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EDITORIAL

Teaching the 8-Second Brain: Rethinking Pedagogy for Generation Z in Health Professions Education

Ulfat Bashir[1], Sana Iqbal[2]

The education of health professionals is at a critical pedagogical crossroads that requires urgent attention. The student population of most current medical, dental, nursing, and allied health schools is made up of Generation Z: students born from 1997 to 2012. They demonstrate radically different thinking patterns, the way they engage, and what they learn compared to previous generations. The so-called 8-second brain generation, often referred to in literature, is a manifestation of short attention spans among Gen Z, likely conditioned by their digital upbringing, being mesmerized by streams of information and multimedia flowing rapidly. Although this tag begs to be oversimplified and generalized, it is true to a significant pedagogical fact: students today do not receive, process, and prioritize information in the same way as past generations did.

The traditional pedagogical practices, which are based on didactic lectures, passive learning, and delayed feedback, constitute a significant part of the curriculum delivered. Such approaches are becoming less in harmony with the changing learning environment that modern learners are taking. It is not the lack of attention span or discipline, but rather the learned adaptive cognitive strategies used in the information saturated environment in Gen Z. Instead of viewing generational traits as an obstacle to interdisciplinary teaching and learning, the educators can exploit normalizing behaviour as the chance to establish new forms of exploration, motivate more personal investment in the learning process, promote clinical reasoning and promote adaptive expertise.

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The Generation Z: Cognitive and Learning Attributes.

Generation Z is Digital Natives, and they were not supposed to know any life without the internet. This generation, therefore, possesses distinctive cognitive patterns, developed within these instruments, as well as through daily exposure to algorithmically filtered information, on-demand content, and online communication. Increasingly sophisticated algorithms have left-fingered shifts to combine, join, and add extant knowledge with new notes, the ability of which can promote rapid scanning over visual prioritization or nonlinear browsing of the data. In this regard, such learners are likely to be attracted to short content presented in a visual, interactive format rather than long text-based materials.

Furthermore, multitasking is generally discussed as an extremely deleterious aspect of the academic environment, and numerous researchers claim that this concept may result in the specialization in one task. Nevertheless, it may also indicate the increased ability to quickly switch between multiple streams of information. This ability enhances flexibility in dynamically evolving operations in heterogeneous learning settings and develops the skills to quickly combine different concepts through active-learning methods. The case of Generation Z is that they are socially conscious and demand genuineness, inclusivity and meaningful work. Learning may be enhanced when real-world impact, ethical responsibility and patient outcomes are related. It is a valuable chance to realize the opportunities of patient-centred and socially responsible pedagogies, which help to form the professional identity in the education of health professions.

Rethinking Pedagogy: Principles for Reform

Even though the characteristics of learners change, most health professions courses still cling firmly to pedagogies based on the industrial-age model of learning (i.e. the long lecture, assessment based on memorizing, and hierarchical teacher-centred delivery). These methods were effective in the past

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for passing on substantial amounts of foundational knowledge; however, they do not bode well for the development of clinical reasoning, adaptive expertise, and lifelong learning competencies that practitioners in human care systems should be capable of in the present day.

Nevertheless, it does not imply that education in health professions among Generation Z should be less demanding or lack a background. Instead, it requires a change in pedagogical orientation informed by learning science, cognitive psychology, and modern research in education.

1. Microlearning and Cognitive Chunking:

Microlearning is an emerging strategy to keep up with the shorter attention span, digital behaviour, higher adaptiveness and better retention of learning among the Generation Z. Segmentation of content into limited-focus, short-form materials aids attention control, as well as reduces cognitive load. Microlearning can be used to engage in a progressive learning process through short videos, case studies, or concept summaries, and to enable students to review the content when necessary. These techniques enhance retention and facilitate spaced repetition when placed in a strategic location.

2. Active and Experiential Learning:

Generation Z learners are active participants rather than passive receivers of information, and such learning conditions foster dynamism and creativity in the learning process. Such strategies as case-based learning, team-based learning, the flipped classroom and problem-based instruction improve clinical reasoning, collaboration, and decision-making skills that are essential in practice.

3. Technology-Rich Learning Environments:

The learning ecosystems that successfully utilize technology should be based on the learning preferences of Generation Z. Technology-enhanced environment must not merely digitalize the conventional lectures; the teachers must employ technology to make the learning process more enriched. The interactive platforms, adaptive learning systems, virtual reality simulations, etc. are such tools that make learning process personal, encourage active interaction and immersive learning environment that is nearly comparable to the manner in which the contemporary learner processes information.

4. Continuous Feedback and Assessment for Learning:

Generation Z is responsive to positive immediate feedback; a tendency reinforced by studies showing that feedback is among the most influential predictors of achievement, with effects on achievement of nearly 0.70 in meta-analysis. Self-regulation and formative learning are facilitated with the help of frequent low-stakes tests, peer feedback, digital quizzes, and reflective exercises. The assessment strategies are supposed to focus on application, logic, and clinical judgment as opposed to memorization. Nevertheless, the level of motivation may decrease in entirely online, self-directed environments, without transparency and social support. Although this generation favors the use of technology in learning, prolonged involvement requires being set with expectations, guided, and specifically with academic support.

