defines patient safety as "the absence of preventable harm and the reduction of risks to an acceptable minimum." Patient

safety is considered one of the fundamental components of high-quality healthcare.[6] As one of the top three causes of death worldwide, medication errors put tremendous pressure on the healthcare system in the form of avoidable morbidity, mortality, and costs. Medication errors account for nearly 200,000 deaths every year in the United States alone.[7] To give an incentive for the incorporation of patient safety into the undergraduate syllabus, the Pakistan Medical and Dental Council (PMDC) dedicated a number of hours for students to learn about patient safety with the aim of providing a safe practice environment once they graduated.[8] Liaquat National Hospital (LNH) recognized the need for quality assurance and the integration of patient safety education for undergraduates as a way of encouraging safe clinical practice in line with the national and international recommendations. Since cinemeducation has the potential to engender cognitive and affective-based learning on pharmaceutical safety, we used it as a novel approach to enhance knowledge and attain positive, long-standing changes.[9] However, previous literature in this field has largely focused on quantitative measures and does not explore students' perceptions or how these perceptions impact professional knowledge.[5,10]

Based on this research gap identified, this study was designed to determine the improvement in medication safety knowledge among third-year medical students following a brief film-based teaching intervention. The study integrated quantitative assessment and qualitative reflection, analyzing not just the gain in knowledge but also the effect of the educational intervention on attitudes, emotional engagement, and the sense of professional responsibility for patient safety.

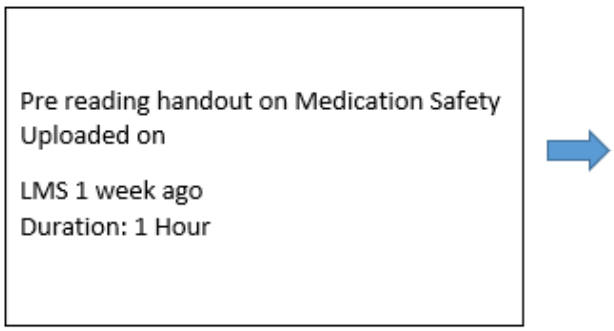
Methodology

This was a mixed-methods educational intervention study conducted at Liaquat National Medical College, Karachi, over a period of three months (July–September 2025). Since the curriculum was introduced in the third year of the MBBS program by the University, the intervention was designed to target learners at the same stage of study. Data collection was initiated after obtaining ethical approval from the Institutional Review Board of Liaquat National Hospital (ERC #1242-2025-LNH-ERC). Before the enrollment of the participants, written informed consent was obtained from all participants.

The sample size was calculated using G*Power based on a previously conducted similar study reported overall mean scores of pretest and posttest score (5.54±1.05 and 7.42±0.82 respectively).[11] Taking a power of 90% and a 95% confidence interval and a correlation of 50%, the required sample size was estimated as 44 participants with effect size of 0. Sampling was performed using a non-probability convenience technique. Third-year students who attended the intervention and provided consent were included; those absent or unwilling were excluded. The total class size was 80 students, all of whom were invited to participate in the study. Of these, 52 attended the session. The non-probability convenience technique may limit the generalizability of findings due to potential selection bias.

This intervention was planned aligning with the principles of Mezirow's transformative learning theory, which emphasizes critical reflection and experiential engagement to challenge existing assumptions.[12] The session was aim to enhanced cognitive understanding and affective aspect of patient safety concept using film-based scenarios and reflective discussions.

The session was facilitated by three faculty members and fifty two students participated. The lesson plan was developed and reviewed by the medical college's patient safety core curriculum committee. In addition, the teaching material, pre and posttest MCQs, and reflection questions developed, were reviewed. The feedback from the expert were incorporated through iterative revisions. Prior implementation, the session's facilitators were oriented to the finalized lesson plan .The teaching session consisted of structured two-hour large-group session, with time allotted to a brief introductory lecture, video clips, group discussion, reflective writing, and debriefing as presented in Figure 1.



Session Component	Duration
Introductory Lecture	35 minutes
Pre intervention MCQs	10 minutes
Video Clips	15 minutes
Debriefing	20 minutes
Reflection (group activity)	20 minutes
Post intervention MCQs	10 minutes
Post session Feedback	10 minutes
Total Duration	120 minutes

Figure 1: Time allocation for different components of the cinemeducation based teaching session

One week before the scheduled teaching session, pre reading material from the WHO Drug Safety Curriculum was shared with the students via college's LMS. During the session, the baseline knowledge was assessed using a pretest MCQ via Google Forms. The session included an introductory lecture on drug safety concepts and high-alert medications, followed by two video clips, a five-minute scene from 'The House' and a ten-minute WHO workshop video, portraying critical medication errors. Students then engaged in small-group discussions (ten-twelve per group) and submitted structured reflections using Gibbs' Reflective Cycle. Reflections were anonymized. The session was completed with a posttest and post session feedback which was filled by students online. The study variables included pre and posttest knowledge scores, students' written reflections, and post session feedback.

Pre and posttest: The recall level MCQs based on medication safety were initially drafted by the committee member, aligned with the predefined learning objectives. The draft questions were shared with the team and their feedback led us to revise the questions, mainly to improve wording, re-

move ambiguity, and ensure each question reflected the intended learning outcomes. Example items included: *'Which of the following is classified as a high-alert medication?' and 'What is the safest strategy to prevent drug resistance in hospital practice?'* Although the items were reviewed by content expert, however the items were not piloted and formal reliability testing (KR-20 or Cronbach's α) could not be carried out because of the small sample size. This remains a limitation of the study. The same set of MCQs was utilized in both the pre and posttests. Each of the eleven items comprising the online quizzes was given a time allocation of ten minutes, administered through Google Forms. Faculty members were present when the quizzes were administered to enhance standard testing conditions. An anonymous identifier mechanism developed by Google Forms was used to match the pre and post responses to protect the privacy of students. Students were awarded a score of one for every correct response and zero for wrong responses.

A 5-point Likert scale (1 = Strongly Disagree through 5 = Strongly Agree) was utilized to collect post session comments via a Google Form. The "Neutral" label on the midpoint allowed students to convey doubt or strike a balance between two choices. Learners' opinions on the session's clarity, relevance, facilitation, and educational value were obtained using the above questionnaire. Both faculty and subject matter experts assessed it for face validity. However, since the instrument was for formative feedback and not psychometric purposes, neither a pilot nor reliability measurements were conducted. The reflection activity was guided by a series of questions, all of which were based on Gibbs's theory of the cycle of reflection. Students were required to submit reflection reports in groups and not reveal their personal identities. This ensured anonymity and confidentiality throughout the process.

Data analysis was performed using SPSS version 27. Frequency and percentage were calculated for all categorical variables. All numerical data were summarized as mean ± standard deviation. The normality of knowledge scores was assessed using the Shapiro-Wilk test. Paired t-tests were used to assess the significance of pre and post meeting scores. Significance levels for all analyses were set at p-values < 0.05. Descriptive statistics were reviewed to assess post meeting feedback. A total of five group reflection reports were reviewed.

This analysis used five sets of group reflection materials. Thematic analysis was conducted following Braun and Clarke's six-step framework, using an inductive approach. Two investigators independently coded the reflections, after which consensus meetings were held to resolve discrepancies and agree on the final coding scheme. Themes were developed directly from the responses provided by participants. The analysis was performed manually.

Result

A total of 52 third-year MBBS students participated in the pretest and posttest assessments. The comparison of correct responses before and after the cinemeducation session is displayed in Table 1. The knowledge score before and after the session was 9.6 ± 1.6 and 10.2 ± 1.7 respectively. Although the increase was statistically significant (p=0.025), the magnitude of change (mean difference 0.60 ± 2.1) was small, indicating only a modest improvement in factual knowledge. Table 1 displays the comparison of pre and post knowledge scores.

Table 1: Pretest and posttest knowledge scores and mean change (post–pre) after a 2-hour film-based session (n = 52)

Variables	Mean ± SD	Mean difference (post-pre)	95% Confidence interval	Cohen's d Effect size	t-statistics	p-value
Pre test score	9.6 ± 1.6					
		0.60 ± 2.1	0.07 - 1.10	0.211	2.290	0.025
Post test score	10.2 ± 1.7					

Paired t-test was applied after assessing normality assumption with Shapiro-Wilk test. Whereas the general upward trend of pre and posttest scores can be seen in Figure 2, with a higher frequency of correct responses observed for Q2, Q3, Q4, Q5, Q8, and Q10.

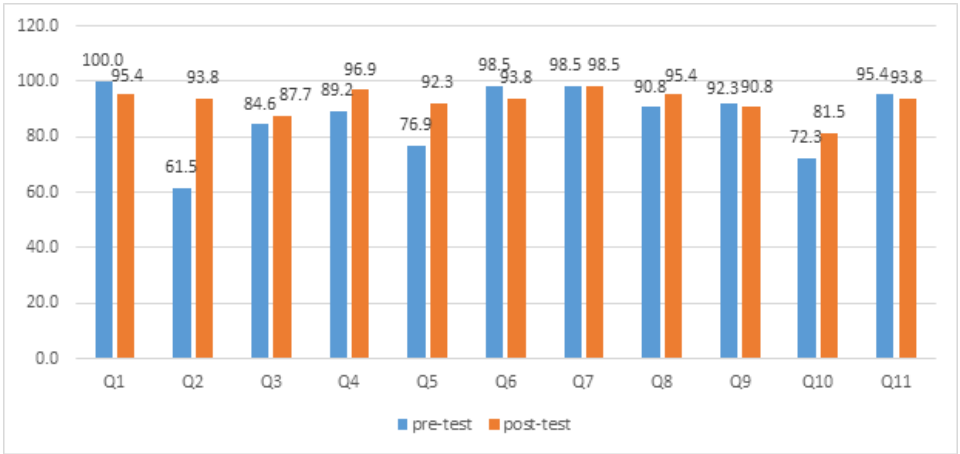


Figure 2: Distribution of correct responses; X-axis represents the number of questions Y-axis represents percentage of correct responses

Post-session feedback was received from 22 out of 52 participants, giving a response rate of 42.3%. Participant feedback was overwhelmingly positive. Agree/Strongly agree were combined for key outcomes. Nearly all agreed that the session objectives were clear (95.4%), the content was relevant (86.4%), and facilitators explained concepts effectively (100%). Most reported improved understanding of drug safety (95.5%) and ability to prevent medication errors (95.5%). Most importantly, multimedia, video, debriefing, and reflection were well received, though group activities were rated lower (50%) agreement. Table 2 outlines data distribution of post-session feedback

Table 2: Frequency distribution of post session feedback (n=22)

Post session Feedback	Strongly agree n(%)	Agree n(%)	Neutral n(%)	Disagree n(%)	Strongly disagree n(%)
The session objectives were clearly defined.	12(54.5)	9(40.9)	1(4.5)	0(0)	0(0)
The content was relevant to my level of training and clinical practice.	10(45.5)	9(40.9)	2(9.1)	0(0)	1(4.5)
The session enhanced my understanding of drug safety and high-alert medications.	8(36.4)	13(59.1)	1(4.5)	0(0)	0(0)
The use of multimedia (PowerPoint, video) helped in understanding the topic.	11(50)	9(40.9)	1(4.5)	0(0)	1(4.5)
Group activities and discussions were engaging and useful.	7(31.8)	4(18.2)	9(40.9)	2(9.1)	0(0)
The facilitators explained the content clearly and responded well to questions.	12(54.5)	10(45.5)	0(0)	0(0)	0(0)
The pre reading material was helpful in preparing for the session.	7(31.8)	10(45.5)	5(22.7)	0(0)	0(0)
The video episode effectively highlighted important drug safety issues.	10(45.5)	10(45.5)	1(4.5)	0(0)	1(4.5)
The timeline debriefing helped connect the video to real-world practice.	7(31.8)	11(50)	3(13.6)	1(4.5)	0(0)
The Reflection exercise helped me reflect on and internalize key lessons.	9(40.9)	9(40.9)	4(18.2)	0(0)	0(0)
The pre and post-session MCQs helped gauge my understanding of the topic.	7(31.8)	14(63.6)	0(0)	1(4.5)	0(0)
The session has improved my ability to recognize and prevent medication errors.	13(59.1)	8(36.4)	0(0)	1(4.5)	0(0)

Thematic analysis of the group reflections resulted in five major themes and their respective subthemes. The themes illustrate that students identified drug safety errors, the emotions they linked with the drug safety concerns, the deficiencies they saw in current practice, the root causes leading to errors, and the solutions they felt would eliminate errors. Students also indicated how they would like to communicate in the future. Tables 3 lists a sample of quotes for each theme and subtheme.

Discussion

This study analyzed methods for teaching drug safety knowledge to undergraduate medical students using film education. The following teaching strategies were employed to motivate students: pre and posttests, interactive lectures, film clips, post class discussions, and structured guided reflective writing. The pre and posttest results showed significant improvement in students' awareness and knowledge of key elements of drug safety. Specifically, students' factual knowledge significantly improved (mean score modest increase from 9.6 ± 1.6 to 10.2 ± 1.7), a change of 0.60 ± 2.1 ($p = 0.025$). Although the average improvement in factual knowledge was small, the results were statistically significant. However, further investigation is needed into how film education influences students' attitudes and their ability to think critically about clinical situations. Furthermore, post-session feedback indicated that students found the course helpful. Almost all students felt the trainers did a good job explaining the topics and that the course improved their ability to identify potential medication errors (95.4%). Most students also found the video clips helpful for their learning (90.9%). After analyzing the themes of the group reflections, five key aspects were identified: how students remembered medication

Table 3: Thematic Analysis of Student Reflections on Drug Safety

Theme	Subtheme	Representative Quotes (Student Responses)
1. Recognition of Drug Safety Errors	Wrong drug and wrong route	*"Wrong medicine administered, without double checking, infrequent monitoring, doctor was irresponsible and didn't observe the patient after administering the drug" (G2)* *"In video A we saw vincristine being administered instead of methotrexate and it was also administered intrathecally which when via IV causes paralysis and an immediate death" (G3)*
	Failure to take allergy/ medical history	*"Clip 2: insufficient allergic history" (G1)* *"In the second video, Dr failed to take any form of history and due to lack of communication and willingness from the side of the doctor resulted in a fatal event" (G5)*
	Inadequate labeling and documentation	*"No labeling on medicine" (G1)* *"ROD, expired date and therapeutic index was not properly checked" (G3)*
	Absence of pharmacovigilance	*"No proper monitoring" (G1) "There was no double check of drug being administered (pharmacovigilance)" ; (G2,G3)*
	Poor communication and teamwork	*"Lack of communication, coordination" (G1, G2, G3) "Lack of professionalism" (G5)*
2. Emotional Responses to Errors	Emotional Impact and Professional Responsibility	*"Sad and disappointment" (G1)* *"Disgust, frustration annoyance"* ; *A sense of personal failure, shame and guilt" (G3)* *"We all got tensed and it was terrifying to see patient dying" (G4)*
3. Pathways to Medication Errors	Individual factors	*"Doctor wanting to sign off, was trying to hurry home which led to patient negligence and violated patient safety" (G3)* *"Lack of training, poor communication, inadequate history taking" (G4,G5)*
	System-level factors	*"High Risk drugs not labelled" (G3,G2,G1)* *"Shortage of staff in video A"; (G4, G5)*
4. Learners' Perspectives on Prevention	Double-checking and labeling	"*Double checking, label high risk and route*"; (G1, G2)
	History-taking and monitoring	*"Proper history should be taken and team should be involved"; (G2,G4,G5,G3)* *"In video B: high alert medication should be separated and should have been administered with extra care and proper monitoring" (G1)*
	Improved teamwork and communication	*"Staff coordination could be better" (G1,G3)* *"Proper communication" (G2)*
5. Intended Professional Practice Changes	Patient-centered care (history, allergy checks)	"*We will take complete history, check MR number, check allergic reaction reactions if any*" (G1)
	Professional behaviors	*"Should not be multitasking, practice proper communication with patient, show some empathy to my patient, take proper history, prioritize my patient's health"(G4,G5)*
	Vigilance in prescriptions and administration	*"To pay more attention and be more careful of the dosage, drug and route of administration along with taking a better and more detailed history, also observe the patient after administering drug for allergic reactions" ; (G2)* *"Verify the medication, good communication with the patient, take care of safety protocols" (G3)*
	Effective Communication	"Proper communication with the patient and the staff" (*G4)* *Better coordination with staff" (G2, G3)*

Note: Clinical facts stated are from quotations of students' reflections and may or may not be accurate.

safety errors, their feelings about these errors, what they believed caused the errors, what different approaches they would take to avoid making the same mistakes, and what experiences they planned to apply to their future careers.

Besides indicating the learning of new knowledge, the students in our study also provided evidence of reflective engagement and affective commitment regarding the issues of patient harm and professional responsibility. These observations are aligned with the previous study, which has also reported that cinemeducation helped strengthen medical students' understanding of patient safety and related professional behaviours.[12] The provision of a pre reading hand out in this study might have contributed to the relatively high baseline scores, this trend is generally observed when students were provided with pre reading material and resources before viewing activities.[13] The significant improvement in overall positive trends across the pre & posttest, are in accordance with the study conducted in Spain which highlighted the significance of structured audiovisual materials and guided discussion in fostering deeper comprehension of patient safety strategies.[14] Similarly, the emphasis on rigorous planning of both the viewing activity and the subsequent debrief likely enhanced engagement and helped consolidate levels of learning assessed through MCQs.[9]

In the study the teaching session was planned in a way that emphasized reflection rather than rote knowledge transfer, which may have produced greater gains in attitudes and awareness than in factual recall. This aligned with literature that highlighted cinemeducation was particularly effective in shaping professionalism and attitudes rather than knowledge alone.[15] In our study, most students reported a high level of satisfaction with the cinemeducation session. This is in line the findings of Sinha et al. (2024), who reported a satisfaction index of 97.6%.[11] The post-test improvements we observed particularly in items that were directly illustrated in the video clips, such as wrong drug or route and failure to check allergy history also align with earlier work, Rueb et al. noted that students were more motivated when films portrayed realistic clinical situations, which appears consistent with the pattern seen in our results.[3] In our study, students' reflections identified systemic and individual factors including inadequate training, poor communication, unlabeled high-risk drugs, and scarcity of staff, that represent the basis of ill- practices. Such findings are in line with those by Kadivar et al. (2018), where it was established that cinemeducation enables the recognition of systems-based errors and arouses reflective thinking about patient safety. [16] Such elements have been hypothesized to develop not only knowledge but also that kind of critical reflection and awareness so crucial for safe clinical practice.

The students' reflections showed strong emotional reactions, such as sadness, guilt, frustration, and helplessness. In line with research by Patel et al. (2022) in relation to the ability of cinemeducation to foster empathy and ethical awareness by engaging students at the emotional level, standard teaching approaches often fail to engage learners in this way and are less likely to be associated with deep learning.[17] The emotional engagement that our participants described appears to be a particular strength of this learning opportunity. A number of preventative techniques and contributing factors were considered by the students, including double-checking, marking high-alert drugs, getting a complete medical history, working in groups, and being watchful of prescriptions. This is also in keeping with the WHO's worldwide patient safety recommendation.[18]

Ninety percent of the student participants rated the video clips as the most useful part of the session since they served to maintain interest and attention in the evaluation that was done at the end of the session. This finding is consistent with previous research that found cinematic cues enhanced motivation, engagement, and learning transfer to the clinical environment.[19]

This study added new insights in the existing literature by demonstrating how film education can enhance students' understanding of drug safety. Students identified numerous drug safety errors and expressed a range of strong emotional responses, including anger, guilt, and heightened professional responsibility. Moreover, they suggested several potential mitigation strategies, including improved teamwork and planning, clearer labeling, and double-checking. Many participants considered how these strategies could be applied in future clinical practice. These findings suggested that this approach not only facilitates immediate cognitive learning but may also contribute to more lasting attitude and behavioral changes. The cognitive and behavioral responses elicited in this study make a noteworthy contribution to the ongoing literature on film education as an instructional intervention.

This study laid the foundation for further exploration of the important but under-researched area of drug safety in undergraduate medical education. By integrating various interactive elements such as videos, summary discussions, reflections, and group activities into the teaching process, this study effectively stimulated students' learning interest and promoted meaningful learning. The preventative strategies proposed by the students made a valuable contribution to this study because they provided perspectives on how future clinicians can understand patient safety situations and address these issues in practice.

Limitations

Generalizability may be affected because this was a single institution study with a small sample size. Convenience sampling may have affected selection bias. There was no comparator or control group present. There may have been some nonresponse bias because less feedback response was collected. There may have been practice effects because the same 11 multiple-choice questions were used for assessments both before and after the intervention. There may have been some variability in how each group performed the session because facilitator adherence, group size, and time allocation were not measured independently. The depth of viewpoints acquired may be less because reflections were taken in groups rather than individually. Long-term memory retention and whether the learning had translated into any clinical behaviors were not considered in this study.

Conclusion

The third-year medical students' knowledge of medication safety was improved after brief film-based session. Medical educators may consider this approach for meaningful educational experience to enhance knowledge gain, motivation and empathy among students. Other longitudinal curriculum topics in undergraduate medical education such as ethics, professionalism, and leadership could similarly be instructed through the cinematography approach. Future studies should look at the long term knowledge retention and behavior through this strategy. The overall efficacy of teaching with the cinema

could be clarified through doing larger research, multi-center studies or executing the sessions at different periods in the curriculum.

Acknowledgement: The authors would like to acknowledge Ms. Noureen Durrani, Biostatistician at Liaquat National Hospital, for her valuable expertise and support in data analysis and sampling methodology

Authors' Contributions: YN conceived the study idea, designed the educational intervention, contributed to data collection, and drafted the initial manuscript. SH assisted in the implementation of the intervention, data collection, and contributed to manuscript drafting. SA contributed to the study design, supervised the research process, and critically reviewed the manuscript for intellectual content. SAN assisted in data analysis, interpretation of results, and critically revised the manuscript.All authors reviewed and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Conflict of Interest: The authors have no conflicts of interest to declare.

Funding: This study was not supported by any external agency.

Data Availability Statement: The data that support the findings of this study, apart from the data already presented in the results section, are available from the corresponding author upon reasonable request.

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Journal of University College of Medicine & Dentistry

Original Article

Frequency of Buccal Bone Fenestration in Anterior maxilla: A Virtual Implant Placement Study

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Submission: 2nd October, 2025
First revision: 20th November, 2025
Second revision: 22nd December, 2025
Acceptance: 5th January, 2026

DOI: https://doi.org/10.51846 jucmd.v5i1.4797

Cite this article as:

Naqvi Z, Haseeb M, Javed S, Bajwa O, Ahmed M. Frequency of buccal bone fenestration in anterior maxilla: a virtual implant placement study. *J Univ Coll Med Dent*. 2026;5(1): 21-26.

Abstract

Objective: To determine the occurrence of buccal bone fenestration of the anterior maxilla and its relationship with the type of prosthesis (screw-retained or cement-retained) and the labial concavity angle (LCA) based on virtual placement of the implants.

Methodology: A Cone-Beam Computed Tomography (CBCT)-based virtual implant simulation study was conducted over 6 months from May to October, 2025 at the Department of Periodontology, University Dental Hospital, University of Lahore. Two hundred anonymized CBCT images for patients over the age of 20 years were analyzed using BlueSky Plan software. Virtual placement of implants was done based on the type of prosthesis- screw retained and cement retained. Buccal bone thickness, presence of fenestration and LCA were documented. Data were analyzed based on the Mann Whitney U test and Fisher's exact test with SPSS at a significance level of p value < 0.05.

Results: The average age of patients was 39.7±10.9 years. The mean coronal bone-to-implant distance was significantly greater in cement-retained implants (2.33 ± 0.93 mm) compared with screw-retained implants (1.52 ± 0.48 mm) ($p < 0.05$). The distance b/w the bone and the implant significantly differed at the middle (1.61 ± 0.48 mm) and apical (1.40 ± 0.59 mm) levels for cement-retained implants as compared to screw-retained implants (1.03 ± 0.62 mm and 0.67 ± 0.88 mm, respectively; $p < 0.05$. The average LCA was 154.7° ± 7.1°. A statistically significant association between prosthesis type and fenestration was identified using Fisher's exact test. In addition, the LCA showed a positive correlation, with significant differences observed between genders ($p < 0.05$).

Conclusion: Screw-retained virtual implant positions demonstrated a higher likelihood of buccal bone fenestration compared to cement-retained positions. Labial concavity angle differed significantly between genders, suggesting anatomical variability may influence fenestration risk.

Keywords: Buccal bone fenestration, anterior maxilla, CBCT, virtual implant placement, screw-retained prosthesis, cement-retained prosthesis

Introduction

Dental implants are now a highly accepted and predictable treatment option for partially or fully edentulous patients.[1] Modern surgical and restorative methods currently emphasize shortening treatment time while maintaining the best esthetic and functional outcomes.[1] Immediate implant placement, especially with simultaneous bone augmentation, has demonstrated the ability to develop and/or maintain the natural periodontal architecture and minimize bone resorption after tooth extraction.[1] However, implant placement in the anterior maxilla has its unique challenges due to proclined antero-inferior angle of the alveolar bone and the presence of a prominent buccal concavity, both of which increase the potential for labial bone fenestration.[2] The thin buccal cortical plate is vulnerable to fenestration and dehiscence, which may negatively impact primary stability and consequently require additional grafting procedures.

Sagittal root positioning (SRP) can further complicate implant placement in this esthetic zone. A study established that approximately 85% of maxillary incisors have Class I SRP with the root positioned near the labial cortical plate.[3] To preserve sufficient buccal bone in such cases, implant placement is recommended 0.5-1.0 mm towards the palatal side.

Ideally, implants should be prosthetically driven to maximize esthetics, force distribution, and hygiene; however, anatomical restrictions dictate practicing the positioning of implants bone-driven. Cone-beam computed tomography (CBCT) plays an important role in the pre-operative evaluation process to understand bone morphology and implant positioning in 3D. A study identified a significant number of labial perforations, mainly in the apical and middle third, based on the implant design and angulation.[4,5] A study conducted by Anna and coworkers reported a higher percentage of perforation at prosthetically driven (80%) compared to bone-driven implants (5%) in central

incisors. It is thought that the differences in perforations about the location could be due to differences in SRP classes and differences, ethnicity in the morphology of the alveolar ridge.[6]

Previous CBCT-based investigations in the anterior maxilla have explored parameters such as screw-retained crown feasibility, ridge morphology, labial bone thickness, undercuts, and sagittal angulation. Across these studies, a consistent finding emerges—there is a substantial risk of labial bone perforation when planning implants in the esthetic zone.[7] However, to date, no study has specifically evaluated the risk of labial bone perforation in relation to screw-retained versus cement-retained implant restorations within the context of sagittal root positioning. However, unlike previous CBCT studies that focused primarily on bone morphology or implant angulation, this study uniquely integrates prosthetic orientation with labial concavity morphology to quantify fenestration risk in anterior maxillary implant planning. This study evaluates the frequency of buccal bone fenestration in screw-retained vs. cement-retained implant positions. This study also investigates the labial concavity angle in our population and its possible association with gender variation and fenestration of buccal bone.

Methodology

Following ethical approval from the Institutional Review Board (Ref No: UCD/ERCA/279; Approved on 17-06-2023), A CBCT-based virtual implant simulation study was conducted over 6 months at the Department of Periodontology. It was conducted over six months from May 15th 2025 to Oct 15th 2025 in the Department of Periodontology, University Dental Hospital, University of Lahore, using non-probability consecutive sampling.

The sample size comprised 200 virtual implant simulations, which were enough to provide the statistical power needed to check the relation between the type of prosthesis and the buccal bone fenestration. OpenEpi (Version 3.01) was used for the priori determination of the necessary sample size. Fenestration rates mentioned in earlier CBCT-based virtual placement studies were the basis for this determination. A total sample size of 200 virtual implant stimulations was calculated with 100 in each group (screw-retained versus cement-retained position). The sample size was calculated using a 95% confidence level and 80% power, based on an expected buccal bone fenestration prevalence of approximately 15.5% for screw-retained implant positions at tooth #21, as reported in previous CBCT-based studies.[6]

Inclusion criteria comprised patients older than 20 years who were medically suitable for implant therapy, presented with bilateral maxillary anterior teeth, sagittal root positioning (SRP) Class I, and Type I extraction sockets. Only those requiring CBCT scans for posterior implant planning and providing informed consent were included. Exclusion criteria included the presence of periodontal disease, a history of radiotherapy or chemotherapy, psychological impairment, unclear or artifact-distorted CBCT images, Type II or III extraction sockets, and pathology affecting the maxillary anterior region.

To minimize selection bias, one maxillary anterior tooth (right or left central or lateral incisor) was randomly selected per scan using a computer-generated randomization sequence. The allocation of each tooth was thus purely random and not affected by the researchers. CBCT scans were obtained using a Planmeca Romexis unit (Planmeca, Helsinki, Finland) with a voxel size of 0.2mm, 90 kV at 10 mA, and a field of view of 8 × 8 cm. The DICOM datasets were then imported into BlueSky Plan software (Version 4.8, BlueSkyBio, USA) for virtual simulation.

Within the BlueSky Plan software, standard cross-sectional slices were utilized. The labial concavity angle was measured on cross-sectional CBCT images at each implant site to assess the curvature of the labial cortical plate. Three reference points were identified for this measurement (Figure 2):

- Point C: the most coronal external point of the labial plate,
- Point I: the most internal point of the labial concavity, and
- Point A: the most external apical point of the labial plate, located superior to Point I.

A digital wax-up was obtained from the software's digital tooth library to produce crown contour and cementoenamel junction (CEJ) contours, secured in position before implant simulation. The virtual bone-level tapered implants (4.1 × 13 mm) were positioned 4 mm apical to the mid-facial CEJ. A standardized implant length of 13 mm was selected to ensure a minimum apical anchorage of 4 mm, which is considered essential for immediate implant placement. Similarly, an implant diameter of 4.1 mm was used, as a 4 mm diameter is commonly regarded as a standard dimension for implants in this region.[8] Different angles were used for cement- and screw-retained implants to reflect clinical prosthetic requirements and assess their impact on buccal bone fenestration

Each site was planned in two orientations;

1. Screw-retained position: The implant was aligned such that the screw access hole emerged through the middle of the lingual groove near the cingulum.

2. Cement-retained position: The implant was aligned along the long axis of the tooth through the incisal edge of the diagnostic wax-up.

At both the positions, buccal bone thickness was measured from the implant shoulder to the outer buccal cortical plate at coronal, middle and apical third (Figure 1). The presence of fenestration (exposure of any implant thread beyond the buccal bone) was recorded at each level as present or absent. Data collection was preceded by the calibration of two operators who collectively assessed 10 CBCT scans and normalized their measuring protocols. The reliability testing showed a very good agreement, with the intra- and inter-observer ICC values both being more than 0.85, which meant that there was a high level of reliability in all the measurements taken.

Every virtual implant simulation, and not individual patients, was regarded as the unit of analysis, which guaranteed that the statistical tests took into account the independence of observations. One anterior tooth per scan was randomly chosen to obviate clustering effects, thus preventing unit-of-analysis errors and subsequently allowing for valid inference to be made.

The reliability was established by means of intra- and inter-observer ICC (intraclass correlation coefficients) which were greater than 0.85 indicating a very good agreement between the two trained operators. All measurements were carried out again on 10% of the sample in order to check the consistency thus ensuring robust and reproducible radiographic assessments. Normality of the data was assessed using the Shapiro–Wilk test. The labial concavity angle (LCA) showed a normal distribution ($p > 0.05$) and was therefore analyzed using parametric independent-sample t-tests. Bone-to-implant distance did not follow a normal distribution and was analyzed using the non-parametric Mann–Whitney U test. Categorical variables, including the presence or absence of fenestration, were analyzed using Fisher's exact test. Continuous variables were reported as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. A p-value < 0.05 was considered statistically significant.

Results

A descriptive analysis of a total of 200 virtual implant simulations demonstrated that, the average age of the patients was 39.7±10.9 years. Of the 100 patients included, 65 were female and 35 were male. The average labial concavity angle (LCA) was 154.7° ± 7.1°, which indicates a moderately convex labial plate contour.

Bone to implant distance by prosthesis type: The average distance from bone to implant in screw retained implants was 1.07±0.66 mm whereas the average distance for cement retained implants was 1.78± 0.66 mm. Table I shows the comparison of the bone distance from the implant to the gingiva in more detail. The results reveal a significant difference between bone width at cement retained and screw retained positions at coronal, middle and apical levels.

Table 1: Comparison of radiographic bone-to-implant distance (mm) between cement-retained and screw-retained implant prosthesis

Distance	Cement-Retained (Mean ± SD)	Screw-Retained (Mean ± SD)	p-value
Bone-to-Implant (Coronal)	2.33 ± 0.93	1.52 ± 0.48	<0.05
Bone-to-Implant (Middle)	1.61 ± 0.48	1.03 ± 0.62	<0.05
Bone-to-Implant (Apical)	1.40 ± 0.59	0.67 ± 0.88	<0.05

Mann-Whitney U test was applied to evaluate the significance between the cement-retained and screw-retained position in table I. Table II shows the Fisher's test for fenestration at different levels. It shows that there is significance difference between middle third and apical third.

In our analysis, the overall prevalence of buccal bone fenestration across both groups was 67% (55 cases in screw retained, 1 in cement retained and 11 in common). The Fisher's exact test indicated a statistically significant correlation between the prosthesis type and the presence of fenestration. Fenestration was analyzed per level, and a single implant could exhibit fenestration at more than one level

Table 2: Frequency of buccal bone fenestration in cement-retained versus screw-retained prosthesis n (%)

Presence of fenestration	Cement-Retained n(%)	Screw-Retained n(%)	p-value
Coronal third	0 (0%)	0 (%)	-
Middle third	3 (3%)	16 (16%)	<0.05
Apical third	10 (10%)	50 (50%)	<0.05

In our analysis, the overall prevalence of buccal bone fenestration across both groups was 67% (55 cases in screw retained, 1 in cement retained and 11 in common). The Fisher's exact test indicated a statistically significant correlation between the prosthesis type and the presence of fenestration. Fenestration was analyzed per level, and a single implant could exhibit fenestration at more than one level

Correlation of Labial Concavity Angle with gender: The mean value of LCA in females was 151° ± 6.01°, signifying a more pronounced buccal concavity compared to males, in whom the angle was 156.52° ± 6.96°. Significant differences were observed between male and female mean labial concavity angles ($p < 0.01$) using the independent sample t-test. Figure 2 shows the measurement of LCA as described.

