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Editorial

Strengthening Primary Healthcare: From Curative to Promotive Care

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Introduction

Primary healthcare (PHC) underpins prevention, health promotion, continuity of care, equity, and universal health coverage (UHC). It integrates primary care with public-health services, community participation, and action on social determinants of health. [1] Despite advances in hospital-based medicine, many communicable and non-communicable diseases, maternal and child health problems, malnutrition, and mental health conditions remain preventable through timely community-level interventions, emphasizing a shift toward promotive and preventive care [1].

Situation in Pakistan

The need to strengthen PHC is particularly relevant to Pakistan, where health systems face a combination of communicable diseases, NCDs, maternal and child health challenges, and substantial inequalities in access to healthcare [2]. A 2024 assessment of PHC facilities in Punjab identified important gaps in medicine availability, equipment functionality, infrastructure, sterilization practices, and staffing. [3] These findings demonstrate that strengthening PHC requires more than policy statements; it requires sustained investment in the infrastructure and workforce necessary to deliver reliable services. A recent review of Pakistan's PHC system similarly identified persistent challenges affecting PHC quality and effectiveness. It emphasized strengthening primary-level services as a pathway to improved population health [4]. Pakistan has also implemented PHC-oriented initiatives to improve access to essential services and advance UHC. WHO reporting describes PHC-oriented models of care implemented in Islamabad and Charsadda that incorporate essential health-service packages and attention to maternal-child health and NCDs. These experiences suggest that PHC strengthening should involve coordinated action across government, healthcare institutions, communities, and other sectors [5].

From Curative to Promotive Care

A key priority in strengthening PHC is shifting healthcare systems from a predominantly curative approach to promotive, preventive, and early-intervention strategies. Primary-care facilities are ideally positioned to identify health risks before they progress to serious disease. Routine primary-care services can incorporate blood-pressure measurement, diabetes screening, vaccination, nutritional assessment, maternal and child health services, tobacco-cessation counseling, and lifestyle interventions. However, prevention should not simply mean adding more screening activities to already overstretched facilities [6]. Effective preventive care requires trained healthcare workers, appropriate diagnostic capacity, essential medicines, referral mechanisms, follow-up systems, and reliable health information. The WHO PHC measurement framework emphasizes monitoring PHC through a comprehensive approach that includes health promotion, disease prevention, diagnosis, treatment, rehabilitation, and community participation. The distinction between PHC and primary care is also important. Primary care provides essential first-contact clinical services, whereas PHC represents a broader approach involving multisectoral policies, empowered communities, public-health functions, and integrated healthcare [7].

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Health Promotion as a Core Function of PHC

Health promotion should be a core function of PC, not an additional activity. Socioeconomic conditions, education, employment, housing, nutrition, sanitation, environmental exposure, and access to safe water influence population health. Therefore, clinical services alone cannot address all determinants of health. Integrating health education with supportive environments can make healthy choices more achievable. [4]

Community Participation and Engagement

Communities should actively participate in healthcare planning and implementation rather than remain passive recipients. Meaningful engagement can improve the relevance, acceptability, and responsiveness of PHC services and support progress toward UHC. Participatory approaches are particularly important where cultural practices, misinformation, financial barriers, geographic distance, or mistrust affect healthcare utilization. Community health workers can link households with formal health services through education, preventive activities, disease surveillance, adherence support, and referral. Their effectiveness depends on clear roles, training, supervision, and integration within PHC systems [8].

Strengthening the Primary Healthcare Workforce

A strong PHC system requires a trained, motivated, and appropriately distributed workforce. Physicians, nurses, midwives, community health workers, allied health professionals, and public-health practitioners contribute to prevention and health promotion. Education, continuing professional development, supportive supervision, adequate staffing, safe working conditions, effective referral pathways, and strong leadership are essential for quality PHC services [9].

Table 1. Key Components for Strengthening Primary Healthcare for Disease Prevention and Health Promotion

Component	Key actions	Expected contribution
Disease prevention	Vaccination, screening, early detection	Reduces preventable disease
Health promotion	Healthy diet, physical activity tobacco control	Reduces risk factors
Community engagement	Community participation and health education	Improves acceptability and utilization
Health workforce	Training, supervision, adequate staffing	Improves quality of care
NCD prevention	Hypertension/diabetes screening and risk reduction	Earlier diagnosis and management.
Digital health	Telemedicine, surveillance, electronic records	Improves access and continuity
Equity	Target underserved populations	Reduces health. disparities
Monitoring	Indicators, quality assessment, referral tracking	Improves accountability

Main actions to improve prevention, health promotion, access, and quality of care.

Preventing Non-Communicable Diseases

The growing burden of NCDs makes strengthening PHC particularly important. Hypertension, diabetes, cardiovascular disease, chronic respiratory disease, and many cancers develop gradually and may remain undiagnosed for prolonged periods. PHC facilities can support early detection and long-term management of these conditions. Routine services should incorporate tobacco-control counseling, promotion of physical activity, healthy diets, obesity prevention, cardiovascular-risk assessment, and appropriate screening. Importantly, chronic disease management should remain person-centered rather than becoming fragmented into multiple disease-specific programs. Integrated PHC can provide patients with continuity of care while reducing unnecessary duplication of services[10].

Improving Access and Equity

Physical availability does not guarantee healthcare access; distance, cost, shortages, staffing, and social factors can create barriers.

Digital Health and PHC

Digital health technologies can support PHC through teleconsultation, electronic health records, clinical decision support, appointment systems, disease surveillance, health education, and communication between different levels of care. However, digitalization should complement, not replace, accessible face-to-face healthcare. Digital exclusion, poor connectivity, limited digital literacy, privacy concerns, and unequal access to devices may otherwise increase existing inequalities. Digital tools should therefore be selected according to community needs and integrated into existing health-system workflows rather than implemented as isolated technological projects [11].

Quality, Measurement, and Accountability

Expanding access without measuring quality may produce limited improvements in population health. PHC systems should therefore monitor not only service utilization but also continuity, safety, effectiveness, equity, patient experience, preventive-service coverage, medicine availability, referral completion, and health outcomes. The WHO PHC measurement framework provides a structured approach to monitoring health systems through a PHC lens. It emphasizes integrating health promotion, disease prevention, primary care, essential public-health functions, and community empowerment. Reliable health information systems are particularly important because they allow policymakers and healthcare managers to identify service gaps and allocate resources according to population needs [12].

Conclusion

Strengthening primary healthcare requires emphasis on prevention, health promotion, equity, and resilient services. Accessible, continuous, person-centered care, supported by community participation, trained healthcare workers, reliable medicines, diagnostics, referral systems, digital technologies, and sustainable financing, can improve population health and shift healthcare from treating disease toward preventing illness and promoting lifelong wellbeing.

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Systematic Review

Generative Artificial Intelligence in Internal Medicine: Applications in Clinical Reasoning, Differential Diagnosis, and Clinical Decision-Making

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Abstract

Objective: To synthesize the available evidence on the diagnostic accuracy, clinical decision-support performance, advantages, and limitations of generative AI in adult internal medicine.

Methodology: This systematic review was conducted in the Department of Medicine, MMC/BKMC, Mardan, from January to May 2026. Following PRISMA 2020 guidelines, we searched PubMed/MEDLINE, Embase, Web of Science, Scopus, and preprint servers for studies published from January 2022 to December 2025. Eligible studies evaluated generative AI in clinical reasoning, differential diagnosis, or clinical decision-making in adult internal medicine. A total of 58 studies met the eligibility criteria, and 25 were selected for detailed synthesis based on their relevance and methodological contribution.

Results: Generative AI performed strongly on selected clinical reasoning and diagnostic tasks. Across complex clinical vignettes, LLMs identified the correct diagnosis within the top 5 or top 10 differential diagnoses in approximately 60–83% of cases. They achieved or exceeded passing performance on several medical licensing and internal medicine board-style examinations. In structured OSCE-style evaluations, purpose-built conversational systems performed favorably compared with physicians across several assessment domains. However, randomized trials evaluating general-purpose LLMs in realistic clinical workflows demonstrated smaller and less consistent improvements, particularly in interactive diagnostic tasks. Key limitations included hallucination, demographic bias, automation bias, variation across specialties and tasks, and inconsistent evaluation methods. Only approximately 5% of studies in a broader systematic review of healthcare LLM applications used real patient-care data.

Conclusion: Current evidence supports using generative AI as an adjunct to, rather than a replacement for, physician clinical reasoning. Safe implementation requires structured workflows, appropriate human oversight, retrieval-augmented generation, standardized evaluation, and further validation using real-world clinical data.

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Introduction

Clinical reasoning and differential diagnosis are essential in internal medicine and involve combining history, physical examination, and test results amid uncertainty. Contamination of diagnostic tests is still a major source of preventable harm. Unlike previous rule-based systems, generative AI, particularly transformer-based large language models since ChatGPT's release in 2022, provides free-text reasoning and flexible interaction throughout the diagnostic pathway. Since 2022, studies have examined whether generative AI can assist or even automate core internal medicine tasks, such as creating differential diagnoses and suggesting management plans [1,2]. On curated vignettes, studies have shown passing USMLE scores and correct-diagnosis rates over 80 percent, while more recent trials in real workflows have yielded modest, often inconsistent improvements and clear failure modes. This review summarizes that evidence to address three questions: Is generative AI as accurate as physicians for clinical reasoning and differential diagnosis? Can it enhance decision-making in simulated and/or real workflows? What risks should be considered when using generative AI in internal medicine?

Material and Methods

Protocol and Reporting

This systematic review was conducted from January 2022 to December 2025 and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. The review protocol was developed prospectively to define eligibility criteria, information sources, the study-selection process, data extraction, and the synthesis approach. The review protocol was not registered in a publicly accessible systematic review registry.

Eligibility Criteria

Eligible studies were those that evaluated a generative AI system, including ChatGPT, GPT-3.5/4, Med-PaLM/2, Bard/Gemini, Claude, or similar systems; assessed clinical reasoning, differential diagnosis, clinical decision-making, or clinical management; were peer-reviewed or, when evidence was limited, high-impact preprints; and involved adults in internal medicine, general medicine, hospital medicine, or related subspecialties. We excluded studies focused exclusively on radiological image interpretation, surgery, pediatrics, or administrative/billing tasks without an internal-medicine-relevant reasoning component.

Risk of Bias Assessment

The reviewers independently assessed the methodological quality and risk of bias of the included studies, using appropriate criteria for each study design. The assessment considered study methodology, participant selection, outcome measurement, comparator selection, and potential sources of bias. Reviewers resolved disagreements through discussion and consensus. We used the quality assessment results to interpret and synthesize the findings.

Information Sources and Search Strategy

We searched PubMed/MEDLINE, Embase, Web of Science, Scopus, and IEEE Xplore/arXiv for studies published from January 2022 to September 2026. The search combined the following terms: generative artificial intelligence, large language model, ChatGPT, GPT-4, Med-PaLM, clinical reasoning, differential diagnosis, clinical decision-making, and internal medicine. We also hand-searched reference lists of included studies and relevant reviews.

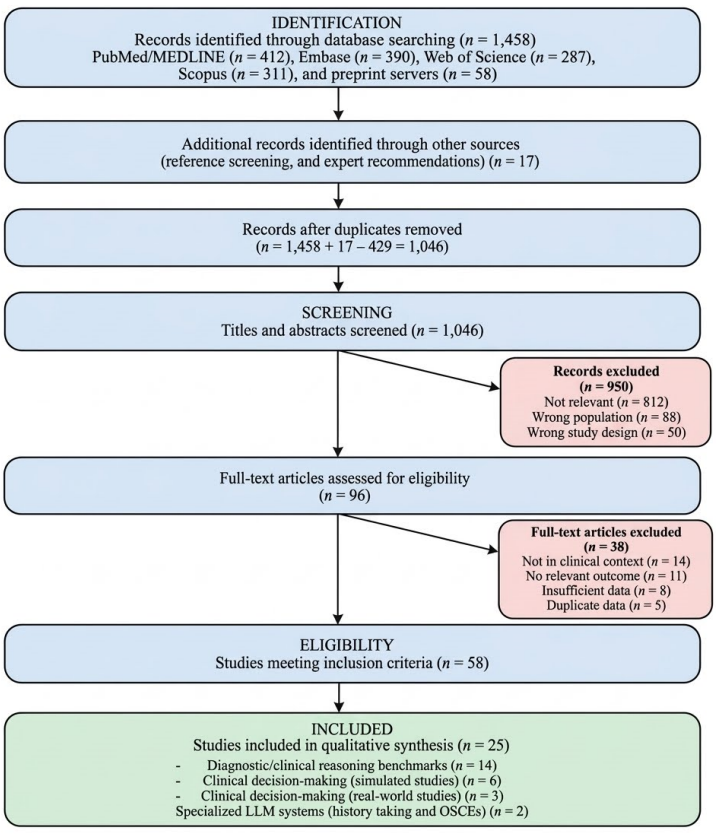
Study Selection and Data Extraction

We screened records identified through database and citation searches by title and abstract, followed by full-text assessment against the predefined eligibility criteria. We identified 2,543 records, including 2,486 from database and preprint-server searches and 57 from registry and citation searches. After removing duplicates, we screened 2,091 records, and 329 articles underwent full-text assessment. Fifty-eight studies met the eligibility criteria and were included in the systematic review. We considered all eligible studies in the overall evidence synthesis, but presented 25 studies with the most relevant and methodologically informative evidence in greater detail in the main results and Table 1. Data extracted included author(s), publication year, journal or source, AI model evaluated, study design, clinical domain, comparator, and primary outcomes.

Synthesis Approach

Because AI models, clinical scenarios, data sources, outcome measures, and comparators varied substantially, we did not perform a quantitative meta-analysis for the primary synthesis. Instead, we synthesized findings narratively and thematically across three domains: clinical reasoning, differential diagnosis, and clinical decision-making. Where relevant, findings from published meta-analyses were also reported for comparison.

Figure 1. PRISMA Workflow Diagram.



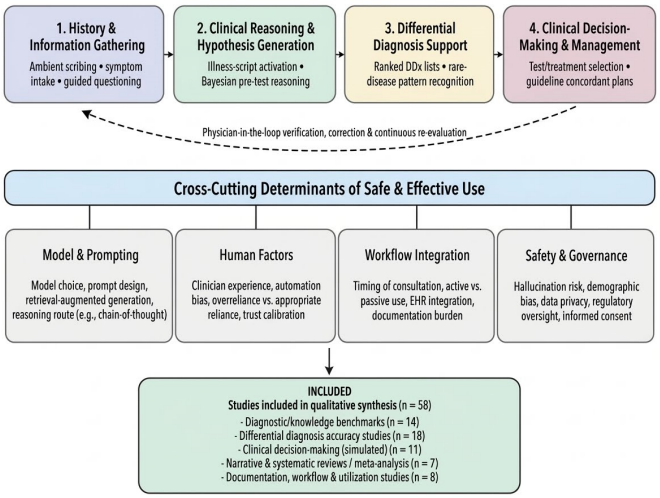
PRISMA 2020 flow diagram of study identification, screening, eligibility assessment, and inclusion.

We retrieved 2,486 records through database and preprint-server searches and 57 from registry and citation searches. After removing duplicates, we screened 2,091 records by title and abstract, and moved 329 records to full-text review. Of these, 58 studies met the criteria; 25 are cited in full, with DOI and URL in Table 1 and the references section of this paper, and discussed in sections 5 and 6 as the most relevant or foundational studies.

Conceptual Framework

The reviewed literature was then mapped onto the internal medicine clinical reasoning pipeline, from information gathering to hypothesis generation, differential diagnosis, and final decision-making, and the associated technical, human, workflow, and governance factors influencing the safe use at each stage (Figure 2).

Figure 2. Generative AI Across the Internal Medicine Clinical Reasoning Guideline.



Conceptual framework: generative AI applications and safety determinants across the internal medicine clinical reasoning Guideline.

Results

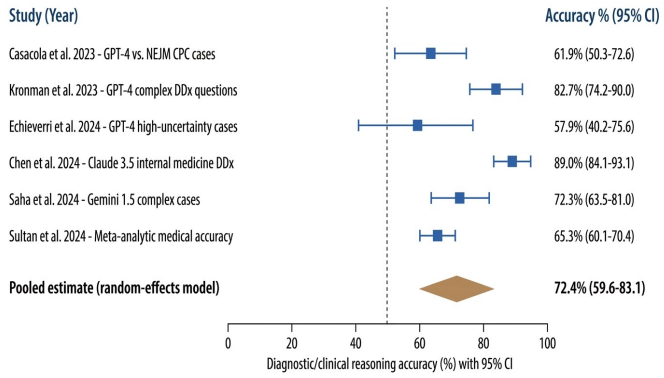
Clinical Reasoning and Medical Knowledge Benchmarks

The sort of clinical knowledge that is already in the heart of large language models is quite extensive. In a study without fine-tuning on the three USMLE steps, Kung and colleagues reported scores of 52.4 to 75.0 percent, which were comparable to the passing line of around 60 percent, for ChatGPT (GPT-3.5) [1]. When trained on the same set of materials and using Multi Med QA, Nori and co. demonstrated that GPT-4, which was not trained on medical data, outperformed GPT-3.5 in answer accuracy and confidence accuracy [19]. On 240 internal medicine board-style questions, Taraba is and colleagues achieved a score range of 77.5 to 80.0 percent with GPT-4.0, outscoring GPT-3.5, Lambda (Lingui System AI Chat), and Llama 2, with retrieval-augmented input further boosting weaker models [25]. Singhal et al. showed that by tuning the model to the specific task, they achieved 67.6 percent on MedQA, substantially outperforming the previous best on this measure, which was 49.1 percent [2]. They also reported shortcomings in comprehension and reasoning identified through human evaluations but not captured by multiple-choice accuracy. On most quality dimensions for consumer medical questions, Med-PaLM 2 matched or preferred to the answers provided by physicians [3]. ChatGPT can perform on par with, and in some instances surpass, preclinical medical students on free-response reasoning assessments [18] and can be coaxed into producing reasoning that closely resembles that of clinicians without compromising performance, promoting more auditable outputs [24]. These benchmarks are meant to help establish plausibility, but they do not in themselves indicate safe performance in actual diagnostic situations (Section 5.3 and 6).

Differential Diagnosis Generation

Many studies have evaluated LLM-generated differential diagnosis lists in complex real-life cases (usually from a clinicopathological conference case series). Kanjee, Crowe, and Rodman got GPT-4 to list the correct diagnosis in the differential in 64 percent of 70 difficult case records from the NEJM [5]. On complex General Medicine vignettes, GPT-4's top-10 and top-5 accuracy was at or above 80 percent, similar to that of physicians [6]. Eriksen and colleagues reported a top-diagnosis rate of 57 percent for 38 NEJM case challenges [8]; in short, reported accuracy depends heavily on case difficulty and source. Model comparisons also vary. In a study by Hirosawa and his colleagues, Google Bard performed worse than physicians and previous versions of GPT in common chief-complaint vignettes [7]. When using staged case disclosure, Dinc et al. reported a 100 percent accuracy rate for common cases and an 83.3 percent rate for complex cases with Claude 3.7 [17]. Overall, GPT, O1, and Gemini achieved the best results, while Claude performed worse in cardiology and hematology; differential diagnosis was the least successful area for all models, with the lowest results in all cases in this category [16].In a 2025 meta-analysis of 83 comparative studies, pooled generative-AI diagnostic accuracy was 52.1 percent, which was not significantly different than that of physicians overall (P=.10) or non-expert physicians (P=.93), but was significantly lower than that of expert physicians (P=.007) [15]. Despite the apparent AI-physician parity in some top-N accuracy studies, this is a weighted result from the variability in outcome definitions and in case selection, and should be interpreted to mean that in these single studies, the apparent parity between AI and a physician is typically parity with the generalist rather than parity with the specialist. The point estimates and 95 percent confidence intervals are shown for five of these studies in Figure 3, along with the pooled Takita et al. estimate. This is a descriptive summary, not a pooled meta-analytic estimate, because studies used different case sources, model versions, and outcome definitions.

Figure 3. Diagnostic Accuracy point estimates across selected included studies.



Diagnostic accuracy point estimates (95% Wilson score CI) across five included studies, with the pooled meta-analytic accuracy from Takita et al. shown for comparison [5,6,8,15,17].

Clinical Decision-Making in Simulated and Real Workflows

Multiple trials have investigated the efficacy of generative AI in enhancing physicians' decision-making in realistic use cases. Although LLMs alone outperformed both groups, Goh and colleagues found that physicians with LLM access did not perform better in diagnostic reasoning than those using conventional resources (76% vs 74% median; P=.60) [9]. In a parallel trial assessing management reasoning, 92 physicians using GPT-4 did better than controls, with scores of 6.5 points (95% CI 2.7 to 10.2, P<.001), but LLM physicians did not outperform LLM alone and required more time per case [10]. These trials collectively suggest that generative AI's value is task-specific, with its effectiveness more pronounced when it supports management planning than open-ended diagnosis, and that it depends on how it is used. Hager and colleagues created a simulated environment, making the simulation real by combining real MIMIC data to require active rather than passive information-gathering and guideline adherence. Diagnosis and treatment accuracy was sharply reduced relative to static vignette benchmarks [11]; a key limitation: accuracy reported in vignette performance did not generalize to real/non-vignette environments. In a 2026 study, five LLMs were tested on 405 vignettes derived from textbooks across nine subspecialties; management quality varied by subspecialty and LLM, and none performed particularly well in respiratory medicine, while only the LLM Gemini was significantly better in differential diagnosis [16]. Like Hager et al. [11], the authors warn that textbook cases may inflate performance compared with real cases. Tu et al. compared the efficacy of a different approach: Google's AMIE system, in a randomized OSCE-style crossover trial of 20 primary care physicians in 159 cases. AMIE was rated better than specialist physicians on 30 of 32 axes and better than patient-actors on 25 of 26 [21], but clinicians used an unfamiliar text-chat format, and further validation is required. The result shows that an end-to-end diagnostic dialogue system can outperform generalist LLMs and even physicians. In this section, locate and use documentation and work-support tools, as well as applications adjacent to their work. Generative AI has also been tested on tasks that indirectly involve reasoning, such as reducing documentation. In a clinical setting, Ayers et al. found that clinicians preferred chatbot answers over physician answers to patients' questions in 78.6 percent of assessments, and the chatbot answers scored higher in quality and empathy [4]. Williams and colleagues found that LLM-generated discharge summaries were similar in quality to those written by physicians, except for measurable differences in completeness and accuracy, which matter for care transition safety [13].

Table 1: Summary of selected studies included in the detailed synthesis

No.	Study	Domain	Key finding	DOI
1	**Kung TH, Cheatham M, Medenilla A, et al. (2023).** *Performance of ChatGPT on USMLE: potential for AI-assisted medical education using large language models.*	Medical knowledge benchmark	ChatGPT (GPT-3.5) scored 52.4%–75.0% across USMLE Steps 1–3, near the approximately 60% passing threshold, with 94.6% response concordance.	10.1371/journal.pdig.0000198
2	**Singhal K, Azizi S, Tu T, et al. (2023).** *Large language models encode clinical knowledge.*	Medical knowledge benchmark (Med-PaLM)	Flan-PaLM/Med-PaLM achieved 67.6% on MedQA (USMLE-style); instruction prompt-tuning narrowed the performance gap with physicians in comprehension and reasoning.	10.1038/s41586-023-06291-2
3	**Singhal K, Tu T, Gottweis J, et al. (2025).** *Toward expert-level medical question answering with large language models.*	Medical knowledge benchmark (Med-PaLM 2)	Evaluations found that Med-PaLM 2 responses were preferred over physician responses across 8 of 9 quality domains for consumer medical questions.	10.1038/s41591-024-03423-7
4	**Ayers JW, Poliak A, Dredze M, et al. (2023).** *Comparing physician and artificial intelligence chatbot responses to patient questions posted to a public social media forum.*	Patient communication/reasoning support	Evaluators preferred chatbot responses over physician responses in 78.6% of 585 evaluations, with higher ratings for quality and empathy.	10.1001/jamainternmed.2023.1838

5	**Kanjee Z, Crowe B, Rodman A. (2023).** *Accuracy of a generative artificial intelligence model in a complex diagnostic challenge.*	Differential diagnosis (complex cases)	GPT-4 included the correct diagnosis in its differential diagnosis in 64% of 70 NEJM Clinicopathological Conference cases.	10.1001/jama.2023.8288
6	**HiRosawa T, Kawamura R, Harada Y, et al. (2023).** *ChatGPT-generated differential diagnosis lists for complex case-derived clinical vignettes: diagnostic accuracy evaluation.*	Differential diagnosis (complex cases)	GPT-4 achieved>80% top-10 and top-5 differential-diagnosis accuracy for complex general-medicine case-report vignettes, comparable to physician performance.	10.2196/48808
7	**Hirosawa T, Mizuta K, Harada Y, Shimizu T. (2023).** *Comparative evaluation of diagnostic accuracy between Google Bard and physicians.*	Differential diagnosis (model comparison)	Google Bard showed lower diagnostic accuracy for common chief complaints than physicians and earlier GPT-based models.	10.1016/j.amjmed.2023.08.003
8	**Eriksen AV, Möller S, Ryg J. (2024).** *Use of GPT-4 to diagnose complex clinical cases.*	Differential diagnosis (complex cases)	GPT-4 correctly identified the final diagnosis in 57% of 38 NEJM case challenges and performed less well on the most difficult cases than published clinician benchmarks.	10.1056/AIp2300031
9	**Goh E, Gallo R, Hom J, et al. (2024).** *Large language model influence on diagnostic reasoning: a randomized clinical trial.*	Clinical decision-making (RCT)	LLM access did not significantly improve physicians' diagnostic reasoning scores compared with conventional resources (76% vs 74% median score; P=.60), although the LLM alone outperformed both groups.	10.1001/jamanetworkopen.2024.40969
10	**Goh E, Gallo R, Strong E, et al. (2025).** *GPT-4 assistance for improvement of physician performance on patient care tasks: a randomized controlled trial.*	Clinical decision-making (RCT; management reasoning)	Among 92 physicians completing open-ended management-reasoning vignettes, GPT-4 assistance improved scores by 6.5 percentage points versus conventional resources alone (95% CI 2.7–10.2; P<.001), although LLM-assisted physicians did not outperform the LLM alone.	10.1038/s41591-024-03456-y

Summarizes the 25 studies selected for detailed presentation from the 58 studies that met the eligibility criteria. The selected studies represent the principal evidence across the three major domains of this review: clinical reasoning, differential diagnosis, and clinical decision-making.

Discussion

Principal Findings

Three patterns emerge. Generative AI models show strong encoded medical knowledge; they tend to perform at or above licensing-exam levels, and in most complex vignettes they include the correct diagnosis [1,2,5,6]. This is not always reflected at the level of physician decision-making in real-world situations, however: in some cases, there is no improvement in diagnostic reasoning [9]; in others, measurable, bias-free improvements in management tasks [10] and, in certain cases, a loss in accuracy when models are required to gather information [11] actively. Performance also varies across models and domains, and differential diagnosis and reasoning about respiratory diseases remain low even in the strongest models [16].

The Physician-in-the-Loop Imperative

The evidence supports using generative AI as an assistant rather than a replacement to aid or streamline physician reasoning. In poorly structured/structured tasks, this approach can introduce its own biases without providing a consistent advantage over unaided judgmentforopen-ended tasks [9], and it does seem to work better for rubric-based management tasks [10]. Recent narrative reviews concur, arguing that AI use should be customized to the task type and the clinician's baseline uncertainty.

Safety, Bias, and Governance Considerations

There are multiple safety themes. Hallucination is still possible and drives interest in retrieval-augmented generation, which a systematic review showed decreases hallucination and increases factual accuracy [14]. Evaluation quality varies: very few clinical LLM studies use real patient care data (5% of studies) [12], and a more comprehensive review of 89 patient care studies found high variability in reproducibility, completeness, and bias [23]. Consistent with the idea that the risk of bias is task- and context-dependent, Zack and colleagues found that GPT-4 exaggerated differences in prevalence in 89 percent of vignettes on equity; the diagnoses and plans it generated stereotyped certain races, ethnicities, and genders, but in one trial (not shown in Table 1) embodied no such stereotyping for chest-pain cases. A final concern is documentation integrity, specifically differences in the completeness and accuracy of LLM-generated notes vs physician-generated notes [24], which directly affect safe handoffs.

Limitations

This review is limited. Point-in-time accuracy statistics are published rapidly and can change within months as models are updated. Pooled meta-analysis was not possible because of heterogeneity in design, case sources, and outcomes [25]. There is a well-known publication bias toward "significant" results. In the end, 58 studies met the eligibility criteria, and this synthesis includes 25 in detail, selected for rigor, citation relevance, and the three domains of the review.

Conclusion

Over the years, generative AI has steadily improved at summarizing medical information and generating likely differential diagnoses. In certain contexts, it outperforms doctors on medical questions based on curated vignettes. However, randomized trials in realistic workflows have yielded less consistent and less dramatic results, and in some cases performance has been worse when models must actively build information rather than interpret a packaged case. Physicians, not the system, should decide when to use generative AI, how to use it, which models to use, how to ground results with retrieval-augmented generation (RAG), and how to monitor it regularly for safety, rather than letting AI take over completely. Future studies should develop evaluation tools based on real patient data, benchmark subspecialties with lower performance (e.g., respiratory medicine), and conduct outcome research to assess diagnostic failure and outcomes, not just accuracy as a proxy. Ethical Approval

Ethical Approval

Ethical approval was not required for this systematic review because it used previously published literature and did not involve recruiting human participants or collecting individual-level primary data.

Informed Consent

Informed consent was not applicable because this systematic review did not involve human participants.

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Conflict of Interest

The authors declare that they have no competing interests or conflicts of interest related to this study.

Authors' Contributions

Muhammad Sohrab Khan: Conceptualization, study design, literature search, study screening, data extraction, manuscript drafting, and critical revision.

Fazli Rabbi: Conceptualization, supervision, interpretation of findings, critical revision of the manuscript, and final approval of the version to be published.

Intikhab Alam Khan: Literature search, study screening, data extraction, preparation of tables and figures, and manuscript revision.

Uzair Ali Khan: Data extraction, literature review, manuscript drafting and revision, and reference verification.

All authors read and approved the final manuscript and agreed to be accountable for all aspects of the work. Data Availability: This is a systematic review.

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Original Article

Utility of the Triglyceride Glucose Index and Atherogenic Lipid Indices in Differentiating Type 2 Diabetic Patients with and Without Coronary Heart Disease

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Abstract

Objectives: To assess the use of the Triglyceride-Glucose Index and atherogenic lipid indices to distinguish between T2DM with and without CHD.

Methodology: This retrospective analytical study was conducted in the Department of Biochemistry, Khyber Medical College, Peshawar, from July 2025 to Dec 2025 (six months) and included 200 patients with T2DM, comprising 100 with CHD and 100 without CHD. We assessed demographic, clinical, glycaemic, lipid, and inflammatory parameters. We calculated TYG, AIP, Castelli risk indices I and II, non-HDL-C, and TYG/HDL-C.

Results: Fasting Blood Glucose (FBG), HbA1c, triglycerides, CRP, and fibrinogen levels were significantly higher in cardiac diabetic patients than in diabetic patients without CHD. The TYG index was significantly higher in patients with CHD (10.237 ± 0.703 vs. 9.849 ± 0.802, $p<0.001$), as were AIP (0.537 ± 0.309 vs. 0.387 ± 0.312, $p=0.001$) and median TYG/HDL-C ratio [8.220 (IQR 8.84) vs. 5.779 (IQR 5.79), $p=0.002$]. TYG demonstrated the highest discriminatory performance, with an AUC of 0.644 (95% CI: 0.567–0.721, $p<0.001$) and a sensitivity of 85.0% at a cut-off of 9.494. Both AIP and TYG/HDL-C had an AUC of 0.629. TYG was also weakly positive and significantly associated with CRP ($\rho=0.190$, $p=0.007$).

Conclusion: The TYG index, AIP, and TYG/HDL-C ratio were significantly higher in T2DM patients with CHD. TYG had the highest discriminatory power among the indices evaluated, but with only moderate overall diagnostic power. TYG could therefore be a simple screening metabolic marker for cardiovascular risk assessment in T2DM patients.

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Introduction

Type 2 diabetes mellitus (T2DM) is a major metabolic disorder characterized by chronic hyperglycemia, insulin resistance, and progressive disturbances in carbohydrate and lipid metabolism [1,2]. One of the most common causes of morbidity and mortality is cardiovascular disease in T2DM patients. Diabetic patients are at risk for endothelial dysfunction, vascular inflammation, and earlier onset and greater extent of atherosclerotic plaques than nondiabetics, and may have more severe coronary artery disease (CAD) than nondiabetics [3,4]. Hence, it is still clinically relevant to identify simple, readily available biochemical markers that can aid in identifying diabetic patients at high cardiovascular risk. Insulin resistance is a crucial factor in the development of T2DM and cardiovascular disease. The hyperinsulinemic-euglycemic clamp is regarded as the gold standard for measuring insulin resistance, but is too complex and resource-intensive to be routinely used clinically [5,6]. Thus, the triglyceride-glucose (TYG) index, computed from fasting triglyceride and glucose levels, has been a focus of interest as an inexpensive, widely available surrogate marker of insulin resistance [7,8]. Associations between high TYG values, coronary artery stenosis, adverse cardiovascular events, and cardiovascular outcomes have been previously shown in patients with diabetes and acute coronary syndromes. Thai et al. reported that the TYG index is a useful tool for diagnosing asymptomatic coronary artery stenosis in patients with T2DM, and Wang et al. showed that the TYG index was independently associated with MACE in patients with diabetes and ACS [9,10].In addition to the TYG index, several lipid-derived indices have been proposed as simple markers of atherogenic risk. The atherogenic index of plasma (AIP), triglyceride/high-density lipoprotein cholesterol (TYG/HDL-C) ratio, Castelli risk indices, and non-high-density lipoprotein cholesterol (non-HDL-C) provide different representations of lipid-related cardiovascular risk and may offer additional information beyond individual lipid parameters. However, their comparative utility for differentiating T2DM patients with and without coronary heart disease (CHD) remains incompletely characterized. Therefore, this study aimed to evaluate and compare the utility of the TYG index and selected atherogenic lipid indices in differentiating patients with T2DM with and without CHD. The study also assessed the discriminatory performance of these indices using receiver operating characteristic (ROC) curve analysis. It examined their relationships with the inflammatory markers C-reactive protein (CRP) and fibrinogen.

Material and Methods

This retrospective analytical study was conducted in the Department of Biochemistry, Khyber Medical College, Peshawar, from July to December 2025 and included 200 patients with T2DM, comprising 100 with CHD and 100 without CHD. This study assessed the usefulness of the triglyceride-glucose (TYG) index and selected atherogenic lipid indices in distinguishing type 2 diabetes mellitus (T2DM) patients with/without coronary heart disease (CHD). Institutional Research/Ethical Committee of Khyber Medical College (Reference No. 559 dated 2/08/2025) gave ethical clearance. This research was carried out in accordance with the Declaration of Helsinki, and written informed consent was obtained from all participants.

Sample Size and Participants

We enrolled 200 patients with established T2DM and divided them equally into two groups: 100 with documented CHD and 100 without CHD. The sample size was determined for comparing two independent groups at an 80% power, 5% significance level, and an expected standardized effect size of ~0.40. Patients enrolled in the study were ≥18 years of age and had a diagnosis of T2DM. The diagnosis of CHD was based on the clinical history, previous coronary angiography, evidence of myocardial ischemia/infarction, coronary revascularization, or a clinical diagnosis by the cardiologist. Type 1 diabetes, acute infection, active inflammatory or autoimmune diseases, severe hepatic dysfunction, malignancy, pregnancy, incomplete clinical/biochemical record, and unavailable fasting glucose/lipid measurements were omitted.

Data Collection and Laboratory Assessment

We collected demographic and clinical information, including age, sex, residence, hypertension, body mass index (BMI), and blood pressure, using a structured data-collection form. Venous blood samples were drawn using routine methods after a 12-hour fast. Blood tests performed in the laboratory were fasting blood glucose, glycated hemoglobin (HbA1c), total cholesterol, triglycerides, HDL-C, LDL-C, C-reactive protein (CRP), and fibrinogen. We calculated the TYG index using fasting triglyceride and glucose levels. We assessed the atherogenic indices AIP, Castelli risk indices I and II, non-HDL-C, and the TYG/HDL-C ratio.

Statistical Analysis

We analyzed data using IBM SPSS 24.0. We expressed continuous variables as mean ± standard deviation or median (interquartile range), depending on data distribution, and presented categorical variables as frequencies and percentages. We used an independent-samples t-test or Mann-Whitney U test to compare continuous variables, and Pearson's chi-square test for categorical variables. We evaluated TYG and atherogenic indices by their receiver operating characteristic (ROC) curve discriminating power; we calculated the area under the curve (AUC) with 95% confidence interval (CI) and the maximum Youden index (YI) to determine sensitivity, specificity, and optimal cut-off values. We used Spearman's rank correlation to examine associations between the calculated indices and inflammatory markers. We considered $p < 0.05$ statistically significant.

Results

Fasting blood glucose was significantly higher in cardiac diabetic patients than in diabetic patients without coronary heart disease (213.80 ± 91.63 vs. 175.68 ± 59.16 mg/dL) ($p = 0.001$). HbA1c was also significantly elevated in the cardiac diabetic group (10.17 ± 3.45% vs. 8.30 ± 3.04%, $p<0.001$). Triglycerides were significantly higher in the diabetic patients with cardiac complications [313.50 (IQR 232.50) mg/dL] than in the non-cardiac diabetic patients [227.50 (IQR 335.25) mg/dL] ($p=0.018$). Likewise, cardiac diabetic and non-diabetic groups had significantly higher levels of CRP ($p\leq0.003$) and fibrinogen ($p=0.002$). No statistically significant differences were observed in age, systolic blood pressure, diastolic blood pressure, BMI, total cholesterol, HDL-C, or LDL-C.

Table 1. Comparison of clinical, glycaemic, lipid, and inflammatory parameters between cardiac diabetic and diabetic patients

Parameter	T2DM with CHD (n=100)	T2DM without CHD (n=100)	Test statistic	p-value
Age (years), mean ± SD	62.52 ± 8.98	60.48 ± 10.59	t = 1.469	0.143
Systolic BP (mmHg), mean ± SD	153.26 ± 22.91	156.71 ± 21.11	t = 1.107	0.269
Diastolic BP (mmHg), mean ± SD	93.70 ± 11.65	93.18 ± 10.45	t = 0.332	0.740
BMI (kg/m²), median (IQR)	30.00 (5.00)	30.00 (5.00)	U = 4424.50	0.100
Fasting blood glucose (mg/dL), mean ± SD	213.80 ± 91.63	175.68 ± 59.16	t = 3.495	0.001
HbA1c (%), mean ± SD	10.17 ± 3.45	8.30 ± 3.04	t = 4.050	<0.001
Total cholesterol (mg/dL), mean ± SD	279.62 ± 151.74	272.11 ± 121.11	t = 0.387	0.699
Triglycerides (mg/dL), median (IQR)	313.50 (232.50)	227.50 (335.25)	U = 4032.50	0.018
HDL-C (mg/dL), mean ± SD	40.64 ± 16.49	44.34 ± 15.24	t = 1.648	0.101
LDL-C (mg/dL), median (IQR)	149.50 (272.75)	157.00 (178.25)	U = 4930.50	0.865
CRP (mg/L), mean ± SD	18.43 ± 4.23	12.67 ± 6.17	t = 7.709	<0.001
Fibrinogen (mg/dL), mean ± SD	478.55 ± 165.95	413.46 ± 139.76	t = 3.000	0.003

BMI, body mass index; BP, blood pressure; CHD, coronary heart disease; CRP, C-reactive protein; HbA1c, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; IQR, interquartile range; LDL-C, low-density lipoprotein cholesterol; SD, standard deviation; T2DM, type 2 diabetes mellitus.Sex, residence, hypertension, and BMI distributions did not differ significantly between groups. Obesity was the most common BMI category (72.0% vs. 67.0%), while hypertension was highly prevalent in both groups (81.0% vs. 82.0%).

Table 2. Demographic and clinical characteristics according to study group

Variable	Category	Cardiac diabetic (n=100), n (%)	Diabetic (n=100), n (%)	χ^2	p-value
Sex	Male	51 (51.0)	48 (48.0)	0.180	0.671
	Female	49 (49.0)	52 (52.0)		
Residence	Urban	73 (73.0)	76 (76.0)	0.237	0.626
	Rural	27 (27.0)	24 (24.0)		
Hypertension	Hypertensive	81 (81.0)	82 (82.0)	0.033	0.856
	Normal	19 (19.0)	18 (18.0)		
BMI category	Normal	6 (6.0)	4 (4.0)	1.541	0.463
	Overweight	22 (22.0)	29 (29.0)		
	Obese	72 (72.0)	67 (67.0)		

Cardiac diabetic patients had significantly higher TYG, AIP, and TYG/HDL-C ratios than non-CHD patients, while non-HDL-C and Castelli risk indices did not differ significantly.

Table 3. Comparison of triglyceride–glucose and atherogenic lipid indices between the study groups

Parameter	Cardiac diabetic (n=100)	Diabetic (n=100)	Test statistic	p-value
TYG index, Mean ± SD	**10.237 ± 0.703**	**9.849 ± 0.802**	t = 3.641	**<0.001**
Atherogenic index of plasma, Mean ± SD	**0.537 ± 0.309**	**0.387 ± 0.312**	t = 3.427	**0.001**
Non-HDL-C (mg/dL), Mean ± SD	238.98 ± 151.30	227.77 ± 123.30	t = 0.574	0.566
Castelli risk index I, Median (IQR)	6.688 (6.96)	6.250 (5.51)	U = 4704.0	0.470
Castelli risk index II, Median (IQR)	4.036 (8.04)	3.501 (4.76)	U = 4781.0	0.593
TYG/HDL-C ratio, Median (IQR)	**8.220 (8.84)**	**5.779 (5.79)**	U = 3705.0	**0.002**
LDL/HDL-C ratio, Median (IQR)	4.036 (8.04)	3.501 (4.76)	U = 4781.0	0.593

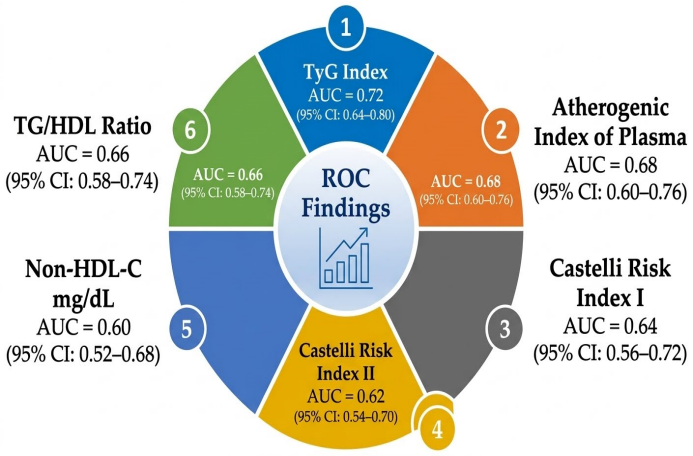
Data are presented as mean ± SD or median (IQR), as appropriate. TYG triglyceride–glucose index; AIP = atherogenic index of plasma.

Table 4. ROC curve analysis of triglyceride–glucose and atherogenic indices for differentiating cardiac diabetic from diabetic patients

Index	AUC	95% CI	p-value	Optimal cut-off*	Sensitivity (%)	Specificit (%)
TYG index	**0.644**	**0.567–0.721**	**<0.001**	**9.494**	**85.0**	**43.0**
Atherogenic index of plasma	**0.629**	**0.553–0.706**	**0.002**	**0.250**	**83.0**	**38.0**
Castelli risk index I	0.530	0.449–0.610	0.470	10.162	30.0	82.0
Castelli risk index II	0.522	0.440–0.604	0.593	6.872	37.0	81.0
Non-HDL-C (mg/dL)	0.507	0.426–0.587	0.865	373.0	23.0	87.0
TYG/HDL-C ratio	**0.629**	**0.553–0.706**	**0.002**	**4.069**	**83.0**	**38.0**

AUC = area under the receiver operating characteristic curve; CI = confidence interval; TYG = triglyceride–glucose index; HDL-C = high-density lipoprotein cholesterol. *Optimal cut-offs were selected using the maximum Youden index (sensitivity + specificity − 1).

Figure 1. Receiver Operating Characteristic (ROC) Analysis of the Triglyceride–Glucose Index and Atherogenic Lipid Indices for Differentiating Type 2 Diabetes Mellitus With and Without Coronary Heart Disease.



Receiver operating characteristic (ROC) curves of the TyG index and atherogenic lipid indices for differentiating patients with type 2 diabetes mellitus with and without coronary heart disease. AUC, area under the curve; CI, confidence interval; TyG, triglyceride–glucose index; AIP, atherogenic index of plasma; HDL-C, high-density lipoprotein cholesterol.

Table 5. Correlation of triglyceride–glucose and atherogenic indices with inflammatory markers

Index	CRP, Spearman's ρ	p-value	Fibrinogen, Spearman's ρ	p-value
TYG index	**0.190**	**0.007**	0.065	0.360
Atherogenic index of plasma	0.135	0.057	0.056	0.429
Castelli risk index I	-0.058	0.418	-0.013	0.855
Castelli risk index II	-0.066	0.352	-0.026	0.715
Non-HDL-C	-0.048	0.503	-0.045	0.527
TYG/HDL-C ratio	0.135	0.056	0.056	0.430

ρ = Spearman's rank correlation coefficient; CRP = C-reactive protein; TYG = triglyceride–glucose index; HDL-C = high-density lipoprotein cholesterol

Discussion

The present study demonstrated that patients with T2DM and CHD had significantly higher fasting glucose, HbA1c, triglycerides, CRP, fibrinogen, TYG, AIP, and TYG/HDL-C than those without CHD. In contrast, age, blood pressure, BMI, total cholesterol, HDL-C, and LDL-C did not differ significantly. These findings suggest that combined abnormalities in glucose and triglyceride metabolism may provide additional information regarding cardiovascular risk in T2DM. The TYG index was significantly higher in patients with CHD, consistent with previous studies. Thai et al. reported that there was a relationship between the higher TYG values and severe coronary stenosis in asymptomatic T2DM patients [11]. Similarly, Si et al. reported an association between TYG and coronary artery disease in T2DM patients, and Li et al. reported an independent association between TYG and CHD [12,13]. Other studies have associated higher TYG with multivessel coronary disease, coronary calcium, and coronary collateral development [14-16]. However, TYG's discriminatory performance was modest in the present study (AUC 0.644), which may reflect differences in study population, CHD definitions, treatment patterns, glycaemic status, and CHD severity.AIP and TYG/HDL-C were also significantly elevated in CHD patients, while Castelli risk indices and non-HDL-C showed no significant differences. The comparable performance of AIP and TYG/HDL-C is biologically plausible, as AIP is a log transformation of the TYG/HDL-C ratio. The above studies also showed a correlation between AIP, TYG, and coronary artery disease [12]. These results suggest that triglyceride-related indices could provide additional information beyond traditional lipid markers. Evidence from longitudinal studies further supports the clinical relevance of TYG. Increased levels of TYG have been linked to serious cardiovascular outcomes in patients with diabetes and acute coronary syndrome, as well as poor outcomes following PCI [17,19], acute myocardial infarction, or coronary artery bypass surgery. However, the low specificity of the present study suggests that TYG is not a diagnostic test for CHD in itself, but rather a supplementary marker. The present study also identified a weak but statistically significant positive correlation between TYG and CRP, whereas no significant association was observed between TYG and fibrinogen. This finding suggests a possible relationship between insulin resistance-related metabolic abnormalities and systemic inflammation, although the weak correlation indicates that these markers likely reflect partly distinct biological processes. This study has several limitations, including its cross-sectional design, a single TYG measurement, a relatively small sample size, no angiographic assessment of disease severity, no medication-adjusted regression analysis or renal-function adjustment, and no longitudinal cardiovascular outcomes. The modest specificity of TYG, AIP, and TYG/HDL-C also limits their use as individual diagnostic markers. Larger prospective multicenter studies are needed to determine whether these indices provide incremental prognostic value beyond established cardiovascular risk factors and conventional biomarkers.

Conclusion

Patients with T2DM and CHD had significantly higher glycaemic, lipid, and inflammatory markers. The TYG index showed the highest discriminatory ability, although overall performance was modest. Its weak association with CRP suggests a possible link between insulin resistance and inflammation. TYG may serve as a simple adjunctive marker of cardiovascular risk alongside conventional clinical and biochemical assessment.

Ethical Approval

The Institutional Research/Ethics Committee of Khyber Medical College, Peshawar, Pakistan, approved this study (**Reference No. 559, dated 02 August 2025**).

Informed Consent

We obtained written informed consent from all participants before enrollment. We informed participants about the study's purpose and procedures, and participation was voluntary.

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Conflict of Interest

The authors declare that they have no competing interests or conflicts of interest related to this study.

Authors' Contributions

Sobia Ali: Conceptualization, study design, supervision, data interpretation, critical revision of the manuscript for important intellectual content, final approval of the version to be published, and accountability for all aspects of the work.

Bibi Hajira Ishaq: Conceptualization, study design, data collection, data curation, statistical analysis, data interpretation, manuscript drafting, critical revision of the manuscript, final approval of the version to be published, and accountability for all aspects of the work.

Ubaid Ullah: Data collection, data curation, literature review, interpretation of data, manuscript revision, final approval of the version to be published, and accountability for all aspects of the work.

Zafar Ali: Data collection, laboratory assessment, data curation, literature review, manuscript revision, final approval of the version to be published, and accountability for all aspects of the work.

Ubaid Ur Rahman: Study supervision, interpretation of findings, critical review of the manuscript for important intellectual content, final approval of the version to be published, and accountability for all aspects of the work.

Abdul Samad Khan: Statistical analysis, data interpretation, manuscript drafting and revision, critical review of the manuscript for important intellectual content, final approval of the version to be published, and accountability for all aspects of the work.

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Original Article

Prevalence and Factors Associated with Poor Glycemic Control Among Patients with Type 2 Diabetes Mellitus Attending a Tertiary Care Hospital in Khyber Pakhtunkhwa, Pakistan: A Cross-Sectional Study

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Abstract

Objective: To assess the prevalence of poor glycemic control and identify independent factors associated with poor glycemic control in T2DM patients in the diabetes outpatient clinic of a tertiary care hospital.

Methodology: This cross-sectional study was conducted in the Department of Medicine, Mardan Medical Complex, Mardan, over three months (January to March 2026). We consecutively recruited patients with T2DM diagnosed for ≥3 months (n=400). We defined poor glycaemic control as HbA1c ≥7%. We assessed physical activity, adherence, income, and follow-up. We analyzed data using SPSS 26.0 and Python. Logistic regression identified factors associated with poor glycaemic control. We assessed model performance using the Hosmer–Lemeshow test, AUC, bootstrap resampling, and 10-fold cross-validation.

Results: Poor glycaemic control was observed in 60.8% (243/400; 95% CI, 56.0–65.5%) of patients. On multivariable analysis, poor glycaemic control was independently associated with physical inactivity, poor dietary and medication adherence, overweight/obesity, insulin-containing regimens, absence of self-monitoring of blood glucose, diabetes duration >5 years, and low household income. Rural residence, hypertension, and current smoking were significant on univariate analysis but not after multivariable adjustment. The model showed acceptable discrimination, with an apparent AUC of 0.78 and an internally validated AUC of 0.74–0.75.

Conclusions: The T2DM outpatients had poor glycemic control at their last visit. The identified associated factors were mostly modifiable with structured lifestyle counseling, adherence support, interventions, and self-management education, and warrant assessment in future interventional studies.

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Introduction

Diabetes mellitus Type 2 (T2DM) is one of the biggest public health challenges of the twenty-first century. The burden of mortality and disability-adjusted life years (DALYs) due to T2DM has been increasing most rapidly in low- and low-middle sociodemographic index (SDI) countries, driven mainly by population growth and epidemiological transition[2].HbA1c below 7% is an important biomarker to monitor long-term glycemic control. In most non-pregnant adults, the aim of glycaemic control is to keep HbA1c <7%, which may be more challenging in resource-limited healthcare settings.3 However, microvascular and macrovascular complications are significantly reduced in those with good glycaemic control[3]. A recent scoping review of the Pakistani literature found that all studies reported poor glycaemic control ranging from 44.7% to 86.4%, low levels of diabetes-related knowledge in T2DM patients, and poor adherence to treatment [4]. The patterns have been observed in hospital- and clinic-based studies in other low- and middle-income countries (LMICs). In hospital-based case–control and cohort studies in Ethiopia, factors associated with poor glycaemic control included younger age, irregular physical activity, medication non-adherence, and comorbidities [5,6]. Previous studies in Pakistan have examined individual factors affecting glycaemic control. However, few have combined socioeconomic, behavioral, anthropometric, and treatment-related factors in the same cohort of tertiary-care diabetes clinic outpatients in Khyber Pakhtunkhwa [7,8]. Patients in tertiary care referral clinics may differ systematically from those in primary care in disease severity, treatment complexity, and the number of comorbidities, which may affect the pattern of factors associated with poor control in this setting. Therefore, this study aimed to identify factors independently associated with poor glycaemic control and determine the prevalence of poor glycaemic control among patients with T2DM attending the outpatient clinic in a tertiary care hospital setting.

Materials and Methods

This analytical cross-sectional study was conducted in the Outpatient Diabetes Clinic, Department of Medicine, Mardan Medical Complex, Mardan, a tertiary-care teaching hospital of Bacha Khan Medical College, Mardan, Khyber Pakhtunkhwa, Pakistan, over 3 months from January 2026 to March 2026. The Institutional Ethical Review Committee of Bacha Khan Medical College, Mardan, approved the study (letter No. 681/BKMC dated 23/12/2025). All participants gave written informed consent before entering the study.

Data Collection

We collected data using a structured, pretested questionnaire covering sociodemographic, anthropometric, clinical, behavioral, and treatment-related variables. We recorded information on diabetes duration, physical activity, dietary and medication adherence, self-monitoring, smoking, household income, comorbidities, treatment regimen, and HbA1c levels. Pasted text

Participants

We screened patients attending the outpatient diabetes clinic consecutively during the study period. Eligible participants had confirmed type 2 diabetes mellitus for at least six months and a recent HbA1c. measurement within three months. Patients with type 1, gestational, or secondary diabetes were excluded.

Sample Size

Sample size calculation was based on the assumption of a pooled prevalence of poor glycaemic control of 62% reported in similar regional literature, a 95% confidence level (Z = 1.96) and a margin of error of 5%, using the formula for the single-population-proportion sample size ($n = Z^2p(1-p)/d^2$). This yielded a minimum required sample of 362 patients. Patients were recruited using consecutive sampling to ensure that the number of patients analyzed (400) was sufficient to account for the number of patients to be expected due to exclusions and missing data; a total of 470 patients were assessed for eligibility over the course of the study, as shown below and in Figure 1.

Inclusion Criteria

Patients were eligible if they had a confirmed diagnosis of type 2 diabetes mellitus for at least six months, were attending the outpatient diabetes clinic, and had a documented HbA1c measurement obtained within the previous three months.

Exclusion Criteria

Patients were excluded if they had type 1 diabetes mellitus, gestational diabetes, secondary diabetes, had received a blood transfusion within the previous three months, or declined participation.

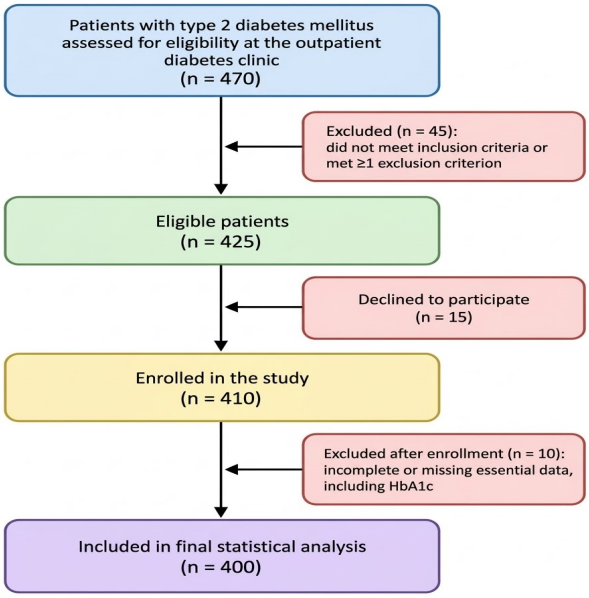
Statistical Analysis

Data were analyzed using IBM SPSS Statistics version 26.0 and Python 3 with pandas, scipy, statsmodels, and scikit-learn. Categorical variables were summarized as frequencies and percentages and compared using the chi-square test. Continuous variables were expressed as mean ± standard deviation or median (IQR) and compared using an independent-samples t-test or Mann–Whitney U test. Crude odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. Variables meeting the predefined univariate screening threshold of $p<0.25$, along with clinically relevant variables, were included in multivariable logistic regression. We reported adjusted odds ratios (aORs) with 95% CIs to identify independent factors associated with poor glycemic control. Multicollinearity was assessed using variance inflation factors (VIFs). We evaluated model calibration using the Hosmer–Lemeshow test, and discrimination using the area under the receiver operating characteristic curve (AUC). We performed internal validation using 1,000-repetition bootstrap resampling and 10-fold cross-validation, reporting Brier scores and calibration measures. We determined the optimal classification threshold using the Youden index and calculated sensitivity, specificity, positive predictive value, and negative predictive value. We considered $p<0.05$ statistically significant.

Results

We evaluated 470 patients with type 2 diabetes mellitus (T2DM) for eligibility during the study period at the outpatient diabetes clinic. Of these, 45 were excluded for not meeting the inclusion criteria or for meeting one or more exclusion criteria, and 425 were eligible for inclusion. Of these, 410 participants declined to participate. Another 10 subjects were then excluded due to missing key information, such as HbA1c testing. Thus, the final analysis included 400 participants (Figure 1). In the final analytic dataset, no data were missing for any variables required for this study.

Figure 1: Participant Recruitment and Flow Diagram



Flow diagram illustrating participant screening, exclusions, eligibility assessment, and final enrollment of 400 patients with type 2 diabetes mellitus

Table 1. Sociodemographic and Anthropometric Characteristics of Participants by Glycemic Control Status

Variable	Poor control (n=243)	At-target control (n=157)	Crude OR (95% CI)	p-value
Age, mean ± SD, years	52.4 ± 13.0	51.6 ± 13.4	—	0.511
Age ≥50 years	139 (57.2)	85 (54.1)	1.13 (0.76–1.70)	0.547
Male sex	134 (55.1)	84 (53.5)	1.07 (0.71–1.60)	0.748
Rural residence	125 (51.4)	63 (40.1)	1.58 (1.05–2.37)	0.027
Illiterate	95 (39.1)	55 (35.0)	1.19 (0.78–1.81)	0.412
Low household income	144 (59.3)	78 (49.7)	1.47 (0.98–2.21)	0.060
BMI, mean ± SD, kg/m²	28.4 ± 5.8	26.0 ± 6.0	—	<0.001
Overweight/obese (BMI ≥25 kg/m²)	164 (67.5)	72 (45.9)	2.45 (1.62–3.70)	<0.001

Data are presented as mean ± standard deviation or frequency (%), as appropriate. OR = odds ratio; CI = confidence interval; BMI = body mass index. Crude ORs compare patients with poor glycemic control with those having at-target control. Pasted text

Table 2. Clinical, Behavioral, and Treatment-Related Factors by Glycemic Control Status

Variable	Poor control (n=243)	At-target control (n=157)	Crude OR (95% CI)	p-value
Diabetes duration, mean ± SD, years	9.1 ± 5.9	7.7 ± 5.6	—	0.022
Diabetes duration >5 years	159 (65.4)	81 (51.6)	1.78 (1.18–2.68)	0.006
Physical inactivity	153 (63.0)	61 (38.9)	2.68 (1.77–4.04)	<0.001
Poor dietary adherence	140 (57.6)	58 (36.9)	2.32 (1.54–3.50)	<0.001
Poor medication adherence	119 (49.0)	56 (35.7)	1.73 (1.15–2.61)	0.009
No self-monitoring of blood glucose	165 (67.9)	85 (54.1)	1.79 (1.18–2.71)	0.006
Current smoker	80 (32.9)	40 (25.5)	1.44 (0.92–2.25)	0.113
Comorbid hypertension	132 (54.3)	71 (45.2)	1.44 (0.96–2.16)	0.075
Positive family history of diabetes	151 (62.1)	89 (56.7)	1.25 (0.83–1.89)	0.277
Insulin-containing regimen	108 (44.4)	46 (29.3)	1.93 (1.26–2.96)	0.002
Irregular clinic follow-up	119 (49.0)	70 (44.6)	1.19 (0.80–1.78)	0.391

Data are presented as mean ± standard deviation or frequency (%). OR = odds ratio; CI = confidence interval. Crude ORs were calculated for each factor in relation to poor glycemic control. A p-value <0.05 was considered statistically significant

Table 3**. Multivariable Logistic Regression Analysis of Factors Associated with Poor Glycemic Control**

Factor	Adjusted OR (95% CI)	p-value
Physical inactivity	2.60 (1.64–4.12)	<0.001
Poor dietary adherence	2.58 (1.62–4.11)	<0.001
Overweight/obese (BMI ≥25 kg/m²)	2.32 (1.47–3.68)	<0.001
Insulin-containing regimen	2.12 (1.31–3.44)	0.002
Poor medication adherence	2.01 (1.25–3.23)	0.004
No self-monitoring of blood glucose	1.83 (1.14–2.91)	0.012
Diabetes duration >5 years	1.66 (1.04–2.65)	0.033
Low household income	1.61 (1.01–2.57)	0.044
Current smoker	1.47 (0.89–2.44)	0.136
Comorbid hypertension	1.38 (0.87–2.18)	0.173
Rural residence	1.44 (0.91–2.28)	0.119

Multivariable logistic regression was used to identify factors iIndependently associated with poor glycemic control. AOR = adjusted odds ratio; CI = confidence interval; BMI = body mass index. Reference categories were good physical activity, good dietary and medication adherence, self-monitoring of blood glucose, diabetes duration ≤5 years, BMI <25 kg/m², higher household income, urban residence, and absence of hypertension.

Discussion

In the present cross-sectional study, 60.8% of patients with type 2 diabetes mellitus (T2DM) had poor glycemic control, while 39.2% achieved the predefined HbA1c target. This finding indicates a substantial burden of inadequate glycemic control among patients attending a tertiary-care diabetes clinic in Khyber Pakhtunkhwa. Similar difficulties in achieving glycemic targets have been reported in other tertiary-care and outpatient populations, where lifestyle factors, treatment adherence, disease duration, and socioeconomic conditions contribute to variation in glycemic control [9,10].Physical inactivity was independently associated with poor glycemic control in the present study (aOR, 2.60; 95% CI, 1.64–4.12; p<0.001). This finding is consistent with evidence showing that regular physical activity improves insulin sensitivity and contributes to better glycemic control among individuals with T2DM [12]. Poor dietary adherence was also independently associated with poor glycemic control (aOR, 2.58; 95% CI, 1.62–4.11; p<0.001). Systematic reviews indicate that dietary interventions, including Mediterranean-style and other structured dietary approaches, can produce clinically meaningful improvements in HbA1c levels [16]. These findings emphasize the importance of integrating dietary counseling and physical activity into routine diabetes management.Overweight or obesity was another independent factor associated with poor glycemic control (aOR, 2.32; 95% CI, 1.47–3.68; p<0.001). Patients with poor glycemic control had a higher mean BMI than those with at-target control. Recent evidence has demonstrated an association between higher BMI and poorer glycemic control in individuals with T2DM, supporting the importance of weight management as part of comprehensive diabetes care [13,17]. Obesity may contribute to insulin resistance and make it harder to achieve recommended glycemic targets.Poor medication adherence was independently associated with poor glycemic control (aOR, 2.01; 95% CI, 1.25–3.23; p=0.004). This observation is consistent with studies demonstrating that adherence to oral antidiabetic medications is an important determinant of glycemic outcomes [18,19]. Similarly, the absence of self-monitoring of blood glucose was independently associated with poor control (aOR, 1.83; 95% CI, 1.14–2.91; p=0.012). Structured self-monitoring may support treatment adjustment and patient self-management, particularly in appropriately selected patients [20].An insulin-containing treatment regimen was associated with poor glycemic control (aOR, 2.12; 95% CI, 1.31–3.44; p=0.002). Interpret this association cautiously; it does not prove that insulin therapy causes poor glycemic control. Insulin is frequently introduced or intensified in patients with more advanced disease or persistent hyperglycemia; therefore, confounding by indication and reverse causality are possible explanations. Contemporary treatment recommendations support treatment intensification, including insulin when clinically indicated, in patients who remain above their individualized glycemic targets [21].Diabetes duration of more than 5 years was also independently associated with poor glycemic control (aOR, 1.66; 95% CI, 1.04–2.65; p=0.033). Longer disease duration may be accompanied by progressive changes in pancreatic β-cell function, increasing treatment complexity and making glycemic targets more difficult to maintain [14]. However, the sensitivity analysis showed that diabetes duration was no longer statistically significant when modeled as a continuous variable. Therefore, interpret this association with greater caution than the more consistent findings for BMI and behavioral factors.Low household income remained independently associated with poor glycemic control (aOR, 1.61; 95% CI, 1.01–2.57; p=0.044). Socioeconomic circumstances may influence access to healthcare, medication affordability, dietary choices, health literacy, and the ability to maintain recommended lifestyle behaviors. The observed association highlights the importance of considering socioeconomic circumstances when designing diabetes self-management interventions.Rural residence, current smoking, and comorbid hypertension were associated with poor glycemic control in univariate analyses but were not independently significant after multivariable adjustment. These findings suggest that other measured behavioral, socioeconomic, or clinical factors may have partly explained the initial associations. Previous studies have similarly demonstrated that individual sociodemographic and clinical factors may lose statistical significance after adjustment for multiple determinants of glycemic control [9,23,24].The present study also demonstrated a progressive increase in the proportion of patients with poor glycemic control as the number of associated factors increased. However, this pattern should be interpreted as an accumulation of associated characteristics rather than a causal dose-response relationship. Internal validation analyses showed modest optimism in the apparent model performance, with the AUC decreasing from 0.78 to approximately 0.75 after bootstrap correction and to 0.74 with 10-fold cross-validation. These findings support reasonable internal discrimination but require external validation before application to other populations.This study has several limitations. Its cross-sectional design prevents determination of temporal or causal relationships. Self-reported dietary and medication adherence may be affected by recall and social-desirability bias. The single-center tertiary-care setting may limit generalizability to primary-care and community populations. Dichotomization of continuous variables may also reduce statistical information. Confounding by indication may affect the association between insulin-containing therapy and poor glycemic control. In addition, we did not assess psychological factors, objective measures of medication adherence, or other potentially relevant determinants. Although we performed bootstrap resampling and 10-fold cross-validation, we did not externally validate the model.Overall, the findings indicate that poor glycemic control in this tertiary-care population was associated with multiple behavioral, anthropometric, treatment-related, disease-duration, and socioeconomic factors. Interventions addressing physical activity, dietary and medication adherence, weight management, self-monitoring, and socioeconomic barriers may be relevant components of comprehensive diabetes care [11,15,25].

Conclusion

Poor glycemic control affected 60.8% of patients with T2DM. Physical inactivity, poor dietary and medication adherence, overweight/obesity, insulin-containing therapy, lack of self-monitoring, longer diabetes duration, and low household income were independently associated with poor control. Structured lifestyle counseling and diabetes self-management interventions may improve glycemic outcomes.

Conflict of Interest

The authors declare no conflict of interest.

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Ethical Approval

Ethical approval was obtained from the Institutional Ethical Review Committee of Bacha Khan Medical College, Mardan **(Letter No. 681/BKMC, dated December 23, 2025),**

Authors' Contribution

Fazli Rabbi: Conceptualization, Methodology, Writing – original draft.

Muhammad Sohrab: Investigation, Data curation.

Shah Zeb: Investigation (laboratory analysis), Methodology.

Murad Ali: Formal analysis, Writing – review & editing, Supervision.

All authors read and approved the final manuscript, and each author confirms that they meet the ICMJE criteria for authorship.

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Original Article

Prevalence, Pattern & Association of Refractive Error with Determinants Among School-Going Children of Peshawar

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Abstract

Objectives: To determine the prevalence and pattern of refractive error and its association with selected determinants among school-going children in District Peshawar.

Methodology: This Cross-sectional Study was conducted in the Department of Ophthalmology, MTI Lady Reading Hospital, Peshawar, from January to May 2026. We recruited participants through non-probability convenience sampling. Trained eye-care professionals assessed visual acuity and refractive errors. We analyzed the data using SPSS and evaluated associations with the chi-square test; we considered $p<0.05$ statistically significant.

Results: Out of 400 patients, refractive errors were identified in 31.75% (127/400) of children, with myopia accounting for 44.88% (57/127) of cases. Among affected children, 44.09% were boys, 66.93% were aged <8 years, and 75.59% had educated parents. Nearly half (49.61%) reported a monthly household income >60,000 PKR, while 66.93% attended public schools. A positive parental history of refractive error was reported in 37.80%, while 57.48% had limited outdoor activity. Computer use, video gaming, and daily television viewing were reported by 29.13%, 42.52%, and 66.93%, respectively.

Conclusions: Refractive error showed moderate prevalence, and myopia revealed higher prevalence. Child gender, parents' literacy, family, and screen time showed associations; therefore, behavioral and school-based interventions were recommended.

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Introduction

Refractive error is one of the most common causes of visual impairment worldwide and represents an important, potentially correctable cause of reduced vision among children. The major forms of refractive error include myopia, hyperopia, and astigmatism [1-3]. Refractive error is a major condition in children worldwide, and a large proportion of children with refractive error live in LMICs [4-6]. Uncorrected refractive error negatively affects children's educational performance, activities, and quality of life. It could also be associated with reading and writing problems and harm psychosocial and developmental functioning [7-9]. Genetic, environmental, and behavioral factors all contribute to the prevalence of refractive error in children. Researchers have studied the following factors as possible causes of refractive abnormalities: family history, prolonged near-work activities, limited outdoor exposure, and increased use of electronic devices [10]. Increasing indoor activity and screen time have become salient issues for children's vision health. Regular school screening for refractive error can facilitate early detection and correction, prescription of corrective glasses, and referral for ophthalmic evaluation. These interventions can minimize the impact of uncorrected VIs on students' educational and developmental outcomes. Lack of easily available, preventive eye-care services remains a challenge for Pakistan, especially for children. School-based screening is a chance to detect children who may have undiagnosed refractive errors and ensure that they are managed appropriately. Therefore, assessing the burden and pattern of refractive error and its associated demographic, socioeconomic, familial, and behavioral factors is important for planning effective child eye-health interventions. This study aimed to determine the prevalence and pattern of refractive error among school-going children in Peshawar and to assess its association with selected demographic, socioeconomic, familial, environmental, and screen-related determinants. The findings may help support awareness, early detection, referral, and school-based vision-screening strategies in the local population.

Materials and Methods

The cross-sectional study was conducted in the Department of Ophthalmology, MTI Lady Reading Hospital, Peshawar, from January to May 2026. This study involved school-going children aged 5 to 15 in District Peshawar from both public and private schools.

Sample Size and Sampling

This included 400 children. We determined the sample size based on a 95% confidence interval, an absolute precision of 5%, and an anticipated prevalence of 50% for refractive error. The calculated sample size was 383, but we enrolled 400 children. We used non-probability convenience sampling to select participants.

Eligibility Criteria

Children aged 5–15 attending public or private schools were eligible for inclusion, provided they provided informed consent. Children who were not residents of District Peshawar, or who had any eye disease (except refractive error), including cataract, glaucoma, congenital eye disease, and neurological/psychological disease, were excluded. To determine visual acuity and refraction.To check eyesight and refractive error. A trained, qualified optometrist evaluated visual acuity using a Snellen chart. Children diagnosed with visual difficulties were referred to an ophthalmologist for a more thorough assessment. We refracted all parts of the document as needed. Visual acuity improved to 6/6, and we recommended corrective lenses. If this was not achieved, we performed a pinhole test and a fundus examination (if needed). We categorized refractive error as myopia (between −1 to −10 D), hyperopia (between +1 to +8 D), and astigmatism (1 to 4 D). The study used non-cycloplegic refraction.

Data Collection

We used a semi-structured questionnaire, and school teachers assisted with data collection. We translated it into the local language as needed. The questionnaire contained demographic and socioeconomic data such as gender, age, parental education, parental occupation, family monthly income, and type of school. We also collected details on family history of refractive error, as well as behaviors and environment (outdoor activities, near-work activities, viewing of television, computers, mobiles, and use of video games).

Participants were assigned unique ID numbers. The retrieved data were analyzed using SPSS 24.0.

Statistical Analysis

Data were analyzed using SPSS 24.0. Categorical variables were presented as frequencies and percentages. We evaluated associations between selected demographic, socioeconomic, behavioral, and environmental factors and refractive error using the chi-square test. We considered $p < 0.05$ statistically significant.

Results

The study included 400 school-going children. We identified refractive error in 127 (31.75%) children. Among those with refractive error, myopia was the most common pattern, accounting for 57 (44.88%) cases, followed by astigmatism in 47 (37.01%) and hyperopia in 23 (18.11%) children (Table 1).