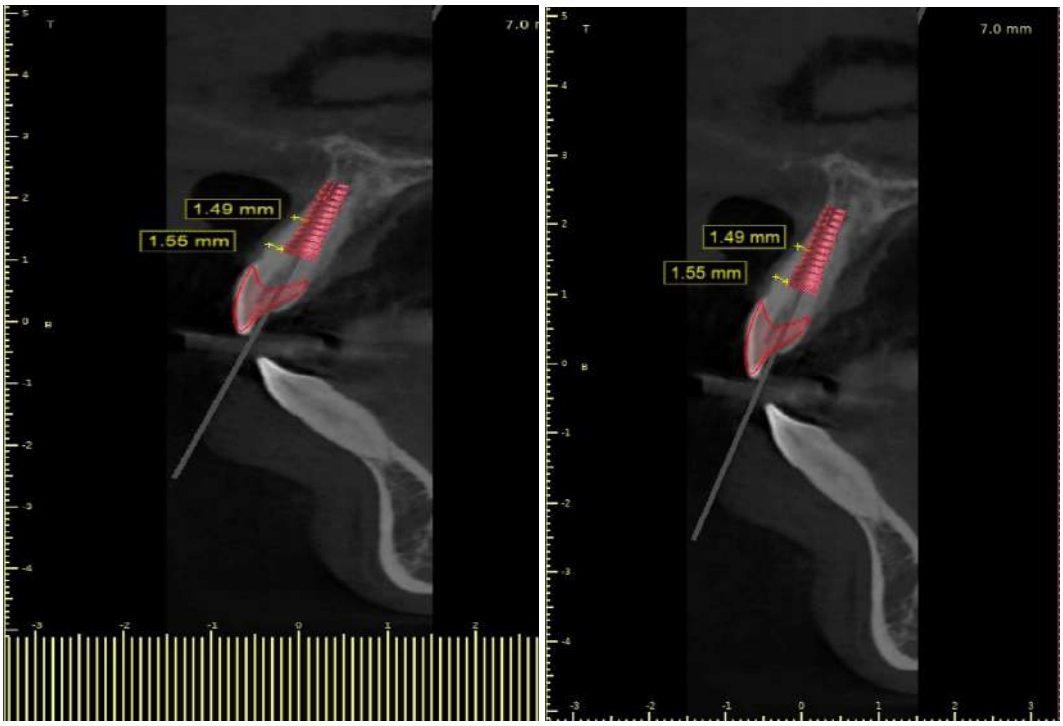

Figure 1: Implant placement in the (a) cement-retained (b) screw-retained position with buccal bone thickness at coronal, middle and apical third

The labial concavity angle (LCA) was measured between the coronal external I, internal concavity (I), and apical external (A) points.

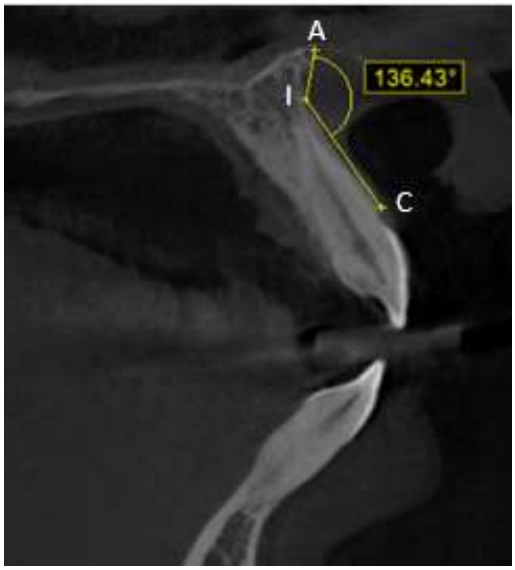

Figure 2: Labial concavity angle

Discussion

The screw-retained position is widely regarded as the optimal choice due to its superior esthetic results but the results of our study show that there is an increased and thread exposure. In such cases, the clinician has to perform guided bone regeneration (GBR) procedures to overcome the defect and implant thread exposure.[9] However, in cases where the bone thickness is not favorable, a cement-retained position is preferred to minimize the risk of perforation and reduce additional cost of the bone graft and membrane. Although it does save the cost, the esthetics is compromised. While this option may offer a cost advantage, it often compromises esthetics, particularly in the anterior maxilla.[10,11]

The mean value of LCA (Figure 2) in females was 151° ± 6.01° signifying a more pronounced buccal concavity as compared to males in which the angle was 156.52 °± 6.96°. The present study found that females exhibited a higher incidence of labial cortical bone perforation compared to males, consistent with the findings of Ikbal et al., (2023).[12] This discrepancy may be attributed to inherent anatomical variations between genders, particularly the generally smaller facial bone volume and thinner cortical plates in women. Such factors should be carefully considered during immediate implant placement (IIP), as they may predispose to labial bone perforation even with optimal virtual implant positioning.[13,14]

In our analysis, we discovered that the prevalence of fenestration was 67%, which is comparable with the previous CBCT evaluations done by Sayer et al. showing a wide range of 50% – 70% in the anterior maxilla area.[15] This again underlines the need for the clinical use of pre-operative assessment for the risk of fenestration using CBCT or virtual planning tools.[16]

The bone-to-implant distances were considerably higher in the cement-retained group at the middle (1.61 ± 0.48 mm vs. 1.03± 0.62 mm, $p < 0.05$) and apical levels (1.40 ± 0.59 mm vs. 0.67 ± 0.88 mm, $p < 0.05$) (Table 1). Anna et al. compared buccal plate perforation between prosthetically driven and bone-driven implant positions, reporting a significantly higher incidence of perforation in the former (80%) than in the latter (5%) which is in agreement with our study.[5] Screw-retained prothesis does provide the benefit that it is easy to retrieve due to the presence of an access channel

and provides better hygiene however it requires very precise implant angulation.[17]

The distribution of buccal bone fenestration varied markedly between prosthetic designs (Table 2). Fenestrations were absent in the coronal third for both cement- and screw-retained positions, suggesting adequate coronal bone support in virtual implant placement. However, a significantly higher frequency of fenestration was observed in the middle and apical thirds in screw-retained implants compared to cement-retained implants ($p < 0.05$). This finding indicates that the angulation required to achieve screw-access emergence may predispose implants to apical and mid-root buccal cortical perforation, particularly in anatomically concave labial plates.[5]

There was a statistically significant relationship between the type of prosthesis and the presence of a fenestration confirming the previously established effect of the restoration approach on peri-implant bone integrity. This is also supported by Severi et al. reporting the significance of surgical and prosthetic planning or coalescing buccal bone defects around anterior implants.[18]

The notable strengths of this study are the large sample size with 200 simulations, which allowed for a meaningful statistical comparison of prosthetic types, including the ability to examine bone morphology in three distinct levels (coronal, middle, apical). The use of virtual implant placement permitted standardized, isolated details in measuring bone-to-implant distance and fenestration risk, minimizing variability associated with clinical imaging methods. The measurement of the labial concavity angle as a morphological correlate is a unique approach and adds to the understanding of anatomical patterns that may predispose to the development of fenestrations.

Limitations

Nevertheless, the study has several limitations. As the imaging modality was a virtual CBCT simulation, biological responses, including soft tissue remodeling, vascularization, and bone healing, during the process in vivo were not captured, nor were clinical implant placement procedural variances accounted for. Additionally, the CBCT scans were obtained for posterior implant planning, which is a consideration for sampling bias and circumvents the anatomical characteristics of patients requiring anterior maxillary rehabilitation. In addition, while intra- and inter-observer reliability was assessed using intraclass correlation coefficients (ICC > 0.85), there are still concerns regarding the value associated with the lack of an independent external source to validate the measurements. Additionally, a single fixed implant size (4.1 × 13 mm) served as a limitation, and reconciling variability in bone morphology or risk of buccal fenestration with different dimensions or designs of implants was not transferable. Furthermore, clinical comparisons with actual implantation outcomes in vivo, including but not limited to survival rate or rates of marginal bone loss or soft tissue stability, were not possible through a virtual study. Finally, the nature of a cross-sectional design limits the study to an association versus causation of prosthesis type, angles of labial concavity, and buccal bone fenestration events.

Conclusion

This research shows a statistically significant association between prosthesis type, labial concavity angle, and buccal bone fenestration in virtual implant placement in the anterior maxilla. Cement-retained prostheses provided decreased rates of fenestration and greater bone-to-implant distances when compared to screw retained prostheses, likely reflecting variation in surgical and prosthetic procedures. The angle of labial concavity emerged as an important morphological feature that influenced fenestration risk. Overall, these findings indicate a need for careful assessment of anatomical features and prosthetic planning of implant cases to decrease buccal bone fenestration while optimizing functional and esthetic results.

Authors' Contribution: Z.N. and M.H. contributed to the conception and design of the study. Z.N. conducted data acquisition and analysis and drafted the methodology. M.H. supervised the study and critically reviewed the manuscript. S.J. provided clinical input and verified data accuracy. O.B. performed statistical analysis and prepared figures and tables. M.A. and M.K. contributed to study design, manuscript revision, and coordination of the final submission. All authors approved the final manuscript and accept responsibility for the work.

Funding: This study did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of Interest: The authors declare no conflict of interest related to this study.

Data Availability Statement: The data that support the findings of this study, apart from the data already presented in the results section, are available from the corresponding author upon reasonable request.

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Journal of University College of Medicine & Dentistry

Original Article

Evolving Patterns of Antibiotic Resistance in Empyema Thoracis: A Descriptive Analysis from Services Hospital, Lahore

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Submission: 20th July, 2025
First revision: 19th September, 2025
Second revision: 16th November, 2025
Final Revision: 23rd December, 2025
Acceptance: 31st December, 2025

DOI: https://doi.org/110.51846 jucmd v5i1.4348

Cite this article as:

Sarwar Z, Nabi MS, Arooj A, Musharraf MS. Evolving patterns of antibiotic resistance in empyema thoracis: a descriptive analysis from Services Hospital Lahore. *J Univ Coll Med Dent*. 2026;5(1): 27-32.

Abstract

Objective: To characterize the microbiological spectrum and antibiotic susceptibility patterns of pathogens causing empyema thoracis in adults at a tertiary care hospital in Lahore, and to describe the prevalence and temporal trends of multidrug-resistant (MDR) isolates.

Methodology: This observational study comprises 581 cases of bacterial empyema thoracis in patients admitted to the Thoracic Surgery Department, Services Hospital, Lahore, Pakistan, from March 2023 to February 2025. We collected the patient's demographic data, culture results, and patterns of antibiotic sensitivity and resistance. Adults aged ≥18 years were included in the study. Descriptive variables were analyzed as means and frequencies. An independent t-test was applied to compare resistance to antibiotics in gram-negative and gram-positive organisms.

Results: This study includes 581 cases of empyema thoracis, out of which 527 cases show positive bacterial culture growth and 54 cases show no growth on culture. From a total of 527 bacterial cultures, 274 (52%) were Multidrug-resistant (MDR). Multidrug-resistant prevalence fluctuated across half-year periods, ranging from 53.7% to 62.7%. Among positive cultures; most common Bacteria isolated was Pseudomonas aeruginosa in 167 (32%) patients, this was followed by Klebsiella pneumonaie in 51 (10%), Acinetobacter species in 47 (9%), E. coli in 48 (9%) and other gram negative organisms. Meropenem shows the highest sensitivity followed by gentamycin.

Conclusion: Empyema thoracis remains prevalent in our country and is now more commonly associated with gram-negative organisms. Antibiotic resistance is increasing alarmingly, producing Multidrug-resistant pathogens upto (62%) in our study.

Keywords: Antibiotic sensitivity, Empyema thoracis, Multidrug resistance, Pleural space

Introduction

Empyema thoracis, defined as infected fluid accumulation in the pleural space, represents a major clinical burden in Pakistan, frequently following pneumonia and rarely after chest trauma. Delay in diagnosis and treatment due to limited rural healthcare access and high cost of therapy amplifies morbidity in resource-constrained settings.[1]

Antimicrobial resistance (AMR) poses a threat globally, especially in developing countries. National surveillance through the Pakistan Antimicrobial Resistance Surveillance System (PASS), aligned with WHO's GLASS, has demonstrated resistance levels more than 50% among E. coli and Klebsiella pneumoniae to third-generation cephalosporins, fluoroquinolones, and trimethoprim–sulfamethoxazole, while carbapenem resistance was detected below 30% in these isolates.[2,3] These trends leads to failure of empirical treatment and prolong hospital stays, increasing both direct and indirect economic burden.

Data on empyema thoracis, specifically AMR patterns in Pakistan remain limited. A descriptive cross-sectional study from Bahawalpur of N = 110 reported a 52.7% culture positive yield, with Pseudomonas aeruginosa (18.8%), Klebsiella spp. (10%), and E. coli (10%) as the most frequently isolated bacteria. Most showed high-level resistance to empirical regimens such as piperacillin/tazobactam, while sensitivity was preserved to agents like colistin, tigecycline, fosfomycin, and vancomycin.[4] A separate cohort in Abbottabad ($n \approx 219$) found culture positivity in 32.9%, with low susceptibility (~28%) to cefotaxime, ciprofloxacin, gentamicin, and co-amoxiclav [5]. Together, these results highlight that one-third to half of cultures yield positive results, and the resistance to most commonly used antibiotics is increasing.

Despite the existence of the National AMR Action Plan and PASS, national surveillance experiences major gaps, especially in under-reported regions like Balochistan, and lacks a standardized, empyema-specific antibiogram to guide empirical therapy.[6] In Pakistan's socio-economic conditions, characterized by a mix of public and private healthcare, delayed or inappropriate antibiotic therapy can have the worst financial and clinical consequences.[2]

This study characterizes the microbiological spectrum and antibiotic susceptibility profiles of empyema thoracis patients in our institute. By formulating local antibiograms and analyzing resistance trends, this work will form empirical guidelines for antibiotic therapy tailored to Pakistani socioeconomic conditions.

Methodology

This ambispective (retrospective–prospective) descriptive case series was conducted in the Department of Thoracic Surgery, Services Hospital, Lahore, Pakistan, from March 1, 2023, to February 28, 2025. The study identified microbial pathogens isolated from empyema thoracis patients and assessed the prevalence of multidrug-resistant (MDR) strains. Multidrug resistance was defined according to international consensus criteria as non-susceptibility to at least one antimicrobial agent in three or more relevant drug classes,[7] applied separately for Gram-negative organisms (β-lactams, cephalosporins, carbapenems, fluoroquinolones, aminoglycosides, folate pathway inhibitors) and Gram-positive organisms (β-lactams, macrolides, lincosamides, fluoroquinolones, aminoglycosides, glycopeptides, tetracyclines)

The study design included both retrospective and prospective components. A structured study questionnaire was formulated in March 2024. From that date onward, pleural fluid culture results of all empyema patients were prospectively collected and entered into a dedicated study database to ensure data completeness. For the retrospective component, records of eligible empyema cases presenting in the initial months of the study period were retrieved from the inpatient department culture register. Data compilation was done between March 1 and April 15, 2024. By prospectively maintaining complete culture records, we minimized common retrospective biases such as missing information and variability in documentation. The study population included consecutive adults aged ≥18 years diagnosed with empyema thoracis, defined by the presence of purulent/infected pleural fluid or a positive culture supported by imaging and clinical features. Patients requiring pleural drainage or surgical management were included. Patients were excluded if records didn't have essential information (demographics, culture results, or susceptibility profiles) or if pleural fluid specimens were inadequate or contaminated.

Pleural fluid specimens were collected under aseptic measures and processed with Gram staining, culture, and identification by MR numbers. Antimicrobial susceptibility testing was performed and interpreted according to the Clinical and Laboratory Standards Institute (CLSI) guidelines. [8, 9]

Data were entered into SPSS version 26.0 for statistical analysis. The ambispective design allowed us to strengthen the study by including a full consecutive series of cases over two years, combining the retrospective data with the prospective data collection. This approach minimized bias by ensuring completeness of data, prospective standardization of data variables, and consistency in MDR classification, while sensitivity checks confirmed that retrospective and prospective datasets were comparable in baseline characteristics.

The study was approved by the Institutional Review Board of the Services Institute of Medical Sciences (reference no. IRB/2025/1535/SIMS, issued February 11, 2025). Written informed consent for diagnostic and surgical procedures, including the use of pleural fluid samples, was obtained at the time of chest intubation from the prospective cohort in accordance with institutional ethics policies.

Results

A total of 581 patients with empyema thoracis were included in this study, of whom 527 (90.7%) had positive bacterial cultures. All patients were ≥ 18 years of age. Males constituted 398 cases (68.5%), while females accounted for 183 cases (31.5%).

Table 1. Baseline demographic characteristics of patients with pleural effusion

Variable	N	%
Total patients	581	100.0
Positive bacterial cultures	527	90.7
Age groups		
≥18 years	581	100.0
Sex		
Male	398	68.5
Female	183	31.5

Among the culture-positive organisms, aerobic Gram-negative bacteria were predominant, representing 386 cases (73.2%), whereas aerobic Gram-positive bacteria accounted for 141 cases (26.8%). Approximately 54 (10%) of cultures yielded no bacterial growth.

Among the culture-positive patients, 280 (53%) had a single pathogen, 184 (35%) had two pathogens, and 63 (12%) had three or more pathogens.

In gram negative organisms the most common isolate was Pseudomonas aeruginosa (167; 32%), followed by Klebsiella spp. (51; 10%), Escherichia coli (48; 9%), and Acinetobacter spp. (47; 9%). Other gram-negative bacterial infections were observed in 19% of cases.

In Gram-positive organisms Staphylococcus aureus was the most frequent isolate identified in 47 patients (33%), followed by streptococcus species in 45 (32%) while all other Gram-positive bacteria accounted for an additional (49) 35% of cases.

The bacterial antibiotic sensitivity results showed that they were more sensitive to the aminoglycosides gentamycin 177 (30.5%) and amikacin 171 (29.4%), the carbapenems meropenem 187 (32.2%) and imipenem 166 (28.6%), and combinations such as piperacillin-Tazobactam 179 (30.8%) as shown in the Figure 3 below.

Antimicrobial resistance predominated among the isolates, as shown in Table 2. The highest resistance was observed for ciprofloxacin (246; 42.3%) and trimethoprim/sulfamethoxazole (175; 30.1%). Penicillin resistance was 28.7% for ampicillin and 22% for amoxicillin/clavulanic acid.

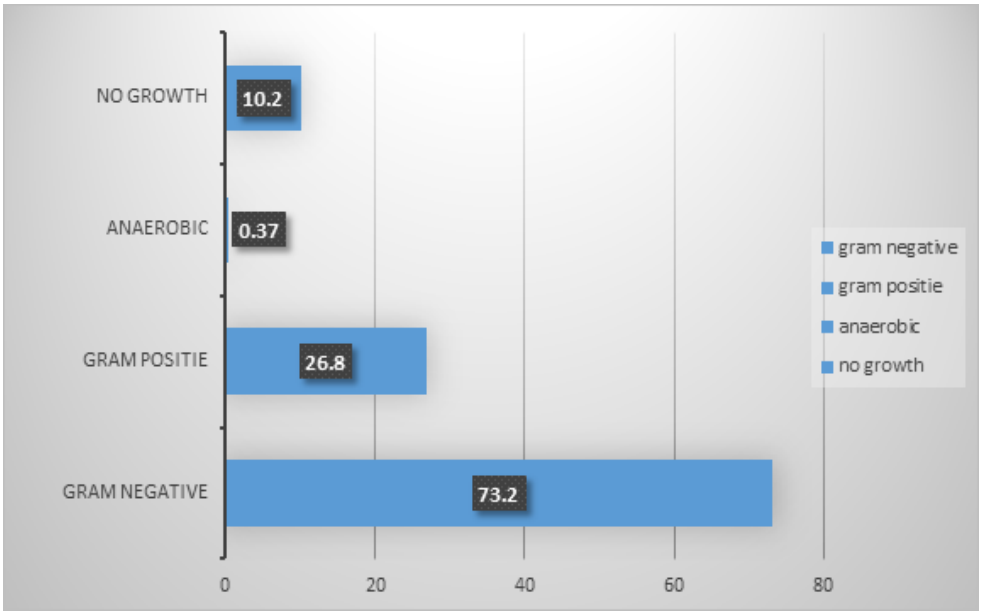

Figure 1: Percentages of Growth on Cultures

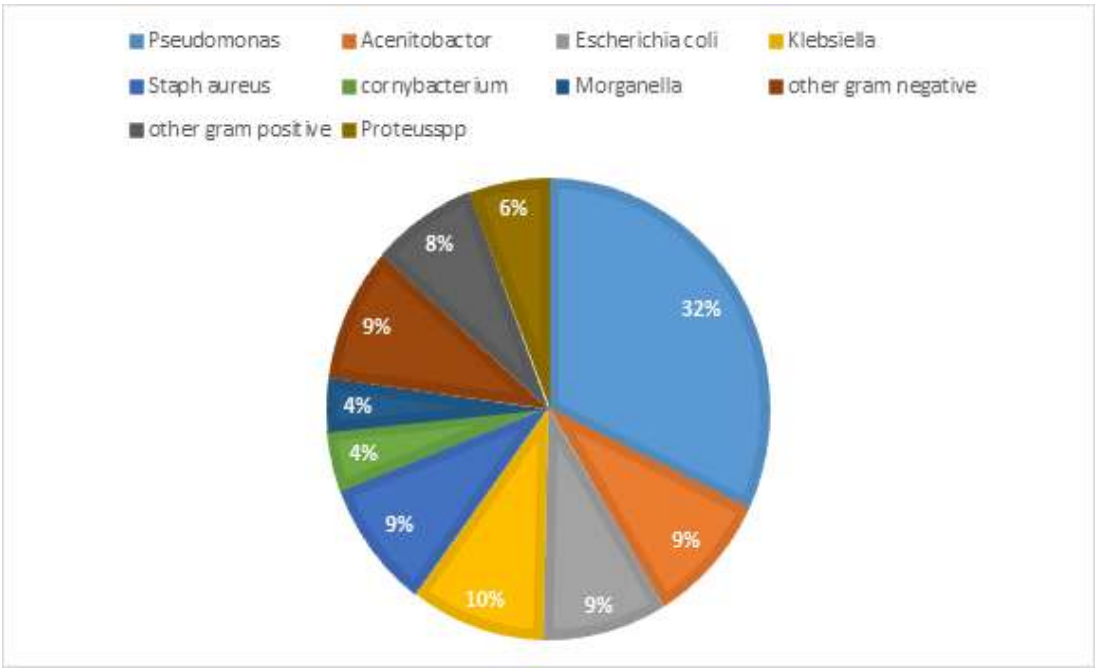

Figure 2: Collective Positive bacterial Cultures

The mean resistance rate for Gram-negative antibiotics was significantly higher compared to Gram-positive antibiotics (22.4% vs. 2.7%, respectively; $p < 0.001$, independent t-test). Gram-negative pathogens, the predominant causative organisms in empyema thoracis, exhibited significantly higher resistance than Gram-positive bacteria, as shown in Table 3.

Across the five half-year periods, from 527 positive bacterial cultures, 274 (52.1%) were MDR, and its prevalence fluctuated between 53.7% and 62.7% across intervals at an average of 55.3%. A chi-square test for association demonstrated significant variation in MDR rates between periods ($p = 0.008$). The observed values demonstrate non-linear temporal fluctuations, showing the MDR pattern in Figure 4.

Discussion

In this large ambispective case series of 581 patients with empyema thoracis (527 culture-positive, 90.7%), three interrelated and clinically important findings stand out. First, aerobic Gram-negative organisms predominated (386/527, 73.2% of culture-positive isolates), with Pseudomonas aeruginosa the single most frequent pathogen (167 isolates, ~32%). Second, polymicrobial infections were common. Third, antimicrobial resistance among Gram-negative pathogens was high and clinically concerning, including substantial levels of carbapenem resistance. These observations have direct implications for the selection of empirical therapy, infection control, and regional antimicrobial stewardship. Our very high culture positivity is likely explained by the selection of patients requiring drainage

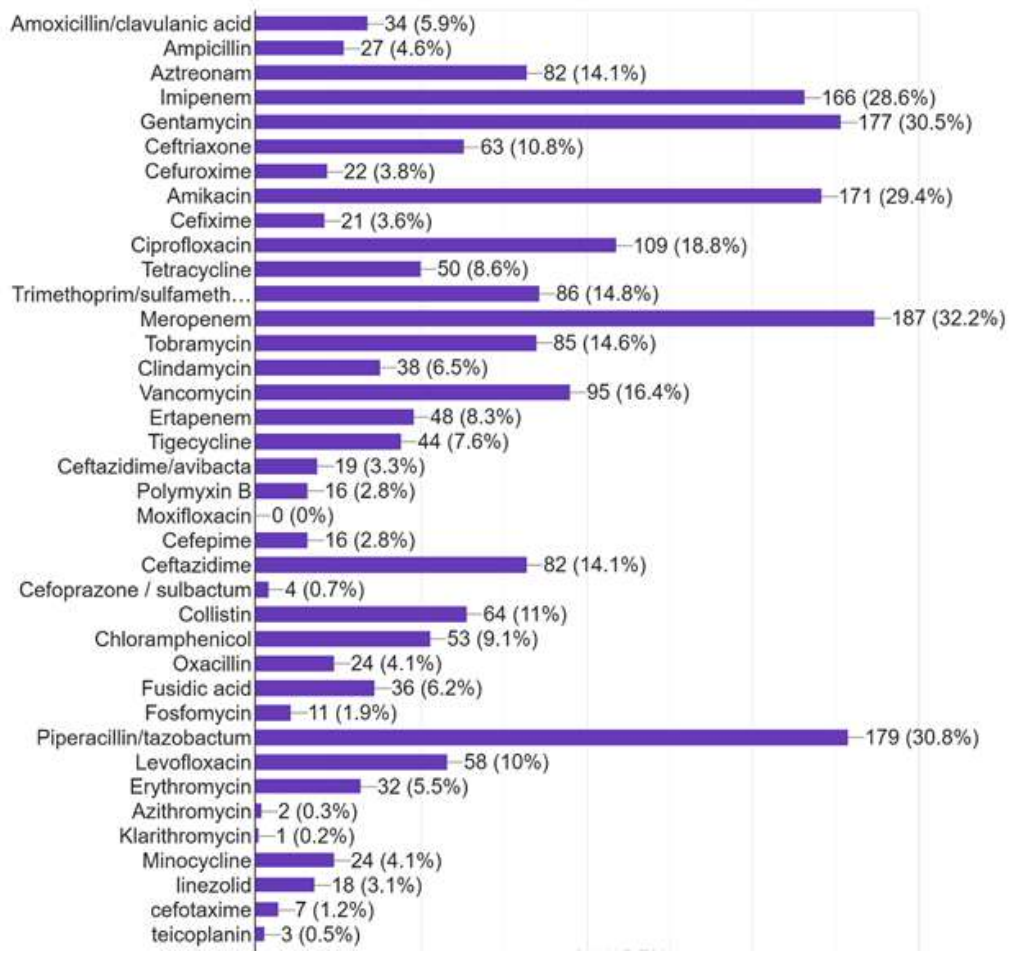

Figure 3: Antibiotic Sensitivity Pattern of Bacterial Organisms

Table 2: Culture-based antibiotic resistance pattern

Antibiotic Class	Antibiotic	Resistance in organisms' n (%)
β-lactams (Penicillins)	Amoxicillin/clavulanic acid	128 (22.0)
	Ampicillin	167 (28.7)
	Piperacillin/tazobactam	173 (29.8)
Cephalosporins	Ceftriaxone	135 (23.2)
	Cefuroxime	117 (20.1)
	Ceftazidime	102 (17.6)
	Cefepime	28 (4.8)
Carbapenems	Imipenem	168 (28.9)
	Meropenem	159 (27.4)
Monobactams	Aztreonam	129 (22.2)
Aminoglycosides	Gentamicin	152 (26.2)
	Amikacin	123 (21.2)
	Tobramycin	82 (14.1)
Fluoroquinolones	Ciprofloxacin	246 (42.3)
	Levofloxacin	138 (23.8)
Folate Pathway Inhibitors	Trimethoprim/sulfamethoxazole	175 (30.1)
Tetracyclines	Tetracycline	75 (12.9)
Glycopeptides	Vancomycin	3 (0.5)
Macrolides	Erythromycin	50 (8.6)

or surgical intervention (enriching for higher bacterial load), prospective and standardized specimen collection with prompt laboratory processing, and the referral bias inherent in a tertiary thoracic surgery service. These factors contrast with retrospective or mixed cohorts, where yields are often lower (50–60%) in Pakistan.[4, 10] Improved culture techniques, such as bedside inoculation into blood culture bottles and use of molecular diagnostics, have also been shown to increase yields internationally.[11, 12]

The predominance of Gram-negative aerobes, particularly P. aeruginosa and Enterobacteriaceae, contrasts with older reports where Gram-positive cocci predominated. Recent national and regional studies have similarly reported a predominance of Gram-negative bacteria in empyema.[13,14.] Comparable trends have been described internationally: in Nigeria, Klebsiella pneumoniae was the leading cause of empyema,[15] while in Qatar, a recent study highlighted Pseudomonas and other Gram-negative organisms in a substantial proportion of cases.[17] Global reviews also confirm this epidemiological shift.[11,18] From an antimicrobial stewardship perspective, our antibiogram is concerning. Fluoroquinolone and TMP-SMX resistance were high, and although carbapenem resistance was not universal, its prevalence (~28%) mirrors regional reports from Pakistan and exceeds 30% in recent global analyses of P. aeruginosa.[14, 18] Preservation of susceptibility to aminoglycosides and glycopeptides was also noted, consistent with other reports from South Asia and beyond.[13, 15]

Our analysis revealed a high overall multi-drug resistance prevalence (55.3%) with significant variability across half-year intervals ($p = 0.008$), indicating that resistance patterns in empyema thoracis are dynamic rather than stable. Such temporal fluctuations are likely caused by medication practices and infection-control measures. Shorter reporting cycles, rather than annual reviews, may better inform empiric therapy and guide effective antimicrobial stewardship.[2, 18]

Our study fills a critical gap for thoracic surgery-treated pleural infections in Pakistan, providing up-to-date, center-level data to guide empiric therapy for empyema thoracis. Future work should focus on multicenter studies, incorporation of anaerobic and molecular diagnostics, and linking microbiological findings to patient outcomes. These steps will help build the evidence base needed for national guidelines and contribute to global antimicrobial resistance (AMR) reporting systems.

Table 3: Mean Antimicrobial Resistance in Gram-negative versus Gram-positive Bacteria

Bacterial Group	Mean Resistance Rate (%)	Statistical Test	p-value
Gram-Negative	22.4	Independent t-test	<0.001
Gram-Positive	2.7		

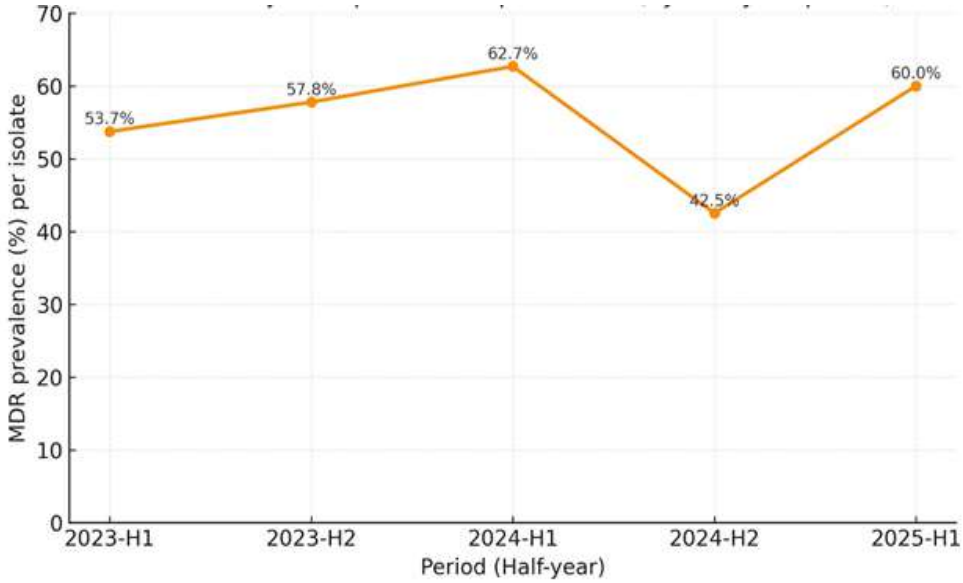

Figure 4: Six-monthly MDR prevalence rates

Limitations

This study has several limitations. Tuberculous and fungal empyema were not properly excluded despite their high regional prevalence. This may have led to the missing of some cases as culture-negative bacterial empyema. The absence of anaerobic cultures and molecular diagnostics likely underreports organisms and resistance mechanisms. Undocumented previous antibiotic exposure among referred patients may have reduced culture yield. The single-center, convenience sampling design from a tertiary-care referral hospital limits generalizability and introduces selection bias. Finally, incomplete outcome data limits meaningful analysis of clinical endpoints, and therefore, the findings should be interpreted as center-level microbiological results informing local empiric therapy and antimicrobial stewardship.

Conclusion

Empyema thoracis in our cohort was predominantly caused by multidrug-resistant Gram-negative organisms, particularly Pseudomonas aeruginosa, with the highest susceptibility mainly to amikacin, carbapenems, and vancomycin. By providing region-specific data from thoracic surgery patients in Pakistan, this study offers clinicians practical guidance for empirical antibiotic therapy and establishes a foundation for multicenter, prospective research. For clinicians, the key message is that dependence on conventional empiric regimens is unsafe in this setting; empiric therapy should be guided by local antibiograms and culture results.

Authors' Contributions: ZS contributed to the conception and design of the study, acquisition and analysis of data, interpretation of findings, and drafting of the original manuscript. MSN contributed to the conception of the study, data curation, statistical analysis, interpretation of findings, and critical revision and editing of the manuscript for important intellectual content. AA contributed to the literature review, verification of data, manuscript preparation, and visualization of data, and assisted in interpretation of findings. All authors reviewed and approved the final version of the manuscript and agree to be accountable for all aspects of the work.