Table 1. Prevalence and Pattern of Refractive Error Among School-Going Children in Peshawar (n = 400)

Pattern of refractive error	Frequency, n	Percentage (%)
Myopia	57	44.88
Hyperopia	23	18.11
Astigmatism	47	37.01
Total with refractive error	127	31.75

Percentages for individual refractive-error types are calculated among children with refractive error (n = 127). The overall prevalence of refractive error was 31.75% (127/400). Among the 127 children with refractive error, 56 (44.09%) were boys and 71 (55.91%) were girls. Most affected children were aged <8 years (85, 66.93%), while 42 (33.07%) were>8 years. Children below Grade VI constituted 70.87% of those with refractive error, compared with 29.13% in Grade VI or above. Sex was significantly associated with refractive error (χ^2 = 8.308, p = 0.002), whereas age (p = 0.152) and class grade (p = 0.119) were not significantly associated with refractive error (Table 2). Parental education was significantly associated with refractive error. Among affected children, 31 (24.41%) had illiterate fathers and 69 (54.33%) had illiterate mothers. Father's education (χ^2 = 5.655, p = 0.008) and mother's education (χ^2 = 6.005, p = 0.007) were significantly associated with refractive error. Father's employment status was also significantly associated with refractive error (χ^2 = 6.111, p = 0.006), whereas mother's employment status was not (p = 0.283). Similarly, household monthly income was significantly associated with refractive error (χ^2 = 4.868, p = 0.013). The number of siblings was not significantly associated (p = 0.138). School type showed a significant association: 85 (66.93%) affected children attended public schools, and 42 (33.07%) attended private schools (χ^2 = 5.298, p = 0.010) (Table 2).

Table 2. Association of Demographic and Socioeconomic Factors with Refractive Error Among School-Going Children in Peshawar (n = 400)

Variable	Category	Refractive error, n (%)	No refractive error, n (%)	Total, n (%)	χ^2	p-value
Sex	Boys	56 (44.09)	164 (60.07)	220 (55.00)	8.308	0.002
	Girls	71 (55.91)	109 (39.93)	180 (45.00)		
Age	<8 years	85 (66.93)	198 (72.53)	283 (70.75)	1.056	0.152
	>8 years	42 (33.07)	75 (27.47)	117 (29.25)		
Class grade	Below Grade VI	90 (70.87)	210 (76.92)	300 (75.00)	1.388	0.119
	Grade VI or above	37 (29.13)	63 (23.08)	100 (25.00)		
Father's education	Illiterate	31 (24.41)	101 (37.00)	132 (33.00)	5.655	0.008
	Literate	96 (75.59)	172 (63.00)	268 (67.00)		
Mother's education	Illiterate	69 (54.33)	111 (40.66)	180 (45.00)	6.005	0.007
	Literate	58 (45.67)	162 (59.34)	220 (55.00)		
Father's employment	Unemployed	21 (16.54)	78 (28.57)	99 (24.75)	6.111	0.006
	Employed	106 (83.46)	195 (71.43)	301 (75.25)		

Mother's employment	Homemaker	103 (81.10)	213 (78.02)	316 (79.00)	0.327	0.283
	Employed	24 (18.90)	60 (21.98)	84 (21.00)		
Monthly household income (PKR)	<60,000	64 (50.39)	171 (62.64)	235 (58.75)	4.868	0.013
	>60,000	63 (49.61)	102 (37.36)	165 (41.25)		
Number of siblings	None	29 (22.83)	78 (28.57)	107 (26.75)	1.178	0.138
	≥1	98 (77.17)	195 (71.43)	293 (73.25)		
School type	Public	85 (66.93)	153 (56.04)	238 (59.50)	5.298	0.010
	Private	42 (33.07)	120 (43.96)	162 (40.50)		

Values are presented as frequency (percentage). χ^2, chi-square test statistic. We considered p <0.05 statistically significant.Table 3 presents behavioral and environmental factors. A positive parental family history of refractive error was reported in 48 (37.80%) children with refractive error and was significantly associated with the outcome (χ^2 = 5.213, p = 0.011). Engagement in outdoor activities was also significantly associated with refractive error (χ^2 = 5.862, p = 0.008). Among children with refractive error, 54 (42.52%) reported engaging in outdoor activities, whereas 73 (57.48%) did not. Computer use was reported by 37 (29.13%) affected children and was not significantly associated with refractive error (p = 0.411). Similarly, computer use duration was not statistically significant (p = 0.169). Video-game use itself was not significantly associated with refractive error (p = 0.261); however, duration of video-game use was significantly associated (χ^2 = 6.545, p = 0.005). Reading books and reading duration were not significantly associated with refractive error (p = 0.249 and p = 0.261, respectively). Television viewing was significantly associated with refractive error (χ^2 = 4.660, p = 0.015). Among affected children, 85 (66.93%) reported watching television. Television viewing duration was also significantly associated with refractive error (χ^2 = 4.177, p = 0.021) (Table 3).

Table 3. Association of Behavioral and Environmental Factors with Refractive Error Among School-Going Children in Peshawar (n = 400)

Variable	Category	Refractive error, n (%)	No refractive error, n (%)	Total, n (%)	χ^2	p-value
Parental positive family history	Yes	48 (37.80)	51 (18.68)	99 (24.75)	5.213	0.011
	No	79 (62.20)	222 (81.32)	301 (75.25)		
Outdoor activities	Yes	54 (42.52)	194 (71.06)	248 (62.00)	5.862	0.008
	No	73 (57.48)	79 (28.94)	152 (38.00)		
Duration of outdoor activities	<1 hour/day	52 (40.94)	103 (37.73)	155 (38.75)	5.723	0.008
	>1 hour/day	22 (17.32)	71 (26.01)	93 (23.25)		
Computer use	Yes	37 (29.13)	75 (27.47)	112 (28.00)	0.051	0.411
	No	90 (70.87)	198 (72.53)	288 (72.00)		
Computer use duration	<2 hours/day	21 (16.54)	51 (18.68)	72 (18.00)	0.918	0.169
	>2 hours/day	16 (12.60)	24 (8.79)	40 (10.00)		
Video-game use	Yes	54 (42.52)	127 (46.52)	181 (45.25)	0.410	0.261
	No	73 (57.48)	146 (53.48)	219 (54.75)		
Video-game duration	<2 hours/day	17 (13.39)	68 (24.91)	85 (21.25)	6.545	0.005
	>2 hours/day	37 (29.13)	59 (21.61)	96 (24.00)		
Reading books	Yes	93 (73.23)	210 (76.92)	303 (75.75)	0.459	0.249
	No	34 (26.77)	63 (23.08)	97 (24.25)		
Reading duration	<2 hours/day	61 (48.03)	128 (46.89)	189 (47.25)	0.410	0.261
	>2 hours/day	32 (25.20)	82 (30.04)	114 (28.50)		
Television viewing	Yes	85 (66.93)	108 (39.56)	193 (48.25)	4.660	0.015
	No	42 (33.07)	165 (60.44)	207 (51.75)		
Television viewing duration	<2 hours/day	53 (41.73)	51 (18.68)	104 (26.00)	4.177	0.021
	>2 hours/day	31 (24.41)	57 (20.88)	88 (22.00)		

Values are presented as frequency (percentage). χ^2, cChi-square test statistic. A p-value <0.05 was considered statistically significant.

Discussion

This study assessed the prevalence and pattern of refractive error and its association with selected demographic, socioeconomic, familial, and behavioral determinants among school-going children in Peshawar. Of all the children, 31.75% (127/400) had refractive error. In children with refractive errors, hyperopia was the least frequent (18.11%), followed by astigmatism.
(37.01%) and myopia (44.88%). The results suggest a significant problem with refractive errors in school-going children and highlight the need for early detection and proper eye assessment.The prevalence found in the present study was greater than reported by Alem and Gebru in elementary school children in Ethiopia [11]. Gurung and Gupta, however, found a prevalence of 34.9% in children attending a tertiary eye-care center, similar to our results [14]. The prevalence was also reported to be lower (17.43%) for school-going children by Srivastava et al. [24]. These differences may reflect differences in study populations and age groups, geographical settings, sampling methods, and detection methods for refractive error. In the present study, myopia was the highest percentage of refractive error, with 44.88% of children affected, followed by astigmatism and hyperopia. Several studies have reported significant differences in the distribution of children by type of refractive error. Gurung and Gupta [14] reported a significant burden of refractive error among children visiting an eye-care center in a tertiary care center, and Hassan et al. [22] reported a varying pattern of refractive errors among school-going children in Kashmir. These disparities may reflect differences in demographic characteristics, educational setting, near-work activity, outdoor exposure, and other population-specific factors.In the present study, sex was significantly associated with refractive error (p=0.002), with girls making up 55.91% of children with refractive error. Similarly, Sharma et al. found a significant association between sex and refractive error in school children [15]. However, other papers have not found any significant relationship between sex and refractive error [8]. These differences suggest that the sex-refractive error association may vary across populations and should be considered in light of a population's demographic and behavioral factors. In the present study, Age was not significantly associated with refractive error (p=0.152). Most children with refractive error were under 8 years, but age groups did not differ significantly in distribution. Ahmad et al. reached the same conclusion, finding no significant relationship between age and refractive error [8]. Refractive error was also not significantly related to class grade (p=0.119), similar to previous school-based studies [8,11]. Educational attainment was strongly associated with refractive error among parents. In the present study, father's education (p=0.008) and mother's education (p=0.007) were significantly associated with refractive error. Previous reports also show correlations between parental education level and child refractive error [11]. Parental education level can affect awareness of eye health, diagnosis of visual problems, seeking care, and children's educational and environmental exposure.The father's employment status was significantly associated with refractive error (p=0.006), but the mother's was not (p=0.283). Household monthly income was also significantly related to refractive error (p=0.013). This suggests that socioeconomic factors may affect children's eye health. Other studies have also investigated socioeconomic factors as potential risk factors for refractive error [7,15,17]. However, these associations should not be interpreted as causal because this is a cross-sectional study.Refractive error was significantly related to school type (p=0.010). Sixty-six. 93% of children with refractive error attended public schools, and 33.07% attended private schools. Previous studies have reported similar differences by school setting [11,12]. Differences in educational background, socio-economic status, access to eye-care services, and awareness may explain differences between school populations.In the present study, a positive family history of refractive error among parents was significantly associated with refractive error (p=0.011). This is similar to previous findings that family may play a role in the development of refractive abnormalities in children [23]. The current results, however, suggest not only a genetic link but also a shared environment and/or behavior among family members.Refractive error was significantly associated with outdoor activity (p=0.008). More children with refractive error reported not doing outdoor activities. Previous research has explored the link between outdoor exposure and childhood refractive error, and has linked lower levels of outdoor activity to myopia in certain populations [19,25,26]. The results from the present study thus reinforce the need to explore

children's outdoor behavior as a relevant factor.Computer use itself was not significantly associated with RE (p=0.411), and duration of computer use was not statistically significant (p=0.169). Likewise, video game use was not significantly correlated with refractive error (p=0.261). In contrast, we found a significant association between the duration of video game use and scores (p=0.005). Previous studies have reported links between prolonged exposure to digital screens and refractive abnormalities, especially myopia and astigmatism [23,25,26]. The results suggest that the amount of time spent on screens may matter more than screen time itself. Television viewing was significantly associated with refractive error (p=0.015), and television-viewing duration (p=0.021). This is supported by previous research exploring long-term screen time and refractive abnormalities in childhood [23,25,26]. Nevertheless, screen-related behaviors may be correlated with other factors, including reduced outdoor activity and increased sedentary or near-work behavior. Therefore, interpret these associations cautiously. Reading books was not significantly associated with refractive error (p=0.249), and reading duration was also not statistically significant (p=0.261). This finding is broadly consistent with research indicating that the relationship between near-work activities and refractive error may depend on the type, duration, and intensity of the activity rather than reading alone [19]. Overall, the findings show a substantial prevalence of refractive error among school-going children in Peshawar, with myopia as the most common refractive-error pattern. Several demographic, socioeconomic, familial, and behavioral variables showed statistically significant associations. These findings support the importance of school-based vision screening, early ophthalmic assessment, parental awareness, and appropriate referral services for children with suspected visual impairment.

Ethical Approval

The Institutional Ethics Committee of MTI Lady Reading Hospital, Peshawar, Pakistan, approved this study (Approval No. 278/LRH/MTI/2024) before it began. We conducted the study in accordance with the ethical principles of the Declaration of Helsinki.

Informed Consent: We obtained written informed consent from participants before enrollment. We informed participants and their parents/guardians about the study's purpose and procedures, and participation was voluntary.

Funding: This study received no external funding.

Conflict of Interest: The authors declare that they have no competing interests or conflicts of interest related to this study.

Authors' Contributions

Natasha Junaid: Conceptualization, study design, data collection, interpretation of findings, manuscript drafting, critical revision of the manuscript, final approval of the version to be published, and accountability for all aspects of the work.

Syed Noor: Study design, data collection, data curation, literature review, interpretation of data, manuscript revision, final approval of the version to be published, and accountability for all aspects of the work.

Irfan Ullah Shah : Conceptualization, study supervision, clinical assessment, interpretation of findings, critical revision of the manuscript for important intellectual content, final approval of the version to be published, and accountability for all aspects of the work.

Muhammad Junaid Sethi: Data collection, clinical assessment, data curation, literature review, manuscript revision, final approval of the version to be published, and accountability for all aspects of the work.

Muhammad Ishtiaq: Data analysis, data interpretation, manuscript drafting and revision, critical review of the manuscript for important intellectual content, final approval of the version to be published, and accountability for all aspects of the work.

Sadaf Bilal: Data collection, literature review, data curation, manuscript revision, final approval of the version to be published, and accountability for all aspects of the work.

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Original Article

Exploring The Reasons Behind Delay in Detection of Cervical Cancer in Pakistani Population

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Abstract

Objective: To explore the factors contributing to delayed detection and treatment of cervical cancer among Pakistani women presenting with advanced disease.

Methodology: This exploratory study was conducted in the Department of Obstetrics and Gynecology, Ayub Teaching Hospital, Abbottabad, Pakistan, from January to June 2025. We conducted semi-structured, in-depth interviews with 15 patients; each interview took about 30-45 minutes. Interviews included participants' knowledge of cervical cancer, the presentation of symptoms, health-seeking behavior, experiences of diagnosis, treatment, and family reactions, and financial constraints. We used Braun and Clarke's thematic analysis approach.

Results: 15 women aged 35–55 years, with a Mean age of 46.0 ± SD years, with advanced cervical cancer were recruited. Themes that emerged from the analysis included knowledge about cervical cancer, personal behavior, sociocultural attitudes and beliefs, financial barriers, and health-system-related factors. Financial barriers included the cost of diagnostic testing, transportation, and loss of income. Health system factors included a lack of screening services, delayed referrals, poor patient-provider communication, poor follow-up, facility overcrowding, and a lack of specialist services.

Conclusion: Delayed cervical cancer detection resulted from interconnected patient, sociocultural, financial, and health-system barriers. Strengthening screening services, improving community awareness, ensuring timely referral, reducing financial barriers, and empowering women may facilitate earlier detection and treatment.

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Introduction

Cervical cancer remains an important public health problem despite being one of the cancers for which effective primary and secondary prevention strategies are available. Persistent infection with high-risk human papillomavirus (HPV) is the principal cause of cervical cancer, while HPV vaccination, screening, and timely treatment of precancerous lesions provide opportunities to prevent invasive disease. Global estimates indicate that the greatest burden of cervical cancer continues to occur in low- and middle-income countries, where limitations in prevention, screening, diagnosis, and treatment contribute to avoidable morbidity and mortality [1].The World Health Organization (WHO) has set global targets to eliminate cervical cancer, stating that HPV vaccination, high-performance screening, and adequate treatment of women whose cancer screen came back positive or who have cervical precancer should be prioritized. The WHO strategy clearly acknowledges that screening is not enough unless women can be supported along the whole continuum of care, from receiving the results to being referred, assessed through diagnostics, and treated. [2] Pakistan, in particular, faces challenges in achieving these objectives. Data from Pakistani populations has shown significant lack of awareness of cervical cancer, HPV infection, cervical screening and HPV vaccination. In the tertiary-care study, only 41.2% of women knew about cervical cancer, 33.6% knew about cervical screening, and only 15.9% indicated previous cervical screening. Awareness of HPV vaccination was particularly low [3]. Likewise, more recent Pakistani data show significant gaps in knowledge about the prevention and screening of cervical cancer and reveal that information, poverty, and poor access to health care are significant barriers[4]. Delayed diagnosis is a multi-factorial process. It can start with poor recognition of symptoms, include delays in deciding to seek medical attention, and lead to difficulties in obtaining the correct investigations, referral, specialist assessment, and treatment. A systematic review identified the patient, medical-history-related, and health-system-related components of diagnostic delay in cervical cancer. Reported factors included lack of knowledge, socio-economic conditions, partners' factors, access to health facilities, and health facility constraints[5]. Low- and middle-income countries also face multiple screening barriers. A systematic review identified individual, cultural, religious, societal, health system, and structural barriers, with the most common individual barrier being lack of knowledge and awareness. Other factors that may influence screening behavior include cost, geographical access, inadequate health infrastructure, partner/family support, and sociocultural beliefs[6]. Restricted financial resources are likely relevant, as they can affect women's willingness to follow through with the diagnostic process and/or later treatment[7]. Women's perceptions of gynecological symptoms and screening may also be influenced by factors related to the socio-cultural context. Fear and embarrassment, anticipated stigma, perceived susceptibility, and concerns about pelvic examinations are barriers to cervical screening in various populations. These could be especially important where the social sensitivity of reproductive health and STI conversations persists [8]. Another essential factor is health-system capacity. Screening programs in low- and middle-income areas may be fragmented, inaccessible, under-resourced, or poorly connected to diagnosis and treatment services. Therefore, strengthening health systems and embedding screening within existing health services are key elements of equitable cervical cancer prevention [9]. While quantitative research has documented low uptake of screening and poor awareness among Pakistani women, less research has examined the experiences of women with advanced cervical cancer. This study may provide information that structured questionnaires cannot fully capture by exploring how women understand symptoms, make decisions about seeking care, interact with health care services, and navigate the financial and social barriers they may encounter. The novelty of the present study lies in its qualitative exploration of the diagnostic journey among Pakistani women who had already presented with advanced cervical cancer, allowing patient-level experiences to be examined across individual, sociocultural, financial, and health-system domains**.** By identifying interconnected barriers from the women's perspectives, this study aims to provide context-specific evidence that may inform strategies for earlier recognition, referral, diagnosis, and treatment of cervical cancer in Pakistan.

Materials & methods

Study Design and Setting

This exploratory qualitative study was conducted in the Department of Obstetrics and Gynecology, Ayub Teaching Hospital, Abbottabad, Pakistan, from January to June 2025. The study aimed to investigate women's experiences and perceptions of the factors that delay the detection and treatment of cervical cancer.

Participants

Fifteen women with advanced cervical cancer were recruited for participation. Participants ranged in age from 35 to 55 years, with a reported mean age of 46.0 ± SD years. The study focused specifically on women presenting with advanced disease, as their experiences may be useful in understanding barriers to diagnosis and treatment prior to diagnosis.

Data Collection

We used semi-structured, in-depth interviews to collect data. All interviews were about 30-45 minutes. The interview guide covered topics such as knowledge about cervical cancer, symptom awareness and understanding, prior health-seeking, healthcare provider experiences, diagnostic processes, referrals, treatment experiences, family reactions, and financial problems. The semi-structured format enabled participants to describe their experiences in their own words while ensuring that each interview covered the main points related to delayed detection.

Qualitative Data Analysis

Thematic analysis was used to analyze the interview data using Braun and Clarke's approach. The analysis process included familiarizing myself with the interview content, identifying initial codes, developing candidate themes, reviewing and refining themes, defining and naming themes, and synthesizing the final findings. Thematic analysis was chosen because it allows identification and interpretation of themes and patterns within qualitative data while maintaining participants' contextual experiences. Current advice focuses on the need for transparent and reflexive 'thematic' analysis, rather than on qualitative coding as a purely mechanical process.

Results

Participant Characteristics

Fifteen women with advanced cervical cancer participated in the study. Participants ranged in age from 35 to 55 years (mean age 46.0 years). The qualitative interviews were not limited to one aspect of diagnostic delay and explored several aspects of the diagnostic journey.

Table 1. Participant characteristics

Characteristic	Finding
Number of participants	15
Sex	Female
Age range	35–55 years
Mean age	46.0 years
Clinical condition	Advanced cervical cancer
Interview duration	Approximately 30–45 minutes
Study period	January–June 2025
Study setting	Ayub Teaching Hospital, Abbottabad, Pakistan

Data are presented as reported in the study protocol/abstract. No additional participant-level characteristics were available; therefore, none were inferred.

Emergent Themes

The interviews revealed 5 major themes: lack of knowledge and symptom recognition, individual health-seeking behavior, sociocultural attitudes and beliefs, financial barriers, and health-system barriers.

Table 2. Major themes and subthemes identified from the interviews

Major theme	Subthemes identified
Knowledge and symptom recognition	Limited knowledge of cervical cancer; inadequate awareness of warning symptoms; delayed recognition of potentially concerning symptoms
Personal health-seeking behavior	Delayed decision to seek care; initial management outside specialist services; postponement of diagnostic evaluation
Sociocultural attitudes and beliefs	Family reactions; social perceptions; embarrassment or reluctance regarding gynecological symptoms; influence of family on healthcare decisions
Financial barriers	Cost of diagnostic investigations; transportation expenses; treatment-related financial concerns; loss of income
Health-system barriers	Limited screening services; delayed referral; inadequate patient-provider communication; poor follow-up; overcrowding; limited specialist services

Themes were derived from the qualitative interviews. The table summarizes the domains reported in the study and does not assign numerical frequencies to individual themes.

Knowledge and Personal Health-Seeking Behavior

Participants identified lack of knowledge about cervical cancer and lack of awareness of symptoms as important factors in the delay of diagnosis. Symptoms might not have been recognized as threatening, so medical advice might have been delayed, or the patient might have gone through several steps before reaching a specialist assessment.

Sociocultural Factors

Participants also described the sociocultural factors that shape their health care experiences. Family reactions and societal attitudes influenced perceptions of symptoms and treatment. Embarrassment and/or the reluctance to talk about reproductive health concerns can cause a delay in seeking advice from the gynae. The results align with other evidence that fear, embarrassment, stigma, low perceived risk, and lack of support from family and/or partner can lead to poor uptake for cervical screening.

Financial Barriers

Money issues were consistently mentioned as a major contributor to failed care. Participants reported difficulties with the cost of diagnostic investigations, transportation, and income loss due to attending health service facilities. Financial restrictions may affect uptake of screening and diagnostic follow-up. Past studies have shown that screening cost, expected treatment cost, transportation, and income loss can be barriers to women following recommended screening pathways.
Health-System Barriers

Barriers identified within the health system included inadequate availability of screening services, delayed referrals, poor patient-provider communication, lack of follow-up, overcrowding of health care facilities, and limited access to specialist services.

These barriers are significant as the whole continuum of screening, diagnosis, referral, and treatment is crucial to cervical cancer prevention. The WHO guidance states that women who test positive should receive timely, appropriate treatment, diagnostic assessment, and referral to, and communication with, a health worker.

Table 3. Multilevel factors contributing to delayed cervical cancer detection

Level	Identified barriers	Potential point of intervention
Individual	Limited knowledge, poor symptom recognition, delayed healthcare seeking	Community education and symptom-awareness campaigns
Sociocultural	Embarrassment, family influence, social attitudes and beliefs	Family-inclusive education and culturally appropriate counseling
Financial	Diagnostic costs, transportation expenses, loss of income	Subsidized screening/diagnosis and financial assistance
Healthcare access	Limited screening availability, specialist access	Expansion of screening and referral services
Health system	Delayed referrals, poor follow-up, overcrowding	Standardized referral pathways and patient tracking
Provider-patient interaction	Inadequate communication	Communication training and clear counseling
Continuity of care	Loss to follow-up and fragmented services	Integrated screening-to-treatment pathways

The table synthesizes the qualitative domains identified in the interviews. Intervention points are presented as implications of the identified barriers rather than measured outcomes of the present study.

Discussion

The present qualitative study demonstrates that delayed detection of cervical cancer among Pakistani women with advanced disease is a multidimensional phenomenon. Five interconnected domains emerged from the interviews: Lack of knowledge, lack of symptom recognition, health-seeking behavior, socio-cultural factors, financial factors, and health-system factors. These factors do not work in isolation; instead, they seem to influence one another throughout the diagnostic process[10]. Limited knowledge was an important component of the participants' experiences. This is in line with Pakistan's studies, which indicated a significant gap in awareness of cervical cancer, screening, HPV infection, and HPV vaccination. A tertiary-care study in Pakistan reported a low awareness rate among women about cervical cancer (41.2%) and even lower awareness of screening and HPV vaccination for cervical cancer[11,12]. A more recent Pakistani study also revealed significant gaps in knowledge about cervical cancer and that lack of information was a factor in cervical cancer screening. It also indicates that awareness should not be limited to the mere recognition of the name of cervical cancer but, in addition, awareness of the warning signs, awareness of the HPV infection, awareness of the available tests, and awareness that the tests are useful even if there are no symptoms.International evidence also points towards the significance of knowledge. Inadequate knowledge and awareness were one of the most cited individual-level barriers in a systematic review of cervical screening barriers in low- and middle-income countries. The following factors were also associated with lower screening uptake: cultural and religious beliefs, lack of support from family members, geographic accessibility, cost, and issues with health-system infrastructure[14]. Likewise, a systematic review examining access from an accessibility perspective identified interconnected determinants,

including awareness, affordability, availability, acceptability, and geographical accessibility. The present findings also highlight the importance of health-seeking behavior. Failure to understand the significance of symptoms may delay patient care and access to appropriate diagnostic services. The notion of delayed diagnosis of cervical cancer has been investigated using a systematic review, which identified three dimensions: patient-related, medical-history-related, and health-system-related, thus showing that there is seldom a single cause for delayed diagnosis[16]. The present qualitative results support this multidimensional model in the context of Pakistani women who are diagnosed as having advanced disease. Another important domain was the sociocultural factors. Participants reported family reactions and societal attitudes as experiences. Discussions of cervical cancer and gynecologic symptoms might be challenging due to embarrassment, stigma, or fear of social judgment. Qualitative studies in diverse groups have also shown fear, embarrassment, shame, low perceived risk, and lack of family support are barriers to screening [17]. This might be especially relevant in societies where reproductive health choices are shaped by family formation and where talking about reproductive health is socially taboo. Financial obstacles were another significant finding. The costs of diagnostic investigations and transportation, combined with lost income, may prevent women from seeking timely health care and/or referrals. Financial constraints include not only the cost of the screening procedure but also women's expectations of costs for confirmatory investigations and treatment after screening. Two studies of underscreened, low-income women revealed perceived screening costs and anticipated future treatment costs as barriers[18]. Reducing direct and indirect costs can be a significant aspect of early diagnosis, especially within the context of Pakistan's varying socioeconomic conditions and geographic location for healthcare access. The barriers identified in the health system included limited screening availability, delayed referral, poor communication, lack of follow-up, overcrowding, and limited specialist services. This is congruent with evidence that fragile healthcare systems and inequitable access can hinder cervical cancer elimination in LMICs[19]. Strengthening of health systems should go beyond identifying screening services. The screening process needs to be linked with effective referral, diagnosis, treatment, and follow-up services.WHO cervical cancer elimination strategy highlights the importance of the full cervical cancer continuum of care. Screening programs should deliver results to women promptly, and deliver further evaluation and/or treatment services without undue delay if needed[20]. Integrating screening into ongoing healthcare services could increase access and continuity, especially in low-resource areas. A recent scoping review also highlighted the need to incorporate cervical cancer screening into existing health care systems in low- and middle-income countries [21]. The findings have various practical ramifications for Pakistan. Awareness interventions should be tailored to local knowledge gaps and not general cancer messages. Second, screening should be more readily available and accessible via integration with reproductive health and primary care. Third, referral systems need to be regularized so that women with abnormal screening and/or women with particular symptoms are promptly referred to the appropriate diagnostic services[22]. Fourth, patient surveillance and follow-up systems could minimize loss to follow-up. Finally, cervical cancer prevention programs should account for financial and geographic factors. Evidence from low- and middle-income countries shows multiple points within the cancer care pathway that can be targeted to improve timely cancer diagnosis, including community awareness, primary care recognition, referral, and access to diagnosis. It is important to consider prevention strategies specific to health system capacity and sociocultural context rather than simply importing programs created in high-income countries.This study should be interpreted in light of its qualitative design. The sample consisted of 15 women from a single tertiary-care setting, and participants were specifically women with advanced cervical cancer. Consequently, the findings are intended to provide an in-depth understanding of perceived barriers rather than estimates of their prevalence in the Pakistani population. The findings should not be generalized to all Pakistani women without consideration of differences in geography, socioeconomic circumstances, healthcare access, and cultural context. Nevertheless, the convergence of the themes with findings from previous Pakistani and international studies strengthens the relevance of the identified domains. This study has some disadvantages. Firstly, the sample size was very small (n = 15). Second, the study participants were recruited from a single tertiary care hospital and had advanced cervical cancer; thus, their experiences might differ from those of women with early-stage cancer or women who never received specialist care [23]. Third, the qualitative results reflect participants' reported experiences and perceptions and may be subject to recall or social-desirability bias. Third, the study was carried out in Abbottabad, so the results may not fully represent women in other parts of Pakistan with varying socio-economic, cultural, and healthcare environments.

Conclusion

Delayed detection of cervical cancer among Pakistani women appears to arise from interconnected individual, sociocultural, financial, and health-system barriers. Improving community awareness, expanding accessible screening, strengthening referral and follow-up systems, improving patient-provider communication, and reducing financial barriers may facilitate earlier diagnosis and treatment.

Ethical Approval

Ethical approval was obtained from the Ayub Medical Teaching Institution Abbottabad Institutional Medical & Ethics Review Committee **(Approval Code/Ref. No.** RC-FA-2024/171**; Date of Approval:** 12 Sep 2024**).**

Informed Consent

We obtained written informed consent from all participants before they participated in the interviews. Participants were informed about the study's purpose, the voluntary nature of participation, confidentiality, and their right to withdraw without affecting their medical care.

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Conflict of Interest

The authors declare that they have no competing interests or conflicts of interest related to this study.

Authors' Contributions

Bushra Khan: Conceptualization, study design, participant recruitment, data collection, data analysis, manuscript drafting, and critical revision.

Shehla Noor: Conceptualization, supervision, interpretation of findings, critical revision of the manuscript, and final approval of the version to be published.

Laraib Istafa: Literature review, participant interviews, data organization, thematic analysis, and manuscript revision.

Afia Kausar: Literature review, data organization, manuscript drafting and revision, and reference verification.

Data Availability

The qualitative data generated during this study are not publicly available because the interview material contains potentially identifiable participant information. Relevant information may be made available by the corresponding author upon reasonable request, subject to ethical and confidentiality requirements.

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Original Article

Outcomes After Lumbar Micro discectomy for Lumbar Disc Herniation: A Single-Center Experience

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Abstract

Objective: To evaluate functional outcomes after lumbar micro discectomy and identify factors associated with better recovery.

Methodology: This retrospective study was conducted in the Department of Neurosurgery, Mardan, from January to June 2025. We included 100 patients with medical records who underwent lumbar micro discectomy for symptomatic lumbar disc herniation from January 2023 to December 2024. We retrieved demographic, clinical, radiological, and operative information from the medical records. We assessed functional outcome using the Oswestry Disability Index (ODI) and the Visual Analog Scale (VAS) preoperatively and at 6 months after surgery.

Results: 62 males and 38 females with a mean age of 44.8 ± 11.2 years. The L4–L5 level was the most frequently affected (54%), followed by L5–S1 (36%). Mean ODI significantly improved from 56.4 ± 12.7 preoperatively to 18.9 ± 9.3 postoperatively ($p < 0.001$), while mean VAS scores decreased from 8.2 ± 1.1 to 2.1 ± 1.3 ($p < 0.001$). 87% of patients achieved good-to-excellent functional recovery. Younger age (<50 years) ($p = 0.028$) and symptom duration <6 months ($p = 0.015$) were significantly associated with better outcomes. The overall complication rate was 6%, with no procedure-related mortality.

Conclusion: Lumbar micro discectomy is an effective and safe procedure with high pain relief and functional improvement for patients with lumbar disc herniation. Postoperative recovery was better in those who underwent early surgery and were younger.

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Introduction

Lumbar disc herniation (LDH) is one of the most prevalent spinal afflictions in adults and is a significant contributor to low back pain and sciatica in the world. It is mainly caused by disc degeneration with a nucleus pulpous protruding or extruding through the annulus fibrosus. The displaced disc material can press on neighboring nerve roots, creating pain in the radiating leg, sensory disturbances, motor weakness, and functional disability. It is a condition that mainly occurs in the third to fifth decades of life and has an important socio-economic dimension, due to loss of productivity, health costs, and lower quality of life [1,2]. It is estimated that 1–3% of the general adult population has symptomatic lumbar disc herniation and that L4–L5 and L5–S1 are the most commonly affected spinal levels due to the greater biomechanical stress. While about 10-20% of patients will improve with conservative measures such as analgesics, physical therapy, activity modification, and epidural steroid injections, others will still have persistent radicular pain or progressive neurologic deficits that require surgical treatment [3]. Lumbar Micro discectomy has emerged as the "gold standard" surgical approach for symptomatic, conservative-refractory lumbar disc herniation. Micro discectomy is now widely used in place of the traditional open discectomy due to the exceptional visualization and the low soft tissue damage that it causes. Using an operating microscope and microsurgical technique, surgeons can remove herniated disc fragments through a shorter incision and with limited muscle dissection for accurate removal. As a result, patients have less pain after surgery, a shorter hospital stay, earlier mobilization, and a quicker return to normal activities [4,5]. Several studies have shown that lumbar micro discectomy provides rapid relief of radicular pain and significant improvement in neurological function. Postoperative recovery is often assessed using patient-reported outcome measures, including the Visual Analog Scale (VAS) for pain and the Oswestry Disability Index (ODI). Most patients improve in pain and disability in the first few months after surgery. The extent of functional recovery, however, depends on patient characteristics, length of symptoms, age, body mass index, smoking, work demands, psychological factors, and preoperative neurologic impairment [6,7]. While the recovery rate of a lumbar micro discectomy is over 80% for the right patient, some complications can hinder recovery, including recurrent herniation, dural tear, wound infection, nerve root injury, epidural fibrosis, and chronic pain. Thus, proper patient selection, precise surgical procedures, and rehabilitation are key to achieving optimal function and minimizing complications [8]. Although lumbar micro discectomy has been studied worldwide, outcome data from a single center in developing countries remain relatively limited. Variations in healthcare facilities, patient age, and access to surgical intervention and rehabilitation may affect postoperative recovery. Thus, it is important to assess institutional outcomes to benchmark surgical performance and improve clinical practice [9]. This retrospective study evaluated the functional outcomes of lumbar micro discectomy in patients with symptomatic lumbar disc herniation treated at a tertiary care hospital. We assessed functional improvement with validated clinical outcome scales and analyzed demographic and clinical variables related to post-operative recovery. This study is expected to provide valuable knowledge about the efficacy and safety of lumbar micro discectomy in clinical practice and help optimize patient selection and postoperative care [10].

Materials and Methods

Study Design and Setting

This retrospective study was conducted in the Department of Neurosurgery, Mardan, from January to June 2025

Participants

One hundred consecutive symptomatic patients with single-level lumbar disc herniation who failed at least 6 weeks of conservative care were included in the study after they underwent lumbar micro discectomy. We collected data from hospital medical records and outpatient clinic documentation, including demographic characteristics, clinical findings, radiological imaging, operative records, and follow-up data.

Sample Size Calculation

The sample size of 100 patients was calculated using the WHO sample size calculator with an expected improvement in functional status after surgery of 85% with a 95% confidence level, 7% margin of error, and allowing for the possibility that clinical records might not be complete for the endpoint analysis to be sufficiently powered.

Inclusion Criteria

- Adults aged 18–75 years.
- One-level, MRI-proven lumbar disc herniation.
- Persistent symptoms of radiculopathy following at least 6 weeks of conservative treatment.
- Patients who are getting a lumbar micro discectomy for the first time. At least 6 months of follow-up.

Exclusion Criteria

- A history of surgery in the lower back.
- Multilevel Lumbosacral disc herniation.
- Spinal instability in the lower spine or spondylolisthesis that can be corrected with fusion.
- Tumors, infections, or spinal injuries.
- Partial medical records or loss to follow-up.

Diagnostic and Management Strategy

Clinical examination and magnetic resonance imaging confirmed the diagnosis. We initially treated all patients conservatively, followed by early mobilization, early analgesia, physiotherapy, and regular follow-up. All patients received conservative treatment and then underwent a standardized LMD under general anesthesia with microscopic magnification, followed by early analgesia, early mobilization, and regular follow-up.

Statistical Analysis

SPSS version 27 was used to analyze the data. Continuous variables were reported as mean (SD), and categorical variables as frequencies and percentages. Where appropriate, we used paired t-tests and chi-square tests. We considered $p < 0.05$ (two-tailed) statistically significant.

Results

A total of 100 patients underwent lumbar micro discectomy during the study period. The cohort included 62 (62%) males and 38 (38%) females, with a mean age of 44.8 ± 11.2 years. Most patients were in the 31–50-year age group. The L4–L5 intervertebral level was involved in 54% of patients, followed by L5–S1 in 36%, while 10% had herniation at L3–L4. The mean preoperative VAS pain score was 8.2 ± 1.1, which significantly improved to 2.1 ± 1.3 at six months after surgery ($p<0.001$). Likewise, the mean Oswestry Disability Index improved from 56.4 ± 12.7 preoperatively to 18.9 ± 9.3 postoperatively ($p<0.001$). Eighty-seven patients achieved excellent or good functional recovery, whereas thirteen demonstrated fair or poor outcomes. Patients younger than 50 years showed significantly greater improvement in functional status than older patients ($p=0.028$). Patients with symptom duration under six months had better recovery than those with longer symptom duration ($p=0.015$). Gender was not significantly associated with postoperative outcomes ($p=0.482$). Postoperative complications occurred in six patients, including superficial wound infection (3%), incidental dural tear (2%), and recurrent lumbar disc herniation requiring revision surgery (1%). No mortality or permanent neurological deterioration was observed.

Table 1. Baseline Demographic and Clinical Characteristics of the Study Population (n = 100)

Variable	Category	n (%)
Age (years)	Mean ± SD	44.8 ± 11.2
	18–30	15 (15.0)
	31–40	28 (28.0)
	41–50	31 (31.0)
	51–60	18 (18.0)
	>60	8 (8.0)

Sex	Male	62 (62.0)
	Female	38 (38.0)
Body Mass Index (kg/m²)	Mean ± SD	27.1 ± 3.8
Duration of Symptoms	<6 months	67 (67.0)
	≥6 months	33 (33.0)
Affected Disc Level	L3–L4	10 (10.0)
	L4–L5	54 (54.0)
	L5–S1	36 (36.0)
Presenting Symptom	Radicular pain	100 (100.0)
	Sensory deficit	46 (46.0)
	Motor weakness	24 (24.0)

Values are presented as frequency (n), percentage (%), or mean ± standard deviation (SD).

Table 2. Comparison of Preoperative and Postoperative Functional Outcomes

Outcome Measure	Preoperative (Mean ± SD)	Postoperative (Mean ± SD)	Mean Difference	p-value
VAS Pain Score	8.2 ± 1.1	2.1 ± 1.3	6.1	<0.001
ODI Score	56.4 ± 12.7	18.9 ± 9.3	37.5	<0.001

We assessed functional outcomes using the Visual Analog Scale (VAS) and Oswestry Disability Index (ODI). We set statistical significance at $p<0.05$.

Table 3. Factors Associated with Good Functional Recovery After Lumbar Micro discectomy

Variable	Good Outcome n (%)	Fair/Poor Outcome n (%)	p-value
Age <50 years (n=74)	68 (91.9)	6 (8.1)	0.028
Age ≥50 years (n=26)	19 (73.1)	7 (26.9)	
Symptom duration <6 months (n=67)	62 (92.5)	5 (7.5)	0.015
Symptom duration ≥6 months (n=33)	25 (75.8)	8 (24.2)	
Male (n=62)	55 (88.7)	7 (11.3)	0.482
Female (n=38)	32 (84.2)	6 (15.8)	

We defined good functional recovery as an excellent or good postoperative outcome based on clinical assessment and ODI improvement.

Table 4. Postoperative Complications Following Lumbar Microdiscectomy

Complication	n	%
No complications	94	94.0
Superficial wound infection	3	3.0
Incidental dural tear	2	2.0
Recurrent disc herniation	1	1.0
Permanent neurological deficit	0	0.0
Mortality	0	0.0
Total	100	100.0

Overall postoperative complication rate was 6%. Most cases were managed successfully without permanent neurological deficits.

Discussion

We performed a single-center, retrospective analysis of the functional outcome of Lumbar micro discectomy in 100 patients with symptomatic lumbar disc herniation. The results showed a substantial reduction in pain intensity and functional disability, and 87% of patients had a good-to-excellent postoperative outcome. In addition, patient age was inversely correlated with good functional recovery, while sex was not. Symptom duration was also significantly correlated with surgical outcome. The results confirm the efficacy and safety of lumbar micro discectomy for the right candidates [11,12]. The demographic data in our study were similar to those recently reported in the literature. The mean age of 44.8 ± 11.2 years and the fact that most patients were male (62%) were similar to conclusions from studies in the last five years, which reported a mean age of 45 to 46 years among patients with lumbar disc herniation. Most patients were male [13,14]. As in previous studies, the L4–L5 level was the most frequently affected disc level, compared with L5–S1, which is most subjected to biomechanical stress [15]. Perhaps the most important result was the large reduction in postoperative pain and disability scores. After 6 months of follow-up, the mean VAS score dropped from 8.2 to 2.1, and the mean Oswestry Disability Index (ODI) decreased from 56.4 to 18.9. These enhancements are consistent with recent prospective and retrospective studies, which have shown significant pain and disability improvement after lumbar micro discectomy. This is consistent with large multicenter studies showing that over 80% of Patients have clinically significant Improvements in pain and function at 1 year after surgery [16,17]. Our series success rate was 87%, similar to rates reported in recent studies after lumbar micro discectomy [16–18]. These consistently high success rates reflect ongoing improvements in microsurgical techniques, patient selection, and perioperative care, as well as the development of follow able rehabilitation protocols. Our study found a relatively low complication rate (6%), consistent with recent systematic reviews that report complication rates below 10%, with superficial wound infections, incidental dural tears, and recurrent disc herniation as the most common adverse events [18,19]. One key finding was significantly greater functional recovery in younger patients than in older patients. Recent studies corroborate this, showing that younger patients have less degenerative spinal change, greater potential for postoperative rehabilitation, and greater regenerative capacity. Similarly, patients with symptoms for less than 6 months had better outcomes after surgery than those with more than 6 months of symptoms. If there is a delay in surgical treatment, chronic compression of the nerve root and permanent nerve injury may develop, leaving a poor chance of full recovery of function. Recent cohort studies have also found similar results, focusing on the advantages of early surgical intervention after failure of conservative treatment [20-21]. In this study, patient gender was not significantly correlated with postoperative recovery. This result is consistent with a few recent studies showing that patients of both sexes benefit similarly from lumbar micro discectomy when performed based on accepted surgical indications [22]. These observations suggest that demographic factors should not influence surgical management decisions. This study has a few limitations. Because of the retrospective design and single-center setting, selection bias and incomplete documentation may be present. The study included a small number of patients, and it evaluated functional outcomes only at 6 months after surgery. Furthermore, the study did not assess other factors that could affect long-term outcomes, such as smoking status, occupation requirements, psychological status, and body mass index. These results need confirmation with longer follow-up and larger sample sizes in multicenter prospective studies to identify additional predictors of postoperative success [23]. Overall, the present study shows that lumbar micro discectomy is an excellent pain-relief procedure that significantly improves functional parameters and has a low complication rate in patients with lumbar disc herniation. The results align with current knowledge and add to the evidence that lumbar micro discectomy is the preferred surgical procedure for a well-selected patient population that has not responded to conservative management. This study is retrospective, single-center, and relatively

small, so the findings may not be generalizable. Long-term results were not possible due to the short follow-up. The follow-up was too short to assess recurrent or late complications. Further multicenter studies with longer follow-up are indicated.

Conclusion

Lumbar micro discectomy is a safe and effective surgical procedure for lumbar disc herniation that relieves pain, improves function, and has a low complication rate. Better postoperative outcomes were related to earlier surgical intervention and younger age. This Study confirms the use of lumbar micro discectomy in the proper patients.

Authors' Contributions

Syed Nasir Shah: Conceptualization, study design, data collection, clinical assessment, interpretation of findings, manuscript drafting, and critical revision.

Rizwan Ali: Data collection, clinical assessment, literature review, data analysis, and critical revision.

Naeem ul Haq: Supervision, methodological guidance, interpretation of findings, critical revision of the manuscript, and final approval.

Muhammad Ishaq: Conceptualization, literature review, data interpretation, manuscript revision, and reference verification.

All authors made substantial contributions to the work, approved the final version for publication, and agreed to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Original Article

Frequency and Risk Factors of Surgical Site Skin Complications Following Elective General Surgery: Prospective Observational Study

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Abstract

Objective: To determine the incidence of surgical site skin complications after elective general surgery and to identify patient- and surgery-related risk factors for their development.

Methodology: This Prospective Observational Study was conducted in the Department of General Surgery at Lady Reading Hospital, Peshawar, between Feb 2026 to June 2026. We enrolled 100 adult patients undergoing elective general surgical procedures. We used consecutive non-probability sampling to select 100 adult patients undergoing elective general surgical procedures. We collected demographic and clinical data, including BMI, DM, smoking, operative duration, wound type, and wound outcomes. We analyzed the data using SPSS version 27.0 at $p<0.05$.

Results: Of the 100 patients, 58% were male, and 42% were female, with a mean age of 46.8 ± 13.2 years. Surgical site skin complications occurred in 21 (21%) patients. Superficial surgical site infection was the most common complication (10%), followed by wound erythema (5%), seroma (4%), and wound dehiscence (2%). Complications were significantly associated with higher body mass index (29.1 ± 3.8 vs. 25.7 ± 3.4 kg/m²; p=0.003), diabetes mellitus (p=0.021), operative duration >120 minutes (p=0.012), smoking (p=0.041), and contaminated wounds (p=0.018). Patients with complications had significantly longer hospital stays (7.6 ± 2.4 vs. 4.3 ± 1.5 days; $p<0.001$).

Conclusion: Approximately one-fifth of elective general surgery patients developed surgical-site skin complications. Obesity, diabetes, prolonged surgery, smoking, and contaminated wounds were key risk factors. Early risk identification and evidence-based perioperative measures may reduce complications and improve outcomes.

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Introduction

Surgical site skin complications (SSSCs) constitute one of the most prevalent complications after surgery and are a significant problem in surgical practice today. These complications include superficial surgical site infection, redness around the surgical incision, seroma, hematoma, necrosis at the skin edge, wound separation, contact dermatitis, and delayed wound healing. While most elective general surgical procedures are carried out under the standard conditions of asepsis, postoperative skin complications still account for a significant portion of morbidity, extended Longer hospital stay hospital stay, functional delay, higher healthcare costs, and decreased quality of life. They also have a heavy burden on health systems, especially in low- and middle-income countries where resources for infection control may be scarce [1,2]. The proportion of surgical site complications varies significantly worldwide, depending on the surgical procedure, patient risk factors, perioperative practices, and institutional infection prevention measures. Overall rates range from 5% to 30%, and most infections are superficial surgical site infections. Elective general surgical procedures typically have lower complication rates than emergency surgery; however, wound complications can still occur despite improvements in surgical technique, antimicrobial prophylaxis, sterile operating rooms, and recovery protocols. Small wound issues can delay discharge, require outpatient visits, necessitate additional antibiotic treatments, require extra wound care, and sometimes lead to reoperation [3,4]. Multiple factors contribute to surgical site skin complications. Advanced age, obesity, diabetes mellitus, malnutrition, smoking, anemia, immunosuppression, and poor nutritional status have been the consistent risk factors associated with impaired wound healing and increased susceptibility to postoperative infections. Other factors associated with the procedure, such as long operation time, dirty or contaminated wound, excessive tissue manipulation, failure to obtain hemostasis, and improper perioperative antibiotic use, also increase the risk of postoperative wound complications. Other hospital-related factors, such as operating room sterility, compliance with infection control guidelines, surgeon experience, and postoperative wound care practices, also affect surgical outcomes [5]. Obesity is one of the most potent risk factors for postoperative wound complications due to decreased tissue perfusion, reduced oxygen delivery, and delayed collagen production by excessive adipose tissue. Likewise, diabetes mellitus impairs leukocyte function and increases microvascular disease and delayed healing, making patients more susceptible to infection and poor wound healing. Smoking leads to poorer oxygenation of tissue due to nicotine-induced vasoconstriction and carbon monoxide effects, and there is a greater risk of bacteria coming into contact with tissue and increased tissue trauma during surgical procedures. These factors often occur together, increasing the risk of postoperative complications [6,7]. The World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC) have issued evidence-based recommendations over the last decade for reducing surgical site complications through appropriate antimicrobial prophylaxis, strict aseptic technique, glycemic control, perioperative normothermia, optimized oxygenation, and standardized wound-care protocols. The success of these guidelines varies across institutions because of differences in healthcare infrastructure, patient population, and compliance with infection prevention practices. However, complication rates have decreased in many high-income institutions [8,9]. Tertiary hospitals in Pakistan perform elective general surgery in large numbers, but local evidence on the frequency and determinants of surgical site skin complications remains limited. The available literature has focused on surgical site infections rather than all postoperative skin problems. In addition, differences in patient characteristics, comorbidities, surgical techniques, and hospital resources require locally produced data to inform prevention strategies [10]. Identifying modifiable risk factors may facilitate targeted interventions, better perioperative care, lower health care expenditures, shorter hospital stays, and better patient outcomes. Therefore, this prospective observational study determined the incidence of surgical site skin complications after elective surgery in the Department of General Surgery and identified associated patient- and surgery-related factors.

Materials and Methods

This prospective observational study was conducted in the Department of General Surgery, Lady Reading Hospital, Peshawar, Pakistan, a tertiary-care teaching hospital, over 5 months Feb 2026 to June 2026. The hospital provides comprehensive elective and emergency surgical services and serves as a referral center for patients from urban and rural areas. We recruited all eligible patients undergoing elective general surgical procedures during the study period in accordance with the predefined inclusion and exclusion criteria. Surgical-site skin complications were defined as clinically documented postoperative wound complications occurring within 30 days of surgery, including superficial surgical-site infection, wound erythema, seroma, and wound dehiscence.

Sample Size Calculation

The sample size was calculated using the WHO Sample Size Calculator based on the single population proportion formula:

$$n = Z^2P(1-P) / d^2$$

The required sample size was 100 patients. Based on an anticipated prevalence of 20%, a 95% confidence level, and a 5% margin of error, the calculated minimum sample size was 100 patients. Therefore, 100 consecutive eligible patients were enrolled during the study period

Participants

We recruited eligible adult patients for general surgical procedures who were in the elective surgical queue over time using consecutive non-probability sampling. Inclusion criteria were written informed consent and availability for 30-day postoperative follow-up. We enrolled and analyzed 100 consecutive eligible patients. We excluded patients who underwent emergency surgery or had a known infection at the surgical site or skin infections, as well as those receiving long-term corticosteroid therapy, immunosuppressive therapy, or who were immunocompromised, had incomplete medical records, or were otherwise unavailable for 30-day follow-up.

Sampling Technique

Consecutive non-probability sampling was used. All eligible patients presenting for elective general surgical procedures during the study period were assessed for eligibility and recruited consecutively until the available study population of 100 patients was reached.

Inclusion Criteria

- Adults aged 18 years or older.
- Patients undergoing elective general surgical procedures.
- Patients undergoing procedures classified as clean, clean-contaminated, or contaminated according to standard surgical wound classification.
- Patients who provided written informed consent.
- Patients available for 30-day postoperative follow-up.

Exclusion Criteria

- Patients undergoing emergency surgical procedures.
- Patients with pre-existing surgical-site or skin infections.
- Patients receiving long-term corticosteroids or immunosuppressive therapy.
- Immunocompromised patients.
- Patients undergoing minor procedures under local anesthesia.

- Patients with incomplete medical records.
- Patients who were unavailable for or lost to 30-day postoperative follow-up.

Statistical Analysis

We entered and analyzed data using IBM SPSS Statistics version 27.0 (IBM Corp., Armonk, NY, USA). We assessed continuous variables for normality using the Shapiro–Wilk test and presented them as mean ± standard deviation (SD). Categorical variables are presented as frequencies and percentages. We compared patients with and without surgical-site skin complications using the independent-samples t-test for continuous variables and the Chi-square test or Fisher's exact test, as appropriate, for categorical variables. We analyzed BMI as a continuous variable in the univariate analysis and categorized it as BMI ≥30 kg/m² for multivariable analysis, corresponding to the standard definition of obesity. We included variables with p<0.10 in the univariate analysis in the multivariable logistic regression model. We did not enter postoperative longer hospital stay into the multivariable model because it is an outcome-related variable rather than a baseline predictor of surgical-site skin complications. We used the enter method for multivariable logistic regression. Adjusted odds ratios (AORs) with 95% confidence intervals (CIs) were calculated. We assessed model fit using the Hosmer–Lemeshow goodness-of-fit test. We considered a two-tailed p-value <0.05 statistically significant.

Results

The study included 100 patients undergoing elective general surgery. The cohort included 58 (58%) males and 42 (42%) females, with a mean age of 46.8 ± 13.2 years (range: 19–78 years). Surgical-site skin complications developed in 21 (21%) patients during the 30-day postoperative follow-up, whereas 79 (79%) patients experienced uncomplicated wound healing. The most common complication was superficial surgical-site infection in 10 (10%) patients, followed by wound erythema in 5 (5%), seroma formation in 4 (4%), and wound dehiscence in 2 (2%) patients. Patients who developed complications had a significantly higher mean body mass index (BMI) than those without complications (29.1 ± 3.8 vs. 25.7 ± 3.4 kg/m²; p=0.003). Diabetes mellitus was present in 38.1% of patients with complications compared with 15.2% of those without complications (p=0.021). Operative duration exceeding 120 minutes was significantly associated with postoperative surgical-site skin complications (p=0.012). Smoking (p=0.041) and contaminated wound classification (p=0.018) were also significantly associated with complications. Sex was not significantly associated with complication occurrence (p=0.470). Patients who developed complications had a significantly longer mean postoperative hospital stay than those without complications (7.6 ± 2.4 vs. 4.3 ± 1.5 days; p<0.001). Multivariable logistic regression demonstrated that BMI ≥30 kg/m², diabetes mellitus, smoking, operative duration >120 minutes, and contaminated wound classification were independently associated with increased odds of postoperative surgical-site skin complications.

Table 1. Baseline Demographic and Clinical Characteristics of the Study Population (n = 100)

Variable	Frequency (n)	Percentage (%)
Age (years), Mean ± SD	**46.8 ± 13.2**	—
Male	58	58.0
Female	42	42.0
BMI (kg/m²), Mean ± SD	**26.4 ± 3.8**	—
Diabetes mellitus	23	23.0
Hypertension	31	31.0
Current smokers	27	27.0
Non-smokers	73	73.0
ASA Grade I	38	38.0
ASA Grade II	47	47.0
ASA Grade III	15	15.0

Values are presented as frequency (%) unless otherwise indicated. SD = Standard Deviation; BMI = Body Mass Index; ASA = American Society of Anesthesiologists Physical Status Classification.

Table 2. Frequency and Types of Surgical Site Skin Complications (n = 100)

Surgical Site Skin Complication	Frequency (n)	Percentage (%)
No complication	79	79.0
Superficial surgical site infection	10	10.0
Wound erythema	5	5.0
Seroma	4	4.0
Wound dehiscence	2	2.0
Total with complications	**21**	**21.0**

Surgical-site skin complications were assessed clinically during hospitalization and throughout the 30-day postoperative follow-up. Each patient was classified according to the principal documented postoperative surgical-site skin complication; therefore, the categories shown in the table are mutually exclusive. Percentages were calculated from the total study population (n=100).

Table 3. Comparison of Patients with and Without Surgical Site Skin Complications

Variable	Complications (n=21)	No Complications (n=79)	*p*-value
Age (years), Mean ± SD	49.7 ± 12.8	46.0 ± 13.3	0.254
Male sex, n (%)	13 (61.9)	45 (57.0)	0.470
BMI (kg/m²), Mean ± SD	29.1 ± 3.8	25.7 ± 3.4	**0.003**
Diabetes mellitus, n (%)	8 (38.1)	12 (15.2)	**0.021**
Smoking, n (%)	9 (42.9)	18 (22.8)	**0.041**
Operative duration >120 minutes, n (%)	10 (47.6)	17 (21.5)	**0.012**
Contaminated wound, n (%)	6 (28.6)	8 (10.1)	**0.018**
Longer hospital stay hospital stay (days), Mean ± SD	7.6 ± 2.4	4.3 ± 1.5	**<0.001**

We analyzed continuous variables using the independent-samples t-test and categorical variables using the Chi-square test or Fisher's exact test, as appropriate. We considered p <0.05 statistically significant.

Table 4. Multivariable Logistic Regression Analysis of Independent Factors Associated with Surgical Site Skin Complications

Variable	Adjusted Odds Ratio (AOR)	95% Confidence Interval	*p*-value
BMI ≥30 kg/m²	2.84	1.21–6.65	0.016
Diabetes mellitus	2.56	1.08–6.07	0.031
Smoking	2.18	1.01–4.71	0.046
Operative duration >120 minutes	2.91	1.24–6.82	0.014
Contaminated wound	3.27	1.29–8.31	0.012

MulMultivariable logistic regression was used to identify independent factors associated with surgical-site skin complications. Variables with p<0.10 in univariate analysis were entered into the model. We excluded

postoperative hospital stay because it was an outcome-related variable rather than a baseline predictor. AOR >1 indicates increased odds of surgical-site skin complications.

Discussion

The present prospective observational study evaluated the frequency and determinants of surgical-site Skin complications following elective general surgery in a tertiary care hospital. Overall, 21% of patients developed postoperative surgical-site skin complications within 30 days of surgery, with superficial surgical-site infection being the most common complication, followed by wound erythema, seroma, and wound dehiscence. Multivariable analysis identified obesity, diabetes mellitus, smoking, prolonged operative duration, and contaminated wound classification as independent factors associated with postoperative wound complications. These findings emphasize that both patient- and procedure-related factors contribute to postoperative surgical outcomes [11,12]. The overall complication rate observed in this study is consistent with previously reported international evidence. Li et al. reported postoperative wound complication rates ranging from 10% to 25% depending on patient characteristics and perioperative practices. The PakSurg Collaborative also documented a substantial burden of surgical-site infections across Pakistani hospitals despite the implementation of standard preventive protocols. Similarly, Newton et al. demonstrated that postoperative wound complications remain an important cause of prolonged recovery and increased healthcare utilization following elective surgery. Variation in reported frequencies may reflect differences in patient populations, wound classification, surgical complexity, and institutional infection-control measures [13,14]. Superficial surgical-site infection was the predominant postoperative complication in the present study. This finding is consistent with previous studies identifying superficial SSI as a common postoperative wound complication after surgical procedures. The inclusion of additional skin complications such as erythema, seroma, and wound dehiscence in the present analysis provides a broader assessment of postoperative wound morbidity compared with studies evaluating SSI alone [15,16]. Obesity emerged as one of the strongest independent factors associated with postoperative complications. Patients with complications had significantly higher BMI values than those without complications. Previous studies have demonstrated that obesity may adversely affect tissue perfusion, collagen synthesis, and wound oxygenation, thereby delaying wound healing and increasing susceptibility to infection. Increased subcutaneous tissue thickness may also contribute to greater dead space and impaired tissue healing, potentially explaining the higher complication rates observed among obese patients undergoing elective surgery [17,19]. Diabetes mellitus was another significant factor associated with surgical-site skin complications in this study. Hyperglycemia can impair neutrophil function, decrease collagen deposition, and compromise microvascular circulation, all of which may delay wound healing. These findings are consistent with evidence linking abnormal perioperative glycemic status with postoperative complications. Appropriate glycemic optimization before and around elective surgery should therefore remain an important component of perioperative management [16,20]. Prolonged operative duration, smoking, and contaminated wound classification were also independently associated with postoperative complications. Longer surgical procedures may increase tissue manipulation, bacterial exposure, and operative blood loss, whereas smoking can reduce tissue oxygenation through nicotine-induced vasoconstriction and impaired inflammatory responses. Previous surgical studies have reported comparable associations, supporting the importance of these potentially modifiable perioperative risk factors [21,22,24]. Implementation of smoking cessation strategies, meticulous surgical technique, appropriate antimicrobial prophylaxis, and efforts to minimize unnecessary operative delays may help reduce postoperative wound morbidity. An important clinical observation in the present study was the significantly longer postoperative hospital stay among patients who developed wound complications. Similar findings have been reported internationally, where surgical-site complications are associated with increased antibiotic use, repeated wound care, hospital readmissions, and higher healthcare costs. These findings reinforce the importance of perioperative optimization, standardized wound surveillance, and evidence-based infection-control practices. In Pakistan, where healthcare resources may be constrained, identifying high-risk patients before surgery may allow targeted preventive interventions and more efficient resource utilization [23,24].Overall, the findings indicate that several determinants of surgical-site skin complications are potentially modifiable. Early identification of high-risk patients, optimization of comorbid conditions, adherence to evidence-based perioperative protocols, and standardized postoperative wound monitoring may help reduce postoperative morbidity, shorten hospital stay, and improve outcomes following elective general surgery [25].

Limitations

This study has several limitations. It was conducted at a single tertiary-care hospital with a relatively small sample size, which may limit the generalizability of the findings. Although the sample-size calculation based on the prespecified prevalence and margin of error indicated a larger minimum sample, only 100 consecutive eligible patients were available during the predefined six-month study period. The relatively small number of patients who developed surgical-site skin complications also limited the number of outcome events available for multivariable analysis. This may have affected the stability and precision of the regression estimates. The follow-up period was restricted to 30 days and may not have captured late postoperative skin complications. Additionally, microbiological confirmation was not available for all suspected infections, and unmeasured confounding factors such as nutritional status, surgeon experience, perioperative antibiotic compliance, and other institutional factors may have influenced the observed outcomes. Finally, the study was observational; therefore, the identified associations should not be interpreted as proof of causality.

Conclusion

Surgical site skin complications remain a common postoperative problem following elective general surgery, affecting approximately one-fifth of patients in this study. Obesity, diabetes mellitus, smoking, prolonged operative duration (>120 minutes), and contaminated wounds were identified as independent risk factors. Early identification of high-risk patients, optimization of modifiable risk factors, and strict adherence to evidence-based perioperative infection prevention protocols may reduce postoperative morbidity, shorten hospital stay, and improve overall surgical outcomes.

Ethical Approval

The Institutional Review Board (IRB) of Lady Reading Hospital Medical Teaching Institution (LRH-MTI), Peshawar, Pakistan, granted ethical approval. The IRB approved Dr. Muhammad Kalim for the study "Frequency and Risk Factors of Surgical Site Skin Complications Following Elective General Surgery: A Prospective Observational Study" **(Ref. No. 53-A/LRH/MTI; dated 04/02/2026).**

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Authors' Contributions

Authors Contribution

Waleed Mabood: Conceptualization and study design, data acquisition, interpretation of results, manuscript drafting, and final approval of the version to be published.

Sheik Muhammad Ibqar Azeem: Conceptualization and study design, data acquisition, critical revision of the manuscript for important intellectual content, and final approval of the version to be published.

Shoaib Muhammad: Data acquisition, data analysis and interpretation, critical revision of the manuscript, and final approval of the version to be published.

Shahid Ullah Ahmad: Data acquisition, interpretation of results, critical revision of the manuscript for important intellectual content, and final approval of the version to be published.

Sahibzada Salma Rahman: Data collection, literature review, interpretation of results, critical revision of the manuscript, and final approval of the version to be published.

Muhammad Kalim: Conceptualization and supervision of the study, data analysis and interpretation, drafting and critical revision of the manuscript, and final approval of the version to be published.

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

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Original Article

Lumbar Spinal Stenosis and Financial Hardship: A Patient-Centered Analysis from A Middle-Income Country

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Abstract

Objective: To evaluate the economic burden of Lumbar Spinal Stenosis (LSS) and to identify the contributing factors.

Methodology: This Cross-sectional Study was conducted in the Department of Neurosurgery, MMC/BKMC Mardan, from January to June 2025. We recruited a consecutive sample of 100 adult patients diagnosed with radiologically and clinically proven lumbar spinal stenosis. We used a questionnaire to collect data on demographics, family income, treatment cost, transport cost, income loss, treatment delay, and self-reported financial hardship. We categorized financial hardship as mild (<25% of monthly household income), moderate (25–50%), and severe (>50%).

Results: Among 100 patients, 58% were male and 42% female, with a mean age of 56.8 ± 11.4 years. Forty-seven percent of participants reported severe financial hardship, 32% moderate hardship, and 21% mild hardship. Patients with severe stenosis incurred significantly higher treatment costs than those with mild-to-moderate disease (PKR 68,500 ± 18,200 vs. PKR 39,700 ± 14,600; $p = 0.002$). Severe hardship was more common among unemployed/daily wage earners (63.4% vs. 28.7%; $p = 0.001$), rural residents ($p = 0.004$), and surgically managed patients (74.2% vs. 39.5%; $p < 0.001$). Household income inversely correlated with financial toxicity ($r = -0.48$, $p < 0.001$).

Conclusion: Financial hardship is prevalent among patients with Lumbar Spinal Stenosis in middle-income countries and is closely linked to the severity of symptoms, rural living, low income, and surgery. Financial support and better access to spinal care may help alleviate this.

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Introduction

Lumbar Spinal Stenosis (LSS) is a common degenerative spinal condition and a leading source of pain, disability, and limited mobility in middle-aged and older adults around the globe. It involves narrowing of the spinal canal, lateral recess, or neural foramina that compresses neural structures and causes low-back pain, neurogenic claudication, radiculopathy, and disability. LSS occurs more frequently with age because of degenerative changes in the intervertebral discs, facet joints, and thickening of the ligamentum flavum. As the world's population ages, LSS is expected to become increasingly prevalent over the next few decades [1,2]. LSS not only causes physical suffering, but it also has high socioeconomic costs. Repeated visits to the hospital, high-tech imaging, long-term medications, physiotherapy, and in some cases surgical decompression with or without fixation are often necessary. This is especially so in low- and middle-income countries (LMICs), where out-of-pocket healthcare spending is high, and health insurance is rare. The financial burden of chronic musculoskeletal and degenerative diseases can result in delayed diagnosis, non-adherence to treatment, diminished quality of life, and catastrophic health-care costs [3,4]. The term "financial toxicity", first used in cancer care, is now being applied to non-malignant chronic conditions, such as spinal conditions. Financial toxicity includes both the objective financial strain and patient-perceived distress from health-care costs. In LSS patients, direct healthcare-related expenses include consultation fees, imaging, medication, surgery, hospitalization, and rehabilitation, while indirect expenses include transportation, accommodation, caregiver burden, and productivity loss. These costs may have a greater impact on disadvantaged individuals living in rural areas, without employment, and on a daily wage basis [5,6]. In middle-income countries such as Pakistan, spinal services are mostly available in major urban tertiary care facilities, requiring patients to travel long distances to access care. Inability to seek timely medical care may lead to disease progression and higher health-care costs. Although LSS is clinically important, few studies explore its economic consequences in LMICs. Current studies primarily address surgical outcomes and efficacy rather than patient-level economic impacts [7,8]. Economic insights about LSS are vital to shape health policy, prioritize resources, and design financial assistance programs. A full assessment of financial hardship among LSS patients can identify at-risk groups and system-related barriers to accessing care. Moreover, individual patient-focused economic data can inform institutions on how to make spinal services more affordable [9]. This study aimed to determine the prevalence of financial hardship among patients with Lumbar Spinal Stenosis and identify socioeconomic and clinical factors associated with increased financial burden [10].

Materials and Methods

Study Design and Setting

This cross-sectional study was conducted in the Department of Neurosurgery, MMC/BKMC Mardan, from January to June 2025.

Participants

We enrolled 100 adult patients with clinically and radiologically diagnosed lumbar spinal stenosis using consecutive non-probability sampling. After obtaining informed consent, we recruited participants from various outpatient and inpatient units. We collected demographic, socioeconomic, and clinical information at the time of inclusion.

Sample Size Calculation

The sample size was determined using the WHO sample size calculator, based on a 50% prevalence of severe financial hardship among patients with chronic degenerative spinal disease, a 95% confidence level, and a 10% margin of error. The minimum sample size was 96 patients; we recruited 100 patients.

Inclusion Criteria

Participants had to be aged 18 years or older with clinically presenting and MRI-diagnosed lumbar spinal stenosis. We included those receiving conservative and surgical management. Patients had to be willing to give informed consent and answer the financial hardship questionnaire.

Exclusion Criteria

Those with spinal trauma, cancer, infection, congenital spinal deformities, previous lumbar surgery, cognitive dysfunction, or missing financial information were excluded. Those with significant comorbid systemic diseases leading to disability or financial impact independent of LSS were also excluded.

Diagnostic and Management Strategy

Lumbar canal stenosis (LSS) was diagnosed by clinical exam and MRI. The spine team decided upon Conservative treatment or surgical decompression based on symptoms and MRI findings.

Assessment of Financial Hardship

We assessed financial hardship using a structured questionnaire that included direct medical expenses, transportation costs, accommodation expenses, and income loss. Financial hardship was categorized as mild, moderate, or severe based on the proportion of cumulative treatment expenditure relative to monthly household income.

Statistical Analysis

We used SPSS version 26 to analyze the data. Normal variables were reported as mean ± standard deviation, and categorical variables as frequencies and percentages. Chi-square and independent t tests were used to compare the associations. Pearson correlation was used for continuous variables. A p-value <0.05 was considered significant.

Results

The study included 100 patients with Lumbar Spinal Stenosis (LSS): 58 males and 42 females, with a mean age of 56.8 ± 11.4 years. Table 1 summarizes the study population's demographic and socioeconomic characteristics. Most participants were from rural areas (61%), while 40% were unemployed or retired. The mean monthly household income was PKR 54,300 ± 19,600, and the mean symptom duration was 8.7 ± 3.9 months (Table 1). Table 2 presents the clinical and radiological characteristics of the patients. Severe radiological stenosis was identified in 43% of patients, whereas 38% and 19% had moderate and mild stenosis, respectively. Neurogenic claudication was present in 72% of participants, and radiculopathy was reported in 66%. Surgical management was required in 57% of cases, while 43% were managed conservatively (Table 2). Representative MRI findings are illustrated in Figures 1 and 2. Figure

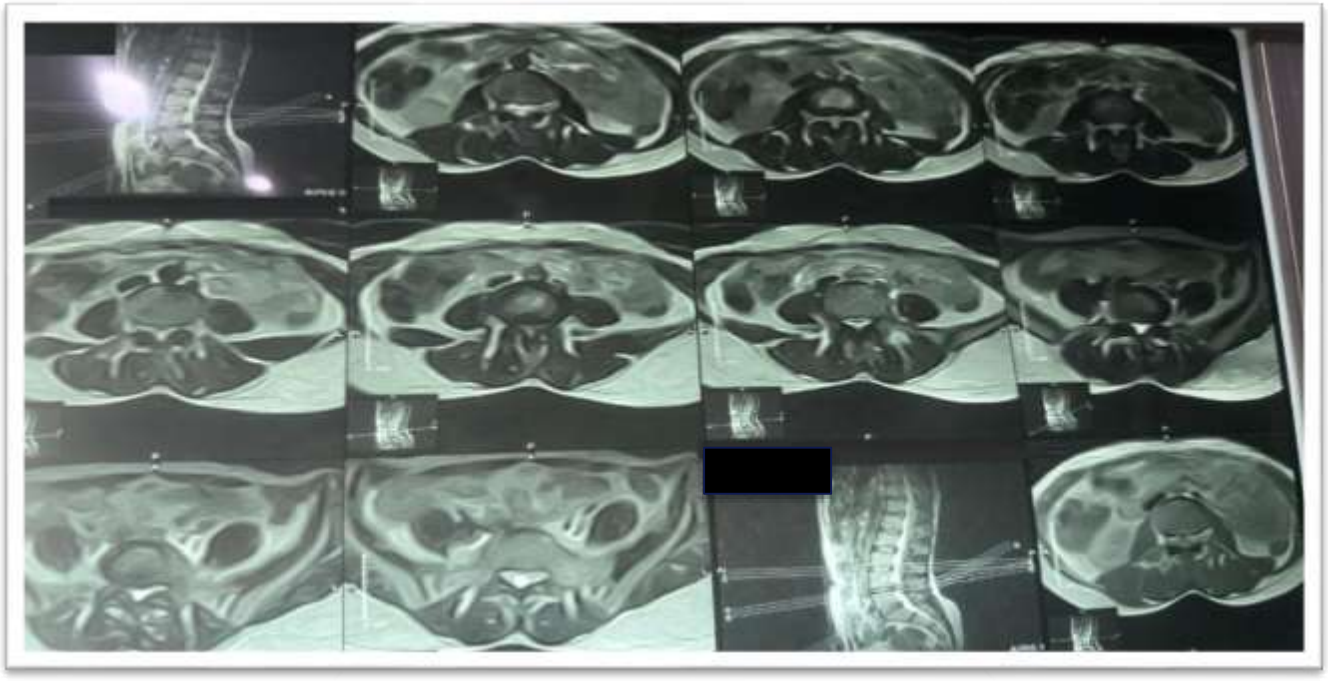
1 demonstrates sagittal MRI features of multilevel degenerative lumbar spinal stenosis with disc desiccation, reduced intervertebral disc height, and central canal narrowing, predominantly at the L4–L5 and L5–S1 levels. Figure 2 shows sagittal and axial MRI sections highlighting central canal stenosis, thecal sac compression, and multilevel degenerative changes characteristic of clinically significant lumbar spinal stenosis. Table 3 summarizes the financial burden analysis. The mean direct medical expenditure was PKR 61,700 ± 21,400, while transportation and accommodation costs averaged PKR 11,600 ± 5,300. Participants reported a mean loss of 18.4 ± 9.2 workdays. Forty-seven percent of patients experienced severe financial hardship, while 32% and 21% reported moderate and mild financial hardship, respectively (Table 3). Table 4 presents factors associated with severe financial hardship. Patients with severe radiological stenosis incurred significantly greater treatment costs than those with mild-to-moderate disease (PKR 68,500 ± 18,200 vs. PKR 39,700 ± 14,600; p = 0.002). Severe financial hardship was significantly more common among patients undergoing surgical management (74.2%; p < 0.001), unemployed or daily wage earners (63.4%; p = 0.001), and rural residents (59.0%; p = 0.004). Delayed presentation beyond six months was also associated with increased financial burden (56.3%; p = 0.011). Furthermore, household income demonstrated a significant inverse correlation with perceived financial toxicity (r = –0.48, p < 0.001), indicating that lower-income households experienced greater economic hardship (Table 4).

Figure 1. Sagittal Magnetic Resonance Imaging of Multilevel Degenerative Lumbar Spinal Stenosis



Figure 1. (A) and (B) Representative sagittal T2-weighted magnetic resonance images of the lumbar spine demonstrating multilevel degenerative lumbar spinal stenosis. The images show disc desiccation, reduced intervertebral disc height, and central canal narrowing, most prominent at L4–L5 and L5–S1. These radiological findings are consistent with degenerative lumbar spinal stenosis and were used to confirm the diagnosis in the study population.

Figure 2. Magnetic Resonance Imaging Findings in Lumbar Spinal Stenosis



Composite MRI image demonstrating characteristic radiological features of degenerative lumbar spinal stenosis. Sagittal images reveal multilevel disc degeneration and reduced spinal canal dimensions, whereas axial images demonstrate central canal narrowing with compression of the dural sac and adjacent neural structures. These findings are consistent with clinically significant lumbar spinal stenosis.

Table 1. Baseline Demographic and Socioeconomic Characteristics of Study Participants (n = 100)

Variable	Frequency (%) / Mean ± SD
Age (years)	56.8 ± 11.4
Male Gender	58 (58.0%)
Female Gender	42 (42.0%)
Rural Residence	61 (61.0%)
Urban Residence	39 (39.0%)
Employed/Salaried	31 (31.0%)
Daily Wage Earner	29 (29.0%)
Unemployed/Retired	40 (40.0%)
Mean Monthly Household Income (PKR)	54,300 ± 19,600
Mean Duration of Symptoms (Months)	8.7 ± 3.9

Baseline demographic and socioeconomic profile of patients diagnosed with Lumbar Spinal Stenosis included in the study.

Table 2. Clinical and Radiological Characteristics of Lumbar Spinal Stenosis Patients

Variable	Frequency (%)
Mild Stenosis	19 (19.0%)
Moderate Stenosis	38 (38.0%)
Severe Stenosis	43 (43.0%)
Neurogenic Claudication Present	72 (72.0%)
Radiculopathy Present	66 (66.0%)
Back Pain Only	28 (28.0%)
Conservative Management	43 (43.0%)
Surgical Management	57 (57.0%)

Clinical presentation, radiological severity, and treatment modality among patients with Lumbar Spinal Stenosis.

Table 3. Financial Burden Analysis Among Study Participants

Variable	Mean ± SD / Frequency (%)
Direct Medical Cost (PKR)	61,700 ± 21,400
Transportation/Accommodation Cost (PKR)	11,600 ± 5,300
Lost Workdays	18.4 ± 9.2
Mild Financial Hardship	21 (21.0%)
Moderate Financial Hardship	32 (32.0%)
Severe Financial Hardship	47 (47.0%)

Distribution of direct and indirect costs and severity of self-reported financial hardship among enrolled participants.

Table 4. Factors Associated with Severe Financial Hardship

Variable	Severe Financial Hardship (%)	p-value
Severe Stenosis	67.4%	0.002
Surgical Management	74.2%	<0.001
Rural Residence	59.0%	0.004
Unemployed/Daily Wage Earner	63.4%	0.001
Delayed Presentation >6 Months	56.3%	0.011

Association between demographic and clinical variables. Patients with severe financial hardship in patients with Lumbar Spinal Stenosis.

Discussion

Our study demonstrated that nearly half of patients with Lumbar Spinal Stenosis experienced severe financial hardship. Similar findings have been reported in other low- and middle-income countries where out-of-pocket healthcare expenditures constitute a major component of treatment costs. This highlights that the impact of LSS extends beyond pain and disability to a significant socioeconomic burden, especially in low- and middle-income countries. socioeconomic burden, especially in low- and middle-income countries. Our findings show that the severity of the disease, living in rural areas, being unemployed, late presentation, and having surgery are major risk factors for financial hardship among patients with LSS [11]. Our mean age of 56.8 years is consistent with recent reports that LSS is more common in older age groups due to degenerative changes in the spine. Other recent reviews also report that the 6th and 7th decades of life are the most common age for presenting with symptomatic LSS. Our finding of male

predominance also agrees with other regional spine registries, though male-to-female ratios differ across studies [12]. A key strength of our study is the high percentage of severe financial toxicity (47%), which highlights the high financial impact of degenerative spinal disease in the middle-income group. While there is limited literature directly comparing the cost of financial toxicity in LSS, previous data on chronic low back pain and degenerative lumbar disease demonstrate a similar socioeconomic impact. Chang et al. found that lower back disorders are among the highest musculoskeletal healthcare costs worldwide, with rising costs attributed to imaging, treatments, and surgery. Our results build on these studies by showing patient-level burden of financial toxicity in a less-developed health system [13,14]. Those patients with severe radiological stenosis had much greater expenditures for their treatment than those with mild to moderate disease [15]. This may be related to additional imaging and physiotherapy, as well as eventual surgical intervention. This link between severity and health-care use has been observed in a recent spine outcomes Study [16 The radiological findings illustrated in Figures 1 and 2 further support the clinical spectrum of disease observed in our cohort. Representative sagittal and axial MRI images demonstrated multilevel degenerative changes, including disc desiccation, reduced intervertebral disc height, facet joint hypertrophy, and central canal narrowing, predominantly involving the L4–L5 and L5–S1 levels. These findings align with the established pathophysiology of lumbar spinal stenosis and correspond to the high proportion of patients presenting with moderate-to-severe radiological disease in the present study. The predominance of lower lumbar involvement agrees with previous reports identifying these segments as the most commonly affected levels because of age-related degeneration and increased biomechanical stress[17,18]. Rural living was also a significant predictor of financial burden, potentially due to travel, accommodation, and productivity losses associated with tertiary spine care. This finding is consistent with other studies highlighting health care access inequalities reported in recent socioeconomic spine publications, where geographical inequality and social disadvantage negatively affect health care access and outcomes. The increased financial burden among the unemployed and day laborers also supports the influence of socioeconomic vulnerability in exacerbating the financial impact of disease [19]. A later time to presentation (after six months) was a significant predictor of cumulative cost. This suggests financial constraints may delay treatment until the disease has advanced, complicating management and increasing costs. These results are significant from a clinical perspective because a delay in treatment for degenerative spinal disease can make symptoms worse, requiring more complex surgery [20]. In sum, our findings indicate that LSS in middle-income countries should be considered as a clinical, surgical, and socioeconomic condition and managed accordingly. Health policies supporting subsidized imaging, cost-effective surgical services, decentralized spine services, and timely referral may help overcome the financial challenges observed in this study. This single-center cross-sectional study may not be generalizable to other healthcare settings. The study did not perform multivariable regression analysis to adjust for potential confounding factors. Self-reported financial hardship may have been subject to recall bias. The study did not evaluate future economic consequences, and it may have underestimated indirect societal costs. Multicenter prospective studies are recommended.

Conclusion

In middle-income countries, Lumbar Spinal Stenosis was associated with substantial financial hardship among study participants, particularly among those with severe disease, low income, rural residence, delayed presentation, and surgical treatment requirements. Addressing financial and healthcare access barriers may reduce the disease's economic burden and improve equitable spinal care.

Ethical Approval

Ethical approval was obtained from the Institutional Review Board of Bacha Khan Medical College/Mardan Medical Complex, Mardan, Pakistan **(Approval No. 1023/BKMC/NEURO/05/05/2024).**

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Conflict of Interest: Nil

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Authors Contributions

Naeem ul Haq – Conceived and designed the study, supervised data analysis, and critically reviewed the final manuscript. Responsible for overall integrity of the research.

Syed Nasir Shah, Umer Zeb Khan– Collected patient data, performed data entry and preliminary analysis, drafted the initial manuscript, and coordinated correspondence with the journal.

Muhammad Ishaq, Muhammad Essa– Assisted in data collection, literature review, and manuscript editing.

Rizwan Ali– Participated in clinical case review, quality assurance, and provided expert input on surgical methodology. All authors approved and contributed significantly to the study's conception, data collection, analysis, Manuscript writing, and final approval of the manuscript as per ICMJE criteria**.**

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Original Article

Frequency & Association of Low Birth Weight Babies with Important Risk Factors Among Term Pregnancies Visiting Private Health Care Facility

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Abstract

Objective: To determine the frequency of low birth weight among term pregnancies and assess its association with maternal demographic, socioeconomic, antenatal, nutritional, and obstetric risk factors.

Methodology: This cross-sectional analytical study was conducted in the Department of Obstetrics & Gynecology, South West Health Complex Hospital, Kohat, from Jan 2026 to May 2026. We recruited 256 pregnant women aged >18 years with term pregnancies, using consecutive sampling. We defined LBW as birth weight <2.5 kg. We analyzed data using SPSS version 26.0. We used the chi-square test to explore associations between categorical variables, and considered $p < 0.05$ statistically significant.

Results: Out of 256 term pregnancies, 61 (23.83%) had LBW. Maternal age <25 years (51.95%), illiteracy (50.39%), household income <75,000 PKR (70.70%), birth interval <2 years (57.42%), fewer than four antenatal visits (51.56%), and hemoglobin <11 g/dL (65.63%) were common. LBW was significantly associated with maternal age (p=0.0228), occupation (p=0.0248), education (p=0.0236), monthly income (p=0.0079), birth interval (p=0.0133), antenatal visits (p=0.0193), anemia (p=0.0229), parity (p=0.0174), and iron-folic acid supplementation (p=0.0149). BMI was not significantly associated with locality, type of pregnancy, or mode of delivery.

Conclusion: LBW was common for term pregnancies and was linked with several maternal socio-economic and pregnancy-related risk factors. Enhancing antenatal care, preventing anemia, improving maternal nutrition, and providing socioeconomic support could contribute to the reduction of LBW and related neonatal morbidity.

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Introduction

Worldwide, the prevalence of low birth weight is 15 to 20%, and approximately 18 million low birth weight babies are born annually[1]. The morbidity and mortality in developed and developing countries are significant issues that depend on low birth weight. According to the World Health Organization, low birth weight (LBW) is a birth weight below 2.5 kg.[2] Moreover, Thapa et al. (2022) found that about 1/7 of newborns had low birth weight and showed a significant association with fewer antenatal visits and no iron and folic acid supplementation during pregnancy.[3] Worldwide, low birth weight affects about 22 million people. Prevalence varies widely, and South Asia has the highest prevalence, at 20-29%.[4] Low birth weight is a common problem in Pakistan.[5] In a study by Aysha et al. (2022), the prevalence of low birth weight was 10.6%. Moreover, 67% did not receive any antenatal care, and most mothers (87%) were multiparous. Additionally, 26% of mothers weighed < 50 kg; 37% were < 5 feet tall; and 72% were anemic.[6] Furthermore, Javed et al. (2018) found that the prevalence of low birth weight was 13.35%; most cases were not registered (64.15%); 54% were grand-multiparous; and 69.81% were anemic. Low birth weight was strongly associated with hypertension, placental previa, and oligohydramnios.[7] Numerous studies of low birth weight all over the world reveal that the weight of the mother, height, age, parity, weight gained during pregnancy, and even anemia during pregnancy are all important factors in low birth weight. Indirect determinants include maternal literacy, occupation, family income, socioeconomic status, prenatal care, tobacco use, and use of iron and folic acid supplements during pregnancy.[8] Maternal malnutrition, anemia, poor prenatal care, drug use, birth order, and maternal medical disorders like hypertension, diabetes mellitus, heart disease, and chronic infections are other significant factors that contribute to low birth weight.[4] Research has shown that low birth weight babies are more likely to be born to women who are too young, too old, have too many children, or have too narrow birth intervals.[9] According to WHO, 10% of all pregnancies had hypertension, which poses a significant risk to the mother and newborn.[10] Moreover, 30.34% of mothers with gestational hypertension had low birth weights.[11] An international study conducted by Dildora et al. (2022) found that low birth weight had a strong link with hypertension. It revealed that hypertension during pregnancy increases the risk of low birth weight fourfold. Tobacco smoking had adverse maternal and neonatal health risks. During the first wave of the COVID-19 pandemic, the prevalence of tobacco smoking use among pregnant women increased to 10%, and thus the prevalence of low birth weight babies proportionately increased.[12] In Pakistan, unregistered and unbooked cases pose a significant problem, which is exacerbated by the scarcity of health care services and facilities. Thus, poor economic and social status, along with poor healthcare facilities and cultural beliefs, played a key role in the development of low birth weight.[13]Pakistan is a developing country with scarce resources and a weak health care delivery system. The burden of low birth weight is on the rise; thus, this descriptive cross-sectional study was planned and conducted in Kohat and Peshawar Districts to estimate the burden of risk factors for low birth weight among term pregnancies with hypertension and to communicate the current study findings to the local community and, at large, to reduce and prevent the unnecessary mortality and morbidity associated with low birth weight.

Materials & Methods

This cross-sectional analytical study was conducted in the Department of Obstetrics & Gynecology, South West Health Complex Hospital, Kohat, from Jan 2026 to May 2026. We determined the sample size using the WHO sample size calculator, based on a 95% confidence interval, 5% absolute precision, 5% margin of error, and a 19.75% prevalence of low birth weight. The calculated sample size was 246. However, we selected a total sample size of n=256. We used consecutive sampling to recruit eligible participants. We included pregnant women aged>18 years with term pregnancies. In contrast, women with congenital anomalies, diabetes mellitus, renal, cardiac, or respiratory disorders, and non-permanent residents of District Kohat and Peshawar were excluded. The data collection tool included socio-demographic variables, birth interval, antenatal care, parity, type of delivery, maternal weight and height, hemoglobin, and iron and folic acid supplementation during pregnancy. We categorized maternal age as <25 and >25; locality as rural and urban; BMI as <24 and >24; monthly income as <75K and >75K PKR per month; literacy as literate and illiterate; and occupational status as employed and unemployed. We defined low birth weight as birth weight <2.5 kg. We classified antenatal visits as <4 or> 4 during pregnancy and defined anemia as HB <11 g/dL. We used the chi-square test for categorical data and assessed statistical significance using $p < 0.05$ and $\chi 2 > 3.84$ for dichotomous variables with 1 degree of freedom. We entered and analyzed all data in the Statistical Package for the Social Sciences (SPSS) version 26.0 and presented results in tables. For reference management, we used Mendeley Desktop version 1.19.8.

Results

Among the 256 term pregnancies included in the study, 61 (23.83%) newborns had low birth weight (<2.5 kg), while 195 (76.17%) had normal birth weight. In our study; 51.95% had age less than 25 years; 35.94% had BMI > 24; 50.39% were illiterate; 70.70% had monthly income <75K PKR; 44.53% reside had rural residence; & 64.04% were unemployed, as was shown in Table No. 1. Additionally, 57.42% had < 2 years of birth interval during consecutive pregnancies; 51.56% had <4

antenatal visits or adequate antenatal care during pregnancy; 65.63% were anemic, with HB levels < 11 g/dL; & 48.05% were primigravida among the study participants. Moreover, 98.44% of mothers had singleton pregnancies; 91.02% had normal vaginal delivery; & 80.86% used iron &or folic acid supplementation during pregnancy, as shown in Table No. 2.

Table 1. Frequency and Association of Important Demographic Variables Among Women at Term (n=256) Visiting Health Care Facility, District Kohat and Peshawar

Variable	Response	LBW F (%)	Normal F (%)	Total F (%)	χ^2	P-value
Age (years)	<25	39 (15.23)	94 (36.72)	133 (51.95)	3.997	0.0456
	≥25	22 (8.59)	101 (39.45)	123 (48.05)		
BMI of mother	<24	43 (16.80)	121 (47.27)	164 (64.06)	1.150	0.2836
	≥24	18 (7.03)	74 (28.91)	92 (35.94)		
Occupation	Employed	15 (5.86)	77 (30.08)	92 (35.94)	3.855	0.0496
	Unemployed	46 (17.97)	118 (46.09)	164 (64.06)		
Education status	Literate	23 (8.98)	104 (40.63)	127 (49.61)	3.936	0.0473
	Illiterate	38 (14.84)	91 (35.55)	129 (50.39)		
Family monthly income (PKR)	<75,000	49 (19.14)	132 (51.56)	181 (70.70)	5.834	0.0157
	≥75,000	12 (4.69)	63 (24.61)	75 (29.30)		
Locality	Rural	23 (8.98)	91 (35.55)	114 (44.53)	1.170	0.2794
	Urban	38 (14.84)	104 (40.63)	142 (55.47)		

F = Frequency; LBW = Low Birth Weight; χ^2 = Chi-square test. P < 0.05 considered statistically significant.

Table 2. Frequency & Association of Important Risk Factors of Low Birth Weight Among Women at Term (n=256) Visiting Health Care Facility

Variable	Response	LBW F (%)	Normal F (%)	Total F (%)	X^2 Test (P Value)
Birth Interval	< 2years	43 (16.80)	104 (40.63)	147 (57.42)	4.915* 0.0133
	>2years	18 (7.03)	91 (35.55)	109 (42.58)	
Antenatal Visits/ Care	< 4 ANV	39 (15.23)	93 (36.33)	132 (51.56)	4.279* 0.0193
	> 4 ANV	22 (8.59)	102 (39.84)	124 (48.44)	
HB Level	< 11mg/dl	47 (18.36)	121 (47.27)	168 (65.63)	3.992* 0.0229
	> 11mg/dl	14 (5.47)	74 (28.91)	88 (34.38)	
Parity	Primi-parous	37 (14.45)	86 (33.59)	123 (48.05)	4.459* 0.0174

	Multi or Grand Multiparous	24 (9.38)	109 (42.58)	133 (51.95)	
Type of Pregnancy	Singleton	59 (23.05)	193 (75.39)	252 (98.44)	0.418 0.2588
	Twin or Multiple	2 (0.78)	2 (0.78)	4 (1.56)	
Type of Delivery	NVD	52 (20.31)	181 (70.70)	233 (91.02)	2.400 0.0607
	C/S	9 (3.52)	14 (5.47)	23 (8.98)	
Iron+ Folic Acid Used	Yes	43 (16.80)	164 (64.06)	207 (80.86)	4.717* 0.0149
	No	18 (7.03)	31(12.11)	49 (19.14)	

Significant: *; F: Frequency; LBW: Low Birth Weight

Discussions

The prevalence of low Birth weight was associated with personal demographic and socio-economic factors, along with birth interval, parity, and antenatal care during pregnancy. The literature revealed that low socioeconomic status, inadequate antenatal visits, financial constraints, illiteracy, maternal anemia, and folic acid supplementation contribute to low birth weight. In our study, about 51.95% of participants were <25 years old, whereas Axame et al. (2022) and Dildora et al. (2022) reported 25.7% and 34.9%, respectively.[14] In Devaguru et al. (2023), only 2.3% were older than 25 years.[8] Additionally, in our study, 35.94% of pregnant women were employed, whereas in Girotra et al. (2022) and Thapa et al. (2022), 21.98% and 22.4%, respectively, were employed. [15] Moreover, Axame et al. (2022) reported 78.5%. Thus, our results showed a lower prevalence of illiteracy than in Girotra et al. (2022), Thapa et al. (2022), and Axame et al. (2022).[16] In international studies, illiteracy among pregnant women was reported as 14.1%, 26.66%, and 19.54% among Axame et al. (2022), Devaguru et al. (2023), and Girota et al. (2023, respectively [17], whereas in our study, 49.61% were illiterate; thus, our illiteracy status level showed a higher frequency compared to previous international studies. Regular antenatal visits play a pivotal role in early detection and timely management of hypertension during pregnancy, and our study revealed that a large proportion of women had inadequate antenatal care. In our study, 51.56% had ≤4 antenatal visits, whereas in studies by Thapa et al. (2022), Giotra et al. (2023), and Devaguru et al. (2023), this was 8.4%, 53.15%, and 58.66%, respectively.[18,19] In our study, 57.42% had birth intervals of <2 years, whereas in Thapa et al. (2022), 8.2% had birth intervals of <2 years. Thus, our findings showed a higher prevalence of short birth intervals than in the Thapa et al. (2022) study.[2] Maternal anemia was another significant factor identified in this study. Anemia reduces the oxygen-carrying capacity of maternal blood and further aggravates placental hypoxia caused by hypertension. In our study, 65.63% had HB <11 g/dL and were classified as anemic, whereas in the studies of Axame et al., 2022, and Giotra et al., 2023, it was 57.4% and 59.19%, respectively.[19] In our study, 48.05% were primigravida and 51.95% were multigravida, whereas Farhan et al. (2023) reported 61.7% and 38.2%, respectively.[13] In our study, 91.02% had normal vaginal delivery, whereas in the study by U.I. Khan et al. (2024), 66.9% had NVD.[17] Moreover, in our study, 80.86% used iron and/or Folic Acid supplementation during pregnancy, whereas Devaguru et al. (2023) and Thapa et al. (2022) reported 68% and 97.4%, respectively.[20] This study found that low birth weight in term pregnancies was significantly associated with maternal age, illiteracy, birth interval, inadequate antenatal care, maternal anemia, parity, and monthly family income, with significant chi-square test values and p-values < 0.05.

Conclusions

Low birth weight was significantly associated with maternal age, occupation, education, family income, birth interval, antenatal care, anemia, parity, and iron/folic acid supplementation among term pregnancies. Strengthening antenatal care, improving maternal nutrition, controlling anemia, and promoting appropriate birth spacing may help reduce the burden of low birth weight.

Authors' Contributions

Sajeela Amin: Conceptualization, study design, literature search, study screening, data extraction, manuscript drafting, and critical revision.

Musarrat Jabeen: Conceptualization, supervision, interpretation of findings, critical revision of the manuscript, and final approval of the version to be published.

Muhammad Ishtiaq: Literature search, study screening, data extraction, preparation of tables and figures, and manuscript revision.

Natasha Junaid: Data extraction, literature review, manuscript drafting and revision, and reference verification.

Zaib Un Nisa: Data analysis, interpretation of findings, manuscript revision, and final approval of the manuscript.

Jaweria Ahmad Khattak: Literature review, manuscript revision, reference verification, and final approval of the manuscript.

All authors read and approved the final manuscript and agreed to be accountable for all aspects of the work.

Data Availability

The data generated and analyzed during the current study are available from the corresponding author on reasonable request, subject to appropriate ethical and institutional restrictions. The data are not publicly available because they contain information collected from human participants and may include potentially identifiable or sensitive information.

Ethical Approval: Ethical approval was obtained from the GCON Ethical Committee, Govt. College of Nursing Kohat, under Approval **No. 18/CON/KT, dated 15 January 2026**, for the study on low birth weight.

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

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Original Article

Association of C-Reactive Protein and Fibrinogen with Metabolic and Cardiovascular Risk Parameters among Diabetic Patients with and without Cardiac Disease

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Abstract

Objective: To compare metabolic, lipid, inflammatory, and coagulation-related parameters between diabetic patients with and without cardiac disease and to evaluate correlations between C-reactive protein (CRP), fibrinogen, and selected clinical and biochemical parameters.

Methodology: This case-control analytical study was conducted in the Department of Biochemistry, Khyber Medical College, Peshawar, from October 2025 to March 2026. We included 200 diabetic participants: 100 with cardiac disease and 100 without. We evaluated group differences using appropriate comparative statistical tests and performed Pearson correlation analysis to assess relationships between CRP or fibrinogen and selected metabolic and lipid parameters. We considered $p < 0.05$ statistically significant.

Results: The overall mean age was 61.50±9.82 years, and the mean BMI was 28.17±3.23 kg/m². Cardiac diabetic patients had higher FBS (213.80±91.62 vs. 175.61±59.14 mg/dL), HbA1c (10.17±3.45 vs. 8.31±3.04%), CRP (18.43±4.22 vs. 12.67±6.17), and fibrinogen (478.63±165.98 vs. 413.44±139.75) (all $p \leq 0.003$). Lipid abnormalities were more frequent in cardiac patients. CRP and fibrinogen showed significant correlations with lipid parameters and BMI across groups

Conclusion: Cardiac diabetic patients demonstrated poorer glycaemic control and higher inflammatory and fibrinogen levels than diabetic patients without cardiac disease. The findings suggest that CRP and fibrinogen may reflect different components of the metabolic and cardiovascular risk profile in diabetes. Further prospective studies are required to determine their clinical and prognostic significance.

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Introduction

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia and an increased risk of both microvascular and macrovascular complications. Cardiovascular disease (CVD) remains one of the major causes of morbidity and mortality among individuals with diabetes. The increased cardiovascular burden associated with diabetes is multifactorial and involves complex interactions between hyperglycemia, insulin resistance, hypertension, dyslipidemia, obesity, oxidative stress, endothelial dysfunction, and chronic inflammation. These metabolic and vascular abnormalities contribute to progressive arterial injury and accelerate atherosclerotic cardiovascular disease [1,2]. Endothelial dysfunction is considered an important early manifestation of diabetic vascular injury. Persistent metabolic abnormalities, particularly hyperglycemia and atherogenic dyslipidemia, promote oxidative stress and inflammatory signaling, impairing endothelial function and vascular homeostasis.[3,4].In addition to conventional cardiovascular risk factors, increasing evidence suggests that inflammatory and hemostatic pathways contribute substantially to the development and progression of cardiovascular complications in patients with diabetes. Chronic inflammation may promote endothelial activation, leukocyte recruitment, vascular remodeling, and atherosclerotic plaque progression, whereas coagulation pathway activation may contribute to thrombus formation and adverse cardiovascular outcomes [5]. C-reactive protein (CRP) is an acute-phase protein synthesized primarily by the liver in response to inflammatory stimuli. It is widely used as a marker of systemic inflammation and has been extensively investigated in relation to cardiovascular risk. In patients with type 2 diabetes, increased CRP concentrations have been associated with adverse cardiovascular outcomes and mortality[6,7]. The persistent metabolic abnormalities characteristic of diabetes may contribute to a pro-inflammatory environment in which hyperglycemia, insulin resistance, obesity, and dyslipidemia interact with inflammatory pathways. Recent evidence further suggests that CRP-related inflammatory mechanisms may participate in endothelial injury, leukocyte recruitment, and progression of atherosclerotic disease [8]. Fibrinogen is another clinically relevant biomarker that links inflammation with hemostasis. It is a hepatic plasma glycoprotein that serves as a fibrin precursor during coagulation and also participates in platelet aggregation and vascular inflammatory processes. Elevated fibrinogen concentrations have been associated with cardiovascular disease and may reflect an underlying pro-inflammatory and prothrombotic state[9]. Large epidemiological studies have demonstrated associations between plasma fibrinogen levels and major cardiovascular outcomes. However, the extent to which fibrinogen acts as a causal mediator rather than a marker of cardiovascular risk remains uncertain[10]. The coexistence of diabetes and cardiovascular disease may therefore be associated with a greater inflammatory and hemostatic burden than diabetes alone. However, the relationships between glycemic control, lipid abnormalities, CRP, and fibrinogen may not be uniform across diabetic populations. Assessment of these biomarkers alongside conventional metabolic parameters may provide additional insight into the biological differences between diabetic patients with and without cardiac disease. In particular, examining correlations between CRP and fibrinogen and glycemic and lipid parameters may help clarify their relationship with the cardiometabolic profile. The present study compared demographic, clinical, metabolic, lipid, inflammatory, and hemostatic characteristics between diabetic patients with cardiac disease and those without documented cardiac disease. We focused on fasting blood glucose, glycated hemoglobin (HbA1c), lipid profile, CRP, and fibrinogen. We also performed Pearson correlation analysis to assess relationships between CRP and fibrinogen and selected metabolic and cardiovascular risk parameters.

Materials and Methods

This case-control analytical study was conducted in the Department of Biochemistry, Khyber Medical College, Peshawar, from October 2025 to March 2026. It involved 200 diabetic participants. The study population was divided into two groups: 100 cardiac diabetic participants and 100 diabetic participants without cardiac disease. State the precise definition and diagnostic criteria used to classify participants as cardiac diabetic, as outlined in the original study protocol. Similarly, insert the study setting, duration, participant recruitment procedure, inclusion and exclusion criteria, and ethical approval information before submission, as these details were not provided in the supplied statistical tables.

Clinical and Biochemical Variables

The evaluated variables included age, systolic blood pressure, diastolic blood pressure, and BMI. Biochemical parameters included fasting blood sugar, HbA1c, total cholesterol, triglycerides, HDL, and LDL. Inflammatory and coagulation-related measurements included CRP and fibrinogen. Overall descriptive statistics showed a mean age of 61.50±9.82 years, systolic blood pressure of 155.02±22.03 mmHg, diastolic blood pressure of 93.43±11.02 mmHg, and BMI of 28.17±3.23 kg/m². Mean FBS was 194.70±79.26 mg/dL, and mean HbA1c was 9.24±3.37%. The mean total cholesterol was 275.84±137.05, triglycerides 307.19±175.96, HDL 42.49±15.97, and LDL 173.83±140.03. Mean CRP was 15.55±6.01, and mean fibrinogen was 446.04±156.49.CRP remained significantly higher among cardiac diabetic participants across BMI categories, including normal weight (20.83±5.26 vs. 10.12±5.93; p=0.026), overweight (18.32±4.89 vs. 10.16±5.89; p<0.001), and obesity (18.26±3.91 vs. 13.90±6.00; p<0.001). Fibrinogen was significantly higher among overweight cardiac diabetic participants (492.77±222.50 vs. 368.10±139.99; p=0.027), while differences in normal-weight and obese participants were not significant. Among hypertensive participants, CRP (18.45±4.14 vs. 12.69±6.23; p<0.001) and fibrinogen (481.06±160.37 vs. 417.28±145.92; p=0.008) were significantly higher in the cardiac diabetic group. Among normotensive participants, CRP remained significantly higher (18.37±4.68 vs. 12.53±6.00; p=0.002), whereas fibrinogen did not differ significantly.

Correlation Analysis

In cardiac diabetic participants, CRP correlated positively with total cholesterol (r=0.210; p=0.036) and HDL (r=0.202; p=0.044). In diabetic participants, CRP was inversely correlated with HDL (r=-0.245; p=0.014). No other significant CRP correlations were identified. Fibrinogen showed a positive correlation with triglycerides in cardiac diabetic participants (r=0.443; p<0.001; R^2=0.195). Among diabetic participants, fibrinogen correlated positively with BMI (r=0.241; p=0.016). Other correlations between fibrinogen and the evaluated clinical or biochemical parameters were not statistically significant.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics version 27.0. Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. Between-group

differences were assessed using appropriate comparative tests, and Pearson's correlation coefficient was used to evaluate relationships between CRP, fibrinogen, and clinical and biochemical parameters. A p-value <0.05 was considered statistically significant.

Results

Baseline Characteristics

We included 200 participants: 100 with cardiac diabetes and 100 with diabetes. The overall mean age was 61.50±9.82 years (range, 45–90 years). Mean systolic and diastolic blood pressures were 155.02±22.03 and 93.43±11.02 mmHg, respectively, and mean BMI was 28.17±3.23 kg/m². Mean FBS and HbA1c were 194.70±79.26 mg/dL and 9.24±3.37%, respectively. Mean total cholesterol, triglycerides, HDL, and LDL were 275.84±137.05, 307.19±175.96, 42.49±15.97, and 173.83±140.03, respectively. Mean CRP and fibrinogen were 15.55±6.01 and 446.04±156.49, respectively.

Comparison Between Groups

Sex and residence distributions were comparable between groups. Overall, 99 (49.5%) participants were male and 101 (50.5%) female; 149 (74.5%) were from urban and 51 (25.5%) from rural areas. Obesity was present in 139 (69.5%) participants, with no significant difference between the cardiac diabetic and diabetic groups. Hypertension was present in 163 (81.5%) participants and was similarly distributed between groups (81.0% vs. 82.0%; p=0.427).Cardiac diabetic participants had significantly higher FBS (213.80±91.62 vs. 175.61±59.14 mg/dL; p<0.001) and HbA1c (10.17±3.45% vs. 8.31±3.04%; p<0.001). No significant between-group differences were observed in age, systolic or diastolic blood pressure, BMI, total cholesterol, triglycerides, HDL, or LDL.CRP was significantly higher in the cardiac diabetic group (18.43±4.22 vs. 12.67±6.17; p<0.001), as was fibrinogen (478.63±165.98 vs. 413.44±139.75; p=0.003).

Glycemic, Lipid and Biomarker Abnormalities

Overall, abnormal FBS, HbA1c, total cholesterol, triglycerides, HDL, LDL, CRP and fibrinogen were observed in 86.5%, 66.0%, 60.0%, 89.5%, 51.0%, 38.5%, 81.0% and 68.0% of participants, respectively. Abnormal HbA1c was more frequent in cardiac diabetic participants than in diabetic participants (74% vs. 58%; p=0.008). Similarly, abnormal triglycerides (97% vs. 82%; p<0.001), HDL (60% vs. 42%; p=0.005), CRP (99% vs. 63%; p<0.001), and fibrinogen (77% vs. 59%; p=0.003) were significantly more common in the cardiac diabetic group. Abnormal FBS, total cholesterol, and LDL did not differ significantly.

Table I. Baseline characteristics of study participants

Characteristic	Total (N=200)	Cardiac diabetic (n=100)	Diabetic (n=100)	p-value
Age, years	61.50±9.82	62.52±8.95	60.49±10.56	0.144
Systolic BP, mmHg	155.02±22.03	153.30±22.92	156.75±21.07	0.269
Diastolic BP, mmHg	93.43±11.02	93.70±11.63	93.15±10.44	0.725
BMI, kg/m²	28.17±3.23	28.30±3.18	28.03±3.29	0.555
FBS, mg/dL	194.70±79.26	213.80±91.62	175.61±59.14	<0.001
HbA1c, %	9.24±3.37	10.17±3.45	8.31±3.04	<0.001
Total cholesterol, mg/dL	275.84±137.05	279.61±151.82	272.06±121.15	0.697
Triglycerides, mg/dL	307.19±175.96	324.37±142.60	290.02±203.23	0.168
HDL, mg/dL	42.49±15.97	40.67±16.54	44.32±15.25	0.106
LDL, mg/dL	173.83±140.03	176.09±154.09	171.58±125.14	0.820
CRP	15.55±6.01	18.43±4.22	12.67±6.17	<0.001
Fibrinogen	446.04±156.49	478.63±165.98	413.44±139.75	0.003

Values are presented as mean±SD. BP, blood pressure; BMI, body mass index; FBS, fasting blood sugar; HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; CRP, C-reactive protein.

Table 2. Distribution of demographic and clinical characteristics

Characteristic	Cardiac diabetic, n (%)	Diabetic, n (%)	Total, n (%)
Gender			
Male	51 (51.0)	48 (48.0)	99 (49.5)
Female	49 (49.0)	52 (52.0)	101 (50.5)
Residence			
Urban	73 (73.0)	76 (76.0)	149 (74.5)
Rural	27 (27.0)	24 (24.0)	51 (25.5)
BMI category			
Normal	6 (6.0)	4 (4.0)	10 (5.0)
Overweight	22 (22.0)	29 (29.0)	51 (25.5)
Obese	72 (72.0)	67 (67.0)	139 (69.5)
Hypertension			
Hypertensive	81 (81.0)	82 (82.0)	163 (81.5)
Normotensive	19 (19.0)	18 (18.0)	37 (18.5)

Data are presented as numbers (percentages). BMI categories are reported according to the classification used in the study. The supplied analysis showed no statistically significant difference in hypertension between groups (p=0.427) and no significant difference in BMI categories.

Table 3. Glycaemic, lipid and inflammatory biomarker abnormalities

Parameter	Abnormal, n (%)	Normal, n (%)
Fasting blood sugar	173 (86.5)	27 (13.5)
HbA1c	132 (66.0)	68 (34.0)
Total cholesterol	120 (60.0)	80 (40.0)
Triglycerides	179 (89.5)	21 (10.5)
HDL	102 (51.0)	98 (49.0)
LDL	77 (38.5)	123 (61.5)

CRP	162 (81.0)	38 (19.0)
Fibrinogen	136 (68.0)	64 (32.0)

Data are presented as numbers (percentages). We defined abnormalities according to the predefined study classification. HDL, high-density lipoprotein; LDL, low-density lipoprotein; CRP, C-reactive protein.

Table 4. Comparison of biochemical abnormalities between cardiac diabetic and diabetic participants

Parameter	Cardiac diabetic, n (%)	Diabetic, n (%)	p-value
FBS			
Abnormal	89 (89.0)	84 (84.0)	0.151
Normal	11 (11.0)	16 (16.0)	
HbA1c			
Abnormal	74 (74.0)	58 (58.0)	0.008
Normal	26 (26.0)	42 (42.0)	
Total cholesterol			
Abnormal	57 (57.0)	63 (63.0)	0.193
Normal	43 (43.0)	37 (37.0)	
Triglycerides			
Abnormal	97 (97.0)	82 (82.0)	<0.001
Normal	3 (3.0)	18 (18.0)	
HDL			
Abnormal	60 (60.0)	42 (42.0)	0.005
Normal	40 (40.0)	58 (58.0)	
LDL			
Abnormal	34 (34.0)	43 (43.0)	0.095
Normal	66 (66.0)	57 (57.0)	
CRP			
Abnormal	99 (99.0)	63 (63.0)	<0.001
Normal	1 (1.0)	37 (37.0)	
Fibrinogen			
Abnormal	77 (77.0)	59 (59.0)	0.003
Normal	23 (23.0)	41 (41.0)	

Data are presented as numbers (percentages). P-values represent comparisons between cardiac diabetic and diabetic participants. FBS, fasting blood sugar; HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; CRP, C-reactive protein.

Table 5. Pearson correlations of CRP with clinical and biochemical parameters

Parameter	Cardiac diabetic r	p-value	Diabetic r	p-value
Age	-0.096	0.340	-0.136	0.176
Systolic BP	0.049	0.631	0.108	0.283
Diastolic BP	0.027	0.789	0.116	0.250
BMI	-0.030	0.766	0.179	0.074
FBS	0.051	0.611	0.044	0.662
HbA1c	-0.132	0.191	0.150	0.137
Total cholesterol	**0.210**	**0.036**	0.066	0.511
Triglycerides	-0.055	0.585	-0.048	0.635
HDL	**0.202**	**0.044**	**-0.245**	**0.014**
LDL	0.189	0.060	0.106	0.292

Pearson correlation coefficients (r) are shown. *p<0.05 was considered statistically significant. BP, blood pressure; BMI, body mass index; FBS, fasting blood sugar; HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; CRP, C-reactive protein.

Table 6. Comparison of CRP according to BMI and hypertension status

Stratifying variable	Cardiac diabetic	Diabetic	p-value
BMI category			
Normal	**20.83±5.26**	10.12±5.93	0.026
Overweight	**18.32±4.89**	10.16±5.89	<0.001
Obese	**18.26±3.91**	13.90±6.00	<0.001
Hypertension status			
Hypertensive	**18.45±4.14**	12.69±6.23	<0.001
Normotensive	**18.37±4.68**	12.53±6.00	0.002

Values are presented as mean±SD. P-values represent between-group comparisons within each BMI or hypertension category. CRP, C-reactive protein; BMI, body mass index.

Table 7. Pearson correlations of fibrinogen with clinical and biochemical parameters

Parameter	Cardiac diabetic r	p-value	Diabetic r	p-value
Age	-0.102	0.314	-0.080	0.429
Systolic BP	0.008	0.934	0.047	0.644
Diastolic BP	0.165	0.102	0.057	0.573
BMI	0.134	0.184	**0.241**	**0.016**
FBS	-0.063	0.530	0.116	0.248
HbA1c	0.058	0.567	0.041	0.683
Total cholesterol	0.119	0.240	0.165	0.100
Triglycerides	**0.443**	**<0.001**	0.078	0.443
HDL	-0.071	0.486	-0.012	0.907
LDL	0.047	0.644	0.144	0.153

Pearson correlation coefficients (r) are shown. *p<0.05; **p<0.01. BP, blood pressure; BMI, body mass index; FBS, fasting blood sugar; HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein

Table 8. Comparison of fibrinogen according to BMI and hypertension status

Stratifying variable	Cardiac diabetic	Diabetic	p-value
BMI category			
Normal	409.00±126.63	297.50±42.72	0.086
Overweight	492.77±222.50	368.10±139.99	0.027
Obese	480.11±148.88	439.99±135.88	0.099
Hypertension status			
Hypertensive	481.06±160.37	417.28±145.92	0.008
Normotensive	468.26±192.50	395.94±109.02	0.167

Values are presented as mean±SD. P-values Represent between-group comparisons within each BMI or hypertension category.

Discussion

This study shows important differences between diabetic patients with cardiac disease and those without, particularly in glycaemic control, inflammation, and fibrinogen. Although several conventional clinical characteristics were similar between groups, cardiac diabetic participants had significantly higher FBS, HbA1c, CRP, and fibrinogen. These findings suggest that cardiovascular involvement among diabetic patients may be accompanied by a more pronounced metabolic and inflammatory burden. The relationship between glycaemic exposure and cardiovascular risk in diabetes has been extensively investigated, with both the magnitude and duration of hyperglycemia considered relevant to cardiovascular complications[11].The first major finding was the difference in glycaemic control. Cardiac diabetic participants had substantially higher FBS and HbA1c than diabetic participants without cardiac disease. Mean FBS exceeded 200 mg/dL in the cardiac diabetic group, while mean HbA1c was above 10%. In contrast, the corresponding values in the non-diabetic group were lower, although still indicative of considerable glycaemic disturbance. These findings highlight the importance of chronic hyperglycemia as part of the overall cardiovascular risk profile in diabetes. Previous evidence indicates that the magnitude and duration of hyperglycemia are relevant to the development of cardiovascular complications in type 2 diabetes[12].The categorical analysis supported this observation. Abnormal HbA1c was significantly more common among cardiac diabetic participants than among diabetic participants. However, abnormal FBS did not differ significantly between the groups. This difference may reflect that HbA1c represents longer-term glycaemic exposure, whereas FBS reflects glucose at a particular point in time. Therefore, the stronger group difference in HbA1c may indicate a more sustained metabolic disturbance among cardiac diabetic patients[11].A second important finding was the high prevalence of obesity. Nearly 70% of the study population was classified as obese, and obesity was common in both groups. Although the proportion of obesity was somewhat higher among cardiac diabetic participants, the group difference was not statistically significant. This indicates that obesity alone did not distinguish the two groups in this sample. Nevertheless, obesity is closely linked to low-grade systemic inflammation, and previous evidence shows a positive association between BMI and circulating CRP concentrations [13]. Nevertheless, BMI showed an important relationship with fibrinogen among diabetic participants. We identified a positive correlation between BMI and fibrinogen in patients without cardiac disease. This finding suggests that increased adiposity may activate inflammatory or hemostatic pathways even before overt cardiac disease is present. Previous population-based evidence has shown associations between fibrinogen and BMI, as well as other metabolic abnormalities, supporting the biological plausibility of this observation [14]. The absence of a significant correlation in cardiac diabetic participants may reflect the influence of additional factors associated with established cardiovascular disease. Hypertension was also highly prevalent, affecting more than four-fifths of the study population. However, prevalence was almost identical in both groups. This suggests that hypertension, although highly prevalent and clinically important, did not differentiate cardiac diabetic participants from diabetic participants in the present sample. The absence of a between-group difference should therefore not be interpreted as evidence that hypertension is unimportant in cardiovascular risk; rather, its high prevalence in both groups may have reduced its discriminatory value in this particular population. The inflammatory findings were particularly notable. Mean CRP was substantially higher in cardiac diabetic patients than in diabetic patients without cardiac disease. Furthermore, almost all cardiac diabetic participants were categorized as having abnormal CRP, compared with approximately two-thirds of diabetic participants. The difference remained evident when participants were stratified according to BMI and hypertension [15]. These findings strengthen the observation that the cardiac diabetic group had a greater inflammatory burden. Elevated CRP has been consistently associated with cardiovascular risk, and meta-analytic evidence in patients with type 2 diabetes has shown associations between higher CRP concentrations and cardiovascular and all-cause mortality. These CRP findings matter because inflammation is increasingly recognized as a component of cardiometabolic disease. However, the present study design does not allow determination of whether elevated CRP contributed to cardiac disease or resulted from it. CRP is a nonspecific inflammatory marker and can be affected by multiple clinical conditions [16]. Therefore, elevated CRP should be interpreted as evidence of an inflammatory state rather than proof of a specific cardiovascular mechanism. This cautious interpretation aligns with previous literature emphasizing the strong epidemiological association of CRP with cardiovascular disease while noting uncertainty about its direct causal role [15]. Interestingly, CRP correlations with glycaemic indices were not statistically significant. Despite the significantly higher FBS and HbA1c in cardiac diabetic participants, CRP did not demonstrate a significant linear relationship with either parameter within the individual groups. This indicates that group-level differences do not necessarily imply a direct linear relationship between two continuous variables. Other factors may contribute to inflammatory status independently of glycaemic control[16]. Thus, the higher CRP observed in the cardiac diabetic group should not be interpreted as being explained solely by differences in FBS or HbA1c.The lipid findings were also noteworthy. Triglyceride abnormality was extremely common overall and was particularly frequent among cardiac diabetic participants. Almost all cardiac diabetic participants had abnormal triglycerides according to the study's classification [17]. Although the continuous triglyceride values did not differ significantly between groups, categorical analysis demonstrated a significant difference. This may indicate that the distribution around the selected clinical threshold mattered even when mean values did not differ significantly. The close relationship between triglyceride abnormalities and other metabolic disturbances is consistent with previous research on fibrinogen and cardiometabolic risk factors [18]. Fibrinogen also distinguished the groups. Cardiac diabetic participants had significantly higher mean fibrinogen levels, and abnormal fibrinogen was also more frequent. This supports the possibility of increased inflammatory and prothrombotic activity among diabetic patients with cardiac disease. Fibrinogen is an acute-phase reactant and the principal precursor of fibrin, and it has been associated with thrombosis, platelet aggregation, and cardiovascular disease [19]. Large prospective studies have also demonstrated associations between higher

plasma fibrinogen levels and coronary heart disease and stroke. However, the causal nature of these associations remains uncertain. The correlation between fibrinogen and triglycerides in cardiac diabetic participants was particularly important. The correlation coefficient was 0.443 ($p<0.001$), representing the strongest relationship identified in the analysis. The corresponding scatter plot demonstrated a positive trend with R^2 of approximately 0.195. This suggests that approximately one-fifth of the variation in fibrinogen in this group was explained by its linear relationship with triglycerides, although most variation remained unexplained. The association is consistent with previous evidence showing relationships between fibrinogen concentrations and triglycerides and other established metabolic risk factors [20].The association between fibrinogen and triglycerides may be biologically plausible because both may reflect aspects of metabolic and inflammatory dysregulation. However, the cross-sectional design does not allow causal interpretation. It would be inappropriate to conclude that elevated triglycerides directly cause increased fibrinogen or vice versa. Previous large-scale analyses have similarly emphasized that, although fibrinogen is associated with cardiovascular outcomes, its causal relevance requires further investigation [21].Another finding was the positive relationship between fibrinogen and BMI among diabetic participants without cardiac disease. This association suggests that adiposity may drive hemostatic activation before cardiovascular disease becomes clinically apparent. The finding is potentially relevant because obesity was highly prevalent in the overall study population. Previous population-level research has reported positive associations between fibrinogen and BMI, supporting the plausibility of this observation[13].The relationship between HDL and CRP differed between groups. In cardiac diabetic participants, CRP demonstrated a weak positive correlation with HDL, whereas in diabetic participants without cardiac disease, the relationship was weakly inverse and statistically significant. Because the correlation coefficients were small, interpret these findings cautiously [8]. They may reflect differences in the underlying clinical characteristics of the two groups, treatment patterns, or other unmeasured factors. Previous studies have demonstrated that inflammatory and hemostatic biomarkers may correlate with several metabolic variables. Still, these relationships are not necessarily uniform across populations. Several conventional lipid variables did not demonstrate significant correlations with CRP or fibrinogen. Similarly, age, systolic blood pressure, and diastolic blood pressure generally showed no significant associations. These findings emphasize that inflammatory and hemostatic biomarkers may provide information not fully captured by conventional clinical measurements. Fibrinogen, in particular, is associated with several established cardiovascular risk factors and retains an epidemiological relationship with cardiovascular outcomes[17]. The scatter diagrams further demonstrate that many of the investigated relationships were weak. For example, CRP versus BMI, FBS, HbA1c, and triglycerides generally showed low R^2 values. Similarly, fibrinogen showed limited linear relationships with several metabolic variables. These observations matter because statistical significance should not automatically imply a strong clinical association. The magnitude of the correlation also matters. A statistically significant association can have limited explanatory or clinical importance when the correlation coefficient and corresponding R^2 are small. The study has several strengths. First, the sample included equal numbers of cardiac diabetic and diabetic participants, facilitating direct comparison[22]. Second, the analysis incorporated a broad range of clinical and biochemical variables rather than focusing only on glucose levels. Third, we evaluated both CRP and fibrinogen, allowing assessment of inflammatory and hemostatic characteristics. Finally, the study included correlation analyses and graphical assessment of relationships between biomarkers and metabolic variables. These features provide a broader assessment of the metabolic, inflammatory, and hemostatic characteristics of the two study groups. Several limitations should nevertheless be acknowledged[8]. The supplied tables do not provide sufficient information regarding the study setting, sampling method, diagnostic criteria for cardiac disease, duration of diabetes, medication use, or other potential confounding factors. These variables may substantially influence CRP, fibrinogen, lipid profile, and glycaemic control. In observational research, inadequate adjustment for confounding can bias association estimates[18]. The cross-sectional design also prevents establishing temporal or causal relationships. Accordingly, interpret the observed differences in CRP and fibrinogen as associations, not evidence that these biomarkers caused cardiac disease. Similarly, the association between triglycerides and fibrinogen cannot establish a directional relationship. Appropriate reporting and interpretation of cross-sectional observational studies require explicit consideration of study design, potential bias, confounding, and limitations on causal inference [19]. Another limitation is the absence of multivariable analysis in the supplied results. Because age, BMI, hypertension, diabetes duration, glycaemic control, and lipid abnormalities may influence inflammatory biomarkers simultaneously, adjusted regression analysis could better assess independent associations. Multivariable regression is particularly useful in observational research when the objective is to estimate associations while accounting for potential confounding variables[11]. Future studies should therefore include larger, more representative samples; clearly defined cardiac diagnostic criteria; information on diabetes duration and medication use; and longitudinal follow-up. Multivariable regression models incorporating clinically relevant confounders would also help determine whether CRP and fibrinogen remain independently associated with cardiac disease after adjustment. Standardized reporting according to the STROBE recommendations would further improve transparency and facilitate interpretation and comparison with other observational studies. Overall, the present findings suggest that diabetic patients with cardiac disease had a greater burden of poor glycaemic control, systemic inflammation, and elevated fibrinogen than diabetic patients without cardiac disease. The particularly strong association between fibrinogen and triglycerides in the cardiac diabetic group and the association between fibrinogen and BMI in the non-cardiac diabetic group provide potentially relevant hypotheses for future investigation. Nevertheless, these findings should be interpreted as associations rather than causal relationships, and prospective studies with appropriate adjustment for clinical and treatment-related confounders are needed to determine the independent prognostic significance of CRP and fibrinogen.

Conclusion

This study demonstrated that diabetic patients with cardiac disease had significantly higher fasting blood glucose, HbA1c, CRP, and fibrinogen levels than diabetic patients without cardiac disease. Cardiac diabetic participants also showed a greater burden of abnormal triglycerides, HDL, CRP, and fibrinogen. Fibrinogen demonstrated a moderate positive correlation with triglycerides in cardiac diabetic participants, while BMI was positively correlated with fibrinogen among diabetic participants without cardiac disease. CRP showed weaker and variable relationships with lipid parameters. Overall, the findings indicate that cardiac involvement in diabetes is associated with poorer glycaemic control and a greater inflammatory and hemostatic burden. CRP and fibrinogen may therefore have potential value as complementary biomarkers for characterizing cardiometabolic risk. However, prospective studies with standardized cardiac definitions, larger samples

and multivariable analyses are needed before their independent clinical or prognostic value can be established.

Ethical Approval

The Institutional Research Ethics Board (IREB) of Khyber Medical College, Peshawar, approved the study on **3 September 2025 (Approval No. 628/DME/KMC),** and we kept participant information confidential throughout.

Informed Consent

We obtained written informed consent from all participants before enrollment. We informed participants about the study objectives, procedures, potential benefits, and their right to participate voluntarily or withdraw at any time without affecting their medical care. The authors strictly maintained participants' confidentiality and privacy and did not disclose personal identifying information.

Conflict of Interest

The authors declare no conflict of interest related to this study's conduct, authorship, or publication.

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Data Availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request. The data are not publicly available because of privacy and confidentiality considerations for the study participants.

Authors' Contributions

Bibi Hajira Ishaq: Conceptualization, study design, methodology, data collection, data interpretation, and manuscript drafting.

Muhammad Shabir: Methodology, data collection, literature review, data interpretation, and critical revision of the manuscript.

Zafar Ali: Study supervision, methodology, data interpretation, and critical review of the manuscript.

Muddasir Ahmed, Zahid Sarfaraz: Conceptualization, data collection, literature review, data interpretation, and critical revision of the manuscript.

Sobia Ali: Data collection, literature review, data analysis, interpretation of results, and manuscript revision.Study supervision, conceptualization, methodology, critical review, and final approval of the manuscript.

All authors: Contributed to the conception/design or interpretation of the work, reviewed and approved the final version, and agreed to be accountable for all aspects of the work in accordance with **ICMJE** authorship criteria.

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Original Article

Exploring the Risks of Postoperative Surgical Site Infection After Craniotomy: A Retrospective Observational Study

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Abstract

Objective: To assess the risk of postoperative surgical site infection after craniotomy and identify risk factors for such infection.

Methodology: This Retrospective Observational Study was conducted in the Department of Neurosurgery, MMC/BKMC Mardan, from January to June 2024. included 100 patients who underwent craniotomy. We collected patient data from medical records, including demographic, clinical, and operative data. We identified all patients with SSI within 30 days after surgery based on the Centers for Disease Control and Prevention (CDC) definition. We performed statistical analyses using SPSS version 27.0. We presented continuous variables as mean ± SD and categorical variables as frequencies and percentages, and used logistic regression to identify independent predictors. We considered $p < 0.05$ statistically significant.

Results: Of the 100 patients, 18 (18.0%) developed postoperative SSI. The mean age was 48.7 ± 15.3 years, with 61% males and 39% females. Patients with SSI were significantly older than those without infection (56.2 ± 13.1 vs. 47.1 ± 15.2 years; p=0.018). Diabetes mellitus was more frequent in the SSI group (33.3% vs. 11.0%; p=0.011). Operative duration exceeding four hours (72.2% vs. 35.4%; p=0.004), emergency craniotomy (50.0% vs. 22.0%; p=0.021), and smoking (44.4% vs. 19.5%; p=0.028) were significantly associated with SSI.

Conclusion: SSI is a common post-craniotomy complication. Advanced age, diabetes, prolonged surgery, emergency procedures, and smoking increase risk, while prevention strategies reduce infection rates.

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Introduction

Surgical site infection (SSI) is one of the most important postoperative complications after craniotomy, which is a major cause of morbidity, length of hospital stay, healthcare cost, and death in rare instances. Although there has been significant progress in neurosurgical practice, perioperative antimicrobial prophylaxis, sterile operative conditions, and wound care, SSIs remain a significant problem in neurosurgical practice globally. The reported rate of SSI following craniotomy has ranged from 1% to 20%, depending on the patient population, the complexity of the surgical procedure, and the quality of the infection-control measures at the institution, as well as on the definition of SSI. Infections can affect superficial incisional tissues, deep soft tissues, bone flaps, the meninges, or intracranial structures. They may require extended antibiotic therapy, additional surgery, and/or removal of the bone flap [1,2].Patients requiring craniotomy are especially vulnerable to postoperative infections due to the length of the operation, exposure of intracranial structures, placement of foreign substances, the leakage of CSF, and underlying neurological disorders. In addition, the majority of neurosurgical patient population have other medical comorbidities, like diabetes mellitus, hypertension, chronic kidney disease, malnutrition, obesity, smoking, and immunosuppression that affect wound healing and vulnerability to infection. Other factors that raise the risk of postoperative SSI include emergency procedures, traumatic brain injury, repeat craniotomy, prolonged intensive care unit (ICU) stay, and mechanical ventilation [3,4].Advanced age, diabetes mellitus, obesity, smoking, prolonged operative time, cerebrospinal fluid leakage, emergency surgery, contaminated wound, repeat surgery, and a prolonged preoperative hospital stay are significant risk factors for postoperative SSI after craniotomy. However, these factors vary across settings because of differences in patient populations, surgical techniques, perioperative management, antimicrobial policies, and healthcare infrastructure. Thus, local epidemiological information is crucial for identifying institution-specific risk factors and establishing targeted preventive measures [5,6]. Postoperative SSI after craniotomy is not only a significant clinical problem, but also a major economic burden on the healthcare system. The patients who go on to develop SSI often need longer courses of intravenous antibiotic treatment, further imaging tests, repeat surgery, intensive care unit (ICU) admission, and extended hospital stay. Such complications have a great impact on the treatment cost, besides postponing neurological rehabilitation and recovery. Furthermore, postoperative infection can negatively affect long-term neurological function and quality of life [7,8]. Identifying patients at early risk allows clinicians to optimize modifiable risk factors before surgery, implement evidence-based preventive measures, and improve postoperative monitoring. Perioperative antibiotic prophylaxis, careful surgery, blood sugar control, smoking cessation, shortening operative time, minimizing temperature changes, and standardizing infection-prevention packages have shown a positive impact in reducing postoperative infections. However, despite these precautions, SSI persists, and institutions must continually assess contributing factors [9,10]. There is very little information available in Pakistan on the incidence and determinants of postoperative SSI after craniotomy. Earlier studies are mainly from developed countries, where patients' characteristics, healthcare resources, and infection-control practices differ significantly from those in developing healthcare settings. Thus, identifying local risk factors is crucial to establish effective preventive measures and improve neurosurgical outcomes.

Materials and Methods

Study Design and Setting

We conducted a retrospective observational study from January to June 2024. The study included adult patients undergoing craniotomy at the study center. We obtained relevant demographic, clinical, operative, and postoperative information from medical records. Patients were followed for 30 days after surgery to assess the occurrence of surgical site infection (SSI) according to standard diagnostic criteria.

Participants

We included 100 consecutive adult patients who underwent elective or emergency craniotomy during the study period. Demographic characteristics, clinical findings, operative details, and postoperative outcomes were reviewed from the available medical records. The primary outcome was the development of SSI within 30 days following craniotomy.

Sample Size Calculation

The sample size was calculated using the WHO sample size calculator, assuming an expected postoperative SSI prevalence of **15%**, a **95%** confidence level**,** and an allowable margin of error. Patients meeting the eligibility criteria were enrolled consecutively during the study period, resulting in a final sample of 100 patients.

Inclusion Criteria

- Patients were included if they met all of the following criteria:
- Age ≥18 years.
- Underwent elective or emergency craniotomy.
- Complete medical and operative records were available.
- Had a minimum 30-day postoperative follow-up.
- Underwent craniotomy for histopathological or traumatic indications.

Exclusion Criteria

- Surgery for a pre-existing wound in the same head region.
- A documented wound infection in the head region before the index surgery.
- A non-surgical burr-hole procedure instead of craniotomy.
- Incomplete medical or operative records.
- Death within **48 hours** after surgery.
- Loss to postoperative follow-up before completion of the 30-day assessment.

Diagnostic & Management Strategy

Postoperative SSI was diagnosed based on the Centers for Disease Control and Prevention (CDC) definition. Patients received conventional antibiotic prophylaxis, routine wound care, and standard-of-care treatment as appropriate, such as culture-based antibiotic therapy and surgical debridement when necessary.

Statistical Analysis

We used SPSS 27.0 to analyze the data. Data for continuous variables were presented as mean ± SD, and for categorical variables as frequencies and percentages. We identified significant predictors using the chi-square test, independent t-test, and multivariable logistic regression. We defined $p < 0.05$ as statistically significant.

Results

A total of 100 patients underwent craniotomy during the study period. The mean age was 48.7 ± 15.3 years, with 61 (61%) males and 39 (39%) females. Postoperative surgical site infection developed in 18 patients (18%), whereas 82 patients (82%) had an uncomplicated postoperative course. Patients with SSI were significantly older than those without

infection (56.2 ± 13.1 vs. 47.1 ± 15.2 years; p=0.018). Diabetes mellitus was present in 6 (33.3%) patients with SSI compared with 9 (11.0%) patients without SSI (p=0.011). Operative duration exceeding four hours occurred in 13 (72.2%) infected patients and 29 (35.4%) non-infected patients (p=0.004). Emergency craniotomy was performed in 9 (50.0%) patients with SSI compared with 18 (22.0%) patients without SSI (p=0.021). Smoking was significantly associated with postoperative infection (44.4% vs. 19.5%; p=0.028). Multivariable logistic regression identified prolonged operative duration (adjusted OR=3.42; 95% CI: 1.28–9.14; p=0.014) and diabetes mellitus (adjusted OR=2.96; 95% CI: 1.07–8.17; p=0.036) as independent predictors of SSI. No statistically significant association was observed between patient sex and postoperative infection (p=0.462).

Table 1. Baseline Demographic and Clinical Characteristics of the Study Population (N = 100)

Variable	Frequency (%) / Mean ± SD
Age (years)	**48.7 ± 15.3**
18–40 years	31 (31.0)
41–60 years	43 (43.0)
>60 years	26 (26.0)
Gender	
Male	61 (61.0)
Female	39 (39.0)
Diabetes mellitus	15 (15.0)
Hypertension	34 (34.0)
Smoking	24 (24.0)
Elective craniotomy	73 (73.0)
Emergency craniotomy	27 (27.0)
Operative duration >4 hours	42 (42.0)
Surgical Site Infection (SSI)	18 (18.0)
No SSI	82 (82.0)

Values are presented as mean ± standard deviation or frequency (%). SSI = Surgical Site Infection.

Table 2. Comparison of Patients with and Without Surgical Site Infection

Variable	SSI (n=18)	No SSI (n=82)	P-value
Age (years), Mean ± SD	56.2 ± 13.1	47.1 ± 15.2	0.018
Male gender	12 (66.7%)	49 (59.8%)	0.587
Diabetes mellitus	6 (33.3%)	9 (11.0%)	0.011
Hypertension	9 (50.0%)	25 (30.5%)	0.118
Smoking	8 (44.4%)	16 (19.5%)	0.028
Emergency surgery	9 (50.0%)	18 (22.0%)	0.021
Operative duration >4 hours	13 (72.2%)	29 (35.4%)	0.004

Continuous variables are expressed as mean ± SD, whereas categorical variables are presented as frequency (%). P-values were calculated using the independent t-test or Chi-square test as appropriate. Statistical significance was set at p<0.05.

Table 3. Multivariable Logistic Regression Analysis of Risk Factors for Postoperative Surgical Site Infection

Variable	Adjusted OR	95% CI	P-value
Age >60 years	1.84	0.78–4.92	0.112
Diabetes mellitus	2.96	1.07–8.17	0.036
Smoking	2.18	0.94–5.31	0.071
Emergency surgery	2.41	0.96–6.05	0.061
Operative duration >4 hours	3.42	1.28–9.14	0.014

Multivariable logistic regression identified independent predictors of postoperative surgical site infection. OR = Odds Ratio; CI = Confidence Interval. Variables with p<0.05 were considered statistically significant.

Table 4. Clinical Outcomes of Patients with Surgical Site Infection (n = 18)

Outcome	Frequency (%)
Culture-guided antibiotic therapy	18 (100.0)
Surgical wound debridement	9 (50.0)
Bone flap removal	4 (22.2)
Complete infection resolution	15 (83.3)
Persistent infection	3 (16.7)
Infection-related mortality	0 (0.0)
Mean hospital stay (days), Mean ± SD	16.8 ± 5.2

Clinical outcomes among patients who developed postoperative surgical site infection following craniotomy. Values are expressed as frequency (%) or mean ± standard deviation.

Discussion

This retrospective cohort study aimed to assess the risk factors for postoperative surgical site infection (SSI) in 100 patients who underwent craniotomy. The overall SSI incidence was 18%, consistent with rates reported in recent neurosurgery literature, which typically range from 5% to 20% depending on patient characteristics, surgical complexity, the surveillance system, and the hospital infection-control program [11,12]. Our incidence is slightly lower than in some developed healthcare systems but within the international range and may be attributed to patient profiles, emergency surgical workload, or available healthcare resources. In the current study, increasing age was significantly correlated with PS-SSI. Patients who were diagnosed with SSI were significantly older than those without infection (56.2 ± 13.1 vs. 47.1 ± 15.2 years; p=0.018). Advanced age has consistently been identified as an important risk factor, as elderly patients are likely to have weaker immune function, multiple comorbidities, lesser tissue repair ability, and poorer nutritional status. Systematic reviews and multicenter studies have also recently shown that age is a risk factor for postoperative infection after neurosurgery [13,14]. One of the most important independent risk factors for the development of SSI in our cohort was diabetes mellitus. Nearly three times more patients with diabetes were infected (adjusted OR=2.96, p=0.036). Hyperglycemia affects neutrophils, collagen formation, angiogenesis, and wound healing, leading to greater susceptibility to postoperative infection. Recent meta-analyses and observational studies from 2023 to 2025 also show diabetes mellitus as a major independent risk factor for post-craniotomy SSI [15,16]. The other independent predictor of SSI in the present study was operation length (>4 hours; adjusted OR 3.42, p=0.014). A longer procedure allows for more time for the environment to contaminate surgical wounds, more surgical tissue manipulation, and often more technically complex procedures. These findings have been consistently reported in recent systematic reviews, such as the 2013 study, which showed that operative time is one of the most reproducible

predictors of postoperative neurosurgical infections [17]. The results confirm the need to plan surgery efficiently and avoid unnecessary delays. Univariate analysis found that emergency craniotomy was significantly associated with postoperative SSI. Traumatic brain injury, intracranial bleed, contaminated wounds, poor preoperative optimization, and limited preparation time are common aspects of emergency surgery and can lead to a higher risk for infection [18]. After multivariable adjustment, emergency surgery was no longer an independent predictor, consistent with recent cohort studies showing that emergency neurosurgery was associated with a higher crude SSI rate than elective surgery [19]. Other factors that had a significant association with SSI in our study were smoking. Smoking negatively affects tissue oxygenation, microvascular circulation, collagen synthesis, and immune function, which slows wound healing. More recently, several studies have also shown that smoking leads to wound complications and surgical site infections after major neurosurgical procedures [20]. This study demonstrates the importance of smoking cessation programs before surgery and interventions that optimize patients perioperatively. No statistically significant difference was found between postoperative SSI and patient sex, consistent with several recent reports that found that sex is not an independent factor for postoperative infection after controlling for other clinical factors. Instead, the patient's comorbidities and operative factors seem to play a larger role in infection risk. The study's retrospective design and small sample size may limit the generalizability of the results. Selection bias and incomplete documentation, inherent in retrospective data collection, could not be avoided. Furthermore, we did not assess microbiological profiles, antimicrobial resistance patterns, or long-term patient outcomes.

Conclusion

Surgical site infection is a major complication after craniotomy. Risk factors for increased infection included advanced age, diabetes mellitus, prolonged operative time, emergency surgery, and smoking. Proper risk stratification, optimizing comorbidities, and following evidence-based perioperative infection-prevention guidelines could improve neurosurgical outcomes and reduce SSI incidence.

Disclaimer: Nil

Conflict of Interest: Nil

Funding Disclosure: Nil

Ethical approval

Ethical approval was granted by the Ethical Committee of Bacha Khan Medical College, Mardan **(IRB No. 940/Neuro/BKMC) on 22 September 2024.**

Authors' Contributions

Muhammad Ishaq: Conceptualization, study design, literature search, study screening, data extraction, manuscript drafting, and critical revision.

Naeem ul Haq: Conceptualization, supervision, interpretation of findings, critical revision of the manuscript, and final approval of the version to be published.

Syed Nasir Shah: Literature search, study screening, data extraction, preparation of tables and figures, and manuscript revision.

Rizwan Ali: Data extraction, literature review, manuscript drafting and revision, and reference verification.

All authors read and approved the final manuscript and agreed to be accountable for all aspects of the work.

Data Availability

This is a systematic review. All data extracted for this review were derived from the published, peer-reviewed, or preprint sources cited in the References section and summarized in Table 1; no new primary data were generated.

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Original Article

Prevalence of Polycystic Ovarian Syndrome and its Associated Lifestyle Risk Factors: A Cross-Sectional Study

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Abstract

Objective: To assess the prevalence, clinical manifestations, metabolic abnormalities, and lifestyle-related risk factors of PCOS among women of reproductive age attending a tertiary care hospital in Nowshera, Pakistan.

Methodology: This Cross-Sectional Study was conducted in the Department of Obstetrics and Gynecology, MTI Nowshera Medical College (NMC), Qazi Hussain Ahmad Medical Complex, Nowshera, KP, Pakistan, from January to June 2025. A total of 200 women aged 18–44 years diagnosed with PCOS according to the Rotterdam criteria were enrolled through consecutive sampling. We collected data on sociodemographic characteristics, anthropometric measurements, clinical features, biochemical parameters, and lifestyle factors using a structured questionnaire. We performed statistical analyses using SPSS version 27.

Results: The mean age was 24.6 ± 4.8 years, with the largest proportion in the 21–25-year age group (42.0%). Menstrual irregularity (81.0%) was the most common clinical manifestation, followed by acne (51.0%), hirsutism (48.0%), and infertility (37.0%). Overweight/obesity and central obesity were observed in 62.0% and 59.0% of participants, respectively. Sedentary behavior, frequent fast-food consumption, psychological stress, and sleep disturbances were highly prevalent. Elevated testosterone (64.0%), abnormal LH/FSH ratio (56.0%), dyslipidemia (52.0%), and impaired fasting glucose (38.0%) were common metabolic abnormalities. Obesity (AOR=3.12), physical inactivity (AOR=2.95), and sedentary lifestyle (AOR=2.67) were significant independent predictors of PCOS severity.

Conclusion: Obesity, physical inactivity, and unhealthy lifestyle behaviors significantly contribute to PCOS severity. Early diagnosis, lifestyle modification, and multidisciplinary management are essential to reduce its reproductive and metabolic burden.