Conflict of Interest: The authors declare that they have no known competing financial interests that could have appeared to influence the work reported in this paper.

Funding: The research was funded by the personal efforts of the authors.

Data availability statement: All data are included in this article; further details are available from the corresponding author upon reasonable request.

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Journal of University College of Medicine & Dentistry

Original Article

Age and Gender Related Morphometric Analysis of the Fourth Ventricle Using MRI in Healthy Adults: A Cross-Sectional Study

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Submission: 15th October, 2025
First revision: 21st November, 2025
Second revision: 18th December, 2025
Final Revision: 28th December, 2025
Acceptance:4th January, 2026

DOI: https:// 10.51846/jucmd v5i1.4817

Cite this article as:

Sughra A, Mohiuddin M, Kumar H, Kumar K. Age- and gender-related morphometric analysis of the fourth ventricle using MRI in healthy adults: a cross-sectional study. J Univ Coll Med Dent. 2026;5(1): 33-38.

Abstract

Objective: To analyze age- and gender-related differences in the length and width of the fourth ventricle using MRI in healthy adults in two different age groups.

Methodology: This cross-sectional study was conducted in the Department of Anatomy and Radiology of Jinnah Postgraduate Medical Centre, Karachi, from November 2019 to December 2021. The study was carried out on 206 healthy subjects. divided into two age groups: Group A (20–40 years) and Group B (41-60 years). Both groups included male and female participants with no clinical symptoms or metallic implants. Images were acquired using a thin-slice (1 mm) 3D brain MRI protocol on a 1.5-Tesla scanner (T1-weighted, T2-weighted, and FLAIR sequences). Fourth-ventricle dimensions were measured on axial images using MicroDicom: length was measured craniocaudally at the midline (roof-to-floor), and width was measured transversely at the level of the lateral recesses.

Results: The fourth ventricle was slightly larger in males than in females in both age groups. In Group A (20–40 years), males had a mean length of 14.3 ± 1.16 and width of 13.6 ± 1.36, compared to females (length 13.8 ± 0.91, width 12.9 ± 1.35; $p = 0.007$). In Group B (41–60 years), males were slightly larger (length 14.7 ± 1.19, width 13.9 ± 1.19) than females (length 14.5 ± 1.02, width 13.6 ± 1.21), without statistical significance. Age-related comparison showed a significant increase in females' length ($p = 0.001$) and width ($p = 0.005$), while males showed no significant change (all values in mm).

Conclusion: The study provides MRI-based normative reference values for fourth-ventricle dimensions in healthy Pakistani adults, demonstrating modest gender differences and age-related enlargement, particularly in females. These population-specific measurements serve as an important baseline for distinguishing normal anatomical variation from pathological ventricular dilation in clinical practice.

Keywords: Fourth ventricle, Magnetic resonance imaging, Normative reference values, Ventricular morphometry

Introduction

The fourth ventricle is a cerebrospinal fluid (CSF)-filled cavity situated in the posterior cranial fossa between the pons, medulla oblongata and the cerebellum. It forms a crucial segment of the brain's ventricular system linking the cerebral aqueduct with the third ventricle above, and central canal of spinal cord below.[1] It is adjacent to critical brainstem structures and CSF pathways so its size and/or shape is often subjected to the changes, associated with conditions such as hydrocephalus, posterior cranial fossa masses, or obstruction to CSF flow.[2,3] Precise evaluation of fourth ventricular dimensions is therefore important to distinguish normal anatomical variations from pathological ventricular enlargements in clinical practice.[4,5]

Neuro-circuitry development in the human brain continues until approximately 30–40 years of age; however, degenerative changes gradually appear as the age advances. Age-related cortical atrophy, accompanied by compensatory ventricular enlargement, poses a significant challenge for physicians, neurologists, and radiologists when distinguishing normal aging from pathological conditions.[6] Pathological dilatation of the ventricles can compress nearby critical structures, further complicating clinical assessment.[7] Before the advent of non-invasive imaging modalities such as CT and MRI, clinicians relied on invasive and hazardous techniques, including pneumoencephalography and contrast ventriculography. In the present study, MRI was selected instead of CT because MRI provides safer imaging without ionizing radiation and offers superior visualization of brain fluids and soft tissues in sagittal, axial, and oblique planes without requiring changes in patient posture.[8,9]

Despite several international studies examining ventricular dimensions to differentiate normal from diseased brains, there remains a clear lack of population-specific, MRI-based normative reference values for the fourth ventricle in Pakistan.

Ventricular size is known to vary with ethnic, genetic, and anthropometric factors, yet no MRI study has established normative fourth-ventricular measurements for Pakistani adults, which represents a significant diagnostic gap. Although some regional studies have addressed ventricular morphometry, most have relied on CT imaging, which provides inferior soft tissues contrast and less accurate delineation of ventricular boundaries compared to MRI.[10,11] Furthermore, age- and gender-related variations in fourth-ventricle dimensions remain poorly documented, particularly in adults aged 20–60 years, despite evidence that ventricular size changes with aging and differs between males and females. This lack of regional reference population datasheet is clinically important because the fourth ventricle lies close to several essential nuclei and plays a critical role in cerebrospinal fluid circulation.[12,13] Even subtle deviations in its dimensions may signal early hydrocephalus, CSF-flow obstruction, posterior-fossa tumors, Chiari malformation, or Dandy–Walker malformations.[7,14]

Despite extensive research on the lateral and third ventricles, global data on fourth-ventricle morphometry remain limited, and to our knowledge, no MRI-based normative measurements exist for the Pakistani population. Accurate morphometric data are essential for identifying abnormal ventricular enlargement or posterior fossa pathologies, yet clinicians in Pakistan currently lack reference standards for comparison. To address this gap, the present study was undertaken to provide detailed morphometric measurements of the fourth ventricle in healthy Pakistani adults aged 20–60 years of both genders. The objective was to evaluate age- and sex-related variations in fourth-ventricle dimensions, thereby establishing foundational MRI-based normative data for clinical and research applications in the local population.

Methodology

This analytical cross-sectional study was conducted in the Department of Anatomy, Basic Medical Sciences Institute (BMSI), in collaboration with the Department of Radiology, Jinnah Postgraduate Medical Centre (JPMC), Karachi. The study was conducted from November 2019 to December 2021 after approval by the Institutional Review Board (Ref. #F.2-81/2019-GENI/35808/JPMC, dated 25 October 2019). The study period was prolonged due to intermittent interruptions in imaging services during the COVID-19 pandemic. All patient data were anonymized and handled with strict confidentiality in accordance with ethical standards. A total of 206 adult volunteers were recruited. Participants were considered clinically healthy for research purposes. However, the sample was not fully representative of the general population. A selection bias was present because many volunteers approached the radiology department for mild, non-specific complaints such as headaches, vertigo, or visual discomfort, and a subset requested MRI due to a family history of brain tumors. These factors are explicitly acknowledged as potential contributors to population bias.
Although these symptoms were not linked to any diagnosed neurological condition and did not meet exclusion criteria, they were unevenly distributed across groups. Participants were divided into two age groups to assess age-related variation in fourth-ventricle morphology: Group A (20–40 years) and Group B (41–60 years). In Group A, reported symptoms included headaches (34%), visual disturbances (29.4%), vertigo (22.8%), and mood changes (17.9%). In Group B, vertigo was more common (44%), followed by visual disturbances (16%), headaches (18%), and mood changes (7%). Notably, approximately 15% of Group B participants were asymptomatic and underwent MRI due to a positive family history of brain tumors. All individuals were clinically evaluated and deemed neurologically fit prior to inclusion.

The sample size was calculated using OpenEpi, with a 95% confidence interval and 5% margin of error. Consecutive sampling was used to recruit healthy adults aged 20–60 years. Participants with neurological disorders, brain abnormalities, or prior cranial surgery were excluded. Both males and females were included, as ventricular measurements may vary with age and gender. Before imaging, all participants received an explanation of the study and signed written informed consent. A brief medical and neurological screening was performed. Exclusion criteria included any history of intracranial surgery, diagnosed neurological disorders (such as stroke, tumors, or demyelinating disease), systemic conditions that could alter brain morphology, and MRI contraindications like pacemakers or metallic implants. MRI scans were obtained using a Toshiba Vantage Elan 1.5-Tesla scanner (2017) at the JPMC Radiology Department. Standardized brain MRI protocols were followed. T1-weighted and T2-weighted images were acquired in the axial plane, while FLAIR sequences were acquired in the coronal plane. All sequences used a 1-mm slice thickness, appropriate for precise morphometric assessment of ventricular boundaries. Repetition time (TR) and echo time (TE) values were selected according to standard diagnostic protocols. Total scan time was approximately 25–30 minutes.15 All scans were performed by a senior MRI technologist with over 10 years of experience, and images were reviewed by an Associate Professor of Radiology.

Fourth-ventricle measurements were performed on axial MRI images using MicroDicom software. Although MRI scans were acquired in 3D, 2D axial measurements were used because these planes provide the clearest and most reproducible view of ventricular boundaries, allow comparison with previous studies, and reflect clinically relevant dimensions. Length was measured craniocaudally at the midline, and width transversely at the lateral recesses. All measurements were repeated by the same observer to assess intra-observer reliability, and a subset was measured independently by a second observer for inter-observer reliability using consistent anatomical landmarks.
Data was analyzed using SPSS version 19.0. Quantitative variables were compared between age groups using the independent samples t-test, provided normality assumptions were satisfied. A p-value < 0.05 was considered statistically significant.

Results

Study subjects were 206, divided into group A, which comprises 106 (51.5%), and group B, which comprises of 100 (48.5%) subjects. The total number of males and females in both groups was 102 (49.5%) and 104 (50.5%), respectively, as shown in Figure 1.

Morphometric measurements of the fourth ventricle were recorded in millimeters (mm) for both length and width. In Group A, males had a greater mean length (14.3 ± 1.16)

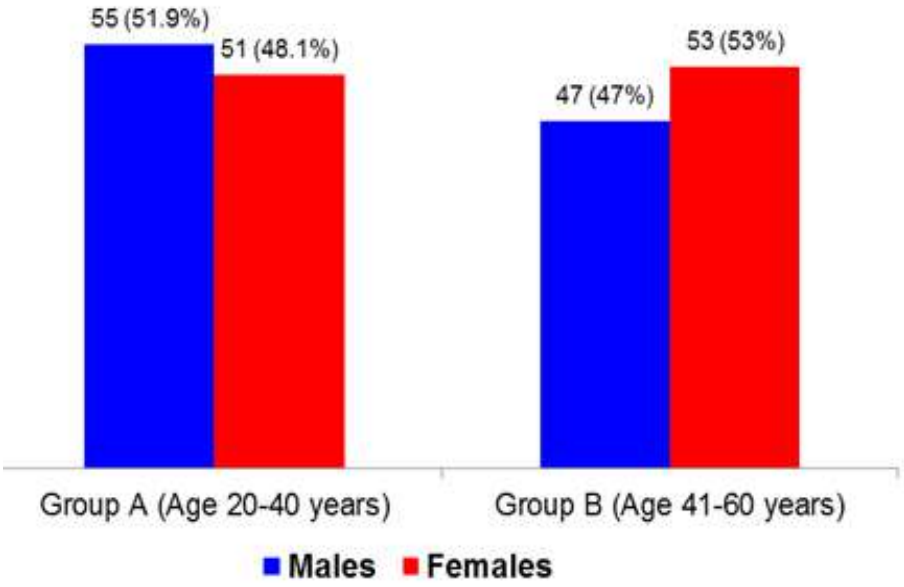

Figure 1: Gender distribution of participants across age groups.

compared with females (13.8 ± 0.91). Similarly, mean width was higher in males (13.6 ± 1.36) than in females (12.9 ± 1.35), with the difference reaching statistical significance (p = 0.007). In Group B, males also showed slightly higher values than females, with mean length of 14.7 ± 1.19 in males versus 14.5 ± 1.02 in females, and mean width of 13.9 ± 1.19 versus 13.6 ± 1.21, although these differences were not statistically significant. The results are summarized in Table 01 and Figure 2.

Table 1: Gender-based comparison of fourth ventricle dimensions within age groups

Dimensions	Male (n=55)	Female (n=51)	P-value
Group A (20-40) years			
Length	14.3 ± 1.16	13.8 ± 0.91	0.007
Width	13.6 ± 1.36	12.9 ± 1.35	0.007
Group B (41-60) years			
Length	14.7 ± 1.19	14.5 ± 1.02	0.317
Width	13.9 ± 1.19	13.6 ± 1.21	0.170

Table 2: Age-based comparison of fourth ventricle dimensions stratified by sex

Dimensions	Age (20-40) years	Age (41-60) years	P-value
Male			
Length	14.3 ± 1.16	14.7 ± 1.19	0.081
Width	13.6 ± 1.36	13.9 ± 1.19	0.184
Female			
Length	13.8 ± 0.91	14.5 ± 1.02	0.001
Width	12.9 ± 1.35	13.6 ± 1.21	0.005

Morphometric measurements were recorded in millimeters (mm) for both length and width. Comparison of males between Group A and Group B showed no significant differences in length (14.3 ± 1.16 vs. 14.7 ± 1.19) or width (13.6 ± 1.36 vs. 13.9 ± 1.19). In females, however, Group B showed significantly larger dimensions than Group A, with length of 14.5 ± 1.02 versus 13.8 ± 0.91 (P = 0.001) and width of 13.6 ± 1.21 versus 12.9 ± 1.35 (P = 0.005). These findings are summarized in Table 02 and Figure 02.

Discussion

The study provides MRI-based morphometric dimensions of fourth-ventricle in Pakistani healthy adults and age- and sex-related variations among two age groups. Observations exhibit that males generally have slightly larger measurements of fourth-ventricle than females. Group A males have length and width 14.3 ± 1.16 mm and 13.6 ± 1.36 mm whereas females have 13.8 ± 0.91 mm and 12.9 ± 1.35 mm respectively (Table 1, Figure 2).

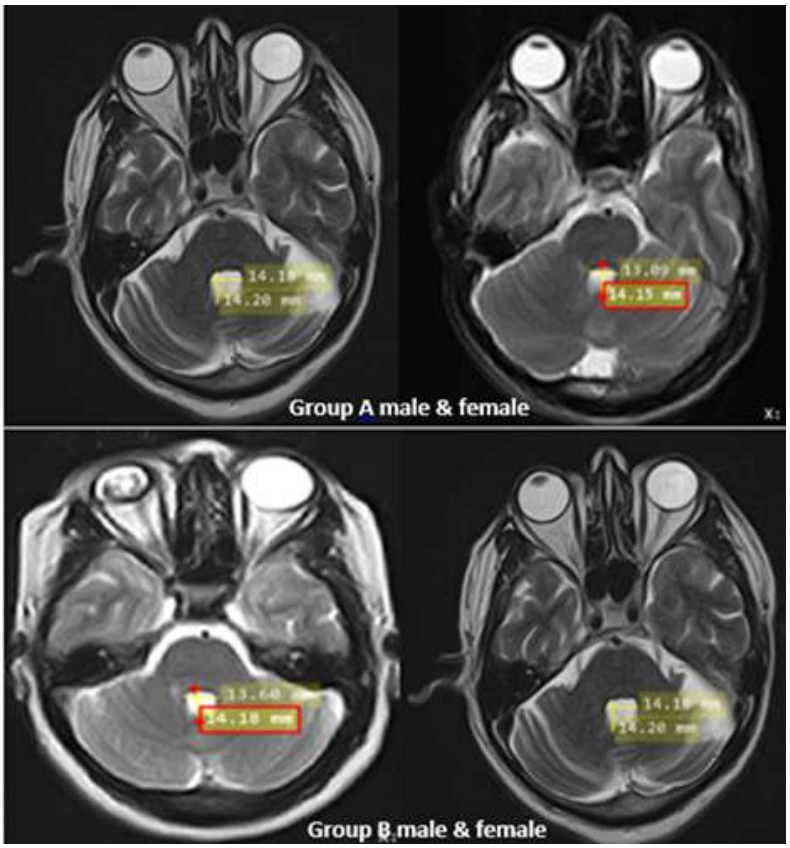

Figure 2: Comparison of fourth ventricle measurements across age groups and sex

Comparison between two age groups show no significant change in males, whereas Group B females in comparison to Group A females demonstrate a significant increase in length as well in width (Table 2, Figure 2). These results provide standard parameters for Pakistani population and distinguish normal anatomical dimensions from pathological enlargement of fourth ventricles.

The observed sex variances are constant with well-known biological patterns, as males typically have larger cranial fossae, contributing to slightly greater ventricular dimensions. Age-related enlargement in females reveals physiological parenchymal atrophy, which gradually decreases posterior fossa parenchymal volume and allows fourth ventricle modest compensatory expansion. These anatomical based changes are physiological rather than pathological or disease-related alterations. These physiological tendencies line up with previous morphometric observations of different regions show mild increases in ventricular measurements with age and gender differences in healthy adults.[15,16] Comparisons with other studies point out both methodological and population-based variations. Multiple Indian CT-based studies have demonstrated larger fourth-ventricle measurements than those in our study. CT-based study from Jaipur reveal fourth-ventricle mean values (12.57 mm in males and 11.58 mm in females), with significant age and sex related variations; and from South Indian reported mean dimensions (12.16 mm in males and 11.38 mm in females), also showing sex-related differences.[18] A study from North India also shows the same result.[19] A Bangladeshi CT research reveal larger fourth-ventricle dimensions in males and with progressively enlargement with age and sex.[20] An MRI- based study from Northern India exhibits fourth-ventricle dimensions of 13.12 mm in males and 12.62 mm in females highlight regional anatomical similarities.[21] MRI-based study in Nepalese reveal that fourth-ventricle sizes increase a little with age and are larger in males than females, reflecting patterns comparable to those in our Pakistani population (Singh et al., 2020; Yadav & Yadav, 2025).[22] In Saudi Arabia, CT-based morphometric study by Gameraddin et al. (2015) reported fourth-ventricle dimensions, endorsing sex-related size variants and reflects the importance of population-specific reference measurements.[23] Similar differences have been shown in a Nigerian study.[24]

All over the South Asia, fourth-ventricle dimensions are influenced by both gender and age, stressing the need for regional data rather than relying on external references (Patra et al.2025).[20] CT-based studies may overvalue dimensions due to thicker slices and partial-volume effects, while our 1-mm thin-slice 3D MRI allows precise dimension (Sinha et al., 2023; Kolsur et al. 2018).[16,18] Variations of measurements in different regional studies might be due to direction and planes of slices, and demographic factors. These factors spot the novelty and clinical status of our MRI-based normal anatomical data sheet for Pakistani population in reference to differentiate from pathological enlargement. Clinically, regional reference values are important for accurate measuremental deviations in fourth-ventricular dimensions that may indicate early hydrocephalus, CSF-flow obstruction, Chiari malformation, or other posterior fossa lesions.[8,25]

These measurements from our study provide a baseline for radiologists and neurosurgeons to distinguish anatomical dimensions from pathological lesions, and should be

interpreted cautiously in old adults; as mild enlargement may be physiological.

Over all, our study gives significant, regional-specific MRI data for our population and align up with global norms indicating age and gender related ventricular dilatation. Meanwhile the observational variations among the populations, highlight the importance of regional reference data sheets for clinical interpretation. It can enhance the diagnostic efficacy of MRI in distinguishing normal anatomical regional variation from pathological ventricular dilatation and play a foundation for future morphometric research in the population of South Asian.

Limitations

The study has many limitations. It was conducted at a single center, which may restrict the generalizability of the results to broader populations. Although the data included 206 participants, divided by age and gender decrease the statistical analyses. Intra-observer and inter-observer reliability was assessed and evaluated for consistency of dimensions. However, 2D linear dimensions were used on selected axial slices rather than full 3D volumetric analysis, which may not catch complete ventricular dimensions. Engaging healthy volunteers for MRI was tough and time-taking, and lead to slower and more selective registration. Yet, this study creates the first MRI-based anatomical reference values for fourth-ventricle measurements in healthy Pakistani population and provides a foundation for future multicenter, longitudinal, and volumetric studies. Moreover, some participants underwent MRI for minor symptoms like headache and vertigo, or family history, which may lead selection bias and limit the presentation of the sample.

Conclusion

This study generates the MRI-based anatomical morphometric dimensions for the fourth ventricle in healthy Pakistani population, demonstrating a major gap in regional reference neuroimaging data. This study establish that fourth-ventricle magnitudes are generally larger in males than females, with gradual age advancement, showing statistical significance observed among females of age groups 20–40 and 41–60 years. This study by developing the baseline measurements, helps the clinicians to distinguish normal age and sex-related changes from abnormal enlargement of the fourth ventricle. These anatomical values can improve diagnostic accuracy for pathological conditions.

Authors' Contributions: AS: Conception and design of the study; data acquisition; drafting of the manuscript; MM: Drafting and revising the manuscript for important intellectual content; HK: Data acquisition and data analysis; critical revision of the manuscript; KK: Critical revision of the manuscript and final approval of the version to be published. All authors meet the ICMJE criteria for authorship and approved the final manuscript.

Conflict of interest: None

Funding: None to declare

Data Availability Statement: The data that support the findings of this study, apart from the data already presented in the results section, are available from the corresponding author upon reasonable request.

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Journal of University College of Medicine & Dentistry

Original Article

Dermatological Manifestations of Chemotherapy in Pediatric Cancer Patients: A Prospective Cohort Study from a Tertiary Center in Pakistan

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Submission: 29th July, 2025
First revision: 16th October, 2025
Second revision: 13th November, 2025
Final Revision: 14th December, 2025
Acceptance: 30th December, 2025

DOI: https://10.51846jucmdv5i1.4373.

Cite this article as:

Khan MR, Yasmeen N, Shaheen H, Manzoor R, Jamshed J. Dermatological manifestations of chemotherapy in pediatric cancer patients: a prospective cohort study from a tertiary center in Pakistan. *J Univ Coll Med Dent*. 2026;5(1): 39-45

Abstract

Objective: Dermatological manifestations are common but under-recognized complications of chemotherapy in children, particularly in low- and middle-income countries (LMICs) such as Pakistan where supportive care systems are limited. This study prospectively assessed the spectrum and onset of dermatological toxicities in pediatric cancer patients at a tertiary care center in Pakistan.

Methodology: A prospective cohort study was conducted from March to December 2023 at the Children's Hospital, Pakistan Institute of Medical Sciences (PIMS) Islamabad, Pakistan. Sixty-eight children (aged 1–13 years) with cancer receiving chemotherapy were enrolled and systematically examined for dermatological manifestations at each cycle by a dermatologist. Dermatological toxicities such as skin, hair, and nail changes were recorded using standardized clinical definitions, and infections were confirmed by microbiological or histopathological testing when indicated. Associations with demographic and treatment characteristics were analyzed using chi-square tests.

Results: Overall, 86.7% of patients developed at least one dermatological toxicity. Nail changes were most frequent (69.1%), followed by skin (57.4%) and hair changes (42.6%). Common findings included Beau's lines (30.9%), maculopapular rash (16.1%), and complete alopecia (25.0%). Most dermatological toxicities appeared within 30 days of treatment initiation and only 7.3% of dermatological toxicities led to temporary treatment delay. Younger children (1–5 years) and those on continuous chemotherapy regimens experienced significantly higher rates of dermatological toxicities (p-value < 0.05). Secondary infections occurred in 29.4% of patients, with viral etiologies predominating.

Conclusion: Dermatological manifestations are highly prevalent and often occur early in pediatric cancer patients receiving chemotherapy, particularly among younger children and those on continuous regimens. Routine dermatological surveillance and timely management should be integrated into pediatric oncology supportive care in Low- and middle-income countries to minimize morbidity and treatment disruption.

Keywords: Chemotherapy, Dermatological toxicities, Low- and middle-income countries, Pediatric cancer, Supportive care

Introduction

Childhood cancer is a growing global health challenge, with approximately 400,000 new cases annually among individuals aged 0–19 years.[1] The burden is disproportionately concentrated in low- and middle-income countries where nearly 90% of childhood cancer deaths occur.[2] Contributing factors include delayed diagnosis, limited treatment access, therapy abandonment, and underdeveloped supportive care systems. In Pakistan, between 8,000 and 12,000 pediatric cancer cases are reported each year; however, underreporting and the absence of comprehensive national registries likely lead to substantial underestimation of the true incidence.[3] Over the past few decades, chemotherapy has transformed outcomes in pediatric malignancies such as acute lymphoblastic leukemia (ALL), lymphomas, and sarcomas, converting previously fatal conditions into treatable diseases.[4] Despite these advances, chemotherapy induces profound immunosuppression and multisystem toxicities, including dermatological adverse effects that are frequently underrecognized in children.[5,6] These cutaneous toxicities manifesting as maculopapular eruptions, alopecia, nail dystrophies, pigmentary alterations, and opportunistic infections are rarely life-threatening but can cause pain, discomfort, psychosocial distress, and, in severe cases, treatment interruption.[7] To date, no pediatric oncology center in Pakistan routinely uses the Common Terminology Criteria for Adverse Events (CTCAE) to grade dermatological toxicities, limiting comparability with global literature.

The pathophysiology of chemotherapy-induced dermatological toxicity is multifactorial, involving direct cytotoxic damage to rapidly dividing epidermal cells, disruption of keratinocyte turnover, drug-related inflammatory responses, and increased susceptibility to infections due to neutropenia and compromised barrier integrity.[8] Agents such as methotrexate, vincristine, doxorubicin, and cytarabine are among the most frequently implicated drugs.[9]

High-income countries (HICs) have established standardized dermatologic surveillance and supportive care protocols, which enable timely recognition and management of chemotherapy-related toxicities.[10] In contrast, Low- and middle-income countries such as Pakistan face critical gaps in detection, documentation, and management of these complications.[11] Key barriers include a shortage of dermatology expertise, limited diagnostic resources for confirmatory testing (e.g., microbiological cultures, skin biopsies), and fragmented follow-up systems. Psychosocial challenges compound these issues, as visible dermatological changes can lead to stigma and significantly impair quality of life in children.

Although previous South Asian studies have examined general chemotherapy adverse effects, few have systematically evaluated dermatological manifestations using predefined criteria, onset timelines, and infection confirmation. Reports from Karachi, Peshawar, and Lahore describe mucocutaneous toxicities as a major source of morbidity but often lack detailed classification of clinical spectrum, temporal onset, and differentiation between infectious and non-infectious etiologies.[12, 13]

This study therefore aimed to comprehensively characterize the onset, duration, clinical patterns, and etiologies (infectious versus non-infectious) of dermatological manifestations in immuno-compromised pediatric patients receiving chemotherapy at a tertiary oncology center in Pakistan. By delineating the frequency and nature of skin, hair, and nail changes, we aim to inform early diagnostic protocols, optimize supportive care, and ultimately improve treatment adherence and quality of life among children with cancer.

Methodology

This prospective observational cohort study was conducted through interdisciplinary collaboration between the Departments of Pediatric Oncology and Dermatology at the Children's Hospital, Pakistan Institute of Medical Sciences (PIMS), Islamabad, Pakistan, from March to December 2023. Ethical approval was obtained from the Institutional Ethical Review Board of Shaheed Zulfiqar Ali Bhutto Medical University (Approval No. F.1-1/2015/ERB/SZABMU/1087, dated 1 March 2023).

Children aged 1–13 years with a confirmed cancer diagnosis who were scheduled to receive chemotherapy were eligible. Patients with pre-existing chronic dermatological disorders unrelated to chemotherapy (e.g., eczema, psoriasis, genetic skin conditions) were excluded. The sample size of 68 children was determined based on the number of newly diagnosed pediatric oncology patients receiving chemotherapy during the study period, allowing comprehensive evaluation of dermatological manifestations across multiple chemotherapy cycles. Written informed consent was obtained from parents or legal guardians, and assent was obtained from children aged ≥ 7 years using age-appropriate forms in both English and Urdu.

Baseline demographic and clinical data, including age, sex, cancer type, chemotherapy regimen, and cycle number, were recorded using a structured proforma developed in consultation with pediatric oncologists, dermatologists, and infectious disease specialists. Chemotherapy regimens were classified as either continuous, with repeated administration of cytotoxic agents without planned breaks, or cyclic, administered in defined cycles with planned recovery periods. Full-body dermatological examinations were performed at baseline and during each chemotherapy cycle by a board-certified dermatologist, with documentation of skin, hair, and nail changes. Laboratory or histopathological investigations, including skin scrapings, nail clippings, bacterial or fungal cultures, and biopsies, were conducted where clinically indicated to differentiate infectious from non-infectious etiologies. Although internationally recognized Common Terminology Criteria for Adverse Events (CTCAE) grading was not used due to resource constraints, detailed qualitative and quantitative documentation of severity was performed.

Dermatological manifestations were categorized into three domains: (i) cutaneous changes (macular, maculopapular, pustular, papular, vesicular, vesiculobullous, maceration, and purpuric lesions); (ii) nail changes (Beau's lines, nail fragility, onycholysis); and (iii) hair changes (partial alopecia, complete alopecia, and hair thinning). Secondary dermatological diagnoses including bacterial, viral, fungal, and parasitic infections, as well as benign drug reactions, were also documented. Figure 1 shows representative clinical features of patients following chemotherapy: (A) cutaneous changes, (B) hair changes, and (C) nail changes. Data were analyzed using IBM SPSS Statistics version 21.0. Descriptive statistics were presented as frequencies and percentages for categorical variables, and as mean ± standard deviation (SD) for continuous variables. Comparative analyses were performed using chi-square test to assess associations between demographic or clinical characteristics (age, sex, diagnosis, and chemotherapy regimen) and dermatological manifestations. To account for cohort size effects, proportion-adjusted comparisons were conducted to ensure that higher toxicity rates in the 1–5 year age group reflected true risk rather than sample distribution. P-values < 0.05 were considered statistically significant.

Results

A total of 68 pediatric cancer patients were enrolled, with a median age of 7 years (IQR: 4–11) and a mean age of 6.2 ± 3.3 years. Males comprised 55.9% (n = 38) and females 44.1% (n = 30). Acute lymphoblastic leukemia (ALL) was the most common malignancy (47.1%), followed by Hodgkin's lymphoma (22.1%) and nephroblastoma (11.8%), while non-Hodgkin's lymphoma, acute myeloid leukemia, and other solid tumors accounted for smaller proportions (Table 1). More than half of the cohort (61.8%) received continuous chemotherapy regimens, and 38.2% received cyclic regimens.

A wide range of chemotherapeutic agents were administered, including vincristine, cytarabine, methotrexate, dexamethasone, etoposide, cyclophosphamide, ifosfamide, doxorubicin, asparaginase, carboplatin, procarbazine, daunorubicin, actinomycin-D, cisplatin, vinblastine, idarubicin, bleomycin, 6-mercaptopurine, cyclosporine, and temozolomide.

Dermatological manifestations were frequent, with hair changes observed in 42.6% (n = 29), nail changes in 69.1% (n = 47), and skin changes in 57.4% (n = 39) (Figure 2). Among cutaneous toxicities, maculopapular rash was most common (16.1%), followed by purpuric lesions (11.8%),

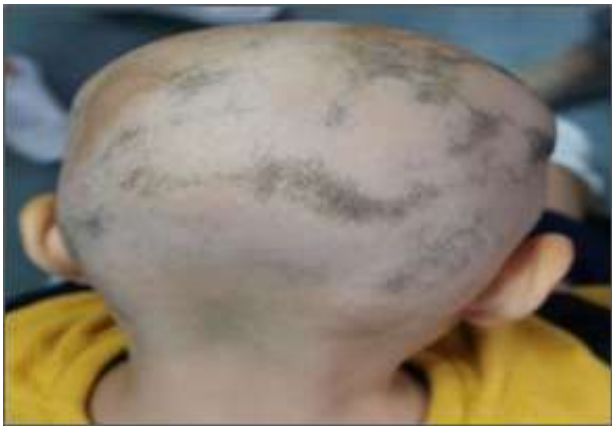
pustular eruptions (10.3%), vesicular rashes (7.3%), macular lesions (5.9%), papular eruptions (2.9%), and vesiculobullous rashes (2.9%). Hair changes included complete alopecia (25.0%), partial alopecia (13.2%), and hair thinning (4.4%). Nail toxicities were dominated by Beau's lines (30.9%) and nail fragility (25.0%), with onycholysis affecting 13.2% of patients. Most manifestations appeared within the first 30 days of treatment initiation ($p < 0.05$) (Table 2).

Table 1: Demographic and clinical information of pediatric patients on chemotherapy.

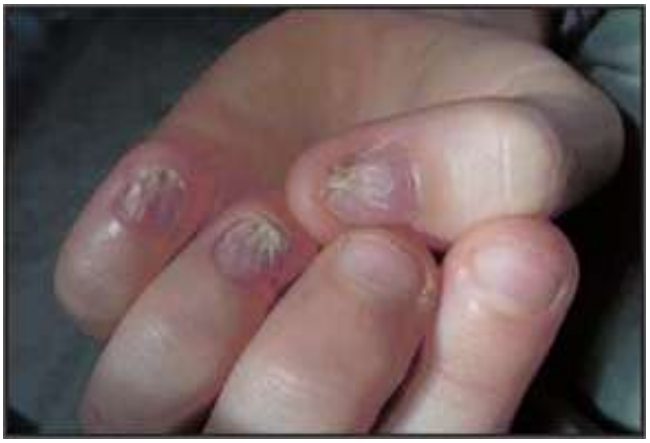
Variable	Categories	N	%
Age (in years)	1-5	34	50
	6-10	22	32.4
	11-13	12	17.6
Sex	Male	38	55.9
	Female	30	44.1
Type of malignancy	Acute Lymphoblastic Leukemia (ALL)	32	47.1
	Non-Hodgkin's Lymphoma (NHL)	6	8.8
	Nephroblastoma (Wilm's Tumor)	8	11.8
	Hodgkin's Lymphoma	15	22.1
	Acute Myeloid Leukemia (AML)	2	2.9
	Others	5	7.3
Chemotherapy regimen	Cyclic	26	38.2
	Continuous	42	61.8

Mean age=6.2 years, SD=3.3

A. Cutaneous changes including erythematous rash.



B. Hair changes demonstrating alopecia



C. Nail changes showing ridging

Figure 1: Dermatological manifestations among pediatric cancer patients

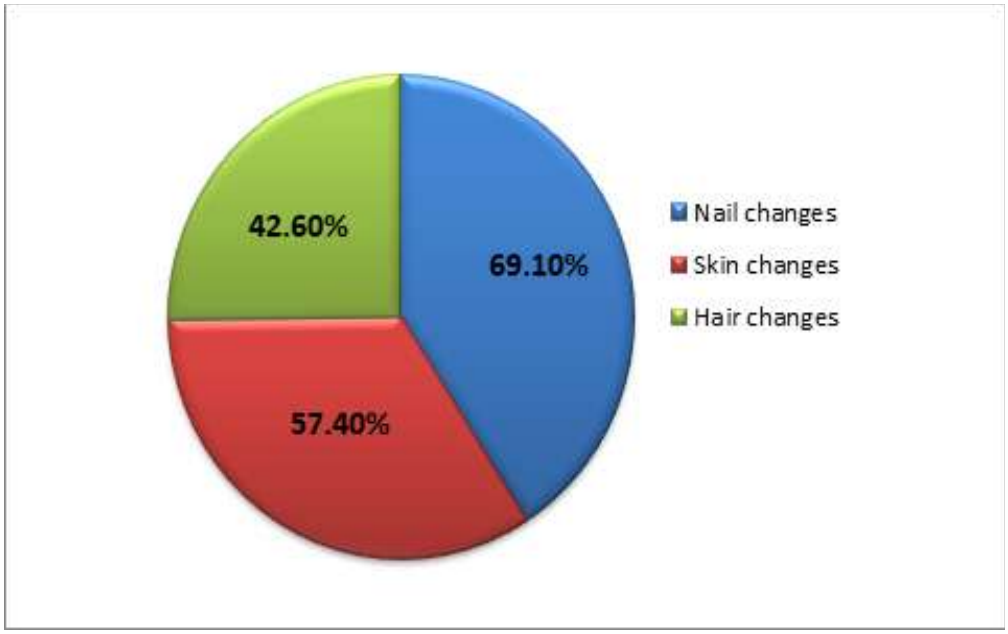


Figure 2: Dermatological manifestations among pediatric cancer patients

Table 2: Frequency and onset of dermatological manifestations among pediatric patients receiving chemotherapy.

Dermatological manifestation		Patients	Time of onset		
			0-30 days	30-90 days	After 90 days
		n (%)	n (%)	n (%)	n (%)
Cutaneous changes	Macular	4 (5.9)	2 (50.0)	1 (25.0)	1 (25.0)
	Maculo-papular	11 (16.1)	7 (63.6)	3 (27.3)	1 (9.1)
	Pustular	7 (10.3)	5 (71.4)	2 (28.6)	0 (0.0)
	Papular	2 (2.9)	1 (50.0)	1 (50.0)	0 (0.0)
	Vesicular	5 (7.3)	3 (60.0)	2 (40.0)	0 (0.0)
	Vesiculobullous	2 (2.9)	2 (100.0)	0 (0.0)	0 (0.0)
	Purpuric	8 (11.8)	5 (62.5)	2 (25.0)	1 (12.5)
Hair changes	Partial hair loss	9 (13.2)	2 (22.2)	4 (44.4)	3 (33.3)
	Complete hair loss	17 (25.0)	3 (17.6)	10 (58.8)	4 (23.6)
	Thinning	3 (4.4)	2 (66.7)	1 (33.3)	0 (0.0)
Nail changes	Beau's lines	21 (30.9)	13 (61.9)	6 (28.6)	2 (9.5)
	Nail fragility	17 (25.0)	11 (64.7)	6 (35.3)	0 (0.0)
	Onycholysis	9 (13.2)	0 (0.0)	6 (66.7)	3 (33.3)

p-value < 0.05

Secondary infections were also observed: viral infections in 19.1%, bacterial infections in 10.3%, fungal infections in 7.3%, and parasitic infestations in 4.4% of patients. Each percentage was calculated using the total study population (n = 68) as the denominator (100%), and categories were not mutually exclusive. Benign drug reactions occurred in 16.2% (Figure 3).

Statistical analysis indicated significant associations between several demographic variables and dermatological toxicities. Age showed a significant association with dermatological manifestations (p-value = 0.04), with the highest frequencies of hair (38.5%), nail (44.7%), and skin changes (37.9%) occurring in children aged 1–5 years. No significant sex-based differences were found (p-value = 0.218), although females showed slightly higher rates of nail and skin toxicities. Trends by malignancy type particularly among children with acute lymphoblastic leukemia and Hodgkin's lymphoma did not reach statistical significance (p-value = 0.062). Chemotherapy regimen demonstrated a significant association, with continuous therapy showing higher rates of dermatological manifestations compared with cyclic therapy (p-value = 0.04) (Table 3)

Table 3: Association of demographic and clinical characteristics with dermatological manifestations among pediatric cancer patients receiving chemotherapy

Variable	Categories	Skin changes	Nail changes	Hair changes	*p*-value
		n(%)	n(%)	n(%)	
Age (years)	1–5	15 (38.5)	21 (44.7)	11 (37.9)	0.04
	6–10	13 (33.3)	16 (34.0)	10 (34.5)	
	11–13	11 (28.2)	10 (21.3)	8 (27.6)	
Sex	Male	21 (53.8)	24 (51.1)	16 (55.2)	0.218
	Female	18 (46.2)	23 (48.9)	13 (44.8)	
Type of malignancy	ALL	17 (43.6)	20 (42.6)	13 (44.8)	0.062
	NHL	3 (7.7)	5 (10.6)	3 (10.3)	
	Nephroblastoma	5 (12.8)	6 (12.8)	4 (13.8)	
	Hodgkin's Lymphoma	8 (20.5)	11 (23.4)	6 (20.7)	
	AML	2 (5.1)	2 (4.3)	1 (3.4)	
	Others	4 (10.3)	3 (6.4)	2 (6.9)	
Chemotherapy regimen	Cyclic	14 (35.9)	17 (36.2)	11 (37.9)	0.04
	Continuous	25 (64.1)	30 (63.8)	18 (62.1)	

Discussion

Chemotherapy frequently causes dermatological adverse effects involving the skin, hair, and nails, since anti-cancer drugs target rapidly proliferating cells. These complications increase morbidity and impair quality of life, and early recognition and management are crucial for maintaining uninterrupted treatment.[13,14] This study characterized the spectrum of dermatological manifestations in pediatric cancer patients on chemotherapy and explored associations with demographic and clinical factors. The findings demonstrated that nail, skin, and hair toxicities were common, often appearing within the first 30 days of treatment. Younger children (1–5 years) and those receiving continuous chemotherapy regimens were significantly more affected, underscoring the need for targeted monitoring and supportive care. Although internationally recognized grading systems such as the Common Terminology Criteria for Adverse Events were not utilized, we employed a structured, dermatologist-validated assessment tool for pediatric patients, ensuring consistent and clinically meaningful classification of toxicities.

We observed that the most frequent malignancies were acute lymphoblastic leukemia (47.1%) and Hodgkin's Lymphoma (22.1%), consistent with Sous et al. (2023), who reported acute lymphoblastic leukemia (42.2%) and Hodgkin's lymphoma (12.0%) as predominant pediatric cancers.[15] In our study, nail changes (69.1%) were the most common adverse effect, followed by skin (57.4%) and hair changes (42.6%), aligning with Deutsch et al. (2020) who reported nail changes in 62.2% of patients.[16] This highlights the importance of identifying and managing dermatological toxicities in pediatric oncology. of pustular rash, often linked to neutropenia, reflects chemotherapy-induced immunosuppression and increased susceptibility to infection.[18] A small proportion of dermatological toxicities (7.3%) led to temporary interruption or delay of chemotherapy, primarily due to severe bacterial or fungal infections requiring stabilization prior to treatment continuation. The early onset of most cutaneous changes supports the need for vigilant monitoring during initial chemotherapy cycles.[19]

Beau's lines were most common (31.0%), consistent with Saraswat et al. (2020), who attributed these to temporary nail matrix arrest during systemic stress.[20] Nail fragility (25.0%) aligned with Günaydın & Çetingül (2015), highlighting impaired keratinization.[21] Onycholysis (13.2%) developed later (30–90 days), consistent with Chen et al. (2007), which described this as a delayed cumulative effect of chemotherapy.[22] These findings suggest different temporal patterns of nail toxicities, reinforcing the importance of ongoing nail examination throughout treatment.

Hair loss was another distressing side effect, with complete alopecia in 25.0% and partial loss in 13.2%. The drugs most often implicated were vincristine, cyclophosphamide, and doxorubicin. Similar patterns were reported by Sanmartín et al. (2019) (alopecia in 50.0%)[23] and Rajashekar et al. (2016) (68.3%).[24] Most hair changes occurred between 30–90 days, consistent with follicular cycle disruption by chemotherapy.[25] Given its psychological impact, hair loss requires pre-treatment counseling and supportive interventions.

Viral skin infections were most common (19.1%), followed by bacterial (10.3%), fungal (7.3%), and parasitic (4.4%). This distribution contrasts with Shedeed et al. (2019), who reported predominantly bacterial infections,[26] but is consistent with Gandhi et al. (2014), who found viral infections to be most frequent.[27] Benign drug reactions were seen in 16.2% of patients, higher than the 9.8% reported by Rajashekar et al. (2016).[24] These variations may reflect differences in chemotherapy regimens, immune status, and regional epidemiology.

Children aged 1–5 years had the highest rates of dermatological toxicities, with age reaching statistical significance. This supports Akbayrak et al. (2021), who linked younger age with higher susceptibility due to rapid cell turnover and immature immune defenses.[28] In contrast, Alkathiri et al. (2025) found no significant age-related effect, likely reflecting variability in regimens and dosing.[29] To ensure that the higher toxicity burden in younger children was not solely due to a larger cohort size, proportional statistical analyses and adjusted chi-square tests were performed, which confirmed a true association beyond group size differences. Our findings reinforce the need for age-tailored supportive care. Dermatological changes were most frequent in ALL and HL, consistent with Pramanik et al. (2025), while continuous chemotherapy regimens were significantly associated with more toxicities.[30] This supports Yan et al. (2024), who reported prolonged exposure as a risk factor,[31] though Tola et al. (2023) did not observe regimen differences. Variability likely reflects drug-specific toxicities and dose intensity.[32]

Limitations

This study was limited by its small sample size, single-center design, and relatively short follow-up (6 months), which restricted assessment of late-onset dermatological complications. The absence of a standardized dermatological toxicity grading system such as CTCAE represents a significant limitation; however, the structured dermatologist-guided assessment ensured consistency in evaluation. Quality-of-life outcomes, which are an important aspect of dermatologic morbidity, were not assessed and should be included in future research. Additionally, treatment delays were recorded, but the sample size limited deeper analysis of their predictors. Larger multicenter studies with extended follow-up, standardized grading scales, and QoL assessment tools are needed.

Conclusion

Dermatological manifestations are frequent, often early, and significantly influenced by age and chemotherapy regimen in pediatric cancer patients. Nail, skin, and hair changes substantially affect quality of life and may disrupt treatment adherence. Although only a minority of cases resulted in temporary chemotherapy delay, these findings highlight the importance of timely diagnosis and appropriate management of severe toxicities. Routine dermatological screening, early intervention, and infection control should be integrated into pediatric oncology protocols to minimize morbidity and ensure treatment continuity. Implementing standardized assessment frameworks and enhancing healthcare provider training, particularly in resource-limited settings, will further improve supportive care and optimize outcomes.

Acknowledgements: The authors thank the staff of the Department of Dermatology, The Children's Hospital PIMS, Islamabad, for their assistance in patient care and data collection. We also acknowledge the families of pediatric patients for their participation.

Author Contributions: MRK and NY Conceptualization, supervision, manuscript review, dermatological assessment. HS Patient recruitment, drafting, and clinical oversight of pediatric oncology patients. RM Interpretation of results, manuscript drafting, dermatological evaluations. JJ Data collection and analysis, literature search, data management, figure and table preparation, manuscript formatting.

Conflicts of Interest: The authors declare no competing interests.

Funding: **No** funding was received for this study.

Disclaimer: The views expressed in this article are those of the authors and do not necessa rily reflect the official policy or position of the Pakistan Institute of Medical Sciences or affiliated institutions.

Data Availability Statement: The data that support the findings of this study, apart from the data already presented in the results section, are available from the corresponding author upon reasonable request.

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Journal of University College of Medicine & Dentistry

Original Article

Association of Age and Body Mass Index with Bone Mineral Density in a Hospital-Based Cohort from Karachi, Pakistan

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Submission: 15th May, 2025
First revision: 1st August, 2025
Second revision: 13th September, 2025
Third Revision: 14th October, 2025
Fourth Revision: 23rd November, 2025
Final Revision: 19th December, 2025
Acceptance: 7th January, 2026

DOI: https:/10.51846jucmd.v5i1.4066.

Cite this article as:

Shahid A, Fahad A, Khan MS. Association of age and body mass index with bone mineral density in a hospital-based cohort from Karachi, Pakistan. *J Univ Coll Med Dent*. 2026;5(1): 46-51.

Abstract

Objective: To investigate the correlation of bone mineral density (BMD) with age and body mass index (BMI) in patients undergoing DEXA scans.

Methodology: This was a retrospective observational study conducted at the Medicare Cardiac and General Hospital, Karachi, crossing over the period from 8th September 2022 to September 2023. The study retrospectively analyzed the data of 154 patients who had undergone DEXA scans. Demographic details included age and sex, while anthropometric measurements included height, weight, and BMI. T-scores of both the lumbar spine and femoral neck were noted. Patients with systemic bone disorders, cancer, kidney diseases, and those on hormonal therapy or smoking were excluded. Data analyses were done on SPSS version 25, applying descriptive statistics and Spearman correlation tests; p-values less than 0.05 were considered significant.

Results: The mean age was 60.6 ± 10.1 years, while the mean BMI was 30.6±6.27 kg/m². For the T-score, the mean was -1.023± 1.66 at the lumbar spine and -.908±1.2 at the femur. The lumbar BMD status was significantly associated with age p = 0.001, whereby older patients have higher proportions of osteopenia and osteoporosis. No significant associations were noted between either BMI or gender and BMD status; however, Spearman correlation demonstrated a weak negative association of age with BMD in both sites and a positive correlation with BMI, especially in the femoral neck (r = 0.285).

Conclusion: With increasing age, there was a strong association with decreasing lumbar BMD, whereas increasing BMI showed a protective effect on the femoral BMD. Routine osteoporosis screening is essential for early detection and prevention, especially in people above 50 years. Lifestyle and hormonal factors should be included in further studies to strengthen the evidence.

Keywords: Aging, Body Mass Index (BMI), Bone Mineral Density (BMD), Dual-Energy X-ray Absorptiometry, Osteoporosis.

Introduction

Osteoporosis is a progressive skeletal disorder characterized by reduced bone mass and microarchitectural deterioration, leading to increased bone fragility and fracture risk. It usually does not manifest clinically until a fracture occurs, and therefore, early detection is important.[1] Osteoporosis is becoming more common worldwide as life expectancy rises, particularly in low- and middle-income nations where resources are scarce and the population is ageing. A major public health concern, osteoporosis increases the risk of fractures, which can result in serious illness, death, and a lower quality of life.[2] BMD, measured using dual-energy X-ray absorptiometry (DEXA), is the gold standard for diagnosing osteoporosis.[3] The World Health Organization defines osteoporosis based on BMD T-scores, with values ≤ –2.5 indicating significant bone loss.[4]

Since the mid-1990s, it's been established that achieving high BMD before late adolescence is crucial, as this period marks the peak of BMD acquisition, impacting bone health and fracture risk later in life.[5] Calcium and other BMD-associated nutrients are critical for fortifying BMD and for bone health, and it seems a prerequisite to increase consumption of calcium-rich and various food items, and weight-loaded physical exercise from childhood to adolescence.[6]Age and BMI are among the most widely studied determinants of BMD. Advancing age is strongly associated with bone loss, and BMI influences skeletal loading, with lower BMI often linked to lower BMD and higher fracture risk.[7,8]

In Pakistan, osteoporosis represents an emerging public health concern. Evidence suggests that nearly 40% of postmenopausal women may be affected, underscoring the need for improved screening and preventive strategies.[9] However, local data on BMD patterns and their association with age and BMI remain limited, particularly in tertiary-care settings. This study adds to the

national data by evaluating BMD trends in an urban Karachi population. Therefore, this study aimed to assess BMD at the lumbar spine and femoral neck and to explore its association with age and BMI in adults undergoing DEXA scanning at a tertiary care hospital in Karachi, Pakistan.

Methodology

This retrospective observational study was conducted at Medicare Cardiac and General Hospital, Karachi, between September 2022 and September 2023. Ethical approval for this study was obtained from the Institutional Review Board of Sohail University, Karachi, Pakistan (Protocol No. 000203/22; approved on 8 September 2022). As this was a retrospective review of hospital records, the IRB granted a waiver of individual informed consent. All data were anonymized before analysis to ensure confidentiality.

We chose a retrospective design because DEXA scanning is not routinely performed in the general population in Karachi, and existing hospital records provided a cost-effective means of exploring early associations in our setting. To minimize the limitations of retrospective data, we used a pre-specified data extraction form, only included records with complete demographic, anthropometric, and T-score entries, and rechecked all entries independently by two reviewers. Completeness thresholds were set (>90% of the data available), and extreme outliers (for example, BMI > 60 kg/m^2) were analyzed for robustness with and without those cases. The primary aim is to explore the relationship of BMD with age and BMI among patients who have undergone DEXA scanning. DEXA scan reports had been routinely archived in the Radiology Department. Each report gave details on demographic and anthropometric information (age, sex, height, weight), calculated BMI, referral clinical notes including chief complaints, and BMD as T-scores for the lumbar spine (L2–L4) and femoral neck. All DEXA scans were carried out by trained radiology technicians according to the hospital's SOPs. Throughout the study period, only two operators carried out all scans. A Medix 90 DEXA system (MEDILINK, France; software version 4.1) was used. Daily calibration of the machine using manufacturer-supplied phantom standards was performed throughout to maintain accuracy and instrument reliability. Sample size calculation was done using OpenEpi v3.01. The required sample size for detecting a correlation of r = 0.48 from the study (S. Sultana1et.al 2021)[23], which shows the T-score of LS and BMI were positively correlated (r=0.484) with a significance level of $\alpha = 0.05$, and a power of 80% was calculated using Fisher's z-transformation formula. The estimated sample size was 50 participants. To enhance the reliability of this study and also take missing data into account, a total of 154 participants were included in this research study. Since this is a retrospective review, all eligible records fitting the inclusion criteria within the study period were recruited until sample size was achieved.

The study enrolled all patients who underwent BMD testing during the study period; thus, both male and female patients were eligible for the study. These patients were excluded if they had systemic conditions known to affect bone metabolism such as hyperparathyroidism, Paget's disease, osteocalcin disorders, renal osteodystrophy, or osteogenesis imperfecta. Subjects with a history of cancer or chronic kidney diseases were excluded. Similarly, patients who had taken hormonal therapy, as well as current or past smokers, were also excluded from the study. Current and past smokers were excluded due to the fact that smoking is an important independent risk factor for osteoporosis. Including smokers in this study could thus introduce a strong confounding effect that will make it difficult to establish the relationship between BMD, age, and BMI in a non-smoking population.

Patients had been selected for BMD testing based on clinical referrals, which included criteria such as possible osteoporosis, fracture risk assessment, or other relevant clinical problems. The careful inclusion of all the relevant records during the study period reduces selection bias and offers a representative overview of persons undergoing DEXA scanning in this clinical setting, although the sample is hospital-based and may not be representative of the general public.

The data analysis was done using IBM SPSS version 25. Continuous variables such as age, BMI, and T-scores were presented as mean ± SD. Categorical variables were presented as frequencies and percentages for gender and BMD categories. Spearman's correlation coefficient was used to test the association between continuous variables of age, BMI, and BMD. The Chi-square test was conducted for categorical comparisons including age group and BMI categories with gender in relation to BMD status. A p-value < 0.05 was considered statistically significant. Scatter plots with regression lines were used to illustrate trends.

Results

A total of 154 patient records met the inclusion criteria and were analyzed to determine the relationships between age, BMI, and bone mineral density. The basic anthropometric characteristics of these patients are presented in Table 1.

Table 1: Characteristics of Study Populations

Variable	Mean(Std. Deviation)	Minimum	Maximum
Age	60.60(10.18)	34	84
BMI	30.6(6.27)	19	48
Lumbar (T-score)	-1.0(1.66)	-4.1	5.8
Femur (T-score)	-.90(1.20)	-5.0	2.0

The relationship between age, gender, and BMI with BMD status of both the lumbar spine and femur was analyzed (Tables 2 and 3).

Table 4 presents the Spearman correlation coefficients between BMD at different skeletal sites (femoral neck and lumbar spine) and two variables: age and BMI. A weak negative correlation was observed between age and femoral neck BMD (r = -0.205), as well as between age and lumbar spine BMD (r = -0.182), suggesting a slight decline in BMD with increasing age at both sites. In contrast, BMI demonstrated a positive correlation with BMD. Specifically, a moderate positive correlation between BMI and femoral neck BMD was observed (r = 0.285), with a weaker positive correlation observed with respect to lumbar spine BMD (r

Table 2: Lumbar Spine BMD Status of the Study Patients

Variable	Normal n (%)	Osteopenia n (%)	Osteoporosis n (%)	p-value
Age (years)				
< 50 years	9 (37.5%)	3 (9.7%)	8 (8.7%)	0.001
≥ 50 years	15 (62.5%)	28 (90.3%)	84 (91.3%)	
BMI (kg/m²)				
Underweight	1 (4.2%)	1 (3.2%)	3 (3.3%)	
Normal weight	1 (4.2%)	1 (3.2%)	14 (15.2%)	
Overweight	8 (33.3%)	7 (22.6%)	31 (33.7%)	0.093
Obese Type I	6 (25.0%)	9 (29.0%)	27 (29.3%)	
Obese Type II	3 (12.5%)	11 (35.5%)	12 (13.0%)	
Obese Type III	5 (20.8%)	2 (6.5%)	5 (5.4%)	
Gender				
Male	1(4.2%)	4(12.9%)	4(4.3%)	0.521
Female	23(95.8%)	27(87.1%)	88(95.7%)	

% and Frequency, *P-value measured by Chi-square (<0.05 considered significant)

= 0.187). This suggests that increasing BMI might result in higher bone density, most notably at the femoral neck. Another finding revealed that there was no significant association between age and BMI (r = 0.003), reflecting again that these are independent variables in this population. These correlation analyses complement the categorical analysis: age was significantly associated with lumbar BMD status in chi-square analysis (Table 2); suggesting BMD categories change across age groups. However, in the context of age as a continuous variable, the association with lumbar and femoral neck BMD was weakly negative, consistent with the relatively younger age distribution of our sample.

Table 3: Femoral Neck BMD Status of the Study Patients

Variable	Normal n (%)	Osteopenia n (%)	Osteoporosis n (%)	p-value
Age (years)				
< 50 years	11(14.7%)	9(13.0%)	0(0%)	0.432
≥ 50 years	64(85.3%)	60(87.0%)	10(100%)	
BMI (kg/m²)				
Underweight	1(1.3%)	3(4.3%)	1(10%)	
Normal weight	9(12.0%)	5(7.2%)	2(20%)	
Overweight	23(30.7%)	24(34.8%)	1(10%)	
Obese Type I	17(22.7%)	24(34.8%)	3(30%)	0.170
Obese Type II	16(21.3%)	8(11.6%)	3(30%)	
Obese Type III	9(12.0%)	5(7.2%)	0(0%)	
Gender				
Male	7(9.3%)	3(4.3%)	0(%)	0.410
Female	68(90.7%)	66(95.7%)	10(100%)	

% and Frequency, *P-value measured by Chi-square (<0.05 considered significant)

Table 4: Spearman Correlation between Age, BMI, and Bone Mineral Density

Variable Pair	Spearman r	Interpretation
Age vs Lumbar Spine BMD	–0.182	Weak negative correlation
Age vs Femoral Neck BMD	–0.205	Weak negative correlation
BMI vs Lumbar Spine BMD	0.187	Weak positive correlation
BMI vs Femoral Neck BMD	0.285	Moderate positive correlation
Age vs BMI	0.003	No correlation

Note: For the assessment of associations between continuous variables, Spearman's rank correlation coefficient (r) was computed; $p < 0.05$ was considered to indicate statistical significance.

Figure 1 A and B describe the types of correlations. BMD with age demonstrates a negative trend of bone density over time. The Femoral neck BMD demonstrates a clearer downward slope with some clustering around the regression line, reflecting a more consistent pattern of age-related bone loss. In contrast, the lumbar spine BMD shows a much weaker negative slope, with data points more widely spread, indicating greater variability and a less consistent relationship with age.

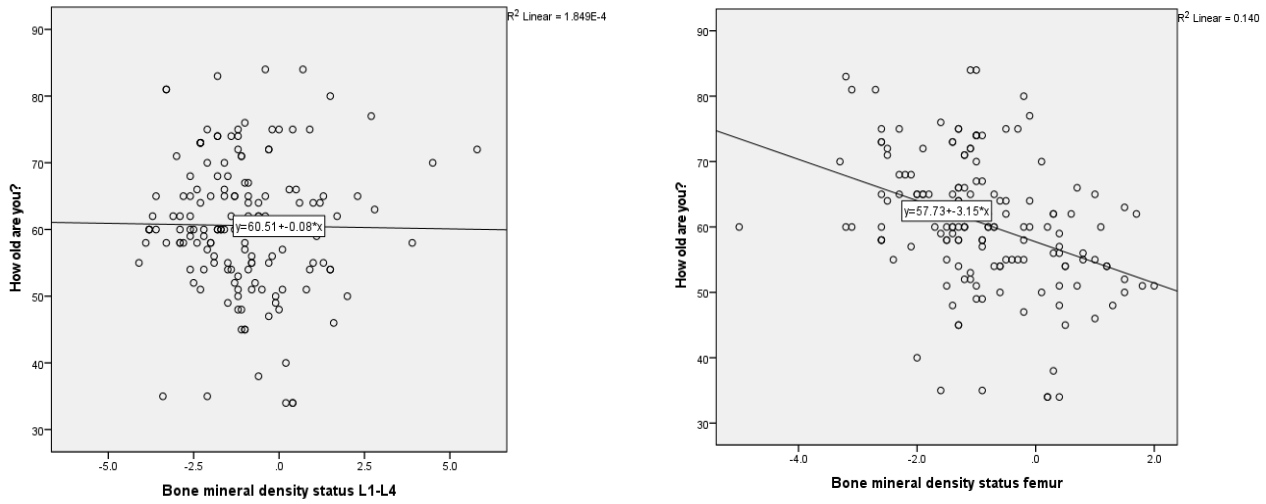

Figure 1. Scatter-plot of (A) lumbar spine BMD and (B) Femoral neck BMD against age.

Multivariable linear regression was considered to adjust for potential confounders such as age, BMI, and menopausal status. While this was not implemented in the current analysis, future phases of this study will incorporate stratified regression models to enhance interpretability

Discussion

This study on 154 patients in Karachi revealed that age was strongly associated with reduced lumbar spine BMD, with osteoporosis and osteopenia more prevalent after 50 years (Tables 2 and 3). As the mean age of 60.6 years reflects a group entering the phase of accelerated age-related bone, which is aligned with worldwide data that indicates a significant decrease in BMD after the fifth decade of life (Table 1).[10] The participant's mean BMI of 30.6 kg/m² indicates that they are obese, which is similar to studies that report obesity incidence is rising in South Asian population, including Pakistan [11]. It is known that lumbar degenerative alterations, such as osteophytes, vertebral sclerosis, and facet hypertrophy, can artificially increase lumbar BMD in older persons, which could be the reason for the higher values that are reported.[12] BMI showed no significant association overall; however, a higher BMI correlated positively with Femoral neck BMD and weakly with lumbar spine BMD, while gender had no significant impact. Notably, the results for the lumbar spine and femoral neck were not always aligned, suggesting that relying on a single skeletal site may miss patients at risk. In our setting, age above 50 years emerged as the strongest predictor of lumbar spine bone loss (Table 2), while BMI demonstrated a modest protective effect at the femur in (Table 3). These findings closely resemble reports from South Asian cohorts, where lumbar spine BMD tends to decline earlier and more sharply with increasing age, particularly in urban populations with high levels of overweight and obesity.[13] In patients with very high BMI, DEXA interpretation can be complicated due to soft-tissue artifacts; however, even after excluding extreme BMI values, the direction and strength of associations in our study remained unchanged. Despite a predominance of overweight and obese participants, bone loss continued to progress with advancing age, reinforcing the need for routine screening in older adults irrespective of body mass.[14] Such findings are consistent with recent Pakistani and Indian studies reporting that high BMI does not uniformly protect the spine against age-related osteoporosis, possibly due to central adiposity related inflammation impairing trabecular bone.[15] Our findings on age-related bone loss align with both local and international reports indicating a higher prevalence of osteopenia and osteoporosis after 50 years, consistent with WHO and FRAX-based assessments.[16,17] However, in contrast to many global datasets, we did not find significant relationships between BMI and either lumbar or femoral BMD.

The lack of a significant BMI–BMD association may reflect unmeasured confounders such as low calcium intake, widespread vitamin D deficiency in Pakistan, limited physical activity, or variations in body fat distribution. All of these factors can attenuate the expected protective effect of BMI on BMD.[18] Previous Studies have shown that higher BMI correlates more strongly with femoral BMD than with lumbar spine BMD, partly due to site-specific mechanical loading.[19,20] Although these correlations were weak (r = 0.285 for femoral neck and r = 0.187 for lumbar spine), our results showed that BMI had a stronger association with femoral BMD than with lumbar spine BMD (Table 4). Taken together, the chi-square analysis showing a significant association between age and lumbar BMD status and the weak negative correlations shown in the table and figure (Table 4 and Figure 1) suggest early-stage bone mineral loss in a relatively young, predominantly middle-aged cohort. Gender showed no significant impact on BMD, likely due to methodological limitations, including the small number of male participants (Table 2 and 3), the markedly skewed sex distribution, and the inherent constraints of a hospital-

based retrospective dataset, all of which may limit the ability to detect true sex-related variations in BMD. Regarding the femur, we observed that no significant association between age and femoral BMD existed, which is somewhat surprising given the common belief that age-related osteoporosis predominantly affects the femoral region, particularly the neck of the femur. A study conducted by (Chen et al. 2013) proposed that the femoral neck is often one of the earliest sites to show osteoporotic changes with advancing age.[21] Our study supported this literature as all the patients with femoral osteoporosis were above 50 according to the data shown in the table (Table 3). However, no significant age-related trend was seen due to homogeneity of the sample as most of them are females which may have masked the real age-related effect on femoral BMD. The literature regarding the adverse effects of ageing on BMD is supported our results. Various studies demonstrated that BMD decreases with advancing age, especially in weight bearing skeletal regions of the lumbar spine and femoral neck, which are the usual sites affected by osteoporosis and fractures in elderly individuals.[22] The weak correlations may indicate that the study population represented the early stage of BMD loss or a relatively younger age group, as BMD is known to decline more steeply in older age groups. Age and BMI did not exhibit any significant association (Table 4). These findings are consistent with previous literature that, although there is a positive correlation between BMI and BMD, age does not appear to be a modifier of this relationship.

In the Pakistani clinical setup, which is burdened by high levels of obesity, widespread vitamin D deficiency, and lack of random sampling, BMI alone cannot be used as a reliable predictor of either lumbar or femoral BMD. In contrast, age remains the single strongest and most consistent determinant of bone loss, particularly in the lumbar spine. Our overall findings indicate that, although BMI exerts a limited site-specific influence on BMD, it cannot serve as a reliable standalone predictor of osteoporosis in clinical settings in Pakistan. Age remains the key determinant of bone loss, especially at the lumbar spine, and should therefore remain central to screening and risk assessment strategies. The weak correlations further underscore the likely contribution of unmeasured lifestyle and biological factors, including but not limited to vitamin D status, physical activity, diet, and hormonal influences, which deserve attention in future prospective studies.

Limitations

This study was conducted at only one private tertiary hospital, which is a limitation to the generalizability of our findings. Being a retrospective design, analysis was done only for systematically recorded variables; records with a lack of essential data were excluded. Lifestyle and hormonal factors, such as dietary intake, physical activity, vitamin D status, menopausal status, and medications, were not available, which may introduce residual confounding. Smokers and patients with systemic bone disorders were excluded, which further limits the applicability to the general population. The male sample was small, further restricting the assessment of sex-specific differences. Despite these limitations, consistency in our results using sensitivity analyses, for example, the exclusion of extreme cases of BMI, lends support to the reliability of the results. Future prospective studies are recommended that would include these additional determinants for a comprehensive assessment of osteoporosis risk factors.

Conclusion

While age is significantly related to BMD decline, especially at the lumbar spine, higher BMI only exerts a modest protective effect at the femoral neck. These findings would, therefore, suggest that adults above 50 years, regardless of BMI, are to be considered the priority for osteoporosis screening among clinicians in Karachi. When there is a difference between the lumbar spine and hip results, the lower score is to be considered clinically relevant. Overweight and obesity may offer only partial protection and should not delay screening in high-risk patients. Further studies are recommended to also include lifestyle and hormonal factors in order to strengthen risk stratification and guide preventive strategies. This paper will help inform local osteoporosis screening and prevention policies, emphasizing early assessment in adults above 50 years of age and ensuring standardized evaluation of both lumbar and hip sites in routine practice

Author' Contributions: A.S. contributed to the study conception, design, and data interpretation; A.F. acquired and interpreted the data; M.S.K. acquired and interpreted the data. All authors contributed substantially to the work and accept equal responsibility for its content

Conflict of Interest: The authors declare no conflict of interest.

Data Availability Statement: The data that support the findings of this study, apart from the data already presented in the results section, are available from the corresponding author upon reasonable request.

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Journal of University College of Medicine & Dentistry

Original Article

Subthalamotomy versus Pallidotomy for Parkinsonian Rigidity: A Quasi-Experimental Study in a Resource Limited Tertiary Center

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Submission: 28th September, 2025
First revision: 25th November, 2025
Second revision:10th December, 2025
Third Revision: 24th December, 2025
Final Revision: 5th of January, 2026
Acceptance: 11th January, 2026

DOI: https://doi.org/10.51846/jucmd.v5i1.4771

Cite this article as:

Ali OA, Ahmad U, Khan RA, John A, Shah SH, Mehmood K. Subthalamotomy versus pallidotomy for Parkinsonian rigidity: a quasi-experimental study in a resource-limited tertiary center. *J Univ Coll Med Dent*. 2026;5(1): 52-57.