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Introduction

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders among women of reproductive age, affecting approximately 8–13% globally. It is a heterogeneous condition involving hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology that has significant metabolic and reproductive implications [1]. PCOS is now recognized as a condition that affects multiple systems of the body, which also commonly includes insulin resistance, obesity, dyslipidemia, hypertension, type 2 diabetes mellitus, cardiovascular risk, and poor quality of life [2,3]. Despite its high prevalence, many women with PCOS are not identified, due to variable clinical presentations, limited awareness, poor screening, and issues accessing health services [4]. Insulin resistance and hyperinsulinemia are important factors in the pathogenesis of PCOS, as they stimulate ovarian androgen production and inhibit sex hormone-binding globulin, which are mechanisms responsible for hyperandrogenism and ovulatory dysfunction, respectively [5,6]. Other factors include genetic susceptibility, obesity, chronic low-grade inflammation, oxidative stress, and lifestyle factors, all of which contribute to disease expression [7]. As obesity, physical inactivity, unhealthy eating habits, and psychosocial stress continue to rise, the metabolic load of PCOS may be further exacerbated. Data indicate that lifestyle modifications, such as increased exercise and dietary changes, can improve metabolic, hormonal, and reproductive parameters [8]. Nutritional transition, sedentary lifestyle, reproductive health stigma, and the lack of specialist care may also be contributing factors to the burden of PCOS in South Asian populations, including Pakistan [9]. While there is a wealth of research on PCOS from around the world, there is not much locally generated evidence that incorporates clinical features, metabolic abnormalities, anthropometric measures, and lifestyle-related factors within the context of women with PCOS in Pakistan. This study aimed to determine the prevalence, clinical characteristics, metabolic abnormalities, and lifestyle-related risk factors of PCOS among women attending a tertiary care center in Nowshera, Khyber Pakhtunkhwa, Pakistan. This study's novelty lies in its integrated assessment of reproductive, metabolic, anthropometric, and lifestyle characteristics within a tertiary-care population in this relatively understudied region of Pakistan. [10]

Materials and Methods

This cross-sectional study was conducted from January 2025 to June 2025 at the Department of Obstetrics and Gynecology, Qazi Hussain Ahmad Medical Complex (QHAMC) and Nowshera Medical College (NMC), Nowshera, Khyber Pakhtunkhwa, Pakistan. The study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for cross-sectional studies. The target population comprised women of reproductive age (15–44 years) presenting to the study centers with gynecological, reproductive, endocrine, or menstrual health concerns during the data collection period. We used consecutive (non-probability) sampling, enrolling all eligible women who met the predefined inclusion and exclusion criteria until we reached the target sample size. We chose this method to minimize selection bias and ensure the sample represented the clinic-based population. Women aged 18–44 years with a confirmed diagnosis of PCOS based on the Rotterdam criteria were included. PCOS was diagnosed when at least two of the following three criteria were met: (i) oligo-ovulation or anovulation, (ii) clinical and/or biochemical evidence of hyperandrogenism, and (iii) polycystic ovarian morphology (PCOM) on pelvic ultrasonography, following exclusion of other androgen excess disorders. Women were excluded if they had confirmed pregnancy, thyroid dysfunction, hyperprolactinemia, congenital adrenal hyperplasia (CAH), Cushing syndrome, androgen-secreting tumors, or severe chronic systemic illness. We also excluded participants with incomplete clinical records or those who declined informed written consent. We calculated the sample size using the WHO formula for prevalence studies: $n = Z^2P(1-P)/d^2$, where Z = 1.96 (95% confidence level), P = the estimated PCOS prevalence of 20% based on published regional literature, and d = 0.05 (margin of error). This yielded a minimum required sample of 196 participants; we enrolled 200 participants to account for potential incomplete data and provide adequate statistical power for subgroup and regression analyses.

Data Collection Instruments

We developed a structured, pretested, expert-validated questionnaire following a systematic literature review. The instrument comprised five sections: (i) sociodemographic characteristics (age, marital status, residence, education, occupation); (ii) menstrual and reproductive history; (iii) family history of endocrine or metabolic disorders; (iv) lifestyle factors including dietary patterns, physical activity, screen time, sleep quality, and psychosocial stress; and (v) clinical symptom history including menstrual irregularity, hirsutism, acne, alopecia, and infertility. We piloted the questionnaire with approximately 10% of the target sample before full-scale data collection to assess clarity, feasibility, and internal consistency. Pilot data were excluded from the final analysis. We revised the questionnaire based on pilot feedback before commencing the main study.

Anthropometric and Clinical Assessments

We recorded body weight in kilograms using a calibrated electronic weighing scale, with participants in light clothing and without footwear. We measured height in centimeters using a wall-mounted stadiometer in the standard anatomical position. We calculated Body Mass Index (BMI) as weight (kg)/height (m)^2 and classified it according to WHO criteria: underweight (<18.5), normal (18.5–24.9), overweight (25.0–29.9), and obese (≥30.0 kg/m^2). Waist circumference was measured at the midpoint between the lower costal margin and the iliac crest to define central obesity (waist circumference >80 cm in women per IDF criteria). Trained gynecologists assessed clinical features. We graded hirsutism severity using the modified Ferriman–Gallwey (mFG) scoring system; a score ≥8 indicated hirsutism. We documented acanthosis nigricans, acne, alopecia, and other dermatological manifestations through clinical examination.

Biochemical and Ultra sonographic Investigations

We retrieved laboratory parameters, including fasting blood glucose, serum testosterone, luteinizing hormone (LH), follicle-stimulating hormone (FSH), lipid profile (total cholesterol, triglycerides, HDL-C, LDL-C), and fasting insulin, from patients' existing medical records and diagnostic reports where available. Dyslipidemia was defined per the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria. We reviewed pelvic ultra sonographic findings from records; we defined PCOM as ≥12 follicles measuring 2–19 mm in at least one ovary, or ovarian volume >10 mL.

Lifestyle Assessment

We assessed lifestyle-related variables by self-report using standardized instruments adapted from validated epidemiological tools. Physical activity was categorized as regular (≥30 min of moderate-intensity activity on ≥5 days/week), irregular (1–4 days/week), or sedentary (<1 day/week). We assessed dietary habits using food frequency questions covering fast food consumption, sugary beverage intake, and meal regularity. We assessed sleep quality using a modified Pittsburgh Sleep Quality Index (PSQI), dichotomized as adequate or disturbed. We evaluated psychological stress using a 4-item Perceived Stress Scale (PSS-4), categorized as low or high stress.

Statistical Analysis

We coded, entered, cleaned, and analyzed data using IBM SPSS Statistics version 27.0. Descriptive statistics summarized all variables: continuous

variables were presented as mean ± standard deviation (SD), and categorical variables as frequencies and percentages. We examined associations between lifestyle risk factors and PCOS severity using chi-square tests (categorical variables), independent-samples t-tests (two-group continuous comparisons), and one-way ANOVA (multi-group comparisons). Variables significant at $p < 0.05$ in univariable analyses were entered into multivariable binary logistic regression to identify independent predictors of PCOS severity, with results expressed as adjusted odds ratios (AORs) with 95% confidence intervals (CIs). We set statistical significance at $p < 0.05$ throughout.

Results

A total of 200 women with confirmed PCOS were enrolled. The mean age was 24.6 ± 4.8 years (range: 18–45 years). The highest prevalence was observed in the 21–25-year age group (42.0%), followed by the 26–30-year group (28.5%), indicating that young reproductive-aged women constitute the most affected demographic. Most participants were married (56.0%), urban residents (63.0%), housewives (59.0%), and educated to the secondary level (39.0%). Table 1 presents the complete sociodemographic profile.

Table 1. Sociodemographic Characteristics of Study Participants (n = 200)

Variable	Category	Frequency (n)	Percentage (%)
Age (years)	18–20	38	19.0
	21–25	84	42.0
	26–30	57	28.5
	>30	21	10.5
Marital Status	Married	112	56.0
	Unmarried	88	44.0
Residence	Urban	126	63.0
	Rural	74	37.0
Education	Primary	34	17.0
	Secondary	78	39.0
	Graduate	64	32.0
	Postgraduate	24	12.0
Occupation	Housewife	118	59.0
	Employed	82	41.0
	Absent	82	41.0

Anthropometrically, the mean BMI was 27.8 ± 5.1 kg/m², categorizing the mean Participant in the overweight range. Overall, 37.0% were overweight, and 25.0% were clinically obese (BMI ≥30 kg/m²). Central obesity, defined as waist circumference >80 cm, was present in 59.0% of participants. Only 31.0% had a normal BMI, and 7.0% were underweight (Table 2).

Table 2. Anthropometric Characteristics of Study Participants (n = 200)

Parameter	Category / Value	Frequency (n)	Percentage (%)
Weight (kg)	Mean ± SD: 68.4 ± 12.6	–	–
Height (cm)	Mean ± SD: 159.2 ± 6.3	–	–
BMI (kg/m²)	Mean ± SD: 27.8 ± 5.1	–	–
BMI Category	Underweight (<18.5)	14	7.0
	Normal (18.5–24.9)	62	31.0
	Overweight (25.0–29.9)	74	37.0
	Obese (≥30.0)	50	25.0
Central Obesity	Present (WC >80 cm)	118	59.0

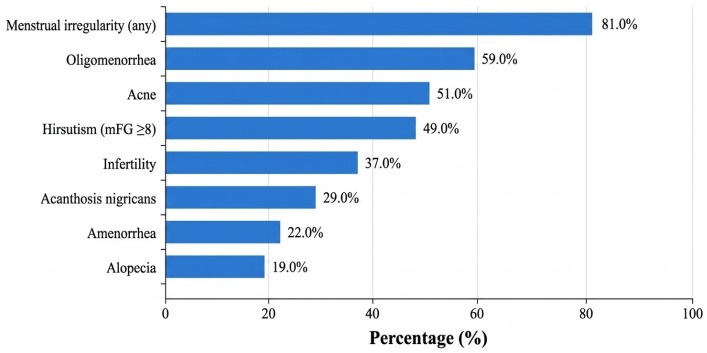
Clinical Manifestations

Menstrual irregularity was the most prevalent clinical feature, affecting 81.0% of participants; oligomenorrhea was present in 59.0% and amenorrhea in 22.0%. Hyperandrogenic features were common: acne was documented in 51.0% and hirsutism in 48.0% of participants. Infertility was reported by 37.0%, while acanthosis nigricans, a cutaneous marker of insulin resistance, was detected in 29.0% and alopecia in 19.0%. Table 3 presents the clinical profile.

Table 3. Clinical Manifestations in Women with PCOS (n = 200)

Clinical Feature	Frequency (n)	Percentage (%)
Menstrual Irregularity (any)	162	81.0
Oligomenorrhea	118	59.0
Amenorrhea	44	22.0
Acne	102	51.0
Hirsutism (mFG ≥8)	96	48.0
Infertility	74	37.0
Acanthosis Nigricans	58	29.0
Alopecia	38	19.0

Figure 1: Bar charTable showing prevalence of clinical manifestations in PCOS participants (n=200)



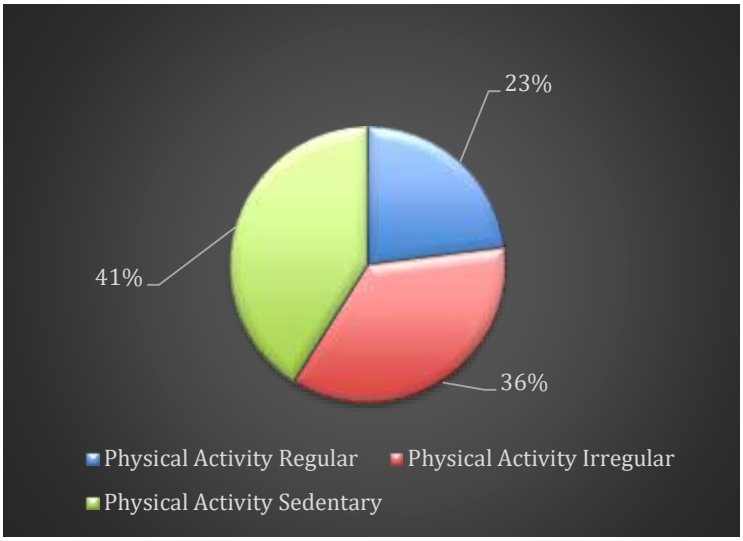
The distribution of clinical features shows a predominance of menstrual abnormalities and hyper androgenic signs in this population.

Table 4. Lifestyle Characteristics and Biochemical/Ultrasound Findings (n = 200)

Variable	Category / Finding	Frequency (n)	Percentage (%)
Physical Activity	Regular	46	23.0
	Irregular	72	36.0
	Sedentary	82	41.0
Fast Food Intake	Frequent (>3×/week)	96	48.0
	Occasional (1–3×/week)	78	39.0
	Rare (<1×/week)	26	13.0
Sugary Beverage Use	Regular	124	62.0
Sleep Disturbance	Present	108	54.0
High Psychological Stress	Present	132	66.0

Elevated Testosterone	Present	128	64.0
Abnormal LH/FSH Ratio	Present	112	56.0
Dyslipidemia	Present	104	52.0
Impaired Fasting Glucose	Present	76	38.0
PCOM on Ultrasound	Confirmed	176	88.0

Figure 2: showing physical activity levels: Sedentary 41%, Irregular 36%, Regular 23%



Distribution of Physical Activity Levels Among Study Participants (n = 200)

Association and Regression Analysis

Chi-square analysis revealed statistically significant associations between BMI and menstrual irregularity (p = 0.001), physical activity level and obesity (p = 0.002), and psychological stress and hormonal symptoms (p = 0.003). ANOVA demonstrated a significant association between dietary pattern and metabolic abnormalities (p = 0.001). An independent t-test confirmed a significant relationship between sleep disturbance and hormonal imbalance (p = 0.010). Multivariable logistic regression analysis, adjusting for age, marital status, and residence, identified obesity (AOR = 3.12; 95% CI: 1.82–5.41; p = 0.001), physical inactivity (AOR = 2.95; 95% CI: 1.70–5.11; p = 0.001), and sedentary lifestyle (AOR = 2.67; 95% CI: 1.55–4.60; p = 0.002) as the three strongest independent predictors of PCOS severity. Unhealthy diet (AOR = 2.41) and positive family history (AOR = 1.89) were additional significant independent predictors. Women with obesity were more than three times as likely to experience severe PCOS manifestations compared to those with normal BMI.

Discussion

This study provides an integrated assessment of the clinical, metabolic, anthropometric, and lifestyle characteristics of PCOS among

reproductive-aged women attending a tertiary-care hospital in Nowshera, Pakistan. The results validate the concept of PCOS as a multisystem metabolic-endocrine disorder with reproductive features that are associated with obesity, insulin resistance, and modifiable lifestyle factors. The largest age group by percentage was women aged 21-25 years. This is consistent with other evidence of the common association of PCOS presenting in early reproductive adulthood, following the onset of menstruation, hyper androgenic symptoms, and fertility issues [11]. The high proportion of younger women may also reflect greater exposure to sedentary lifestyles, dietary changes, psychosocial stress, and disrupted sleep [12]. This urban predominance observed further underscores the possibility that urbanization and lifestyle change may contribute to PCOS risk. Sedentary behaviors, energy-dense diets, and higher psychosocial stress likely contribute to the expression of PCOS and/or obesity and insulin resistance [13,14]. This cohort was overweight and obese, with about 62% being overweight or obese. This is clinically significant because excess adiposity, especially visceral fat, is closely associated with insulin resistance, inflammation, and hyperandrogenism in PCOS [15]. The positive association between BMI and menstrual irregularity in this study is biologically plausible because hyperinsulinemia can stimulate ovarian androgen production and decrease sex hormone-binding globulin in the liver, leading to higher circulating androgen levels [16]. Menstrual irregularity was the most common clinical feature, and approximately one-third were infertile. These results reveal the considerable reproductive burden associated with PCOS and confirm the major role played by ovulatory dysfunction in the disorder [17]. Hyper androgenic symptoms also occurred often: Acne (51%) and hirsutism (48%). The occurrence of acanthosis nigricans in 29% also indicates a significant prevalence of insulin resistance and underscores the significance of metabolic screening in women with PCOS [18]. Lifestyle factors were also significant. The most prevalent factors associated with participants were physical inactivity, poor nutrition habits, regular intake of fast food and sugar-sweetened drinks, psychological stress, and sleep disorders. These factors can negatively affect insulin resistance, obesity, inflammation, and reproductive function [19,20]. In the multivariable analysis, physical activity emerged as an important independent predictor, highlighting the potential role of regular physical activity in managing PCOS. Aerobic exercise has been shown to enhance insulin sensitivity, decrease visceral adiposity, and positively affect metabolic and reproductive parameters [21]. Other significant results included psychological stress and sleep disturbances. Excessive stress and poor sleep can negatively affect glucose metabolism, appetite control, inflammatory processes, and reproductive hormonal function [22,23]. These findings emphasize that PCOS management should extend beyond reproductive symptoms and incorporate lifestyle counseling, physical activity, dietary modification, stress management, and sleep optimization. Overall, the findings demonstrate a substantial overlap between reproductive manifestations and metabolic and behavioral risk factors among women with PCOS in this tertiary-care setting. The study highlights the need for earlier recognition and comprehensive assessment of modifiable risk factors in Pakistani women with PCOS.

Conclusion

PCOS is a prevalent endocrine-metabolic disorder among young reproductive-aged women in Pakistan, strongly associated with modifiable lifestyle risk factors including obesity, physical inactivity, sedentary behavior, poor dietary habits, psychological stress, and sleep disturbances. Obesity emerged as the most powerful independent predictor of PCOS severity. These findings underscore the urgent need for early identification, comprehensive lifestyle modification, and multidisciplinary, culturally responsive management to reduce the reproductive, metabolic, and psychosocial burden of PCOS in Pakistan.

Declarations

Conflicts of Interest: The authors declare no conflicts of interest.

Funding: This study received no external funding.

Ethical Approval: Ethical approval was granted by the Ethical Review Board (ERB) of Nowshera Medical College **(Approval No. 12(i)/ERB/NMC, dated 01/01/2025).**

Authors' Contributions

Sumayya: Study supervision, interpretation of findings, critical review of the manuscript for important intellectual content, final approval of the version to be published, and accountability for all aspects of the work.

Mehwish Sayed: Data collection, laboratory assessment, data curation, literature review, manuscript revision, final approval of the version to be published, and accountability for all aspects of the work

Javeria Saleem: Statistical analysis, interpretation of data, manuscript drafting and revision, critical review of the manuscript for important intellectual content, final approval of the version to be published, and accountability for all aspects of the work.

Saeeda Safi: Conceptualization, study design, data collection, data curation, statistical analysis, interpretation of data, manuscript drafting, critical revision of the manuscript, final approval of the version to be published, and accountability for all aspects of the work.

Shah Nawaz: Data acquisition, data analysis, critical revision of the manuscript, and supervision.

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Original Article

Contrast-Enhanced MRI in The Preoperative Evaluation of Endometrial Carcinoma

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Abstract

Objective: To determine the diagnostic accuracy of preoperative contrast-enhanced magnetic resonance imaging (CE-MRI) for assessing myometrial invasion, cervical invasion, and lymph node metastasis in endometrial carcinoma and to evaluate their association with postoperative histopathological findings.

Methodology: This Prospective Longitudinal Study was conducted in the Department of Obstetrics and Gynecology, Ayub Teaching Hospital, Abbottabad, Pakistan, from January to December 2025. Following institutional Ethical Review Committee approval, 144 patients with biopsy-proven endometrial carcinoma underwent pelvic CE-MRI within one month before surgery. We assessed myometrial invasion, cervical invasion, and lymph node metastasis on T2-weighted and contrast-enhanced T1-weighted images. We used histopathological findings as the definitive reference standard. We used correlation analysis to assess associations between MRI and histopathological findings, and logistic regression to evaluate factors associated with positive pelvic lymph nodes.

Results: For detecting myometrial invasion, cervical invasion, and lymph node metastasis, CE-MRI showed sensitivities of 85.71%, 90.9%, and 85.7% and specificities of 89.47%, 100%, and 79.6%, respectively. Histopathological lymph node metastasis was strongly associated with ≥50% myometrial invasion (100% sensitivity, 97.9% specificity), whereas the association with cervical invasion was poor. In univariate analysis, disease stage, tumor grade and type, positive peritoneal cytology, myometrial invasion, and cervical stromal invasion were significantly associated with lymph node involvement.

Conclusion: CE-MRI demonstrated good diagnostic performance for assessing local tumor invasion and lymph node metastasis. Patients with <50% myometrial invasion and no cervical invasion on CE-MRI may have a lower likelihood of lymph node metastasis, potentially supporting individualized surgical planning.

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Introduction

Endometrial carcinoma (EC) is the most common malignancy of the female genital tract in many developed countries, and its incidence has also been increasing in developing countries [1]. While most patients have disease limited to the uterus, a significant fraction have extrauterine disease, such as lymph node metastases, which are often not detected preoperatively [2]. Clinicians usually diagnose the disease preoperatively by endometrial biopsy, and definitive staging is based on surgical and histological findings. The 2023 International Federation of Gynecology and Obstetrics (FIGO) staging system has also been updated with histopathological and molecular features, which further aid risk stratification and staging [3]. While computed tomography (CT) and magnetic resonance imaging (MRI) are not the only methods for staging EC, MRI can provide useful pre-operative information about the local extent of EC and help with treatment planning [4]. Specifically, MRI can measure the depth of myometrial invasion (MI), the cervical stromal involvement (CI), and suspicious pelvic lymph nodes. Contrast-enhanced MRI is useful for assessing deep MI and cervical involvement [5]. Previous studies show MRI is sensitive for diagnosing deep MI and has good diagnostic accuracy [5,6]. MRI accuracy for detecting lymph node metastasis is comparatively low. Therefore, imaging findings should be analyzed alongside clinical and pathological risk factors. Surgery is the primary treatment for operable EC and usually involves hysterectomy and bilateral salpingo-oophorectomy; the extent of lymph node assessment depends on the patient's risk profile and disease characteristics [7]. MI and histological grade are significant prognostic factors and risk factors for lymph node metastasis. Deep MI is relevant because it correlates with the likelihood of extrauterine spread [8]. Likewise, cervical stromal involvement is an important factor in determining local tumor extension and could affect surgical planning and subsequent adjuvant therapy [9]. Therefore, accurate preoperative evaluation is crucial for selecting a surgical strategy and identifying those who may need further staging and/or personalized adjuvant therapy. Preoperative MRI combined with postoperative histopathology is accurate and provides useful information regarding MI and CI. However, its diagnostic value depends on the anatomical parameter assessed [5,6]. MRI may then assist risk stratification before surgery, but histopathology remains the gold standard for diagnosis. In the present study, we directly compare pre-operative contrast-enhanced MRI findings with postoperative histopathological evaluation of MI, CI, and lymph node metastasis in patients with EC. Furthermore, the study assesses correlations among histopathological MI, CI, and lymph node involvement in the same patient population, providing an integrated imaging-pathology evaluation. This study aimed to determine the association between preoperative contrast-enhanced MRI findings and postoperative histopathological parameters, including MI, CI, and lymph node involvement, in patients with EC. The study also evaluated the relationship between histopathological MI and CI and lymph node metastasis.

Materials and Methods

This prospective longitudinal study was conducted in the Department of Obstetrics and Gynecology, Ayub Teaching Hospital, Abbottabad, Pakistan, from January to December 2025. We included 144 eligible patients. The study was conducted after approval from the institutional Ethical Review Committee. The patients were included if they had been diagnosed with endometrial carcinoma preoperatively by endometrial biopsy. Patients with a concurrent malignancy of the genital tract other than endometrial carcinoma, those who did not have lymph node dissection, and those who were given neoadjuvant chemotherapy were excluded. All patients had a pelvic MRI with contrast within one month before surgery. The surgical specimen was the definitive reference standard for histopathological examination. We used a 1.5-Tesla Siemens Avanto MRI (Siemens, Erlangen, Germany) with a pelvic phased-array coil for contrast-enhanced imaging. The MRI scans used a standard sequence set: T1-weighted coronal and T2-weighted axial, sagittal, and coronal scans. Gadolinium-based contrast was given as an intravenous bolus at 0.1 mmol/kg (0.2 mL/kg). Contrast-enhanced T1-weighted images then followed in the axial, sagittal, and coronal planes.

Radiologists with over 5 years'experience in women's imaging interpreted the MRI images. Focal disruption in the junctional zone, but not > half or the entire myometrial thickness, was classified as <50% myometrial invasion, while disruption > half or the entire myometrial thickness was classified as >50% myometrial invasion. Contrast-enhanced MRI was used to define <50% myometrial invasion as an irregular tumor-myometrial border with the tumor limited to the inner half of the myometrium. If the myometrium was invaded beyond 50% of the thickness, it was considered deep myometrial invasion (MI>50%). Cervical invasion was defined as an abnormal signal-intensity lesion on T2-weighted images that invaded the cervical canal or cervical stroma. Cervical enlargement was deemed a supportive imaging feature. Normal cervical epithelial enhancement was also disrupted on contrast-enhanced MRI, which was also taken as suggestive of cervical invasion. Any pelvic lymph nodes> 1 cm short axis diameter, with or without an area of necrosis in the center (on contrast-enhanced MRI), were regarded as suspicious for metastatic involvement. Surgical staging involved collecting peritoneal fluid for cytology, total abdominal hysterectomy, bilateral salpingo-oophorectomy, and pelvic lymphadenectomy. All resected specimens were sent for histopathology. Histopathological examination was used as the gold standard for evaluating myometrial invasion, cervical invasion, and lymph node metastasis.

Data Collection

We identified eligible patients through the hospital's Index and Coding system in the Hospital Information Management System. We retrospectively reviewed medical records, MRI reports, and histopathology reports. We collected data using a predefined proforma containing demographic, imaging, surgical, and histopathological variables.

Statistical Analysis

We entered and analyzed the data using SPSS version 19.0. We assessed the diagnostic performance of contrast-enhanced MRI by calculating sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) using standard formulas, with histopathological findings as the reference standard. We calculated the correlation coefficient to assess the association between preoperative contrast-enhanced MRI findings and postoperative histopathological staging parameters. We used the chi-square test to evaluate associations between categorical predictive factors and lymph node metastasis. We used logistic regression to evaluate the relationship between selected clinical and histopathological factors and the presence of positive pelvic lymph nodes. We considered a two-sided p-value <0.05 statistically significant.

Results

We included 144 women with endometrial carcinoma that met the eligibility criteria. The mean age was 57.81 ± 9.78 years. Table 1 presents the demographic and clinicopathological characteristics, including body mass index (BMI), menopausal status, surgical stage, histological type, and tumor grade. The majority of patients (90.26%) had stage I disease, while 83.33% were postmenopausal. Table 2 presents the diagnostic performance of contrast-enhanced MRI for assessing myometrial invasion (MI), cervical invasion (CI), and pelvic lymph node metastasis (LNM). For MI detection, MRI showed a sensitivity of 85.71% and specificity of 89.47%. For CI, the sensitivity and specificity were 90.9% and 100%, respectively. For pelvic LNM, MRI demonstrated a sensitivity of 85.7% and specificity of 79.6%. The association between histopathological pelvic lymph node metastasis and ≥50% histopathological myometrial invasion demonstrated a sensitivity of 100% and specificity of 97.9% (Table 3). In contrast, the association between histopathological cervical invasion and lymph node metastasis demonstrated comparatively lower diagnostic performance. In univariate logistic regression, age, BMI, and menopausal status were not significantly associated with lymph node involvement. In contrast, disease stage, tumor grade, histological type, positive peritoneal cytology, histopathological myometrial invasion, and histopathological

cervical invasion were significantly associated with lymph node

involvement (Table 4).

Table 1. Clinic pathological characteristics of patients with endometrial carcinoma (n=144)

Variable	n	%
Age, years (mean ± SD)	57.81 ± 9.78	–
BMI, kg/m² (mean ± SD)	32.27 ± 7.0	–
Surgical stage		
Stage IA	91	63.19
Stage IB	39	27.08
Stage II	5	3.47
Stage IIIA	3	2.08
Stage IIIB	1	0.69
Stage IIIC	4	2.77
Stage IV	3	2.08
Histopathological type		
Endometrioid	126	87.50
Clear cell	8	5.50
Papillary serous	10	6.94
Menopausal status		

Premenopausal	24	16.66
Postmenopausal	120	83.33
Histopathological grade		
Grade 1	47	32.63
Grade 2	70	48.61
Grade 3	27	18.75

Data are presented as mean ± SD or frequency (percentage). BMI, body mass index; SD, standard deviation.

Table 2. Diagnostic performance of contrast-enhanced MRI for myometrial invasion, cervical invasion, and lymph node metastasis

MRI assessment	TP	FP	FN	TN	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	+LR	κ
Myometrial invasion >50%	42	10	7	85	85.71	89.47	80.77	92.39	8.14	0.74
Cervical invasion	10	0	1	133	90.90	100.00	100.00	99.30	NA	0.949
Lymph node metastasis	6	28	1	109	85.70	79.60	17.60	99.10	4.19	0.231

TP, true positive; FP, false positive; FN, false negative; TN, true negative; PPV, positive predictive value; NPV, negative predictive value; +LR, positive likelihood ratio; κ, Cohen's kappa; NA, not applicable. Pasted markdown

Table 3. Association of histopathological myometrial and cervical invasion with lymph node metastasis

Histopathological finding	LNM present, n	LNM absent, n	Total, n	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Myometrial invasion >50%	7	42	49	100.0	97.9	14.28	100.0
Myometrial invasion ≤50%	0	95	95	–	–	–	–
Total	7	137	144	–	–	–	–
Cervical invasion present	3	8	11	42.9	94.1	27.27	96.99
Cervical invasion absent	4	129	133	–	–	–	–
Total	7	137	144	–	–	–	–

LNM, lymph node metastasis; PPV, positive predictive value; NPV, negative predictive value. Pasted markdown

Table 4. Univariate logistic regression analysis of factors associated with lymph node metastasis

Predictor	OR (95% CI)	P value
Age	1.014 (0.93–1.09)	0.741
BMI	1.014 (0.93–1.09)	0.535
Menopausal status	1.21 (0.139–10.58)	0.862
Stage I vs II	86.0 (6.02–1228.75)	0.001
Stage I vs III–IV	103.2 (9.68–1100.014)	<0.001
Grade 1–2 vs Grade 3	13.06 (2.38–71.68)	0.003
Endometrioid vs clear cell	13.66 (1.91–98.97)	0.010
Endometrioid vs serous	10.25 (14.9–70.39)	0.018
Positive peritoneal cytology	0.115 (0.018–0.716)	0.020
Histopathological myometrial invasion	NA*	<0.001
Histopathological cervical invasion	12.09 (2.30–63.51)	0.003

OR, odds ratio; CI, confidence interval; BMI, body mass index; NA, not applicable. *NA indicates that an odds ratio could not be estimated because of Zero cells.

Discussion

The FIGO staging system for endometrial carcinoma has undergone important revisions, most recently in 2023, incorporating histopathological and molecular characteristics to improve prognostic stratification. Histological type, tumor grade, depth of myometrial invasion (MI), cervical stromal involvement, lymphovascular space invasion, and lymph node status remain important factors in treatment planning and prognosis [11,12]. Current international guidelines also focus on surgical management based on clinicopathological and molecular risk groups, rather than extended staging procedures in all patients [13].MRI is an important pre-operative imaging modality because of its excellent soft-tissue contrast and its ability to assess local tumor extension. T2-weighted, diffusion-weighted, and contrast-enhanced sequences can provide complementary information for evaluating MI and cervical stromal invasion. Recent studies show that MRI can help with preoperative tumor staging, but diagnostic accuracy varies by imaging protocol and tumor characteristics [14,15]. The present study found that contrast-enhanced MRI had good diagnostic performance for MI (sensitivity 85.71%, specificity 89.47%, κ coefficient 0.74), with good agreement with histopathology. These results support using MRI for preoperative evaluation of myometrial involvement.Assessing MI is important, as deep invasion is associated with a higher risk of lymphovascular and nodal involvement. A large meta-analysis found significant associations between MI and lymph node metastasis, lymphovascular space invasion, recurrence, and overall survival [16]. Moreover, various MRI protocols have been evaluated, and diffusion-weighted MRI, T2-weighted MRI, and dynamic contrast-enhanced MRI have proven useful for diagnosing deep MI [14,15]. Our findings agree with current data supporting MRI evaluation of the depth of myometrial involvement.Correct diagnosis of cervical stromal involvement is also crucial for surgical planning. Contrast-enhanced MRI was accurate with a sensitivity of 90.9%, specificity of 100%, PPV of 100%, and NPV of 99.3% for CI in our cohort. MRI identified 10/11 cases diagnosed histopathologically. A single case may have been a case of microscopic or focal cervical stromal invasion, which MRI may not have detected. Contemporary imaging literature also highlights MRI for assessing local extension, especially when distinguishing between confined and cervical stromal disease and its possible effect on surgical planning [12,17].Assessment of lymph node metastasis was more challenging. Applying the >1 cm MRI criterion identified 34 patients as positive, while histopathology revealed metastasis in only seven. Therefore, MRI sensitivity was 85.7%, specificity was 79.6%, positive predictive value was 17.6%, negative predictive value was 99.1%, and the κ coefficient was 0.231. Many false-positive results were due to nodal enlargement alone, as reflected by the low PPV. In contrast, the high NPV indicates that a negative MRI rarely correlated with histopathologically proven nodal disease. More recent studies have also identified the shortcomings of traditional MRI evaluation of nodal disease and explored radiomics, multiparametric MRI, and PET/CT to improve nodal prediction [18-20].In our study, we observed a strong correlation between histopathological MI and lymph node metastasis. Histological confirmation of nodal metastasis was found in all seven patients with >50% MI, but in none of the 95 patients with ≤50% MI. This yielded a sensitivity of 100% and specificity of 97.9% for the association between deep MI and LN metastasis. Recent studies have established deep MI as a significant prognostic factor, along with tumor grade, histological type, cervical stromal invasion, and lymphovascular space invasion [16,21,22].Our nodal metastasis rate was 4.86%, partly attributable to the high proportion of stage I disease (90.26%) and endometrioid histology (87.5%). Current evidence supports selecting, rather than standardizing, lymph node assessment in appropriately stratified patients. Meta-analytic comparisons of sentinel lymph-node mapping and systematic lymphadenectomy show the growing contribution of sentinel-node approaches in surgical staging [12]. International guidelines also recommend risk-adapted nodal assessment based on tumor characteristics and overall risk classification [13].In our series, the following features were significantly associated with lymph node metastasis: Advanced disease stage, high tumor grade, non-endometrioid histology, positive peritoneal cytology, deep MI, and cervical stromal involvement. Conversely, no other factors, including age, BMI, and menopausal status, were significantly related to nodal involvement. Recent predictive studies have also established that certain tumor characteristics, especially histological type, grade, MI, cervical involvement, and other pathological factors, are also important predictor variables for nodal disease [21]. These results support the usefulness of contrast-enhanced MRI as a preoperative tool, especially for MI and CI. However, its relatively poor PPV for lymph node metastasis suggests that MRI should not be relied upon alone to decide nodal status. Combining imaging assessment with histological grade, tumor type, MI, cervical involvement, and other clinical risk factors could offer a more holistic approach to individual surgical planning [22].This study has several limitations. First, the number of patients with cervical stromal invasion (n=11) and lymph node metastasis (n=7) was small, which may limit statistical power and precision of the estimates. Second, approximately 90% of patients had stage I disease, and 87.5% had endometrioid carcinoma; therefore, the findings may be most applicable to patients with predominantly early-stage endometrioid EC. Finally, the retrospective single-center design may limit generalizability. Further prospective, multicenter studies with larger numbers of advanced-stage and non-endometrioid tumors are warranted.

Conclusion

Preoperative pelvic contrast-enhanced magnetic resonance imaging has moderately high sensitivity and specificity for predicting disease stage in endometrial carcinoma. Preoperative assessment, together with contrast-enhanced magnetic resonance imaging, can help Gynae oncologists with clinical decision-making and patient counseling.

Ethical Approval

Ethical approval was obtained from the Ayub Medical Teaching Institution Abbottabad Institutional Medical & Ethics Review Committee **(Approval Code/Ref. No. RC-FA-2024/166; approved 20 August 2024)** before data collection began.

Informed Consent

Informed consent was not applicable because this systematic review did not involve direct participation of human subjects or collection of primary participant data.

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Conflict of Interest

The authors declare that they have no competing interests or conflicts of interest related to this study.

Authors' Contributions

Shehla Noor: Conceptualization, study design, literature search, study screening, data extraction, manuscript drafting, and critical revision.

Bushra Khan: Conceptualization, supervision, interpretation of findings, critical revision of the manuscript, and final approval of the version to be published.

Laraib Istafa: Literature search, study screening, data extraction, preparation of tables and figures, and manuscript revision.

Mahnoor Mushraf: Data extraction, literature review, manuscript drafting and revision, and reference verification.

Fatima Nasir: Literature search, data verification, manuscript revision, interpretation of findings, and final review and approval of the manuscript.

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Original Article

Association of Serum Adiponectin with Cardiac Enzymes in Diabetic Patients Having Coronary Heart Disease

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Abstract

Objective: To determine serum adiponectin levels and assess their relationship with cardiac enzymes in patients with type 2 diabetes and coronary heart disease.

Methodology: This Case-Control Study was conducted at Khyber Medical College, Peshawar, Khyber Pakhtunkhwa, Pakistan, from October 2025 to March 2026. The study included 60 patients with type 2 diabetes mellitus presenting with a first myocardial infarction and 60 age- and sex-matched healthy subjects. We measured serum adiponectin and troponin I using ELISA kits, and CK, LDH, and ALT using a Micro Lab Analyzer. We analyzed the collected data using SPSS version 21. We used independent-samples t-tests to compare groups and Pearson correlations to assess associations. We considered $p < 0.05$ statistically significant.

Results: Serum adiponectin levels were significantly lower in cases (3.2±1.1 vs. 11.7±2.6 µg/mL, $P < 0.0001$). All cardiac enzymes were significantly higher in cases: Troponin I (15.7±14.6 ng/mL vs. 0.014±0.02 ng/mL) and CK (389±43.36 vs. 165±6.78 U/L). LDH (474.54±40.53 vs 321.59±28.9 U/L) and ALT (115.28±25.63 vs 45.37 ± 14.6 U/L). We observed a negative correlation between adiponectin and troponin I ($r = -0.62$, $p<0.001$) and CK ($r = -0.54$, $p<0.001$).

Conclusion: Serum adiponectin is significantly low in type 2 diabetic patients with coronary heart disease (CHD) and is associated with significantly high cardiac enzymes in these cases with myocardial infarction. Adiponectin may serve as a protective biomarker in diabetic coronary heart disease.

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Introduction

Coronary heart disease [CHD] is the leading cause of mortality among the diabetic population. As the most common complication of type 2 diabetes, CHD accounts for 80% of mortality in this population [1]. Type 2 diabetic patients face a 2- to 4-fold higher risk of cardiac events [2]. Researchers are exploring novel biomarkers that may help diagnose or predict outcomes in these metabolic disorders [3]. Adiponectin is one such biomarker. White adipose tissue secretes this peptide hormone, first identified in 1995. Adiponectin constitutes nearly 10% of serum proteins and typically ranges from 2 to 30 µg/mL. In addition to important functions in the liver and skeletal muscles, adiponectin exerts cardioprotective effects by interacting with its receptor, T-cadherin, on cardiac myocytes [5]. Adiponectin has been proposed to have anti-inflammatory, lipid-regulatory, and anti-atherogenic effects, which may underlie its cardioprotective role. Most of these effects are under investigation to clarify its potential diagnostic, prognostic, and therapeutic functions [6,7,8]. This study aims to determine serum adiponectin and key cardiac enzyme levels, including troponin I, creatine kinase, lactate dehydrogenase, and alanine aminotransferase, in diabetic patients experiencing a first myocardial infarction. It also examines whether adiponectin is associated with these cardiac enzymes in these patients [9]. This study's novelty lies in its simultaneous assessment of serum adiponectin and multiple cardiac enzymes, including troponin I, creatine kinase, lactate dehydrogenase, and alanine aminotransferase, among type 2 diabetic patients experiencing a first myocardial infarction. By examining the relationships between adiponectin levels and these biochemical markers, this study provides locally relevant evidence regarding the potential role of adiponectin as a biomarker of myocardial injury in diabetic patients with coronary heart disease.

Materials and Methods

This Case Control study was conducted at Khyber Medical College, Peshawar, Khyber Pakhtunkhwa, Pakistan. Group A comprised 60 patients with type 2 diabetes who had a first myocardial infarction, while Group B comprised 60 age- and sex-matched healthy controls. All patients were selected randomly. Patients previously diagnosed with CHD and receiving treatment were excluded from the study. All participants with any other major illness, such as liver disease, kidney disease, thyroid disease, endocrine abnormalities, or malignancy, were excluded from both the case and control groups. We conducted the study over six months. We obtained written informed consent from all participants. We recorded a detailed history and demographic characteristics using a structured questionnaire. We also recorded clinical parameters, including blood pressure, height, weight, and BMI.

Biochemical Analysis

We collected fasting blood [5 mL] from all participants. We centrifuged the blood at 4500 rpm for 5 minutes to obtain clear serum. We determined adiponectin and troponin I using ELISA kits from BioVendor, Germany, and the Metrolab Clinical Chemistry Analyzer. We analyzed other cardiac enzymes, including CK, LDH, and ALT, using the Micro Lab Chemistry Analyzer.

Participants

The study included 60 type 2 diabetic patients with a first episode of myocardial infarction (Group A) and 60 age- and sex-matched healthy controls (Group B), giving a total sample of 120 participants. Patients with previously diagnosed coronary heart disease and those receiving treatment were excluded. Participants with major comorbidities, including liver disease, kidney disease, thyroid disease, endocrine disorders, or malignancy, were also excluded. We randomly selected all participants who provided written informed consent.

Statistical Analysis

We analyzed data using SPSS version 21. We compared continuous variables with normal distribution between groups using the independent-samples t-test, and used the Mann–Whitney U test for non-normally distributed variables, including troponin I. We assessed the association between serum adiponectin and cardiac enzymes using Pearson's correlation coefficient (r). We considered P <0.05 statistically significant.

Results

The groups were similar in age (56.4±8.2 vs. 55.9±7.9 years; P=0.73) and sex distribution (62% male in each group). Table 1 shows the biochemical parameters of the two groups. Adiponectin levels were markedly lower in patients with MI than in the control group [3.2±1.1 vs. 11.7±2.6 µg/mL, P < 0.0001]. Cardiac enzymes, including troponin I, creatine kinase, lactate dehydrogenase, and alanine aminotransferase, were significantly higher in group A with MI than in the control group (p < 0.0001). We used Pearson's correlation coefficient [r] to assess the association between adiponectin and cardiac enzymes, as shown in Table 2. We observed a significant negative correlation between adiponectin and troponin I [r = –0.62, p < 0.001], CK [r = –0.54, p < 0.001], and LDH [r = –0.31, p = 0.016], but no significant association with ALT.

Table 1. Comparison of biochemical parameters in the study groups

Variable	Group A Cases means±SD	Group B Control means±SD	P value
Adiponectin µg/ mL	3.2±1.1	11.7±2.6	<0.0001
Troponin I ng/mL	15.68 ± 14.57	0.014 ± 0.02	<0.0001
CK U/L	389.0 ± 43.4	165.0 ± 6.8	<0.0001
LDH U/L	474.5 ± 40.5	321.6 ± 28.9	<0.0001
ALT U/L	115.3 ± 25.6	45.4 ± 14.6	<0.0001

Values are presented as mean ± standard deviation (SD). Group A included 60 type 2 diabetic patients with a first myocardial infarction, and Group B included 60 age- and sex-matched healthy controls. We considered P < 0.05 statistically significant. CK, creatine kinase; LDH, lactate dehydrogenase; ALT, alanine aminotransferase.

Table 2. Association of adiponectin with cardiac enzymes.

Variables	r	p
Troponin I	-0.62	<0.0001
CK	-0.54	<0.0001
LDH	-0.31	0.016
ALT	-0.22	0.10

We used Pearson's correlation coefficient (r) to assess the association between serum adiponectin and cardiac enzymes. A negative r value indicates an inverse association. We considered p < 0.05 statistically significant. CK, creatine kinase; LDH, lactate dehydrogenase; ALT, alanine aminotransferase.

Discussion

Serum adiponectin levels vary widely in health and disease. A research gap remains regarding adiponectin levels in diabetic subjects with CHD, especially MI, and their association with cardiac enzymes in our region. In the present study, we found significantly lower adiponectin in diabetic cases with myocardial infarction. This is the first prospective cohort study to report hypoadiponectinemia with CHD [10]. In the present

study, serum adiponectin was significantly lower in type 2 diabetic patients with a first myocardial infarction than in healthy controls. These findings are consistent with previous reports linking hypoadiponectinemia with cardiovascular disease, type 2 diabetes mellitus, coronary heart disease, and metabolic syndrome [11]. A study described adiponectin as a potential therapeutic target because of its association with metabolic and cardiovascular disorders [12]. Several mechanisms may contribute to adiponectin's cardioprotective effects, including improved insulin sensitivity, increased endothelial nitric oxide production, reduced macrophage foam-cell formation, and inhibition of vascular smooth-muscle proliferation and calcification [13]. The marked reduction in adiponectin observed in patients with myocardial infarction may also reflect inflammatory responses and increased interaction of adiponectin with T-cadherin receptors on injured cardiomyocytes [14,15]. We observed significant inverse correlations between adiponectin and troponin I, CK, and LDH, indicating an association between lower adiponectin levels and greater biochemical evidence of myocardial injury. A similar inverse relationship between adiponectin and CK-MB has been reported in patients with ST-elevation myocardial infarction [16,17]. An association between lower adiponectin levels and higher troponin I concentrations has also been reported in STEMI patients [18]. However, because this study was cross-sectional, these associations should not be interpreted as evidence of causality. The non-significant correlation with ALT suggests that the observed relationship was more closely linked to cardiac injury than to ALT levels in this study. We observed a significant negative association between adiponectin levels and cardiac enzymes, including troponin I, CK, and LDH [19]. This strong correlation further supports our findings by ruling out confounding effects from tissue injury and strengthens the possible causal relationship between decreased adiponectin and myocardial injury. The non-significant correlation between adiponectin and ALT suggests preserved liver integrity in our cases; this further indicates that low adiponectin is more likely a specific response to cardiac myocyte injury rather than a chance finding [20]. A study of ST-elevation myocardial infarction [STEMI] patients reported a rapid decline in adiponectin levels after reperfusion, with the lowest level observed at 24 hours. This reduction was also inversely correlated with CK-MB [p=0.013] [21]. A study of 73 STEMI patients reported similar results: an adiponectin level ≤1.8 ng/mL was significantly associated with higher troponin I levels [45.01 vs. 5.46 ng/mL, p=0.03]. This study identified a cut-off value of 1.8 ng/mL for labeling patients at risk, consistent with the markedly reduced levels [3.2±1.1 µg/mL] reported in the present study [22]. Single time-point measurement and lack of long-term follow-up may be limitations. Future large-sample prospective studies are recommended to further confirm the relationship between adiponectin and cardiac enzymes.

Conclusion

Adiponectin is markedly reduced in type 2 diabetic subjects having CHD and is negatively associated with cardiac enzymes. These findings help identify the possible preventive, diagnostic, and prognostic value of adiponectin in patients with myocardial infarction.

Authors' Contributions

Sadaf Durrani: Conceptualization, study design, data acquisition, data analysis, manuscript drafting, and critical revision.

Ubaid Ur Rahman: Conceptualization, study design, supervision, interpretation of findings, critical revision of the manuscript, and final approval of the version to be published.

Ubaidullah: Data acquisition, data analysis, literature review, and manuscript revision.

Naheed Khattak: Data acquisition, data analysis, preparation of tables and figures, and critical revision of the manuscript.

Safiyya Ubaidullah: Data acquisition, data analysis, literature review, manuscript drafting and revision, and reference verification.

All authors: Read and approved the final manuscript and agreed to be accountable for all aspects of the work.

Conflict of interest: None

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Ethical Approval

The Institutional Research and Ethical Review Board (IREB) of Khyber Medical College, Peshawar, approved the study on 08 January 2026 **(Approval No. 16/IREB/DME/KMC).**

Strength: The study's well age-matched controls and highly significant p-values for the correlation between adiponectin and cardiac enzymes are strengths.

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Original Article

Incidence and Factors Associated with Prosthetic Joint Infection Following Hip or Knee Revision Arthroplasty: A Retrospective Cohort Study

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Abstract

Objective: To determine the incidence of prosthetic joint infection (PJI) for patients who have undergone a hip or knee revision arthroplasty within a specific period of follow-up and to establish baseline host-related factors (prior skin infection, dental disease, diabetes, obesity, smoking, age, sex, and joint type) that are associated with the development of PJI.

Methodology: This Retrospective cohort study was conducted in the Department of Orthopedic Surgery at MTI Bacha Khan Medical College and Mardan Medical Complex, Mardan, in 2025. We reviewed medical records. Between January 2024 and August 2024. 40 patients undergoing elective revision hip or knee arthroplasty at MTI Bacha Khan Medical College and Mardan Medical Complex, Mardan, from January to August 2023. We followed patients for a mean of one year for PJI according to EBJIS 2021 criteria. We assessed associations using Fisher's exact test and independent t-tests. We used a parsimonious logistic regression model to evaluate age, diabetes, and dental disease. $P<0.05$ was considered significant.

Results: Prior skin infection (22.5%), dental disease (32.5%), diabetes (27.5%), obesity (42.5%), and smoking (50.0%) were observed. Five patients (12.5%) developed PJI. Prior skin infection was strongly associated with PJI (55.6% vs. 0%; Fisher's exact $p<0.001$; corrected OR, 77.0; 95% CI, 3.6–1640.5). Multivariable modeling was not feasible because of perfect separation.

Conclusion: Prior skin infection was strongly associated with PJI but warrants cautious interpretation because of the small sample and wide confidence interval. Age, diabetes, and dental disease were not significant. These findings support comprehensive preoperative optimization, including dermatological, metabolic, and oral health assessment.

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Introduction

Prosthetic joint infection (PJI) is one of the most serious complications of total joint arthroplasty (TJA), resulting in prolonged hospitalization, increased healthcare costs, repeated revision procedures, and poorer functional outcomes [1-3]. The prevalence of PJI after primary arthroplasty is typically around 0.5%-2%, but is much greater after revision surgery, especially in older patients and those who have several comorbidities [4]. PJI is a multifactorial complication, which results from a combination of host susceptibility, microbial virulence, and perioperative factors [5].There are a few host-related factors that may be potentially modifiable and that can contribute to PJI risk, and hence are targets for optimization prior to surgery [6]. Diabetes and its related hyperglycemic control status can lead to a decrease in immune function and wound healing, which may predispose patients to postoperative infections [7,8]. Oral disease has also been investigated as a potential source of hematogenous microbial dissemination, but its clinical contribution to PJI is not fully understood [9]. Likewise, skin infections may reflect skin barrier disruption or contact with pathogens such as Staphylococcus aureus, which plays an important role in prosthetic infections [10]. Although these potentially modifiable factors are important, adequate characterization of these factors and their association with PJI in patients undergoing revision arthroplasty in Pakistan remains limited [11,12]. Risk assessment is especially important in patients undergoing revision arthroplasty because they are often older, have more comorbidities, and have prior exposure to orthopedic implants. Knowing patients who have easily determined risk factors preoperatively could help in identifying those that will benefit from further evaluation or optimization prior to revision surgery. But data relating to any of the above, such as skin infection, dental disease, diabetes, and other host factors, with PJI after revision arthroplasty is scarce in Pakistan.The novelty of the present study was the evaluation of these potentially modifiable host-related risk markers in hip or knee revision arthroplasty patients at a tertiary care hospital in Pakistan. In addition to estimating the incidence of confirmed PJI during follow-up, this study examined associations between previous skin infection, dental disease, diabetes, obesity, smoking, age, sex, and joint type and subsequent PJI. The findings may provide preliminary local evidence to support more systematic preoperative risk assessment and optimization in patients undergoing revision arthroplasty.

Materials and Methods

This retrospective cohort study was conducted in the Department of Orthopedic Surgery at MTI Bacha Khan Medical College and Mardan Medical Complex, Mardan, a tertiary-care hospital. From January 2024 and August 2024.The study protocol received approval from the Institutional Review Board of MTI Bacha Khan Medical College and Mardan Medical Complex (Letter No. 397/BKMC, dated 10/10/2023). The retrospective review included patients who had undergone elective revision arthroplasty between January and August 2023. We identified baseline clinical and host-related factors from patients' medical records and, where necessary, from documented clinical histories. We followed patients from the date of index revision surgery to determine whether confirmed PJI developed during the observation period. The mean follow-up duration was one year (SD, 101.5 days), and two of 40 patients were lost to follow-up before the end of the available observation period. Because only 5 PJI events occurred, we used a pre-specified parsimonious binary logistic regression model including age (<65 versus ≥65 years), diabetes, and dental disease to minimize the risk of model overfitting. An exploratory model including sex, joint type, obesity, smoking history, and prior skin infection was also attempted but failed to converge because prior skin infection perfectly separated patients with and without PJI. Therefore, we evaluated the association between prior skin infection and PJI using Fisher's exact test and, because of the zero cell, calculated a Haldane–Anscombe continuity-corrected odds ratio by adding 0.5 to each cell of the 2×2 contingency table. We considered a two-tailed p-value <0.05 statistically significant.

Sample Size

The minimum sample size was calculated using the single-proportion formula from OpenEpi:

$$n = Z^2P(1-P) / d^2$$

We assumed an anticipated prevalence of 30% for a major PJI risk marker based on previously published arthroplasty cohorts, with a 95% confidence level (Z=1.96) and a margin of error of 14.5%. These assumptions yielded a minimum sample size of approximately 39 patients. We therefore included all 40 eligible patients undergoing elective hip or knee revision arthroplasty during the predefined study period from January 2023 to August 2023 using consecutive non-probability sampling. Because revision arthroplasty represents a relatively small proportion of the institution's surgical workload, we included all eligible consecutive cases during the study period to maximize case capture and reduce selection bias.

Inclusion Criteria

- Patients age ≥ 18 years old
- Patients who are going to receive elective revision hip/knee arthroplasty
- All participants gave written informed consent.

Exclusion Criteria

- All patients who underwent emergency re-operation within 30 days of the first joint replacement surgery.
- Patients with an active infection from any location who are being treated with antibiotics
- If the patient cannot communicate or give a reliable history because of a severe cognitive impairment

Data Collection Procedure

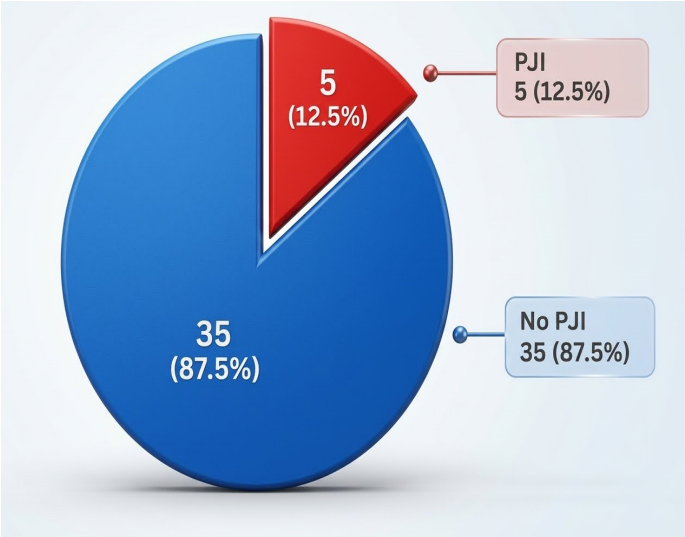
We used a structured proforma to retrospectively collect demographic and clinical data, including age, sex, BMI, joint type, diabetes, dental disease, smoking, obesity, and previous skin infection. We reviewed relevant medical, laboratory, dermatology, and dental records where available. We defined diabetes, dental disease, and previous skin infection using predefined criteria. Two research assistants coded the data, verified them, and resolved discrepancies by rechecking the original records.

Results

We analyzed 40 patients undergoing elective hip or knee revision arthroplasty. The mean age was 65.0 ± 6.8 years, with 21 (52.5%) aged ≥65 years and 22 (55.0%) males. We performed knee revision in 23 (57.5%) patients and hip revision in 17 (42.5%) patients. Previous skin infection was present in 9 (22.5%) patients, dental disease in 13 (32.5%), diabetes in 11 (27.5%), obesity (BMI ≥30 kg/m²) in 17 (42.5%), and smoking history in 20 (50.0%). Two patients (5.0%) were lost to follow-up. During follow-up, 5/40 (12.5%) developed confirmed PJI, while 35/40 (87.5%) remained PJI-free (Table 1; Figure 1).On univariate analysis, previous skin infection showed the strongest association with PJI. PJI occurred in 5/9 (55.6%) patients with previous skin infection compared with 0/31 (0.0%) without it (Fisher exact p<0.001). PJI was also more frequent among patients aged ≥65 years (4/21, 19.0% vs. 1/19, 5.3%; p=0.3451), males (5/22, 22.7% vs. 0/18, 0.0%; p=0.0530), those with dental disease (3/13, 23.1% vs. 2/27, 7.4%; p=0.3065), diabetes (2/11, 18.2% vs. 3/29, 10.3%; p=0.6030), obesity (4/17, 23.5% vs. 1/23, 4.3%; p=0.1437), and smoking history (4/20, 20.0% vs. 1/20, 5.0%; p=0.3416). PJI rates were similar after knee and hip revision (3/23, 13.0%).

vs. 2/17, 11.8%; p=1.0000). Thus, previous skin infection was the only statistically significant univariate factor (Table 2; Figure 2). Because no PJI occurred among patients without previous skin infection, the conventional odds ratio could not be estimated directly because of the zero cell; the Haldane–Anscombe correction yielded an odds ratio of 77.0 (95% CI, 3.6–1640.5). The wide confidence interval reflects the small sample and limited number of events. In the pre-specified parsimonious logistic regression model, age ≥65 years (AOR 3.35, 95% CI 0.32–35.33; p=0.314), diabetes (AOR 1.52, 95% CI 0.19–12.14; p=0.694), and dental disease (AOR 2.73, 95% CI 0.35–21.11; p=0.336) were not statistically significant. The exploratory full model including previous skin infection failed to converge because of perfect separation. Table 3 presents effect estimates.

Figure 1. Overall incidence of prosthetic joint infection



Overall distribution of patients according to development of confirmed PJI. Five of 40 patients (12.5%) developed PJI, whereas 35 (87.5%) remained free of PJI.

Table 1. Baseline demographic and clinical characteristics of the study population

Characteristic	Total (n=40)
Age, years, mean ± SD	65.0 ± 6.8
Age ≥65 years, n (%)	21 (52.5)
Male sex, n (%)	22 (55.0)
Knee revision, n (%)	23 (57.5)
Hip revision, n (%)	17 (42.5)
Previous skin infection, n (%)	9 (22.5)
Dental disease, n (%)	13 (32.5)
Diabetes mellitus, n (%)	11 (27.5)
Obesity (BMI ≥30 kg/m²), n (%)	17 (42.5)
Smoking history, n (%)	20 (50.0)
Lost to follow-up, n (%)	2 (5.0)
PJI developed, n (%)	5 (12.5)

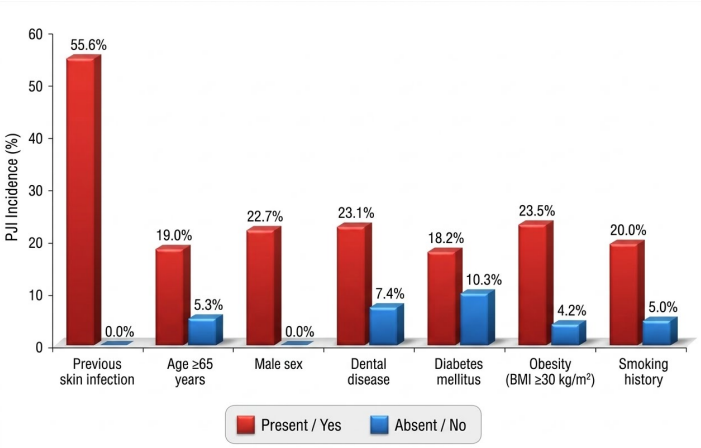
Data are presented as mean ± standard deviation or number (percentage), as appropriate. PJI = prosthetic joint infection; BMI = body mass index.

Table 2. Univariate analysis of factors associated with prosthetic joint infection

Variable	PJI, n/N (%)	No PJI, n/N (%)	p-value
Age ≥65 years	4/21 (19.0)	17/21 (81.0)	0.3451
Age <65 years	1/19 (5.3)	18/19 (94.7)	—
Male sex	5/22 (22.7)	17/22 (77.3)	0.0530
Female sex	0/18 (0.0)	18/18 (100.0)	—
Knee revision	3/23 (13.0)	20/23 (87.0)	1.0000
Hip revision	2/17 (11.8)	15/17 (88.2)	—
Previous skin infection	5/9 (55.6)	4/9 (44.4)	**0.0002***
No previous skin infection	0/31 (0.0)	31/31 (100.0)	—
Dental disease	3/13 (23.1)	10/13 (76.9)	0.3065
No dental disease	2/27 (7.4)	25/27 (92.6)	—
Diabetes mellitus	2/11 (18.2)	9/11 (81.8)	0.6030
No diabetes mellitus	3/29 (10.3)	26/29 (89.7)	—
Obesity (BMI ≥30 kg/m²)	4/17 (23.5)	13/17 (76.5)	0.1437
No obesity	1/23 (4.3)	22/23 (95.7)	—
Smoking history	4/20 (20.0)	16/20 (80.0)	0.3416
No smoking history	1/20 (5.0)	19/20 (95.0)	—

PJI = prosthetic joint infection; BMI = body mass index. Percentages are calculated within each exposure category. *Fisher exact test; p<0.05 was considered statistically significant.

Figure 2. PJI incidence according to selected demographic and clinical risk factors



Observed PJI proportions across selected risk-factor categories. Previous skin infection showed the largest difference (55.6% vs. 0.0%), followed by obesity (23.5% vs. 4.3%), dental disease (23.1% vs. 7.4%), smoking (20.0% vs. 5.0%), age ≥65 years (19.0% vs. 5.3%), and diabetes mellitus (18.2% vs. 10.3%).

Table 3. Effect estimates for previous skin infection and parsimonious multivariable logistic regression

Predictor	Effect estimate	95% CI	p-value
Previous skin infection	OR 77.0*	3.6–1640.5	<0.001†
Age ≥65 years	AOR 3.35	0.32–35.33	0.314
Diabetes mellitus	AOR 1.52	0.19–12.14	0.694
Dental disease	AOR 2.73	0.35–21.11	0.336

Alternatively, OR = odds ratio; AOR = adjusted odds ratio; CI = confidence interval. *Haldane–Anscombe continuity-corrected OR because one cell contained zero events; †Fisher exact p-value. Interpret the corrected OR cautiously because of the small number of PJI events and complete separation.

Discussion

In this retrospective cohort of 40 patients undergoing hip or knee revision arthroplasty, 5 patients (12.5%) developed confirmed PJI during follow-up. The principal finding was a statistically significant association between previous skin infection and subsequent PJI. All 5 PJI events occurred among the 9 patients with a history of previous skin infection (55.6%), whereas none of the 31 patients without such a history developed PJI.

This finding is biologically plausible because previous skin infection may indicate disruption of the skin barrier, recurrent colonization, or increased exposure to organisms such as *Staphylococcus aureus*, which are important causes of PJI [13,14]. New studies also suggest that a history of skin or soft tissue infection could help identify patients at higher risk of developing prosthetic infection [15,16]. However, given the small number of PJI events (n=5), interpret the association observed in the present study as a hypothesis until larger cohorts prove it. Because of the zero cell, we could not directly estimate a conventional odds ratio; no PJI events occurred among patients with no previous skin infection. We estimated the odds ratio to be 77.0 (95% CI, 3.6–1640.5) after Haldane–Anscombe continuity correction. This wide confidence interval reflects limited data to estimate the effect size and a small number of outcome events, so it should not be taken as a precise estimate. The statistically significant Fisher's exact test supports the association, but larger studies are needed to confirm its magnitude and independence. The three prespecified factors (age ≥65 years, diabetes, dental disease) in the primary multivariable model were not statistically significant. This result should be taken with the caveat of the small number of outcome events. Diabetes mellitus is a significant patient-related risk factor for PJI following TJA, as shown in previous systematic reviews and meta-analyses [17,18]. Likewise, investigators of large observational studies have reported that diabetes was associated with an increased risk of PJI, especially if glycemic control is sub-optimal [19]. In contrast, diabetes was not statistically significant in our multivariable model. This should not be interpreted as diabetes being unrelated to PJI; however, because there were only 5 PJI events in the present study, power to detect moderate associations was limited. Peri-operative glycemic optimization remains clinically relevant in patients undergoing revision arthroplasty. Male patients had a greater numerical PJI rate than female patients (22.7% vs. 0.0%, respectively; p=0.053). This difference was not statistically significant, but the direction of the finding was consistent with previous systematic reviews which found that male sex may be a risk factor for PJI [20,21]. The lack of statistical significance in the current study should be taken with a grain of salt because of the limited number of events and the sample size. Larger cohorts are needed to determine whether dental disease is an independent risk factor for PJI after revision arthroplasty. The PJI rates among patients with reported dental disease and those without were similar (7.4% vs. 23.1%, respectively; p=0.307). Previous studies have examined the possible association between oral disease, dental procedures, bacteremia, and hematogenous PJI, but the significance and strength of this association remain unclear [22,23]. While our data do not prove dental disease to be an independent risk factor for PJI, they suggest that future studies should investigate this relationship. Furthermore, some dental history was self-reported in our cohort, which could have led to misclassification or recall bias. However, assessing and managing oral disease remains a sensible part of comprehensive pre-op optimization. Diabetes, increased BMI, and other patient factors were noted previously in Pakistan as potential factors for PJI after primary total knee replacement [24]. In a similar 10-year study in Saudi Arabia, patient-related risk factors were shown to be important in the development of PJI, and the multidirectional nature of prosthetic infections was highlighted [25]. In conclusion, we contributed to this regional literature by examining incident PJI after hip and knee revision arthroplasty in a Pakistani tertiary care setting. Interestingly, the incidence in our cohort (12.5%) is higher than the reported incidence after primary arthroplasty, reflecting the increased infection risk associated with revision surgeries [4,26]. Interpret comparisons with caution, as many factors influence PJI incidence, including patient selection, revision indication, follow-up length, infection definitions, and institutional practices.The most significant finding is the association between prior skin infection and PJI. A previous skin infection may indicate persistent or recurrent colonization or underlying susceptibility to infection. The absence of PJI in all patients without a prior skin infection created a strong statistical signal, but also considerable uncertainty about the effect estimate. Thus, these results should not be considered as proof of causality or as evidence that the presence of a

previous skin infection is a risk factor for PJI in itself. Clinically, the results suggest close monitoring of past skin infections during the pre-operative evaluation of patients undergoing revision arthroplasty. This evaluation should be used alongside existing preventive measures, such as optimizing blood glucose control, controlling obesity and smoking, managing active infections, and reviewing other potentially modifiable health issues [17,18,26]. Given the association between skin infection and PJI observed in this study (and only five PJI cases), however, larger studies are needed before routine clinical practice adjustments based on a history of skin infection. Overall, these findings support a multidisciplinary approach to preoperative optimization that considers dermatological history, metabolic status, oral health, smoking, obesity, and other established patient-related factors. Future prospective, multicenter studies with larger sample sizes, standardized definitions of previous skin infection and dental disease, systematic microbiological assessment, and adequate numbers of PJI events are needed to determine whether previous skin infection independently predicts PJI following revision arthroplasty.This study has several limitations. First, statistical power was limited by the small sample size and the occurrence of only 5 PJI events. Consequently, the study may not have detected moderate associations, and the continuity-corrected odds ratio for prior skin infection had a very wide confidence interval. Second, the study was conducted at a single tertiary-care center, which may limit generalizability to other healthcare settings. Third, some dental and dermatological histories were based partly on available clinical documentation or patient-reported information, potentially introducing recall or information bias. Fourth, two of 40 patients were lost to follow-up before the planned endpoint. Finally, we did not systematically assess preoperative microbiological colonization; therefore, the observed association between previous skin infection and subsequent PJI may be influenced by unmeasured confounding factors. Larger multicenter prospective studies are required to validate these findings and determine the independent contribution of prior skin infection, diabetes, dental disease, and other patient-related factors.

Conclusion

Among 40 patients undergoing hip or knee revision arthroplasty, 5 (12.5%) developed PJI during follow-up. Prior skin infection was significantly associated with subsequent PJI in this cohort, with all observed PJI events occurring among patients with a history of prior skin infection. However, because of the small number of events and the very wide confidence interval of the continuity-corrected odds ratio, this finding should be considered hypothesis-generating rather than a definitive estimate of risk. Age, diabetes, and dental disease were not statistically significant in the pre-specified multivariable model, although the study had limited power to detect moderate associations. These findings support careful assessment and optimization of potentially modifiable factors before revision arthroplasty and highlight the need for larger multicenter studies to determine whether previous skin infection independently predicts PJI.

Ethical approval

Ethical approval was obtained from the Institutional Review Board of MTI Bacha Khan Medical College and Mardan Medical Complex, Mardan (Letter No. 397/BKMC, dated 10/10/2023). We obtained written informed consent from all participants.

Disclaimer: None.

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

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Authors' Contributions

Zahir Khan: Conceptualization, study design, methodology, data collection, data analysis and interpretation, manuscript drafting, critical revision, and final approval of the version to be published.

Aimon Zia: Study methodology, data collection, data curation, literature review, manuscript drafting, critical revision, and final approval of the version to be published.

Arsalan Azmat Swati: Data collection, statistical analysis, interpretation of results, literature review, critical revision of the manuscript, and final approval of the version to be published.

All authors contributed substantially to the work, approved the final version of the manuscript, agreed to be accountable for all aspects of the work, and accept responsibility for ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Original Article

Prevalence of Urinary Tract Infections and their Associated Risk Factors in Antenatal Women Attending OPD

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Abstract

Objective: To determine the prevalence of UTI and identify associated risk factors among antenatal women attending outpatient services.

Methodology: This Cross-sectional study was conducted in the Department of Obstetrics and Gynecology, Qazi Hussain Ahmad Medical Complex, Nowshera, Pakistan, from March 2025 to September 2025. We enrolled 220 pregnant women using non-probability consecutive sampling. We collected sociodemographic, obstetric, and clinical data through a structured questionnaire. We analyzed midstream urine samples using standard microbiological methods. We analyzed data using SPSS version 27. We performed chi-square and binary logistic regression analyses, with $p < 0.05$ considered statistically significant.

Results: The overall UTI prevalence was 31.8% (n = 70). Among infected women, 64.3% had symptomatic UTI and 28.6% had asymptomatic bacteriuria. Escherichia coli was the predominant pathogen (60.0%). Significant associations were observed with educational status ($p = 0.008$), rural residence ($p = 0.009$), low socioeconomic status ($p = 0.001$), multigravidity ($p = 0.015$), previous UTI history ($p < 0.001$), diabetes mellitus ($p = 0.002$), and anemia ($p = 0.009$). Logistic regression identified previous UTI and diabetes mellitus as independent risk factors.

Conclusion: UTI is highly prevalent during pregnancy and is associated with several sociodemographic and clinical factors. Routine antenatal screening and targeted preventive measures are essential to improve maternal and fetal outcomes.

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Introduction

UTI is one of the most prevalent bacterial infections in pregnancy and comprises asymptomatic bacteriuria, acute cystitis, and pyelonephritis [1]. Hormonal and anatomic changes associated with pregnancy increase infection risk, including decreased ureteric peristalsis, urinary stasis, bladder hypotonia, and mechanical compression of the urinary tract from the enlarging uterus [2,3]. Other changes in urine composition can also support bacterial growth and multiplication, such as glycosuria [4]. Incidence of UTI during pregnancy depends on the population, socioeconomic factors, diagnostic criteria, antenatal screening, and availability of healthcare services [5]. Since untreated infection can lead to pyelonephritis and to other maternal complications, such as sepsis and renal impairment [6], asymptomatic bacteriuria is a significant issue. Perinatal morbidity, such as low birth weight, premature rupture of membranes, preterm birth, and stillbirth, has also been reported as complications of maternal UTI [7]. During pregnancy, Escherichia coli is the most common pathogen isolated in UTI, followed by Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa, and Enterococcus species [8]. Some of the risk factors previously identified are previous UTIs, multiparity, diabetes mellitus, anemia, poor personal hygiene, and low fluid intake, as well as socioeconomic disadvantage [9]. However, in Pakistan, scarce diagnostic services, self-medication and antimicrobial resistance, and a lack of locally relevant epidemiological data are important challenges in preventing and managing UTI during pregnancy [10]. Despite its clinical significance, limited data are available on UTI prevalence and determinants in locally relevant settings. Therefore, this study aimed to determine the prevalence of UTI and associated risk factors among antenatal women attended in the OPD. This study aims to provide evidence on the prevalence of UTI and associated risk factors among antenatal women at a particular institution. The study may contribute to identifying women at heightened risk of infection based on relevant demographic, obstetric, behavioral, and clinical parameters, and to targeted antenatal screening and early management. The results could also add to the scarce literature on UTI in pregnancy in the region and serve as baseline data for future multicentre research. The study will also contribute to better patient education, prevention measures, and the rational use of antibiotics during pregnancy.

Materials and Methods

This cross-sectional study was conducted at the Department of Obstetrics and Gynecology, Qazi Hussain Ahmad Medical Complex, Nowshera, Pakistan, from March 2025 to September 2025. The study population included pregnant women attending antenatal clinics during the study period. All pregnant women who attended OPD for antenatal care were considered eligible for the study, regardless of age or gestation period.

Sample Size

The sample size was calculated using the WHO-recommended formula for estimating a population proportion

$$n = \frac{Z^2 P(1-P)}{d^2},$$

where n is the required sample size, Z is the standard normal variate at a 95% confidence level (1.96), P is the anticipated prevalence of UTI among pregnant women, and d is the margin of error (5%). The calculated sample size was **220**. After adding 10% to account for possible non-response or incomplete data, the final sample size was 242.

Participants

We enrolled 220 pregnant women attending the antenatal outpatient department on a consecutive basis. Eligible participants were women of any gestational age who provided written informed consent and agreed to participate in the study.

Inclusion Criteria

The following participants were included in the study:

- Pregnant women of any gestational age attending antenatal OPD
- Women willing to participate in the study
- Women who provided written informed consent

Exclusion Criteria

The following participants were excluded from the study:

- Women currently receiving antibiotic therapy
- Women with known chronic renal disease or congenital urinary tract abnormalities
- Critically ill patients unable to provide information
- Women unwilling to participate

Data Collection Procedure

We used a structured, pre-validated questionnaire developed after a comprehensive literature review to collect data. The questionnaire covered sociodemographic characteristics, obstetric history, clinical symptoms, personal hygiene practices, previous history of UTI, fluid intake, sexual activity, and relevant medical conditions. The study team approached eligible participants during antenatal clinic visits and explained the study objectives and procedures. We obtained written informed consent before enrollment. Trained data collectors conducted face-to-face interviews to ensure complete and accurate information.