Abstract

Objective: To compare motor outcomes and postoperative complications of subthalamotomy versus pallidotomy for Parkinsonian rigidity in a resource-limited setting where deep-brain stimulation is not affordable.

Methodology: This quasi-experimental study was carried out at the Department of Neurosurgery, Punjab Institute of Neurosciences, Lahore, from 2016 to 2021. Forty patients with Parkinson's disease were included. Twenty patients underwent pallidotomy, in which a small, precisely targeted lesion was made in the globus pallidus region of the brain, and twenty had a subthalamotomy, involving a lesion in the subthalamic nucleus. Each patient's motor function was assessed before surgery and at regular follow-ups using the Unified Parkinson's Disease Rating Scale (UPDRS) part III, a standard measure of movement difficulty in Parkinson's disease. Postoperative complications were also recorded. The changes in UPDRS scores and complications were compared within and between groups.

Results: The mean age was 47.6 ± 8.7 years, and 85% of patients were male. Both procedures produced significant postoperative improvement in motor scores ($p < 0.001$). In the pallidotomy group, the UPDRS Part III score improved from 24.9 ± 1.47 to 10.47 ± 0.86 (42% improvement), and in the subthalamotomy group from 25.48 ± 1.55 to 10.26 ± 1.18 (40.2% improvement). Although pallidotomy showed a slightly greater numerical reduction in UPDRS scores, the difference between groups was not statistically significant ($p > 0.05$). Complications were less frequent after pallidotomy (10%) compared with subthalamotomy (35%), but this difference was not statistically significant.

Conclusion: Both procedures are effective in treating Parkinsonian rigidity. No statistically significant difference was observed between the two procedures in terms of relief of symptoms. Fewer complications were associated with pallidotomies as compared with subthalamotomies.

Keywords: Parkinson's disease, Pallidotomy, Subthalamotomy, STN lesioning, Unified Parkinson's Disease Rating Scale

Introduction

Parkinson's disease (PD) is a chronic, progressive neurodegenerative disorder named after James Parkinson, and is the second most common neurodegenerative disease worldwide after Alzheimer's disease. It is an incurable, debilitating condition affecting approximately 11.7 million people globally.[1,2] The classical motor manifestations include resting tremor, bradykinesia, muscular rigidity, and postural instability, with a male predominance of about 1.5:1 compared to females.[3,4] Clinically overt motor symptoms typically emerge after the substantia nigra has lost more than about 50% of dopaminergic neurons. Although no medical or surgical treatment can halt or reverse the disease process, symptom progression can be mitigated with antiparkinsonian drugs such as levodopa, anticholinergics, dopamine agonists, and catechol-O-methyltransferase inhibitors, used alone or in combination. However, long-term pharmacotherapy is frequently complicated by motor fluctuations and dyskinesias, prompting consideration of surgical options in advanced cases.

Surgical interventions are generally reserved for patients with severe, medically refractory symptoms. Contemporary neurosurgical strategies include deep brain stimulation (DBS), medication infusion systems, and ablative (lesioning) procedures targeting specific basal ganglia structures.[5] DBS has become the preferred surgical approach for advanced PD in many centers because it is adjustable, reversible, and associated with a favorable safety profile. Nevertheless, the high cost of hardware, need for device maintenance, and long-term follow-up substantially limit its accessibility in low- and middle-income countries.[6] In such resource-constrained settings, lesioning procedures remain an important, pragmatic alternative for carefully selected patients.[7]

Among ablative procedures, pallidotomy targets the internal segment of the globus pallidus (GPi), whereas subthalamotomy targets the subthalamic nucleus (STN). The STN is a relatively newer lesioning target compared with the GPi; its use was initially supported by encouraging results in primate models of PD,[8] although early

concerns about inducing hemiballismus delayed broader application in humans. Subsequent clinical experience has shown that STN lesioning can improve all cardinal motor features of PD and reduce levodopa requirements by approximately 42%, thereby potentially decreasing the drug-induced complications; significant motor gains are typically observed within 6–8 months,[9] with reports of around 50% improvement in rigidity and other motor symptoms. Clinical series by McCarter and Alvarez reported no major adverse effects on cognition, balance, or swallowing,[10] although other studies have documented procedure-related complications such as dyskinesias, speech disturbances, and ataxia.[11] These data support lesioning of the STN as a viable, cost-conscious option in appropriately selected patients when DBS is not feasible. Despite International reports describing the effectiveness of subthalamotomy and pallidotomy, direct comparative evidence between the two procedures remains limited, especially in low-resource health systems where DBS is not financially accessible. Most available studies are small, single-arm case series conducted in high-income countries, and there is little published data on surgical outcomes, complication rates, and short-term functional improvement in South Asian populations.

Because lesioning procedures remain a practical alternative in Pakistan due to cost constraints, there is a critical need for locally generated comparative data to guide decision-making. This study addresses this gap by directly comparing motor improvement and postoperative complications between stereotactic subthalamotomy and pallidotomy in patients with Parkinsonian rigidity in the local population.

Methodology

This prospective quasi-experimental study was carried out at Neurosurgery unit II of Punjab Institute of Neurosciences, Lahore General Hospital, for five years, from 2016 to 2021, after approval from the Ethical Review Board (LGH/00/156/16). Given the low annual procedural volume for these lesioning techniques and the need for standardized postoperative follow-up, the study was designed as a multi-year prospective cohort. Ethical approval covered the entire recruitment and follow-up period. Forty participants were recruited in the study. Allocation into groups was done through non-probability convenience sampling by a consultant neurosurgeon, without any specific criteria, as it was difficult to dichotomize the patients due to their diverse clinical presentations. Allocation was based on surgeon judgment, as rigid randomization was not feasible due to heterogeneity of clinical presentations. Twenty participants each were assigned to the pallidotomy and subthalamotomy groups.

Those patients with Parkinsonian rigidity were included in the study who had initially shown a good response to antiparkinsonian medication but later experienced either a diminished therapeutic effect or the development of treatment-related complications, of either gender, between 30 and 70 years of age. Patients with a history of stroke, intracranial tumour, or prior surgery for head trauma were excluded, as were those with malignant diseases or evidence of cognitive decline. Individuals with any form of bleeding diathesis were also not considered eligible for inclusion in the study.

The following variables were recorded for each patient: age, categorized as <40 years, 40–60 years, or >60 years; gender; and presenting symptoms, which included rigidity (unilateral or bilateral, with left predominance, right predominance, or symmetrical involvement), bradykinesia, gait disturbances or ataxia, micrographia, and tremors (left- or right-predominant). Motor severity was assessed using Part III of the UPDRS, which focuses on the motor examination. although UPDRS comprises four parts, only Part III (motor examination) was used in this study, and all reported UPDRS scores refer exclusively to this section. UPDRS Part III consists of 18 items, each scored from 0 (normal) to 4 (severe disability), yielding a maximum total score of 72. UPDRS scoring before and after the intervention was calculated, assessed, and analyzed by a consultant neurosurgeon who was not involved in the study and was therefore blinded.

Postoperative complications were also documented and included vascular complications (hematoma, stroke, or infarction), wound-related complications (infection, cerebrospinal fluid fistula), motor complications (motor weakness, dyskinesias, swallowing difficulties, and dysphasias), and cognitive complications (cognitive decline and memory deficits). In addition, any mortality occurring within the 3-month postoperative follow-up period was recorded.

Patients fulfilling the inclusion criteria were enrolled from the outpatient department. Informed consent was taken from the patient after they were informed of the details of the procedure, its outcome, and associated risks. The assessor was blinded to the procedure. Patients fulfilling the inclusion criteria were admitted through OPD, and UPDRS was noted. The motor component of UPDRS was considered in the study. After taking informed consent from the patients, they were subjected to surgery under local anaesthesia. Any drugs the patient was taking for PD were discontinued. The procedures were guided by metal frames placed on the patients' heads. Four pins, two in front and two at the back, were applied to fix the frame. Once a square was ensured, the fiducial box was applied. The box fitted snugly only if the frame was square. The MRI was used to locate the STN and GPi, which were the exact brain targets responsible for Parkinsonian movement difficulties.

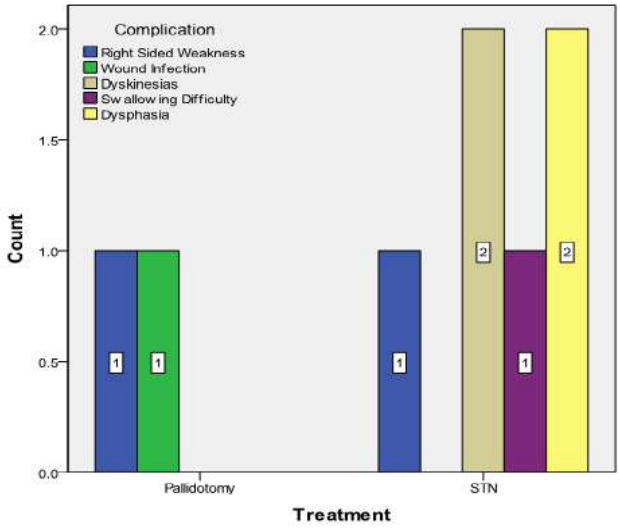
Both procedures were performed under local anesthesia using MRI guidance to accurately locate the target areas in the brain. A small electrode was inserted through a tiny opening in the skull, and controlled heat was applied to create a lesion in the region responsible for Parkinsonian rigidity.After the procedure, patients were observed in the recovery room for an hour and then transferred to the ward. A postoperative CT scan was performed 8–12 hours later to check for any bleeding or other complications, and antiparkinsonian medications that had been paused were restarted. The following morning, patients were evaluated, and UPDRS scores and complications were documented. A postoperative MRI was also obtained to confirm lesion placement. Patients were then discharged with instructions to continue their medications and attend follow-up visits. At the 3-month follow-up, UPDRS scores were recorded again and any complications noted during hospitalization or the follow-up period were documented.

Data were analyzed using IBM SPSS Statistics version 27. Continuous variables (age and UPDRS Part III scores) were summarized as mean ± standard deviation, while categorical variables (sex and postoperative complications) were presented as frequencies and percentages. Normality of continuous variables was assessed (assuming approximate normal distribution for UPDRS scores). Within-group comparisons of preoperative and 3-month postoperative UPDRS Part III scores were performed using paired t-tests. Between-group comparisons of 3-month postoperative UPDRS Part III scores (pallidotomy vs. subthalamotomy) were performed using independent samples t-tests. Associations between categorical variables, including postoperative complication rates, were evaluated using chi-square tests. A p-value ≤0.05 was considered statistically significant.

Results

In this study, the mean age of the patients was 47.58±8.69 years. 11 (27.5%) patients were younger than 40 years of age, 14 (35%) were between 40 and 50 years of age, and 15 (37.5%) were older than 60 years. 34 (85%) patients were male, and 6 (15%) were female. In the pallidotomy group, 14 (70%) were male and 6 (30%) were female, whereas in the STN group, all (100%) were male. Mean baseline UPDRS Part III scores were 24.90 ± 1.47 in the pallidotomy group and 25.48 ± 1.55 in the subthalamotomy group, with no statistically significant difference between groups. However, sex distribution differed between groups, with all patients in the subthalamotomy group being male.

In the pallidotomy group (n = 20), the most frequent presenting pattern was bilateral rigidity with bradykinesia in 5 patients (25.0%), followed by bilateral rigidity with bradykinesia and ataxia in 4 patients (20.0%), bilateral rigidity was more marked on the right side in 4 patients (20.0%), and bilateral rigidity was more marked on the left side in 3 patients (15.0%); in addition, 4 patients (20.0%) presented with difficulty in walking, Micrographia, bradykinesia, and bilateral rigidity. In the STN group (n = 20), right-sided tremors with predominant right-sided rigidity and bradykinesia were observed in 6 patients (30.0%), left-sided tremors with predominant left-sided rigidity and bradykinesia in 5 patients (25.0%), while 9 patients (45.0%) had predominantly bilateral rigidity. UPDRS part III scores were recorded for both pallidotomy and subthalamotomy groups. The patients scored the following:



Graph 1: Comparison of postoperative complications between pallidotomy and subthalamotomy at 3 months

Table 1: Mean and standard deviation of preoperative and 3-month postoperative UPDRS Part III total motor scores (pallidotomy group)

	Mean	Std. Deviation
pre-op UPDRS	24.90	1.470
3 months	10.47	.860

There was a 42% improvement in mean UPDRS score postoperatively. The difference between preoperative and 3-month post-operative UPDRS was statistically significant (p <0.001) in the pallidotomy group.

Table 2: Mean and standard deviation of preoperative and 3-month postoperative UPDRS Part III total motor scores (subthalamotomy group

Treatment	Mean	Std. Deviation
pre-op UPDRS	25.48	1.546
3 months	10.26	1.182

There was a 40.2% improvement in mean UPDRS score postoperatively. The difference between preoperative and 3-month post-operative UPDRS was statistically significant (p <0.001) in the subthalamotomy group.

Table 3: Comparison of Stereotactic Subthalamotomy and Pallidotomy UPDRS Part III total motor scores

	Treatment	Mean	Std. Deviation	Std. Error Mean
3 months	Pallidotomy	10.47	0.86	0.157
	STN	10.26	1.18	0.212

The difference between Stereotactic Subthalamotomy and Pallidotomy in terms of UPDRS at 3 months post op was statistically insignificant (p-value=0.435)

Postoperative complications were found to be few and far between, with none of the patients developing any vascular complications (hematoma, stroke/infarction) or cognitive complications (cognitive decline or memory deficits). There was, however, 1 wound complication (infection but no CSF fistula), and 7 motor complications (2 motor weakness, 2 dyskinesias, 1 swallowing difficulty, and 2 dysphasia).

There was no statistically significant association between treatment modality and complications (p-value=0.127). Although this difference did not reach statistical significance, the higher complication rate observed with subthalamotomy may be clinically relevant in resource-limited settings and warrants caution. In our sample of 40 patients, no mortalities were encountered during the study period.

Discussion

In this quasi-experimental study of 40 patients, both pallidotomy and subthalamotomy significantly improved UPDRS Part III scores at 3 months, with no statistically significant difference between the groups. Complications, however, were more frequent in the subthalamotomy group, though the difference was statistically insignificant. The modern surgical treatment of choice for PD is Deep Brain Stimulation of the STN, but lesioning is still performed and is a valuable option in non-affording populations.[12] Although the upfront cost for lesional techniques is comparable to deep brain stimulation, AL Green & Kalhoro et al reported cost-effective results of pallidotomy (especially unilateral)

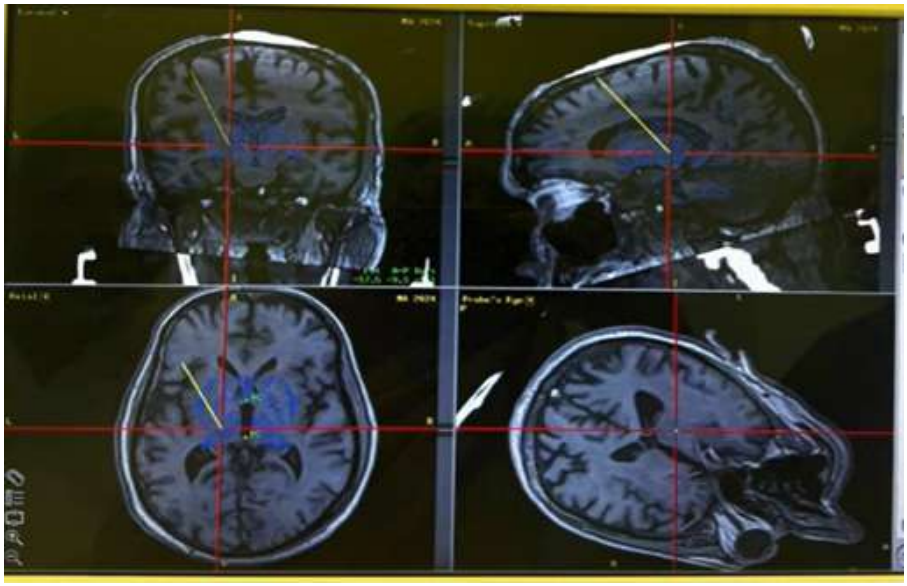


Figure 1. Preoperative stereotactic MRI-based target planning showing localization of the globus pallidus internus (GPi) and subthalamic nucleus (STN) for ablative surgery in Parkinson's disease. Red lines: marking target at point of intersection. Yellow line: marking trajectory from skull surface site to ablative target.

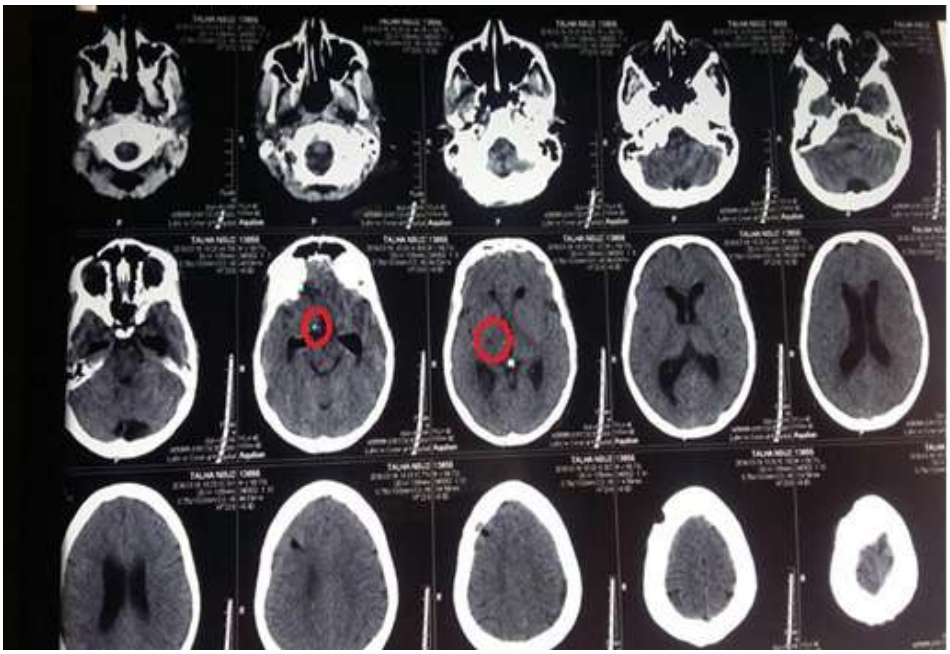


Figure 2. Postoperative CT scan following pallidotomy demonstrating the stereotactic lesion within the globus pallidus internus (encircled red), obtained to confirm target placement and exclude postoperative complications.

secondary to improvement in UPDRS score, reduced need for medication, and fewer postoperative complications.[13,14] Thus, these lesioning techniques serve as a viable alternative to the gold standard in the non-affording population of Pakistan.

Traditionally, pallidotomy was the preferred lesioning procedure for PD, but gradually, subthalamotomy started emerging as a potential alternative. In 1997, two separate pilot studies by Gill et al and Obeso et al were conducted to check the safety and efficacy of subthalamotomy, and the results were very encouraging. Both studies concluded that subthalamotomy can be done without any noticeable side effects.[15,16] Alvarez et al described their series of 11 patients

in 2001, in which they showed significant improvement in the symptoms at 6 months without many complications except in one patient who had dyskinesias.[9] Su et al in 2002 described subthalamotomy as a safe procedure thatameliorates all the symptoms of Parkinson's disease without significant complications.[11]
Laitinen et al. (1992) observed in 92% of 38 patients undergoing pallidotomy that the symptom of rigidity had nearly completely abated, and Alvarez et al. described approximately 75% improvement in contralateral limb rigidity following subthalamotomy.[17] A study showed larger improvements in the off-drug phase in the STN group compared with the GPi group in the mean change in UPDRS motor examination scores (20.3±16.3 vs 11.4±16.1). It suggests that STN is the preferred target for DBS in patients with advanced Parkinson's disease.[18] But there was no comparative data to ascertain the efficacy of lesioning in these two nuclei.

In this study, Pallidotomy was compared with the STN lesioning to determine the more effective technique in terms of improvement in UPDRS and associated with fewer complications. Baseline disease severity varied across patients; however, both procedures resulted in significant improvement in overall motor function as reflected by UPDRS Part III scores. In this study, in terms of UPDRS, the improvement was 42% and 40% in the pallidotomy and subthalamotomy groups, respectively, at 3-month follow-up.[18] Previously described studies have yielded results comparable to these findings. Alvarez in 2001 described a 50% improvement in UPDRS postoperatively.[7]

Dogali et al in 1995 described 60% improvement after pallidotomy.[8] Complications reported didn't reach statistical significance, but were more frequent in the subthalamotomy group (35%) as compared with the pallidotomy group (10%). This is in accordance with previous studies, which showed that complications such as speech difficulties and swallowing difficulties, along with dyskinesias, are related to STN lesioning.[19] Similar findings were reported by Alvarez et al. (2009), who observed higher rates of speech and swallowing disturbances following unilateral subthalamotomy.[20] In contrast, studies evaluating pallidotomy, including the randomized trial by Vitek et al. (2003), have demonstrated comparatively lower rates of procedure-related motor and bulbar complications.[21]

Some studies comparing the outcomes of lesioning techniques and DBS have concluded that although STN-DBS offers long-term benefit and medication reduction lesioning procedures, particularly unilateral, offer greater motor improvement.[22,23] A recent systematic review and metanalysis showed that unilateral lesioning offers comparable short-term improvement in UPDRS motor scores, with lower device-related complications, although DBS remains superior for bilateral symptom control.[23] These findings support the continued role of ablative surgery where DBS is unavailable or unaffordable.

Overall, this study adds practical, real-world evidence comparing subthalamotomy and pallidotomy for Parkinsonian rigidity in a resource-limited setting, reinforcing the role of ablative surgery as a viable and relatively cost-effective option when deep brain stimulation is not feasible. Future work should include larger, preferably randomized multicenter studies with longer follow-up, broader motor and non-motor assessments, quality-of-life measures, and systematic evaluation of cognitive and psychiatric outcomes to better define the place of these procedures in modern Parkinson's disease surgery. For a resource-limited setting like Pakistan, pallidotomy and subthalamotomy may be clinically and more economically accessible options for patients with severe symptoms of PD.

Limitations

This study has several limitations that should be considered and addressed in future research. The relatively small sample size reduces statistical power and increases the risk of selection bias. The non-randomized convenience allocation of patients into either group increases the risk of sampling bias, and in future studies, this could be mitigated by performing subgroup analysis. There was only a single blind observer for calculation of the UPDRS score, and the inter-rater variability was not controlled for this study. Being a single-center study with a marked gender imbalance further limits the generalizability of our findings to broader Parkinson's disease populations. In addition, the short follow-up period of 3 months and reliance on UPDRS Part III motor scores alone preclude comprehensive assessment of long-term outcomes, non-motor symptoms, and quality of life. Additionally, improvement in motor scores does not necessarily reflect true functional recovery in daily activities or improved quality of life. Finally, as all procedures were performed by a limited number of surgeons, possible operator bias cannot be excluded.

Conclusion

The study shows that both the lesioning techniques are equally effective in reducing the rigidity in patients of Parkinson's disease, but complications associated with subthalamotomy are more common compared to pallidotomy, although not statistically significant.

Authors' contributions: OAA contributed to study conception, design, methodology, and drafting of the manuscript. UA conducted the literature review and contributed to the writing of the discussion. RAK performed the statistical analysis and contributed to data interpretation. AJ contributed to the interpretation of results. TA was responsible for data acquisition. SSHS and KM contributed to data analysis and quality assurance. All authors critically reviewed and approved the final manuscript and agree to be accountable for the integrity and accuracy of the work.

Conflict of Interest: None to declare

Funding Disclosure: This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Data Availability Statement: The data that support the findings of this study, apart from the data already presented in the results section, are available from the corresponding author upon reasonable request.

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Journal of University College of Medicine & Dentistry

Original Article

Clinical Spectrum of Focal Dystonia in Patients at Tertiary Care Hospital in Karachi: A Cross-Sectional Study

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Submission: 20th September, 2025
First revision: 25th October, 2025
Second revision: 15th November, 2025
Final Revision: 28th of December, 2025
Acceptance: 2nd January, 2026

DOI: https://doi.org/10.51846/jucmd.v5i1.4695

Cite this article as:

Khan R, Qamar-un-Nisa Q, Faruqi SJ, Umer SR, Iqbal R, Jawaid W. Clinical spectrum of focal dystonia in patients at a tertiary care hospital in Karachi: a cross-sectional study. *J Univ Coll Med Dent*. 2026;5(1): 58-62.

Abstract

Objective: To describe the clinical patterns and types of focal dystonia among patients presenting to the neurology department of a tertiary care hospital in Karachi.

Methodology: This descriptive cross-sectional study was undertaken at Dr. Ruth K. M. Pfau Civil Hospital, a tertiary care institution in Karachi, from 21st March 2025 to 20th September 2025, including individuals aged 15 to 60 years of both genders. The exclusion criteria included patients with clinical conditions mimicking dystonia (neck extensor myopathy, post-traumatic deformities, Isaacs syndrome, neuromuscular junction disorders, and hemifacial spasm) and non-consenting patients. Following the acquisition of ethical clearance, participants were selected via convenience sampling methodology, with recruitment of consecutive patients presenting with focal dystonia to our department. Comprehensive data regarding demographic characteristics, clinical manifestations, and classification of focal dystonia (blepharospasm, oromandibular dystonia, laryngeal dystonia, cervical dystonia, and limb dystonia) were systematically gathered. Statistical evaluation was conducted utilizing SPSS software, with a significance threshold established at $p \leq 0.05$, using the Chi-square test.

Results: There were a total of 75 patients, with a mean age of 32.09 ±11.68 years . Most participants were men (59, 78.7%), while 16 (21.3%) were women. The most frequent form of dystonia involved the neck muscles, causing involuntary twisting of the head (cervical dystonia, 28 patients-37.3%). This was followed by dystonia affecting the arms or legs (limb dystonia, 18 -24.0%), eyelid spasms leading to repeated blinking (blepharospasm, 14 patients -18.7%), voice muscle involvement causing a strained or interrupted voice (laryngeal dystonia, 8 patients 10.7%), and jaw or facial muscle contractions (oromandibular dystonia, 7 patients - 9.3%). Dystonia subtype was strongly connected with both gender (p=0.001) and duration (p=0.050) exhibiting different clinical patterns. Concerning the variability of symptoms, 77.3% experienced persistent dystonia, 10.7% had paroxysmal symptoms, and 12.0% reported diurnal fluctuation.

Conclusion: This study identified cervical dystonia as the most frequent form of focal dystonia, followed by limb dystonia and blepharospasm. Beyond defining subtype distribution, these findings highlight the need for improved awareness and earlier recognition of dystonia among general clinicians to prevent diagnostic delays.

Keywords: Focal dystonia; Neurological disorders; Blepharospasm; Cervical dystonia

Introduction

Dystonia is a hyperkinetic movement disorder characterized by involuntary, sustained, and often patterned contractions of muscles, resulting in twisting movements or abnormal postures.[1] These movements are typically repetitive and may be associated with overflow activation of adjacent muscles, which helps differentiate dystonia from other movement disorders.[2] Etiologically, dystonia is classified as primary (idiopathic), where no structural or metabolic cause is evident, or secondary (symptomatic), which may be related to underlying lesions, systemic disease, or drug exposure.[3,4] Anatomically, it can present as focal, segmental, multifocal, or generalized, with focal dystonia being the most frequently encountered in outpatient neurology clinics.[5,6]

Dystonia is termed as "focal dystonia" when it involves only one anatomical portion of the body.[1] The global prevalence of idiopathic focal dystonia ranges from 30 to 732 per 100,000 population, reflecting wide variability across geographic and ethnic populations.[7]Among focal dystonias, the most commonly involved sites include the neck (cervical dystonia), eyelids (blepharospasm), oromandibular region, larynx, and limbs, particularly in task-specific presentations like writer's cramp or musician's dystonia.[6] In a study conducted in India, Prasad et al. reported upper limb dystonia as the most prevalent subtype (47.7%), followed by blepharospasm (26.1%) and oromandibular dystonia(18.2%).[8]

Beyond anatomical patterns, dystonia can also be classified by its temporal features as persistent, action-specific, paroxysmal, or diurnally fluctuating. Persistent dystonia remains all the time. Action-specific dystonias manifest only during tasks, paroxysmal dystonia appears episodically, while diurnal variation is typically seen in dopamine-responsive dystonia.[2,9] Diagnosis is primarily clinical and requires exclusion of mimics such as neuromuscular junction abnormalities, neck extensor myopathy, hemifacial spasm, and functional neurological disorders.[3,10]

While numerous international studies have explored the epidemiology and clinical characteristics of dystonia, such data from Pakistan remains scarce. A regional study reported that focal dystonias accounted for a significant portion of movement disorder referrals, yet sub type-specific data are largely lacking.[11] Incorporating local data into movement disorder research is essential not only for accurate diagnosis and management, but also for aligning with regional public health priorities.[12]

This study was therefore undertaken to describe the clinical spectrum of focal dystonia among patients attending neurology department of a tertiary care hospital in Karachi. By characterizing the prevalent sub-types and demographic patterns, the study aims to contribute to local data, enhance clinical recognition, and inform patient-centered management strategies in Pakistan's health-care setting. The objective of this study was to evaluate the clinical spectrum of patients with focal dystonia attending the neurology department at a tertiary care hospital in Karachi.

Methodology

This descriptive cross-sectional study was carried out at the Neurology Department of Dr. Ruth K. M. Pfau Civil Hospital, which is a tertiary care teaching hospital affiliated with Dow University of Health Sciences Karachi. The study was approved by the Institutional Review Board of the university on 18th of February, 2025 (Ref: IRB-3816/DUHS/Approval/2025/64). The study duration was six months, from 21st March 2025 to 20th September2025. Using WHO calculator, sample size of 75 cases was calculated with 95% confidence interval, 9% margin of error and percentage of oromandibular dystonia i.e. 18.18%.[13] This sample size was considered sufficient to describe the overall clinical spectrum of focal dystonia. Subsequent analyses of other focal dystonia subtypes (cervical, limb, blepharospasm, laryngeal) were performed descriptively, as the study was not powered to detect subtype-specific differences. We did not collect personally identifiable information such as names, addresses, email addresses, or phone numbers. To ensure anonymity, each participant was assigned a pseudonym. In order to maintain confidentiality all the paper based data was kept in areas where only investigators could access it . Electronic based data was saved in computers with limited access with password protection and regular backups. The inclusion criteria was participants between the age of 15 and 60 years of either sex, with focal dystonia. The exclusion criteria included patients with clinical conditions mimicking dystonia (neck extensor myopathy, post-traumatic deformities, Isaacs syndrome, neuromuscular junction disorders, and hemifacial spasm) and non-consenting patients. The participants were recruited using non-probability method of convenience sampling.

Eligible participants included both newly diagnosed with focal dystonia at the time of enrollment or had existing diagnosis prior to study entry. Diagnosis was determined by consultant neurologists with expertise in movement disorders, ensuring accuracy in recognition and classification. Focal dystonia was defined clinically as sustained, patterned, and often task-specific muscle contractions localized to a single body region. This aligns with established diagnostic frameworks and international movement disorder society guidelines.[2,3] After obtaining informed written consent, eligible patients were evaluated and data was recorded using a structured proforma capturing demographic information (age, gender, residence, education, occupation), clinical characteristics (age at onset, duration of illness, family history), and the specific type of focal dystonia. The spectrum of dystonia assessed included blepharospasm (involuntary spasm of orbicularis oculi muscles), oromandibular dystonia (involuntary movements of the jaw, tongue, or lower face), laryngeal dystonia (laryngeal muscle contractions resulting in dysphonia), cervical dystonia (involuntary twisting of the neck), and upper or lower limb dystonia. As temporal features (persistent, paroxysmal, and diurnal variation) reflect symptom behavior over time, classification was primarily based on patient-reported history, with clinical assessment at presentation used to corroborate task specificity, persistence, and fluctuation where demonstrable. This approach is consistent with established clinical practice and previously described classification systems for dystonia. Task-specific limb dystonias were explicitly screened during clinical assessment.

Data analysis was performed using IBM SPSS version 26.0. Continuous variables were reported as mean ± standard deviation, while categorical variables were reported in terms of frequencies and percentages. Statistical associations were explored using the Chi-square test, with a p-value ≤ 0.05 considered statistically significant. Given the exploratory nature of the study and small sizes of certain dystonia subgroups, results were interpreted cautiously.

Results

The study included 75 participants with a mean age of 32.09±11.68 years (95%CI:29.40–34.78), and the mean age at onset of dystonia was 29.02 ± 10.57 years (95% CI: 26.59–31.45). The average duration of illness was3.88±3.69 years (95%CI:3.03–4.73). The majority of participants were male (59, 78.7%), while 16 (21.3%) were female. A significant proportion of participants were from urban areas (89.3%), and 10.7% belonged to rural regions. In terms of educational status, 66.7% were illiterate, 22.7% had an education under matric level, and only 10.6% were graduates or above. Regarding employment, 57.3% were employed, and 42.7% were unemployed. Most participants had an active lifestyle (89.3%), while 10.7% reported a sedentary lifestyle. A family history of dystonia was present in 22.7% of the participants. Concerning the variability of symptoms, 77.3% experienced persistent dystonia, 10.7% had paroxysmal symptoms, and 12.0% reported diurnal fluctuation. No cases of focal dystonia in our study met criteria for task-specific presentation. Mean age differed significantly ($p<0.001$), being lowest in laryngeal (19.50±4.81years) and highest in cervical dystonia (39.25±10.76years). Duration of illness also varied ($p = 0.05$), with the longest in cervical (5.50 ± 4.58 years) and shortest in laryngeal dystonia (2.00 ± 1.06 years). Gender was significantly associated ($p<0.001$), with all blepharospasm patients being female and others predominantly male. Symptom variability showed significant differences ($p<0.001$): blepharospasm and oromandibular dystonia were entirely persistent, laryngeal was 50% persistent and 50% paroxysmal, while cervical presentation was 75% persistent and 25% had diurnal fluctuation.

Table 1: Association of Patient Characteristics with Clinical Spectrum of Focal Dystonia(n=75)

Patient Characteristics		Clinical Spectrum					P-Value
		Cervical Dystonia(n=28)	Limb Dystonia (n=18)	Blepharospasm (n=14)	Laryngeal dystonia (n=8)	Oromandibular dystonia (n=7)	
Age in years		39.25±10.76	29.00± 12.40	32.71± 6.91	19.50± 4.81	24.57±7.13	<0.001*
Duration of Illness in years		5.50±4.58	2.89±3.40	3.24±2.90	2.00±1.06	3.42±0.78	0.050*
Gender	**Male**	28(100.0)	16(88.9)	0 (0.0)	8(100.0)	7(100.0)	<0.001*
	Female	0 (0.0)	2(11.1)	14(100.0)	0 (0.0)	0 (0.0)	
Variability	**Persistent**	21(75.0)	12(66.7)	14(100.0)	4(50.0)	7(100.0)	<0.001*
	Paroxysmal	0 (0.0)	4(22.2)	0 (0.0)	4(50.0)	0 (0.0)	
	Diurnal fluctuation	7(25.0)	2(11.1)	0 (0.0)	0 (0.0)	0 (0.0)	

Discussion

This study provides a focused evaluation of the clinical spectrum of focal dystonia in a tertiary care hospital in Karachi, with particular emphasis on demographic patterns, subtype prevalence, and symptom variability. Cervical dystonia emerged as the most frequently observed sub-type in our cohort, accounting for 37.3% of cases, followed by limb dystonia (24.0%), blepharospasm (18.7%), laryngeal dystonia (10.7%), and oromandibular dystonia (9.3%) as shown in Table 1. This pattern differs somewhat from the findings of Prasad et al.[8] who reported upper limb dystonia as most prevalent in their Indian cohort, Similarly, Rajan et al. found that brachial dystonia accounted for 65.8% of cases, followed by cranial (27.1%) and cervical (15.7%) subtypes.[1] In contrast, results of our study are consistent with broader global trends suggesting increased recognition of cervical dystonia in clinical practice.[1,14]

The observed gender distribution in our study, where all blepharospasm cases were female and whereas other focal subtypes were predominantly observed in male patients (Table 1), contrasts with earlier reports that commonly describe a female predominance across most focal dystonia types, including cervical and cranial forms.[5,15] For example, a large European multicenter study reported a female-to-male ratio of nearly 2:1 in cranial and cervical dystonias.[16] This discrepancy may reflect regional sociocultural factors, differential care-seeking behavior, or referral biases rather than true epidemiological distributions. In our setting, male patients, who are often primary income earners, are more likely to seek neurological consultation when focal dystonia interferes with work performance, while cranial dystonias such as blepharospasm may prompt earlier consultation among female patients due to functional and cosmetic concerns. Notably, laryngeal dystonia showed the youngest mean age at onset (19.5years) , raising the possibility of early-onset idiopathic or hereditary forms, as supported by genetic studies in dystonia cohorts.[4,17] Young mean age at onset of laryngeal dystonia (19.5 ± 4.81 years), as shown in Table 1, is an intriguing finding from our study, which significantly differs from international data where onset is typically in mid-life (average 31–35 years).[18,19]

In terms of symptom variability, most cases were persistent, particularly among blepharospasm and cervical sub-types (Table 1), which is in line with findings from both SouthAsian and Western populations.[9,10] Moreover, recent reviews have underlined that focal dystonias, though relatively rare, remain under diagnosed and often misclassified, particularly in resource-constrained healthcare systems.[12] Interestingly, the average duration of illness prior to presentation varied significantly by subtype, with cervical dystonia patients having the longest mean duration (5.50 ± 4.58 years) as shown in Table 1. This finding reflects trends seen globally, where diagnostic delays are common, particularly for cervical and laryngeal dystonias.[18] One study reported an average diagnostic delay of over four years for laryngeal dystonia, often due to misdiagnosis as psychiatric or functional voice disorders.[18,19] This reinforces the need for broader awareness among non-neurologists, particularly ENT and primary care physicians, in identifying focal dystonias.

Another notable finding was the high proportion of illiterate (66.7%) patients, potentially reflecting disparities in access to care and information. This demographic skew warrants attention, as educational status may influence both care-seeking behavior and awareness of neurological symptoms, potentially contributing to delayed diagnosis and underreporting in rural settings.[13,19] A family history of dystonia was noted in 22.7% of our participants, comparable to reports from international registries and clinical cohorts.[20] This highlights the potential utility of developing national dystonia registries in Pakistan to support early identification of hereditary forms and contribute to global genomic research efforts.

The overall shortage of structured epidemiological data on dystonia in Pakistan reflects broader challenges in neurology infrastructure and research prioritization.[21] We advocate for enhanced clinician training, multidisciplinary collaboration, and public awareness campaigns to improve diagnostic accuracy and treatment outcomes. Botulinum toxin remains the mainstay of treatment for cervical and other focal dystonias; however, access and treatment outcomes may vary across regions due to resource availability and expertise.[22] Studies comparing treatment efficacy in European and Latin American populations emphasize the importance of localized treatment protocols and outcome monitoring.[22] In

the Pakistani context, such data are lacking, underscoring the need for research on therapeutic response and long-term management. The overall shortage of structured epidemiological data on dystonia in Pakistan reflects broader challenges in neurology infrastructure and research prioritization.[20] This study underscores the clinical utility of subtype classification in improving diagnostic accuracy and tailoring patient management. It supports the growing consensus that earlier recognition, broader awareness among clinicians, and local registry development are vital to advancing care for dystonia patients in developing regions.[6,16] Furthermore, understanding the distribution of focal dystonia subtypes will support timely referrals, reduce misdiagnosis, and guide effective treatment approaches.[16]

Limitations

Several limitations of this study warrant acknowledgement. First, the research was conducted at a single tertiary care facility, Dr. Ruth K. M. Pfau Civil Hospital, as an initial, exploratory effort to generate baseline data on focal dystonia in Pakistan, where subtype-specific data are currently scarce. This setting allowed for diagnostic consistency by expert neurologists within available time, resource constraints and ethical approvals. While this center serves a large and diverse patient population, the single-center design, modest sample size, and reliance on convenience sampling may introduce selection and referral bias. Consequently, the observed clinical spectrum may not be fully representative of the general population. The observed sex distribution across focal dystonia subtypes should be interpreted with caution. The predominance of females in blepharospasm and males in other subtypes likely reflects referral patterns, health seeking behaviour and center-specific sampling rather than true biological differences, hence the findings are not intended to represent population-level sex distribution. Additionally, the use of Chi-square testing in small subgroup analyses may have resulted in violations of test assumptions, and effect sizes or confidence intervals were not calculated. Therefore, statistically significant associations should be interpreted as exploratory and hypothesis-generating rather than definitive. Since the diagnoses were made by multiple clinicians without formal inter-rater reliability assessment, some degree of diagnostic variability cannot be excluded. One limitation of our study is that our assessment of cervical dystonia did not include documentation of its phenomenological subtype and directionality. Specific subtypes - including torticollis, retrocollis, laterocollis, anterocollis were not systematically recorded hence subtype specific comparisons could not be performed.

Despite these constraints, our findings contribute meaningful insights into the presentation of focal dystonia within the Pakistani context, where data on movement disorders remain scarce.

Conclusion

This study highlights cervical dystonia as the most prevalent form of focal dystonia in a tertiary care setting, followed by limb dystonia and blepharospasm. The findings underscore the clinical variability and demographic associations among sub-types. Recognizing these patterns can enhance diagnostic accuracy and inform targeted management strategies, particularly in regions with limited data on movement disorders like Pakistan.

Author Contributions: RK: Conceptualization, study design, data collection, data interpretation, writing original draft, review & editing; QN: Conceptualization, data analysis, review & editing, Supervision; SJF: Data analysis, data interpretation, review & editing; SRU: Data analysis, data interpretation, review & editing; RI: Data collection, writing original draft; WJ: Conceptualization, study design, data analysis, data interpretation, review & editing, Supervision. All authors approved the final manuscript and are accountable for all aspects of the work.

Conflict of Interest: The authors declare no conflict of interest.

Funding Disclosure: This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Data Availability Statement: The data that support the findings of this study, apart from the data already presented in the results section, are available from the corresponding author upon reasonable request

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Journal of University College of Medicine & Dentistry

Original Article

Analysis of Caesarean Sections Using Robson's Ten-Group Classification System in a Tertiary Care Hospital: A Descriptive Study

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Submission: 18th July, 2025
First revision: 30th October, 2025
Second revision: 14th November, 2025
Third Revision: 4th December, 2025
Fourth Revision: 23rd December, 2025
Final Revision: 5th January, 2026
Acceptance: 13th January, 2026

DOI: https://doi.org/10.51846 jucmd.v5i1.4338

Cite this article as:

Fatima F, Waheed G, Safdar Z, Zia U, Sohail SG, Rasheed M. Analysis of caesarean section by using Robson's group classification system in a tertiary care hospital. *J Univ Coll Med Dent*. 2026;5(1): 63-70

Abstract

Objective: To evaluate the impact of subgroups and the frequency of cesarean sections using the Robson's Ten-Group Classification system at a tertiary care center in Lahore, Pakistan.

Methodology: This descriptive examination of a cross-section included all births that took place at Avicenna Hospital, Lahore, from July 1, 2024, to March 31, 2025. A total of 550 deliveries were classified according to the Robson ten-group classification system. Maternal demographics, obstetric characteristics, indications for caesarean sections, and the results for mothers and newborns were also recorded. Data were analyzed using SPSS version 26, and the results are presented as frequencies and percentages.

Results: Among 550 deliveries, 200 were caesarean sections, yielding an in general caesarean section (rate of 36.4% (200/550 deliveries). The average maternal age of women having cesareans (29.3 ± 5.4 years. Robson ten-group classification system analysis showed that Robson ten-group classification system analysis showed that Group 4 (women who are multiparous but do not have a uterine scar,induced or pre-labor caesarean sections) comprised the largest segment of caesarean sections (cases (27.5%), succeeded in contribution by Group 5 (Uterine scarred multiparous women) (27.0%) of all caesarean deliveries. Failed induction and failure to progress were the most common indications for these groups.

Conclusion: The application of Robson ten-group classification system demonstrated that multiparous women, particularly those in Groups 4 and 5, were significantly associated with higher rates of caesarean sections. Focused clinical audits and targeted obstetric interventions in these groups may help optimize caesarean section practices and reduce unnecessary procedures.

Keywords: Caesarean section, Obstetrics, Pregnancy Robson Ten-Group Classification System

Introduction

Medically indicated caesarean section (CS) is a vital obstetric intervention that can improve maternal and neonatal outcomes and safeguard both lives.[1] Examples of clinical indications for CS include fetal distress, placenta previa, obstructed labor, and other situations in which the risks associated with vaginal delivery are high. Through the use of prompt surgical intervention, CS minimizes the risks of maternal and neonatal morbidity and mortality from complications such as severe maternal hemorrhage, uterine rupture, or neonatal asphyxia. Furthermore, CS may improve long term health outcomes and enhance maternal psychosocial well-being by preventing trauma to the mother and baby, and ensuring a safer recovery. Global surveys indicate that the percentage of cesarean deliveries was 21.1% in 2021 and is predicted to rise to almost 29% in 2023.[2] This increase can be attributed to multiple factors, like the improvement of prenatal diagnoses, advancements of medical equipment, and refinements of clinical practices that prioritize the safety of the mother and baby. The increasing demand for cesarean sections is also attributed to maternal age, older first-time mothers, and the increased presence of comorbidities. Given the trend, it is concerning that the overutilization of cesarean sections may pose unwarranted surgical risks, prolonged recovery, and increased cost of care without any added value.

The disparity is still quite notable. While CS rates are at 8.2% for low-income countries and 24.2% for middle-income countries, depending on the location, there are quite complex cases of both under and over utilization.[2] In low-income countries, the underutilization of CS often contributes to readily preventable deaths of mothers and newborns due to the lack of access to emergency obstetric care and surgical services. Middle-income countries, on the other hand, face dual problems: disparate access, where some areas have over-utilization, and other areas have under-utilization, due to non-medical reasons such as provider payment incentives, cultural norms, and systemic healthcare inefficiencies. The dissimilarity of the zones reinforces the need for tailored strategies to address both availability and

the lessening of potential unnecessary caesarean sections. Pakistan faces alarming rates of cesarean births which appear to exceed the WHO optimal use guidelines based on national data from the Demographic and Health Survey.[3,4]The cesarean birth rate worldwide is ideally kept between 10-15% in order to limit the risks associated with having a cesarean. Anything beyond this risk threshold is without a doubt a medical overuse driven by patient wants, physician convenience, or socioeconomic factors. Such overuse would likely increase the risks of operative morbidity, prolonged admissions, and the strain on the healthcare system. The data provided necessitate a systematic review on the assessment of cesarean birth procedures. In order to improve the outcomes of mothers and babies, the processes must be evidence based and effectively streamlined. Standardized clinical processes, enhanced provider education, and improved patient education will help align the use of cesareans with best practices, and will focus on increasing the safety and resource efficiency of cesarean practices.

Methodology

This retrospective cross-sectional study was conducted using delivery records from the Avicenna Hospital's Department of Obstetrics & Gynecology, affiliated with Avicenna Medical College, Lahore, Pakistan. Every delivery occurring between July 1, 2024, and March 31, 2025, were eligible for inclusion, which included 550 deliveries. The ERB approval was obtained from the institution under reference number IRB-53/06/24/AVC on 20-04-2024. Women included in this study reported having given live birth or stillbirth at gestational weeks 24 or more.

Table 1: Robson's Ten Group Classification System.[5]

Group	Description
1	First-time mothers having one fetus in cephalic position during the term[a] who go into labor naturally.
2	Women who are nulliparous and have one cephalic-term[a] pregnancy whose either induced or natural labor or scheduled for caesarean delivery.
3	Women who are multiparous yet lack previous uterine scar, carrying a single cephalic fetus at term[a] with spontaneous labor onset.
4	Women who are multiparous but no scarred uterus, utilizing a singleton cephalic-term[a] pregnancy, undergoing either induced labor or planned CS.
5	Women with one or more prior caesarean sections, carrying a single cephalic fetus at term[a].
6	First-time mothers carrying a single fetus in breech presentation.
7	Women who are multiparous and breech presenting singleton pregnancy, including those with prior uterine surgery.
8	All women carrying twins or higher-order multiples, regardless of previous CS status.
9	Women with a singleton fetus in transverse or oblique lie, with or without a uterine scar.
10	All women delivering a single cephalic fetus before 37 weeks of gestation[b], including those with previous CS.

a refers to at least 37 weeks of gestation at the time of delivery. b refers to a gestational age of less than 37 full weeks at the time of delivery.

All deliveries were categorized using Robson's Ten-Group Classification System (RTGCS), which facilitated group classification and size calculations. Clinical breakdowns were restricted, however, to the 200 CS cases for the baseline maternal characteristics, the reasons for the operation, any complications intra- or post-operatively, and the outcomes for the neonates. Records for deliveries prior to 24 weeks gestation and the record sets without the necessary variables to construct a Robson group were eliminated from consideration in the study.

Using a structured proforma, the study acquired data from labor ward records, operating theatre registers, and the study period individual clinical records. Variables included maternal age, gravida, parity, prior abortions, and gestational age at delivery, and obstetric and demographic characteristics, labor onset (pre- CS labor, spontaneous, induced, augmented), CS primary reason, maternal medical comorbidities/ complications, Apgar score, and other neonatal parameters. Source registers and the clinical team for the case were consulted to fill any gaps identified.

To analyze the data, SPSS version 26 was utilized. Continuous variables' lowest and highest values are shown as mean ± standard deviation (SD). Frequencies (n) and percentages (%) are used to display categorical variables. Unless otherwise specified, percentages for baseline characteristics, indications, complications, and neonatal outcomes used the denominator of all caesarean sections. For the Robson analysis, the relative contribution to CS (%) used all CS as the denominator, and its absolute contribution to CS rate (%) used all deliveries (N=550) as the denominator. The size of each group (%) and the group CS rate (%) require the total number of deliveries within each Robson group; however, these totals were unavailable and therefore could not be calculated. As this was a descriptive institutional audit, no hypothesis testing was conducted a priori.

For the Robson analysis, the following measures were

defined (denominators shown in brackets): Group size (%) = (Robson group delivery count ÷ total deliveries [N=550]) × 100 (not computed in this analysis since group totals were not available) ; CS rate within group (%) = (number of CS in the Robson group ÷ number of deliveries in that group) × 100 (not computed in this analysis since group totals were not available); The total percentage of the CS rate is equal to the number of CS in the Robson group divided by the total number of deliveries (N = 550) times 100; In the Robson group, the number of CS divided by the total number of CS (N = 200) equals the relative contribution to all CS (%); Robson's "relative contribution to all CS" and "group size (%)" percentages were computed with all deliveries as the denominator and were verified to add up to almost 100%.

Results

Throughout the research period, there were 550 deliveries recorded, including 200 caesarean sections, yielding an overall CS rate of 36.4% (200/550). Unless otherwise specified, the results below describe women who underwent CS (N=200). The baseline maternal and obstetric characteristics of the CS cases are summarized in Table 2. The average age of mothers was 29.3 ± 5.4 years and the mean gestational age at delivery was 37.2 ± 1.7 weeks. Regarding labor status at the time of caesarean section, pre-labour caesarean section was the most common, accounting for 79 cases (39.5%). This was followed by caesarean section after spontaneous labour in 74 cases (37.0%). Caesarean sections performed after induced labour comprised 37 cases (18.5%), while 10 cases (5.0%) occurred following augmentation of labour.

The minimum and maximum values of continuous variables are displayed as mean ± standard deviation (SD). Categorical variables are presented as n (%). Percentages for labor status were calculated using the total number of caesarean sections (N = 200) as the denominator.

Table 2. Maternal characteristics and labor status among women undergoing caesarean section (N = 200)

Characteristic	Value	Range / %
Age (years)	29.3 ± 5.4	17–39
Gravida	3.0 ± 1.7	1–9
Parity	1.8 ± 1.7	0–8
Previous abortions	0.3 ± 0.7	0–3
Gestational age (weeks)	37.2 ± 1.7	26–41
Pre-labour CS	79	39.5%
Spontaneous labour	74	37.0%
Induced labour	37	18.5%
Augmented labour	10	5.0%

The primary indications for CS are listed in the figure (Figure 1). The most frequent indications were previous caesarean section, fetal distress, and failure to progress, with other indications contributing to smaller proportions. Bars show the percentage of CS cases for each recorded primary indication, Percentages used N=200 as the denominator.

The maternal comorbidities/complications recorded in the CS cases are shown in the figure (Figure 2). A substantial

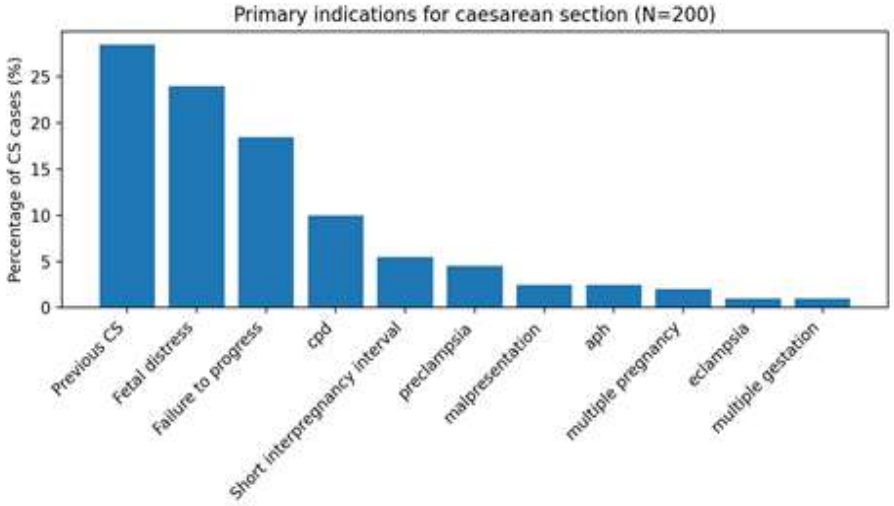

Figure 1. Primary indications for caesarean section among CS cases (N=200).

proportion had no recorded comorbidity/complication, while anemia and decreased fetal movement were among the most commonly recorded conditions. Each case was assigned a single primary comorbidity/complication category; therefore, the categories were mutually exclusive. Bars show the percentage of CS cases in each primary comorbidity/complication category. Categories are mutually exclusive, and percentages use N=200 as the denominator.

Most neonates were viable at birth 196(98%), with a small

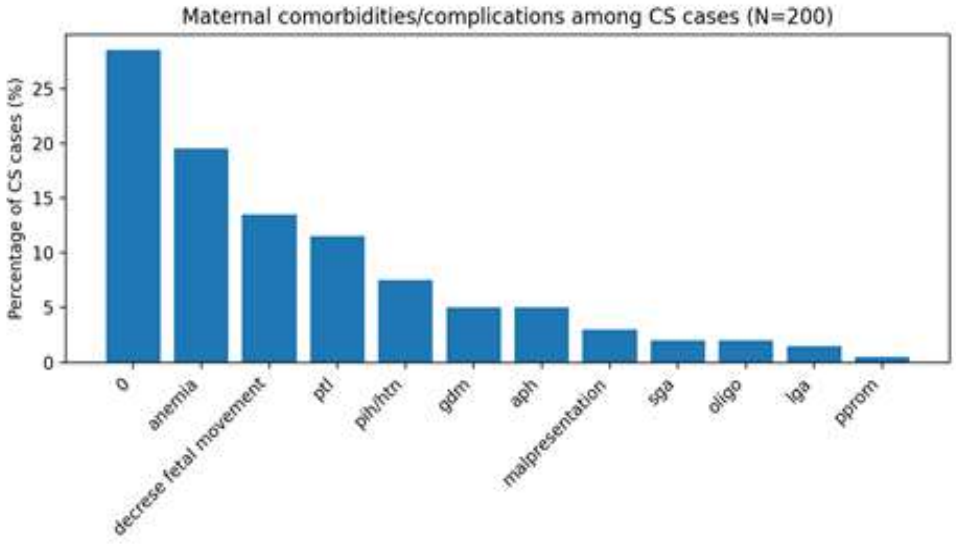

Figure 2. Maternal comorbidities among caesarean section cases (N=200).

proportion of them being stillbirths 3(1.5%). Apgar categories are reported in Table 3, with the majority achieving Apgar ≥7, and smaller proportions with low Apgar or Apgar 0. Values are presented as n (%). Percentages were calculated using N=200 caesarean sections as the denominator.
Values are presented as n (%). Percentages were calculated

Table 3. Indications for caesarean section, maternal comorbidities, and neonatal outcomes (N = 200)

Category	n	%
Indications for caesarean section		
Previous caesarean section	54	27.0
Fetal distress	48	24.0
Failure to progress	36	18.0
Other indications	62	31.0
Maternal comorbidities		
Anemia	42	21.0
Reduced fetal movements	26	[13].0
No comorbidity	102	51.0
Neonatal outcomes		
Live birth	197	98.5
Stillbirth	3	1.5
Apgar score at 5 minutes		
≥ 7	191	95.5
< 7	6	3.0
0	3	1.5

using N = 200 caesarean sections as the denominator. Indications for caesarean section are mutually exclusive and sum to 100%. Maternal comorbidity categories represent the most frequently recorded conditions and therefore do not sum to 100%. An Apgar score of 0 corresponds to stillbirths. NR = Not reported due to absence of total deliveries within each Robson group. Group size (%) = (N = 550) x 100 (number of women in each Robson group ÷ total deliveries). The CS rate within a group is calculated by multiplying the number of caesarean sections by the total number of women in the group by 100. Relative contribution to total CS (%) = (group caesarean sections ÷ total [N = 200]) × 100. Because Robson group delivery totals were unavailable, NR = Not recorded. OB group definitions and reporting indicators follow the WHO Robson categorization implementation guideline.[6]

Table 4. Robson Ten-Group Classification of caesarean sections with relative contribution to total CS

Robson Group	Obstetric group (WHO definition)[15]	CS (n)	Group size (%)	CS rate within group (%)	Relative contribution to total CS (%)
1	Singular, cephalic, nulliparous, term, spontaneous labor	24	NR	NR	12.0
2	Term, induced, pre-labor, singleton, nulliparous, or cephalic CS	5	NR	NR	2.5
3	Singleton, cephalic, term, spontaneous labor, and multiparous (no scar)	7	NR	NR	3.5
4	Singular, cephalic, term, induced, or pre-labor CS, multiparous (no scar)	55	NR	NR	27.5
5	Multiparous, ≥1 previous CS, singleton, cephalic, term	54	NR	NR	27
6	Nulliparous, singleton breech	2	NR	NR	1.0
7	Singleton breech and multiparous (including prior CS)	10	NR	NR	5.0
8	Previous CS and several pregnancies	8	NR	NR	4.0
9	Transverse or oblique lie, singleton pregnancy	13	NR	NR	6.5
10	Singleton, cephalic, preterm (<37 weeks)	22	NR	NR	11
Total		**200**			**100**

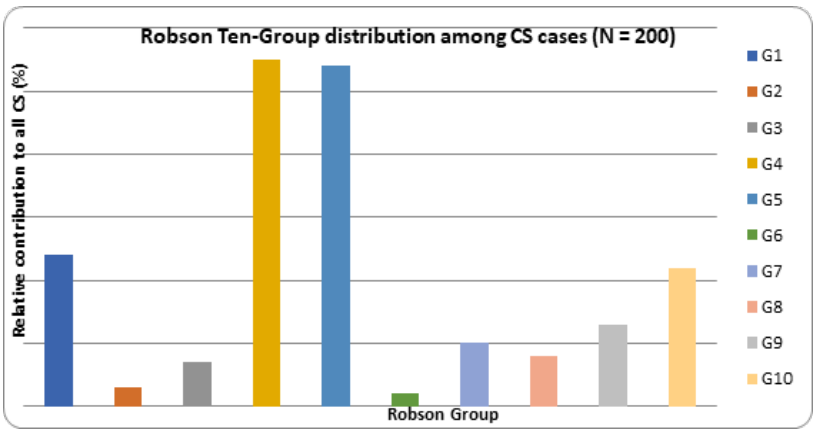

Figure 3: Relative contribution of RTGCS to all caesarean sections (N=200). Bars show the percentage of all CS accounted for by each Robson group (denominator: all CS, N=200).

Discussion

This hospital-based audit applied the Robson Ten-Group Classification System to 550 deliveries at a tertiary care center and found that Groups 4 and 5 accounted for more than half of all caesarean sections, yielding an overall CS rate of 36.4%. Institutional audits of this type are critical because they not only quantify operative workload but also highlight the obstetric groups in which targeted interventions may reduce unnecessary CS. As a developing country, Pakistan is at 5th rank with a greater population rate, and according to the WHO with a 340/100,000 mortality rate.[7] The rising section rate may be attributed to complications such as breech presentation, placenta previa, and prior pregnancies. WHO cautions against the widespread assumption that surgical birth offers greater safety than vaginal delivery, a perception that has fueled rising rates of non-medically indicated procedures and heightened medico-legal anxiety among healthcare providers.[6,7] Other factors such as scarred uterus, induced labour, escalated utilization of postoperative antibacterial agents, and higher maternal illness and death can be optimized by regular antenatal visits.[8] Numerous efforts have been made to curb the increasing trend of c-sections by conducting various clinical audits and developing guidelines for the indications for c-sections but none of these strategies have been successful.[9,10]

Over time, CS rates in Pakistan have increased significantly, exceeding WHO guidelines as reported in the most recent demographic and health census. The necessity for rigorous institutional audits is underscored by the much higher rates that have been documented at tertiary care hospitals.[11,12]

This hospital-based audit reported a caesarean section rate of 36.4%, with 200 procedures performed out of 550 total deliveries. Baseline maternal traits and labor status are summarized in Table 2. Fetal discomfort, prior cesarean section, and lack of improvement were the most common indications for surgery, while anemia was the most frequent maternal comorbidity (Table 3). Neonatal outcomes were generally favorable, with the majority of neonates achieving an Apgar score ≥7 at five minutes (Table 3). Robson analysis showed that Groups 4 and 5 caused most of the workload related to cesarean sections (Table 4).

The RTGCS analyzed the distribution and individual contribution of the obstetric team members towards the total CS rate. The main contributors to the CS workload were Groups 4 and 5, followed by Groups 1 and 10. RTGCS provides a consistent and systematic approach to evaluating the CS rate and identifying focus groups that may be eligible for quality improvement interventions. When compared to other audits conducted using the RTGCS, it has been noted that there are often significant contributions from multiparous women, particularly those in Groups 4 and 5. This has been documented in numerous facility-based studies, particularly those where the clinicians faced challenges in managing the labor and repeat CS. It is reasonable to expect variation between institutions, and this is often the result of a variety of influences, including referral patterns, a case mix that includes higher risk pregnancies, the availability of safe labor induction, active labor monitoring, and institutional policies about the timing of repeat caesarean sections.[13]An audit from a tertiary teaching hospital in Northern Uganda using the Robson classification also documented the ability to define the most contributing groups, and this could be used to inform quality improvement efforts in the USE of CS.[14] International experience adds depth to Robson's classification, showing it can do more than measure CS rates and assist in quality assessment and policy development. For instance, Robson strata have been used in population-based assessments to analyze and track certain postpartum complications, like postpartum hemorrhage, and to assess changes in obstetrician and obstetrician-gynecologist practice over time.[8] WHO recommends RTGCS as the standard for global CS auditing and suggests the regular use of Robson-based reporting to support intracountry comparisons and facility-based assessments.[15,16] From the perspective of institutional policy, the clustering of CS in Groups 4 and 5 underscores the prioritizable action areas. First, for women with a previous CS (Group 5), strengthening structured antenatal counselling and standardized eligibility assessment for trial of labor after caesarean (TOLAC/VBAC), where clinically appropriate and safely supported, may reduce repeat CS. Second, for Groups 1–4, refining induction protocols, standardizing labor progress assessment (including clear definitions of labor arrest), and strengthening fetal monitoring interpretation and response pathways may reduce potentially avoidable CS for fetal distress or failure to progress. Third, routine quarterly RTGCS audit with feedback to clinical teams can support continuous quality improvement and track the impact of implemented changes. Besides positive therapeutic indications, Caesarean section rates are also strongly influenced by institutional and broader health system factors. Recent Pakistan Demographic and Health Surveys reveal that the likelihood of having a caesarean delivery is higher in private maternal health care than in public. This implies that non-medical CS may be practiced when there are financial opportunities and loose regulatory frameworks.[17] In addition, the expanding field of studies in South Asia emphasizes health system components such as the patterns of provider practice, institutional practices, and resource limitations as critical in influencing CS decisions, in addition to individual clinical risk factors.[18]

Limitations

This was a single-center audit over a limited duration, and detailed clinical analyses were performed for CS cases (N=200). In addition, because the totals for all deliveries in each Robson group were not available, we reported the Robson distribution among CS cases (relative contribution to CS) and absolute contribution to the overall CS rate, rather than the full WHO-style group size and within-group CS rates. Data were reliant on accurate medical records of a limited duration of nine months and a limited number of patients. The result's generalizability was limited because the investigation was only carried out in one tertiary facility; however, multicenter studies would be more conclusive, as they would manage a higher proportion of complex pregnancies. In addition, the general distribution of group contributions seems to stand in alignment with the existing literature in the field, contributing to the overall validity of the Robson classification system in any context. However, this particular study has a number of pertinent issues. First, the analysis did not go beyond the bounds of descriptive statistics to embrace the multivariable techniques required to pinpoint independent predictors of a cesarean section. Second, there is a potential for bias in the reliance on hospital

records and the records kept by the hospital which can lead to misclassification bias due to the absence of complete or inaccurate records.

The restricted application of the RTGCS to one particular institution, in this case, may limit the extent to which the findings can be extrapolated to the wider community, especially considering the exclusion of women who gave birth at home or in the private hospital setting. In addition, due to the fact that the neonatal outcomes were presented in a batch, this restricted the overall integration of the outcomes with the principal framework for analysis of the study, the RTGCS. It is accepted that the absence of neonatal outcomes by Robson group constitutes a significant gap in this study. More research of this type is required to articulate more precisely the relationship that exists between the patterns of cesarean delivery and the outcomes for infants in the various obstetric group.

Conclusion

The use of the RTGCS showed that the two groups of multiparous women defined as Group 4 and Group 5 had the highest percentages of caesarean deliveries at 27.5% and 27.0%, respectively, which identifies the primary contributors to the total CS rate. With the most recent data highlighting the need for specific, immediate clinical measures, this includes the auditing of CS indications for Group 4, the advocacy of safe VBAC for Group 5, the adjustment of the CS for the less than ideal indications, and the improvement of the standards of care for the induction and augmentation. There is also a need for the government to facilitate the first steps towards a national RTGCS surveillance for the continued setting of benchmarks and the alignment of organizational practices for childbirth with the goals of health-optimizing policy.

Authors' contributions: FF contributed to study conception and design, data acquisition and interpretation, drafting of the manuscript, critical revisions, and formulation of the conclusion; GW provided overall supervision, contributed to study design, guided the literature review, and critically revised the manuscript for intellectual content; ZS contributed to supervisory oversight, reviewed the study methodology, and critically revised the manuscript; UZ contributed to study design and data collection and reviewed the manuscript; SGS contributed to data collection and assisted in manuscript review**;** MR contributed to data collection and assisted in manuscript review. All authors reviewed and approved the final version of the manuscript and agree to be accountable for all aspects of the work in accordance with ICMJE criteria.

Conflict of interest: The authors declare no conflicts of interest.

Funding Disclosure: This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Data Availability Statement: The data that support the findings of this study, apart from the data already presented in the Results section, are available from the corresponding author upon reasonable request.