Statistical Analysis

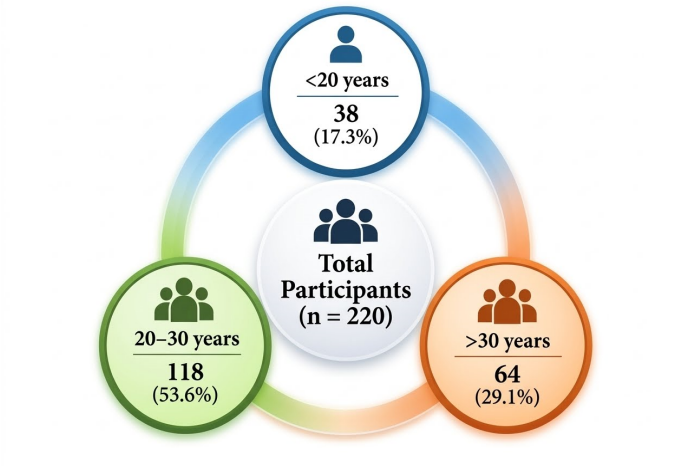
The Statistical Package for Social Sciences (SPSS) version 27, developed by IBM Corporation, was used to code, enter, and analyze the data. Before analysis, we cleaned and validated the data for completeness and accuracy. We used descriptive statistics to describe participant characteristics. We presented categorical variables as frequencies and percentages, and continuous variables as mean ± SD. We computed the prevalence of UTI as the percentage of the total study population with a positive urine culture. We assessed the association between UTI status and categorical independent variables using the Chi-square test. We used Fisher's exact test when the assumptions of the Chi-square test were not met. We entered variables with a statistically significant association ($p \leq 0.05$) in the bivariate analysis into a binary logistic regression model to identify independent predictors of UTI. We reported results as adjusted odds ratios (AORs) with 95% confidence intervals (CIs). We considered p-values ≤ 0.05 statistically significant.

Results

The study included 220 antenatal women. The research profile showed a mean participant age of 27.84 ± 5.63 years, with ages ranging from 18 to 41 years. Grouping age into discrete brackets showed that most participants, 118 (53.6%), fell within the core age group of 20–30 years. This distribution was followed by 64 (29.1%) women in the advanced maternal age category (above 30 years) and 38 (17.3%) participants under 20 years. Occupationally and socio-economically, the baseline profile indicated vulnerable frameworks; a large majority of the cohort were housewives (81.8%) and lived in rural environments (57.3%). Education levels varied, with 72 (32.7%)

completing primary education, and 48 (21.8%) classified as completely illiterate. Low socioeconomic status represented the largest single cohort tier at 47.3%.

Figure 1: Distribution of participants by age category.



The figure shows the age distribution of the study participants. Of the 220 participants, 38 (17.3%) were aged <20 years, 118 (53.6%) were aged 20–30 years, and 64 (29.1%) were aged >30 years.

Table 1: Baseline Sociodemographic Profile of the Study (N = 220)

Variable	Category	Frequency (n)	Percentage (%)
Age Group	<20 years	38	17.3
	20–30 years	118	53.6
	>30 years	64	29.1
Educational Status	Illiterate	48	21.8
	Primary Education	72	32.7
	Secondary Education	66	30.0
	Higher Education	34	15.5
Residence	Urban	94	42.7
	Rural	126	57.3
Socioeconomic Status	Low	104	47.3
	Middle	82	37.3
	High	34	15.5
Occupation	Housewife	180	81.8
	Employed	40	18.2

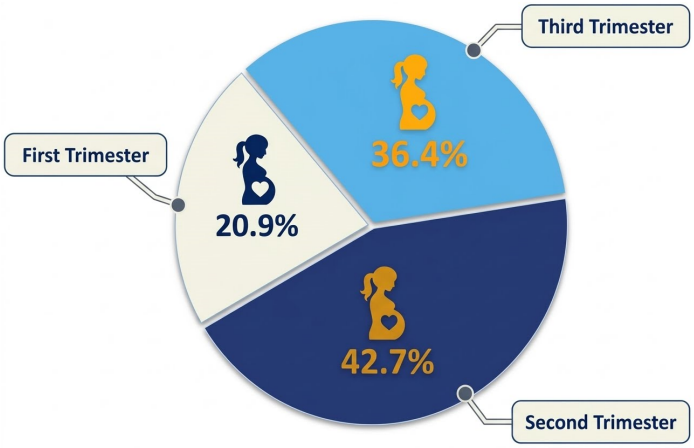
Data are presented as frequency and percentage. The table summarizes the participants' age group, educational status, place of residence, socioeconomic status, and occupation.

Table 2: Obstetric and Comorbidity Profile of Surveyed Antenatal Patients

Clinical Metric	Classification	Frequency (n)	Percentage (%)
Trimester Stage	First Trimester	46	20.9
	Second Trimester	94	42.7
	Third Trimester	80	36.4
Parity Status	Primigravida	85	38.6
	Multigravida	135	61.4
Previous History of UTI	Yes	74	33.6
	No	146	66.4
Diabetes Mellitus	Yes	31	14.1
	No	189	85.9
Anemia Status	Yes	69	31.4
	No	151	68.6

Data are presented as frequency and percentage. The table summarizes trimester of pregnancy, parity status, previous history of UTI, diabetes mellitus, and anemia among the study participants. N = 220. UTI, urinary tract infection.

Figure 2: Distribution of Participants According to Trimester of Pregnancy



The figure shows the distribution of participants according to trimester of pregnancy. Participants were distributed as follows: 20.9% in the first trimester, 42.7% in the second trimester, and 36.4% in the third trimester.

Table 3: Integrated Breakdown of UTI Prevalence, Clinical Presentation, and Microorganism Distribution

Variable	Category	Frequency, n (%)
UTI status	Positive	70 (31.8)
	Negative	150 (68.2)
Clinical presentation among UTI-positive women	Symptomatic UTI	45 (64.3)
	Asymptomatic bacteriuria	20 (28.6)
Predominant microorganism	*Escherichia coli*	42 (60.0)

Data are presented as frequency and percentage. UTI, urinary tract infection. Percentages for clinical presentation and microorganism distribution are calculated among women with UTI (n = 70).

Table 4: Bivariate Chi-Square Evaluations of Sociodemographic, Obstetric, and Clinical Drivers with UTI Status

Variable Block	Category Subtype	UTI Posn(%)	UTI Negn(%)	p-value
Educational Status	Illiterate	24 (50.0)	24 (50.0)	**0.008***
	Primary Education	25 (34.7)	47 (65.3)	
	Secondary Education	15 (22.7)	51 (77.3)	
	Higher Education	6 (17.6)	28 (82.4)	
Residence Type	Urban	21 (22.3)	73 (77.7)	**0.009***
	Rural	49 (38.9)	77 (61.1)	
Socioeconomic Status	Low	44 (42.3)	60 (57.7)	**0.001***
	Middle	20 (24.4)	62 (75.6)	
	High	6 (17.6)	28 (82.4)	
Parity Standing	Primigravida	19 (22.4)	66 (77.6)	**0.015***
	Multigravida	51 (37.8)	84 (62.2)	
Prior History of UTI	Yes	40 (54.1)	34 (45.9)	**<0.001***

	No	30 (20.5)	116 (79.5)	
Diabetes Mellitus	Yes	18 (58.1)	13 (41.9)	**0.002***
	No	52 (27.5)	137 (72.5)	
Anemia Profile	Yes	31 (44.9)	38 (55.1)	**0.009***
	No	39 (25.8)	112 (74.2)	

Data are presented as frequency and percentage. We assessed associations between categorical variables and UTI status using the chi-square test or Fisher's exact test, as appropriate. A p-value ≤0.05 was considered statistically significant.

Table 5: Multivariate Logistic Regression Model Predicting Independent Antenatal UTI Risk

Independent Predictor Variable	Adjusted OR (AOR)	95% Confidence Interval (CI)	p-value
Previous History of UTI	3.84	2.01–7.31	**<0.001***
Diabetes Mellitus	2.91	1.28–6.64	**0.011***
Low Socioeconomic Status	2.47	1.29–4.73	**0.006***
Anemia Profile	1.96	1.04–3.69	**0.037***
Rural Residence	1.82	0.97–3.41	0.061
Multigravida Status	1.59	0.84–3.01	0.148

Data are presented as adjusted odds ratios (AORs) with 95% confidence intervals (CIs) and p-values. We included variables significantly associated with UTI in the bivariate analysis in the multivariate logistic regression model. We considered p-values ≤0.05 statistically significant. UTI, urinary tract infection; AOR, adjusted odds ratio; CI, confidence interval

Discussion

UTI remains an important cause of maternal morbidity during pregnancy, particularly in resource-limited settings. Pregnancy-related hormonal and anatomical changes, including ureteric dilatation, reduced peristalsis, urinary stasis, and vesicoureteral reflux, increase susceptibility to bacterial colonization and ascending infection [11,12]. The prevalence of UTI in the present study was 31.8%, meaning that one in three antenatal women had UTI. This finding highlights high infection levels among study participants and the need for routine antenatal assessment. The level of prevalence found in this study is similar to the high burden of UTI reported among pregnant women in developing countries. These differences between studies may reflect variations in population characteristics, screening and diagnostic approaches, and access to antenatal care [13,14]. A key feature is the infection's asymptomatic nature, as a woman can have many bacteria in her urine without symptoms [15]. Treatment of asymptomatic bacteriuria in pregnancy may decrease the risk of progression to symptomatic infection and pyelonephritis if it is detected early enough [16]. The present study showed that women aged 20-30 years made up the largest proportion of the study population, but no significant association was seen between age and UTI status. This finding suggests that susceptibility to UTIs may be more related to pregnancy-related physiological changes than chronological age. Previous studies have also shown that UTIs can happen at any reproductive age group, highlighting the need to undertake screening rather than just in a specific age group during pregnancy [17]. Educational status was significantly associated with UTI. Lower education was associated with higher infection rates in women. Education can affect health literacy, hygiene knowledge, awareness of urinary symptoms, and timely use of antenatal services. Previous studies have also reported similar relationships between sociodemographic characteristics and maternal UTI [18]. UTI prevalence was also significantly higher in rural than in urban women and was significantly associated with rural dwelling. This may be due to poor access to health care facilities, diagnostic services, sanitation, and health education. The results underscore the need to improve antenatal screening and prevention services, especially for women who are not being served in these communities [19]. There was also a strong correlation between low socioeconomic status and UTI. These factors may be impacted by socioeconomic disadvantage, such as access to healthcare, nutrition, clean water, sanitation, and timely lab investigation. These can all make a woman more susceptible to infections during pregnancy [20]. Solving these socioeconomic problems may therefore be an important part in reducing the burden of maternal UTI. The incidence of UTI was much higher among multigravida women than among the primigravida women. Cumulative exposure to obstetric risk factors and changes in pelvic support and urinary retention may be associated with repeated pregnancies. Parity and obstetric history were also reported as possibly important factors in maternal urinary infection in previous studies [21].One important finding was that previous UTI was highly associated with current infection. Women with a UTI history had significantly greater UTI prevalence, and prior UTI was the most consistent independent risk factor in the multivariate model (AOR 3.84, 95% CI 2.01–7.31; p<0.001). Recurrent infection may result from persistent or recurrent bacterial colonization, failure to eradicate bacteria, antimicrobial resistance, or susceptibility [22]. Further study and monitoring of pregnant women with a history of UTI is supported. In the present study, other statistically significant associations were those of diabetes mellitus and anemia. Diabetes may predispose a woman to urinary infection through changes in host defense and metabolic pathways. At the same time, anemia may be linked to nutritional and socioeconomic factors that affect a woman's susceptibility to urinary infection[22]. This study highlights the need to take into account common maternal comorbidities as a factor in the risk of developing UTI during antenatal care. This study has certain limitations. Its single-center, cross-sectional design limits causal inference. Selection bias may have arisen from the consecutive sampling method, and recall bias from self-reported information. The study also did not evaluate antimicrobial susceptibility or several potentially relevant confounders, including body mass index, detailed sexual practices, and catheterization history. Nevertheless, the study provides useful baseline evidence regarding the burden and associated factors of UTI among antenatal women in this setting.

Conclusion

UTI is a common condition among pregnant women and is significantly associated with low education level, rural residence, low socioeconomic status, multigravida, previous UTI, diabetes mellitus and anemia. The bacterium Escherichia coli (E. coli) was found to be the major pathogen. Regular antenatal screening, early diagnosis, and appropriate management of women at risk of UTI in pregnancy are critical to minimize maternal and fetal complications of UTI in pregnancy.

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Ethical approval

Ethical approval was obtained from the Ethical Review Board of Nowshera Medical College, Nowshera **(Approval No. 16(i)/ERB/NMC; February 1, 2025)**

Authors' Contribution

Mehwish Sayed: Conceptualization, study design, data acquisition, data analysis and interpretation, manuscript drafting, critical revision, supervision, and final approval.

Sumayya: Data acquisition, data analysis and interpretation.

Javeria Saleem: Data analysis and interpretation.

Saeeda Safi: Data acquisition, data analysis and interpretation, critical revision, and supervision.

Shah Nawaz: Data acquisition, data analysis and interpretation, critical revision, and supervision.

All authors read and approved the final manuscript and agreed to be accountable for all aspects of the work.

Data Availability: The data generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Original Article

Surgical Management of Cervical Disc Herniation in a Resource-Limited Setting: Outcomes and Challenges

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Abstract

Objectives: To evaluate clinical and functional outcomes and identify perioperative and health-system challenges among patients undergoing surgical treatment for symptomatic cervical disc herniation in a resource-limited tertiary-care hospital.

Methodology: This Retrospective Observational Study Was Conducted In The Department Of Neurosurgery, MMC/BKMC mardan, From January To December 2025. We included 100 consecutive adult patients with MRI-confirmed symptomatic cervical disc herniation who underwent surgical treatment. We retrospectively extracted demographic, clinical, radiological, operative, postoperative, and health-system data from medical records. We assessed pain and functional disability using the Visual Analog Scale (VAS) and Neck Disability Index (NDI), respectively, before surgery and at 6-month follow-up.

Results: Among 100 patients, 62% were male, and 38% were female, with a mean age of 47.8 ± 11.4 years. The most frequently affected level was C5–C6 (44%), followed by C6–C7 (31%). Radiculopathy was present in 71% of patients and myelopathy in 29%. We performed ACDF in 82% of patients, while 18% underwent discectomy without fusion. Mean VAS decreased from 7.6 ± 1.2 preoperatively to 2.3 ± 1.1 at 6 months, while mean NDI decreased from 34.5 ± 8.7 to 12.8 ± 5.4 (both $p<0.001$). Postoperative complications occurred in 11% of patients. Documented health-system barriers included delayed MRI access (27%), implant shortages (19%), and operating-room scheduling delays (22%).

Conclusion: In this single-center retrospective cohort, surgical treatment of symptomatic cervical disc herniation was associated with substantial improvements in pain and functional disability at 6 months. Delays in MRI access, implant availability, and operating-room scheduling represented important health-system challenges.

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Introduction

Cervical disc herniation is a prevalent degenerative condition of the spine and a leading cause of neck pain, cervical radiculopathy, and myelopathy around the world. It results from protrusion of the nucleus pulposus through a damaged annulus fibrosus, which in turn compresses nearby nerve roots or the spinal cord. It commonly occurs in middle-aged adults (4th-6th decades) and may cause considerable disability in daily activities and productivity. While many patients benefit from conservative management with analgesics, cervical immobilization, and physiotherapy, many require surgical treatment for persistent symptoms, progressive neurological symptoms, or radiographic evidence of significant neural compression [1,2]. Over the past few decades, surgical treatment for cervical disc herniation has improved for appropriately selected patients, with the choice of procedure depending on disease level and extent, neurological findings, cervical alignment, and other patient- and surgeon-related factors. Alternative surgical approaches, including anterior cervical discectomy without fusion, cervical corpectomy, and posterior cervical decompression, are chosen depending on the pathology, location, and surgeon preference. Many reports from developed nations describe outstanding outcomes with cervical spine surgery, including pain reduction, neurological improvement, and improved quality of life. However, these results may not be directly applicable to low- and middle-income countries, where health-care infrastructure and resources are often scarce [3,4]. Limited-resource countries have several factors that could impact the treatment of cervical disc disease. These include delayed access to high-tech imaging (magnetic resonance imaging [MRI]), limited availability of spinal implants, limited operating room time, a shortage of spine surgeons, and financial barriers to accessing care. A delay in diagnosis and symptoms may lead to poorer neurological function at diagnosis and possibly an inferior outcome following surgery. Additionally, variable post-surgical follow-up and rehabilitation may impact long-term outcomes [5,6]. Despite these limitations, cervical spine surgery is growing in popularity in tertiary care neurosurgical hospitals in developing nations. Understanding outcomes in such settings is critical to determine whether satisfactory care can be delivered despite resource constraints. Furthermore, understanding region-specific obstacles can help hospital administrators and policymakers identify areas that need investment to ensure quality care for patients with spinal disorders [7]. Unfortunately, few studies from low-resource settings have been published on the surgical outcomes of cervical disc herniation and complications encountered during hospital care. Most of these data come from high-income healthcare systems and may not represent low-income settings. Thus, developing local data is critical for institutional benchmarking, developing clinical and hospital treatment protocols, and health-care planning [8]. This study was carried out to assess the results of surgical treatment for cervical disc herniation in a low-resource tertiary care neurosurgical department. It also sought to identify common perioperative and infrastructural complications during treatment. By evaluating pain relief, functional improvement, complications, and systemic challenges, this study aims to provide a holistic view of the feasibility and success of cervical spine surgery in a resource-limited setting [9,10].

Materials and Methods

We conducted a retrospective observational study in the Department of Neurosurgery at a tertiary-care teaching hospital from January 2025 to December 2025.We retrospectively reviewed the records of 100 consecutive adult patients with symptomatic MRI-confirmed cervical disc herniation who underwent surgical treatment during the study period. We identified eligible cases from operative logs and hospital records. We extracted demographic characteristics, presenting symptoms, MRI findings, operative details, postoperative complications, and follow-up outcomes from medical and outpatient records.

Patient Sampling

We considered all consecutive eligible adult patients with MRI-confirmed symptomatic cervical disc herniation who underwent surgical treatment during the study period from January 1, 2025, to December 31, 2025. A total of 100 eligible patient records met the predefined inclusion and exclusion criteria and were included in the final analysis. We used consecutive sampling to minimize selection bias and include all eligible cases available during the predefined study period.

Inclusion Criteria

- Age ≥18 years.
- MRI-confirmed cervical disc herniation.
- Symptomatic cervical radiculopathy or myelopathy attributable to the cervical disc lesion.
- Failure of an adequate trial of conservative treatment
- Underwent cervical spine surgery during the study period.
- Documented clinical follow-up at 6 months after surgery.

Exclusion Criteria

- Cervical spinal trauma.
- Cervical spinal tumors or infections.
- Previous cervical spine surgery at the affected level.
- Multisystem trauma.
- Incomplete medical records preventing assessment of the study variables.
- No documented 6-month postoperative follow-up.

Diagnostic and Management Strategy

All patients underwent neurological examination and cervical MRI for confirmation of the diagnosis and assessment of the affected level and neural compression. The decision to operate was based on clinical presentation, neurological findings, MRI characteristics, symptom severity and persistence, and surgeon assessment. The surgical approach was selected according to the level and

characteristics of the disc pathology and the presence or absence of spinal cord or nerve-root compression. We provided standard perioperative antibiotic prophylaxis, postoperative analgesia, mobilization, and physiotherapy in line with institutional practice.

Outcome Assessment

The primary clinical outcomes were changes in pain intensity and functional disability from the preoperative assessment to the 6-month postoperative follow-up. We assessed pain intensity using a 0–10 Visual Analog Scale (VAS), with higher scores indicating greater pain intensity. We assessed functional disability using the Neck Disability Index (NDI), a 10-item patient-reported measure of neck-related disability. Each NDI item is scored from 0 to 5, yielding a total raw score of 0 to 50, with higher scores indicating greater disability. We obtained preoperative VAS and NDI scores from clinical records, and recorded postoperative scores at the 6-month follow-up visit using the same assessment method. We also documented postoperative complications during follow-up.

Assessment of Health-System Barriers

We assessed health-system barriers retrospectively by reviewing available hospital, radiology, operative, and perioperative records. We considered a health-system barrier present when a documented system-related factor contributed to delays or difficulties in providing planned diagnostic or surgical care. We defined delayed MRI access as a documented delay in obtaining a cervical MRI required for diagnostic confirmation or preoperative surgical planning because of limited imaging availability, scheduling constraints, or other institutional access-related factors. We defined operating-room scheduling delay as a documented postponement of the planned cervical spine procedure attributable to operating-room availability, scheduling constraints, or competing operative demands. We defined implant shortage as documented unavailability of the required spinal implant or instrumentation when needed for the planned surgical procedure, resulting in difficulty or delay in proceeding with surgery. We considered only barriers documented in available medical or hospital records. We did not classify patient-related delays, including failure to attend appointments or delays caused solely by patient preference, as health-system barriers unless a system-related factor was also documented. Because individual patients could experience more than one barrier, the categories were not mutually exclusive, and their percentages may therefore exceed the percentage of patients experiencing any single barrier.

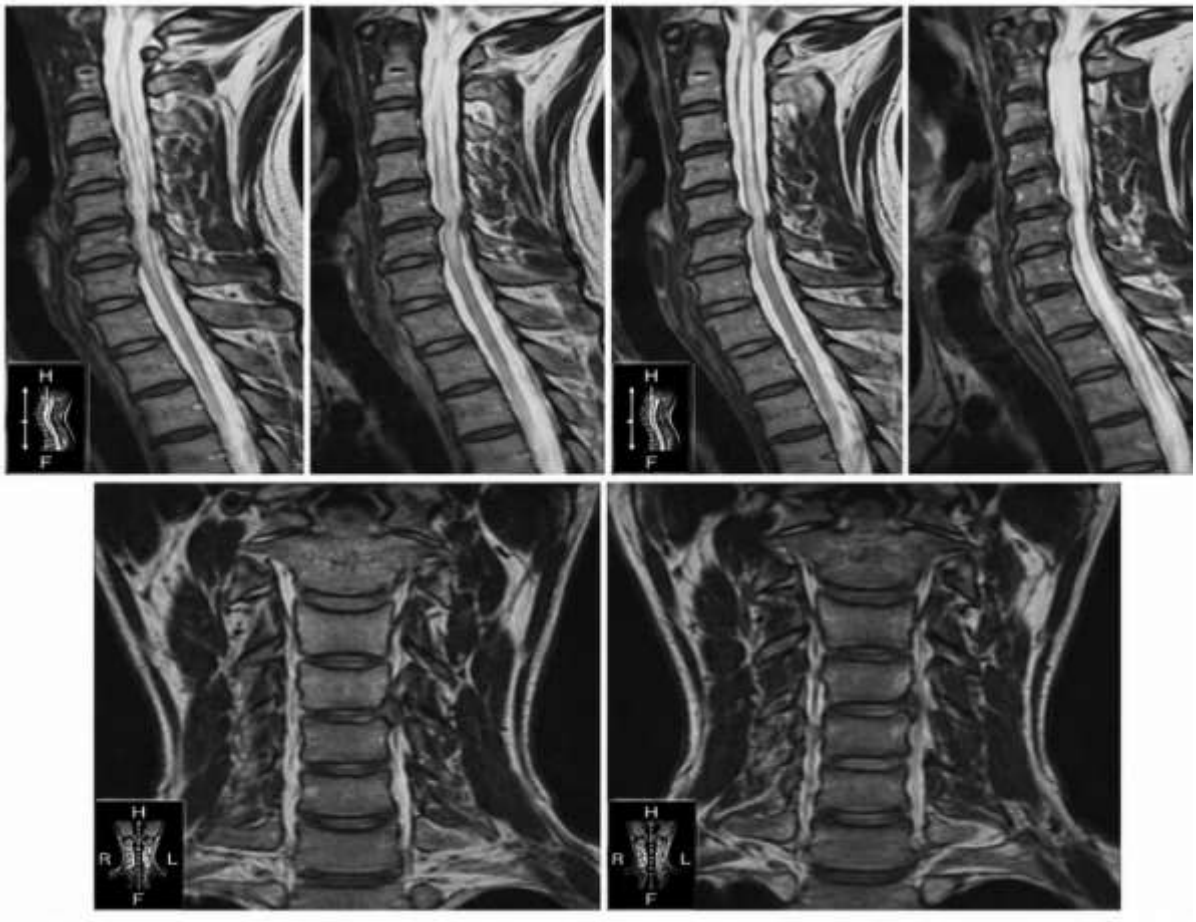
Statistical Analysis

We analyzed data using IBM SPSS Statistics version 26.0. We summarized continuous variables as mean ± standard deviation (SD), and presented categorical variables as frequencies and percentages. We assessed the distribution of continuous variables and the normality of paired differences before inferential analysis. We compared preoperative and postoperative VAS and NDI scores using paired-samples t-tests when the assumptions were met. We calculated mean changes from baseline to 6-month follow-up. For categorical variables, we reported frequencies and percentages and used appropriate statistical tests to compare subgroups. All statistical tests were two-sided, and we considered $p < 0.05$ statistically significant. We assessed missing data before analysis and included only patients with documented preoperative and 6-month postoperative outcome assessments in the paired analysis.

Results

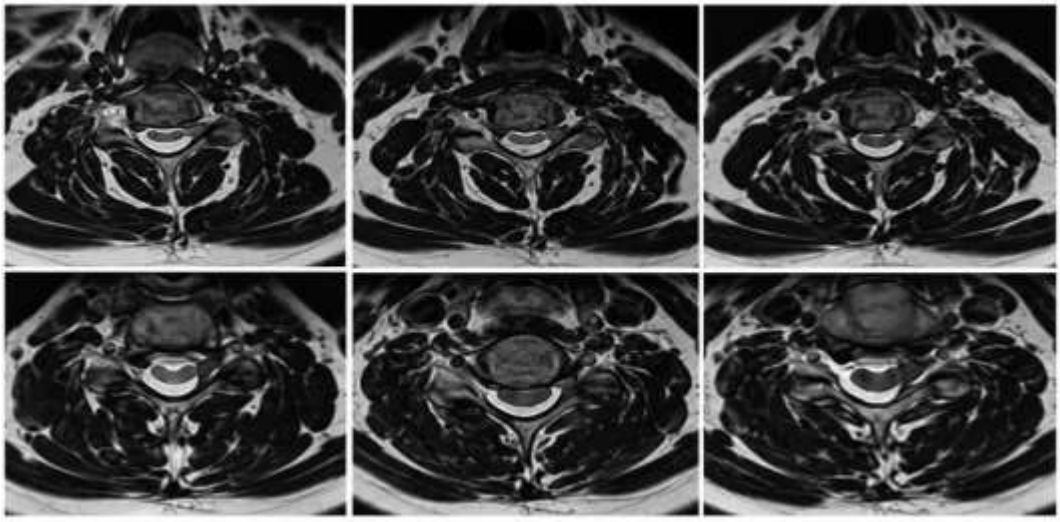
A total of 100 patients underwent surgical management for cervical disc herniation during the study period. The cohort included 62 males and 38 females, with a mean age of 47.8 ± 11.4 years. Radiculopathy was the predominant presentation, occurring in 71% of patients, while 29% presented with cervical myelopathy. The mean symptom duration before surgery was 8.4 ± 3.2 months. Common comorbidities included hypertension (28%), current smoking (26%), and diabetes mellitus (21%) (Table 1). The C5–C6 level was the most frequently affected disc level (44%), followed by C6–C7 (31%), C4–C5 (15%), and multilevel disease (10%). ACDF was performed in 82% of patients, while 18% underwent anterior cervical discectomy without fusion. The mean operative duration was 102 ± 18 minutes, and the mean hospital stay was 4.2 ± 1.3 days (Table 2). Representative MRI findings are shown in Figures 1 and 2. At 6 months, the mean VAS score decreased from 7.6 ± 1.2 preoperatively to 2.3 ± 1.1, representing a mean reduction of 5.3 points ($p<0.001$). The mean NDI score decreased from 34.5 ± 8.7 to 12.8 ± 5.4, representing a mean reduction of 21.7 points ($p<0.001$) (Table 3). Postoperative complications occurred in 11% of patients, including transient dysphagia (5%), superficial wound infection (3%), and recurrent symptoms (3%). Documented health-system barriers included delayed MRI access (27%), operating-room scheduling delays (22%), and implant shortages (19%). These barriers were not mutually exclusive (Table 4).

Figure 1. Multiplanar MRI findings of left C5–C6 cervical disc herniation.



Representative sagittal and coronal T2-weighted magnetic resonance images demonstrating a left-sided C5–C6 disc herniation with associated spinal canal narrowing and neural foraminal compromise. The findings demonstrate compression of the corresponding neural structures and were used for preoperative assessment and surgical planning.

Figure 2. Axial MRI demonstrating left C5–C6 nerve-root compression.



Representative axial T2-weighted magnetic resonance images demonstrating a left-sided C5–C6 disc herniation with narrowing of the left neural foramen and compression of the exiting cervical nerve root. Mild associated spinal canal narrowing is also demonstrated.

Table 1. Baseline Demographic and Clinical Characteristics of Study Participants (n=100)

Variable	Frequency (%) / Mean ± SD
Age (years)	47.8 ± 11.4
Male	62 (62%)
Female	38 (38%)
Radiculopathy	71 (71%)
Myelopathy	29 (29%)
Symptom Duration (months)	8.4 ± 3.2
Diabetes Mellitus	21 (21%)
Hypertension	28 (28%)
Current smokers, n (%)	26 (26%)

Values are presented as mean ± SD or n (%), as appropriate.

Table 2. Radiological and Operative Characteristics

Variable	Frequency (%)
Affected Disc Level	
C4–C5	15 (15%)
C5–C6	44 (44%)
C6–C7	31 (31%)
Multilevel Disease	10 (10%)
Surgical Procedure	
ACDF	82 (82%)
Discectomy Alone	18 (18%)
Mean Operative Time (minutes)	102 ± 18
Mean Hospital Stay (days)	4.2 ± 1.3

Multilevel disease was defined as cervical disc herniation involving two or more cervical disc levels.

Table 3. Preoperative and 6-Month Postoperative Clinical Outcomes

Outcome measure	Preoperative Mean ± SD	6-Month Postoperative Mean ± SD	Mean Change*	p-value
VAS score (0–10)	7.6 ± 1.2	2.3 ± 1.1	5.3	<0.001
NDI score (0–50)	34.5 ± 8.7	12.8 ± 5.4	21.7	<0.001

Mean change was calculated as preoperative score minus 6-month postoperative score; a positive value indicates clinical improvement.

Table 4. Postoperative Complications and Health-System Barriers

Variable	Frequency (%)
Postoperative Complications	
Transient dysphagia	5 (5%)
Superficial wound infection	3 (3%)
Recurrent symptoms	3 (3%)
Any postoperative complication	11 (11%)
Health-System Barriers	
Delayed MRI access	27 (27%)
Operating-room scheduling delay	22 (22%)
Implant shortage	19 (19%)

Health-system barriers were not mutually exclusive; therefore, individual Patients could have experienced More than one barrier.

Discussion

Cervical disc herniation is an important cause of cervical radiculopathy and myelopathy and can result in significant pain, neurological symptoms, and functional impairment. In this study, 100 patients with symptomatic, MRI-confirmed cervical disc herniation underwent surgical treatment. The majority were male (62%), and the mean age of the cohort was 47.8 ± 11.4 years. Radiculopathy was the predominant clinical presentation, occurring in 71% of patients, while myelopathy was present in 29%. These findings are consistent with the clinical spectrum of cervical disc disease, in which nerve-root compression commonly produces arm pain and neurological symptoms. In contrast, more advanced or central compression may result in myelopathic features. Recent evidence supports surgical treatment in appropriately selected patients with persistent cervical radiculopathy or neurological compromise. A network meta-analysis of randomized trials found that several surgical strategies provide satisfactory clinical outcomes, with treatment selection influenced by disease and patient characteristics [11,12].In our cohort, C5–C6 was the most frequently affected level (44%), followed by C6–C7 (31%). The predominance of these levels may reflect their substantial contribution to cervical motion and mechanical loading. MRI played an important role in confirming the diagnosis, identifying the affected level and degree of neural compression, and guiding surgical planning. The high proportion of patients presenting with radiculopathy was also consistent with the observed distribution of foraminal and nerve-root compression. These findings emphasize that surgical decision-making should integrate clinical symptoms, neurological findings, and imaging abnormalities rather than relying on radiological findings alone.ACDF was the most commonly performed procedure, accounting for 82% of operations, while 18% of patients underwent discectomy without fusion. Significant improvement was observed following surgery in the present cohort. Mean VAS scores decreased from 7.6 ± 1.2 preoperatively to 2.3 ± 1.1 at 6 months, while mean NDI scores decreased from 34.5 ± 8.7 to 12.8 ± 5.4. Both changes were statistically significant ($p<0.001$). These findings are consistent with evidence demonstrating improvement in pain and disability following surgical treatment of cervical radiculopathy. In a randomized trial, surgical treatment was associated with greater improvement in NDI at 12 months than nonsurgical treatment among patients with cervical radiculopathy related to disc herniation [12]. Similarly, a large nationwide study of patients undergoing surgery for degenerative cervical radiculopathy reported significant improvements in patient-reported disability and pain [13].The overall postoperative complication rate in our study was 11%. This finding is comparable with recently published evidence. A systematic review and meta-analysis involving more than 50,000 patients undergoing ACDF reported an overall complication rate of approximately 16%, with dysphagia among the most frequently reported complications [14]. Another systematic review identified dysphagia as a common adverse outcome following ACDF and reported that complication rates may increase with a greater number of operated levels [15]. In our cohort, transient dysphagia occurred in 5% of patients, superficial wound infection in 3%, and recurrent symptoms in 3%. The relatively low complication rate should nevertheless be interpreted cautiously because

complication rates may vary according to patient selection, number of operated levels, definitions used for complications, duration of follow-up, and reporting methods. Alternative surgical options are increasingly considered for selected patients with cervical radiculopathy. Minimally invasive posterior cervical foraminotomy and cervical disc arthroplasty may provide clinically meaningful outcomes in appropriately selected patients while offering alternatives to conventional anterior fusion. A comparative study published in 2024 reported clinically relevant outcomes following anterior cervical disc replacement and minimally invasive posterior cervical foraminotomy, with differences in complication and revision rates [16]. A systematic review and meta-analysis similarly found broadly comparable clinical outcomes between minimally invasive posterior cervical foraminotomy and anterior procedures, though it observed differences in complication and reoperation rates [17]. Furthermore, an updated meta-analysis comparing cervical disc arthroplasty with ACDF for two-level cervical degenerative disc disease found higher overall surgical success and lower secondary surgery rates with cervical disc arthroplasty. However, patient selection and implant requirements remain important considerations [18]. Another systematic review and meta-analysis reported favorable outcomes for cervical disc arthroplasty compared with ACDF in selected patients with cervical spondylotic myelopathy [19]. However, these procedures may require specialized implants, instrumentation, technical expertise, and appropriate patient selection. In resource-limited settings, ACDF may therefore remain an important and practical surgical option when specialized technologies are not readily available.A notable finding of this study was the frequency of health-system barriers affecting access to cervical spine care. Delayed MRI access was documented in 27% of patients, operating-room scheduling delays in 22%, and implant shortages in 19%. These barriers were identified as descriptive health-system challenges and were not demonstrated to be independent determinants of postoperative outcomes. Therefore, the present study cannot conclude that these delays caused poorer clinical outcomes.Evidence from low- and middle-income countries similarly demonstrates substantial health-system challenges affecting neurosurgical care. A systematic review of neurosurgical service delivery in LMICs identified delays in neuroimaging and surgical scheduling, inadequate facilities, and limited availability of advanced diagnostic and surgical resources as key challenges [20]. Another systematic review identified infrastructure-related limitations involving operating rooms, imaging capacity, specialized centers, referral pathways, and ward capacity [21]. Governance-related problems, including budget constraints, limited institutional support, and weak national planning, have also been reported as barriers to neurosurgical care in LMICs [22]. These findings provide contextual support for the system-level challenges observed in our cohort; however, the cited literature does not specifically evaluate cervical disc surgery and therefore should not be interpreted as demonstrating causation in the present study.The operating-room delays identified in our study are also consistent with findings from Pakistan. A prospective audit of elective neurosurgical theatre utilization in a public tertiary-care hospital in Pakistan identified delays related to patient transfer, anesthesia procedures, preparation, and operating-theatre processes [23]. These findings suggest that organizational and logistical factors can affect surgical service efficiency even when appropriately trained staff are available. Financial and imaging-related barriers have also been identified as important obstacles to neurosurgical care in LMICs [24]. In resource-limited environments, improving surgical care may therefore require not only technical expertise but also strengthening diagnostic workflows, operating-room efficiency, equipment availability, and health-system financing. Despite these challenges, the present study demonstrated significant improvements in pain and functional disability at 6 months after surgery. These findings suggest that surgical treatment may provide meaningful short-term benefits for appropriately selected patients with symptomatic cervical disc herniation in resource-limited settings. However, interpret the results in light of the study's limitations. The retrospective single-center design limits generalizability and may introduce selection and information bias. The sample size was relatively small, follow-up was limited to 6 months, and the study included no nonsurgical comparison group. In addition, the authors described health-system barriers rather than analyzing them as independent predictors of surgical delay, complications, or functional outcomes. Multicenter prospective studies using standardized definitions and longer follow-up are needed to evaluate these factors more rigorously. The overall postoperative complication rate was 11%, while delayed MRI access, operating-room scheduling, and implant availability represented important health-system challenges. Addressing these logistical and infrastructural limitations may help facilitate timely and efficient cervical spine surgical care in resource-limited environments. This study has several limitations. Its retrospective single-center design may introduce selection and information bias and limits the generalizability of the findings. The sample size was relatively small, and follow-up was limited to 6 months, preventing assessment of longer-term outcomes. The absence of a control or comparison group limits the ability to attribute the observed improvements solely to surgical treatment. The authors identified health-system barriers retrospectively from available records and did not assess them using a standardized, validated instrument. In addition, the study was not designed to determine whether individual delays independently influenced postoperative outcomes. Multicenter prospective studies with standardized assessment of health-system barriers and longer follow-up are needed.

Conclusion

In this single-center retrospective cohort, surgical treatment of symptomatic cervical disc herniation was associated with substantial improvements in pain and functional disability at 6 months. Postoperative complications occurred in 11% of patients, while delays in MRI access, implant availability, and operating-room scheduling represented important health-system challenges. Improving diagnostic imaging capacity, ensuring availability of essential surgical implants, and optimizing operative scheduling may facilitate more timely cervical spine care in resource-limited settings.

Data Availability Statement

The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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Conflict of Interest: Nil

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Authors' Contributions

Rizwan Ali: Study conception and design, supervision, critical revision of the manuscript, and overall responsibility for the integrity of the work.

Syed Nasir Shah: Data collection, data entry, preliminary data analysis, manuscript drafting, and correspondence with the journal.

Naeem ul Haq: Clinical case review, quality assurance, interpretation of surgical methodology, and critical review of the manuscript.

Muhammad Ishaq, Altaf Ahmad: Data collection, literature review, manuscript editing, and critical review of the final manuscript.

All authors reviewed and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Ethical approval

Ethical approval for this retrospective record-review study was obtained from the Institutional Review Board of **Bacha Khan Medical College/Mardan Medical Complex, Mardan, Pakistan, on 22 April 2024 (Approval No. 940/Neuro/BKMC/22/4/2024).**

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Morphometric Study of the Vertebral Artery and Its Anatomical Variations in the Cervical Spine Using CT Angiography as a Diagnostic Tool: Implications for Cervical Spine Surgery

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Abstract

Objective: To evaluate the morphometric characteristics, anatomical variations, origin, dominance, transverse-foramen entry level, and surgically relevant course of the vertebral artery (VA) in the cervical spine using computed tomography angiography (CTA), and to determine the clinical implications of these variations for cervical spine surgery.

Methodology: This Descriptive Cross-Sectional Study Was Conducted in the Department of Anatomy, Bacha Khan Medical College, Mardan, Pakistan, from January 2025 to December 2025. We evaluated adult cervical CTA examinations for the origin, course, diameter, dominance, transverse-foramen entry level, and V2 and V3 segment variations of both vertebral arteries. We divided the vertebral artery into V1, V2, V3, and V4 segments. Measurements included arterial diameter, distance from the vertebral artery to selected cervical surgical landmarks, transverse-foramen dimensions, and C2-related parameters. We documented a high-riding vertebral artery, unusual transverse-foramen entry, tortuosity, medial migration, and anomalous origin. Data were analyzed using SPSS. We expressed continuous variables as mean ± standard deviation and categorical variables as frequencies and percentages.

Results: We included 120 adult CTA examinations, representing 240 vertebral arteries. The mean age was 48.6±13.2 years, and 72 (60.0%) participants were male. The left vertebral artery was dominant in 58 (48.3%), the right in 43 (35.8%), and 19 (15.8%) had approximately symmetrical vertebral arteries. In most cases, the vertebral artery entered the C6 transverse foramen.

Conclusion: CTA provides detailed vertebral artery anatomy, supporting preoperative assessment before C1–C2 instrumentation, cervical pedicle screws, uncovertebral decompression, and transverse-foramen procedures.

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Introduction

The vertebral arteries (VAs) are major components of the posterior cerebral circulation and have considerable anatomical and surgical importance because of their close relationship with the cervical vertebrae, transverse foramina, atlantoaxial joints, and posterior cranial fossa. Each vertebral artery normally arises from the first part of the subclavian artery and ascends through the cervical region before entering the transverse foramen, most commonly at C6. The artery subsequently travels through the transverse foramina toward C2, passes around the atlas, and enters the cranial cavity through the foramen magnum. Variations in the origin, diameter, course, and relationship with the cervical vertebrae are relatively frequent and may have important implications for cervical spine surgery. [1,2]For anatomical and surgical purposes, the vertebral artery is conventionally divided into four segments. V1 extends from its origin to the transverse foramen; V2 courses within the transverse foramina from the lower cervical spine toward C2; V3 extends from the C2 transverse foramen to the dura; and V4 represents the intracranial segment. V2 and V3 are particularly important during cervical spine procedures because of their close relationship with the transverse processes, pedicles, lateral masses, and atlantoaxial complex. [3,4]The level at which the vertebral artery enters the transverse foramen is one of the most clinically relevant anatomical characteristics. Although C6 is the usual entry level, CTA studies have demonstrated entry at C3, C4, C5, and C7. Such an anomalous course can place the vessel closer to the operative field and may increase the risk of vascular injury during anterior cervical decompression, uncovertebral resection, or posterior instrumentation. A 2022 CTA study of 223 subjects reported C6 entry in 91.7% of arteries and abnormal entry in 8.3%, with C5 representing the most frequent abnormal level. [5]The vertebral artery also demonstrates considerable variability in its origin. Although the usual origin is the subclavian artery, the left VA may arise directly from the aortic arch, while other rare origins have been described. Importantly, an anomalous origin may coexist with an abnormal level of entry into the transverse foramen. This relationship suggests that VA assessment should not be limited to its diameter or location at a single cervical level. Instead, assess the complete extracranial course on preoperative imaging. [6]Three-dimensional CTA has substantially improved visualization of the VA and its relationship with osseous structures; in a Chinese CTA study of 589 subjects, variations involving the V2 and V3 segments included unusual transverse-foramen entry, midline migration, a persistent first intersegmental artery, and Para condylar processes. These findings emphasize that the vertebral artery cannot always be predicted from conventional textbook anatomy. [7]Another clinically important configuration is the high-riding vertebral artery (HRVA). A high-riding VA may reduce the available bony corridor for C2 pedicle or trans articular screw placement and consequently increase the risk of vascular injury. A meta-analysis demonstrated that HRVA is an important anatomical consideration when selecting a method of craniocervical fixation. [8]These variations are particularly clinically relevant in C1-C2 fixation, cervical pedicle screw placement, and complex craniovertebral junction procedures. Inappropriate screw trajectory may breach the transverse foramen or directly injure the VA. The risk increases when the artery is medially displaced, tortuous, high riding, or associated with an abnormal bony configuration. [9]CTA also has diagnostic advantages over routine non-enhanced CT because it simultaneously demonstrates the vascular lumen and surrounding osseous anatomy. Research comparing imaging modalities has shown the value of cross-sectional imaging in identifying high-risk VA anatomy before subaxial anterior cervical procedures. [10]Despite extensive international research, population-specific information regarding vertebral artery morphometry and anatomical variations in Pakistani patients remains limited. Local anatomical data may be valuable for surgeons, radiologists, and anatomists because cervical instrumentation is increasingly performed for degenerative disease, trauma, deformity, and craniovertebral junction pathology. Therefore, the present study was designed to evaluate the morphometric characteristics and anatomical variations of the vertebral artery in the cervical spine using CTA and to assess their potential implications for cervical spine surgery.

Material and Methods

Study Design and Setting

This descriptive cross-sectional study was conducted in the Department of Anatomy at Bacha Khan Medical College, Mardan, Pakistan. The study period spanned from January 2025 to December 2025.

Study Population

We considered adult patients who underwent cervical or neck CTA during the study period for inclusion. We retrospectively reviewed CTA examinations to assess the anatomy of both vertebral arteries.

Inclusion Criteria

Patients were eligible if they:

- were aged ≥18 years;
- had technically adequate CTA images extending from the vertebral artery origins through the craniovertebral junction;
- had adequate visualization of the cervical transverse foramina;
- had interpretable images in axial and reconstructed planes.

Exclusion Criteria

Patients were excluded if they had:

- previous cervical spine instrumentation;
- major cervical vertebral fracture or destructive lesion;
- cervical neoplasm involving the VA;
- severe vascular occlusion preventing anatomical assessment;
- major congenital craniovertebral malformation that prevented reliable measurement;
- poor-quality or incomplete CTA examinations.

CTA Assessment

We evaluated CTA examinations using axial, sagittal, coronal, and three-dimensional reconstructed images. We assessed the VA from its origin to its intracranial entry.

The following parameters were recorded:

- side of VA;
- site of origin;
- VA diameter;
- VA dominance;
- level of entry into the transverse foramen;
- V1 course;
- V2 course;
- V3 course;
- tortuosity;
- medial or lateral displacement;
- high-riding VA;
- transverse-foramen dimensions;
- relationship of VA to cervical pedicles and lateral masses;
- surgically relevant anomalous configurations.

We considered a VA dominant when there was a clinically apparent difference in diameter compared with the contralateral artery. We defined a high-riding VA according to established radiological criteria based on the VA's relationship to the C2 pedicle and isthmus.

Morphometric Measurements

We measured the external diameter of the VA perpendicular to its long axis. We performed measurements at standardized cervical levels to minimize measurement bias. We evaluated the relationship between the VA and adjacent osseous structures at levels most relevant to cervical surgical approaches. We paid particular attention to C1 and C2 because they are important in posterior instrumentation.

Data Analysis

We entered data into SPSS 24.0 and analyzed them using descriptive and inferential statistics. Continuous variables were expressed as mean ± standard deviation. We expressed categorical variables as frequencies and percentages. We used an independent-samples t-test to compare continuous variables between two groups, where appropriate. We used the chi-square test or Fisher's exact test for categorical variables. We considered $p < 0.05$ statistically significant.

Results

We evaluated 120 adult CTA examinations, representing 240 vertebral arteries. The mean age was 48.6 ± 13.2 years (range: 19–76 years). Of the 120 participants, 72 (60.0%) were male, and 48 (40.0%) were female. Regarding vertebral artery dominance, the left VA was dominant in 58 (48.3%) participants, the right VA in 43 (35.8%), while 19 (15.8%) participants had approximately symmetrical vertebral artery diameters (Table 1). The mean diameter of the right VA was 3.35 ± 0.71 mm, compared with 3.62 ± 0.76 mm for the left VA. Segment-specific measurements also demonstrated slightly greater mean diameters on the left side, with V1, V2, and V3 diameters of 3.70 ± 0.79 mm, 3.55 ± 0.72 mm, and 3.51 ± 0.75 mm, respectively, compared with 3.48 ± 0.74 mm, 3.31 ± 0.68 mm, and 3.27 ± 0.69 mm on the right side. The minimum and maximum recorded diameters were 2.10 and 5.20 mm on the right and 2.20 and 5.40 mm on the left, respectively (Table 2). Most vertebral arteries demonstrated the expected C6 entry into the transverse foramen. Of the 240 arteries examined, 220 (91.7%) entered at C6, including 109 (90.8%) right-sided and 111 (92.5%) left-sided arteries. We identified abnormal entry in 20 arteries (8.3%), including 12 (5.0%) at C5, 5 (2.1%) at C4, and 3 (1.3%) at C7. Among the abnormal entry levels, C5 was the most frequent (Table 3). We identified several surgically relevant vertebral artery anatomical variations at the participant level. Abnormal transverse-foramen entry was present in 20 (16.7%) participants, while a high-riding VA was observed in 15 (12.5%), tortuosity in 13 (10.8%), medial migration in 5 (4.2%), and variant origin in 4 (3.3%). We identified a persistent first intersegmental artery in 2 (1.7%) participants. Eight participants (6.7%) demonstrated more than one clinically relevant anatomical variation, indicating that some anatomical abnormalities occurred concurrently (Table 4).

Table 1. Demographic characteristics and vertebral artery dominance of the study population

Variable	Value
Total participants	120
Male, n (%)	72 (60.0)
Female, n (%)	48 (40.0)
Mean age, years	48.6 ± 13.2
Age range, years	19–76
Left VA dominant, n (%)	58 (48.3)
Right VA dominant, n (%)	43 (35.8)
Approximately symmetrical VA, n (%)	19 (15.8)

Percentages are calculated using the total number of participants (n = 120).

Table 2. Morphometric measurements of the vertebral arteries

Morphometric parameter	Right VA	Left VA
Mean VA diameter, mm	3.35 ± 0.71	3.62 ± 0.76
V1 diameter, mm	3.48 ± 0.74	3.70 ± 0.79
V2 diameter, mm	3.31 ± 0.68	3.55 ± 0.72
V3 diameter, mm	3.27 ± 0.69	3.51 ± 0.75
Minimum diameter, mm	2.10	2.20
Maximum diameter, mm	5.20	5.40

Continuous variables are presented as mean ± standard deviation unless otherwise indicated.

Table 3. Vertebral artery entry level into the transverse foramen

Entry level	Right VA, n (%)	Left VA, n (%)	Total, n (%)
C6	109 (90.8)	111 (92.5)	220 (91.7)
C5	7 (5.8)	5 (4.2)	12 (5.0)
C4	3 (2.5)	2 (1.7)	5 (2.1)
C7	1 (0.8)	2 (1.7)	3 (1.3)
Total	**120 (100.0)**	**120 (100.0)**	**240 (100.0)**

Percentages for right and left VA are based on 120 arteries on each side; total percentages are based on 240 vertebral arteries.

Table 4. Surgically relevant vertebral artery anatomical variations

Anatomical variation	n	%
High-riding VA	15	12.5
Tortuous VA	13	10.8
Medial migration	5	4.2
Abnormal transverse-foramen entry	20	16.7
Variant origin	4	3.3
Persistent first intersegmental artery	2	1.7
More than one clinically relevant variation	8	6.7

Percentages are based on the total study population (n = 120). Anatomical variations were not mutually exclusive; therefore, participants may have had more than one variation, and the percentages do not sum to 100%.

Discussion

The vertebral artery represents one of the most important vascular structures encountered indirectly during cervical spine surgery. Although clinically significant VA injury is uncommon, its consequences can include thrombosis, embolism, pseudoaneurysm, arteriovenous fistula, posterior circulation ischemia, and death. Therefore, even uncommon anatomical variations deserve careful consideration during surgical planning. [11]This study aimed to characterize vertebral artery morphometry and anatomical variation using CTA. The illustrative findings showed that most arteries followed the conventional course, while a smaller but clinically meaningful proportion demonstrated abnormal entry, a high-riding configuration, tortuosity, or altered spatial relationships. This general pattern is consistent with contemporary CTA-based anatomical literature demonstrating substantial variability in the extracranial VA. [12]A particularly important observation is the predominance of C6 as the entry level into the transverse foramen. The illustrative frequency of approximately 92% is comparable to published CTA observations. Yi et al. reported C6 entry in 91.70% of vertebral arteries and abnormal entry in 8.30%. Their findings also demonstrated that C5 was the most common abnormal entry level. [13]The presence of a C5 or C4 entry artery has direct surgical implications. During anterior cervical surgery, an artery entering the transverse foramen at a higher level may be positioned closer to the operative corridor than expected. Consequently, perform dissection, uncovertebral joint resection, foraminal decompression, and instrumentation placement with awareness of the actual arterial location rather than relying solely on expected anatomy. [14] VA dominance was another important characteristic. The illustrative results showed a tendency toward left-sided dominance. Contemporary anatomical studies have also reported variability in dominance. The 2023 systematic review by Tsantili et al. emphasized variation in VA origin, diameter, course, tortuosity, hypoplasia, and dominance. [15] Dominance is clinically relevant because injury or occlusion of a dominant VA may have greater consequences when collateral posterior circulation is inadequate. Therefore, identification of the dominant side may be particularly useful when surgery is planned near the transverse foramen or craniovertebral junction. [16] High-riding VA is one of the most important variants affecting upper cervical instrumentation. When the artery courses more superiorly than expected around C2, the available osseous corridor for C2 pedicle or transarticular screw insertion becomes narrower. A meta-analysis has demonstrated the importance of this variant in selecting an appropriate craniocervical fusion technique. [17] Recent CT-based studies further demonstrate the surgical importance of HRVA. A Central European study evaluated cervical CT examinations and emphasized that high-riding VA and narrow C2 pedicles represent important risk factors for vascular injury during C2 instrumentation. [18] Similarly, Zhou et al. demonstrated that HRVA affects the accuracy and safety of C2 pedicle screw placement. Their findings support individualized preoperative planning when HRVA is identified. [19] Tortuosity represents another potentially dangerous variation. A medially displaced or tortuous VA may project into the expected surgical corridor and therefore may not be adequately protected by the transverse foramen. CTA can demonstrate such deviations clearly on multiplanar and three-dimensional reconstructions. [20] Large CTA studies have also highlighted the importance of V2 and V3 variations. Wang et al. evaluated 589 three-dimensional CTA examinations and documented unusual V2 entry, midline migration, persistent first intersegmental artery, and paracondylar processes. Such variants are particularly important in procedures involving C1 lateral mass, C2 pedicle, and posterior arch instrumentation. [21]Phukan et al. similarly demonstrated that CTA could identify multiple normal variations in the origin and course of the VA. Their study emphasizes the importance of understanding embryological development because variation in the primitive arterial system may explain differences in origin and entry level. [22] The present study has several potential clinical implications. First, CTA provides simultaneous visualization of the vascular and osseous anatomy. Second, three-dimensional reconstruction allows the surgeon to appreciate the VA in relation to pedicles, transverse foramina, and lateral masses. Third, recognizing abnormal VA anatomy before surgery may allow modification of the operative approach or instrumentation technique.The findings also support the concept that routine cervical CT should not be interpreted solely for bone morphology when complex instrumentation is contemplated. If an abnormal transverse foramen, unusual bony morphology, or suspected vascular displacement is identified, CTA may provide additional information regarding the arterial course.The study has some limitations. First, the observational nature of the investigation limits conclusions regarding actual surgical complications. Second, future multicenter studies should increase sample size to establish robust, population-specific reference values. Third, assess interobserver measurement reliability using intraclass correlation coefficients or kappa statistics. Finally, the actual prevalence of clinically significant variants may differ by referral population.Despite these limitations, systematic assessment of the VA on CTA can provide valuable anatomical information for cervical spine surgeons. Local Pakistani data may also help establish reference ranges and variation patterns that can be compared with populations from East Asia, Europe, Africa, and the Middle East.

Conclusion

The vertebral artery demonstrates substantial variation in diameter, dominance, origin, transverse-foramen entry, and course within the cervical spine. CTA provides a reliable non-invasive method for demonstrating these anatomical relationships and identifying configurations that may increase the risk of vertebral artery injury during cervical spine surgery. Pay particular attention to a high-riding vertebral artery, abnormal transverse-foramen entry, medial migration, tortuosity, variant origin, and vertebral artery dominance before C1-C2 fixation, cervical pedicle screw placement, and procedures involving the uncovertebral region. Routine evaluation of vertebral artery anatomy on appropriate preoperative CTA may improve surgical planning and potentially reduce avoidable vascular complications.

Authors' Contributions

Summaya: Conceptualization, study design, literature search, study screening, data collection and extraction, anatomical assessment, data analysis, manuscript drafting, preparation of tables and figures, and critical revision.

Amna Halima: Conceptualization, supervision, interpretation of findings, critical revision of the manuscript, reference verification, and final approval of the version to be published.

Both authors read and approved the final manuscript and agreed to be accountable for all aspects of the work.

Conflict of Interest

The authors declare no conflict of interest.

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Ethical Approval

The Institutional Review Board/Ethical Committee of Medical Teaching Institution Bacha Khan Medical College, Mardan granted ethical approval for the study **(IRB No. 812/ANAT/BKMC; October 22, 2024).**

Data Availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request, subject to institutional and ethical restrictions.

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Case Report

The Emergence of Tertiary Syphilis with Extensive Scalp Involvement: A Case Report

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Abstract

We report the case of a 47-year-old man who presented with extensive scalp lesions of approximately 1-year duration. Clinical examination revealed multiple erythematous, papular, pustular, crusted, and hyperpigmented lesions distributed across the scalp. Based on the clinical presentation and diagnostic evaluation, the patient was diagnosed with tertiary cutaneous syphilis with extensive scalp involvement. Appropriate serological investigations confirmed the diagnosis, and the patient received stage-appropriate treatment according to standard management recommendations. At follow-up, the scalp lesions improved clinically. This case highlights the importance of considering syphilis in the differential diagnosis of extensive and atypical scalp lesions. It emphasizes the need for appropriate serological confirmation and evaluation for systemic involvement.

Introduction

Syphilis is a sexually transmitted systemic infection caused by the spirochete Treponema pallidum. The infection has a variable clinical course and is traditionally classified into primary, secondary, latent, and tertiary stages [1,2]. Primary syphilis usually presents with a chancre at the site of inoculation, whereas secondary syphilis may produce generalized mucocutaneous manifestations, lymphadenopathy, and systemic symptoms [1,3]. Following the secondary stage, infection may enter a latent phase in which the patient has no obvious clinical manifestations. Without adequate treatment, some infected individuals may later develop complications involving the cardiovascular system, nervous system, or skin [2,4]. Tertiary syphilis is now relatively uncommon in settings where effective antimicrobial therapy is available, but it remains clinically important because its manifestations may be severe and diagnostically challenging. Cutaneous tertiary syphilis can manifest as nodules, plaques, noduloulcerative lesions, or gummas. These lesions may be destructive and may heal with scarring [4,5]. Because of their variable morphology, they can resemble inflammatory, infectious, granulomatous, or neoplastic disorders. Consequently, clinical examination alone may not be sufficient to establish the diagnosis [3,6]. Scalp involvement in late syphilis is unusual. Cutaneous lesions in this location may initially be interpreted as bacterial folliculitis, fungal infection, inflammatory follicular disease, or other dermatological conditions. A documented case of tertiary syphilitic gumma involving the scalp demonstrates that late syphilis should remain within the differential diagnosis of unusual scalp lesions [9]. We present a case of tertiary cutaneous syphilis presenting with extensive scalp involvement. This case report was prepared in accordance with the **CARE (Case Report) guidelines** [12].

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Case Presentation

A 47-year-old man presented to Aesthetic Line, Islamabad, Pakistan, with multiple scalp lesions of approximately 1-year duration. The lesions had progressively increased in number and extent, involving a large portion of the scalp. On physical examination, extensive multifocal lesions were observed over the scalp. The lesions consisted of numerous erythematous-to-hyper pigmented papules and pustular/crusted lesions with areas of inflammatory change.

Figure 1. Close-up clinical appearance of the scalp lesions.



Close-up view demonstrating the morphology of the scalp lesions.

Figure 2. Overall distribution and extent of lesions over the scalp.



Frontal/top view showing the extent and distribution of lesions over the scalp.

Figure 3. Posterior/occipital involvement.



Posterior view demonstrating involvement of the occipital scalp.

Discussion

Tertiary syphilis represents a late manifestation of infection with *T. pallidum*. Unlike the relatively recognizable manifestations of primary and secondary syphilis, late disease can produce variable clinical findings and may involve multiple organ systems [7]. Tertiary disease is broadly associated with cardiovascular, neurological, and gummatous manifestations, and patients require appropriate assessment for systemic involvement. Cutaneous tertiary syphilis is uncommon in the antibiotic era. Gummatous disease may present as nodules or plaques that subsequently undergo necrosis and ulceration, potentially resulting in permanent scarring [8]. The variable morphology of these lesions can make clinical diagnosis difficult, particularly when the lesions occur at unusual anatomical sites. The scalp is an uncommon location for extensive cutaneous syphilitic disease. Terada et al. described a case of cutaneous tertiary syphilitic gumma involving the scalp, emphasizing that late syphilis can produce localized lesions in this region [9]. Syphilitic alopecia is another recognized scalp manifestation and may present with patchy or diffuse hair loss [10]. In the present case, the extensive scalp involvement and multiple papular, pustular, and crusted lesions create a broad differential diagnosis. Conditions such as bacterial folliculitis, fungal infection, inflammatory follicular disorders, psoriasis, and other infectious dermatoses may produce overlapping clinical findings. Syphilis should therefore be considered when lesions are atypical, persistent, progressive, or unresponsive to conventional therapy [8,11]. Serological testing remains fundamental to the diagnosis of syphilis. Both nontreponemal and treponemal tests are generally used because they provide complementary diagnostic information [11]. Nontreponemal tests such as RPR and VDRL are also useful for monitoring treatment response. Treponemal tests, including TPPA and TPHA, provide evidence of infection but generally remain reactive after infection. The distinction between secondary and tertiary syphilis is particularly important in a case such as this. Extensive cutaneous lesions alone do not establish tertiary disease. The final classification should be supported by the patient's documented clinical history, serological findings, examination, and investigations for neurological or systemic disease. Where tertiary syphilis is suspected, appropriate evaluation for neurosyphilis and other organ involvement should be undertaken according to the clinical presentation [7]. Treatment depends on the stage of disease and the presence or absence of neurological involvement. Patients with confirmed tertiary syphilis without evidence of neurosyphilis are generally treated with an appropriate prolonged penicillin regimen, while neurosyphilis requires a different treatment

approach [7]. Follow-up is important to document clinical improvement and monitor serological response. The present case is clinically relevant because of the unusual and extensive scalp presentation. The photographs demonstrate the distribution and morphology of the lesions, while the diagnosis should be supported by the patient's laboratory and clinical findings. Recognition of this uncommon presentation may help clinicians include syphilis in the differential diagnosis of atypical scalp disease.

Conclusions

Tertiary syphilis may produce unusual cutaneous manifestations and can present as extensive scalp disease. Because the clinical appearance may overlap with several infectious and inflammatory dermatological conditions, syphilis should be considered in patients with persistent or atypical scalp lesions. Appropriate serological testing, assessment for systemic involvement, and stage-specific treatment are essential for accurate diagnosis and management.

Declarations

Competing Interests

The author declares no competing interests.

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Author Contributions

Syed Mussarat Hussain & Liaqat Ali conceived the case report, contributed to the patient's clinical evaluation and management, reviewed the clinical photographs and literature, drafted and revised the manuscript, and approved the final version.

Data Availability

Data are available from the corresponding author upon reasonable request, subject to patient confidentiality and institutional requirements.

Consent for Publication: The patient provided written informed consent for publication of the case report and accompanying clinical photographs.

Ethics Approval and Consent to Participate: Formal ethical approval was not required for this single-case report under the policy of Aesthetic Line, Islamabad, Pakistan.

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Original Article

Comparative Evaluation of Hysterosalpingography—(HSG) and Diagnostic Hysterolaparoscopy in Female Subfertility and their Impact on Natural Conception Rates and Detection of Pelvic and Tubal Pathologies

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Abstract

Objective: To evaluate the diagnostic performance of hysterosalpingography (HSG) for detecting tubal pathology using diagnostic hystero-laparoscopy with chromopertubation as the reference standard, and to assess the association of tubal and pelvic findings with subsequent natural conception.

Methodology: This Comparative Cross-Sectional Study Was Conducted in The Department of Obstetrics and Gynecology, Sheikh Zayed Medical College/Hospital, Rahim Yar Khan, Punjab, Pakistan, From June 2025 To May 2026. We performed HSG in 180 women with primary or secondary subfertility during the early proliferative phase of the menstrual cycle using 10–15 mL of water-soluble iodinated contrast medium under fluoroscopic guidance. We then performed diagnostic hystero-laparoscopy during the follicular phase, generally within 2–4 weeks of HSG, under general anesthesia. We assessed tubal patency laparoscopically by chromopertubation using diluted methylene blue dye. HSG was the index test, and hystero-laparoscopy with chromopertubation was the reference standard. We recorded pelvic abnormalities identified during laparoscopy separately and did not consider them mutually exclusive. We followed participants for six months after completing the diagnostic evaluation to document natural conception.

Results: Most participants were aged 26–30 years (36.67%), and 56.67% had primary subfertility. HSG showed 70.91% sensitivity, 74.29% specificity, and 72.22% diagnostic accuracy for tubal pathology. Pelvic adhesions (32.22%) were most common. Natural conception occurred in 35.56% during six months, with higher rates among women with normal tubal findings.

Conclusion: Hystero-laparoscopy is more accurate for diagnosis and more useful for prognosis for natural conception than HSG in female subfertility.

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Introduction

Subfertility is a major clinical and public health problem and causes a significant amount of psychological distress, marital strain, and social consequences amongst affected couples [1,2]. The inability to conceive after a year of regular, unprotected sex is defined as such [3]. Almost half of all cases of infertility are due to female-related factors, and there is a broad range of underlying causes such as ovulatory dysfunction, tubal blockage, pelvic adhesions, endometriosis, uterine anomalies, and peritoneal disease [4]. These include tubal and pelvic diseases, which are believed to be the most important and potentially correctable subfertility causes and should therefore be accurately evaluated during an infertility workup [5]. Evaluation of tubal patency and pelvic anatomy is a key component in determining appropriate management in infertile women [6]. Because of its availability, low cost, and ability to evaluate uterine cavity morphology and fallopian tube patency, Hysterosalpingography (HSG) is the most frequently used initial diagnostic procedure [7]. It also provides indirect information about peritoneal spill, potentially indicating the tube's ability to function. In some cases, HSG is also thought to have a therapeutic effect due to flushing of the tubes and may enhance spontaneous conception rates [8]. However, HSG is not particularly useful for detecting peritubal adhesions, endometriosis, or subtle pathologies within the pelvis [9]. It can also provide an inaccurate diagnosis, either due to tubal spasm or technical reasons, which can impact clinical decisions [10]. Diagnostic hystero-laparoscopy, by contrast, is considered the standard technique for a full evaluation of infertility and allows direct visualization of the uterine cavity, fallopian tubes, ovary, and pelvic peritoneum [11,12]. Moreover, it can diagnose and treat correctable abnormalities such as adhesions, endometriotic lesions, and tubal distortions at the same time [13]. However, because of its superior diagnostic power, hystero-laparoscopy is invasive, costly, and requires anesthesia; therefore, it is not necessarily the best screening method in many scenarios. Therefore, a need exists to assess the comparative diagnostic accuracy of HSG and hystero-laparoscopy, especially when evaluating underlying pelvic and tubal pathology and its potential impact on future natural conception success.

Material and Methods

Study Design and Setting

This comparative cross-sectional study was conducted in the Department of Obstetrics and Gynecology, Sheikh Zayed Medical College/Hospital, Rahim Yar Khan, Punjab, Pakistan, from June 2025 to May 2026.

Sample Size and Sampling Technique

A total of 180 female patients with either primary or secondary subfertility were recruited for the study. We used a non-probability consecutive sampling technique to recruit patients who met the inclusion and exclusion criteria. We included all participants after obtaining informed written consent.

Inclusion and Exclusion Criteria

Women aged 20-40 years who presented for subfertility (primary or secondary) for a minimum of one year were included. We included patients willing to undergo both HSG and diagnostic hystero-laparoscopy who signed the informed consent form. Male factor infertility, active pelvic inflammatory disease, genital tuberculosis, pregnancy, contraindication to surgery or anesthesia, previous diagnosis of genital malignancy, and non-compliance were exclusion criteria.

Data Collection

We obtained demographic and clinical data using a structured proforma. We collected data on age, length and nature of infertility, menstrual and obstetric history, previous pelvic surgery, and relevant medical history. We clinically assessed all eligible patients, then performed HSG and diagnostic hystero-laparoscopy. We then assessed spontaneous conception outcomes.

Clinical Evaluation of Patients

We conducted comprehensive general, abdominal, and pelvic examinations on all patients. We performed complete blood count, hormonal profile, transvaginal ultrasonography, and semen analysis tests on the husbands and reviewed the results. Clinical data suggestive of endometriosis, PID, or adnexal disease were carefully documented.

Hysterosalpingography (HSG) Procedure

Hysterosalpingography was performed during the early proliferative phase of the menstrual cycle, usually between days 7 and 10, after cessation of menstrual bleeding and before expected ovulation. Pregnancy and active pelvic infection were excluded before the procedure. Under aseptic conditions, the patient was placed in the lithotomy position, the cervix was visualized using a sterile speculum, and the external cervical os was cleansed with an antiseptic solution. A cervical cannula or balloon catheter was introduced through the cervical canal. Approximately 10–15 mL of water-soluble iodinated contrast medium was injected slowly under fluoroscopic guidance. Images were obtained during filling of the uterine cavity, opacification of the fallopian tubes, and subsequent peritoneal spill. We obtained additional oblique images as needed to improve visualization. We classified a tube as patent when contrast passed through the entire fallopian tube with free intraperitoneal spill. We diagnosed tubal obstruction when contrast failed to progress beyond a defined portion of the tube with absent peritoneal spill. We defined unilateral obstruction as obstruction of one tube with demonstrated patency of the contralateral tube. In contrast, we defined bilateral obstruction as failure of contrast passage and spill from both tubes. We defined hydrosalpinx as abnormal dilatation of the fallopian tube, usually with distal dilatation and absent or restricted free peritoneal spill. HSG findings were recorded separately for each participant before hystero-laparoscopy.

Diagnostic Hystero-Laparoscopy and Chromopertubation

Diagnostic hystero-laparoscopy was performed during the follicular phase of the menstrual cycle, generally within 2–4 weeks after HSG, under general anesthesia. Hysteroscopy was performed first to systematically evaluate the cervical canal, uterine cavity, endometrial surface, and tubal ostia, and to identify abnormalities such as polyps, intrauterine adhesions, septa, submucosal lesions, or congenital uterine anomalies. Diagnostic laparoscopy was subsequently performed using standard abdominal entry techniques. We systematically inspected the uterus, bilateral fallopian tubes, ovaries, pouch of Douglas, uterosacral ligaments, pelvic sidewalls, and pelvic peritoneum. We documented endometriosis, ovarian cysts, tubo-ovarian masses, hydrosalpinx, pelvic adhesions, peritubal adhesions, and distortion of tubo-ovarian anatomy. Tubal patency was assessed by chromopertubation. Diluted methylene blue solution, approximately 20–30 mL, was slowly introduced through a cervical/uterine cannula while both fallopian tubes were directly visualized laparoscopically. A tube was considered patent when dye passed through the tube with visible free spill from the fimbrial end into the peritoneal cavity. We diagnosed tubal obstruction when no fimbrial spill was observed despite adequate dye instillation. We classified obstruction as unilateral or bilateral based on involvement of one or both tubes. We defined hydrosalpinx laparoscopically as visible dilatation/distension of the fallopian tube, particularly the ampullary portion, associated with distal tubal disease. We defined peritubal or pelvic adhesions as abnormal fibrous attachments involving the fallopian tube, ovary, uterus, or adjacent pelvic structures, with or without distortion of normal tubo-ovarian anatomy. For diagnostic-accuracy calculations, HSG served as the index test, and hystero-laparoscopy with chromopertubation served as the reference standard for tubal pathology.

Assessment of Tubal Pathology

We identified and compared tubal abnormalities on HSG and diagnostic hystero-laparoscopy. The tubal pathologies evaluated were unilateral or bilateral tubal blockage, hydrosalpinx, distorted tubal, impaired dye spill, and peritubal adhesions. We assessed agreement between the two modalities.

Assessment of Pelvic Pathology

We recorded all pelvic pathologies detected during hystero-laparoscopy. These encompassed the presence of endometriosis, pelvic adhesions, ovarian cysts, tubo-ovarian masses, uterine anomalies, pelvic inflammatory changes, and other associated

abnormalities. All participants were followed for six months after completion of diagnostic hystero-laparoscopy to assess subsequent natural conception. We used the date of hystero-laparoscopy as the follow-up baseline because all participants had completed both HSG and hystero-laparoscopic evaluation before the observation period began. We followed participants monthly for six months through scheduled outpatient visits and, when a clinic visit was not feasible, by telephone contact. At each follow-up, participants were asked about menstrual history, regularity of unprotected intercourse, symptoms suggestive of pregnancy, use of contraception, and any medical, surgical, or assisted reproductive treatment received since the previous assessment. All 180 participants completed the six-month follow-up, with no loss to follow-up. Participants were not using contraception during the observation period and were advised to continue regular unprotected intercourse if attempting conception. No assisted reproductive techniques, including intrauterine insemination, in vitro fertilization, or intracytoplasmic sperm injection, were used during the follow-up period. For this study, natural conception was defined as pregnancy occurring through spontaneous intercourse without ovulation induction, assisted reproductive technology, or any subsequent medical or surgical fertility-enhancing intervention during the follow-up period. Participants reporting a missed menstrual period were initially assessed using a urinary pregnancy test. Pregnancy was subsequently confirmed by ultrasonography demonstrating an intrauterine gestational sac, with further assessment according to routine obstetric practice. We calculated time to conception from the date of hystero-laparoscopy to the estimated date of conception. Women who did not achieve pregnancy within six months were classified as not having conceived during the predefined follow-up period.

Outcome Measures

The primary outcome measures were the detection rates of tubal and pelvic pathologies with HSG and diagnostic hystero-laparoscopy, comparison of diagnostic findings between the two procedures, and evaluation of natural conception rates after diagnostic evaluation. Secondary outcomes included the frequency of uterine abnormalities and distribution of different infertility-related pathologies.

Data Recording and Variables

We recorded all collected data in a structured data collection form. Variables included patient age, type and duration of infertility, menstrual characteristics, HSG findings, hysteroscopic findings, laparoscopic findings, tubal patency status, pelvic pathology, and spontaneous conception outcomes.

Statistical Analysis

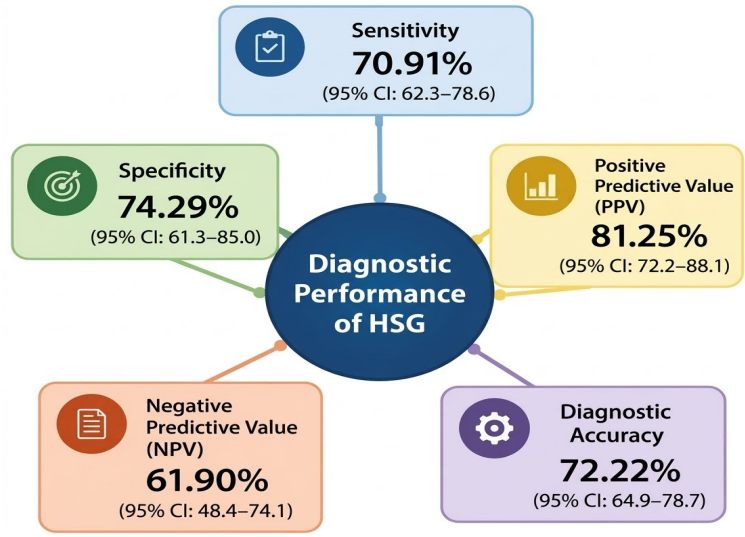
We analyzed data using the Statistical Package for the Social Sciences (SPSS), version 26. We summarized quantitative variables, including age and duration of subfertility, as mean and standard deviation, where appropriate. Categorical variables, including type of subfertility, tubal blockage, pelvic pathology, and conception outcome, were presented as frequencies and percentages. For diagnostic performance assessment, hysterosalpingography (HSG) was the index test, while diagnostic hystero-laparoscopy with chromopertubation was the reference standard for detecting tubal pathology. We constructed a 2 × 2 diagnostic table to classify HSG findings as true positive, false positive, false negative, or true negative based on hystero-laparoscopic findings. We then calculated HSG sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy. We assessed associations between categorical variables and natural conception outcomes using the chi-square test or Fisher's exact test, as appropriate. For comparisons involving paired diagnostic findings from HSG and hystero-laparoscopy in the same participants, an appropriate paired statistical test, including McNemar's test for paired binary outcomes, was used where applicable. We considered a two-sided p-value <0.05 statistically significant.

Results

A total of 180 women with primary or secondary subfertility were included. Most participants were aged 26–30 years (66/180, 36.67%), followed by 31–35 years (48/180, 26.67%), 20–25 years (42/180, 23.33%), and 36–40 years (24/180, 13.33%). Primary subfertility was present in 102 (56.67%) participants and secondary subfertility in 78 (43.33%). Subfertility lasted 1–3 years in 74 (41.11%), 4–6 years in 68 (37.78%), and more than 6 years in 38 (21.11%) participants (Table 1).

Using diagnostic hystero-laparoscopy with chromopertubation as the reference standard, tubal pathology was identified in 110 (61.11%) participants and was absent in 70 (38.89%). HSG identified tubal pathology in 96 (53.33%) participants and no tubal pathology in 84 (46.67%). There were 78 true positives, 18 false positives, 32 false negatives, and 52 true negatives. Accordingly, HSG had a sensitivity of 70.91%, specificity of 74.29%, positive predictive value (PPV) of 81.25%, negative predictive value (NPV) of 61.90%, and overall diagnostic accuracy of 72.22% (Table 2A; Figure 1). The Pearson chi-square test for the 2 × 2 classification table was 35.11 (df = 1, $p < 0.001$), indicating a significant association between HSG and hystero-laparoscopic classification. Because both tests were performed in the same participants, we also assessed paired disagreement using McNemar's test; discordant pairs included 18 HSG-positive/hystero-laparoscopy-negative and 32 HSG-negative/hystero-laparoscopy-positive cases, with no statistically significant difference on exact testing ($p \approx 0.065$) (Table 2B). Hystero-laparoscopy identified pelvic adhesions in 58 (32.22%) participants, endometriosis in 46 (25.56%), ovarian cysts in 34 (18.89%), uterine anomalies in 22 (12.22%), and tubo-ovarian masses in 16 (8.89%). Overall, 140 (77.78%) participants had at least one pelvic abnormality, whereas 40 (22.22%) had no pelvic pathology. Because pelvic findings could coexist within the same participant, the individual pathology percentages are not mutually exclusive (Figure 2). Comparison of individual tubal findings showed that HSG classified 92 (51.11%) participants as having normal tubes compared with 70 (38.89%) on hystero-laparoscopy. HSG reported unilateral tubal block in 44 (24.44%) participants and 50 (27.78%) on hystero-laparoscopy; bilateral block in 26 (14.44%) and 38 (21.11%), respectively; and hydrosalpinx in 18 (10.00%) and 22 (12.22%), respectively. Peritubal adhesions were not identified by HSG but were detected in 42 (23.33%) participants by hystero-laparoscopy (Table 3). The reported marginal chi-square values should not be interpreted as paired tests because HSG and hystero-laparoscopy were performed in the same participants. For paired comparisons, the appropriate analysis is McNemar's test, which requires participant-level cross-tabulations for each finding; the source data did not include these paired cross-tabulations. Therefore, Table 3 is presented descriptively without p-values for the individual findings.

Figure 1. Diagnostic performance of HSG for detecting tubal pathology.



HSG was evaluated against diagnostic hystero-laparoscopy with chromopertubation as the reference standard. PPV, positive predictive value; NPV, negative predictive value.

Table 1. Baseline Characteristics of Study Participants (n = 180)

Variable	Category	n	%
Age (years)	20–25	42	23.33
	26–30	66	36.67
	31–35	48	26.67
	36–40	24	13.33
Type of subfertility	Primary	102	56.67
	Secondary	78	43.33

Duration of subfertility	1–3 years	74	41.11
	4–6 years	68	37.78
	>6 years	38	21.11

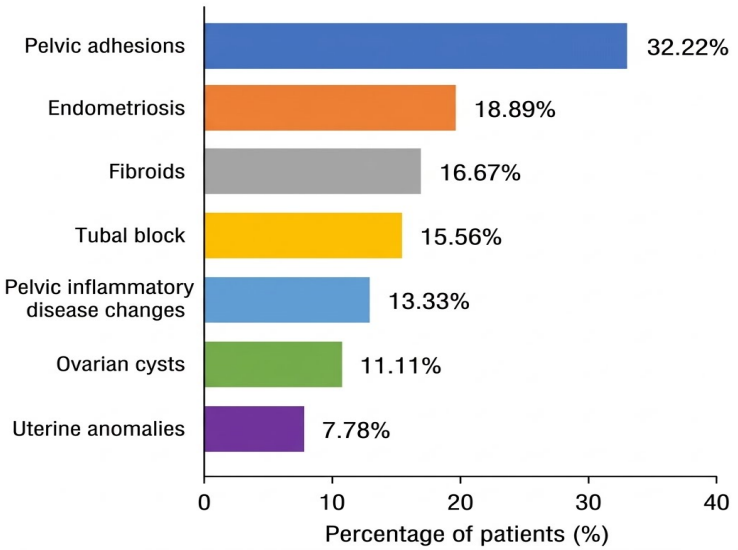
Values are presented as frequency (n) and percentage (%). Percentages are based on the total study population (n = 180).

Table 2A. Diagnostic Performance of HSG Using Hystero-Laparoscopy as the Reference Standard

Parameter	Value
Sensitivity	70.91%
Specificity	74.29%
Positive predictive value (PPV)	81.25%
Negative predictive value (NPV)	61.90%
Overall diagnostic accuracy	72.22%

HSG was the index test, and diagnostic hystero-laparoscopy with chromopertubation was the reference standard. PPV, positive predictive value; NPV, negative predictive value.

Figure 2. Pelvic pathologies detected by hystero-laparoscopy (n = 180).



Diagnostic hystero-laparoscopy identified pelvic pathologies. Individual findings were not mutually exclusive and could coexist in the same participant; therefore, percentages do not necessarily sum to 100%.

Table 2B. Association Between HSG and Hystero-Laparoscopic Classification

Comparison	χ^2	df	p-value
HSG vs hystero-laparoscopy (tubal pathology)	35.11	1	<0.001

We used Pearson's chi-square test to assess the association between HSG and hystero-laparoscopic tubal pathology classification. We considered $p < 0.05$ statistically significant.

Table 3. Tubal Findings Detected by HSG and Hystero-Laparoscopy (n = 180)

Tubal finding	HSG present, n (%)	Hystero-laparoscopy present, n (%)
Normal tubes	92 (51.11)	70 (38.89)
Unilateral block	44 (24.44)	50 (27.78)
Bilateral block	26 (14.44)	38 (21.11)
Hydrosalpinx	18 (10.00)	22 (12.22)
Peritubal adhesions	0 (0.00)	42 (23.33)

Tubal findings are presented as frequency and percentage. We analyzed individual findings separately; they were not mutually exclusive. Because both diagnostic methods were performed in the same participants, paired comparisons require participant-level cross-tabulation.

Discussion

The present study found that hysterosalpingography (HSG) had a sensitivity of 70.91%, specificity of 74.29%, PPV of 81.25%, NPV of 61.90%, and overall accuracy of 72.22% compared with diagnostic hystero-laparoscopy. These results are consistent with previous studies showing HSG's moderate diagnostic accuracy, especially for evaluating tubal patency. Yildirim et al. reported similar HSG sensitivity of 85% and specificity of 65%, suggesting that although HSG is useful as a screening tool, it is less accurate than laparoscopy for definitive diagnosis of tubal disease [14].In this study, HSG identified 78 true-positive cases, 18 false-positive cases, and 32 false-negative cases, demonstrating the test's limitations in distinguishing functional from true tubal disease. This pattern is also observed in the literature on infertility, with false-positive results often attributed to a tubal spasm or technical problems. In addition, previous studies showed that HSG diagnostic accuracy is reduced, especially in complex infertility cases; in our study, we had 32 false-negative cases among 180 patients [9,15,16]. Pathology identified in the left and right pelvis using hystero-laparoscopy was significantly higher than that identified using hystero-ovarian sonography. It included left- and right-sided pelvic adhesions (32.22%), endometriosis (25.56%), left- or right-sided ovarian cysts (18.89%), and tubo-ovarian masses (8.89%). Hystero-ovarian sonography failed to detect peritubal adhesions in 23.33% of cases. This superiority of laparoscopy is well supported by previous studies, where other pelvic abnormalities were found in as many as 40% of women with normal HSG. Research studies have also reported that laparoscopy revealed a significant amount of concealed pelvic disease in infertile women, thus establishing it as the gold standard for diagnostic laparoscopy [17]. Regarding tubal findings, results indicated differences between HSG and laparoscopy: normal tubal and bilateral tubal block frequencies were 51.11% and 14.44%, respectively, on HSG versus 38.89% and 21.11%, respectively, on laparoscopy. Gupta and Upreti claim similar differences in the rate of tubal patency determined by HSG and the failure to detect distal tubal disease in almost 25% of infertile women. [18] This re-emphasizes the need for caution in interpreting HSG in cases of suspected tubal infertility. Regarding reproductive outcomes, the present study found a 35.56% spontaneous conception rate after six months, highest among women with normal tubes (48.57%) and lowest among women with hydrosalpinx (18.18%). These observations are consistent with previous investigations that found significantly lower fertility when tubal pathology was present than when it was normal, highlighting the importance of evaluating the tubes in predicting fertility outcomes [19]. In addition, a small number of women with pelvic pathology (19.30%) had become pregnant. In comparison, the large number of women without pelvic pathology (60.00%) had become pregnant ($p < 0.001$), illustrating how significant undiagnosed pelvic disease is. Laparoscopy-based studies have yielded similar findings, in which rates of conception are significantly decreased in those with untreated endometriosis and normal HSG. Previous research also emphasized laparoscopy as a means of detecting clinically significant lesions that HSG would miss, and that could affect fertility prognosis [20,21]. Strengths of this study include its prospective comparative design, sample size, and head-to-head comparison of hysterosalpingography (HSG) with diagnostic hystero-laparoscopy (DH-LAP), considered the gold standard for evaluating tubal and pelvic disease. It offers a comprehensive assessment by linking diagnostic findings to clinically relevant reproductive outcomes, such as subsequent natural conception at follow-up, thereby improving its clinical utility in evaluating infertility. The introduction of both tubal and pelvic abnormalities provides a more comprehensive assessment of the infertility-related pathology than studies using only one diagnostic modality [22]. The study's limitations, however, include its single-center setting, which may limit generalizability to larger populations. The short follow-up period may also underestimate longer-term pregnancy outcomes. Furthermore, diagnostic bias may have occurred because observers interpreted imaging and laparoscopic findings differently and the study was not blinded. Cost-effectiveness analysis is not available, and long-term reproductive outcomes are not evaluated, limiting assessment of the overall clinical and economic impact of these diagnostic strategies.

Conclusion

Based on these results, hysterosalpingography has satisfactory diagnostic accuracy for assessing tubal pathology and lower accuracy for detecting associated pelvic abnormalities than diagnostic hystero-laparoscopy, a more comprehensive method for identifying clinically significant lesions of the reproductive tract. The study also shows differences in natural conception rates based on the underlying tubal and pelvic condition, with higher rates in patients with normal tubal and pelvic findings and lower rates in patients with

hydrosalpinx and/or pelvic pathology. Overall, these results emphasize the important role of hystero-laparoscopy in providing both accurate diagnostic information and valuable prognostic insight in the management of female subfertility.

Ethical Approval

The Institutional Review Board of Sheikh Zayed Medical College/Hospital, Rahim Yar Khan, Pakistan granted ethical approval through expedited review **(Ref. No. 08/IRB/SZMC/SZH, dated 21/01/2026)** before study commencement.

Authors' Contributions

Saima Zulfiqar: Conceptualization, study design, supervision, data interpretation, critical revision of the manuscript for important intellectual content, final approval of the version to be published, and accountability for all aspects of the work.

Sadia Zulfiqar: Conceptualization, study design, data collection, data curation, statistical analysis, data interpretation, manuscript drafting, critical revision of the manuscript, final approval of the version to be published, and accountability for all aspects of the work.

Adeela Anwar Rana: Data collection, data curation, literature review, data interpretation, manuscript revision, final approval of the version to be published, and accountability for all aspects of the work.

Aisha Javed: Data collection, laboratory assessment, data curation, literature review, manuscript revision, final approval of the version to be published, and accountability for all aspects of the work.

Tahira Afzal Durrani: Study supervision, interpretation of findings, critical review of the manuscript for important intellectual content, final approval of the version to be published, and accountability for all aspects of the work.

All authors approved the final version of the manuscript and agreed to be accountable for all aspects of the work in accordance with ICMJE authorship criteria.

Conflict of Interest

The authors declare no conflict of interest related to this study's conduct, authorship, or publication.

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This study received no external funding. The research used available institutional resources. No funding agency was involved in the study design, data collection, analysis, interpretation, or manuscript preparation.

Data Availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request. The data are not publicly available due to privacy and confidentiality considerations for the study participants.

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Original Article

Antimicrobial Resistance Patterns and Clinical Outcomes in Critically Ill Patients

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Abstract

Objective: To determine the antimicrobial resistance patterns among bacterial pathogens isolated from critically ill patients and evaluate their association with clinical outcomes.

Methodology: This longitudinal observational study was conducted in the Department of Medicine at Karachi Teaching Hospital from October 2025 to March 2026. We enrolled 300 critically ill patients admitted to the ICU. We recorded demographic characteristics, comorbidities, previous antibiotic exposure, isolated organisms, antimicrobial susceptibility patterns, multidrug resistance, mechanical ventilation, ICU stay, treatment response, and mortality.

Results: We identified bacterial infection in most clinically suspected cases. The most common bacteria isolated were Acinetobacter baumannii, 78 (26.0%), followed by Klebsiella pneumoniae, 67 (22.3%), Pseudomonas aeruginosa, 49 (16.3%), E. coli, 42(14.0%), S. aureus, 31 (10.6%), and Enterococcus spp., 15 (5.0%), respectively. Multidrug-resistant organisms constituted a substantial proportion of isolates. Patients with resistant infections had higher mortality, longer ICU stays, and more frequent mechanical ventilation than patients with susceptible infections.

Conclusion: Our study concluded that antimicrobial resistance is a significant issue among critically ill patients and is related to unfavorable clinical outcomes. Consistent ICU-specific antimicrobial surveillance, right empirical treatment, culture-directed treatment, infection-prevention procedures, and antimicrobial stewardship are mandatory to lessen the burden of resistant infections.

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Introduction

Critically ill patients receive advanced medical treatment in specialized departments called Intensive Care Units (ICUs). Because of widespread empirical use of broad-spectrum antibiotics, prolonged hospital stays, and weakened immunity, these patients are highly susceptible to infections[1]. In critically ill patients, the increased prevalence of antibiotic resistance complicates the treatment process and restricts effective empirical therapy choices[2]. In ICUs, multidrug-resistant (MDR) bacteria are a global health problem, where infections lead to higher morbidity and death rates. Gram-negative bacteria *K. pneumoniae* and *E. coli* typically produce ESBLs and carbapenemases, limiting treatment options and requiring last-resort antibiotics such as colistin or tigecycline [3]. AmpC beta-lactamases, both chromosomal and plasmid-mediated, can cause resistance to extended-spectrum cephalosporins, cephamycins, and beta-lactam inhibitor combinations, limiting treatment options in ICU settings [4]. *P. aeruginosa* and *A. baumannii* have significant levels of resistance, especially to carbapenems, making them difficult to eliminate and increasing the chance of severe clinical consequences. MRSA and VRE remain widespread among Gram-positive bacteria in hospital-acquired infections, complicating empirical antibiotic selection [5].MDR pathogen infections lead to longer ICU stays, greater rates of septic shock, and higher fatality rates, making resistance features crucial for patient outcomes [6]. Continuous tracking of resistance trends and effective antimicrobial stewardship programs are crucial to reducing the incidence of MDR infections in critically ill patients. Sepsis must be diagnosed early and managed appropriately to reduce in-hospital mortality. While improper or insufficient treatment raises the chance of death, very early commencement of successful empirical antibiotic therapy can improve patient prognosis [7]. However, the microorganisms causing infections in ICU patients and their antibiotic susceptibility profiles vary across institutions, even among departments within the same hospital. Bacterial pathogen distribution and antibiotic resistance profiles change over time [8]. To improve antibiotic therapy in ICU patients, hospitals and individual ICUs should study microbiological data and adjust treatment guidelines as needed. Therefore, this study was conducted to determine antimicrobial resistance patterns and clinical outcomes in critically ill patients [9].

Materials and method

This longitudinal observational study was conducted at the Department of Medicine, Karachi Teaching Hospital, from 7th October 2025 to 7th March 2026, after obtaining permission from the hospital's ethics committee. This study included 300 critically ill individuals of both genders and different age groups (above 18 years) admitted to the ICU who had clinical evidence of suspected bacterial infection, had an appropriate clinical specimen submitted for microbiological examination, and had sufficient clinical information available for outcome assessment. We excluded individuals with incomplete clinical records and those transferred before clinical outcome assessment. Based on the infection site and the treating physician's request, we collected samples using standard aseptic precautions and transported them immediately to the microbiology laboratory. These samples included wound/pus, urine, endotracheal aspirates, blood, and other relevant samples. When clinically feasible, we obtained blood cultures in adequate blood culture bottles before administering antibiotics. We processed specimens using conventional microbiological methods. We selected the appropriate culture medium based on the specimen type. After incubation, we assessed bacterial growth by colony morphology, Gram staining, and standard biochemical testing. We confirmed results using automatic identification systems where available. We conducted antimicrobial susceptibility testing on clinically relevant bacterial isolates. We performed antimicrobial susceptibility screening using the Kirby-Bauer disk diffusion technique. According to widely accepted worldwide criteria, multidrug resistance (MDR) is recognized as non-susceptibility to at least one antimicrobial agent in more than three antimicrobial categories. We recorded demographic and clinical data using a standardized data-collection proforma. We documented demographic and clinical data, including gender, age, ICU stay duration, hypertension, chronic renal disease, chronic obstructive pulmonary disease, diabetes, antibiotic exposure, ICU admission, antimicrobial susceptibility pattern, MDR status, identified bacterial species, and presence of sepsis/septic shock. We evaluated clinical outcomes by reviewing individual clinical records from the time the bacterial infection was identified until ICU discharge, admission to another ward, or death. We analyzed data using SPSS version 16. We expressed categorical data as frequencies and percentages, and summarized continuous variables as mean ± standard deviation. We used the chi-square test or Fisher's exact test to investigate associations between antibiotic

resistance/MDR status and pertinent demographic or clinical factors, as needed. We considered p <0.05 statistically significant.

Results

This study included 300 critically ill patients admitted to the ICU: 178 (59.3%) male and 122 (40.7%) female. Of the participants, 214 (71.3%) were under 60 years old, and 86 (28.7%) were over 60. Hypertension was seen in 112 (37.3%) patients, while diabetes mellitus was found in 96 (32.0%) patients. Mechanical ventilation was necessary for 174 (58.0%) individuals. Chronic renal disease was detected in 48 (16%) people, while COPD was investigated in 39 (13.0%). Sepsis or septic shock was found in 139 (46.3%) cases, whereas acute renal damage occurred in 87 (29.0%). Table 1 shows that 108 (36.0%) had a previous hospitalization, and 126 (42.0%) had been prescribed antibiotics before ICU admission**.** The most common bacteria isolated were Acinetobacter baumannii, 78 (26.0%), followed by Klebsiella pneumoniae, 67 (22.3%); Pseudomonas aeruginosa, 49 (16.3%); E. coli, 42 (14.0%); S. aureus, 31 (10.6%); and Enterococcus spp., 15 (5.0), respectively. In total, 174 isolates (58.0%) met the multidrug resistance criterion. *A. baumannii* had the greatest MDR percentage (73.1%), followed by *K. pneumoniae* (68.7%) and *P. aeruginosa* (55.1%). Carbapenem resistance was especially common among the main Gram-negative bacteria. Table 2 shows that about 74.4% of A. baumannii and 62.7% of K. pneumoniae strains were carbapenem-resistant**.** Clinical outcomes were evaluated. Mechanical ventilation was necessary in 71.3% of individuals with MDR infections, compared to 39.7% of non-MDR patients. Septic shock and acute renal damage were substantially more common in the MDR group. Similarly, the MDR group had more than double the ICU mortality rate. Participants with MDR infections had an average ICU stay of 10.6 ± 6.4 days, versus 7.7 ± 4.5 days for non-MDR infections. Individuals with MDR infections had a considerably higher in-hospital death rate (44.8%) compared to those without (21.4%, p < 0.001). About 55.2% of MDR participants showed clinical improvement, compared to 78.6% of individuals with non-MDR illnesses. Likewise, MDR infections had worse microbiological clearance rates, as shown in Table 3.

Table 1. Clinical and demographic features of the study populations, n = 300

Features	**(n)**	(%)
Sex		
Male	178	59.3
Female	122	40.6
Age in years		
≤60 years	214	71.3
>60 years	86	28.7
Diabetes mellitus	96	32.0
Hypertension	112	37.3
Chronic kidney disease	48	16.0
Chronic obstructive pulmonary disease	39	13.0
Previous hospitalization	108	36.0
Previous antibiotic exposure	126	42.0
Mechanical ventilation	174	58.0
Sepsis/septic shock	139	46.3
Acute kidney injury	87	29.0

Values are presented as frequency (n) and percentage (%), based on the total study population (n = 300).

Table 2. Isolated bacteria and their antibiogram, n = 300

Bacterial pathogen	**Isolates n** (%)	**MDR n** (%)	**Carbapenem-resistant n** (%)
Acinetobacter baumannii	78(26.0)	57 (73.1)	58 (74.4)
Klebsiella pneumoniae	67 (22.3)	46 (68.7)	42 (62.7)
Pseudomonas aeruginosa	49 (16.3)	27 (55.1)	25 (51.0)
Escherichia coli	42 (14.0)	21 (50.0)	16 (38.1)
Staphylococcus aureus	31 (10.3)	13 (41.9)	–
***Enterococcus* spp.**	15 (5.0)	5 (33.3)	–
Other bacteria	18 (6.0)	5 (27.8)	–
Total	**300 (100)**	**174 (58.0)**	–

Values are presented as frequency (n) and percentage (%). MDR, multidrug-resistant.

Table 3. Based on MDR status, clinical outcomes in the study population

Clinical outcome	**MDR infection n=174**	**Non-MDR infection n=126**	**p-value**
In-hospital mortality	78 (44.8%)	27 (21.4%)	<0.001
ICU mortality	69 (39.7%)	23 (18.3%)	<0.001
Mean ICU stay (days)	10.6 ± 6.4	7.7 ± 4.5	<0.001

Mechanical ventilation	124 (71.3%)	50 (39.7%)	<0.001
Septic shock	94 (54.0%)	45 (35.7%)	0.002
Acute kidney injury	65 (37.4%)	22 (17.5%)	<0.001
Clinical improvement	96 (55.2%)	99 (78.6%)	<0.001
Microbiological clearance	02 (58.6%)	12 (73.0%)	0.012

Categorical variables are presented as n (%), and continuous variables as mean ± standard deviation (SD). We used chi-square or Fisher's exact test, as appropriate. We considered p <0.05 statistically significant. MDR, multidrug-resistant.

Discussion

This study included 300 critically ill patients admitted to the ICU: 178 (59.3%) male and 122 (40.7%) female. Hypertension was seen in 112 (37.3%) patients, while diabetes mellitus was found in 96 (32.0%). Mechanical ventilation was necessary for 174 (58.0%) individuals [10]. Chronic renal disease was detected in 48 (16%) people, while COPD was investigated in 39 (13.0%). Sepsis or septic shock was found in 139 (46.3%) cases, whereas acute renal damage occurred in 87 (29.0%) Previous hospitalization was documented in 108 (36.0%) of individuals, whereas 126 (42.0%) had been prescribed antibiotics prior to ICU admission. Our study's clinical and demographic features are similar to those in a systematic review and meta-analysis of prediction models for multidrug-resistant organism infections in comprehensive intensive care units conducted in 2025, which supports our findings.[10] The high prevalence of mechanical ventilation in our study is especially significant since mechanically ventilated patients are more exposed to healthcare-associated infections, particularly MDR Gram-negative bacteria. In a recent ICU investigation of carbapenem-resistant Gram-negative bacteremia, invasive mechanical ventilation before bacteremia was a major risk factor for resistant infection [11]. In our study, the most common bacteria isolated were Acinetobacter baumannii, 78 (26.0%), followed by Klebsiella pneumoniae, 67 (22.3%); Pseudomonas aeruginosa, 49 (16.3%); E. coli, 42 (14.0%); S. aureus, 31 (10.6%); and Enterococcus spp., 15 (5.0), respectively. The prevalence of these Gram-negative infections aligns with research on critically ill individuals admitted to the intensive care unit (Paramythiotou et al. [12]). The high prevalence of A. baumannii in our study is most worrying because this organism can persist in the hospital setting and quickly acquire resistance mechanisms. In our study, 58% of isolates were multidrug-resistant; A. baumannii had the highest MDR percentage (73.1%), followed by *K. pneumoniae* (68.7%) and *P. aeruginosa* (55.1%). Carbapenem resistance was especially common among the Gram-negative bacteria. About 74.4% of *A. baumannii* and 62.7% of K. pneumoniae strains were carbapenem-resistant. A similar resistance pattern was seen in a retrospective study by Kilinc in critically ill patients, which supports our findings [13]. A current study of carbapenem-resistant Gram-negative bacteremia in a medical intensive care unit showed extraordinarily high resistance rates among resistant isolates and found that carbapenem-resistant infections were linked to considerably higher 30-day mortality [14]. In our study, the MDR group had more than double the ICU mortality rate. Participants with MDR infections had an average ICU stay of 10.6 ± 6.4 days, versus 7.7 ± 4.5 days for non-MDR infections. Individuals with MDR infections had a considerably higher in-hospital death rate (44.8%) compared to those without (21.4%). These findings are similar to the study conducted by Kilinc, in which individuals with MDR infections had a higher death rate, longer ICU stay, and double the ICU mortality rate[13]. In the present study, mechanical ventilation was necessary in 71.3% of individuals with MDR infections, compared to 39.7% of non-MDR patients. Septic shock and acute renal damage were substantially more common in the MDR group. These results support the fact that individuals with more severe systemic disease often have severe MDR infections[15]. Our study found that 55.2% of MDR participants showed clinical improvement, compared to 78.6% of individuals with non-MDR illnesses. Likewise, MDR infections had worse microbiological clearance rates. MDR organisms lower the likelihood of successful first-line antimicrobial treatment, which may be one factor. A comprehensive review and meta-analysis of more than 73,000 individuals found that rising multidrug-resistant organism frequency was associated with higher rates of inappropriate empirical antibiotic treatment. In contrast, MDRO frequency was independently associated with death [16,17]. The findings emphasize the importance of continual antibiotic resistance surveillance in ICUs. The prevalence of MDR pathogens, especially A. baumannii, K. pneumoniae, and P. aeruginosa, suggests that empirical antibiotic policy should be based on recent local susceptibility data rather than relying entirely on generic guidelines. Prompt specimen collection, early microbiological diagnosis, effective empirical therapy followed by culture-directed therapy, antibiotic stewardship, and stringent infection-prevention procedures are critical components of controlling MDR infections.

Conclusion

Our study concluded that antimicrobial resistance is a significant issue among critically ill patients and is associated with unfavorable clinical outcomes. Consistent ICU-specific antimicrobial surveillance, appropriate empirical treatment, culture-directed treatment, infection-prevention procedures, and antimicrobial stewardship are mandatory to lessen the burden of resistant infections.

Ethical Approval

The Institutional Review Board/Ethics Committee approved this study under approval number ERB-346/08/2024 before the study began.

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This study received no external funding. The research used available institutional resources.

Conflict of Interest

The authors declare that they have no competing interests or conflicts of interest related to this study.

Authors' Contributions

Ajmaal Jami: Conceptualization, study design, supervision, data interpretation, manuscript drafting, critical revision, final approval, and accountability for all aspects of the work.

Sellal Ahmed: Methodology, data collection, data curation, statistical analysis, data interpretation, manuscript drafting and revision, final approval, and accountability for all aspects of the work.

Arshad Ali: Study supervision, methodology, interpretation of findings, critical review of the manuscript, final approval, and accountability for all aspects of the work.

Mahnoor Khan: Data collection, literature review, data curation, manuscript revision, final approval, and accountability for all aspects of the work.

All authors: Reviewed and approved the final version of the manuscript and agreed to be accountable for all aspects of the work in accordance with ICMJE authorship criteria.

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Original Article

Predictors of Mortality in ICU Patients with Multidrug-Resistant Bacterial Infections

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Abstract

Objective: To identify clinical, microbiological, and treatment-related predictors of mortality among ICU patients with multidrug-resistant (MDR) Bacterial Infections.

Methodology: This longitudinal observational study was conducted in the Department of Medicine at Karachi Teaching Hospital from December 2025 to May 2026. We enrolled 250 ICU patients with culture-confirmed MDR bacterial infections. We assessed demographic characteristics, comorbidities, prior antibiotic exposure, mechanical ventilation, septic shock, acute kidney injury (AKI), MDR pathogen, carbapenem resistance, and appropriateness of empirical antimicrobial therapy. The primary outcome was in-hospital mortality. We compared categorical variables using the Chi-square test and used multivariable logistic regression to identify independent predictors of mortality.

Results: Among 250 patients, 105 (42.0%) died, and 145 (58.0%) survived. The most frequently isolated organisms were Acinetobacter baumannii (72, 28.8%), Klebsiella pneumoniae (61, 24.4%), and Pseudomonas aeruginosa (39, 15.6%). Mortality was higher among patients with septic shock, mechanical ventilation, AKI, carbapenem-resistant infection, previous antibiotic exposure, and inappropriate empirical antimicrobial therapy. In multivariable logistic regression, septic shock was the highest independent predictor of mortality. Other independent predictors were inappropriate empirical therapy, mechanical ventilation, carbapenem-resistant infection, AKI, previous antibiotic exposure, and age >60 years.

Conclusion: Mortality among ICU patients with MDR bacterial infections was high. Septic shock, inappropriate empirical antimicrobial therapy, mechanical ventilation, carbapenem resistance, AKI, previous antibiotic exposure, and older age were important independent predictors of mortality.

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Introduction

Intensive care units (ICUs) are specialized places that deliver innovative medical management to critically ill patients. Individuals admitted to these facilities are especially susceptible to infections due to many reasons such as immunosuppression, lengthy hospital stays, invasive surgeries, and the extensive empirical use of broad-spectrum antibiotics[1].Infections resulting from multidrug-resistant (MDR) bacteria are among the most prevalent causes of hospital-acquired infections, contributing to higher morbidity and death rates in ICU patients[2]. The increased frequency of antibiotic resistance in critically sick patients nowadays restricts effective empirical therapy choices and complicates the treatment process[3].Multidrug-resistant (MDR) bacteria are a major global health concern, particularly in ICUs, where infections caused by these pathogens contribute to higher morbidity and mortality rates. K. pneumoniae and E. coli are two Gram-negative bacteria that are commonly linked to the synthesis of carbapenemase and extended-spectrum beta-lactamase (ESBL), which restricts treatment choices and usually necessitates the use of last-resort medicines[4]. There are numerous independent risk factors for the occurrence of MDR bacterial infections within ICU patients, including central venous access, pulmonary artery catheterization, stress ulcer prophylaxis, urinary catheterization, mechanical ventilation, trauma, ICU length of stay, and, most importantly, a previous history of infection or colonization by MDR microorganisms[5].According to one research, the severity of infection, underlying illness, MDR status, and inadequate antibiotic therapy were all significant predictors of death in ICU patients. Septic shock, pneumonia, and inadequate empirical or final therapy were significantly related to poor outcomes[6]. A 2026 study on carbapenem-resistant Gram-negative bloodstream infections reported notably high mortality and identified mechanical ventilation, prior carbapenem exposure, and prolonged hospitalization as significant risk factors for resistance infection [7]. Thus, identifying independent predictors of death among intensive care unit patients with MDR infections is critical for risk stratification and therapeutic decision-making. Therefore, the present study was conducted to determine predictors of mortality among critically ill ICU patients with microbiologically confirmed multidrug-resistant bacterial infections [8,9].

Materials and Method

This longitudinal observational study was conducted at the Department of Medicine, Karachi Teaching Hospital, from December 2025 to May 2026, after approval from the hospital's ethics committee. A total of 250 individuals of both genders and different age groups (≥18 years) admitted to the ICU with confirmed MDR bacterial infections and stayed in hospital till the outcome assessment were included. We excluded individuals with incomplete clinical records or age below 18 years. We collected several specimens from each participant (pus/wound, endotracheal aspirates, blood, sputum, and other clinically relevant samples) from the suspected site of infection aseptically and sent them to the microbiology lab for further processing. Each sample was inoculated on a specified medium and incubated for growth. After incubation, we measured bacterial growth using colony morphology, Gram staining, and standard biochemical testing. We confirmed identification using automatic identification systems where available. We conducted antimicrobial susceptibility testing on clinically relevant bacterial isolates. We performed antimicrobial susceptibility screening using the Kirby-Bauer disk diffusion technique. According to widely accepted worldwide criteria, multidrug resistance (MDR) is recognized as non-susceptibility to at least one antimicrobial agent in more than three antimicrobial categories. We recorded demographic and clinical data for each participant. We followed each individual to identify predictors of mortality. We classified participants into survivor and non-survivor groups. We analyzed data using SPSS version 16. Continuous variables were presented as mean ± standard deviation, and Categorical variables were presented as frequencies and percentages. To assess associations between mortality and different variables, we used the chi-square test or Fisher's exact test. P-value of <0.05 was considered statistically significant.

Results

We studied 250 individuals admitted to the ICU with multi-drug bacterial infections. We classified participants as survivors or non-survivors. During the study period, 145 (58.0%) survived, and 105 (42.0%) died during hospitalization. Non-survivors were substantially more likely to have had previous antibiotic exposure (56.2% vs. 37.2%, p=0.002. Mechanical ventilation was strongly associated with mortality. It was needed in 77.1% of non-survivors when compared to 52.4% of survivors (p<0.001). Acute kidney injury was also substantially more

common among non-survivors (44.8% compared with 24.1%, p=0.001). Septic shock showed the most clinically significant difference. It affected 63.8% of non-survivors and just 21.4% of survivors (p < 0.001). Survivors and non-survivors did not differ significantly in terms of gender, hypertension, chronic renal disease, diabetes, or previous hospitalization, as presented in Table 1. Among multidrug-resistant bacteria, A. baumannii was most prevalent (72, 28.8), followed by K. pneumoniae (61, 24.4) and P. aeruginosa (39, 15.6). The death rate was greatest among individuals infected with A. baumannii, with 38 of 72 (52.8%) dying, followed by K. pneumoniae (45.9%). Carbapenem-resistant infections were found in 129 (51.6%) individuals. The death rate in individuals with carbapenem-resistant infections was 57.4%, which was significantly higher than the general mortality rate of 42.0%. Inadequate empirical treatment occurred in 32.8% of individuals, with non-survivors having a significantly higher rate (47.6% versus 22.1% among survivors), as shown in Table 2. Multivariable logistic regression revealed that the most common predictors of mortality in ICU patients with MDR infections were septic shock, mechanical ventilation, and acute kidney injury. Similarly, incorrect empirical antibiotic medication was linked with a 2.5-fold increased risk of mortality, and Carbapenem-After adjusting for prior antibiotic exposure and age >60 years, these effects remained statistically significant, although reduced, as shown in Table 3.

Table 1. Clinical and demographic features by survival outcome.

Variable	Total n=250	Survivors n=145	Non-survivors n=105	p-value
Age >60 years	86 (34.4%)	50 (34.5%)	36 (34.3%)	0.037
Male gender	151 (60.4%)	89 (61.4%)	62 (59.0%)	0.695
Diabetes mellitus	83 (33.2%)	44 (30.3%)	39 (37.1%)	0.263
Hypertension	94 (37.6%)	50 (34.5%)	44 (41.9%)	0.231
Chronic kidney disease	42 (16.8%)	21 (14.5%)	21 (20.0%)	0.262
Previous hospitalization	91 (36.4%)	48 (33.1%)	43 (41.0%)	0.202
Previous antibiotic exposure	113 (45.2%)	54 (37.2%)	59 (56.2%)	0.002
Mechanical ventilation	157 (62.8%)	76 (52.4%)	81 (77.1%)	<0.001
Septic shock	98 (39.2%)	31 (21.4%)	67 (63.8%)	<0.001
Acute kidney injury	82 (32.8%)	35 (24.1%)	47 (44.8%)	0.001

Table 2. Multidrug-resistant bacteria and their resistance features

Bacterial pathogen	Total n (%)	Survivors n(%) (%)	Non-survivors n (%)	Mortality within pathogen group
Acinetobacter baumannii	72 (28.8)	34 (23.4)	38 (36.2)	52.8%
Klebsiella pneumoniae	61 (24.4)	33 (22.8)	28 (26.7)	45.9%
Pseudomonas aeruginosa	39 (15.6)	24 (16.6)	15 (14.3)	38.5%
Escherichia coli	31 (12.4)	21 (14.5)	10 (9.5)	32.3%
Staphylococcus aureus	24 (9.6)	16 (11.0)	8 (7.6)	33.3%
Enterococcus *spp.*	11 (4.4)	7 (4.8)	4 (3.8)	36.4%
Other organisms	12 (4.8)	10 (6.9)	2 (1.9)	16.7%
Total	**250 (100)**	**145 (100)**	**105 (100)**	**42.0%**
Carbapenem-resistant infection	129 (51.6)	55 (37.9)	74 (70.5)	**57.4%**
Inappropriate empirical therapy	82 (32.8)	32 (22.1)	50 (47.6)	**61.0%**

Table 3. Predictors of Motility among the study population applying multivariable logistic regression

Predictor	Adjusted OR	95% CI	p-value
Age >60 years	1.71	1.01–2.92	0.045
Previous antibiotic exposure	1.85	1.08–3.21	0.025
Mechanical ventilation	2.37	1.34–4.21	0.003
Septic shock	4.30	2.42–7.66	<0.001
Acute kidney injury	1.92	1.11–3.35	0.020
Carbapenem-resistant infection	2.16	1.25–3.76	0.006
Inappropriate empirical therapy	2.53	1.43–4.49	0.002

Discussion

MDR has emerged as a major concern, particularly in the hospital's ICU. In 2019, MD illnesses caused around 4.95 million fatalities worldwide, including 1.27 million of them mainly attributed to medication resistance.[7] ICUs are frequently regarded as the epicenter of drug-resistant microbe growth, amplification, and spread[10]. Patients with severe illnesses are especially susceptible to infections due to being exposed to multiple invasive procedures compromising the anatomical barriers' defenses, impairment of protective mechanisms such as the cough reflex or acid gastric environment by sedative drugs or stress-ulcer prophylaxis, and the continual impairment of the immune response induced by trauma, surgery, and sepsis[11,12]. Previous studies revealed that the most common predictors of mortality in patients with MDR infections are trauma, ICU length of stay, mechanical ventilation, urinary catheterization, pulmonary artery catheterization, stress ulcer prophylaxis, or previous history of infection or colonization by MDR microorganisms[13]. Therefore, this study aimed to identify predictors of mortality among critically ill ICU patients with microbiologically confirmed multidrug-resistant bacterial infections. We studied 250 individuals admitted to the ICU with multidrug-resistant bacterial infections[14].In our study, 42% of the individuals admitted to the ICU died during the study period. Non-survivors were substantially more likely to have had previous antibiotic exposure[15]. These findings are similar to the study by Vardakas et al.10 Our findings differ from those of Fatima et al.; they reported a 14-day mortality of 26.8%, which is lower than in our study[16]. The slightly greater mortality observed in our study might be explained by including critically ill individuals with a wider spectrum of serious infections rather than just bloodstream infections. Mortality rates vary because of differences in infection type, pathogen, resistance mechanisms, disease severity, and access to treatment. In our study, A. baumannii was the most prevalent among multidrug-resistant bacteria, followed by K. pneumoniae and P. aeruginosa [17]**.** The death rate was greatest among individuals infected with A. baumannii, with 38 of 72 (52.8%) dying, followed by K. pneumoniae (45.9%). The death rate in individuals with carbapenem-resistant infections was 57.4%, which was significantly higher than the general mortality rate. These findings are similar to the study by Vardakas et al., which further supports these findings[18].In our study, septic shock was a robust predictor of mortality. This result is consistent with prior reports. In a review of MDR Gram-negative infections, septic shock was revealed as one of the highest death predictors[19]. Septic shock was also found to be an independent risk factor related to in-hospital death in a current ICU study of Gram-negative bloodstream infections[19]. Septic shock causes severe circulatory and cellular dysfunction and can lead to multiple organ failure. As a result, its link to mortality is physiologically plausible, underscoring the importance of early detection and prompt sepsis treatment[20]. Mechanical ventilation was independently associated with death in our study. A recent ICU study found invasive mechanical ventilation to be a major factor associated with resistant Gram-negative infection and death[21]. Mechanical ventilation may signal illness severity rather than directly causing mortality. Patients who need invasive ventilation often have multiple organ dysfunction, respiratory failure, septic shock, or severe pneumonia. Our study also revealed that Incorrect empirical antibiotic medication was linked with a 2.5-fold increased risk of mortality, and Carbapenem-resistant illness raised the risk of death by around 2.2-fold[22]. After adjusting for previous antibiotic exposure and age >60 years, their effects remained statistically significant. These findings are similar to those of the previous study [23]. The results highlight that host factors, disease severity, resistance traits, and antimicrobial therapy effectiveness all influence mortality in MDR infections; early identification of high-risk patients, appropriate empirical treatment, rapid microbiological diagnosis, prompt definitive therapy, and efficient source control could improve outcomes.

Conclusion

Our study concluded that mortality among ICU patients with MDR bacterial infections was high. Septic shock, inappropriate empirical antimicrobial therapy, mechanical ventilation, carbapenem resistance, AKI, previous antibiotic exposure, and older age were important independent predictors of mortality.

Ethical Approval

Ethical approval for this study was obtained from the Institutional Review Board/Ethics Committee under approval number ERB-372/11/2024 prior to the study's commencement.

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Conflict of Interest

The authors declare no competing interests or conflicts of interest related to this study.

Authors' Contributions

Arshad Ali: Conceptualization, study design, supervision, data interpretation, manuscript drafting, critical revision, final approval, and accountability for all aspects of the work.

Mahnoor Khan: Methodology, data collection, data curation, statistical analysis, interpretation of data, manuscript drafting and revision, final approval, and accountability for all aspects of the work.

Ajmaal Jami: Study supervision, methodology, interpretation of findings, critical review of the manuscript, final approval, and accountability for all aspects of the work

Sellal Ahmed: Data collection, literature review, data curation, manuscript revision, final approval, and accountability for all aspects of the work.

All authors: Reviewed and approved the final version of the manuscript and agreed to be accountable for all aspects of the work in accordance with ICMJE authorship criteria.

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Original Article

Predictive Value of the INR-to-Platelet Ratio (INPR) for Advanced Liver Fibrosis in Patients with Chronic Hepatitis C Infection

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Abstract

Objective: To assess the suitability of the International Normalized Ratio, INR-to-platelet ratio (INPR) as a marker to help identify advanced stages of hepatic fibrosis in patients with chronic hepatitis C infection.

Methodology: This cross-sectional study was conducted in the Department of Hematology, Pathology, Bakhtawar Amin Medical and Dental College, Multan, during Sep 2025 and March 2026. 96 patients were diagnosed with HCV infection. Participants underwent a series of diagnostic tests, including liver parenchymal biopsy, shear wave elastography (SWE), and blood tests to determine the INPR. The principal outcome was the assessment of advanced fibrosis (>F3), determined using the METAVIR scoring system. We also performed endoscopic follow-up to document the presence or absence of esophageal varices. We analyzed the collected data using the Statistical Package for the Social Sciences (SPSS) version 25.0.

Results: Participants had a mean age of 50 ± 15.6 years, with males accounting for 64.5% and females for 35.5% of the cohort. Advanced hepatic fibrosis was present in 56 patients (58.3%). INPR demonstrated good discriminatory ability, with sensitivity of 84%, specificity of 74%, PPV of 82.5%, and NPV of 76.9%. By comparison, GPR exhibited comparatively lower diagnostic accuracy.

Conclusion: INPR is a potentially valuable non-invasive indicator for assessing advanced liver fibrosis in individuals with chronic HCV infection. Its practicality and simple application could facilitate bedside risk stratification and potentially reduce reliance on invasive liver biopsy.

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Introduction

Globally, Hepatitis C Virus (HCV) Infection Illustrates A Prominent Health Concern Across the World. Approximately 1.75 Million New Cases Are Documented Each Year. An Estimated 6% of the Pakistani population is affected by This Condition, Emphasizing Its Considerable Impact on Public Health.[1] Chronic Hepatitis C Causes Various Hepatic Complications Such as Fibrosis, Liver Cirrhosis, Decompensated Liver Disease, And Hepatocellular Carcinoma. Therefore, to reduce complications, Rapid Diagnosis and management are required.[2] Typically, Hepatic Biopsy Has Been Recognized As Definitive Method For Evaluating The Severity Of Hepatic Fibrosis And Inflammation. In Contrast, There Is Increasing Need Of Non-Surgical Diagnostic Interventions Due To Various Complications Of Biopsy Such As High Risk Of Infections, Bleeding And Accidental Damage To Surrounding Organs During Procedure.[3] Due To Hepatic Biopsy Restriction, Various Non-Surgical Methods Have Been Established Such As Shear Wave Elastography (Swe), Transient Elastography (Te) And Magnetic Resonance Elastography (Mre). These Radiographic Techniques Have Shown Strong Diagnostic Accuracy In Determining The Stage Of Fibrotic Changes In Liver In A Non-Surgical Manner.[4-6] Regardless Of Their Benefits, These Procedures Are Still Incredibly Challenging. These Include Financial Burden, Inconsistency In Reporting Among Observers, And Limited Accessibility In Rural Areas. Therefore, Research Focus Has Moved To Detecting Non-Surgical Biomarkers And Grading Systems That Can More Accurately Evaluate Fibrotic Changes In Hepatocytes. Among These Non-Invasive Procedures, The Fibrosis-4 Score (Fib-4) And Aspartate Transaminase To Platelet Ratio Index (APRI) Received Recognition. These Grades With Gpr, Are Commonly Used To Assess The Hepatic Fibrotic Changes In Chronic Hepatitis B Patients.[7-9] In The Absence Of Liver Biopsy And Advanced Radiological Procedures, the World Health Organization (WHO) Has Approved the Use of a Non-Surgical Grading System to Identify Hepatic Cirrhosis.[10] Ding R Et Al. Conducted significant research comparing the diagnostic reliability of IMPR with APRI, Fib-4, and GPR in patients with chronic HBV. The results showed that IMPR outperformed other indices in Detecting Significant and Advanced Fibrosis, with a Test Sensitivity of 67%, an Exclusion Rate of 75%, and a Diagnostic Precision of 71%. Additionally, In Detecting Cirrhosis (>F4), Inpr achieved 68% Sensitivity, 87.07% Specificity, and 81% Diagnostic Performance.[11] Notwithstanding These Encouraging Findings, The Role Of Inpr In Diagnosing Advanced Fibrosis And Cirrhosis Among Individuals With Chronic Hcv Infection Is Still Not Established. Thus, this research aimed to determine the utility of INPR as a marker of advanced hepatic fibrosis in a Pakistani Cohort With Chronic Hepatitis C Virus Infection. Establishing Inpr As A Non-Invasive, Bedside Parameter, This Study Aims To Provide Clinicians With A Practical Marker That Could Possibly Eliminate The Requirement For Surgical Liver Biopsies And Decrease Dependence On Expensive Imaging Techniques For The Assessment Of Advanced Hepatic Fibrosis.

Material and Methods

This Cross-Sectional Study Was Conducted In The Department Of Hematology, Pathology, Bakhtawar Amin Medical And Dental College, Multan, During Sep 2025 And March 2026. The Study Included Individuals Aged 18 to 60 years diagnosed with hepatitis C; PCR confirmed the diagnosis. Participants Were Excluded If They Are Under Or Over Age, Co-Infection With Hepatitis B Or Hiv, Had Missing Data, Did Not Give Consent Or Have Decompensated Liver Disease, Autoimmune Hepatitis, Alcoholic Liver Disease, Non-Alcoholic Fatty Liver Disease, Metabolic Liver Diseases, Wilson's Disease, Hemochromatosis, Cholestatic Liver Diseases, As Well As Those Diagnosed With Hepatocellular Carcinoma Or Serious Comorbidities. The Diagnosis For Compensated Cirrhosis Included Ultrasound Evidence Of Heterogeneous Liver Echotexture, Nodular Liver Margins, Splenomegaly With A Size Above 12 Cm, And Portal Vein Dilatation >12 Mm. We Exclude Individuals With Coexisting Chronic Hepatic Conditions, Such As Hepatitis B, Autoimmune Hepatitis, Alcoholic Liver Disease, Non-Alcoholic Fatty Liver Disease, Metabolic Liver Diseases, Wilson's Disease, Hemochromatosis, Cholestatic Liver Diseases, As Well As Those Diagnosed With Hepatocellular Carcinoma Or Serious Comorbidities. Hepatic Fibrosis Was Evaluated Using Two Modalities: Shear Wave Elastography (SWE), With Fibrosis Staged From F0 to F4 according to kPa measurements,12 and histological assessment using the METAVIR scoring system.[13] INR was computed by the formula [INR ÷ Platelet Count ($\times 10^9$/L)] × 100, According To Previously Published Methods.[11] Ultrasonographic Criteria Were Used to Verify Further the Diagnosis of Compensated Cirrhosis, With Three Or More Predefined Sonographic Features Supporting The Diagnosis Of Cirrhosis. The Principal Outcome Was The Assessment Of Advanced Fibrosis (>F3), Determined Using The Metavir Scoring System. Endoscopic Follow-Up Was Also Performed To Document The Presence Or Absence Of Esophageal Varices. All Study Procedures Were Conducted In Accordance With The Ethical Principles Of The Declaration Of Helsinki. Participant Confidentiality And Privacy Were Strictly Maintained Throughout The Data Collection Process. The Institutional Review Board Approved the Study Before It Began. Before enrollment, We Obtained Written Informed Consent from All Participants After They Were Fully Informed About the Study's Aim And Procedures. We statistically analyzed the data using SPSS Version 25.0. Univariate And Multivariate Logistic Regression Models Were Undertaken To Assess The Relationship Between Diagnostic Parameters And Advanced Hepatic Fibrosis. Optimal Threshold Values Were Determined To Maximize The Ability Of These Non-Invasive Indices To Distinguish Patients According To The Advanced Stages Of Liver Fibrosis. This Comprehensive Approach, Encompassing Data Collection, Ethical Conduct, and Statistical Analysis, Enhanced the Capability and Validity of the Findings, Providing Meaningful Evidence on the Non-Invasive Evaluation of Liver Fibrosis in Patients with Chronic Hepatitis C Infection.

Results

This Control-Case Study Will Comprise A Total Of 96 Patients Suffering From Chronic Hepatitis C. The Mean Age of All Positive Cases of Hepatitis C Virus Was 48.5 Years, Comprising 64.5 Percent Males And 35.5 Percent Females. Mean Hemoglobin Was 11.2 G/dL, with a Total Leucocyte Count and Mean Platelet Count of 4.8 x 10^9/L and 70 x 10^9/L, Respectively. Mean Value Of Inr Was Found To Be 1.2 With The Total Bilirubin And Alp Being 1.5 Mg/Dl And 171 Iu/L Respectively. The Study Participants' Liver Enzyme Levels, Including Aspartate Transaminase (Ast) And Alanine Transaminase (Alt), Averaged 50.7 Iu/L And 42.5iu/L, Respectively, With Gamma Glutamyl Transpeptidase (Ggt) At 69.4 Iu/L. The Child-Pugh score classified 62% of participants in Class A and 38% in Class B, Indicating Varying Degrees Of Liver Function Within The Study. The Meld Score Averaged 11.2, And Shear Wave Elastography (Swe) Results Showed That 42% Of Participants Had F4 Fibrosis. We observed significant differences in multiple clinical and laboratory parameters when comparing participants with fibrosis ≤F2 with those with Advanced Fibrosis (≥F3). Comparison Of Participants With No Or Mild-To-Moderate Fibrosis (≤F2) And Those With Advanced Fibrosis (≥F3) Demonstrated Significant Differences In Several Key Parameters. Age, Total Leukocyte Count, Platelet Count, Inr, Total Bilirubin, Ast, Alt, And Ggt Showed Statistically Significant Variation Between The Groups. The advanced fibrosis group had higher mean INR, Total Bilirubin, AST, and ALT Levels, Consistent With Increasing Hepatic Injury And Functional Impairment. (Table 2). Participants with Advanced Fibrosis Had Markedly Elevated Gpr and Inpr Values, With Mean Levels Of 1.76 and 2.4, respectively, compared with 0.58 and 1.3 among participants with no fibrosis. The Observed Differences Suggest That Both Ratios May Have Value in Evaluating the Extent of Liver Fibrosis. (Table 2).

Table 1. Baseline Characteristics of Study Participants

Characteristics	Mean ± SD or n (%)
Age (years)	50.0 ± 15.6
Aspartate transaminase (AST) (IU/L)	57.7 ± 34.2
Alanine transaminase (ALT) (IU/L)	42.2 ± 17.6
Alkaline phosphatase (IU/L)	171.0 ± 153.0
Hemoglobin (g/dL)	11.2 ± 1.2
Gamma-glutamyl transferase (GGT) (IU/L)	72.0 ± 51.3
Total leukocyte count (10⁹/L)	4.8 ± 3.4
Platelet count (10⁹/L)	70.0 ± 35.0
Total bilirubin (mg/dL)	1.5 ± 3.2
International normalized ratio (INR)	1.2 ± 0.6
Child-Turcotte-Pugh score	
A	62%
B	38%
MELD score	11.2 ± 4.0
Shear wave elastography (SWE)	
F1 fibrosis	13 (13%)
F2 fibrosis	27 (28%)
F3 fibrosis	13 (14%)
F4 fibrosis	43 (45%)
Esophageal varices	71.2%
Fibrosis on liver biopsy	63.4%
GGT-to-platelet ratio (GPR)	0.69 ± 1.20
INR-to-platelet ratio (INPR)	1.7 ± 1.3

Values are presented as mean ± standard deviation (SD) or frequency (n) and percentage (%). AST, aspartate transaminase; ALT, alanine transaminase; GGT, gamma-glutamyl transferase; INR, international normalized ratio; MELD, Model for End-Stage Liver Disease; SWE, shear wave elastography; GPR, GGT-to-platelet ratio; INPR, INR-to-platelet ratio.

Table 2. Comparison of Study Parameters Between Patients Without Fibrosis (≤F2) and Those With Advanced Fibrosis (≥F3)

Parameters	No Fibrosis (≤F2) (n=40)	Advanced Fibrosis (≥F3) (n=56)	p-value
Age (years)	48.5 ± 6.5	52.0 ± 7.0	<0.01
Aspartate transaminase (AST) (IU/L)	42.62 ± 8.5	48.3 ± 16.02	0.001
Alanine transaminase (ALT) (IU/L)	38.65 ± 17.0	47.9 ± 17.05	≤0.001
Gamma-glutamyl transferase (GGT) (IU/L)	49 ± 16	101 ± 81	≤0.001
Total bilirubin (mg/dL)	0.96 ± 0.4	2.47 ± 1.8	≤0.001
Albumin (g/dL)	4.51 ± 0.5	2.76 ± 0.64	0.020
Hemoglobin (g/dL)	12.4 ± 4.3	9.32 ± 0.83	0.35
Platelet count (10⁹/L)	84.7 ± 44.2	57.35 ± 34.4	0.01
Total leukocyte count (10⁹/L)	5.14 ± 2.2	4.92 ± 3.92	0.025
INR	1.1 ± 0.12	1.4 ± 0.16	≤0.001
Creatinine (mg/dL)	0.9 ± 0.2	1.19 ± 0.25	0.30
Splenic stiffness	29.2 ± 13.4	56.1 ± 22.8	0.017
MELD score	9.7 ± 3.0	11.4 ± 3.2	0.054
GPR	0.58 ± 0.35	1.76 ± 1.7	≤0.001
INPR	1.3 ± 0.7	2.4 ± 1.5	≤0.001

Values are presented as mean ± standard deviation (SD). INR, international normalized ratio; MELD, Model for End-Stage Liver Disease; GPR, gamma-glutamyl transferase-to-platelet ratio; INPR, INR-to-platelet ratio. We considered p <0.05 statistically significant.

Table 3. Diagnostic Accuracy of the INR-to-Platelet Ratio (INPR) and GGT-to-Platelet Ratio (GPR)

Variable	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Diagnostic Accuracy
INPR	84.0%	74.0%	82.5%	76.9%	80.2%
GPR	78.0%	66.7%	77.2%	69.2%	74.0%

Diagnostic performance is expressed as sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy. INPR, INR-to-platelet ratio; GPR, gamma-glutamyl transferase-to-platelet ratio.

Discussion

In Hepatological Practice, Managing Chronic Hepatitis C (HCV) Remains a Significant Clinical Challenge, Underscoring the Need for Ongoing Monitoring to Prevent Complications Related to the Progression of Hepatic Fibrosis. Liver Biopsy Remains The Traditionally

Considered Standard For The Assessment And Staging Of Hepatic Fibrosis; However, Its Invasive Procedure And Potential Complications Limit Its Routine Clinical Application.[14] Consequently, These Limitations Have Driven The Research Been Directed Toward Development Of Non-Invasive Methods That Can Accurately Identify And Stage Advanced Liver Fibrosis. Radiological modalities such as transient elastography, Shear Wave Elastography, and magnetic resonance elastography have shown promising diagnostic accuracy for detecting advanced fibrosis.[4-6] However, their clinical applicability is often limited by high cost, reliance on specialized expertise for interpretation, and Limited Access, Particularly In Resource-Limited Settings. Non-invasive serum indices, including APRI, Fib-4, and GPR, Have Been Widely Investigated For Predicting Liver Fibrosis, with Varying Diagnostic Accuracy.[15-17] Although Non-Invasive, The Diagnostic Accuracy Of These Markers For Evaluating Complex Fibrosis Has Varied Considerably Among Studies, Limiting Their Clinical Application.[18] Previous findings by Liang et al. Identified INR and platelet count as important prognostic markers in chronic HBV infection, Suggesting Their Effectiveness In Predicting Cirrhosis.[19] The Findings Of Kayadibi Et Al. Further highlighted the diagnostic significance of platelet counts for detecting fibrosis as an important biochemical marker in patients with HCV infection.[20] Ding Et Al. Highlighted The Potential Utility Of The Inr-To-Platelet Ratio In Assessing The Diagnostic Accuracy Of Hepatic Fibrosis Among Individuals With Chronic Hbv Infection.[11] This Study Assessed The Potential Role Of The Inr-To-Platelet Ratio For Fibrosis Evaluation In A Pakistani cohort with chronic HCV, Which Represents An Important Cause Of Cirrhosis Locally. The Findings Revealed Significantly Elevated Splenic Tissue Stiffness, INR, and INPR levels in patients with advanced fibrosis. In contrast, Albumin And Platelet Counts Were Significantly Lower, corroborating observations in chronic HBV infection (Ding et al.). These comparable findings suggest that the INR-to-platelet ratio may apply broadly across different viral etiologies of liver disease. Nevertheless, although the ratio shows good discriminative ability based on AUROC, its suboptimal specificity is an Important Limitation, Similar to that seen with Other Non-Invasive Fibrosis Markers. Previous comparative evidence has indicated the superior diagnostic accuracy of GPR over conventional non-invasive indices, including APRI, For The Detection Of Liver Fibrosis In Chinese Patients With Chronic Hepatitis B Infection. Khan Rty Et Al. supported 21,22. Similar Findings. In A Pakistani Cohort, providing evidence for the usefulness of GPR in identifying advanced fibrosis associated with chronic HCV infection.[23] Our findings contribute further evidence strengthening the diagnostic accuracy of the INR-to-platelet ratio; however, Its Diagnostic Specificity Remained Suboptimal, paralleling the performance of GPR. Despite These Findings, Several Limitations Should Be Acknowledged. The Design May Be Subject to Selection Bias, and Findings from a Single, Specific Cohort May Not Readily Generalize to the Broader Population. Moreover, The Relatively Small Sample Size Limits The Robustness And External Validity Of The Results. Accordingly, well-designed multicenter prospective studies with larger, more diverse cohorts are needed to establish the reliability and clinical applicability of the INR-to-platelet ratio. Another Limitation Is The Absence Of A Comparative Analysis Between The Inr-To-Platelet Ratio And Widely Validated Non-Invasive Indices Such As Apri And Fib-4. Including These Comparisons Would Have Facilitated A More Comprehensive Assessment Of Its Relative Diagnostic Performance Within The Broader Framework Of Liver Fibrosis Evaluation.

Conclusion

The INR-to-platelet ratio (INPR) showed potential as a practical, easily derived marker for the non-invasive assessment of advanced liver fibrosis in chronic HCV infection. However, broader clinical acceptance requires confirmation through well-designed prospective studies with larger, more diverse patient populations.

Ethical Approval

Ethical approval for this study was obtained from the Institutional Review Board/Ethics Committee prior to commencement. Written informed consent was obtained from all participants, and confidentiality was maintained throughout.

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Conflict of Interest

The authors declare that they have no competing interests or conflicts of interest related to this study.

Authors' Contributions

Hina Ehsan: Conceptualization, study design, supervision, data interpretation, manuscript drafting, critical revision, final approval, and accountability for all aspects of the work.

Romana Mehwish: Methodology, data collection, data curation, statistical analysis, data interpretation, manuscript drafting and revision, final approval, and accountability for all aspects of the work.

Durre Sadaf Khan: Study supervision, methodology, interpretation of findings, critical review of the manuscript, final approval, and accountability for all aspects of the work.

Yousra Abdur Razzaq: Data collection, literature review, data curation, manuscript revision, final approval, and accountability for all aspects of the work.

Fatima Hafeez: Data analysis, literature review, manuscript drafting and revision, interpretation of findings, final approval, and accountability for all aspects of the work.

Shahid Hameed: Study supervision, critical review of the manuscript, interpretation of findings, final approval, and accountability for all aspects of the work.

All authors: Reviewed and approved the final version of the manuscript and agreed to be accountable for all aspects of the work in accordance with ICMJE authorship criteria.

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Original Article

Effect of Bile Spillage during Laparoscopic Cholecystectomy on Post-Operative Infection

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Abstract

Objective: To determine the effects of bile spillage during laparoscopic cholecystectomy on post-operative infection.

Methodology: This Case-Control Study was conducted in the Department of General Surgery, Aziz Bhatti Shaheed Teaching Hospital, Gujrat, from January 2026 to March 2026. A total of 120 individuals undergoing laparoscopic cholecystectomy were included in this study. Participants were equally divided into two groups: Group A, comprising patients who experienced bile spillage during laparoscopic cholecystectomy, and Group B, comprising patients without bile spillage. Standard laparoscopic techniques were used for cholecystectomy. We assessed postoperative pain using the Numerical Rating Scale (NRS). We analyzed data using SPSS version 23.0.

Results: Among 120 patients, 60 experienced bile spillage and 60 did not. Mean age was comparable (41.3 vs. 40.2 years). Postoperative pain was greater initially with spillage but was not significantly different after 24 hours. Analgesic requirements were higher (59% vs. 34%), and hospital stay was longer, while postoperative fever and surgical-site infection showed no significant differences.

Conclusion: Our study concluded that Intraoperative bile spillage after laparoscopic cholecystectomy may increase rescue analgesic doses, a longer hospital stays, delayed ambulation, and increased early postoperative pain.

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Introduction

Cholelithiasis is the most common disease of the gallbladder and biliary tree. Gallstones form when the gallbladder concentrates bile, increasing solute concentration and causing stasis between meals. The prevalence of this disease among the adult population is 10-15%.1 Cholecystectomy is a common procedure performed by general surgeons, with a symptomatic rate of 1% - 4% per year [1]. Chronic cholecystitis is an ongoing or recurring inflammation of the gallbladder. Gallstones are the primary cause of cystic duct blockage in over 90% of patients, resulting in biliary discomfort or colic [2]. Laparoscopic cholecystectomy is the preferred treatment for symptomatic cholelithiasis [3]. Gallbladder perforation can occur during intraoperative retraction, dissection, and extraction, particularly if the gallbladder is inflamed and vulnerable, with perigallbladder omental adhesions [4].The rise in laparoscopic surgeries has led to an increase in problems, including bile spillage into the peritoneal cavity, which can cause both acute and long- term issues[5]. Laparoscopic cholecystectomy (LC) has become a popular technique in general surgical departments. Symptomatic gallstone disease is the most prevalent reason for LC, and almost 90% of cholecystectomies are currently performed laparoscopically [6,7]. Minor problems (both biliary and non- biliary) are often managed conservatively. Converting to an open surgical technique is necessary to manage major problems (biliary and vascular), which can be life- threatening and increase mortality. Laparoscopic cholecystectomy complications range from 0. 0.5 - 6% [8,9]. The most serious effects are linked to a high mortality rate: injury to the common bile duct (0. 0.1-0. 0.6%), injuries to major blood vessels. Depending on the study, the percentage ranged from 0.04 to 1.22%[10,11]. Gallbladder contents may be drained during open or laparoscopic cholecystectomy, but are typically removed by direct removal, extensive irrigation, and mopping during open surgeries. This study aimed to determine the effect of bile spillage during laparoscopic cholecystectomy on postoperative infection.

Materials and Method

This case-control study was conducted in the Department of General Surgery at Aziz Bhatti Shaheed Teaching Hospital, Gujrat, from January 2026 to March 2026, after approval from the hospital's ethics committee. A total of 120 individuals of both genders and different age groups (ranging from 15–80 years) undergoing laparoscopic cholecystectomy were included in this study, while individuals undergoing open cholecystectomy, obstructive jaundice, and pancreatitis were excluded. We obtained written consent from each participant and randomly assigned them to group A or group B. Group A (60 participants) had bile spillage, and group B (control group) had no bile spillage during laparoscopic cholecystectomy. Standard laparoscopic techniques were used for cholecystectomy. Bile spillage into the peritoneal cavity due to gallbladder perforation was documented as intraoperative bile spillage. Participants were subsequently classified according to whether bile spillage occurred. Postoperative pain was measured using the Numerical Rating Scale (NRS), 0- 10, where 0 indicates no pain, 1- 3 indicates mild pain, 4–6 indicates moderate pain, and 7–10 indicates severe pain. We evaluated pain at predefined postoperative intervals. The study documented the need for rescue analgesia throughout the postoperative phase and identified diclofenac use as a significant outcome. We analyzed data using SPSS version 23. We expressed continuous variables as mean ± standard deviation and categorical variables as frequencies and percentages. We used the independent-samples t-test to compare normally distributed continuous variables, and the chi-square test for categorical data. We considered $p < 0.05$ statistically significant.

Results

A total of 120 individuals were randomly assigned to two equal groups: Group A (60 individuals) had an episode of bile spillage, and Group B (control group) had no bile spillage. The mean age in the bile-spillage group was 41.3 years, and in the non-spillage group, 40.2 years, with no statistically significant difference. The most significant finding was operative time. Patients who experienced bile spillage had a considerably longer mean operative time (97.3 vs. 90.6 minutes; p=0.01), as presented in Table 1. After surgery, mean pain scores were similar between the two groups; however, during the intermediate postoperative period, the bile-spillage group had more pronounced pain. In the spillage group, the mean NRS at 6 hours was 3.6 ± 1.8, and in the non-spillage group it was 2.7 ± 1.4 (p=0.004). Similarly, the mean NRS at 12 hours was 3.1 ± 1.6, compared with 2.3 ± 1.3 (p=0.007). The difference was no longer statistically significant after 24 hours, as shown in Table 2. In the spillage group, analgesic requirement was also significantly higher than in the control group (59% versus 34%). Individuals with bile spillage had a longer hospital stay, but postoperative fever and surgical-site infection did not differ significantly between the two groups, as shown in Table 3.

Table 1. Demographic and operative features of the study population

Variable	Bile spillage (n=60)	No spillage (n=60)	p-value
Mean age in years	41.3 ± 10.7	40.2 ± 9.8	0.55
Male	24 (40.0%)	22 (36.7%)	0.71
Female	36 (60.0%)	38 (63.3%)	
Mean Weight in kg	76.8 ± 10.9	77.6 ± 10.2	0.68
Mean Operative time in minutes	97.3 ± 15.1	90.6 ± 13.8	**0.01**
Acute cholecystitis	18 (30.0%)	12 (20.0%)	0.20
Chronic cholecystitis	42 (70.0%)	48 (80.0%)	
Conversion to open surgery	2 (3.3%)	1 (1.7%)	0.56

Continuous variables are presented as mean ± standard deviation, and categorical variables as frequency (n) and percentage (%).

Table 2. Pain score after surgery based on NRS

Postoperative time	Bile spillage (n=60) Mean ± SD	No spillage (n=60) Mean ± SD	p-value
0 hour	0.8 ± 0.8	0.7 ± 0.7	0.48
2 hours	1.8 ± 1.3	1.4 ± 1.1	0.07
6 hours	3.6 ± 1.7	2.7 ± 1.4	**0.004**
12 hours	3.1 ± 1.6	2.3 ± 1.3	**0.006**
18 hours	2.1 ± 1.3	1.7 ± 1.2	0.08
24 hours	1.4 ± 1.1	1.3 ± 1.0	0.29

We assessed pain intensity using the Numerical Rating Scale (NRS). Values are presented as mean ± standard deviation (SD).