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Journal of University College of Medicine & Dentistry

Original Article

Frequency, Causes, and Complications of Re-Cannulation After Peripheral Intravenous Catheterization in Surgical Patients: A Cross-Sectional Study

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Submission: 1st October, 2025
First revision: 30th October, 2025
Second revision: 18th November, 2025
Final Revision: 25th December, 2025
Acceptance: 8th January, 2026

DOI: https://doi.org/10.51846/jucmd.v5i1.4712

Cite this article as:

Waqar SH, Khaliq M, Hussain AT, Wajahat H, Khan M, Abidin ZU. Frequency, causes, and complications of re-cannulation after peripheral intravenous catheterization in surgical patients: a cross-sectional study. *J Univ Coll Med Dent*. 2026;5(1): 71-76

Abstract

Objective: To assess the size of the cannulas, frequency, causes, as well as the complications associated with re-cannulations among patients admitted within the surgical wards of the Pakistan Institute of Medical Sciences (PIMS), Islamabad, Pakistan.

Methodology: A cross-sectional study was conducted in the General Surgery Department of PIMS, Islamabad, on 225 cases who received peripheral intravenous fluid from January to March 2025. Patients in the age group of 14 to 75 years administered with intravenous fluid were included in the study, but those referred from other healthcare institutions who already have an established intravenous access were excluded. Demographic information, such as gender, age group, and presence of co-morbidities recorded along with the complications developing in patients after peripheral intravenous catheterization, like phlebitis, infiltration, and extravasation of the fluids. Additionally, the other details, such as the infusion rates of the intravenous fluids, the size of the peripheral intravenous fluid access, the site of the peripheral intravenous fluid access, and the dwell time, are recorded.

Results: A total of 225 patients were studied, with a mean age of 43.96 ± 17.1 years. In IV cannula replacement due to complications, including pain, swelling, and inflammation in 104 patients (46.2%), patients did not undergo additional procedures except for the replacement of the cannula. The 20-G cannula was most commonly used in patients (n = 113; 50.0%). The duration of the cannula was below four days in 212 patients (94.2%), with eight patients (3.6%) over four days, while in five patients (2.2%), duration was unspecified. Regarding the insertion area of the cannula, the arm was the foremost site in 117 patients (52%), while others included the hand in 74 patients (32.8%), antecubital fossa in 11 patients (4.9%), lower limbs in 10 patients (4.4%), and instep in five patients (2.2%).

Conclusion: Swelling with pain was the key clinical outcome associated with the use of peripheral IV catheterization in surgical patients. Patient's age, dwell time, and insertion site were found to be associated factors for the complications of peripheral IV catheterization.

Keywords: Infusions, Intravenous; Continuous Infusion; Intermittent Infusion; Drug Administration Schedule; Catheterization, Peripheral.

Introduction

Peripheral intravenous catheterization is one of the most frequently performed invasive procedures in clinical settings, especially among surgical patients.[1] It is a fundamental component of perioperative care employed for the administration of fluids, drugs, blood products, and nutritional aids. Despite its regular employment, it would seem that simple intervention is not devoid of complications, and its efficiency and safety are significant concerns in patient care and hospital management.[2] In the perioperative setting, peripheral intravenous access cannot be avoided. Surgical patients, by the nature of their condition and the intervention they have, present an increased risk for fluid imbalance, sepsis, drug-related reactions, and other complications that require quick intravenous management.[3] PIVC has an essential role to play in reaching these clinical objectives. However, inappropriate catheter selection, suboptimal insertion site, bad maintenance, and long-term catheter dwell times can give rise to serious adverse effects such as phlebitis, infiltration, obstruction, dislocation, chaos, and catheter-related bloodstream infections.[4] These complications may cause delays in treatment, increasing the patient's discomfort, prolonging hospital stay, and increasing the cost of health care.[5]

Certain studies have identified concerns linked to the use of PIVCs with variable outcomes depending on the demographic data and the level of expertise.[6,7] Although some studies highlight the low complexity rates utilizing standardized care protocols, others underline the difficulties of ensuring successful catheter placement and care. These anomalies are clear in surgical patients, especially in surgical patients due to physical stresses imposed by anaesthesia, tissue trauma, and converted immune responses.[8] Postoperatively, conditions such as hypotension, hypothermia, and immobility lead this patient's population on catheter related issues. In addition, surgical patients often require many drugs that can disturb the vascular endothelium,

which can reduce the risks associated with the PIVC.[9] It remains the most commonly used method to establish vascular access, enabling liquids and drug administration in a wide range of patient groups. It is estimated that about 30% to 80% of hospitalized patients receive a PIVC during their stay.[10,11] A PIVC insertion done immediately after the patient's entry, often in induction or operating room settings. This initial placement facilitates quick handling of fluid management, anaesthetic administration, and perioperative complications. Since the procedure was conducted, the patient is still conscious, primarily due to the administration of anaesthesia, which can be quite associated with discomfort and crisis. Repeated unsuccessful efforts on cannulation can increase anxiety for both patient and healthcare providers, increase local irritation and inflammation, increase the risk of microbial contamination, and require the use of alternative insertion sites that may be technically more difficult or reduce additional risks.[12]

In recent years, the healthcare system has placed an increasing emphasis on patient-focused care, quality improvement, and infection prevention. PIVC-related complications are now considered the major indicator of care, especially in surgical units where vascular access is important. The occurrence, type, and underlying determinants of such complications must be identified to design specific interventions and educational programs. The role of overview studies in this respect is found to be indispensable, allowing real-time observations on practices in the clinical environment, patient response, and outcomes. Based on an assessment of convertible risk factors and general failure modes, these studies have a potential role in making specific clinical practices more effective, with reduced complexity rates and enhanced patient satisfaction.

Methodology

This observational cross-sectional study investigated 225 patients in the General Surgery Department, PIMS, Islamabad, from January to March 2025. Patients aged 14 to 75 years who required intravenous liquid therapy and were admitted to the Department of General Surgery, PIMS, Islamabad, after receiving ethical approval from the Ethics Research Review Board (F-5-2/2024(ERRB)/PIMS dated 1st March 2024) were included. All patients presenting in the general surgery Emergency Room or Outpatient Department who required intravenous access were enrolled by non-probability convenience sampling. Patients referred from other healthcare facilities with already maintained intravenous access, referred/shifted to different departments, and those who left against medical advice were excluded. Data was collected through direct observation and patient record reviews in the post-anesthesia care units of the surgical ward, operating room, and selected hospital. A structured data collection form used for patient demographics, PIVC insertion, as well as any catheter-related complications, including phlebitis, infiltration, and extravasation. IV infusion setting, PIVC catheter size, Insertion site, and Catheter dwell time were recorded. Patients were monitored daily until the catheter was removed.

The data were recorded and analyzed using SPSS version 27. Descriptive figures such as frequencies, percentages, means, and standard deviations are used to summarize patient characteristics and complexity rates. Factors associated with complications after peripheral intravenous catheterization, such as age, comorbidities, IV infusion setting, catheter size, insertion sites, and catheter dwell time, were identified and determined using the Chi-square test (X2) by taking a 95% confidence interval and <5% (0.05) as the level of significance.

Results

The overall mean age was 43.96±17.1 years. Of 225 patients, 144 (64%) were male, and 81 (36%) were female. Patient's distribution based on their age was as follows: 40 (17.8%), 14-30 years, 80 (35.6%), 31-45 years, 56 (24.9%), 46-60 years, and 49 (21.8%), 61-75 years. Of the total 225 patients, an IV Cannula was changed in 104 (46.2%) cases. Swelling and pain were the main reasons for cannula changes, followed by swelling and inflammation in 16 (7.1%) cases. The majority of patients were administered by cannula no 20G 113 (50%), followed by 18G 80 (35%). Diabetes was the major comorbidity found in 48 (21.3%). The majority of patients, 94.2% (n=212), had a catheter dwelling time less than 4 days, followed by 3.6% (n=8) >4 days, and 2.22% (n=5) unknown. The arm was the prominent insertion site used in 117 (52%) patients as catheter insertion sites followed by the hand 74 (32.8%), arm crook 11 (4.9%), leg 10 (4.4%), Head 5 (2.2%), instep 5 (2.2%), and Ankle 3 (1.3%). Demographic and baseline details are presented in Table 1. Figure 1 illustrates the change in the cannula status. Factors associated with complications after peripheral intravenous catheterization are presented in Table 2.

Table 1: Demographic and baseline details (N=225)

Parameters	N (%)
Age (years)	43.96±17.1
Gender	
Male	144 (64%)
Female	81 (36%)
Comorbidities	
Diabetes Mellitus (DM)	48 (21.3%)
Hypertension (HTN)	8 (3.6%)
HTN+DM	16 (7.1%)

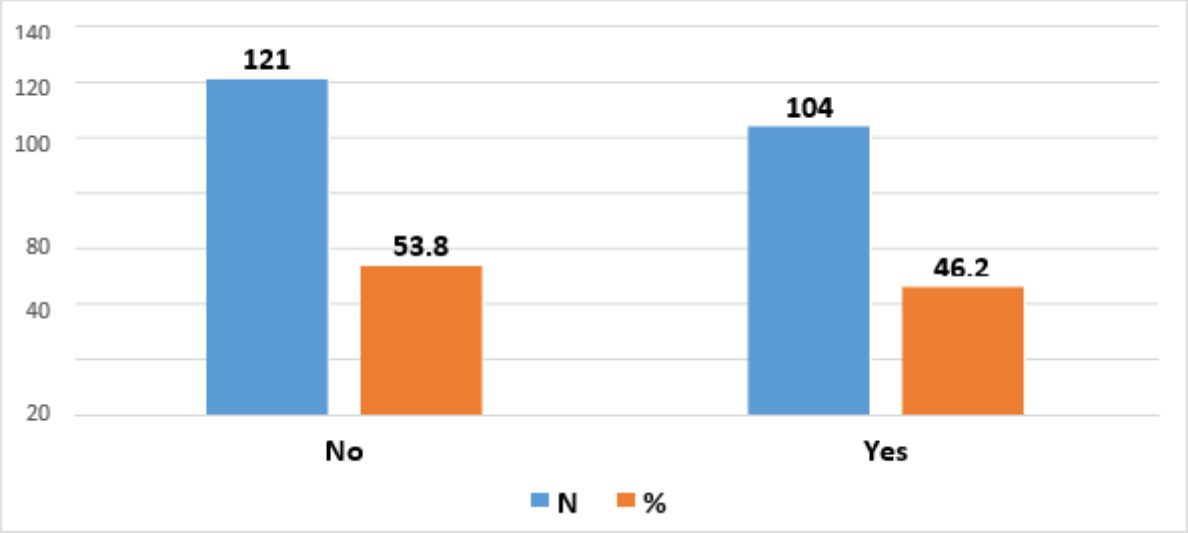

Figure 1: Change of cannula status (N=225)

Table 2: Factors associated with complications after peripheral intravenous catheterization

Parameters/Factors	N (%)	P-value
IV infusion setting		
Continuous	121 (53.8%)	0.184
Intermittent	104 (46.2%)	
Catheter Size		
16 gauge	8 (3.6%)	
18 gauge	80 (35.5%)	
20 gauge	113 (50.2%)	
22 gauge	8 (3.6%)	0.091
24 gauge	16 (7.1%)	
Site		
Arm	117 (52%)	
Hand	74 (32.8%)	
Arm crook	11 (4.9%)	
Leg	10 (4.4%)	
Instep	5 (2.2%)	0.032*
Head	5 (2.2%)	
Ankle	3 (1.3%)	
Dressing		
Sterile	218 (96.9%)	0.268
Nonsterile	7 (3.1%)	
Catheter dwell time		
<4 days	212 (94.2%)	
>4 days	8 (3.6%)	0.001*
Unknown	5 (2.22%)	

*Statistically significant at $p < 0.05$

Discussion

The present study mainly focused on the frequency, causes, and complications of peripheral intravenous catheterization in surgical patients and reported that patient age, catheter dwelling time, and insertion site contribute to the postoperative complications of peripheral intravenous catheterization. Additionally, pain and swelling are other associated factors for peripheral intravenous catheterization in surgical patients. The frequency of cannula changes reported in the present study was 46.2%. Numerous factors, such as insertion site preparation, catheter dwell time, catheter size, dressing types, and infusion types, contributed to the development of complications. In the current study, the majority of PIVCs were inserted in the arm 117 (52%) and the hand 74 (32.8%).

In this study, the average age of patients was 43.96 ± 17.1 years, indicating a diverse patient population consisting of both young adults and the elderly. The majority of patients (35.6%) belonged to the age range 31-45 years, aligning with the prior studies reported statistics that due to higher surgical workload in this age group, requiring cannulated surgeries.[13]

The male population predominance (64%) is also consistent with local and regional trends observed in hospital-based surgical admissions, possibly reflecting gender-related health-seeking behavior or disease distribution patterns.[14] Gender distribution showed a high ratio of male patients (64%) compared to women (36%). While the vein itself may not be a direct factor affecting the catheter results, previous literature suggests that patients often present with prominent veins, potentially allowing easy canals, although it does not always translate into low complexity rates. An earlier study reported similar results in terms of gender distribution.[15]

The reported rate of re-cannulation (46.2%) is notably higher and suggests the substantial burden of IV catheter-related complications. Besides additional workload, re-cannulation increases the patient discomfort and risk of infection.[16,17] The primary causes quoted for replacement were inflammation and pain, which are early symptoms of local tissue irritation and infiltration. Swelling and pain (39.1%) and swelling with inflammation (7.1%) were the main causes of re-cannulation, indicating that phlebitis, infiltration, or extravasation were the predominant underlying complications. Various patient populations align the conclusions with the events already reported - including medical, surgical, and other categories.[18,19]

Regarding the cannula size in the present study, half of the patients (50%) were cannulated with 20G catheters, followed by 35% 18G catheters. For rapid administration of fluid in surgical patients, larger gauge catheters are preferred, but their use increases the risk of endothelial injury in fragile veins, leading to pain and infiltration, which may explain the higher failure rates and the need for re-cannulation. The larger catheter (20G) preference in the current study reflects an attempt to balance flow rate for patient comfort and lower complication risk. Low incidence of complications attributed to the length of the long catheter living within the vein, which limits the catheter movement and reduces the mechanical irritation of the vessel wall.[20,21]

The successful insertion is significantly affected by the insertion site. The arm (52%) and hand (32.8%) were frequently used sites for catheterization. The higher risk of mechanical irritation and movement-related complications is associated with distal sites such as the hand, despite the accessibility. In contrast, an arm provides a stable site, potentially reducing the dislodgment, but is vulnerable to phlebitis if the catheter remains for prolonged durations. Previous studies have demonstrated similar trends, where the choice of site significantly influenced the longevity and complication rates of peripheral IV lines.[22]

The majority of patients (94.2%) had a catheter dwelling time less than 4 days, which aligned with recommendations by current guidelines, according to which regular assessment and replacement within 72-96 hours reduce the risk of phlebitis and infections. Nevertheless, some complications were also observed within the target time interval, indicating that, in addition to its duration, other factors such as aseptic practices, patient-related factors, and the method of catheter placement can also have an important bearing on the integrity. The study recognized diabetes mellitus as the highest prevalence of comorbidities, with 21.3% occurrence in patients. It is already known that diabetic patients affect the integrity of the vascular system and the ability of tissues to treat infection, where infiltration, infection, and inflammation caused by the catheter pose a delaying factor in the recovery process from infiltration, infection, or inflammation. Research supports that there are definitely influences on the outcomes from the catheter, which form part of the patient evaluation process, due to these comorbid conditions. Active steps, such as regular site evaluation, miniaturized cannulas if appropriate, and possibly initial infection for alternative solutions for the vascular access devices, are recommended for these patients in the event of complications. Several complications, including swelling and inflammation in 29.72%, have been recorded in earlier research within the first 24 hours after it occurred.[23]

This proves the relevance of personal care in the peripheral IV catheterization procedure. The improvement in the high penetration rate because of complications like inflammation and pain has emphasized the importance of catheter care techniques. Optimal insertion techniques, regular inspection protocols, and training of clinical staff on patient education can reduce adverse outcomes related to early signs of complications. In addition, findings suggest a possible advantage in developing the risk stratification devices that include age, comorbidity, and venous conditions to direct the selection of cannula site and size. The use of vein visualization technologies and safe equipment can also contribute to reducing the catheter failure rates, especially in patients at high risk.

Limitations

This study was limited by its cross-sectional design, which restricts causal inference. There is a potential selection bias in convenience sampling. Also, a single-center design may limit generalizability. Furthermore, the inserter's skill and experience level, as well as whether IV fluids were aseptically or non-aseptically inserted, were not evaluated that might alter results. A stronger study design, like a prospective study design, would include looking at complications and catheter dwell time.

Conclusion

The contributing factors to post-procedure complications identified in the current study are patient age, dwell time, and the site of insertion for peripheral IV catheterization. Factors such as the type of catheter used and the patient's condition contribute to a high incidence of cannula replacement due to pain, swelling, and inflammation, as well as the typical use of 20G cannulas. The risks associated with a higher incidence of phlebitis, the dwelling time for the cannula, and the presence of other diseases such as diabetes and hypertension in the patients.

Authors' Contributions: SHW conceptualized and designed the study, interpreted the data, critically revised the manuscript, and approved the final version. MK contributed to the study design, performed data analysis, drafted the manuscript, and approved the

final version. ATH was involved in data acquisition, interpretation, statistical analysis, manuscript drafting, and final approval. HW participated in data acquisition and analysis, contributed to manuscript drafting, and approved the final version. ZA assisted with data acquisition and analysis, contributed to manuscript drafting. All authors approved the final manuscript and are accountable for all aspects of the work.

Acknowledgements: We acknowledge the work of the statistician for statistical analysis and the computer operator for the write-up.

Source of Funding: None

Conflict of interest: None

Data Availability Statement: The data that support the findings of this study, apart from the data already presented in the results section, are available from the corresponding author upon reasonable request.

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Journal of University College of Medicine & Dentistry

Narrative Review

Epidemiological Landscape of Human Immunodeficiency Virus in Pakistan

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Submission: 22nd October, 2025
First revision: 21st November, 2025
Second revision: 8th December, 2025
Final Revision: 11th January, 2026
Acceptance: 14th January, 2026

DOI: https://doi.org/10.51846/jucmd.v5i1.4768.

Cite this article as:

Hamid Khan I, Kanathasan JS, Das SK. Epidemiological landscape of human immunodeficiency virus in Pakistan. *J Univ Coll Med Dent*. 2026;5(1): 77-83

Abstract

Objective: To summarize the epidemiological trends of HIV Pakistan and address the major gaps in the prevention and access to treatment among key populations of HIV.

Methodology: This narrative review was conducted between March-June 2025. PubMed, Scopus, The Lancet, Google Scholar, UNAIDS, the National AIDS Control Programme (NACP), WHO, and World Bank databases, as well as national and provincial reports were also searched to support evidence. The data were tabulated according to key populations, province, and chronology to identify the trends and treatment gaps. Pakistan focused sources that addressed prevalence, epidemiology, and access to care of interest to Pakistan were taken into considerations.

Results: The HIV prevalence in Pakistan is approximately 0.1% with the estimated number of PLHIV being 260,000 though very high prevalence rates of HIV are reported among key populations of individuals at high risk, including transgender people and sex workers. The healthcare system is skewed towards metropolitan sites, and the antiretroviral therapy (ART) is more easily accessible there than in rural areas. The progress towards UNAIDS goals is insufficient and there is a significant gap in diagnosis, initiation of ART, and viral suppression, especially among vulnerable groups.

Conclusion: The HIV epidemic in Pakistan is a high public health challenge and disproportionately affects key populations, and it rapidly affects marginalized populations despite the country having a low national prevalence. The persistence stigmatization, uneven access to ART, and health system limitations need to be addressed with decentralized rights-based HIV care and targeted preventive strategies to prevent further expansion of the epidemics.

Keywords: Epidemiology, Public Health, HIV, UNAIDS, Health disparities, Pakistan

Introduction

Human Immunodeficiency Virus (HIV) remains one of the most pressing global health challenges, with an estimated 38 million people living with HIV (PLHIV) worldwide in 2021. Despite substantial advances in Antiretroviral therapy (ART), prevention strategies, and global control initiatives, HIV continues to disproportionately affect certain regions and key populations, resulting in millions of deaths globally.[1] Sub-Saharan Africa remains the most severely affected region; however, South Asia including Pakistan, has experienced a steadily increasing burden, driven by complex social, economic, and healthcare-related factors.[2]

Across South Asia, the HIV epidemic continues to contribute significantly to morbidity and mortality.[2] India bears the highest burden in the region, with approximately 2.1 million PLHIV. Within India, states such as Tamil Nadu, Maharashtra, and Karnataka report particularly high prevalence among key populations, with infection rates among men who have sex with men (MSM) reaching up to 9.6% in major urban centers such as Mumbai and Chennai.[3] In Nepal, an estimated 11,000 individuals are living with HIV.[4] Sri Lanka has maintained a low national prevalence of less than 0.1%.[5] Bangladesh reports a general population prevalence of around 0.1%, with approximately 12,000 PLHIV.[6] Afghanistan has an estimated 1,000–2,000 PLHIV, predominantly among injecting drug users (IDUs), where prevalence reaches nearly 3% in Kabul.[7]

This regional concentration of HIV within key populations reflects patterns similar to those observed in Pakistan, where cross-border migration, drug routes, and refugee movements play an important role in shaping the country's HIV epidemiology.

HIV is an emerging health issue in Pakistan particularly among key populations such as people who inject drugs (PWID), MSM, transgender individuals, and sex workers, who experience disproportionately high infection rates. Socio-cultural stigma, poor healthcare infrastructure, and poor access to prevention and treatment services, especially in rural and under-serviced areas, contribute to the spread of HIV in Pakistan. Such difficulties make the fight against the epidemic and global targets such as the UNAIDS goals quite challenging.[8]

Despite the overall low prevalence of HIV in Pakistan, it is clear that there are significant regional and demographic

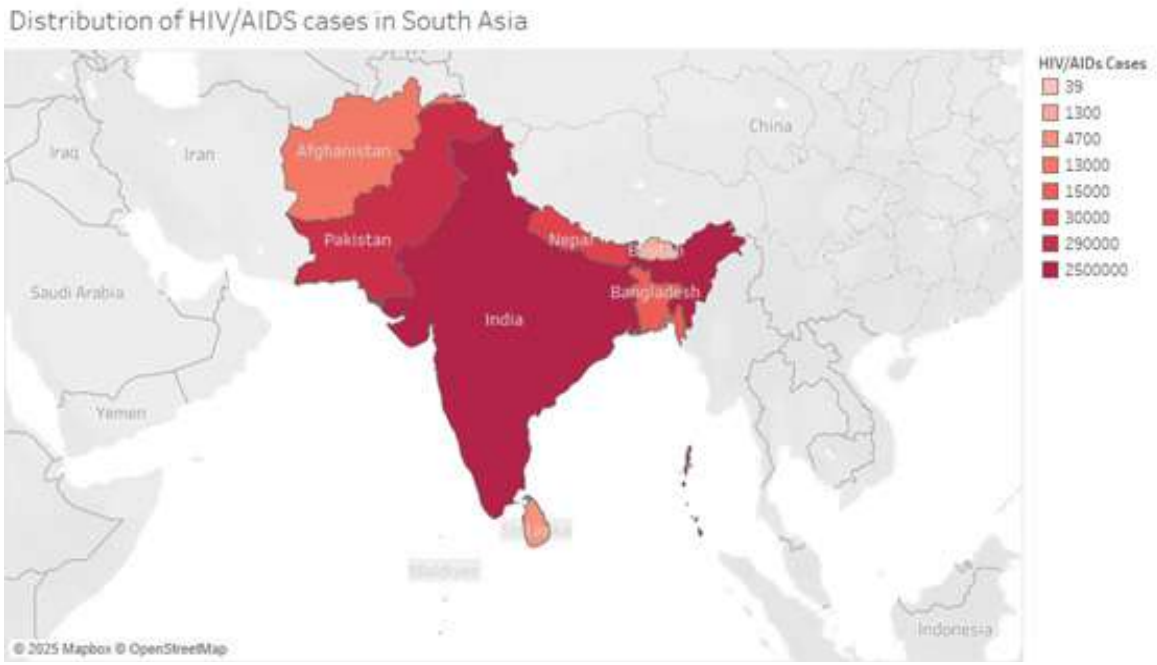

Figure 1: Distribution of cases of PLHIV in South Asian countries as per UNAIDS 2023 Global AIDS updates.

variations in the country, which are concealed by the national averages. The HIV prevalence rates are much higher in high-risk populations, including PWIDs and MSM, transgender people, and sex workers. For example, high-risk behavior and poor access to HIV prevention and care services have led to a high prevalence of HIV among PWID in Pakistan, estimated to be 28.94%,[9] whereas MSM and transgender individuals have an increased risk of developing the disease, and rural areas such as Balochistan and Khyber Pakhtunkhwa continue to experience poorer outcomes of accessing HIV prevention and care services. Major outbreaks in the regions of Sindh including Larkana has been highlighted by the vulnerability of certain communities, further underlining the urgency of addressing HIV in these high-risk groups. Despite the national efforts, treatment access is still uneven with urban centers like Lahore, Karachi, and Faisalabad showing better availability of ART services compared to rural provinces like Balochistan and Khyber Pakhtunkhwa.[10]

Although other studies have addressed a number of issues concerning HIV epidemic in Pakistan, the country still has a huge gap in terms of reviews that can be used to analyse not only the nature of the epidemiological processes but also the problem in accessing treatment. Despite the establishment of National AIDS control program in 1987, Pakistan continues to face substantial barriers in controlling this epidemic.[11] These barriers include persistent stigma, underreporting, social exclusion, and inequities in healthcare access. Additionally, the UNAIDS targets remain unmet, and the country struggles with regional and demographic disparities that hinder the effectiveness of HIV programs.

Multiple studies have examined individual components of the epidemic so there remains no consolidated, updated review synthesizing epidemiological trends alongside structural barriers to treatment access. This review addresses this gap by providing a comprehensive, narrative synthesis of Pakistan HIV landscape by highlighting current epidemiological patterns, treatment inequities and public health priorities.

Methodology

This narrative review was conducted between March and June 2025. The data was obtained through a wide range of credible international and national sources. As a narrative review, search strategy was not structured, the screening framework was not present, therefore, sources were selected according to relevance, credibility and contribution to understanding epidemiological trends, access to treatment, and barriers to health in Pakistan. The information sources included PubMed, Scopus, The Lancet, and Google Scholar, as well as the reports of the Joint United Nations Programme on HIV and data of the National AIDS Control Programme (NACP) in Pakistan that has been managing national HIV prevention and treatment programs since 1987. Additional data was obtained through the World Health Organization (WHO), the World Bank and provincial health authorities across Pakistan.

Literature and reports were reviewed to extract information about epidemiological patterns, access to treatment, and inequity related to healthcare in Pakistan as far as HIV is concerned. The data was well-organized in chronological position, by province and by the populations that are most important to identify major trends, treatment gap and geographical differences. No systematic search strategy/ method, and as the review aimed to provide a descriptive and contextual synthesis rather than a meta-analysis.

Inclusion criteria involved peer-reviewed articles, official reports, and datasets that studied HIV prevalence and epidemiological trends in Pakistan and treatment accessibility were included as the inclusion criteria. The selection of the data sources was made according to their credibility, relevance, and timeliness i.e., they had to be sources that offer current information regarding the state of HIV management and health concerns of the population in the country. The exclusion criterion included the research that focused only on the other countries other than South Asian

region, which did not have a direct relevance in Pakistan, and those that assessed the effect of HIV treatment in the absence of epidemiological background.

All the derived data were categorized into thematic matters in order to explain the development of the HIV epidemic in Pakistan, regional variations, and the state of high-risk groups, which formed the basis of the later findings and discussion.

Results

HIV Trends in Pakistan (1987-2025)

The national prevalence of HIV in Pakistan is estimated to be 0.1% of the adult population, which is approximately 260,000 PLHIV.[12] The first HIV case was reported in 1987, marking the beginning of the epidemic initiative of AIDS in Pakistan.[13] The NACP was established in 1988 in response to the cases and to establish the preventive measures of AIDS in the country. The first official case of AIDS was reported soon thereafter, signaling the onset of AIDS-related mortality in the country.[14]

The 2001, Antenatal Clinic (ANC) was the first study to present the evidence on HIV prevalence among pregnant women.[15] In 2003, an outbreak among intravenous drug users in Larkana, Sindh, drew the national attention to the growing epidemic. The Enhanced AIDS Control Programme (EACP), initiated in 2004, sought to improve data collection, enhance awareness, and strengthen intervention measures through the launch of the HIV/AIDS Surveillance Project (HASP).[16] In 2005, ART centers were established to provide treatment for individuals living with HIV, while NACP and other agencies expanded monitoring efforts between 2006 and 2007, focusing on key populations such as IDUs, male sex workers (MSWs), and MSM.[15]

HIV incidences in Pakistan have been on the rise since 2010 particularly among the high-risk groups. By 2015, there were more than 45,000 people who are HIV-positive, which was accompanied by AIDS-related deaths.[17] In the first part of this decade, it was 38.4% among PWIDs, 7.2% among transgender individuals, and 5.6% among MSM. With these alarming statistics, it was still only 54% of HIV-affected individuals who enrolled on ART treatment.[18] Twenty-five studies conducted during this period described seven localized HIV outbreaks across Pakistan.[19] Studies conducted in this period had reported seven localized epidemics of HIV in Pakistan, the highest being 1.3% prevalence in Kot Imrana, Sargodha, in 2018.[20]

The Larkana outbreak was investigated along with the United Nations and local health officials, and the problem of hazardous injection methods and inadequate measures to control the infection were found to be the primary methods of transmission.[14] The current estimates show that there are approximately 350,000 HIV-infected people in Pakistan, which has led to 14,000 AIDS-related deaths. However, only 16% of PLHIV are under ART, which also indicates that there is a disparity in the availability of treatment and healthcare facilities. It is estimated that about 7% of these people have achieved a number of viral loads.[21] December 2024 statistics indicate that there are about 0.33 million people with HIV of which 74,619 know about their status, and only 51,821 (15.7) are currently under ART care as of 94 treatment sites across Punjab.[22]

Current Burden and Key Populations

The epidemic in Pakistan remains relatively localized in specific significant areas of demography. The affected PWIDs and show a prevalence rate of 28.94%,[23] which is the indicator of high vulnerability among this group of people. Moreover, MSM also demonstrated the prevalence of 18.3% driven by stigma.[24] Female sex workers (FSWs) and transgender also remain vulnerable due to the nature of their work and limited access to the protection and health care. A recent study showed a prevalence rate of 3.3% among FSWs.[25] Prison populations represent a high-risk population with a prevalence rate of 2.28% compared to a national average. The most commonly reported risk behaviors in prisons are extra-marital sex (43.7%), homosexual (22.7%), and needle sharing (21.42%). Hepatitis B, C and TB co-infections are a common occurrence that complicates the management of HIV. Transgender population is highly vulnerable, with a prevalence rate of 4.4%.[26]

Mother-to-child transmission accounts for approximately 1% of new infections.[27] Migrant workers remain an emerging high-risk group due to unsafe sexual practices, lack of access to healthcare in host countries, and inadequate testing services during migration. The surge in the incidence has especially affected the children that could jeopardize the future of Pakistan. In several outbreaks, 80% of detected cases involved children.[28] Children are increasingly being affected. New cases among those aged 0-14 years surged from 530 cases in 2010 to 1800 in 2023.[21]

Treatment gaps

High-risk populations in Pakistan face disproportionately higher HIV prevalence than in the general population. This disparity is increased by factors such as poverty, unemployment, and lack of access to healthcare. The actions and marginalization of these individuals in society often stop their pursuit of therapy, exacerbating the current trend of disease increment of HIV. Being a notably troubling trend, the incidence among PWIDs has hit a record high of 25.4%, that is an alarming trend.[29]

Similarly, MSM continue to experience high infection rates of about 18.3% along with stigma serving as a major barrier to treatment uptake.[24] FSWs face additional challenges like low literacy, poor awareness of transmission risks and limited healthcare access. Prison populations usually require policy-based interventions to ensure regular screening and treatment while transgender individuals face obstacles related to lack of identification documents and social discrimination both of which restrict access to HIV prevention services. Migrant workers face similar vulnerabilities due to inconsistent access to HIV testing and delayed diagnosis during or after migration. Co-infections with hepatitis B, hepatitis C, and tuberculosis are also common among HIV positive individuals, further complicating treatment outcomes and long-term disease management.[30]

Regional disparities

Geographical discrepancies are high in Pakistan either in terms of diagnosis, accessibility to treatment and access to ART. The provinces with the most amount of ART centers are Punjab (45), followed by Sindh (24), Khyber Pakhtunkhwa (13), and Balochistan (5). The Islamabad Capital Territory with a population of more than a million operates only three ART centers. Although there is a high growth rate, the imbalance in services remains a big challenge in the management of the epidemic with the number of ART facilities approximating 90 nationally by 2024, with urban cities dominating the provision of ART leaving rural areas as underserved.[31]

Progress on UNAIDS 90-90-90 targets

Pakistan continues to struggle with the challenges of achieving the UNAIDS 90-90-90 targets that stipulate that 90% of PLHIV be aware of their HIV status, 90% of those who are diagnosed to receive ART and 90% of patients on ART achieve viral suppression. It is estimated that there are 350,000 HIV-positive people in the country.[32] Of them, only 21% are diagnosed with HIV, which is very low in comparison with the initial goal of 90, specifically in high-risk groups, including people who inject drugs, transgender people, and migrants. The third 90 target of viral suppression has been achieved in about 7% of people, but this figure is not optimal due to irregular follow-up, a delay in the initiation of treatment, and an inability to monitor viral loads in rural areas.[33]

Discussion

This study highlights a transition in the HIV epidemiology in Pakistan, which has shifted from a largely sporadic pattern to a more concentrated epidemic, predominantly affecting specific high-risk groups. This transition has unfolded alongside persistent inequities in healthcare access between urban and rural areas. Although the number of ART centres has increased to 90 by 2024, several provinces, including Balochistan, Khyber Pakhtunkhwa, and parts of Sindh remain critically under-served, with a small number of facilities covering very large populations, reflecting marked provincial disparities. The widening urban–rural divide further exacerbates these gaps, leaving many people in remote settings with limited or no access to basic HIV care and treatment.