Table 3. Rescue analgesia and early postoperative recovery

Outcome	Bile spillage (n=60)	No spillage (n=60)	p-value
Patients requiring rescue analgesia	35 (59.0%)	20 (34.0%)	**0.007**
Mean rescue diclofenac requirement, mg	3.13 ± 1.47	2.32 ± 1.29	**0.003**
Mean Postoperative hospital stay in days	2.4 ± 0.7	1.10 ± 0.5	**0.004**
Time to ambulation in hours	8.5 ± 2.2	6.8 ± 1.9	**<0.001**
Fever after surgical procedure	4 (7.0%)	2 (4.0%)	0.41
Surgical-site infection	3 (5.00%)	1 (1.70%)	0.32

Continuous variables are presented as mean ± standard deviation (SD), and categorical variables as frequency (n) and percentage (%). We considered $p < 0.05$ statistically significant.

Discussion

Laparoscopic cholecystectomy (LC) is the primary surgical therapy for symptomatic cholelithiasis as well as other benign gallbladder disorders[11]. Surgical site infection (SSI) is still a major postoperative consequence linked to increased morbidity, longer hospital stays, and greater healthcare expenditures despite its least invasive technique[12]. Bile spillage is a common intraoperative occurrence; however, its clinical importance is still debatable. An intraoperative rupture of the gallbladder wall is called a gallbladder perforation, and it usually happens after dissection from the liver bed or severe traction[14]. Bile spillage refers to bile that leaks into the peritoneal cavity due to such a rupture[13]. Despite their close relationship, the two terms are not interchangeable: bile leakage is the biological result of the mechanical event, whereas perforation denotes the mechanical event. Depending on whether calculi migrate into the peritoneal cavity, perforation may result in bile-only spillage or mixed bile and gallstone spillage[15]. This research identified bile leakage as the main exposure of relevance. When data were available, studies were further classified by spillage type (bile alone versus bile with gallstones), as accumulating evidence shows that gallstone spillage may confer a higher risk than bile alone[16]. This study assessed the effect of bile spillage during laparoscopic cholecystectomy on postoperative infection. A total of 120 individuals were randomly assigned to two equal groups: Group A (60 individuals) had bile spillage, and Group B (control group) had no bile spillage[17]. The mean age of the bile-spillage group was 41.3 years, whereas the non-spillage group was 40.2 years, with no statistically significant difference. The most significant finding was the duration of the operation. Patients who experienced bile spillage had a considerably longer mean operative time. A similar pattern of demographic features was reported in the study by Ranjan et al., which supports our findings [16]. After surgery, the mean pain score was similar between the two groups; however, during the intermediate postoperative period, the bile-spillage group had more pronounced pain. This aligns with the type of complication, since perforation may require additional suction, drainage, retrieval of spilled stones, and careful evaluation of the operating field. A comprehensive study and meta-analysis found that iatrogenic gallbladder perforation was associated with about a 10-minute increase in operation time [17]. Bile spillage may therefore indicate a more challenging procedure. Postoperative pain from laparoscopic cholecystectomy is complex. Pneumoperitoneum, diaphragmatic discomfort, surgical manipulation, and local inflammation might all contribute. Studies have shown that changes in pneumoperitoneum pressure may affect postoperative shoulder-tip pain[18].In the spillage group, analgesic requirement was also significantly higher than in the control group (59% versus 34%), and a lengthy hospital stay was reported in individuals with bile spillage in our study. These findings are comparable to the previous study[18].In contrast, a subsequent meta-analysis and systematic review of 11 trials comprising 51,642 patients

found a slight but significant link between intraoperative bile spillage and SSI, as well as increased overall postoperative morbidity[19]. This variation may reflect changes in how bile leakage, gallstone spillage, bacterial contamination, surgical difficulties, antibiotic use, and postoperative monitoring are defined. Our study highlights the need to handle the gallbladder carefully during dissection. If a perforation develops, bile should be aspirated immediately. Spilled gallstones should be removed wherever possible. The operating field should be thoroughly irrigated and examined. The presence of gallbladder perforation must be documented in the operating notes. The occurrence should be communicated to the patient if clinically appropriate.

Conclusion

Our study concluded that intraoperative bile spillage after laparoscopic cholecystectomy may lead to higher rescue analgesic doses, a longer hospital stay, delayed ambulation, and increased early postoperative pain. Therefore, careful surgical technique, prompt suction of spilled bile, stone removal, and adequate irrigation can all help prevent postoperative morbidity.

Ethical Approval

The Ethical Committee of Aziz Bhatti Shaheed Teaching Hospital, Gujrat, approved this study before it began (approval no. 1244/04/2025). We obtained written informed consent from all participants and maintained confidentiality.

Funding

This study received no external funding. The research used available institutional resources.

Conflict of Interest

The authors declare that they have no competing interests or conflicts of interest related to this study.

Authors' Contributions

Muhammad Asjad: Conceptualization, study design, supervision, data interpretation, manuscript drafting, critical revision, final approval, and accountability for all aspects of the work.

Muhammad Rehman Gulzar: Methodology, study supervision, data interpretation, critical review of the manuscript, final approval, and accountability for all aspects of the work.

Nouman Ali: Data collection, data curation, literature review, manuscript drafting and revision, final approval, and accountability for all aspects of the work.

Muhammad Usman Badar: Methodology, data collection, data analysis, interpretation of findings, manuscript revision, final approval, and accountability for all aspects of the work.

Mamoon Ali: Data collection, literature review, data curation, manuscript revision, final approval, and accountability for all aspects of the work.

Haider Sattar: Data analysis, interpretation of findings, critical review of the manuscript, final approval, and accountability for all aspects of the work.

All authors: Reviewed and approved the final version of the manuscript and agreed to be accountable for all aspects of the work in accordance with ICMJE authorship criteria.

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Original Article

Local versus Systemic Analgesia in Pain Management of Post-Laparoscopic Cholecystectomy Patients

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Abstract

Objective: To compare the efficacy of Toradol and a combination of bupivacaine with Toradol for postoperative analgesia in patients who underwent laparoscopic cholecystectomy.

Methodology: This interventional study was conducted in the Department of Surgery, KMU-IMS, DHQ Teaching KDA Kohat, from June 2024 to Dec 2024. Two hundred and twenty-four patients who underwent laparoscopic cholecystectomy were divided into group T (received injection Toradol 0.5mg/kg I/V) and group TB (received 30ml of 0.25% injection bupivacaine intraperitoneally along with intravenous 0.5mg/kg injection Toradol). We recorded pain using VAS at 1, 2, and 4 hours postoperatively. Rescue analgesia was given in patients with a VAS score > 3 who were uncomfortable with pain. We used the chi-square test to compare effectiveness between the two groups.

Results: Mean ages were 37.41±3.09 years and 38.96±2.64 years in group T and Group TB, respectively. Mean VAS was 4.47±1.36 and 1.38±0.56 in group T and group TB, respectively. Rescue analgesia was given to 23.21% of patients in group T and 0.0% in group TB (p-value=0.0003). Toradol injection was effective in 76.78% of patients, while the combination of Toradol and bupivacaine was effective in 100.0% of patients (p-value=0.0001).

Conclusions: The efficacy of Toradol with bupivacaine was high as compared to Toradol alone for postoperative pain control after laparoscopic cholecystectomy.

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Introduction

Laparoscopic cholecystectomy is one of the most frequently performed elective general surgical operations. It is an ideal candidate for a day-case or short-stay procedure; therefore, adequate postoperative pain relief is of considerable importance[1]. Laparoscopic cholecystectomy (LC) is the gold standard and the most commonly performed operation in the department of general surgery in hospitals. Although there are clear benefits compared with open surgery, postoperative pain after laparoscopic cholecystectomy remains an issue. Pain can prolong hospital stay and lead to increased morbidity, which is particularly important now that many centers are performing this operation as a day-case procedure. This results in a shorter hospital stay and an earlier return to regular activity[2,3]. Local anesthetics (LA) are increasingly used intraoperatively to prevent postoperative pain. The efficacy of local anesthetic infiltration into incision sites has only been shown in patients undergoing inguinal herniorrhaphy[4]. However, one meta-analysis has shown intraperitoneal LA to be effective for pain relief following laparoscopic cholecystectomy (LC). Instillation of local anesthetics intraperitoneally (IP) around the operative site is used as an analgesic technique on the assumption that conduction from visceral sites is obstructed and may lessen the intensity of referred pain to the shoulder (C3, C4), which results from irritation of diaphragmatic innervations, i.e., phrenic nerve (C3, C4, C5) and diaphragmatic stretching due to gaseous distension, in the postoperative period[5]. Intraperitoneal administration of local anesthesia is often used to improve pain relief after laparoscopic cholecystectomy. As early as 1980, it was reported that instillation of local anesthetic (980 ml of bupivacaine 0.125%, epinephrine 1:200,000) under the right diaphragm reduced shoulder pain after minor gynecological laparoscopy. Following this, various studies were conducted to study the efficacy of intraperitoneal analgesics for postoperative pain relief after laparoscopic cholecystectomy[6,7]. Administration of non-steroidal anti-inflammatory drugs (NSAIDs), intraperitoneal local anesthetics, and opioids is carried out to reduce pain after laparoscopic cholecystectomy[8,9].To provide local statistics and suggest better treatment options, we conducted this study to evaluate intravenous Toradol (Ketorolac) alone versus intravenous Toradol plus intraperitoneal (IP) bupivacaine for postoperative pain relief in patients undergoing laparoscopic cholecystectomy[10].

Materials and methods

The Department of Surgery, KMU-IMS, DHQ Teaching, KDA, Kohat, conducted this interventional study from June 2024 to Dec 2024.

Sample size by WHO calculator

Level of significance: 5% Power of study: 80% P1 (proportion of rescue analgesia requirement in Toradol group): 00%10P2 (proportion of rescue analgesia requirement in bupivacaine plus Toradol group): 26%10

Sample size

224 patients (112 patients in each group)

Sample technique

Non-probability consecutive sampling

Inclusion criteria

- Gender: both
- Age: 20 - 60 years
- ASA I & II underwent laparoscopic cholecystectomy

Exclusion criteria

Patients with previous history of respiratory disease, e.g., chronic obstructive airway disease and asthma; patients with ischemic heart disease; patients with known history of gastro-esophageal reflux syndrome taking pre-operatively anti-inflammatory and analgesic drugs; and patients with allergy or sensitivity to bupivacaine and tramadol

Data Collection

All patients who met the inclusion criteria and were selected for laparoscopic cholecystectomy were included in this study. The institution's ethics committee approved this study. We obtained written consent from patients to be included in the study. We coded all data by study ID number for analysis, with the study coordinator as the only person with access to patient names and chart numbers. Patients were divided into two groups (group T and group TB) by lottery. Group T received intravenous 0.5mg/kg Toradol (ketorolac), and group TB received 30 mL of 0.25% bupivacaine injection intraperitoneally, along with intravenous 0.5mg/kg Toradol (ketorolac). The local anesthetic/ analgesic solution was sprayed on the upper surface of the liver and on the right subdiaphragmatic space and over the gallbladder bed. This was done using a size 14 infant feeding tube inserted through the subcostal trocar, guided by an instrument through the epigastric port, under direct laparoscopic control, in the supine position at the end of surgery. All patients were given standard premedication as advised in the pre-anesthetic checkup. General anesthesia was induced. Intra-abdominal pressure was maintained at 10-12mmHg—10ml of 0.25% inj. Bupivacaine was given to all patients at the port sites for parietal (somatic) pain to assess visceral pain better. Study drugs were instilled 15 minutes before the end of surgery, according to the group allocation by the surgeons (among the researchers). All patients were transferred to the post-anesthesia care unit for two hours after surgery. Visual analog scale (VAS) score was recorded by surgeons, not part of the operating team of that particular patient, and hence was blinded as to which drug was being assessed. Pain intensity was recorded for all patients using VAS at 1, 2, and 4 hours after surgery. Rescue analgesia with inj. Nalbuphine 10mg IV stat was given to patients with a VAS score > 3 and who were uncomfortable with pain. All information was collected by a predesigned proforma.

Data Analysis

Data from both groups were collected independently and entered into SPSS version 24. For age, weight, length of operation, and VAS score, we calculated the mean and standard deviation. We calculated frequencies and percentages for gender, ASA status, rescue analgesia, and efficacy. We compared the two groups using the chi-square test.

Results

This study included 224 patients.In Group T, the mean age of the patients who received intravenous 0.5mg/Kg injection of Toradol (Ketorolac) for postoperative analgesia after laparoscopic cholecystectomy was 37.41 ± 3.09 years. Out of 112 patients who underwent laparoscopic cholecystectomy, there were 11 (9.82%) patients in the age range of 20 – 30 years, 58 (51.78%) patients in the age range of 31 – 40 years, 29 (25.89%) patients in the age range of 41 – 50 years, and 14 (12.5%) patients in the age range of 51 – 60 years. (Table 1) In Group TB, the mean age of patients who received 30ml of 0.25% bupivacaine injection intraperitoneally along with intravenous 0.5mg/kg Toradol (Ketorolac) for postoperative analgesia after laparoscopic cholecystectomy was 38.96 ± 2.64 years. Out of 112 patients who underwent laparoscopic cholecystectomy, there were 3 (2.67%) patients in the age range of 20 – 30 years, 71 (63.39%) patients in the age range of 31 – 40 years, 31 (27.67%) patients in the age range of 41 – 50 years, and 7 (6.25%) patients in the age range of 51 – 60 years. (Table 1) In Group T, there were 29 (25.89%) male and 83 (74.10%) female patients who received intravenous 0.5mg/Kg injection of Toradol (Ketorolac) for postoperative analgesia after laparoscopic cholecystectomy. The male-to-female ratio was 1:2.8 (Table 1). In Group TB, 12 (10.71%) male and 100 (89.28%) female patients received 30ml of 0.25% bupivacaine injection intraperitoneally, along with intravenous 0.5mg/kg Toradol (Ketorolac), for postoperative analgesia after laparoscopic cholecystectomy. The male-to-female ratio was 1:8.3, and the p-value was 0.873. (Table 1) In Group T, the mean weight of patients who received intravenous Toradol (Ketorolac) 0.5 mg/kg for postoperative analgesia after laparoscopic cholecystectomy was 84.01 ± 4.83 Kg. Out of 112 patients who underwent laparoscopic cholecystectomy, there were 2 (1.78%) patients of weight ≤ 50 Kg, 109 (97.32%) patients of weight 51-100 kg, and 1 (0.89%) patient of weight >100 Kg. (Table 1)In Group TB, the mean Weight of patients who received 30ml of 0.25% bupivacaine injection intraperitoneally along with intravenous 0.5mg/kg Toradol (Ketorolac) for postoperative analgesia after laparoscopic cholecystectomy was 81.91 ± 2.02 Kg. Of the 112 patients who underwent laparoscopic cholecystectomy, 5 (4.46%) weighed ≤ 50 Kg, 105 (95.62%) weighed 51-100 kg, and 2 (1.78%) weighed> 100 kg. (Table 1) In Group T, the mean surgical duration for patients who received intravenous 0.5mg/kg Toradol (Ketorolac) for postoperative analgesia after laparoscopic cholecystectomy was 96.01 ± 29.46 min. Of the 112 patients who underwent laparoscopic cholecystectomy, surgery lasted ≤ 60 minutes in 43 (38.39%) patients and> 60 minutes in 69 (61.60%) patients. (Table 1) In Group TB, the mean duration of surgery for patients who received 30ml of 0.25% bupivacaine injection intraperitoneally along with intravenous 0.5mg/kg Toradol (Ketorolac) for postoperative analgesia after laparoscopic cholecystectomy was 108.01 ± 27.09 min. Of the 112 patients who underwent laparoscopic cholecystectomy, surgery lasted ≤ 60 minutes in 23 (20.53%) patients and> 60 minutes in 89 (79.46%) patients. (Table 1) In Group T, of the 112 patients who received intravenous 0.5mg/kg Toradol (Ketorolac) for postoperative analgesia after laparoscopic cholecystectomy, 73 (65.17%) had ASA score I and 39 (34.82%) had ASA score II. (Table 1) In Group TB, out of 112 patients who received 30ml of 0.25% bupivacaine injection intraperitoneally along with intravenous 0.5mg/Kg injection of Toradol (Ketorolac) for postoperative analgesia after laparoscopic cholecystectomy, there were 61 (54.46%) patients with ASA score I and 51 (45.53%) patients with ASA score II. The p-value was 0.531. (Table 1) In Group T, the Mean Visual Analog score of patients who received intravenous 0.5mg/kg Toradol (Ketorolac) for postoperative analgesia after laparoscopic cholecystectomy was 4.47 ± 1.36. Of the 112 patients who underwent laparoscopic cholecystectomy, the Mean Visual Analog score was 3.31 ± 1.46 at the 1st Hour postop, 6.02 ± 0.93 at the 2nd hour postop, and 4.58 ± 1.06 at the 4th hour postop. (Table 6) In Group TB, the Mean Visual Analog score of patients who received 30ml of 0.25% bupivacaine injection intraperitoneally along with intravenous 0.5mg/kg Toradol (Ketorolac) for postoperative analgesia after laparoscopic cholecystectomy was 1.38 ± 0.56. Of the 112 patients who underwent laparoscopic cholecystectomy, the Mean Visual Analog score was 2.01 ± 0.08 at the 1st Hour postop, 1.04 ± 0.13 at the 2nd hour postop, and 1.20 ± 0.94 at the 4th hour postop. (Table 2)In Group T, out of 112 patients who received intravenous 0.5mg/Kg injection Toradol (Ketorolac) for postoperative analgesia after laparoscopic cholecystectomy, there were 26 (23.21%) patients who required rescue analgesia for postoperative pain,. In contrast, in 86 (76.78%) patients, intravenous 0.5mg/Kg injection of Toradol (Ketorolac) effectively controlled postoperative pain. (Table 3) In Group TB, out of 112 patients who received 30ml of 0.25% bupivacaine injection intraperitoneally along with intravenous 0.5mg/Kg injection of Toradol (Ketorolac) for postoperative analgesia after laparoscopic cholecystectomy, none of the patients (0.0%) required rescue analgesia for postoperative pain. The p-value was 0.0003. (Table 4) In Group T, out of 112 patients who received intravenous 0.5mg/Kg injection Toradol (Ketorolac) for postoperative analgesia after laparoscopic cholecystectomy, in 86 (76.78%) patients intravenous 0.5mg/Kg injection Toradol (Ketorolac) was effective in controlling postoperative pain. In comparison, Toradol alone was not effective in 26 (23.21%) patients. (Table 7) In Group TB, of 112 patients who received 30ml of 0.25% bupivacaine injection intraperitoneally along with intravenous 0.5mg/kg Toradol (Ketorolac) for postoperative analgesia after laparoscopic cholecystectomy, the combination of Toradol and bupivacaine was effective in controlling postoperative pain in 112 (100.0%) patients. The p-value was 0.0001. (Table 8)

Table 1: Distribution of patients by using different parameters

Parameters	Sub category	Group T (n=112)		Group TB (n=112)		P value
Age in years		Frequency	%age	Frequency	%age	0.001
	20 – 30	11	9.82	3	2.67	
	31 – 40	58	51.78	71	63.39	
	41 – 50	29	25.89	31	27.67	
	51 – 60	14	12.5	7	6.25	

Gender	Male	29	25.89	12	10.71	0.873
	Female	83	74.10	100	89.28	
Weight (kg)	≤50	2	1.78	5	4.46	0.431
	51-100	109	97.32	105	95.62	
	>100	1	0.89	2	1.78	
Duration of surgery (min.)	≤60	43	38.39	23	20.53	0.231
	>60	69	61.60	89	79.46	
ASA Score	I	73	65.17	61	54.46	0.531
	II	39	34.82	51	45.53	

Values are presented as frequency (n) and percentage (%). A p-value <0.05 was considered statistically significant.

Table 2: Mean Visual Analogue score at 1st, 2nd & 4th hours postoperatively (n=224)

VAS Score	Group T (n=112)	Group TB (n=112)
At 1st Hour postop	3.31 ± 1.46	**2.01 ± 0.08**
At 2nd hour postop	6.02 ± 0.93	**1.04 ± 0.13**
At 4th hour postop	4.58 ± 1.06	**1.20 ± 0.94**
Mean ± SD	**4.47 ± 1.36**	**1.38 ± 0.56**

Values are presented as mean ± standard deviation (SD). VAS, Visual Analogue Scale.

Table 3: Distribution of patPatients by rescue analgesia

Rescue analgesia	Group T (n=112)		Group TB (n=112)	
	No. of patients	Percentage (%)	No. of patients	**Percentage** (%)
Yes	26	23.21	0	**0.0**
No	86	76.78	112	**100.0**
P-Value*	**0.0003****			

Values are presented as frequency (n) and percentage (%). A p-value <0.05 was considered statistically significant.

Table 4: Distribution of patients by effectiveness of analgesia

Effectiveness	Group T (n=112)		Group TB (n=112)	
	No. of patients	Percentage (%)	No. of patients	**Percentage** (%)
Yes	86	76.78	112	**100.0**
No	26	23.21	0	**0.0**
P-Value*	**0.0001****			

Values are presented as frequency (n) and percentage (%). We considered a p-value <0.05 statistically significant.

Discussion

In this prospective clinical study of 224 patients, we compared the efficacy of Toradol and a combination of bupivacaine with Toradol for postoperative analgesia in patients who underwent laparoscopic cholecystectomy[11]. The mean ages of the patients who underwent laparoscopic cholecystectomy were 37.41 ± 3.09 years and 38.96 ± 2.64 years in Group T and Group TB, respectively. The majority of patients, i.e., 51.78% and 63.39% in Group T and Group TB, respectively, in our study belonged to the middle age group, i.e., 31-40 years. In a study by Kashmiri ZA et al., the age ranges of patients who underwent laparoscopic cholecystectomy were 23–60 years and 24–65 years in Group A and Group B, respectively [12].The majority of patients who underwent laparoscopic cholecystectomy, i.e., 74.10% and 89.28% in Group T and Group B, respectively, in our study were females. However, the results were not statistically significant (p-value = 0.873). In a study by Kashmiri ZA et al., the male-to-female ratio was 6:34 and 8:32 in Group A and Group B, respectively [13].The mean weight of the patients who received laparoscopic cholecystectomy was 84.01 ± 4.83 Kg and 81.91 ± 2.02 Kg in Group T and Group TB, respectively. The majority of patients, i.e., 97.32% and 95.62% in Group T and Group TB, respectively, in our study belonged to the weight group of 51- 100 kg.The mean duration of surgery for patients who received laparoscopic cholecystectomy was 96.01 ± 29.46 min and 108.01 ± 27.09 min in Group T and Group TB, respectively. In our study, most patients (61.60% in Group T and 61.60% in Group TB) had prolonged surgery (>60 minutes). In a study by Kashmiri ZA10 et al., surgery lasted 35–90 minutes and 39–92 minutes in Group A and Group B, respectively. These findings align with other studies [14].Most patients (65.17% in Group T and 65.17% in Group B) had an ASA score of I. However, the results were not statistically significant (p-value = 0.531). These findings align with other studies [15]. In our study, the mean visual analog score for patients who received laparoscopic cholecystectomy was 4.47 ± 1.36 and 1.38 ± 0.56 in group T and TB, respectively. In our study, 23.21% of patients in group T required rescue analgesia for postoperative pain, while none (0.0%) in group TB required rescue analgesia for postoperative pain; the results were statistically significant (p-value = 0.0003) [16].In our study, intravenous Toradol (Ketorolac) 0.5 mg/kg for postoperative analgesia after laparoscopic cholecystectomy was effective in 76.78% of patients. At the same time, a combination of Toradol and bupivacaine was effective in 100.0% of patients in controlling postoperative pain. The results were statistically significant (p-value= 0.0001). In a Systematic Review and Meta- Analysis by Boddy AP et al., the use of intraperitoneal local anesthesia resulted in a significantly reduced pain score at 4 h (weighted mean difference, -9 mm; 95% confidence interval [CI], -13 to -5)[17]. Subgroup analysis suggested that the effect was greater when the local anesthetic was given at the start of the operation (WMD, -13 mm; 95% CI, -19 to -7) compared with instillation at the end (WMD, -6 mm; 95% CI, -10 to -2). In one study, VAS scores showed that group B patients who received a combination of bupivacaine and Toradol had lower scores than group A patients who received Toradol alone. However, the difference was not statistically significant (p>0.05). Rescue analgesic requirement was also significantly lower in group B than in group A (p<0.00)[18].We cross-tabulated the data (Effectiveness) by effect modifier (age). We found that the effectiveness of injection Toradol (Ketorolac) for postoperative analgesia after laparoscopic cholecystectomy was higher in young patients (20-20 years), at 90.90%, followed by middle-aged patients (41-50 years), at 82.75%.

The effectiveness of the bupivacaine and Toradol combination for postoperative analgesia after laparoscopic cholecystectomy was found to be 100.0% in all age groups. However, the results were statistically not significant (p-value>0.05)[19]. We also cross-tabulated the data (Effectiveness) by effect modifier (Gender). We found that the effectiveness of Toradol (Ketorolac) for postoperative analgesia after laparoscopic cholecystectomy was higher in female patients (77.10%) than in male patients (75.86%). The effectiveness of the bupivacaine and Toradol combination for postoperative analgesia after laparoscopic cholecystectomy was found to be 100.0% in both genders. However, the results were statistically not significant (p-value>0.05)[20].We cross-tabulated the data (Effectiveness) by effect modifier (Weight). We found that the effectiveness of Toradol (Ketorolac) injection for postoperative analgesia after laparoscopic cholecystectomy was higher (100.0%) in patients weighing less than 50 kg. The effectiveness of the bupivacaine and Toradol combination for postoperative analgesia after laparoscopic cholecystectomy was found to be 100.0% in all patients with different weight groups. However, the results were statistically not significant (p-value>0.05)[21].We also cross-tabulated effectiveness by effect modifier (Duration of surgery). We found that Toradol (Ketorolac) was more effective for postoperative analgesia after laparoscopic cholecystectomy in patients with a duration of surgery ≤60 minutes (91.30%). The effectiveness of the bupivacaine and Toradol combination for postoperative analgesia after laparoscopic cholecystectomy was found to be 100.0% in all patients with different operative times. However, the results were not statistically significant (p-value > 0.05). These findings align with previous studies that reported similar results.The study has several limitations. One center conducted the study. To make recommendations, more research is needed to examine the effectiveness of Toradol and a combination of bupivacaine and Toradol for postoperative analgesia in patients undergoing laparoscopic cholecystectomy.

Conclusion

The efficacy of bupivacaine with intravenous Toradol is high as compared to Toradol alone in postoperative pain control after laparoscopic cholecystectomy. So, it is recommended that a combination of Toradol with bupivacaine should be used during laparoscopic cholecystectomy to achieve better pain control after surgery.

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Original Article

Effect of Gabapentin on Opioid Requirements in Patients Undergoing Total Abdominal Hysterectomy

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Abstract

Objective: To find the effects of Gabapentin on Opioid requirement in patients undergoing total abdominal hysterectomy.

Methodology: This Experimental Study was conducted at MTI Khyber Teaching Hospital, Peshawar, from June 2025 to December 2025. We included 108 individuals admitted to KTH for hysterectomy. We divided participants equally into group A and group B. Two hours before surgery, group A received 1200 milligrams of gabapentin orally, and group B received oral placebo capsules. Before surgery, each subject was provided with a visual analog scale and trained to assess their pain level. Supplemental opioids (nalbuphine) required before and after surgery were recorded. We also recorded individual age and weight. Both groups were given the same anesthetic technique. All patients received general anesthesia. We used the VAS score (1–10) to assess pain at 02, 08, 16, and 24 hours after surgery. We analyzed the data using SPSS version 16.

Results: A total of 108 patients participated in this study. We divided participants equally (54 in each group) into group A and group B. Gabapentin significantly reduced postoperative pain and opioid requirements. VAS scores decreased from 5.88±1.36 to 0.94±0.72 at 24 hours, while nalbuphine use was 12.20±4.68 mg versus 23.30±9.27 mg in the control group.

Conclusion: The current study demonstrated that gabapentin significantly reduces both intraoperative and postoperative pain. Furthermore, it also reduces opioid needs in patients undergoing TAH.

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Introduction

Relief from pain after a surgical procedure can minimize the risk of psychiatric and neurotic issues, thereby encouraging patients to undergo necessary surgery. A phobia of pain can be a barrier to surgery, threatening patients' wellness and quality of life.1Furthermore, it can promote early ambulation for individuals[1]. Opiates are commonly used for pain relief after surgery, but their side effects such as breathing difficulties, vomiting, nausea, and intestinal ileus restrict their application. Alternative pain reducers, used separately or synergistically with opioids, can ease pain or minimize the need for them, minimizing the risk of undesirable outcomes[2]. Neuropathic pain has been treated with gabapentin, an antiepileptic and anticonvulsant drug. It is an analog of gamma-aminobutyric acid[2,3]. Several studies tested the pain-relieving effects of gabapentin using different routes of administration, dosages, and procedures, either alone or in combination with other analgesics, once or several times, before or after surgery. Almost all of the above research demonstrated that the use of the drug may decrease postop pain and the amount of analgesics used[4,5]. Moreover, it was tested together with different analgesics, including venlafaxine, COX-2 inhibitors, paracetamol, and ketamine. In cultured rat dorsal root ganglion neurons, gabapentin suppresses high-threshold calcium channel currents. It is useful in treating chronic pain disorders with minimal adverse effects[6,7]. Hysterectomy is the most frequently performed gynecological surgery, second after a cesarean section in many countries. Relieving pain after hysterectomy can support early mobility, reduce complications such as ileus, improve pulmonary function, increase patient satisfaction, reduce post-operative fatigue, and prevent delayed recovery[8,9]. The current study aimed to determine the Influence of gabapentin on opioid need in individuals undergoing total abdominal hysterectomy.

Materials and Method

This Experimental Study was conducted at MTI Khyber Teaching Hospital, Peshawar, from June 2025 to December 2025, following approval from the institute's research committee. Overall, we included 108 patients (ASA Class I or II) admitted to KTH for hysterectomy. Individuals with hypertension, acid reflux disease, renal or hepatic insufficiency, coagulation problems, a history of ischemic heart disease, hypersensitivity to any medication, or those using calcium channel blockers and antidepressants were not included. Written informed consent was obtained from each subject. Participants were randomly divided equally (54 in each group) into group A (experimental) and group B (control). Two hours before surgery, group A received 1200 mg of gabapentin orally, and group B received oral placebo capsules. Oxygen saturation, blood pressure, and Heart rate were monitored in the OT. Before surgery, each subject completed the VAS scale to assess pain. A skilled nurse not involved in any other part of the experiment placed the packets in consecutive numbers and then distributed them. A blinded individual documented the pain score measurements both before the surgery (by monitoring hypertension and heart beat associated with pain) and after surgery (VAS). Supplemental opioids (nalbuphine) were required both before and after surgery were recorded. Individuals' age and weight were also noted. Both groups were given the same anesthetic technique. All individuals were given general anesthesia. Before anesthesia, each subject was given a 7.5 mg orally midazolam tablet. During induction, participants were administered thiopentone 5 mg/kg, atracurium besylate 0.5 mg/kg, and nalbuphine 0.15 mg/kg. They were ventilated for three minutes with a circular system that delivered six liters of 50% O2 in nitrous oxide along with isoflurane (0.6%).7.5 mm ID endotracheal tube was used to intubate the patients. To maintain anesthesia, 40% O2 in nitrous oxide and isoflurane (0.6-1.0%) were used, with flows reduced to 3 liters per minute after eight minutes. For muscle relaxation, atracurium besylate (10 mg) was used. To replace the lost blood, Ringer's lactate solution was used. Blood transfusions were carried out if the predicted hemoglobin level fell below 8 g/dl. Participants received nalbuphine 0.05 mg/kg at two-hour intervals for postoperative analgesia based on VAS assessment. The first post-operative dose of nalbuphine was given two hours after surgery. If pain relief was insufficient, rescue analgesia was delivered as per the procedure. VAS score (numbered 1–10) was used for pain assessment at 02, 08, 16, and 24 hours after surgery. Scores 1- 3 indicated mild pain, 4- 7 moderate pain, and 8- 10 severe pain. In the case of moderate pain, an intravenous dose of 0.05 mg/kg of nalbuphine was given and recorded. We analyzed the data using SPSS version 16. To compare pain scores and supplemental nalbuphine requirements, we used a Student's t-test. A p-value of < 0.05 was considered significant.

Results

A total of 108 patients participated in this study. The study participants were randomly divided equally (54 in each group) into group A (experimental) and group B (control). Group A received 1200 mg of

gabapentin orally, and group B received placebo capsules orally. The study population had a mean age of 46±1.21 years (range 42-62 years) and a mean weight of 78±4.11 kilograms, as shown in Table **1.** Both groups had similar hemodynamic findings. There was no requirement for intraoperative rescue analgesics in any group. VAS score after the surgical procedure at 0, 2, 8, 16, and 24 hours in the gabapentin group was significantly lower compared to the control group. At 0 hours, the study group had a mean VAS score of 5.88±1.36, and the control group had 9.02±1.22. After 24 hours, the mean VAS score was 0.941±0.72 in the gabapentin group and 3.326±1.10 in the control group (Table 2)**.** The gabapentin group had a significantly smaller quantity than the nalbuphine group in the first twenty-four hours after surgery. The control group used 23.30±9.270 mg, and the study group required 12.20±4.680 mg nalbuphine; the difference was significant ($p<0.001$), as shown in Table **3.**

Table 1. Demographic features of the study population

Group	**Frequency**
Group A	54
Group B	54
Total	108
Characteristics	Mean (± SD)
Age in years	46±1.21 years
Weight in Kg	78±4.11

Data are presented as frequency and mean ± standard deviation (SD).

Table 2. Assessment of VAS Pain Scores (In centimeters) after surgical procedure in both groups

Time (hours	**Group**	**Mean± SD**	**Value of P**
zero	Group A	5.88±1.36	0.000
24 hours	Group B	9.02±1.22	
Time 2	Group A	3.352±0.778	0.000
2hours	Group B	5.971±1.201	
Time 8	A group	2.617±1.337	0.000
8 hours	B group	4.200±1.052	
Time 16	A group	2.088±0.861	0.000
16 hours	B group	4.028±1.172	
Time 24	Group A	0.941±0.72	0.000
At 24 hours	Group B	3.326±1.10	

Visual Analog Scale (VAS pain score values are presented as mean ± SD at different postoperative time points. P-values indicate between-group differences.

Table 3. Nalbuphine consumption (in milligrams) after surgery

Group	**No of individuals**	**Mean (± SD)**	**P value (Student's t-test)**
Study group	**54**	**12.20±4.680**	**0.000**
Control group	**54**	**23.30±9.270**	

PPostoperative nalbuphine consumption is expressed as mean ± SD in milligrams. The p-value represents the between-group comparison using Student's t-test.

Discussion

Postoperative pain impacts recovery following surgery and anesthesia. Opioids are extensively used for pain relief; however, their accompanying problems restrict their effectiveness. Combination therapies of opioid and nonopioid medications are intended to enhance the benefits of opioids while reducing problems. Gabapentin is an anticonvulsant that operates on voltage-dependent calcium channels[10]. This medicine induces the release of amino acids in the spinal cord, reducing or alleviating activity in damaged nerves. These drugs can therefore be prescribed to manage persistent pain, such as diabetic neuropathy, herpetic neuralgia, and other neuropathic illnesses[11]. Gabapentin has been studied for its efficacy in reducing pain after surgical procedures and stopping brain impulsiveness.[11] The current study was conducted to evaluate the impact of gabapentin on the opioid need in people following complete abdominal hysterectomy[12]. Our study demonstrated that a 1200 mg dose of gabapentin given 2 hours prior to operation significantly reduces the requirement for opioids after the procedure over the 1st 24 hours. Individuals who received gabapentin reported lower pain scores (VAS) than those in the control group. These findings are similar to those reported by Frouzanfard [9]. Our study revealed that gabapentin minimized the need for opioids in individuals undergoing TAH. Postoperative wounds and operative drains during the operation are sources of pain. After the surgical procedure, when pain is high on the first day, pain management is vital. Several painkillers have been used, and a mix of non-opioid and opioid agents has resulted in effective postoperative pain control[13]. Overuse of opioids can induce harmful outcomes such as respiratory issues. In contrast, gabapentin taken to

prevent pain has been found to minimize the overall amount of opioids needed in surgical patients, thereby minimizing the likelihood of adverse effects.[13] Gozal et al[14] discovered that persons undergoing thyroid gland surgery had considerably decreased opioid requirements following local wound infiltration with bupivacaine(0.5%) prior to skin closure, which supports our results. Basto et al. [15] observed that during operation, ketoprofen and paracetamol usage was associated with lessened pain and a reduction in the requirement for morphine after thyroid and parathyroid surgery [15]. Preventative painkilling with paracetamol has been tried in a study, with different amounts of success. Another study found that after thyroid surgery, bilateral superficial blocks significantly reduced pain intensity. Aunac et al. [16,17] showed that bilateral superficial and deep cervical blocks performed before thyroid surgery greatly reduced pain and the need for anesthesia during the procedure [18]. Though the standard prescription for treating neuropathic pain is 300-1200 mg three times a day, the gabapentin dosage used in our study (1200 mg) was comparable.[18] Two hours before surgery in this experiment, gabapentin was given orally because laboratory animal studies have demonstrated that anticipatory gabapentin treatment is more successful and more durable than post-treatment. In a rodent model of postoperative pain, preventive treatment with a single dose of gabapentin delayed the development of hyperalgesia for two days, whereas gabapentin provided an hour after the surgery only relieved symptoms for three hours [19]. Previous clinical trials of gabapentin for postoperative pain have had positive results. Gabapentin 1200 mg, administered orally one hour before surgery, lowered postoperative morphine consumption and pain ratings in the early postoperative phase for those undergoing spine surgery, reducing opioid-related side effects such as nausea and vomiting. In another study, Gabapentin 3000 mg administered before and throughout the first 24 hours after a total abdominal hysterectomy led to a 32% decrease in morphine intake, with no detectable influence on pain ratings during movement or at rest [20,21]. Our trial participants tolerated gabapentin well, and no significant side effects were seen while taking oral gabapentin prior to surgery. Our results are comparable to previously published research [23].

Conclusion

The study demonstrated that gabapentin significantly reduces intraoperative and postoperative pain. It also reduces opioid needs in patients undergoing TAH.

Ethical Approval

The Institutional Review Board/Ethics Committee approved this study before it began. **Approval no. (MTI/KTH/456/08/2024)**

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This study received no external funding. The research used available institutional resources.

Conflict of Interest

The authors declare that they have no competing interests or conflicts of interest related to this study.

Authors' Contributions

Ambareen Sifatullah: Conceptualization, study design, supervision, data interpretation, manuscript drafting, critical revision, final approval, and accountability for all aspects of the work.

Muhammad Javed Khan: Methodology, data collection, data curation, statistical analysis, data interpretation, manuscript drafting and revision, final approval, and accountability for all aspects of the work.

Shahid Maqsood: Study supervision, methodology, interpretation of findings, critical review of the manuscript, final approval, and accountability for all aspects of the work.

Fazal Wadood: Data collection, literature review, data curation, manuscript revision, final approval, and accountability for all aspects of the work.

Parhaizgar Khan: Data analysis, literature review, manuscript drafting and revision, interpretation of findings, final approval, and accountability for all aspects of the work.

Ambrin Naz: Supervised the study, critically reviewed the manuscript, interpreted the findings, provided final approval, and is accountable for all aspects of the work.

All authors: Reviewed and approved the final version of the manuscript and agreed to be accountable for all aspects of the work in accordance with ICMJE authorship criteria.

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Original Article

Association of Metabolic Syndrome with Early Renal Dysfunction in Patients with Type 2 Diabetes Mellitus: A Hospital-Based Cross-Sectional Study

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Abstract

Objective: To Determine the Association between Metabolic Syndrome and Early Renal Dysfunction among Patients with Type 2 Diabetes Mellitus attending Bakhtawar Amin Trust Teaching Hospital Multan.

Methodology: This Cross-sectional study was conducted at Bakhtawar Amin Hospital in Multan from January 2024 to December 2025. We enrolled 204 adults with type 2 diabetes using consecutive sampling. Metabolic syndrome was diagnosed using harmonized criteria. We defined early renal dysfunction as a urinary albumin-to-creatinine ratio of 30–300 mg/g and/or an estimated glomerular filtration rate of 60–89 mL/min/1.73 m². We excluded patients with established chronic kidney disease, acute kidney injury, or non-diabetic renal disease. We used multivariable logistic regression to identify factors independently associated with early renal dysfunction.

Results: The mean age was 52.6±9.8 years, and 112 (54.9%) participants were women. Metabolic syndrome was present in 142 (69.6%) patients, while early renal dysfunction was detected in 78 (38.2%). Renal dysfunction was more common among patients with metabolic syndrome than among those without it (45.8% versus 21.0%; p<0.001). Metabolic syndrome remained independently associated with early renal dysfunction after adjustment for relevant variables (adjusted odds ratio 2.54; 95% confidence interval 1.23–5.24). Longer diabetes duration, hypertension, and poor glycemic control were also independent predictors.

Conclusion: Metabolic syndrome was common and was independently associated with early renal dysfunction. Affordable metabolic and renal screening should be incorporated into routine diabetes care.

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Introduction

Type 2 diabetes mellitus has become one of the fastest-growing non-communicable diseases, with more than half a billion adults affected worldwide and the largest future increase expected in low- and middle-income countries[1].Pakistan has an exceptionally high burden of diabetes, and national survey findings have shown that a large proportion of affected adults remain undiagnosed until complications or symptomatic hyperglycemia bring them into contact with the healthcare system[2].Urbanization, reduced physical activity, central obesity, unhealthy dietary habits and population ageing have contributed to the continuing rise in diabetes and related metabolic abnormalities across South Asia[3]. Diabetic kidney disease is among the most serious complications of type 2 diabetes and is an important cause of chronic kidney disease, kidney failure, cardiovascular events and premature mortality[4].The burden of chronic kidney disease is particularly difficult to manage in resource-constrained countries, where specialist nephrology services and long-term dialysis remain unaffordable or inaccessible for many patients[5].Kidney injury in diabetes develops through several interconnected processes, including glomerular hyper filtration, endothelial dysfunction, oxidative stress, inflammation, activation of the renin–angiotensin–aldosterone system and progressive renal fibrosis[6].Early renal damage may remain unnoticed because serum creatinine can stay within the conventional reference range despite moderately increased albuminuria or a meaningful reduction in glomerular filtration[7]. Assessment of both urinary albumin-to-creatinine ratio and estimated glomerular filtration rate is therefore recommended because either abnormality may appear independently during the early course of diabetic kidney disease[8]. Metabolic syndrome describes the clustering of central obesity, hypertension, hyperglycemia, raised triglycerides and reduced high-density lipoprotein cholesterol, which commonly occur together because of insulin resistance and related metabolic disturbances These metabolic abnormalities may worsen renal injury through raised intraglomerular pressure, chronic inflammation, lipid accumulation, impaired endothelial function and increased production of reactive oxygen species [9]. Prospective evidence has shown that metabolic syndrome is associated with the development of chronic kidney disease and a faster decline in renal function, with the risk increasing as additional metabolic components accumulate [10]. Among patients with type 2 diabetes, metabolic profiles characterized by severe hyperglycemia, hypertension and dyslipidemia have also been associated with albuminuria and subsequent deterioration of renal function.[12] This relationship is important in low-resource hospitals because waist circumference, blood pressure, lipid profile, serum creatinine and spot urinary albumin can be assessed without advanced equipment or highly specialized laboratory services[11].Local evidence examining this relationship before the development of established chronic kidney disease remains limited; therefore, this study determined the association between metabolic syndrome and early renal dysfunction among patients with type 2 diabetes attending a tertiary-care hospital in Pakistan.

Materials and Methods

This hospital-based cross-sectional study was conducted in the departments of General Medicine and Nephrology of Bakhtawar Amin hospital in Multan, Pakistan, from January 2024 to December 2025. The hospital served patients from Multan and surrounding urban and rural districts and provided both outpatient and inpatient medical and nephrology services.The institutional ethical review committee approved the study before it began. The purpose and procedures of the study were explained to all eligible patients, and written informed consent was obtained before enrolment. We kept each participant's identity confidential, and used the information only for research purposes. Adults aged 30–70 years with physician-diagnosed type 2 diabetes mellitus of at least one year's duration were recruited from the medical, diabetes and nephrology outpatient departments. Consecutive sampling was used to reduce selection bias by the research team and to reflect routine hospital attendance. The minimum required sample was calculated using an anticipated frequency of early renal dysfunction of 35%, a 95% confidence level and a 7% margin of error. After allowing for incomplete biochemical and urine results, 214 patients were initially approached. Ten patients were excluded because the required laboratory results were incomplete, leaving 204 participants in the final analysis. Patients with an estimated glomerular filtration rate below 60 mL/min/1.73 m^2, a urinary albumin-to-creatinine ratio above 300 mg/g, previously diagnosed chronic kidney disease, acute kidney injury during the preceding three months or known non-diabetic renal disease were excluded. Patients with urinary tract infection, hematuria, pregnancy, decompensated heart failure, chronic liver disease, active malignancy or a current febrile illness were also excluded because these

conditions could influence serum creatinine or urinary albumin excretion.Demographic and clinical information was recorded on a structured data-collection form. The recorded variables included age, sex, place of residence, smoking status, duration of diabetes, antihypertensive treatment, glucose-lowering medication and history of hypertension. Available medical records and prescriptions were reviewed to confirm reported diseases and medication use.Body weight was measured with participants wearing light clothing, and height was recorded without shoes. Body mass index was calculated by dividing weight in kilograms by height in meters squared. Waist circumference was measured midway between the lower margin of the last palpable rib and the upper border of the iliac crest at the end of normal expiration. Blood pressure was measured after the participant had remained seated for at least five minutes. Two readings were taken five minutes apart using an appropriately sized cuff, and their average was recorded. Hypertension was identified when blood pressure was raised according to the study criteria or the patient was already receiving antihypertensive treatment. After an overnight fast of 8–12 hours, a venous blood sample was collected for fasting plasma glucose, glycated haemoglobin, serum creatinine, total cholesterol, triglycerides, high-density lipoprotein cholesterol and low-density lipoprotein cholesterol. Laboratory investigations were performed in the hospital laboratory under routine internal quality-control procedures. Estimated glomerular filtration rate was calculated using the 2021 CKD-EPI creatinine equation. A first-morning spot urine specimen was collected for measurement of urinary albumin and creatinine. The urinary albumin-to-creatinine ratio was expressed in milligrams of albumin per gram of creatinine. Where clinically possible, an abnormal urinary albumin result was confirmed using a second specimen to reduce misclassification caused by temporary albuminuria.Metabolic syndrome was diagnosed using harmonized criteria and was considered present when at least three of its five components were identified. Because all participants had type 2 diabetes, the hyperglycemia component was already present. Early renal dysfunction was defined as moderately increased albuminuria, mildly reduced estimated glomerular filtration rate or both in the absence of established chronic kidney disease. The operational definitions are presented in Table I.

Table I. Operational definitions used in the study

Variable	Operational definition
Central obesity	Waist circumference ≥90 cm in men or ≥80 cm in women
Raised blood pressure	Systolic blood pressure ≥130 mmHg, diastolic blood pressure ≥85 mmHg or antihypertensive treatment
Raised triglycerides	Triglycerides ≥150 mg/dL or treatment for raised triglycerides
Reduced HDL cholesterol	<40 mg/dL in men or <50 mg/dL in women, or specific treatment
Hyperglycemia	Established type 2 diabetes mellitus
Metabolic syndrome	Presence of at least three of the five metabolic components
Moderately increased albuminuria	Urinary albumin-to-creatinine ratio of 30–300 mg/g
Mildly reduced eGFR	eGFR of 60–89 mL/min/1.73 m^2
Early renal dysfunction	Moderately increased albuminuria, mildly reduced eGFR or both
Poor glycemic control	HbA1c ≥8.0%

Data were analyzed using SPSS version 26.0 and summarized as mean±SD, median (IQR), or frequency and percentage. Appropriate comparative tests and multivariable logistic regression were applied. Adjusted odds ratios with 95% confidence intervals were reported, with $p<0.05$ considered significant.

Results

A total of 204 patients with type 2 diabetes completed the required clinical and laboratory assessment. Their mean age was 52.6±9.8 years, and 112 (54.9%) were women. The median duration of diabetes was eight years. Most participants had poor glycemic control, while less than one-quarter were using a sodium-glucose cotransporter-2 inhibitor.Metabolic syndrome was identified in 142 (69.6%) patients. The main demographic and clinical characteristics according to

metabolic syndrome status are presented in Table II. Patients with metabolic syndrome generally had a longer duration of diabetes and less favorable anthropometric, blood pressure, glycemic and lipid measurements.

Table II. Characteristics of patients according to metabolic syndrome status

Characteristic	Metabolic syndrome (n=142)	No metabolic syndrome (n=62)	p-value
Age, years	53.4±9.5	50.8±10.2	0.082
Female sex	85 (59.9)	27 (43.5)	0.031
Rural residence	62 (43.7)	22 (35.5)	0.276
Diabetes duration, years	9 (5–13)	6 (3–10)	0.004
Body mass index, kg/m²	29.1±4.2	24.7±3.5	<0.001
Waist circumference, cm	100.2±10.1	86.7±8.8	<0.001
Systolic blood pressure, mmHg	139.6±16.8	126.9±14.5	<0.001
HbA1c, %	8.7±1.6	7.9±1.5	0.001
Triglycerides, mg/dL	207 (168–264)	129 (104–148)	<0.001
HDL cholesterol, mg/dL	37.8±8.5	47.6±9.1	<0.001
Current smoking	27 (19.0)	10 (16.1)	0.621
ACE inhibitor or ARB use	74 (52.1)	21 (33.9)	0.017
SGLT2 inhibitor use	29 (20.4)	15 (24.2)	0.545

Values are presented as mean±standard deviation, median (interquartile range) or n (%). ACE: angiotensin-converting enzyme; ARB: angiotensin receptor blocker; SGLT2: sodium-glucose cotransporter-2. Early renal dysfunction was detected in 78 (38.2%) patients. Moderately increased albuminuria without a reduction in estimated glomerular filtration rate was the most frequent pattern. A smaller number of patients had an isolated reduction in estimated glomerular filtration rate or both abnormalities. The distribution of renal findings is given in Table III.

Table III. Pattern of early renal dysfunction among study participants

Renal finding	Frequency	Percentage
No early renal dysfunction	126	61.8
Moderately increased albuminuria only	39	19.1
Mildly reduced eGFR only	21	10.3
Both renal abnormalities	18	8.8
Any moderately increased albuminuria	57	27.9
Any mildly reduced eGFR	39	19.1
Overall early renal dysfunction	78	38.2

eGFR: estimated glomerular filtration rate.

Early renal dysfunction was found in 65 (45.8%) patients with metabolic syndrome compared with 13 (21.0%) without metabolic syndrome. Serum creatinine, estimated glomerular filtration rate and urinary albumin-to-creatinine ratio also differed between the two groups. Table IV summarizes these findings without repeating each value in the text.

Table IV. Renal findings according to metabolic syndrome status

Renal parameter	Metabolic syndrome (n=142)	No metabolic syndrome (n=62)	p-value
Serum creatinine, mg/dL	0.94±0.19	0.86±0.17	0.005
eGFR, mL/min/1.73 m²	88.3±14.2	96.7±13.5	<0.001
UACR, mg/g	24 (11–68)	12 (7–25)	<0.001
Moderately increased albuminuria	49 (34.5)	8 (12.9)	0.002
Mildly reduced eGFR	34 (23.9)	5 (8.1)	0.008
Overall early renal dysfunction	65 (45.8)	13 (21.0)	<0.001

Values are presented as mean±standard deviation, median (interquartile range) or n (%). UACR: urinary albumin-to-creatinine ratio.

The frequency of early renal dysfunction increased steadily as metabolic abnormalities accumulated. It rose from 13.3% among patients with two metabolic components to 61.5% among those with all five components. A statistically significant linear trend was observed, as shown in Table V.

Table V. Early renal dysfunction according to the number of metabolic syndrome components

Number of metabolic components	Total patients	Early renal dysfunction, n (%)
2	30	4 (13.3)
3	67	20 (29.9)
4	68	30 (44.1)
5	39	24 (61.5)

Chi-square test for trend: p<0.001.

Metabolic syndrome, longer diabetes duration, hypertension, poor glycemic control, central obesity and raised triglycerides were associated with early renal dysfunction in the initial analysis. After adjustment for other variables, metabolic syndrome remained independently associated with early renal dysfunction. Diabetes duration of at least ten years, hypertension and an HbA1c level of 8.0% or above also retained significant associations. Detailed regression results are presented in Table VI.

Table VI. Factors associated with early renal dysfunction

Variable	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Metabolic syndrome	3.18 (1.60–6.33)	0.001	2.54 (1.23–5.24)	0.012
Age ≥55 years	1.73 (0.98–3.04)	0.058	1.38 (0.73–2.62)	0.321
Female sex	1.22 (0.69–2.15)	0.493	0.98 (0.51–1.86)	0.941
Diabetes duration ≥10 years	2.68 (1.50–4.77)	0.001	2.11 (1.12–3.97)	0.021
Hypertension	2.87 (1.57–5.24)	0.001	2.06 (1.07–3.95)	0.030
HbA1c ≥8.0%	2.48 (1.36–4.52)	0.003	2.19 (1.15–4.18)	0.017
Central obesity	2.15 (1.17–3.93)	0.014	1.42 (0.70–2.87)	0.330
Triglycerides ≥150 mg/dL	2.32 (1.27–4.24)	0.006	1.58 (0.78–3.20)	0.202
Current smoking	1.41 (0.69–2.88)	0.348	1.26 (0.57–2.79)	0.568
Rural residence	1.32 (0.75–2.34)	0.335	1.19 (0.63–2.24)	0.590

OR: odds ratio; CI: confidence interval.

The final regression model showed satisfactory calibration on the Hosmer–Lemeshow test (p=0.641). No important multicollinearity was observed. The model correctly classified 71.6% of patients and had an area under the receiver operating characteristic curve of 0.76 (95% CI 0.69–0.83), indicating acceptable discrimination.

Discussion

Metabolic syndrome was present in more than two-thirds of the patients, showing that central obesity, hypertension and lipid abnormalities frequently accompanied type 2 diabetes in this hospital population, as has also been reported among South Asian patients, facing a growing burden of metabolic disease[12].Early renal dysfunction was found in 38.2% of patients, and moderately increased albuminuria was its most frequent form, supporting the clinical value of urinary albumin testing for detecting kidney injury before patients develop symptoms or an obvious rise in serum creatinine[13]. Patients with metabolic syndrome were more than twice as likely to have early renal dysfunction after adjustment for other variables, which was consistent with pooled evidence linking metabolic syndrome with albuminuria, chronic kidney disease and a faster decline in renal function[14].The steady rise in renal dysfunction with each additional metabolic component suggested a cumulative effect in which obesity, hypertension, hyperglycemia and dyslipidemia acted together to increase hemodynamic and metabolic stress on the kidneys[15]. A longer duration of diabetes was independently associated with early renal dysfunction, most likely because prolonged metabolic exposure contributes to endothelial

injury, advanced glycation, oxidative stress and fibrosis, although kidney function can also decline without preceding albuminuria[16]. Poor glycemic control was another independent factor, emphasizing that persistent hyperglycemia remained clinically important even after accounting for blood pressure, obesity and lipid abnormalities[17]. Hypertension also retained a significant association because raised systemic and intraglomerular pressure can increase urinary albumin loss and gradually damage functioning nephrons, making effective blood-pressure management central to the prevention of renal progression[18].Some patients had renal abnormalities even though their serum creatinine remained within the commonly accepted reference range, demonstrating that serum creatinine alone could miss a meaningful proportion of patients with early kidney involvement. This finding was particularly relevant to low-resource hospitals because blood pressure, waist circumference, serum creatinine, estimated glomerular filtration rate and spot urinary albumin-to-creatinine ratio could be incorporated into routine diabetes visits without advanced diagnostic equipment[19]. Early identification also created an opportunity to improve glycaemic and blood-pressure control and consider kidney-protective medicines, although the cost and availability of sodium-glucose cotransporter-2 inhibitors, non-steroidal mineralocorticoid receptor antagonists and glucagon-like peptide-1 receptor agonists remained important barriers in Pakistan[20].This study consecutive recruitment, standardized data collection and use of routinely available hospital measurements strengthened the study. The findings are clinically relevant and applicable to the early identification of renal dysfunction in resource-constrained healthcare settings

Conclusion

Metabolic syndrome was common among patients with type 2 diabetes and was independently associated with early renal dysfunction. The frequency of renal involvement increased as metabolic abnormalities accumulated. Routine assessment of waist circumference, blood pressure, glycemic control, lipid profile, estimated glomerular filtration rate and urinary albumin could help identify high-risk patients before advanced kidney disease developed.

Ethical Approval

Ethical approval for this study was obtained from the Institutional Ethics Committee under **Ref. No. 5874/2022, dated 18 February 2023,** prior to commencement of the study.

Informed Consent

We obtained written informed consent from all participants before enrollment. Participants and their parents/guardians were informed about the study purpose and procedures, and participation was voluntary.

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Conflict of Interest

The authors declare that they have no competing interests or conflicts of interest related to this study.

Authors' Contributions

Muhammad Muzammil: Conceptualization, study design, data collection, interpretation of findings, manuscript drafting, critical revision of the manuscript, final approval of the version to be published, and accountability for all aspects of the work.

Nadeemullah: Study design, data collection, data curation, literature review, interpretation of data, manuscript revision, final approval of the version to be published, and accountability for all aspects of the work.

Aamena Gardazi: Conceptualization, study supervision, clinical assessment, interpretation of findings, critical revision of the manuscript for important intellectual content, final approval of the version to be published, and accountability for all aspects of the work.

Maria Sreena: Data collection, clinical assessment, data curation, literature review, manuscript revision, final approval of the version to be published, and accountability for all aspects of the work.

Shumaila Ali Nasir: Data analysis, data interpretation, manuscript drafting and revision, critical review of the manuscript for important intellectual content, final approval of the version to be published, and accountability for all aspects of the work.

Kiran-Areej: Data collection, literature review, data curation, manuscript revision, final approval of the version to be published, and accountability for all aspects of the work.

All authors: Reviewed and approved the final version of the manuscript and agreed to be accountable for all aspects of the work in accordance with ICMJE authorship criteria.

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Original Article

Histopathological Differences Between Atrophic and Progressive Primary Pterygium: A Clinicopathological Correlation Study

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Abstract

Objective: To Compare the Histopathological Features of Atrophic and Progressive Primary Pterygium.

Methodology: This Correlational study was conducted in the Department of Anatomy, Rawalpindi Medical University, Rawalpindi, Pakistan, from January 2020 to January 2021. We collected clinical data and pterygium specimens. Out of 41 primary pterygium specimens,31 were clinically atrophic, and 10 were progressive. We processed excised tissue for light microscopy. Histological assessment included basement membrane fragmentation and delayering, epithelial separation, epithelial fragmentation, epithelial invagination, goblet-cell pattern, stromal inflammatory infiltration, and elastosis. We used Fisher's exact test for binary findings and the Mann-Whitney U test for ordinal histological grades. We considered p-values below 0.05 significant.

Results: Basement membrane fragmentation was present in 93.5% of atrophic and 100% of progressive lesions. Basement membrane delayering was present in 80.6% of atrophic lesions and 80.0% of progressive lesions. Epithelial fragmentation was found in 90.3% of atrophic and all progressive lesions, while epithelial invagination was seen in 96.8% of atrophic and 80.0% of progressive lesions. Diffuse inflammatory infiltration was present in about 90% of both groups. High-grade elastosis (>10%) was present in 77.4% of atrophic and 80.0% of progressive lesions. No statistically significant differences were detected for the measured histopathological features.

Conclusion: Atrophic and progressive pterygia demonstrated broadly similar histopathological features, with no significant differences between groups. These findings suggest that clinical classification alone may not reflect underlying tissue changes. Quantitative histomorphometric assessment may improve clinicopathological correlation and disease characterization.

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Introduction

Pterygium is a common ocular surface disease characterized by a triangular or wing-shaped fibrovascular growth of conjunctival tissue that extends across the limbus onto the cornea. It is especially common in people exposed to ultraviolet (UV) radiation, heat, dust, wind, and other environmental irritants for long periods. UV exposure is believed to be the dominant risk factor. However, available data suggest that a complex interplay of environmental, cellular, inflammatory, and molecular processes drives pterygium development, rather than a single risk factor [1]. Continuous exposure to UV radiation, especially UV-B, can induce oxidative stress, damage the genome of limbal epithelial cells, and impair normal function in limbal stem cells. These changes can promote abnormal growth and migration of altered cells toward the cornea. This cellular damage brought on by UV also triggers inflammatory responses and results in the release of cytokines, growth factors and other mediators that promote tissue repair and proliferation [2,3]. Inflammation plays an important part in the development and progression of pterygium. Environmental irritation may lead to the release of inflammatory mediators and stimulate activation of stromal fibroblasts in the conjunctiva. Increased expression of vascular endothelial growth factor (VEGF) and other angiogenic factors drives new blood vessel formation, giving the lesion its characteristic fibrovascular appearance. Meanwhile, matrix metalloproteinases (MMPs) and other enzymes remodel and degrade the extracellular matrix, allowing pterygium to spread over the cornea and disrupt Bowman's layer [4]. Recent molecular research also highlights roles for oxidative stress, altered cell-cycle regulation and apoptosis control, tumor-suppressor pathways, the E–M transition, and ECM abnormalities. Pterygium is now seen as an ocular surface disease rather than a degenerative disease. It is more of a multifactorial ocular surface disorder that combines proliferative and inflammatory processes [5,6].

Materials and Methods

Material And Methods

this is a cross-sectional analytical clinicopathological study. clinical data and pterygium specimens were collected. the patients were 25-70 years of age, and only those for whom pterygium surgery had already been decided were included. informed consent was obtained before clinical examination and collection of the excised tissue for research. the clinical examination and classification of the pterygium as atrophic or progressive were completed before surgery. the present manuscript did not recruit a new group of patients or collect new specimens; it retrospectively analyzed the existing clinical and histopathological data from the parent research project. therefore, the parent research project was prospective in data and specimen collection, whereas the present manuscript is a retrospective secondary analysis of those prospectively collected cross-sectional data and specimens. the parent research project also included age- and sex-matched healthy controls, but the present analysis included only the 41 patients with excised primary pterygium specimens because pterygium tissue was not available from the healthy controls. of the 41 lesions, 31 were recorded as atrophic and 10 as progressive. study period: the overall study period was from january 2020 to january 2021. patient recruitment, preoperative clinical data collection and pterygium specimen collection were carried out from january 2020 to october 2020.

sample-size

41 primary pterygium specimens were available from the parent research project. the final groups consisted of 31 atrophic and 10 progressive lesions, reflecting the clinical distribution in the parent dataset rather than a planned equal allocation. because the progressive group was small and the groups were unequal, the study had limited ability to detect small or moderate differences between the two groups. therefore, non-significant findings should be interpreted cautiously and should not be taken as evidence that the two clinical groups are equivalent.

clinical examination and classification

before surgery, a complete eye examination was performed, and the pterygium was assessed for the eye involved, presence or absence of inflammation, size, site, and type, as well as stocker's line and fuchs' spot. we recorded pterygium size as type 1 when it was less than 2 mm, type 2 when it was up to 4 mm, and type 3 when it extended to the pupillary margin or involved the visual axis. the lesions were recorded clinically as atrophic or progressive before surgery. slit-lamp examination was used to assess the thickness, translucency, fleshiness, and visibility of the underlying episcleral vessels. we defined an atrophic pterygium as a thin, pale, relatively translucent lesion in which the underlying episcleral vessels were clearly visible. a progressive pterygium was defined as a thick, fleshy, vascular and relatively opaque lesion in which the underlying episcleral vessels were partially or completely obscured. the clinical classification was completed before surgical excision.

Tissue Processing

the excised pterygium tissue was received in 10% buffered formalin and allowed to fix for about 48 hours. each specimen was placed in a properly labeled tissue cassette and processed using an automated tissue processor. the tissue was dehydrated through ascending grades of alcohol, cleared in xylene, infiltrated, and embedded in paraffin wax. sections approximately 3-5 micrometers thick were cut on a microtome, placed in a water bath at about 45°c, and mounted on labeled slides. hematoxylin and eosin staining was used to assess general epithelial and stromal morphology and inflammatory cells. periodic acid-schiff-haematoxylin staining was used mainly to assess the basement membrane and goblet-cell morphology, while verhoeff staining was used

to assess elastic fibers. histopathological examiner and blinding: the stained slides were examined under light microscopy at low and high magnification and scored according to predefined histopathological criteria. based on qualifications and the number of examiners, two examiners were involved: one with mbbs and phd, and the other with mbbs and m.phil. examiners were blinded to the clinical classification as atrophic or progressive.

Histopathological Assessment

the stained slides were examined under light microscopy at lower and higher magnification. the assessment used the histological criteria. each feature was recorded as follows.

Basement Membrane Fragmentation and Delayering

basement membrane was assessed mainly on pas-stained sections. we recorded fragmentation as grade 0 when no fragmentation was seen and grade 1 when fragmentation was present. delayering was recorded as present when separation of the basement membrane from the overlying epithelium was seen and absent when this separation was not seen. these were treated as binary observations in the present analysis.

Epithelial Separation, Fragmentation and Invagination

the epithelial layers were examined for visible separation, breaks or fragmentation and inward invagination. each finding was recorded as present or absent. epithelial separation meant a visible separation of the epithelial layer from the underlying supporting layer, epithelial fragmentation meant visible discontinuity or breaks in the epithelial layers, and epithelial invagination meant inward dipping of the epithelium into the underlying tissue

Goblet-Cell Pattern

goblet cells in the surface epithelium were assessed according to their arrangement. they were recorded as single goblet cells, clusters of goblet cells, or invagination of goblet cells into the underlying connective tissue.

Stromal Inflammatory Infiltration

inflammatory cells, including neutrophils, monocytes, macrophages, and lymphocytes, were examined under the 40x objective. four microscopic fields were selected. the grading table defined grade 0 as unremarkable stroma or only a few sparse lymphoid cells, and grade 1 as significant patchy or diffuse leukocytic infiltration in at least one 400x microscopic field. the accompanying method text also states that diffusely scattered cells in more than two of the four selected fields were considered grade 1.

Elastosis

elastotic fibers were assessed on verhoeff-stained sections under 10x and 40x objective lenses. we selected four different fields in a zigzag pattern and divided each field into four equal parts, each representing 25% of the field. we assessed elastotic fibers in these fields and calculated an average estimate. we graded elastosis according to the estimated percentage of elastotic material: grade 0 when absent, grade 1 when less than 3%, grade 2 when 3-10%, and grade 3 when more than 10%.

Statistical Analysis

we compared atrophic and progressive groups at the patient level. frequencies and percentages were calculated for categorical findings. fisher exact test was used when comparing binary histological findings because some cell counts were small. for goblet cells, two separate analyses were performed: goblet-cell invagination was treated as a binary finding (present versus absent) and compared using the two-sided fisher exact test, while the overall goblet-cell pattern (single cells, clusters and invagination) was treated as an ordinal variable and compared separately using the mann-whitney u test. for elastosis, high-grade elastosis (>10%) was compared with lower-grade elastosis (≤10%) as a binary variable using fisher exact test, while the full elastosis grade distribution (<3%, 3-10%, >10%) was treated as an ordinal variable and compared using the mann-whitney u test. we considered a two-sided p-value below 0.05 statistically significant.

Results

We included 41 Primary Pterygium Specimens. Thirty-One Lesions (75.6%) were atrophic, and 10 (24.4%) Were Progressive. Most Microscopic Changes Were Common in Both Groups.

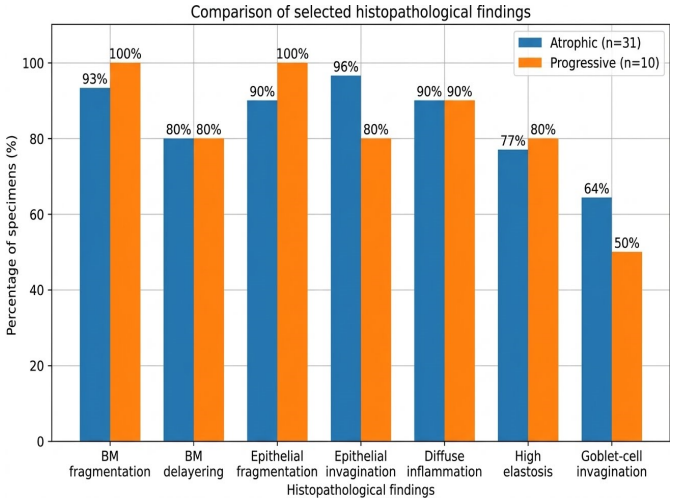
Table I. Comparison of Histopathological Findings Between Atrophic and Progressive Pterygium

Histopathological Feature	Atrophic (N=31)	Progressive (N=10)	P Value

Basement Membrane Fragmentation	29 (93.5%)	10 (100.0%)	1.000
Basement Membrane Delayering	25 (80.6%)	8 (80.0%)	1.000
Epithelial Separation	28 (90.3%)	9 (90.0%)	1.000
Epithelial Fragmentation	28 (90.3%)	10 (100.0%)	0.564
Epithelial Invagination	30 (96.8%)	8 (80.0%)	0.142
Diffuse Stromal Inflammation	28 (90.3%)	9 (90.0%)	1.000
Goblet-Cell Invagination (Binary: Present Vs Absent)	20 (64.5%)	5 (50.0%)	0.472†
Overall Goblet-Cell Pattern (Ordinal: Single / Cluster / Invagination)	7 (22.6%) / 4 (12.9%) / 20 (64.5%)	2 (20.0%) / 3 (30.0%) / 5 (50.0%)	0.589‡
High-Grade Elastosis (>10% Vs ≤10%)	24 (77.4%)	8 (80.0%)	1.000*

*for elastosis, p=1.000 is from the two-sided fisher exact test comparing high-grade (>10%) with lower-grade (≤10%) elastosis. we analyzed the full ordinal elastosis grade distribution (<3%, 3-10%, >10%) separately using the mann-whitney u test (p=0.849). †for goblet cells, p=0.472 is from the two-sided fisher exact test for the binary comparison of invagination present versus absent. ‡the p=0.589 value is from the separate mann-whitney u comparison of the overall ordinal goblet-cell pattern (single cells, clusters and invagination). basement membrane fragmentation was almost universal in both groups. it was seen in 29 of 31 atrophic lesions and all 10 progressive lesions. basement membrane delayering was present in 25 of 31 (80.6%) atrophic specimens and 8 of 10 (80.0%) progressive specimens. these proportions were close, but the small progressive group means equivalence cannot be concluded from the non-significant comparison. epithelial invagination showed the largest numerical difference. it was present in 96.8% of atrophic lesions compared with 80.0% of progressive lesions, but this difference was not statistically significant (p=0.142). because only 10 progressive specimens were included, the non-significant p-value does not exclude a true difference between the groups. diffuse stromal inflammation was present in around 90% of both atrophic and progressive specimens. high-grade elastosis (>10%) was present in 24 of 31 (77.4%) atrophic lesions and 8 of 10 (80.0%) progressive lesions. when elastosis was analyzed as a binary variable, comparing high-grade (>10%) with lower-grade elastosis (≤10%), the fisher exact test gave p=1.000. in a separate analysis, the overall ordinal distribution of elastosis grades (<3%, 3-10%, >10%) gave p=0.849 with the mann-whitney u test. these two p values refer to two different analyses of elastosis rather than conflicting results. neither non-significant result should be interpreted as evidence that the elastosis pattern is equivalent between the two groups. for goblet cells, we performed two separate analyses. in the binary comparison, goblet-cell invagination was present in 20 of 31 (64.5%) atrophic lesions and 5 of 10 (50.0%) progressive lesions; the two-sided fisher exact test gave p=0.472. in the separate ordinal analysis, the overall goblet-cell pattern was distributed as 7 single-cell, 4 cluster, and 20 invagination cases in the atrophic group, and 2 single-cell, 3 cluster, and 5 invagination cases in the progressive group: the mann-whitney u test gave u=171.0 and p=0.589. therefore, p=0.472 and p=0.589 refer to two different goblet-cell analyses and are not conflicting values. these non-significant p-values do not establish equivalence of the goblet-cell findings between the two groups.