Stigma and discrimination remain a major obstacle to effective management of HIV, particularly among marginalized populations such as PWIDs and MSM as well as transgender persons. These groups often feel discouraged to seek testing or treatment because of the social exclusion and discriminatory attitudes they face at hospitals. Such marginalization reinforces stigma and spreads the virus among these groups of people, whereas oppressive legal systems, especially banning drug use and homosexual relations, act as critical barriers to outreach and service delivery to high-risk groups.[34]

The healthcare system in Pakistan is not well developed, particularly in rural and peri-urban regions whereby access to services as far as HIV and healthcare providers and providers are limited consequently leading to a poor treatment outcome and low rates of viral suppression. The solution to these systemic barriers requires an in-depth approach that incorporates equitable access, reduction of stigma, and evidence-based policy implementation. The expansion and decentralization of the ART services to the provinces that have been neglected especially those of Balochistan, Khyber Pakhtunkhwa, and Sindh should be prioritized.[35] High-risk populations can actively participate in prevention by introducing pre-exposure prophylaxis (PrEP) and self-testing kits, which can be delivered to the community through continuous awareness-raising campaigns.

Stigma reduction activities on the community level are also essential. Training healthcare providers in non-judgmental and inclusive practices can improve treatment uptake and retention among PLHIV and retention of individuals with HIV, as decriminalization of behaviors associated with HIV transmission, such as drug use and consensual same-sex relations, would permit those with HIV to pursue medical care without fear of prosecution, allowing a rights-based approach to HIV prevention and treatment to be maintained.[36] It is also important to improve the national surveillance systems. A better surveillance of HIV will mean that the high-risk areas can be identified faster and that timely limited areas.

Some of these governance barriers also have an impact on health outcomes. The regulatory environments in Pakistan, especially the Control of Narcotic Substances Act, and lack of legal safeguards over MSM, and inconsistent access to harm reduction services, provide opportunities where critical populations avoid accessing health facilities because of their citizenship characteristics, leading to treatment deserts despite a growing documented rate.[39] There are also cases where the critical populations avoid accessing health facilities due to the fear of being imprisoned, be socially exposed or harassed by the inconsistent access to harm reduction services. These gaps highlight misalignment between public-health objectives and legal/policy environments.

Nevertheless, despite national initiatives to address the HIV epidemic, policy and governance barriers continue to exist, limiting equal access to prevention and treatment services in Pakistan,[40] among such critical populations as PWIDs,

interventions can be implemented through the acquisition of real-time data that can inform evidence-based public health strategies.[37] Migration of neighboring countries, particularly Afghanistan remains one of the unexplored areas of HIV spread in Pakistan. Transgender population is also disproportionately affected by gender-based discrimination and the lack of specialized healthcare services affect migrants most of the time, making them vulnerable. Specific studies on healthcare disparities in gender minorities are necessary to establish inclusive and equitable HIV policy frameworks. The existing inequality of HIV prevalence and treatment accessibility in the regions, especially the Balochistan and Khyber Pakhtunkhwa shows the need to employ culturally sensitive and regionally specific interventions.[38] It could be possible to implement rural models of HIV care, such as mobile clinics, community outreach, and task-sharing with local health workers, to enhance the results of diagnosis and adherence to long-term treatment. A combination of these strategies and awareness campaigns can significantly improve healthcare service and HIV literacy in the resource-

MSM and transgender people, it leads to poor healthcare seeking behavior and late diagnoses. The legal framework criminalizing drug use and same-sex relations creates fear of disclosure among key populations such as PWID, MSM, and transgender communities, leading to reduced healthcare-seeking behaviour and delayed diagnosis. Furthermore, weak inter-provincial coordination, fragmented surveillance systems, and inconsistent implementation of national HIV strategies contribute to disparities in service availability and quality across regions.

The transmission risks have been increased by the low integration of HIV services into the general public health system and imperfect regulatory oversight of medical practices especially unsafe injecting behavior and unqualified medical workers. Such policy gaps are apparent through harm reduction, migrant health provision, and the social protection of marginalized communities. All these advantages help to perpetuate stigma, reduce access to care, and slow down the progress of Pakistan in achieving its national and global HIV targets.

Strengths and Limitations

This discussion is based on the national and regional surveillance data, UNAIDS reports and the peer-reviewed literature to provide a comprehensive review of HIV epidemiology in Pakistan and its South Asian neighbors. It incorporates numerous top-end data sources such as international surveillance reports, national data sets, and peer-reviewed literature allowing it to provide a broad and uniform view of the HIV burden in Pakistan. The analysis has a focus on epidemiology and treatment services which will be integrated by integrating epidemiological trends, gaps in treatment, capacity of health systems and policy constraints to provide a comprehensive picture of the epidemic.

The limitations include a narrative, non-systematic review and a large proportion of epidemiological data in Pakistan are obtained through government surveillance systems, UNAIDS modeling and programmatic reporting. These sources are inherently biased such as under-reporting, long reporting cycles and variation in data collection methods across provinces. The surveillance mechanisms of Pakistan are notably wanting when it comes to the rural and conflict areas, informal healthcare settings, and hidden communities such as people who inject drugs, transgender, migrants, and MSM. Therefore, the true prevalence and treatment outcomes can be different than recorded estimates.

Conclusion

The HIV pandemic in Pakistan is defined by a low level of overall prevalence rate of 0.1% and this is highly concentrated among the most at risk populations indicating potential failure in their prevention, harm reduction, and equal access to treatment as opposed to medical impossibility. The continued stigma, criminalization of transmission-related behaviors, unequal access to ART and reliance on fragmented surveillance frameworks have continued to hinder progress in the HIV care continuum, especially in Balochistan, rural Sindh, Khyber Pakhtunkhwa, and among transgender people, those who inject drugs, and migrants.

Recommendations

To address such disparities, Pakistan must develop a decentralized, rights-based approach in public health with better provision of ART by communities, developing lower cost prevention programs such as PrEP and self-testing, strengthening harm-reduction initiatives, and policy changes that undermine care-seeking behavior. Improved national surveillance schemes, superior provincial data, and particular investigation of the transgender health, migratory people and rural epidemiological patterns are important in the formation of precise evidence and reaction to programming. Pakistan can take big steps towards meeting the UNAIDs goals of 95-95-95 and counteract the structural vulnerability which has sustained its concentrated epidemic by strategic investment, legal change and addressing equality.

Future progress depends on strengthening Pakistan's HIV response by ensuring equal distribution of resources, decentralization of ART centers, and inclusion of stigma-reduction efforts as part of national health efforts. By increasing the availability of PrEP and HIV self-testing, particularly in vulnerable groups, people will be able to take charge of prevention. Similar attempts to enhance national surveillance systems will allow making timely diagnoses and focused treatment. To achieve sustainable success, it is required to have data-driven, inclusive, and context-specific approaches, which would address the diverse socio-cultural context of Pakistan and support global HIV eradication priorities. To address the growing provincial inequity in regional implementation, mobile ART units in rural Balochistan, community-based outreach in Sindh, telehealth connection to care systems in Khyber Pakhtunkhwa, and growth of hub-and-spoke treatment networks in Punjab should be prioritized to provide an equal access to all provinces.

Authors' Contributions: IHK contributed to the study conception and design, manuscript drafting, and overall responsibility for the integrity of the work. JSK was involved in data acquisition and data management. SKD contributed to critical revision of the manuscript for important intellectual content and approved the final version.

Conflict of Interest: The authors declare that they have no known competing financial interests that could have appeared to influence the work reported in this paper.

Funding: None to declare

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Journal of University College of Medicine & Dentistry

Systematic Review

Impact of Lifestyle Interventions on Mental Health: A Comprehensive Review from Pakistan

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Submission: 1st November, 2025
First revision: 27th November, 2025
Second revision: 18th December, 2025
Final Revision: 1st January, 2026
Acceptance: 16th January, 2026

DOI: https://doi.org/10.51846/jucmd.v5i1.4981

Cite this article as:

Taj R, Khan AM, Khan AYR, Mehmood K, Nawaz A. Impact of Lifestyle Interventions on Mental Health: A Comprehensive Review from Pakistan. *J Univ Coll Med Dent.* 2026;5(1):84-89.

Abstract

Objective: Mental health disorders such as anxiety, depression, and stress-related conditions contribute significantly to global disease burden, including in Pakistan where socioeconomic instability, stigma, and limited access to services worsen outcomes. Lifestyle interventions have emerged as promising non-pharmacological strategies for promoting psychological well-being. This systematic review evaluated the impact of lifestyle interventions on mental health outcomes within Pakistani populations from January 2020 to April 2025.

Methodology: A systematic search was conducted across PubMed and Google Scholar for peer-reviewed studies assessing at least one lifestyle intervention (e.g., physical activity, diet, mindfulness) and reporting at least one mental health-related outcome (e.g., stress, anxiety, depression, or psychological well-being). Study selection followed PCC criteria and PRISMA guidelines.

Results: Twenty-one studies met initial eligibility, of which ten were verified as interventional with measurable mental health outcomes and were included for synthesis. Across studies, interventions involving physical activity, nutrition modification, mindfulness, and culturally adapted cognitive-behavioral techniques demonstrated positive effects on stress, anxiety, depression, mood, sleep, and coping. Study designs primarily included randomized, quasi-experimental, and feasibility trials. Risk of bias was generally moderate due to methodological constraints, shorter durations, and self-reported outcomes.

Conclusion: Pakistani evidence supports the beneficial role of lifestyle interventions in improving mental health outcomes, aligning with international findings and highlighting scalable, low-cost approaches relevant to resource-constrained settings. Integration into primary care, educational, and community settings represents a promising avenue for mental health promotion in Pakistan.

Keywords: Mental health; lifestyle interventions; anxiety; depression; mindfulness; Pakistan

Introduction

Mental health conditions such as anxiety, depression, and stress-related disorders contribute substantially to the global burden of disease.[1] Approximately one in eight individuals worldwide is affected, according to WHO estimates (2022). Beyond pharmacological treatments, there is increased recognition of non-pharmacological approaches, including lifestyle interventions, for prevention and symptom improvement.[2,3] Lifestyle interventions encompass behavioral and environmental modifications, such as physical activity, nutritional and sleep improvements, mindfulness practices, and psychoeducation, targeting mechanisms influencing mood, cognition, and stress regulation.[3,4] Evidence from high-income countries indicates that structured physical activity and diet can reduce anxiety and improve sleep quality,[3] while Mediterranean dietary patterns have demonstrated benefits for depressive symptoms[4]. Digital mindfulness has also shown promise for emotional regulation[5].

Research in low- and middle-income countries (LMICs), including Pakistan, remains comparatively limited and fragmented. Challenges include stigma, limited mental health literacy, scarcity of trained professionals, and poor access to care.[7,8] Lifestyle interventions may offer culturally adaptable, affordable, and scalable strategies. Local interventional studies suggest that yoga, walking, dietary counseling, and culturally adapted CBT may reduce anxiety, depression, and stress among adolescents and young adults.[7,9] Considering these contextual needs, this systematic review aimed to evaluate the impact of lifestyle interventions on mental health outcomes in Pakistan between January 2020 and April 2025 and to compare findings with international evidence for scalability, adaptability, and policy relevance.The Review was based on the following question: What improvements in mental health outcomes have been reported following lifestyle interventions among Pakistani populations?

Methodology

Eligibility using PCC Framework

Population: individuals of any age/gender experiencing

mental health-related outcomes (stress, anxiety, depression, psychological well-being) Concept: lifestyle interventions including physical activity, diet, sleep hygiene, stress management, or related behavioral modifications Context: any setting (clinical, community, academic, workplace), no design restrictions

Eligibility Criteria

Studies were eligible for inclusion if they involved human participants, implemented at least one lifestyle intervention, and assessed one or more mental health outcomes. Only peer-reviewed articles published in English between 2020 and 2025 were considered. Studies were excluded if they exclusively examined pharmacological treatments or psychotherapy, consisted of observational or other non-interventional designs, or did not report any mental health outcome.

Search Strategy

To identify relevant studies, the search strategy incorporated key terms such as "lifestyle intervention" and "mental health," along with their conceptual synonyms. For the exposure construct, synonyms included "physical activity," "exercise," "diet," "nutrition," "sleep hygiene," "mindfulness," "psychoeducation," "behavioral therapy," and "digital intervention." For the outcome construct, corresponding terms included "depression," "anxiety," "stress," and "psychological well-being." An iterative field-based search strategy was used to progressively refine these terms, resulting in the Boolean string: ((("lifestyle intervention" OR "physical activity" OR "exercise" OR "diet" OR "nutrition" OR "sleep hygiene" OR "mindfulness" OR "psychoeducation" OR "behavioral therapy" OR "digital intervention")) AND (("mental health" OR "depression" OR "anxiety" OR "stress" OR "psychological well-being")) AND (("Pakistan") OR ("Pakistan")) AND ("2020/01/01"[Date-Publication]:"2025/04/25"[Date-Publication]). Synonyms were grouped into logical concept categories and combined using Boolean operators (OR within concepts and AND across concepts) to ensure a comprehensive and transparent search strategy. Filters for publication dates from January 2020 to April 2025 were applied.

The study selection process adhered to PRISMA guidelines. Titles and abstracts retrieved from PubMed and Google Scholar were screened systematically. All citations were first exported to EndNote reference management software where duplicates were removed. Screening was conducted independently by two reviewers who assessed relevance based on the predefined eligibility criteria. Any discrepancies between reviewers were resolved through discussion or, when necessary, consultation with a third reviewer. Full-text articles deemed potentially eligible were subsequently retrieved and evaluated for final inclusion. The selection process was documented using a PRISMA flow diagram, detailing the number of records identified, screened, excluded, and included at each stage.

Results

Study Selection

The search identified 1835 records. After removal of 1296 duplicates, 539 remained for title/abstract screening. Of these, 426 were excluded, and 113 underwent full-text review. Ninety-two were excluded, resulting in 21 initially eligible studies. Following methodological verification, ten studies with confirmed lifestyle interventions and mental health outcomes were retained for synthesis.
The included studies represent a range of lifestyle-

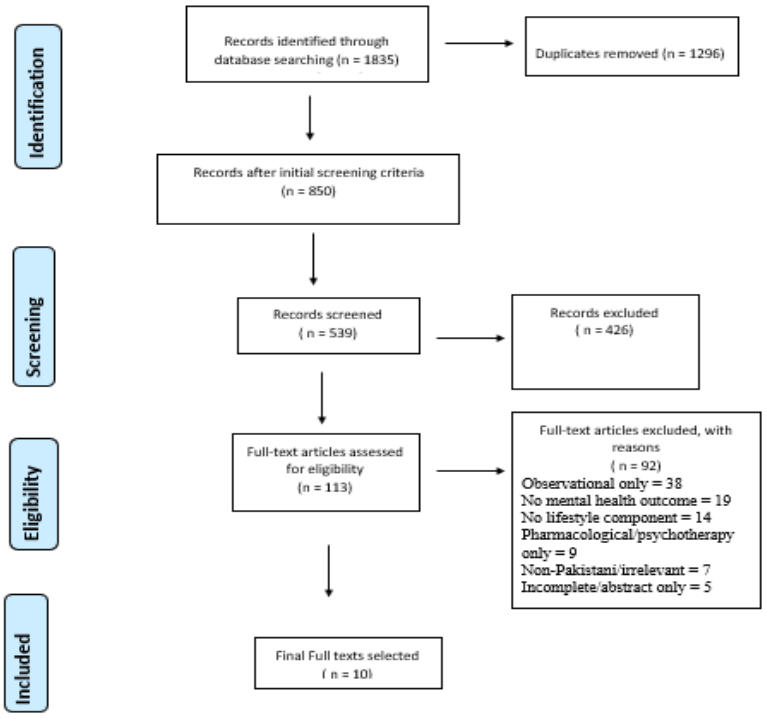

Figure 1: PRISMA Flow Diagram of Study Selection Characteristics of Included Studies

Table 1: Verified Pakistani Studies (n = 10)

Study	Intervention	Sample	Population	Duration	Outcome
Ahmed et al. (2021)[9]	Walking + Group Therapy	150	Univ students	6 wks	↓ Anxiety, ↑ Mood
Khan et al. (2022)[10]	Dietary Modification	120	Adolescents	3 mo	↓ Depression
Riaz et al. (2023)[7]	Yoga + Breathing	180	College students	10 wks	↓ Stress
Malik et al. (2021)[8]	Aerobic Activity	130	Young adults	12 wks	↑ Sleep, ↓ Anxiety
Fatima et al. (2020)[11]	Nutritional Counseling	110	Women	8 wks	↓ Depressive symptoms
Amin et al. (2020)[18]	CACBT	76	Adolescents	8 wks	↓ Social Anxiety
Noor et al. (2024)[13]	Faith-Integrated Mindfulness	110	College females	8 wks	↑ Coping
Rasheed et al. (2023)[14]	Peer-Led Exercise	140	Adolescents	6 wks	↓ Emotional distress
Mustafa et al. (2023)[21]	Aerobic Workout	40	Male adults	12 wks	↓ Stress, ↓ Cortisol
Sarfraz et al. (2023)[22]	Online Mindfulness	102	Univ students	6 wks	↓ Burnout, ↑ Well-being

Note: Univ = University; wks = weeks; mo = months; CACBT = Culturally Adapted Cognitive Behavioral Therapy; ↓ = reduction in negative symptoms (e.g., stress, anxiety, depressive symptoms); ↑ = increase in positive outcomes (e.g., mood, coping, sleep, well-being).

based interventions spanning physical activity, nutrition, mindfulness, and hybrid behavioral approaches conducted in Pakistani populations. Samples primarily consisted of university students and adolescents, with intervention durations ranging from six weeks to twelve weeks and consistent reporting of improvements in stress, anxiety, coping, mood, and well-being.

The overall risk of bias across studies was moderate. Key contributing factors included quasi-experimental designs, brief intervention periods, and dependence on self-reported psychological outcomes, coupled with minimal opportunities for blinding, issues frequently encountered in behavioral trials conducted in LMIC settings. Despite these limitations, feasibility RCTs achieved satisfactory levels of participant recruitment and adherence, indicating that such interventions may be scalable and implementable in both university and community environments.

Table 2: Risk of Bias Across Studies

Study	Design	Sel	Perf	Detect	Outcome	Report
Ahmed 2021[9]	Quasi	Mod	Mod	Mod	Mod	Low
Khan 2022[10]	Quasi	Mod	Mod	High	Mod	Low
Riaz 2023	Quasi	Mod	Mod	Mod	Mod	Low
Malik 2021[7]	Quasi	Mod	Mod	Mod	Mod	Low
Fatima 2020[11]	Quasi	Mod	High	High	Mod	Mod
Amin 2020[18]	RCT	Low	Mod	Mod	Mod	Low
Noor 2024[13]	RCT	Low	Mod	Mod	Low	Low
Rasheed 2023[14]	Quasi	Mod	Mod	Mod	Mod	Low
Mustafa 2023[21]	Controlled	Mod	Mod	High	Mod	Low
Sarfraz 2023[22]	RCT	Low	Mod	Mod	Mod	Low

Note: Study designs included Quasi-experimental (Quasi), Controlled trials, and randomized controlled trials (RCT). ROB domains reflect risk of Selection (Sel), Performance (Perf), Detection (Detect), Outcome assessment (Outcome), and Reporting (Report) bias. Ratings indicate Low, Moderate (Mod), or High risk of bias.

Discussion

This review synthesized evidence from ten interventional studies conducted in Pakistan between January 2020 and April 2025, all of which evaluated lifestyle-based strategies for improving mental health outcomes (Figure 1). Collectively, these studies assessed physical activity, nutrition-related interventions, mindfulness-based approaches, and culturally adapted cognitive-behavioral strategies across adolescents, university students, and adults (Table 1). Overall, the pattern of findings supports the role of non-pharmacological, lifestyle-oriented interventions in reducing symptoms of depression, anxiety, and stress, and in enhancing coping, sleep, and psychological well-being. These results are broadly consistent with the international literature demonstrating beneficial effects of exercise, diet, and mindfulness on emotional regulation and mental health.[3,4]

Physical activity emerged as one of the most frequently studied modalities in Pakistani settings. Structured aerobic exercise, walking programs, and peer-led group activity were associated with reductions in stress and anxiety and improvements in sleep and mood among young adults and adolescents.[7,8,14] These effects mirror international data in which exercise interventions have been shown to regulate stress physiology, improve sleep architecture, and enhance affective stability.[9] However, not all exercise-based interventions produced uniformly strong or sustained effects. In some studies, improvements were modest, confined to specific subscales, or not statistically significant across all measured mental health outcomes. This variation may reflect short intervention duration, variability in session intensity, differences in adherence, or high baseline functioning among relatively healthy student samples, all of which can attenuate detectable changes despite meaningful subjective benefit.

Dietary modification and nutritional counseling also showed promising but not uniformly robust effects. Pakistani trials reported reductions in depressive symptoms and emotional distress following structured counseling or dietary pattern changes.[10,11] These findings align with international evidence linking Mediterranean and plant-based dietary patterns to better mood and reduced depressive symptoms.[4,15] At the same time, several contextual challenges may explain why dietary interventions did not yield strong improvements in every outcome. These include reliance on self-reported diet rather than objective nutritional markers, variability in participants' baseline diet quality, economic barriers to sustaining healthier food choices, and limited follow-up periods that may be insufficient for metabolic and psychological benefits to fully manifest.

Mindfulness-based, digital, and culturally adapted cognitive-behavioral interventions—including faith-integrated mindfulness, guided online mindfulness, and culturally adapted CBT demonstrated notable reductions in anxiety, social anxiety, burnout, and emotional distress, along with improved coping.[13,18,22] These results parallel findings from high-income countries where mindfulness and CBT-based digital interventions have been associated with improvements in stress management, resilience, and well-being.[5,6] Yet, again, effects were not uniformly large across all domains or all studies. In some cases, changes were more evident in coping or specific anxiety subdomains than in global distress scores. This pattern likely reflects differences in baseline severity, partial adherence to home practice, and the fact that relatively brief interventions may not fully transform entrenched cognitive and behavioral patterns.

Importantly, Pakistani studies increasingly incorporated culturally sensitive design elements, such as female-only groups, faith-aligned content, and peer-led delivery models, which appeared to enhance engagement and acceptability in a collectivist, stigma-prone context.[13,14] This cultural adaptation may partly explain why some interventions, particularly faith-integrated mindfulness and peer-led exercise, achieved stronger or more consistent outcomes compared to more generic programs. Where improvements were weaker or absent, a lack of such tailoring, combined with time constraints, competing academic pressures, or limited family support, may have dampened the effectiveness of interventions despite sound theoretical foundations.

Taken together, the heterogeneity of findings across the ten Pakistani studies suggests that lifestyle interventions are beneficial overall, but their impact is contingent on multiple contextual and methodological factors. These include intervention type and dosage, cultural fit, delivery mode (in-person vs online), participant characteristics (age, gender, baseline severity), and structural constraints such as time, space, and institutional support. Rather than weakening the conclusions of this review, the presence of mixed or partial effects underlines that lifestyle interventions are not a uniform "cure-all," but tools whose effectiveness depends on thoughtful design, implementation quality, and sustained engagement. From a health systems perspective, this nuance is critical: it indicates that scaling lifestyle interventions in Pakistan will require not only replication but also refinement, contextualization, and integration within existing educational and primary care structures.[5,6]

Limitations

Several limitations must be considered when interpreting these findings. At the study level, most trials exhibited a moderate risk of bias. Quasi-experimental designs, lack of randomization or concealed allocation, and limited use of active control groups restrict causal inference. Short follow-up periods, often six to twelve weeks, limit understanding of the durability of observed benefits, particularly for outcomes such as depression, burnout, and coping that may fluctuate with academic and social stressors.

Outcome assessment relied predominantly on self-reported scales, which are susceptible to recall bias, social desirability, and response shift over time. No study incorporated biological markers (e.g., cortisol, inflammatory markers) or objective digital indicators (e.g., actigraphy for sleep, step counters for activity), which would strengthen mechanistic interpretation. In addition, some studies reported improvements in only one or a subset of measured outcomes, or presented results without effect sizes, making it difficult to compare magnitude of benefit across interventions or to distinguish clinically meaningful from minimal changes.

At the review level, this synthesis was limited to studies published in English and indexed in selected databases, which may have resulted in omission of unpublished or locally disseminated interventions. The focus on Pakistan enhances contextual relevance but also limits generalizability to other

LMICs with different cultural and health system structures. Finally, heterogeneity in intervention content, duration, population, and measurement tools precluded meta-analysis and required narrative synthesis, which, while appropriate, is inherently more interpretive.

Future Recommendations

Future research in Pakistan should prioritize more rigorous and sufficiently powered randomized controlled trials with clearly defined control conditions and longer follow-up periods to assess the sustainability of mental health benefits. Incorporating objective measures, such as digital activity trackers, sleep monitoring, and, where feasible, biological markers, would strengthen mechanistic understanding and reduce reliance on self-report alone. Intervention manuals and fidelity checks should be reported in greater detail to allow replication and meta-analytic comparison.

Given the promising but variable effects observed, future interventions should increasingly combine modalities—such as integrating physical activity, dietary improvements, and mindfulness or CBT elements, into multimodal programs tailored to local cultural and socioeconomic realities. Implementation research is needed to identify optimal delivery formats (e.g., school-based, university-based, primary care–embedded, or community-led), and to evaluate cost-effectiveness, scalability, and equity of access, particularly for women, low-income groups, and rural populations.

At a policy level, lifestyle-based mental health promotion could be incorporated into national non-communicable disease and mental health strategies, aligning with stepped-care models that prioritize low-intensity, community-compatible interventions before specialist referral.[56] Partnerships between universities, schools, primary care centers, and faith or community organizations may offer sustainable platforms for delivering culturally congruent lifestyle programs. Training non-specialist facilitators—such as peer leaders, teachers, and community health workers—in basic lifestyle and behavioral mental health interventions could help bridge the substantial treatment gap in Pakistan.
Finally, future work should deliberately examine barriers to and facilitators of engagement, including stigma, family support, digital access, and gender norms. Qualitative and mixed-methods studies embedded within intervention trials could provide insight into why some participants show strong improvements while others benefit less, thereby informing refinement of content, delivery, and support mechanisms. Such an evidence base would allow Pakistan to move from promising pilot projects toward integrated, contextually grounded lifestyle mental health programs that are both scalable and sustainable.

Conclusion

Evidence from Pakistan aligns with international findings and supports the utility of lifestyle interventions, including physical activity, nutritional optimization, mindfulness, and culturally adapted CBT, in improving mental health outcomes across populations. Given feasibility, affordability, and cultural adaptability, these interventions warrant scale-up through academic institutions, primary care, and community health systems. More rigorous and powered trials with standardized psychological outcomes and long-term follow-up are required.

Authors' Contributions: RT contributed to conceptualization of the review, development of the study protocol, oversight of methodology, critical revision of content, and final approval of the manuscript. AMK completed the literature search, conducted data extraction, drafted the initial manuscript sections, and participated in revisions. AYRK assisted with data screening and eligibility assessment, constructed study tables, and synthesized results for presentation. KM contributed to interpretation of findings, drafting and refinement of the discussion section, and editorial polishing. AN provided supervision and methodological guidance, contributed to policy contextualization, and approved the final manuscript version. All authors fulfill ICMJE authorship criteria and agree to be accountable for all aspects of the work.

Conflict of Interest: The authors declare no conflict of interest.

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Journal of University College of Medicine & Dentistry

Short Communication

Robotic Gynecologic Surgery in Pakistan: Challenges and Local Realities

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Submission: 1st November 2025
Revision: 10th December, 2025
Acceptance: 25th December, 2025

DOI: https://doi.org/10.51846/jucmd.v5i1.4842

Cite this article as:

Ahmad SM. Robotic gynecologic surgery in Pakistan: promise, proof, and a path that includes everyone. *J Univ Coll Med Dent*. 2026;5(1): 90-92.

Abstract

Robotic-assisted gynecologic surgery is increasingly used worldwide for complex pelvic procedures, but its adoption in Pakistan remains limited. Robotic platforms may facilitate minimally invasive surgery in select complex cases, but their high cost and resource requirements raise concerns about value and equity. For many routine gynecologic procedures, conventional laparoscopy offers comparable outcomes at lower cost. This short communication discusses the evolving role of robotic gynecology in Pakistan and emphasizes the importance of selective use, structured team training, and outcome monitoring to ensure that technological advancement improves women's surgical care without widening existing disparities.

Introduction

Robotic-assisted surgery has transformed the practice of gynecology over the past two decades, particularly in developed countries where it is now routinely used for both benign and oncologic pelvic procedures. Since its initial years of use, in the early 2000s, robotic technology has been promoted as part of minimally invasive surgery, offering enhanced visualization, instrument articulation, and improved surgeon ergonomics in complex anatomical settings.[1,2] These attributes have been especially valuable in procedures such as deep infiltrating endometriosis excision, complex hysterectomy, sacrocolpopexy, and re-operative pelvic surgery.[3]

In Pakistan, robotic gynecologic surgery is relatively recent. Access is largely confined to a small number of private-sector hospitals and tertiary academic institutions, resulting in less exposure among gynecologists and restricted availability for the general population. Interest in robotic platforms is increasing, driven by global trends, patient perceptions, and institutional aspirations to introduce advanced surgical technologies. Pakistan is at an important decision point where robotic gynecology could either strengthen advanced minimally invasive care or worsen existing inequities and cause a financial strain within an already constrained healthcare system.

The rationale for this short communication is threefold. First, the introduction of robotic gynecologic surgery in Pakistan has occurred in the absence of nationally defined indications, credentialing pathways, or outcome reporting mechanisms. Second, internationally robotic surgery is used without considering local cost structures, surgical volume, and training capacities. Third, there is a growing risk that robotic technology may be perceived as a "premium" service in Pakistan, accessible primarily to self-paying patients, thus widening disparities in women's surgical care. Addressing these issues requires a more evidence-informed discussion focused on value, equity, and governance.

Main Text

Robotic surgery and the evolution of minimally invasive gynecology

The global shift towards minimally invasive surgery has been a critical innovation in gynecology, with laparoscopic and vaginal approaches consistently demonstrating superior outcomes compared with open surgery, including reduced postoperative pain, shorter hospital stay, and faster return to normal activity.[4] Robotic surgery emerged as a response to some of the technical limitations of conventional laparoscopy, especially in pelvic procedures requiring fine dissection and advanced suturing.

Several large comparative studies and systematic reviews have shown that, for many benign gynecologic procedures, robotic and laparoscopic approaches yield similar clinical outcomes.[5,6] The primary benefit of robotics does not lie in replacing laparoscopy for routine cases, but rather in facilitating minimally invasive, technically demanding surgeries that might otherwise require laparotomy. This distinction is critical for healthcare systems such as

Pakistan's, where resource optimization and avoidance of unnecessary costs are essential.

Where robotic surgery may add value

Robotic systems provide magnified three-dimensional vision and flexible instruments that allow more precise movement in narrow spaces. These features can be helpful in complex situations such as severe endometriosis, repeated pelvic surgery, or advanced pelvic organ prolapse, where anatomy is often distorted and conventional laparoscopy may be technically challenging.[3,7]

Avoiding open surgery is particularly important in Pakistan, where laparotomy is often associated with longer hospital stays and delayed recovery due to higher risk of wound-related complications. When robotic surgery allows complex cases to be managed minimally invasively, it supports better postoperative recovery, reduces surgical stress, promotes early mobilization, and shortens hospital stay.[8,9]

Where benefits are limited and costs increase

Despite its technical advantages, robotic surgery is associated with significantly higher costs compared with conventional laparoscopy, largely due to capital investment, maintenance contracts, limited instruments' lifespan, and longer operating times during the learning curve.[5] In high-income settings, these costs may be partially offset by surgical volume and negotiated procurement contracts. In Pakistan, lower case volumes and fragmented purchasing mechanisms amplify per-case expenditure. For routine gynecologic procedures, including uncomplicated benign hysterectomy, multiple studies have demonstrated equivalent outcomes between robotic and laparoscopic approaches, without clear clinical superiority of robotics.[5,6] The use of robotic platforms may represent inefficient resource utilization and the diverting of funds from higher-impact services such as training, infrastructure, and access to basic minimally invasive care.

Equity and access considerations

Keeping Pakistan's current healthcare system in mind, equity is a central concern when it comes to introducing advanced surgical technologies. Without deliberate planning, robotic gynecologic surgery risks becoming accessible only to patients who can afford out-of-pocket payment, reinforcing a two-tier system of care.

Concentrating robotic services in a limited number of high-volume centers may improve efficiency, reduce per-case costs, and facilitate structured training. Transparent patient counseling is equally important, ensuring that women are offered the surgical approach which may be most appropriate to their clinical condition rather than one driven by technology availability, cultural stigma or perceived prestige.

Training, credentialing, and outcome monitoring

The success of robotic gynecologic surgery programs depend not only on surgeon skill but on the coordinated performance of the entire operating team. Evidence from established programs emphasize the importance of structured, competency-based training pathways, including simulation, proctored cases, and ongoing performance assessment.[10] Credentialing based on objective metrics rather than seniority alone is essential to maintain safety and quality.\
Systematic outcome monitoring is equally important. Indicators such as operation time, blood loss, complications, length of stay, and cost per case provide objective measures of value and safety. Registry-based data collection has been advocated internationally as a means of guiding responsible expansion and ensuring accountability in robotic surgery programs.[11]

Policy Implications

The introduction of robotic gynecologic surgery in Pakistan has implications for health policy and resource allocation. In the absence of national guidance, adoption may be driven by market forces rather than clinical need, increasing costs without improving access. Policy frameworks should be made for selective use of robotics for complex cases, concentration of services in high-volume centers, and competency-based credentialing. Transparent costing and routine outcome reporting are essential.

Conclusion

Robotic gynecologic surgery offers potential benefits for selected complex cases in Pakistan, minimally invasive management that would otherwise require laparotomy. However, its value is highly context-dependent and closely linked to appropriate case selection, structured team-based training, and transparent outcome evaluation. Without these safeguards, robotic surgery risks increasing healthcare costs and exacerbating inequities. A cautious, evidence-informed approach is essential to ensure that technological advancement translates into meaningful improvement in women's surgical care.

Disclosure: The author serves as a visiting gynecologist to Pakistan and is regularly invited as a speaker at national and international academic conferences and educational forums in gynecology and minimally invasive surgery. In his routine clinical practice, he has performed over 2,000 minimal invasive robotic and laparoscopic gynecologic surgeries.

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