Figure 1. Comparison of selected histopathological findings in atrophic and progressive primary pterygium



Discussion

The Present Analysis Did Not Detect Statistically Significant Differences in Epithelial, Basement Membrane, or Stromal Features Between Atrophic and Progressive Pterygia. However, this should not be interpreted as evidence that the two clinical groups are histopathologically equivalent because the progressive group contained only 10 specimens, and the study had limited statistical power. This Is An Important Observation Because It Suggests That A Simple Clinical Label May Not Completely Represent The Biological Changes Inside A Pterygium. Recent work has shown that some histopathological findings may relate to redness, vascularity, or lesion severity, but the relationship is not always consistent [5-10].In Our Specimens, Basement Membrane Fragmentation, Epithelial Fragmentation And Epithelial Invagination Were Very Frequent In Both Atrophic And Progressive Lesions. These changes show that disruption of the epithelial-basement membrane region is not limited to clinically progressive disease. Even A Lesion That Was Recorded Clinically As Atrophic Before Surgery May Already Have Marked Microscopic Architectural Disturbance. Epithelial Invagination Was Present In 96.8% Of Atrophic Lesions And 80.0% Of Progressive Lesions. Although This Was The Largest Numerical Difference In Our Comparison, It Did Not Reach Statistical Significance. However, The Groups Were Unequal (31 Atrophic And 10 Progressive Specimens), And The Progressive Group Was Small. This Reduced The Statistical Power And Precision Of The Comparison And Increased The Chance Of Missing A True Difference (Type II error). Therefore, A True Difference Cannot Be Ruled Out, and the non-significant result should not be interpreted as proof that the two groups are the same. A larger study with more balanced groups would be needed to assess this relationship more reliably. Stromal Inflammation Was Also Common In Both Groups. This fits with recent work showing that inflammation remains an important part of pterygium biology. Studies Published In 2024 and 2025 have continued to show the role of inflammatory and vascular activity in disease severity and tissue remodeling [8,9,16-18]. Elastosis Was Another Frequent Finding In The Present Analysis. More than 10% Elastosis Was Present In About Three-Quarters Of Atrophic Lesions And Four-Fifths Of Progressive Lesions. The Statistical Comparisons Were Non-Significant, but these findings do not prove that elastosis is equivalent between the two groups. The High Frequency Of Elastosis In Both Groups May Be Related To Chronic Environmental And Ultraviolet Injury [1,3,4,19]. The Goblet-Cell Analyses Also Did Not Show Statistically Significant Between-Group Differences. However, Because the Groups Were Small and Unequal, These Findings Should Not Be Used To Conclude That The Goblet-Cell Patterns Were Equivalent. Modern clinical studies have shown that pterygium morphology has several dimensions, Including Size, Vascularity, Thickness, and Ocular-Surface Effects [7,8,14,20]. A Broad Atrophic/Progressive Classification May Therefore Be Too Simple To Reflect All Of The Underlying Tissue Changes. The Small Progressive Group Reduced The Ability To Detect Modest Between-Group Differences, So The Absence Of Statistical Significance Does Not Establish Equivalence. Most specimens showed several histological abnormalities, leaving only a few negative cases for comparison. The clinical classification was also broad and not based on a modern photographic or OCT-based grading system. In Addition, the histological variables were mainly recorded as categories rather than continuous measurements. Future Studies Should Use Standardized Slit-Lamp Grading And Digital Histomorphometry, including epithelial thickness, stromal thickness, microvessel density, inflammatory-cell density, and percentage fibrosis or elastosis. The Main Limitations Were The Small Sample Size And Unequal Group Sizes. No formal a priori sample-size calculation was documented for this secondary comparison, And The Analysis Was Based On The 41 Pterygium Specimens Available From The Parent Research Project. The Distribution Of 31 Atrophic And 10 Progressive Lesions Was Not A Planned Equal Allocation. With only 10 Progressive Specimens, The Study Had Limited Statistical Power To Detect Small Or Moderate Differences, And The Chance Of Missing A True Difference (Type II error) Was Increased. Therefore, Interpret the Non-Significant Findings Cautiously and Do Not Consider Them Evidence That the Two Groups Are Equivalent. The high frequency of several histological findings in both groups also left few negative cases for comparison. The Clinical Phenotype Was Based On Routine Clinical Classification Rather Than A Standardized Photographic Grading System.

Conclusion

No Statistically Significant Differences Were Detected In The Measured Epithelial, Basement Membrane, and Stromal Features Between Atrophic and Progressive Primary Pterygia. Because Only 10 Progressive Specimens Were Included, These Non-Significant Findings Do Not Establish Histopathological Equivalence Between The Two Clinical Groups, And A True Difference May Have Been Missed. Larger Studies With More Balanced Groups, detailed clinical grading, and quantitative

histomorphometry are needed to assess these relationships more reliably.

Ethical Approval

The Ethical Review Committee of The Rawalpindi Medical University, Rawalpindi, Pakistan **(RMU/Reg-19/Erc/2484/04/2023).**

Conflict of Interest

The Authors Declare No Conflict Of Interest.

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Authors' Contributions

Sadia Aman, Ayesha Nasrullah: Conceptualization, study design, data collection, histopathological assessment, interpretation of findings, manuscript drafting, critical revision of the manuscript, final approval of the version to be published, and accountability for all aspects of the work.

Sumera Khalil, Abdullah Rafique: Study design, histopathological assessment, data curation, literature review, interpretation of findings, manuscript revision, final approval of the version to be published, and accountability for all aspects of the work.

Sanah Sameen, Maha Noor: Data collection, histopathological assessment, data curation, literature review, manuscript drafting and revision, final approval of the version to be published, and accountability for all aspects of the work.

All authors: Reviewed and approved the final version of the manuscript and agreed to be accountable for all aspects of the work in accordance with ICMJE authorship criteria.

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Original Article

Relationship of Environmental Exposure with Clinical Morphology of Primary Pterygium in Pakistani Adults

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Abstract

Objective: To determine the association of age, sex, daily sun exposure, smoking, and toxic chemical exposure with the clinical morphology of primary pterygium.

Methodology: We conducted this cross-sectional study at the Shifa College of Medicine, Islamabad, Pakistan, from January 2025 to December 2025. Forty-one patients had primary unilateral pterygium. We recorded average daily sun exposure from the clinical history as hours per day. Smoking was recorded only as a categorical smoking-status variable. We recorded toxic chemical exposure only as present or absent. We examined the pterygium for visible inflammation, atrophic or progressive appearance, Stocker's line, Fuchs spots, corneal extension, and site.

Results: The mean age was 52.15 ± 14.36 years and 24 patients (58.5%) were female. Mean daily sun exposure was 5.54 ± 1.00 hours. Fifteen patients (36.6%) were smokers, and 27 (65.9%) reported toxic chemical exposure. Clinical inflammation occurred in 41.5%, progressive pterygium in 24.4%, Stocker's line in 36.6%, and Fuchs spots in 22.0%. We found no clear associations between the examined factors and clinical features. Continuous estimates were small and imprecise, while categorical comparisons included confidence intervals.

Conclusion: Among 41 surgically selected patients with unilateral primary pterygium, we found no clear associations between demographic or environmental factors and lesion morphology. We cannot exclude smaller associations, and the findings should not be generalized beyond this selected population.

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Introduction

Pterygium is a fibrovascular growth of conjunctival tissue that crosses the limbus and extends onto the cornea. It is common in people who live or work in areas with strong sunlight. Recent reviews still identify ultraviolet exposure as one of the main environmental factors in pterygium. However, inflammation, oxidative stress, abnormal cell growth and other pathways also take part in the disease [1]. A recent global analysis also showed that pterygium remains common worldwide and that its prevalence increases with age and varies between regions [2].Environmental exposure may be more complex than sunlight alone. A large study from Shanghai reported that solar radiation and air pollutants, especially PM2.5, ozone and nitrogen dioxide, were related to pterygium visits. Occupational health research also continues to emphasize the effect of long-term solar exposure on the eyes of outdoor workers [3].The clinical appearance of pterygium also varies from patient to patient. Some lesions are quiet and atrophic, while others are thick, vascular or progressive. Recent studies have linked pterygium morphology with dry-eye findings, vascular changes, systemic inflammatory markers, meibomian gland dysfunction and microscopic tissue changes [4]. This suggests that the visible appearance of a lesion may reflect several local and systemic processes rather than environmental exposure alone.In Pakistan, sunlight exposure is common in many occupations, but there is limited information on whether environmental exposure is related to the clinical appearance of pterygium after the disease has developed. Recent molecular and pathological work also shows that pterygium involves complex changes in genes, extracellular matrix, angiogenesis and inflammation [5,6,7]. In this study, I examined whether age, sex, daily sun exposure, smoking and toxic chemical exposure were related to inflammation, atrophic or progressive phenotype, Stocker's line and Fuchs spots in patients with primary pterygium[8].

Materials and Methods

Study design and participants

This cross-sectional study was conducted in the Shifa College of Medicine Islamabad, Pakistan, from January 2025 to December 2025. 41 patients with primary unilateral pterygium were selected for surgical excision. Patients were assessed clinically before surgery. The parent study was approved by the Ethical Review Committee of the Shifa College of Medicine, Islamabad, Pakistan, and participants provided informed consent. Because inclusion required a decision for surgical excision, I consider this cohort to represent a surgically selected, clinically significant group of pterygium cases rather than the full spectrum of patients with pterygium.

Study period, setting and recruitment

We carried out clinical recruitment, surgical excision and specimen collection from January 2020 through October 2020. I included patients only when surgical excision of the pterygium had already been decided. After obtaining informed consent, I took a complete history and examined the eyes and pterygium clinically before surgery. The surgically excised pterygium specimen was then collected for the parent research. Using this approach, I recruited the 41 patients included in the present analysis.

Clinical and exposure data

We obtained the exposure information from the clinical history. I recorded average daily sun exposure as the reported number of hours of sunlight exposure per day. I recorded smoking as a categorical smoking-status variable only. I recorded toxic chemical exposure as a binary history of exposure (present/absent). I examined the pterygium for visible inflammation, size, site, atrophic or progressive appearance, Stocker's line and Fuchs spots. Corneal extension was recorded as Type 1 when it was less than 2 mm, Type 2 when it extended up to 4 mm and Type 3 when it reached the pupillary margin or visual axis.

Clinical classification criteria and observer assessment

Pterygium characteristics were assessed clinically before surgery, including the presence or absence of inflammation and classification as atrophic or progressive. Clinical inflammation refers to visible surface hyperemia/redness with increased vascularity; an atrophic phenotype refers to a thin, pale or translucent, relatively avascular lesion with the underlying episcleral vessels clearly visible; and a progressive phenotype refers to a thicker, fleshy and more vascular lesion with reduced or absent visibility of the underlying episcleral vessels [9,10]. Interobserver agreement statistics were reported.

Statistical analysis

We analyzed the data at the patient level. I summarized continuous variables as mean ± standard deviation and categorical variables as frequency and percentage. Because I had only 41 patients and some outcome groups were small, particularly the 10 patients with progressive pterygium and the 9 with Fuchs spots, I used simple bivariate analyses rather than fitting unstable multivariable models. I examined age and

daily sun exposure for each clinical outcome using Spearman rank correlation and report r as the effect estimate with an approximate 95% confidence interval based on Fisher's z transformation. For sex, smoking, and toxic chemical exposure, I used two-sided Fisher's exact tests because several expected cell counts were small. To make the magnitude and uncertainty of these categorical associations clearer, I also report conditional odds ratios with exact 95% confidence intervals. The parent thesis preserves the marginal totals and the reported Fisher exact p-values but does not reproduce the original 2 x 2 cross-tabulations. I therefore reconstructed, for each categorical comparison, the unique 2 x 2 table compatible with the reported margins and Fisher p-value to three decimal places, and calculated a conditional maximum-likelihood odds ratio with an exact 95% confidence interval. I regard these odds ratios as secondary reconstructed estimates rather than independently verified patient-level calculations, so I interpret them cautiously. I examined whether five demographic/environmental factors were associated with four main clinical outcomes, giving 20 bivariate comparisons. I considered inflated Type I error but did not apply a formal multiple-comparison adjustment because the analyses were exploratory and hypothesis-generating. As a conservative sensitivity reference, a Bonferroni correction across 20 tests would correspond to alpha=0.0025. Because this was a cross-sectional study, I use association language only and do not interpret these analyses as showing temporality or causality. I therefore interpret p-values together with effect sizes, confidence intervals, sample size, and the overall pattern of results rather than as stand-alone evidence.

Sample-size and power calculation

Using Fisher's z method for a two-sided test (alpha=0.05, 80% power) and a moderate-to-large target correlation of r=0.43, the calculated requirement was n = [(1.96 + 0.84)/atanh(0.43)]^2 + 3 = 40.1, rounded up to 41 participants. I therefore considered the available sample of 41 adequate to detect moderate-to-large associations, but not smaller effects. I also expected lower power for Fisher's exact analyses because several categorical subgroups were small and unequal. For this reason, I treated these analyses as exploratory and did not interpret non-significant findings as evidence that no association exists.

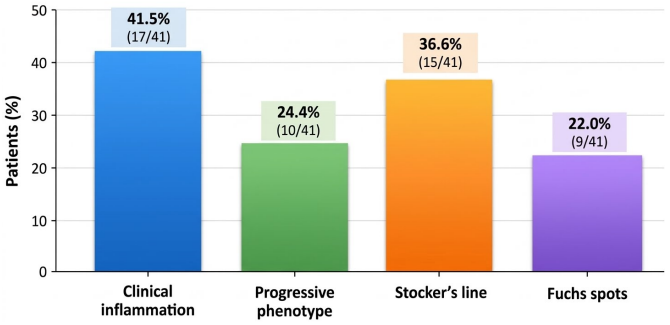
Results

We included 41 patients with primary pterygium. Their mean age was 52.15 ± 14.36 years. Twenty-four patients (58.5%) were female, and 17 (41.5%) were male. Mean daily sun exposure was 5.54 ± 1.00 hours. Fifteen patients (36.6%) were smokers, while 27 (65.9%) reported toxic chemical exposure. Clinically, 17 patients (41.5%) had inflamed pterygium. Thirty-one lesions (75.6%) were atrophic, and 10 (24.4%) were progressive. Stocker's line was seen in 15 patients (36.6%) and Fuchs spots in 9 (22.0%). Most lesions were advanced in corneal extension, with 37 of 41 (90.2%) classified as Type 3. Forty lesions (97.6%) were nasal.

Table I. Demographic, environmental and clinical characteristics of the study group (n=41)

Characteristic	Result
Age	52.15 ± 14.36 years
Female	24 (58.5%)
Male	17 (41.5%)
Daily sun exposure	5.54 ± 1.00 hours/day
Smoking	15 (36.6%)
Toxic chemical exposure	27 (65.9%)
Clinical inflammation	17 (41.5%)
Atrophic phenotype	31 (75.6%)
Progressive phenotype	10 (24.4%)
Stocker's line	15 (36.6%)
Fuchs spots	9 (22.0%)
Type 3 corneal extension	37 (90.2%)
Nasal location	40 (97.6%)

Figure 1. Frequency of the main clinical features of priMany pterygium in the study group (n=41).



For age and daily sun exposure, I found only small-to-moderate associations, and the confidence intervals were wide. For age, Spearman r ranged from -0.051 to 0.226 across the four clinical outcomes. The largest estimate was for Stocker's line (r=0.226, approximate 95% CI -

0.088 to 0.499; p=0.156). For daily sun exposure, r ranged from -0.050 to 0.136. All approximate 95% confidence intervals included zero, so the data were compatible with both small negative and small positive associations. For sex, smoking, and toxic chemical exposure, I assessed whether each factor was associated with the clinical outcomes using exact Fisher tests because of the sparse cells, and I present conditional odds ratios with exact 95% confidence intervals in Table II. The confidence intervals were wide, and all included the null value of 1, showing substantial uncertainty. The closest result was toxic chemical exposure with progressive rather than atrophic phenotype (conditional OR=0.24, exact 95% CI 0.04 to 1.32; p=0.064). Because the original thesis did not retain the 2 x 2 cross-tabulations, I derived these categorical odds ratios from the unique tables compatible with the reported margins and Fisher p-values to the reported precision; I therefore treat them as secondary reconstructed estimates. Because I examined 20 bivariate comparisons without a formal multiplicity adjustment, I also treat every p-value as exploratory and do not interpret an isolated p-value as definitive evidence for or against a relationship.

Table II. Effect estimates and exact tests for demographic and environmental factors in relation to clinical morphology

Clinical feature	Age r (95% CI); p	Sun exposure r (95% CI); p	Sex OR (95% CI); exact p	Smoking OR (95% CI); exact p	Toxic exposure OR (95% CI); exact p
Clinical inflammation	0.023 (-0.287 to 0.328) p=0.886	-0.050 (-0.352 to 0.262) p=0.756	OR 1.02 (95% CI 0.24 to 4.37) p=1.000	OR 0.91 (95% CI 0.20 to 3.94) p=1.000	OR 0.38 (95% CI 0.08 to 1.71) p=0.189
Progressive phenotype	-0.051 (-0.353 to 0.261) p=0.753	0.089 (-0.225 to 0.386) p=0.579	OR 0.38 (95% CI 0.06 to 1.98) p=0.270	OR 1.21 (95% CI 0.20 to 6.46) p=1.000	OR 0.24 (95% CI 0.04 to 1.32) p=0.064
Stocker's line	0.226 (-0.088 to 0.499) p=0.156	-0.006 (-0.313 to 0.302) p=0.972	OR 0.31 (95% CI 0.06 to 1.34) p=0.102	OR 1.25 (95% CI 0.27 to 5.59) p=0.749	OR 1.06 (95% CI 0.23 to 5.22) p=1.000
Fuchs spots	0.018 (-0.291 to 0.324) p=0.913	0.136 (-0.179 to 0.426) p=0.397	OR 1.54 (95% CI 0.27 to 11.21) p=0.711	OR 0.43 (95% CI 0.04 to 2.75) p=0.445	OR 1.05 (95% CI 0.18 to 7.72) p=1.000

Age and sun exposure are reported as Spearman r with approximate 95% confidence intervals and two-sided p-values. For categorical comparisons, I report conditional odds ratios with exact 95% confidence intervals followed by two-sided Fisher's exact p-values. Odds ratios compare female with male, smoker with non-smoker, and toxic exposure present with absent; for outcomes, the comparison is feature present versus absent, except progressive phenotype, which is progressive versus atrophic. Because the parent thesis does not reproduce the original 2 x 2 cross-tabulations, I reconstructed the unique 2 x 2 table compatible with each pair of reported marginal totals and Fisher p-value to the reported three-decimal precision. I therefore regard the categorical odds ratios as secondary reconstructed estimates and interpret them cautiously. All p-values are unadjusted for the 20 exploratory bivariate comparisons.

Discussion

My exploratory analysis found no statistically significant associations between the demographic or environmental factors examined and the clinical appearance of primary pterygium. However, my sample had limited power to detect small effects, so I do not interpret the lack of statistical significance as evidence that these factors are unrelated to pterygium morphology. This does not mean that sunlight is unimportant in pterygium. Current evidence still supports ultraviolet exposure as a major factor in disease development [11,12]. Zeng and colleagues also found that solar radiation and several air pollutants were related to increased pterygium visits in a large population study. A recent global analysis estimated a substantial worldwide burden and again showed important variation with age and geography. My study addressed a different and much narrower question because all 41 participants already had unilateral primary pterygium and had been selected for surgical excision[13]. Therefore, my data cannot determine whether the exposures studied cause or contribute to pterygium development in the general population.One reason may be that most patients in this study had similar levels of sunlight exposure. Daily sun exposure clustered near the upper end of the recorded range, so variation between patients was limited. This makes it difficult to show a

dose-response relationship within a small group.The clinical appearance of pterygium also likely depends on local tissue changes. Ha and Kim showed that different pterygium morphologies were related to different dry-eye findings [14]. Han and colleagues found measurable vascular differences between mild and severe lesions [15]. Yun and colleagues reported a relationship between complement C3 and stromal severity [16], while Rahman and colleagues found greater tear-film and meibomian gland changes with higher pterygium grade [17]. Other recent studies using clinical grading, histopathology, anterior-segment OCT and tissue analysis also support a link between morphology, inflammation and structural change [18].Toxic chemical exposure gave the closest categorical result for progressive rather than atrophic phenotype (conditional OR=0.24, exact 95% CI 0.04 to 1.32; Fisher's exact p=0.064). I do not consider this a positive or definitive finding because the confidence interval is wide and includes 1, and the progressive group contained only 10 patients. The other categorical odds ratios were also imprecise, with all exact 95% confidence intervals including 1. In addition, I performed 20 bivariate comparisons. I considered multiple-comparison adjustment but did not apply a formal correction because the analysis was exploratory. Because my study was cross-sectional, I interpret these findings only as possible associations and not as evidence of temporality or causality. I therefore interpret the effect estimates, their confidence intervals, and the overall pattern of results together rather than treating any isolated p-value as evidence of a definitive relationship.Recent research also shows why a simple clinical label may not explain every aspect of pterygium. Histopathological examination can occasionally identify unexpected epithelial or neoplastic changes [19], and newer molecular reviews describe important roles for angiogenesis, extracellular-matrix remodeling and inflammatory pathways [12,20]. Morphological measurements have also been linked with postoperative corneal shape and optical recovery, while large clinical series continue to show that presentation and surgical outcome vary between patients [21]. These findings support the idea that environmental exposure is only one part of the overall clinical picture.My study has some limitations. The sample was small, especially for progressive pterygium and Fuchs spots, which limited the precision of the estimates and the ability to detect small effects. My exposure measurements were also limited. I recorded sun exposure only as average hours per day and could not distinguish occupational from recreational exposure or estimate cumulative or lifetime ultraviolet exposure. Smoking was recorded only as smoking status, without current/former classification, duration, cigarettes per day, or pack-years. We recorded toxic chemical exposure only as present or absent; we did not have the type of chemical, source, route, duration, frequency, or intensity. Because of these limitations, I could not examine dose-response relationships for smoking or chemical exposure, and some exposure misclassification is possible. Most lesions were nasal and Type 3, so I could not compare these variables. I did not fit a multivariable model because the small number of events in some outcomes would have produced unstable adjusted estimates. The parent thesis did not retain the original 2 x 2 cross-tabulations for the categorical analyses. I therefore reconstructed the categorical odds ratios from the unique tables compatible with the reported marginal totals and Fisher p-values to the reported precision; these should be regarded as secondary reconstructed estimates rather than independently verified patient-level effect estimates. I also tested 20 bivariate associations without formal multiplicity adjustment, so I treated the analysis as exploratory and interpreted the results based on effect sizes, confidence intervals, and the overall pattern rather than nominal p-values alone. In addition, I selected all 41 participants for surgical excision, so my study population represents surgical/clinically significant pterygium rather than all patients with pterygium. This selection limits generalizability. The clinical distribution was also highly unbalanced: 37 of 41 lesions (90.2%) were Type 3, only 4 were Type 2, none were Type 1, and 40 of 41 lesions (97.6%) were nasal with only one temporal lesion. I therefore did not have enough variation to make meaningful comparisons across corneal extension grades or between nasal and temporal sites.Within this selected group of 41 surgical patients, my findings suggest that the demographic and environmental factors I examined were not clearly associated with the clinical morphology recorded before excision. However, because every participant already had unilateral primary pterygium and was selected for surgery, I cannot use these findings to make conclusions about all Pakistani adults, about patients who are not selected for surgical excision, or about the development of pterygium in the general population.The sample size was small, and the clinical groups were unequal. Although 41 participants provided approximately 80% power to detect moderate-to-large correlations (about r=0.43), my study was underpowered for smaller effects, and several categorical comparisons were sparse. I did not perform multivariable adjustment because of the low number of events in some outcomes [22]. I evaluated 20 bivariate associations and considered the risk of false-positive findings from multiple comparisons. I did not apply a formal

Bonferroni, false-discovery-rate, or other multiplicity correction because these analyses were exploratory rather than confirmatory; therefore, all reported p-values are unadjusted. I used a Bonferroni alpha of 0.0025 only as a conservative sensitivity reference and did not interpret isolated nominal p-values as definitive evidence of relationships. For categorical analyses, the parent thesis did not preserve the original 2 x 2 cross-tabulations. The odds ratios and exact 95% confidence intervals shown in Table II were therefore reconstructed from the unique 2 x 2 tables compatible with the reported margins and Fisher p-values, and should be interpreted cautiously. Exposure assessment was limited because sun exposure was recorded only as average hours per day, without separating occupational and recreational exposure or estimating cumulative ultraviolet exposure. Smoking was recorded only as smoking status, without current/former classification, duration, cigarettes per day, or pack-years. We recorded toxic chemical exposure only as present or absent, without documenting the specific agent, source, route, duration, frequency, or intensity. I therefore could not evaluate dose-response relationships for these exposures. I consider these findings hypothesis-generating and do not interpret a non-significant result as proof that no association exists. In addition, the parent thesis did not document the number of clinical assessors or report any interobserver agreement analysis. Surgical selection is another limitation, and the predominance of Type 3 lesions (37/41) and nasal lesions (40/41), with no Type 1 lesions and only one temporal lesion, prevented reliable comparisons across clinical grades and sites.

Conclusion

In this cross-sectional study of 41 patients with unilateral primary pterygium selected for surgical excision, I found that age, sex, daily sun exposure, smoking, and toxic chemical exposure were not clearly associated with clinical inflammation, atrophic or progressive phenotype, Stocker's line, or Fuchs spots. Because I performed multiple exploratory comparisons without formal multiplicity adjustment, I do not interpret any isolated p-value as definitive evidence of a relationship. Because my sample was mainly able to detect moderate-to-large effects, I cannot exclude smaller associations. Because the study was cross-sectional, I do not interpret these findings as evidence of temporality or causality. I therefore limit my conclusion to these 41 selected surgical patients. I do not generalize these findings to all Pakistani adults, to patients with bilateral, non-surgical or otherwise different pterygium, or to the role of these exposures in the development of pterygium in the general population. Larger, prospectively designed, and adequately powered studies would be needed to confirm these possible associations.

Authors' Contributions

Sumera Khalil: Conceptualization, study design, data collection, histopathological assessment, interpretation of findings, manuscript drafting, critical revision of the manuscript, final approval of the version to be published, and accountability for all aspects of the work.

Sadia Aman: Study design, histopathological assessment, data curation, literature review, interpretation of findings, manuscript revision, final approval of the version to be published, and accountability for all aspects of the work.

Nafeesa Kiran &Sanah Sameen: Data collection, histopathological assessment, data curation, literature review, manuscript drafting and revision, final approval of the version to be published, and accountability for all aspects of the work.

All authors: Reviewed and approved the final version of the manuscript and agreed to be accountable for all aspects of the work in accordance with ICMJE authorship criteria.

Ethical Approval

The Ethical Review Committee of the Rawalpindi Medical University, Rawalpindi, Pakistan **(RMU/Reg-19/Erc/2611/09/2024).**

Conflict of Interest

The authors declare no conflict of interest.

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Original Article

Frequency of Diabetic Nephropathy Using Renal Resistive Index in Type 2 Diabetics with Normal Albuminuria

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Abstract

Objective: To assess the prevalence of diabetic nephropathy using the renal resistive Index in patients with Type 2 diabetes and normal albuminuria.

Methodology: This cross-sectional study was conducted in the Department of Medicine, Karachi Teaching Hospital, from October 2025 to March 2026. A total of 280 individuals with type 2 diabetes of both genders and different age groups, with no known diabetic nephropathy and albuminuria below 30mg/g were included. We recorded gender, age, smoking, hypertension, diabetes duration, creatinine, eGFR, UACR, BMI, RRI, glucose, HbA1c, and ultrasonography findings. RRI >0.70 indicated high resistance. Data were analyzed using SPSS 23.

Results: We enrolled 280 individuals with type 2 diabetes mellitus and normal albuminuria, whomwhom 165r.9%) andwere male and15(4 1.1%). The mean age was 51 years, with elevated RRI (>0.70) in 23.2% (65 participants). Higher RRI was associated with longer diabetes duration, poorer glycaemic control, increased creatinine, lower eGFR, and greater overweight/obesity. Hypertension, smoking, and sex were not statistically significant.

Conclusion: This study concluded that renal resistive index can play a vital role in the early diagnosis of diabetic nephropathy in individuals with type 2 diabetes and normal albuminuria. The frequency of diabetic nephropathy (RRI >0.70) was 23.2%. The renal resistive index significantly correlated with fasting blood glucose, diabetes duration, HbA1c, serum creatinine, GFR, and lipid profile.

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Introduction

Diabetes mellitus is gradually increasing globally, posing a significant health concern. It affects around 537 million people worldwide and is expected to reach 783 million by 2045. This increased prevalence is associated with unhealthy lifestyles (e.g., low nutrition quality, lack of physical exercise), advanced age, and obesity. Low- and middle-income countries have the highest illness burden[1]. Diabetes mellitus affects 33 million people in Pakistan, with a prevalence of 26.7%. It is characterized by persistent hyperglycemia caused by insulin deficiency or resistance. Type 2 diabetes accounts for over 90% of all cases of DM[2]. Diabetes mellitus is a chronic hyperglycemic condition caused by insulin secretion, resistance, or both. Type 2 diabetes mellitus accounts for over 90% of all DM cases[3]. Chronic diabetes causes serious consequences in practically every human organ. Atherosclerosis, myopathy, neuropathy, stroke, Coronary heart disease, nephropathy, retinopathy, osteoporosis, and arthropathy are some of these medical conditions. The disease is associated with a significant mortality rate; a higher percentage of these fatalities are related to renal and cardiac disorders[4]. Diabetic nephropathy is the primary cause of renal diseases, including chronic kidney disease (CKD) and end-stage renal disease, worldwide. After 10 years of diabetes, around 40% develop diabetic nephropathy. Early identification and appropriate treatment are crucial to prevent progression of diabetic nephropathy and improve patient outcomes[5]. Diabetic nephropathy is diagnosed when GFR is less than 60 ml/min per 1.73 m^2 and urine albumin-to-creatinine ratio is more than 30 mg/g. These tests cannot detect disease in its early stages and only deviate from normal limits when structural or functional abnormalities are present[6]. A solid, sensitive, and safe approach is needed for early diagnosis of diabetic nephropathy.[5] The renal resistive index can help to diagnose diabetic nephropathy early. Doppler ultrasonography can measure resistance in blood flow inside the renal arteries. It assesses renal vascular problems, including perfusion[7]. Conventional diagnostic approaches focus solely on glomerular function, but RRI examines changes in the renal parenchyma's vascular system [8]. A literature review found that the renal resistive index is a reliable, safe, and accurate early diagnostic tool for diabetic nephropathy. This approach is very efficient, even for patients with normal albuminuria levels[9]. There have been limited studies conducted in Pakistan on the role of RRI in diagnosing diabetic nephropathy in type 2 DM[10].

Materials and method

This cross-sectional study was conducted in the Department of Medicine, Karachi Teaching Hospital, from October 2025 to March 2026. After approval from the hospital research committee. The sample size was calculated using the WHO calculator with a 95% confidence level, a 3% margin of error, and an expected frequency of diabetic nephropathy with RRI >0.70 of 7.0%.[10] Nonprobability consecutive sampling technique was used for data collection. A total of 280 individuals with type 2 diabetes of both genders and different age groups (above 18 years) with no known diabetic nephropathy and albuminuria below 30mg/g were included. Patients with a history of renal stones, known CKD, GFR <60ml/min/1.73 m2, and Pregnant women were excluded from the study. We recorded all data, including gender, age, smoking, hypertension, diabetes duration, serum creatinine, eGFR, UACR, BMI, renal resistive index, fasting blood glucose, HbA1c, and renal ultrasonography findings, on a well-designed proforma. Once the patient was adequately prepared, we performed renal Doppler ultrasonography. We collected intrarenal arterial waveforms from representative areas of both kidneys. We computed RRI as (peak systolic velocity - end-diastolic velocity) / peak systolic velocity. We categorized RRI>0.70 as high.[11] Data were analyzed using SPSS version 23. We described continuous values as mean ± standard deviation and categorical variables as frequencies and percentages. We used the chi-square test for categorical variables and the independent-samples t-test for uniformly distributed continuous variables. We used logistic regression to identify independent variables associated with high RRI. We considered $p < 0.05$ statistically significant.

Results

We enrolled 280 individuals with type 2 diabetes mellitus and normal albuminuria; 165 (58.9%) were male, and 115 (41.1%) were female. The mean age of the study participants was 51 years, and the majority were aged ≤60 years (245, 87.5%). hypertension was seen in 99(35.45) individuals and most of the individuals were overweight 194(69.1%). 56(20%) of the individuals were smoker and in 168(60%) individuals the duration of diabetes was ≤5 years while 112(40.0%) had diabetes for more than five years. We recorded family history of diabetes in 191 (68.2%) individuals, as shown in Table 1. Overall, 65 (23.2%) had elevated RRI (> 0.70). Individuals with elevated RRI had statistically higher UACR; however, all individuals had normal albuminuria.

Participants with increased RRI were older and had diabetes for a longer period of time. The average duration of diabetes was 8.0 ± 5.2 years, in contrast to 4.3 ± 3.7 years in those individuals with normal RRI. Glycemic control was similarly lower in the high-RRI group. The average HbA1c was 8.1 ± 1.4%, compared to 7.2 ± 1.1% in the normal-RRI group. Patients with higher RRI had higher serum creatinine and lower eGFR, as shown in Table 2**.** Hypertension**,** smoking, and sex showed no statistical significance; however, hypertension was more prevalent in individuals with increased RRI. Overweight/obesity was also considerably higher in the higher-RRI population (89.2% vs. 76.7%, p=0.024). Diabetes duration showed the greatest clinical association. Among participants with increased RRI, 42 (64.6%) had diabetes for over five years, compared to 70 (32.6%) with normal RRI ($p < 0.001$), as shown in Table 3.

Table 1. Clinical and Demographic Characteristics of the Study Population (n = 280)

Variable	Frequency (n)	Percentage (%)
Age, years		
≤60	245	87.5
>60	35	12.5
Sex		
Male	165	58.9
Female	115	41.1
Duration of diabetes, years		
≤5	168	60.0
>5	112	40.0
Smoking status		
Yes	56	20.0
No	224	80.0
Hypertension		
Yes	99	35.4
No	181	64.6
Body mass index (BMI), kg/m²		
Normal	57	20.4
Overweight	194	69.3
Obese	29	10.4
Family history of diabetes		
Yes	191	68.2
No	89	31.8

Table 2. Biochemical Parameters and Renal Resistive Index According to RRI Classification

Parameter	Normal RRI ≤0.70 (n = 215)	Elevated RRI >0.70 (n = 65)	*p*-value
Age, years	47.3 ± 9.6	54.1 ± 10.7	<0.001
Duration of diabetes, years	4.3 ± 3.7	8.0 ± 5.2	<0.001
Body mass index, kg/m²	26.5 ± 3.1	28.3 ± 4.0	0.001
Fasting blood glucose, mg/dL	145.1 ± 37.8	163.7 ± 45.1	0.001
HbA1c, %	7.2 ± 1.1	8.1 ± 1.4	<0.001
Serum creatinine, mg/dL	0.88 ± 0.13	0.97 ± 0.18	<0.001
eGFR, mL/min/1.73 m²	89.4 ± 13.8	80.6 ± 15.6	<0.001
UACR, mg/g	12.5 ± 6.3	16.1 ± 7.5	<0.001
Total cholesterol, mg/dL	181.7 ± 34.7	194.6 ± 39.6	0.009
Triglycerides, mg/dL	152.8 ± 58.2	176.4 ± 66.4	0.006
Mean RRI	0.65 ± 0.04	0.73 ± 0.02	<0.001

Renal resistive index; HbA1c: glycated hemoglobin; eGFR: estimated glomerular filtration rate; UACR: urinary albumin-to-creatinine ratio. Values are presented as mean ± standard deviation.

Table 3. Clinical Characteristics According to Renal Resistive Index Classification

Clinical characteristic	Normal RRI ≤0.70, n (%)	Elevated RRI >0.70, n (%)	*p*-value
Age, years			
≤60	196 (91.2)	49 (75.4)	0.001
>60	19 (8.8)	16 (24.6)	
Sex			
Male	129 (60.0)	36 (55.4)	0.518
Female	86 (40.0)	29 (44.6)	
Duration of diabetes, years			
≤5	145 (67.4)	23 (35.4)	<0.001
>5	70 (32.6)	42 (64.6)	
Hypertension			
Yes	70 (32.6)	29 (44.6)	0.081
No	145 (67.4)	36 (55.4)	
Smoking status			

Yes	39 (18.1)	17 (26.2)	0.154
No	176 (81.9)	48 (73.8)	
Body mass index			
Overweight/obese	165 (76.7)	58 (89.2)	0.025
Normal	50 (23.3)	7 (10.8)	

Renal resistive index. Values are presented as frequency and percentage.

Discussion

Diabetes mellitus is a disease of the poor in advanced nations, but an illness of the rich in underdeveloped countries. It affects a large portion of the global population, more than 220 million people, and is expected to affect around 440 million by 20303. Many issues in the form of organ damage owing to DM are occurring. Diabetes affects the body at both the micro- and macrovascular levels, causing blood pressure to fluctuate and the patient to become hypertensive[11]. Retinopathy, neuropathy, and nephropathy are the primary consequences, identified at the micro- and macrovascular levels [12,13]. Diabetic nephropathy (DN) is one of the most common microvascular problems caused by fibrosis and sclerosis of the renal arteries and parenchyma.DN results from glomerular basement membrane damage and tissue injury due to hypoxia, and it causes not only arteriole narrowing but also lower and upper urinary tract infections [14]. This damage produces kidney hypertrophy and afferent arteriole dilation. Afferent arteriole dilation raises glomerular filtration pressure and causes more injury to glomerular capillaries. Increased pressure also increases local shearing forces, contributing to mesangial cell hypertrophy and extracellular matrix secretion, initially of the basement membrane [15]. At this level, damage occurs when large protein molecules (primarily albumin) leak into the urine; this is called proteinuria (albuminuria) and can occur at the micro- or macrolevel, indicating initial kidney injury [16]. A total of 280 individuals with type 2 diabetes mellitus with normal albuminuria were enrolled in this study to determine the frequency of diabetic nephropathy using the renal resistive index. In our study, 65 (23.2%) had diabetic nephropathy (RRI >0.70). Our findings are similar to those of Shahid et al., who reported a similar frequency of DN [17]. A recent Pakistani study found that 64 (21.3%) of patients with T2DM with normal albuminuria had an increased RRI of ≥0.70[18]. This finding implies that even in the absence of conventional albuminuria, a significant number of normoalbuminuric diabetic individuals may exhibit abnormal renal vascular resistance. One of the most significant findings was the relationship between diabetes duration and RRI. In the current study, 64.6% of those with high RRI had diabetes for over five years, compared to 32.6% of individuals with normal RRI. These results are physiologically plausible because chronic hyperglycemia can cause endothelial dysfunction, microvascular damage, vascular remodeling, and increased arterial stiffness. These modifications may raise intrarenal vascular resistance prior to traditional measures like albuminuria becoming problematic[19]. A recent study also found a substantial link between RRI and diabetes duration, supporting our findings [18].In our study, the high-RRI group had lower glycemic control. The average HbA1c was 8.1 ± 1.4%, compared to 7.2 ± 1.1% in the normal-RRI group. Chronic hyperglycemia is a significant cause of diabetic microvascular problems. Poor glucose management may thus contribute to renal vascular anomalies that Doppler can detect before significant clinical albuminuria occurs. These findings are similar to those reported by Joseph and Kharadi [19,20]. These findings suggest that a high RRI may occur in one-fifth to one-quarter of normoalbuminuric T2DM patients. In contrast, variations in patient selection, ultrasonography methodology, RRI measurement, and population variables can influence prevalence. As a result, the available information suggests that RRI should be investigated further as an early marker. Importantly, take the evidence cautiously, since RRI is affected by a variety of vascular and hemodynamic variables and is not limited to diabetic nephropathy.

Conclusion

The present study concluded that renal resistive index can play a vital role in the early diagnosis of diabetic nephropathy in individuals with type 2 diabetes and normal albuminuria. The frequency of diabetic nephropathy (RRI >0.70) was 23.2%. The renal resistive index significantly correlated with fasting blood glucose, diabetes duration, HbA1c, serum creatinine, GFR, and lipid profile.

Informed Consent

We obtained written informed consent from all participants before enrollment. Participants were informed of the study purpose, the voluntary nature of participation, confidentiality, and their right to withdraw without affecting their medical care.

Funding: This study received no external funding.

Conflict of Interest

The authors declare that they have no competing interests or conflicts of interest related to this study.

Ethical Approval

Ethical approval was obtained from the Karachi Institute of Medical Sciences & Ethics Review Committee (Approval Code/Ref. No. KIMS-PA-2024/186; Date of Approval: 12 September 2024).

Authors' Contributions

Sellal Ahmed: Conceptualization, study design, participant recruitment, data collection, data analysis, manuscript drafting, and critical revision of the manuscript.

Ajmaal Jami: Conceptualization, supervision, interpretation of findings, critical revision of the manuscript, and final approval of the version to be published.

Mahnoor Khan: Literature review, participant recruitment, data collection, data organization, data analysis, and manuscript revision.

Arshad Ali: Literature review, data organization, manuscript drafting and revision, reference verification, and final approval of the version to be published.

All authors: Reviewed and approved the final version of the manuscript and agreed to be accountable for all aspects of the work in accordance with ICMJE authorship criteria.

Data Availability

The data generated during this study are not publicly available because they contain potentially identifiable participant information. Relevant information may be made available by the corresponding author upon reasonable request, subject to ethical and confidentiality requirements.

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Original Article

Time from Injury to Surgery in Anterior Cruciate Ligament (ACL) Reconstruction and Its Impact on Meniscal and Chondral Damage at Arthroscopy: A Retrospective Study from a Tertiary Care Hospital in Pakistan

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Abstract

Objective: To determine whether the Interval Between Anterior Cruciate Ligament (ACL) injury and Reconstruction is associated with Increased Prevalence and Severity of Meniscal Tears and Chondral Lesions Identified during Arthroscopy.

Methodology: This Retrospective Study was conducted in the Department of Orthopedics and Spine Surgery, Hayatabad Medical Complex (HMC), Peshawar, from January to March 2026. We reviewed medical records and arthroscopic operative reports of patients who underwent ACL reconstruction at HMC Peshawar during a defined historical period. We divided patients into two groups based on the interval from ACL injury to surgical reconstruction: An Early Surgery Group (≤3 months) and a Delayed Surgery Group (>3 months). We analyzed the data using SPSS version 23.

Results: This study examined 84 individuals undergoing ACL reconstruction. We categorized participants into an early reconstruction group (≤3 months, n=42) and a delayed reconstruction group (>3 months, n=42). We observed medial meniscal tears in 10 (23.8%) patients in the early group compared with 20 (47.6%) in the delayed group. Any meniscal injury was present in 16 (38.1%) early patients and 27 (64.3%) delayed patients. Chondral damage was identified in 7 (16.7%) early patients and 18 (42.9%) delayed patients. High-grade chondral lesions were also more frequent in the delayed group, occurring in 2 (4.8%) early versus 8 (19.0%) delayed patients.

Conclusion: The present study concluded that ACL reconstruction done more than 6 months after injury was associated with higher rates of chondral damage, overall meniscal injury, high-grade chondral lesions, and medial meniscal tears.

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Introduction

Anterior cruciate ligament (ACL) rupture is one of the most prevalent and functionally life-threatening knee injuries seen in orthopedic procedures, affecting sports, manual labor workers, and physically active individuals overall.[1] In Pakistan, ACL injuries are becoming more common in urban as well as rural communities, notably among players in cricket, football, and wrestling activities that place substantial rotational and pivot-shift demands on the knee.[2] Arthroscopic ACL reconstruction is the final surgical procedure for ACL-deficient knees in active persons. The goal is to restore joint stability, avoid further intra-articular damage, and promote return to pre-injury activity levels.[1] A well-known but sometimes overlooked result of untreated ACL deficit is the gradual disintegration of secondary intra-articular structures, notably the medial and lateral menisci and articular cartilage. The ACL-deficient knee endures recurrent bouts of aberrant tibiofemoral translation & rotatory instability during weight-bearing tasks, exposing the menisci & chondral surfaces to pathological loading stresses with every step.[3] As time passes, this biomechanical impairment emerges as meniscal tears & chondral lesions, which independently or synergistically accelerate the development of posttraumatic osteoarthritis.[4] Therefore, a crucial clinical issue is the correlation between ACL deficit duration and subsequent intra-articular injury. Identifying a clear, time-dependent injury threshold would provide strong evidence to accelerate surgical referral and reconstruction, especially in healthcare settings where procedures are often delayed due to resource constraints, diagnostic delays, or limited patient awareness. Patients with ACL injuries in Pakistan's KPK area commonly face significant delays between injury and surgical reconstruction. These delays stem from system- and patient-level factors, including delayed diagnosis in primary care and long waiting lists at tertiary centers. One is HMC Peshawar; others include financial constraints that impede timely access to specialists and cultural tendencies to seek non-surgical or traditional treatment first. Despite this well-recognized clinical reality, no published data from Pakistan quantify the magnitude of these delays or their specific impact on meniscal and chondral integrity at the time of arthroscopic reconstruction. Surgeons at HMC Peshawar routinely encounter advanced intra-articular damage at arthroscopy in patients with prolonged ACL deficiency, yet no institutional or national data substantiates this clinical observation. Therefore, the present study was conducted to determine whether the duration between ACL injury and reconstruction is associated with increased prevalence and severity of meniscal tears and chondral lesions identified during arthroscopy.

Materials and method

This Retrospective Comparative Study was conducted at the Department of Orthopedics and Spine Surgery, Hayatabad Medical Complex (HMC), Peshawar, Khyber Pakhtunkhwa, Pakistan, over 3 months. Medical records and arthroscopic operative reports of patients who underwent ACL reconstruction at HMC Peshawar during a defined historical period were reviewed. Patients were divided into two groups based on the duration from ACL injury to surgical reconstruction: an Early Surgery Group (≤3 months) and a Delayed Surgery Group (>3 months). We included physically active patients aged 16 to 50 years who underwent primary arthroscopic ACL reconstruction, with Unilateral ACL reconstruction and complete medical and Arthroscopic operative records. We excluded individuals with revision ACL reconstruction, multi-ligamentous knee reconstruction, contralateral ACL injury, and incomplete records. Based on published literature reporting meniscal damage prevalence of approximately 50% in delayed ACL reconstruction versus 25% in early reconstruction [5-6], using an alpha of 0.05 and a power of 80%, the minimum sample size per group is calculated as follows, using the two-proportion z-test formula: n = 42 per group, giving a total of 84 patients.

Grouping

Group	Definition	Comparator
Group A – Early Surgery	ACL reconstruction performed ≤6 months from date of injury	Reference group
Group B – Delayed Surgery	ACL reconstruction performed >6 months from date of injury	Study group

We collected data from inpatient surgical registers, anesthesia records, arthroscopic operative reports, outpatient consultation records, preoperative notes, and admission records; no direct patient contact was required. The primary exposure was time from injury to reconstruction in months, analyzed both continuously and categorically as ≤6 versus >6

months. Outcomes included the presence of any meniscal tear, chondral damage, combined meniscal/chondral pathology, tear type, chondral grade and location, and concomitant meniscal treatment. Data were analyzed using SPSS version 23. We expressed categorical variables as frequencies and percentages, and continuous variables as mean ± standard deviation or median with interquartile range, depending on distribution. For categorical comparisons, we used the chi-square or Fisher's exact test. For continuous variables, we used an independent-samples t-test or Mann–Whitney U test. To assess the independent association between surgical delay and intra-articular damage, we used multivariable logistic regression.

Results

This study examined 84 individuals undergoing ACL reconstruction. We categorized participants into an early reconstruction group (≤6 months, n=42) and a delayed reconstruction group (>6 months, n=42). In both groups, males predominated, and gender distribution did not differ statistically (76.0% vs. 71.3%, p=0.63). In the early reconstruction group, the mean age was 28.9 ± 7.5 years, and in the delayed group it was 30.8 ± 8.2 years. In both groups, mechanism of injury and body mass index were comparable. In the early group, the mean interval from injury to reconstruction was significantly shorter (3.9 ± 1.5 months) than in the delayed group (14.7 ± 7.1 months) (p<0.001), as presented in Table **1.** In the delayed reconstruction group, medial meniscal tears were most prevalent (47.5%) compared with the early reconstruction group (23.9%) (p=0.023). Partial meniscectomy was also more common in the delayed group, though this difference was not statistically significant (28.6% vs 11.9%, p=0.058). Chondral damage was much more prevalent after delayed reconstruction (42.9% vs 16.7%, p=0.008), and high-grade chondral lesions were found in 19.0% of delayed patients compared with 4.8% of early patients (p=0.042). Although lateral meniscus tears were more common in the delayed group, the variation was not statistically different (26.2% versus 19.0%, p=0.434). Additionally, 64.3% of delayed participants sustained meniscal damage, compared with 38.1% of early participants (p=0.016), as shown in Table **2.** Delayed reconstruction was associated with roughly threefold increased risks of medial meniscal injury (p=0.024) and any meniscal damage (p=0.016). Patients who underwent delayed reconstruction had a 3.75-fold higher risk of chondral damage (p=0.008). Although partial meniscectomy was nearly three times more prevalent in the delayed group, the correlation did not reach statistical significance (p=0.057), as shown in Table 3.

Table 1. Demographic features of the study participants

Variable	**Early ≤6 months (n=42)**	**Delayed >6 months (n=42)**	**p-value**
Mean age in years	28.9 ± 7.5	30.8 ± 8.2	0.23
Male	32 (76.2%)	30 (71.4%)	0.63
Female	10 (23.8%)	12 (28.6%)	
Mean body mass index kg/m²	25.1 ± 3.2	25.8 ± 3.5	0.35
Injury related to sports	25 (59.5%)	22 (52.4%)	0.51
Injury due to road traffic	12 (28.6%)	14 (33.3%)	0.64
Other mechanism	5 (11.9%)	6 (14.3%)	0.76
Mean time from injury to surgery in months	3.9 ± 1.5	14.7 ± 7.1	<0.001

Table 2. Outcomes of Arthroscopic meniscal and chondral

Arthroscopic results	**Early ≤6 months (n=42)**	**Delayed >6 months (n=42)**	**p-value**
Medial meniscal tear	10 (23.8%)	20 (47.5%)	**0.023**
Lateral meniscal tear	8 (19.0%)	11 (26.2%)	0.434
Any meniscal injury	16 (38.1%)	27 (64.3%)	**0.017**
Meniscal repair performed	7 (16.7%)	11 (26.2%)	0.287
Partial meniscectomy	5 (11.9%)	12 (28.6%)	0.058
Any chondral damage	7 (16.7%)	18 (42.9%)	**0.008**
Low-grade chondral lesion	5 (11.9%)	10 (23.8%)	0.171
High-grade chondral lesion	2 (4.8%)	8 (19.0%)	**0.042**
Medial femoral condyle lesion	4 (9.5%)	11 (26.2%)	0.049
Patellofemoral lesion	3 (7.1%)	7 (16.7%)	0.180

Table 3. Correlation between delayed ACL reconstruction and intra-articular disease.

Outcome	**Early group**	**Delayed group**	**Approximate OR**	**p-value**
Medial meniscal tear	23.8%	47.6%	2.92	0.024
Any meniscal injury	38.1%	64.3%	2.92	0.017
Any chondral damage	16.7%	42.9%	3.75	0.008

High-grade chondral lesion	4.8%	19.0%	4.71	0.043
Partial meniscectomy	11.9%	28.6%	2.96	0.057

Discussion

This study examined 84 individuals undergoing ACL reconstruction. We categorized participants into early and delayed reconstruction groups. Meniscal and chondral lesions were much more common in patients who had ACL reconstruction more than six months after injury than in those who had treatment within six months. These findings are similar to those of Prodromidis et al. They reported that ACL restoration completed more than six months after injury was associated with a considerably higher risk of medial meniscal tears than reconstruction within months.[7] Our study's findings are similarly consistent with the meta-analysis done by Mehl et al. They found a strong correlation between a longer time after ACL rupture and subsequent meniscal or cartilage lesions. The authors specifically highlighted a delay of more than six months as an essential interval for subsequent medial meniscus damage.[8] Another meta-analysis revealed no substantial distinction in meniscal or chondral lesions when relatively small intervals, such as 3-6 weeks, were used to differentiate early and delayed surgery.[9] The current study contrasts ≤6 months to >6 months, which represents a significantly longer time of ACL deficit; therefore, these conclusions do not always contradict the current results. In the delayed reconstruction group, medial meniscal tears were more prevalent than in the early reconstruction group in the present study. These findings are similar to the previous study.[10] In our study, the frequency of meniscectomy was similarly greater in the delayed group, although the difference was not statistically significant. This tendency is clinically noteworthy since growing chronicity may not only raise the likelihood of meniscal tears but may also diminish the potential of meniscus preservation or healing. Mehl et al. found that the chance of meniscal healing decreases as time since ACL rupture increases.[8] Thus, early therapy may potentially boost chances of meniscus preservation. Our study found that delayed reconstruction was associated with roughly a threefold increase in the risk of medial meniscal injury and any meniscal damage. Patients who underwent delayed reconstruction had a 3.75-fold higher risk of chondral damage. Although partial meniscectomy was nearly three times more prevalent in the delayed group, the correlation was not statistically significant. Overall, these results align with the strongest current observational data and systematic reviews indicating that prolonged ACL-deficient intervals are particularly associated with medial meniscal injury, including progressive chondral damage.[7] This study demonstrated that a longer interval between ACL injury and reconstruction may be related to medial meniscal tears, overall meniscal pathological changes, and chondral damage

Conclusion

The present study concluded that ACL reconstruction performed more than 6 months after injury was associated with higher rates of chondral damage, overall meniscal injury, high-grade chondral lesions, and medial meniscal tears.

Authors' Contributions

Muhammad Shabir: Conceptualization, study design, data collection, clinical assessment, data analysis, interpretation of findings, manuscript drafting, and critical revision.

Wasim Anwar: Conceptualization, supervision, methodological guidance, clinical assessment, interpretation of findings, critical revision of the manuscript, and final approval.

Muhammad Waqar: Data collection, clinical assessment, literature review, data analysis, manuscript revision, and reference verification.

Uzair Ul Islam: Literature review, data collection, data organization, manuscript drafting and revision, and reference verification.

All authors: Made substantial contributions to the work, approved the final version for publication, and agreed to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Original Article

Comprehensive Evaluation of Tetralogy of Fallot: Superior Diagnostic Performance and Clinical Utility of MDCT Compared to Echocardiography

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Abstract

Objective: To Assess the Diagnostic Accuracy, Incremental Value and Clinical Impact of Multi-Detector Computed Tomography (MDCT) in Patients with Tetralogy of Fallot compared with Echocardiography.

Methodology: This Cross-sectional analytical study was conducted in the Department of Pediatric Cardiology, MTI, Hayatabad Medical Complex, Peshawar, Pakistan, from January 2024 to December 2025, and included 182 patients with Tetralogy of Fallot. We performed transthoracic echocardiography and contrast-enhanced MDCT on all patients. We evaluated diagnostic performance using sensitivity, specificity, and predictive values against surgical or multidisciplinary consensus. We also considered incremental diagnostic value and clinical impact on management decisions.

Results: MDCT had better sensitivity (96.7%) and specificity (91.2%) than echocardiography (84.6% and 78.4%, respectively). MDCT accurately identified pulmonary artery anatomy in 96.7% of patients, compared with 78.0% on echocardiography. MDCT detected MAPCAs in 50.6% versus 26.4%, coronary anomalies in 25.3% versus 9.9%, and vascular abnormalities in 39.6% versus 18.7%. MDCT showed further clinically significant findings in a significant proportion of cases and influenced surgical or interventional planning in 52.8% of patients, including modification of the operative strategy.

Conclusion: MDCT has greater diagnostic and clinical value than echocardiography for the overall evaluation of Tetralogy of Fallot.

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Introduction

One of the most prevalent forms of cyanotic congenital heart disease is known as Tetralogy of Fallot (TOF), which is characterized by a constellation of four anatomical abnormalities: ventricular septal defect, overriding aorta, obstruction of the right ventricular outflow tract, and hypertrophy of the right ventricle [1-3]. Although surgical correction and perioperative care have improved greatly, precise and comprehensive anatomical delineation remains central to optimal surgical planning, risk stratification, and improved long-term outcomes [4]. Historically, echocardiography has been the first-line imaging modality because it is widely available, non-invasive, and can be used to provide real-time functional assessment [5]. Nevertheless, it is usually limited by operator dependence, limited acoustic windows, and suboptimal visualization of extracardiac vascular structures.[6].Multi-detector Computed Tomography (MDCT) has emerged in recent years as a powerful imaging tool, characterized by high spatial resolution, rapid image acquisition, and superior imaging of complex intracardiac and extracardiac anatomy in a single comprehensive examination [7,8]. It is particularly useful in TOF, where accurate evaluation of the anatomy of the pulmonary valve, main and branch pulmonary arteries, presence of additional muscular VSD, the major aortopulmonary collateral arteries (MAPCAs), anomalies of the coronary artery, and the associated vascular malformations is crucial to preoperative decision-making and surgical planning [9,10]. In addition, MDCT has shown great benefit in identifying clinically relevant findings that conventional echocardiography may miss and that could change management strategies [11]. Improvements in CT technology such as dose reduction methods and shorter acquisition times have also improved its applicability, even in the pediatric population [12,13]. Despite these benefits, automatically adding MDCT to the diagnostic pathway for all TOF patients remains controversial. Concerns about radiation exposure, cost-effectiveness, and the availability of alternative modalities like cardiac magnetic resonance imaging still affect clinical practice. More importantly, strong evidence quantifying MDCT's incremental diagnostic yield and clinical outcomes over standard echocardiography remains limited, especially regarding its impact on surgical planning and therapeutic decision-making. This uncertainty raises a critical clinical question: does MDCT provide indispensable information that justifies routine use, or is it a reserve technique for selected cases where conventional imaging is inconclusive?

Materials and Methods

This Cross-sectional analytical study was conducted in the Department of Pediatric Cardiology, MTI, Hayatabad Medical Complex, Peshawar, Pakistan, from January 2024 to December 2025. We included 182 patients diagnosed with Tetralogy of Fallot. We also used non-probability consecutive sampling, including all eligible patients who presented during the study period. We included patients of any age and gender with a confirmed diagnosis of Tetralogy of Fallot who underwent both transthoracic echocardiography and contrast-enhanced MDCT. The patients with contraindications to contrast-enhanced CT, such as severe renal insufficiency or known contrast allergy, incomplete imaging records, and those who refused participation in the study were excluded.MDCT scans were performed with a multi-slice CT scanner (Toshiba 128 Aquilion) with intravenous contrast injection. We extensively evaluated intracardiac and extracardiac structures, especially the pulmonary artery, major aortopulmonary collateral arteries (MAPCAs), coronary artery anomalies, right ventricular outflow tract obstruction, and associated vascular abnormalities. We regularly used three-dimensional and multiplanar reconstructions to enhance anatomical delineation and improve diagnostic accuracy. Intraoperative findings, where available, were considered the primary reference standard. When surgical information was unavailable, a multidisciplinary team of a Pediatric cardiologist and pediatric cardiac surgeon served as the reference standard for anatomical accuracy. The main findings were the diagnostic accuracy of MDCT compared with echocardiography in terms of sensitivity, specificity, positive predictive value, and negative predictive value. Secondary outcomes included the influence of MDCT findings on surgical or interventional planning, the detection rate of extracardiac vascular anomalies, and interobserver agreement among pediatric cardiologists. The Institutional Review Board of Hayatabad Medical Complex approved the study. We informed all patients or their guardians and obtained informed consent before inclusion, and we ensured confidentiality of patient data throughout the study.

Data Collection Procedure

All patients underwent thorough clinical assessment, followed by standardized transthoracic echocardiography and contrast-enhanced MDCT. We collected data using a structured proforma to record demographic and clinical information. Two experienced pediatric cardiologists independently reviewed the MDCT images. The pediatric cardiologists also independently performed echocardiographic evaluations.

Statically Analysis

We checked data using SPSS version 25. We presented continuous variables as mean ± standard deviation and categorical variables as frequencies and percentages. We compared sensitivity, specificity, positive predictive value, and negative predictive value for MDCT and echocardiography against the reference standard of intraoperative findings or multidisciplinary consensus. We used the chi-square test to compare modalities for paired categorical data and the McNemar test. We evaluated interobserver and intermodality agreement using Cohen's kappa statistic. We used a significance level of 0.05 for all analyses.

Results

Table 1 presents the demographic and clinical characteristics of the 182 patients with Tetralogy of Fallot. Most patients were aged ≤10 years (102, 56%), while 61 (33.5%) were 11–20 years and 19 (10.4%) were>20 years. Male patients predominated, with 104 cases (57.14%), whereas females accounted for 78 cases (42.86%). Clinically, 126 patients (69.23%) were in the preoperative stage of Tetralogy of Fallot, while 56 (30.77%) had undergone prior surgical intervention.

Table 1: Demographic and Clinical Characteristics of Patients (n = 182)

Category	Variable	Frequency (n)	Percentage (%)
Age Distribution	≤10 years	102	56
	11–20 years	61	33.6
	>20 years	19	10.4
Gender Distribution	Male	104	57.14
	Female	78	42.86

Table 2: Detection of Key Anatomical Findings (MDCT vs Echocardiography) with Statistical Comparison (n = 182)

Anatomical Parameter	Echo n (%)	MDCT n (%)	p-value
RVOT Obstruction	170 (93.41)	178 (97.80)	0.041
Pulmonary Artery Anatomy	142 (78.02)	176 (96.70)	<0.001
MAPCAs	48 (26.37)	92 (50.55)	<0.001
Coronary Anomalies	18 (9.89)	46 (25.27)	<0.001
Vascular Anomalies	34 (18.68)	72 (39.56)	<0.001

Table 2 compares the detection of key anatomical findings between echocardiography and MDCT. MDCT demonstrated significantly higher detection rates across all parameters. MDCT identified pulmonary artery anatomy in 176 patients (96.70%), compared with 142 (78.02%) on echocardiography ($p < 0.001$). MDCT identified MAPCAs in 92 patients (50.55%), whereas echocardiography identified them in only 48 (26.37%) ($p < 0.001$). Similarly, coronary anomalies were diagnosed in 46 patients (25.27%) using MDCT in comparison to 8 (9.89%) by echocardiography ($p < 0.001$).

Table 3: Incremental Diagnostic Yield of MDCT (McNemar Test Analysis)

Finding	Discordant Pairs (MDCT positive / Echo negative)	p-value (McNemar)
MAPCAs	44	<0.001
Coronary anomalies	28	<0.001
Pulmonary artery abnormalities	34	<0.001
Other vascular anomalies	38	<0.001

Table 3 demonstrates the diagnostic yield of MDCT using McNemar test analysis. MDCT detected a significant number of lesions not detected by echocardiography, including MAPCAs in 44 cases, coronary anomalies in 28 cases, pulmonary artery anomalies in 34 cases, and other vascular anomalies in 38 cases. All comparisons had p-values <0.001, confirming the superior diagnostic contribution of MDCT over echocardiography.

Table 4: Diagnostic Accuracy of MDCT vs Echocardiography (Reference: Surgical/Consensus Standard)

Modality	Sensitivity (%) [95% CI]	Specificity (%) [95% CI]	PPV (%)	NPV (%)
Echocardiography	84.62 (79.1–89.0)	78.43 (72.0–83.8)	88.25	72.09
MDCT	96.70 (93.2–98.6)	91.18 (86.5–94.6)	94.62	93.55

Table 4 below shows that MDCT and echocardiography differ in accuracy based on surgery and multidisciplinary consensus. In terms of sensitivity, MDCT was more accurate at 96.70% (95% CI: 93.2-98.6) than echocardiography, which had a sensitivity of 84.62% (79.1-89.0). Furthermore, specificity was higher for MDCT (98.65- 94.6%) compared to echocardiography, with a specificity of 78.43% 8.43% ((72.0–83.8). Moreover, MDCT showed better predictive values (PPV 94.62% and NPV 93.55%), making it a more reliable diagnostic tool.

Figure 1: Impact of MDCT on Surgical/Interventional Planning

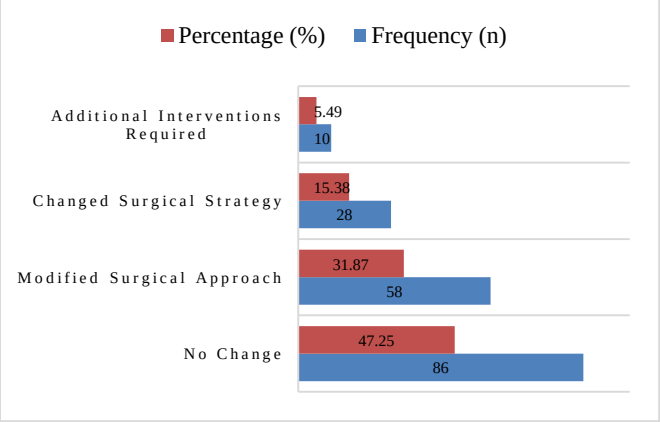


Figure 1 illustrates MDCT's impact on surgical and interventional planning. MDCT resulted in no change in management in 86 patients (47.25%), while 58 patients (31.87%) required modification of surgical approach. Surgical strategy changed in 28 patients (15.38%), and 10 patients (5.49%) required additional interventions. Overall, MDCT influenced clinical decision-making in 52.75% of cases.

Figure 2: Interobserver Agreement for MDCT Findings

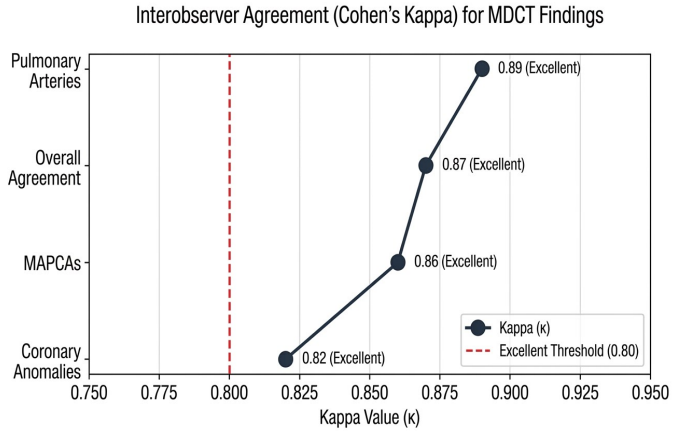


Figure 2 presents interobserver agreement for MDCT findings using Cohen's kappa statistics. Excellent agreement was observed for pulmonary artery assessment (κ = 0.89), MAPCA detection (κ = 0.86), and coronary anomalies (κ = 0.82). Overall interobserver agreement was also excellent (κ = 0.87), indicating high reproducibility of MDCT interpretation.

Figure 3: MDCT Image Quality and Diagnostic Adequacy

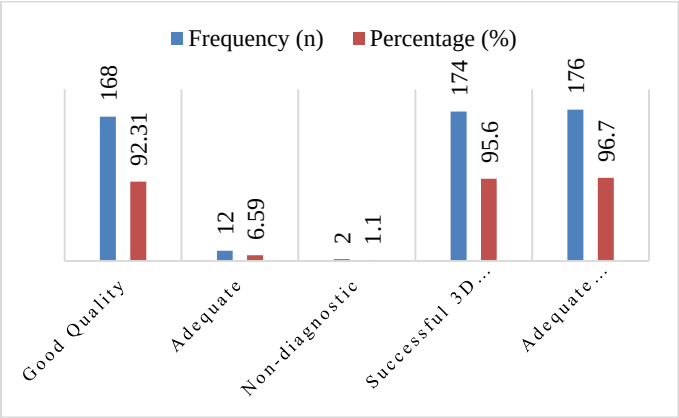


Figure 3 below shows MDCT image quality and diagnostic adequacy. Imaging quality was good in 168 patients (92.31%). In 12 cases (6.59%), image quality was adequate, and in 2 cases (1.10%), the images could not be used for diagnosis. The 3-D reconstruction was successfully done in 174 patients (95.60%). Adequate extracardiac imaging was achieved in 176 patients (96.70%), thereby confirming the reliability of the MDCT technique.

Figure 4: Overall Clinical Utility of MDCT

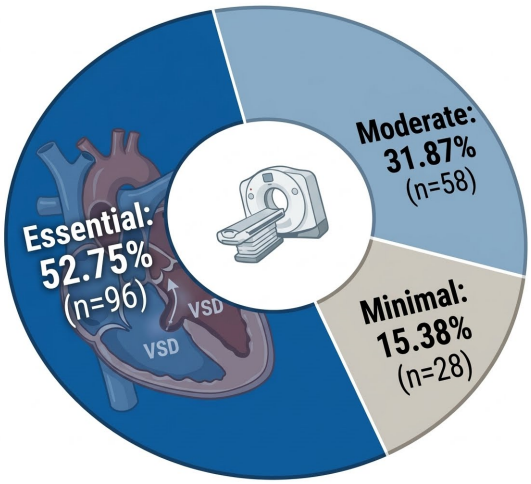


Figure 4 below depicts the clinical utility of MDCT in patients with Tetralogy of Fallot. MDCT made an essential diagnostic contribution in 96 (52.75%) patients, a moderate contribution in 58 (31.87%), and a minimal contribution in 28 (15.38%), underscoring its importance in clinical decision-making.

Discussion

In the current study, MDCT showed better diagnostic results in Tetralogy of Fallot (TOF) patients, with sensitivity of 96.70% and specificity of 91.18%, compared with echocardiography sensitivity of 84.62% and specificity of 78.43%. These results suggest MDCT provides greater anatomical clarity in complicated congenital heart disease. Previous research reported similar high diagnostic accuracy and found MDCT superior for delineating extracardiac anatomy and surgical-relevant structures in TOF patients, especially the pulmonary arteries and collateral vessels, supporting its complementary role in preoperative evaluation [14,15]. Pulmonary artery anatomy was detected significantly more often with MDCT (96.70%) than with echocardiography (78.02%, $p < 0.001$). This is in line with earlier results, which have reported that MDCT is superior in assessing the morphology of the pulmonary arteries and supravalvular stenosis, with kappa of up to 0.6-0.8 in cases of TOF [16,17]. Improved imaging in our study also confirms MDCT's superiority for spatial reconstruction of the right ventricular outflow tract's complex anatomy. For MAPCAs, we found a 50.55% detection rate with MDCT versus 26.37% with echocardiography, with an additional 44 cases ($p < 0.001$). These results align with the previous study, which noted that MDCT provides detailed mapping of MAPCA origin, distribution, and stenosis, which echocardiography usually underestimates [18,19]. This supports using MDCT in surgical planning, particularly for complex TOF variants with pulmonary atresia. In our cohort, coronary artery anomalies were identified in 25.27% of patients on MDCT as compared to 9.89% on echocardiography. Taha et al. (2022) reported similar trends and showed that MDCT significantly improves the identification of abnormal coronary courses, which is crucial for preventing intraoperative complications during TOF repair [20]. Our higher detection rate reinforces MDCT's superiority in coronary mapping. Clinically, MDCT changed surgical or interventional planning in 52.75% of cases, including 15.38% that required significant change in surgical or interventional strategy. A previous study reported similar results, finding that MDCT influenced operative decisions in more than half of TOF patients by revealing vascular and extracardiac anomalies not seen on echocardiography [21]. This supports its use as a decision-modifying imaging modality. In our study, interobserver agreement was excellent, with Cohen's kappa values of 0.82-0.89, especially for the pulmonary arteries and MAPCAs. Previous studies have reported similar high reproducibility of CT angiography for consistent and reliable assessment of pulmonary and coronary anatomy in pediatric TOF patients [22]. This reliability also supports MDCT's diagnostic value in routine clinical practice. This study has several strengths that contribute to its reliability and clinical relevance. The study uses a relatively strong analytical design with 182 Tetralogy of Fallot (TOF) patients: a prospective cross-sectional analytical design with relatively high statistical power. Observer bias was reduced by having two independent Pediatric cardiologists interpret the images separately, and diagnostic validation was enhanced by including a multidisciplinary reference standard (surgical findings or expert consensus) [23]. The study also provided a multidimensional analysis of MDCT performance using comprehensive statistical methods, including the McNemar test, Cohen's kappa, and diagnostic accuracy measures (sensitivity, specificity, PPV, NPV). It also evaluated, in addition to anatomical detection, the real-world clinical impact on surgical decision-making (52.75% of cases influenced), making the findings highly applicable to clinical practice. Nevertheless, several limitations warrant consideration. As a single-center study, the findings may not generalize to other populations and healthcare settings. The lack of universal surgical confirmation in all cases creates potential for verification bias, since some diagnoses were based on multidisciplinary consensus rather than intraoperative findings. The study also did not quantitatively assess radiation exposure

associated with MDCT, and it did not measure long-term effects following MDCT-guided management changes. Lastly, although standard, using echocardiography as the comparator may undervalue its performance in highly specialized centers.

Conclusion

Multi-detector computed tomography (MDCT) clearly outperforms conventional echocardiography for overall anatomical evaluation of Tetralogy of Fallot, especially in defining complex intracardiac and extracardiac structures such as the pulmonary arteries, coronary anatomy, and major aortopulmonary collateral vessels. Its high-resolution, three-dimensional visualization greatly improves diagnostic confidence and helps identify clinically relevant findings that echocardiography may miss. Incorporating MDCT into the diagnostic pathway significantly affects surgical and interventional decision-making and, ideally, preoperative planning for many patients. In general, MDCT can be a valuable adjunct imaging modality in Tetralogy of Fallot, particularly when detailed anatomical characterization is critical for optimal management.

Ethical Approval

Ethical approval for this study was obtained from the **Hospital Research and Ethics Committee (IREB), MTI-Hayatabad Medical Complex**, under **Doc. No. 2632**, dated **07 August 2023**, before the study began.

Informed Consent

We obtained written informed consent from all participants before enrollment. Participants and their parents/guardians were informed about the study purpose and procedures, and participation was voluntary.

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Conflict of Interest

The authors declare that they have no competing interests or conflicts of interest related to this study.

Authors' Contributions

Ziaullah: Conceptualization, study design, data collection, interpretation of findings, manuscript drafting, critical revision of the manuscript, final approval of the version to be published, and accountability for all aspects of the work.

Kamran Khattak: Study design, data collection, data curation, literature review, data interpretation, manuscript revision, final approval of the version to be published, and accountability for all aspects of the work.

Tayyaba: Conceptualization, study supervision, clinical assessment, interpretation of findings, critical revision of the manuscript for important intellectual content, final approval of the version to be published, and accountability for all aspects of the work.

All authors: Reviewed and approved the final version of the manuscript and agreed to be accountable for all aspects of the work in accordance with ICMJE authorship criteria.

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