5. Development of Self-Managed and Life-Long Learning:

Due to the dynamism of medical knowledge, the ability to learn is as significant as the knowledge itself. Metacognitive strategies, critical thinking and reflecting practices should be explicitly taught by instructors, whereas guided consideration, mentoring and contemplation models can be used to promote self-regulated learning and professional growth.

6. Passionate Learning and Patient-Centred Learning:

By connecting educational material to patient outcomes, community health needs, and ethical responsibilities, motivation and professional identity development are enhanced. Service learning and community engagement initiatives, as well as patient stories, reflect the social responsibility of health professionals and align well with those of Generation Z.

The 8-second brain labelling poses the risk of making students look deficient rather than differently endowed. Attention is not a trait but rather a process involving relevance, cognitive load, emotional investment, and instructional design. In cases where learning activities are interactive, clinically significant, and cognitively adaptable, learners show sustained engagement and intensive information processing.

Thus, the key issue is not the process of teaching learners with a short attention span, but rather how to design learning activities that truly capture their attention.

Faculty development is required in pedagogical change. Teachers should be empowered to shift from being movers of knowledge to facilitators, designers, and coaches. Educational technology, assessment literacy and active learning methodologies training and development are essential.

Institutional leadership is also very important. To sustain the course, a flexible curriculum, investment in simulation and online resources and acknowledgement of educational creativity are needed.

Health professional education can bring adaptive expertise, clinical judgement and ongoing learning by reorganizing teaching strategies in terms of modern learning science and student traits. Educators may use them to create more responsive, effective, and compassionate training rather than viewing generational differences as issues.

Generation Z will bring with them distinct cognitive skills, digital literacy, and intentional resolve into health professional education. generate novel cognitive skills, digital literacy, and intentional resolve into health professional education. The current existence of outdated teaching methods, which are not compatible with these qualities, endanger interactions and produce incompetent professionals. Rediscovering the world of pedagogy in terms of microlearning, active interaction, digital technologies, continuous feedback, and patient-centered meaning may transform the learning experience and improve the readiness of graduates to the modern healthcare practice.

The concept of the 8- second brain should not state that there has been less ability, but it is an invitation to redesign the learning spaces that capture attention through relevance, interaction and purpose. The future of the education of health professionals cannot be based on maintaining traditional methods, but on their adaptation to the needs of learners and the modern healthcare environment.

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EDITORIAL

Editorial: Analytical Challenges in Drugs of Abuse Testing

Muhammad Aamir

Drugs of Abuse (DOA) group includes drugs ranging from therapeutic drugs e.g., benzodiazepines, opioids to illegal drugs e.g., Phencyclidine, lysergic acid diethylamide etc. Prevalence of DOA is on the rise in our society.[1] According to United Nations Office of Drugs and Crime(UNODC) there are 6.7million drug users in Pakistan which also happens to be the largest consumer of heroin in south east Asia.[2] Besides addiction, drug abuse is linked to a variety of health problems, including HIV/AIDS, cancer, heart disease, and many more. It is also linked to homelessness, crime, and violence. In essence, DOA addiction is costly to both individuals and society. Keeping in view the increasing use of DOA in our society, its testing has become an indispensable service in modern laboratories and many large or medium sized medical laboratories in Pakistan are involved in DOA testing. From emergency departments and workplace compliance programs to pain management clinics and forensic investigations, laboratories play a central role in detecting these drugs that can impair judgement, threaten safety or contribute to morbidity and mortality. However, as new patterns of substance of abuse evolve and analytical technologies advance, laboratories face mounting scientific, operational, ethical and regulatory challenges in delivering accurate and clinically meaningful results. One of the most pressing challenges is the rapid proliferation of new psychoactive substances leading to shifting in patterns of drug abuse.[3] Synthetic cannabinoids, designer stimulants, novel benzodiazepines and synthetic opioids like fentanyl analogues have complicated traditional testing paradigms. Standard immunoassay screening panels that are designed to detect common drugs like opiates, cannabinoids, cocaine, amphetamines, benzodiazepines and barbiturates often fail to identify newer compounds or cross react unpredictably. This puts the laboratories under pressure to develop and validate methods for the new drugs that have joined the DOA menu.

Most laboratories rely on a two-tiered approach: rapid immunoassay screening followed by confirmatory testing using Gas Chromatography-mass spectrometry (GC-MS) or Liquid chromatography-tandem mass spectrometry (LC-MS/MS).[4] While immunoassays offer speed and cost effectiveness, they are inherently limited by cross reactivity (False positive results) and variable sensitivity (False Negative results).[5] False positive results due to administration of some over the counter prescriptions can have devastating consequences in clinical, occupational or legal contexts. Conversely false negative results may provide false reassurance particularly in overdose settings.[6] Confirmatory technologies though are more specific but have very high upfront costs, require specialized expertise to handle the technology and may not be available around the clock in smaller institutions. Laboratories must therefore strike a delicate balance between turnaround time and analytical rigor especially in emergency medicine where clinical decisions are time-sensitive.

Interpretation of results of DOA are also complex and context-dependant. Factors such as drug metabolism, timing of ingestion, Specimen type (Urine, blood, oral fluid, hair) and individual variability can specifically influence findings.[7] For example, urine testing reflects prior exposure rather than current impairment.[8] Blood concentrations may correlate closely with intoxication but are more invasive and logistically demanding. Laboratories bear the responsibility of not only generating accurate results but also educating clinicians about the limitations of drug testing. Misinterpretation can strain patient-provider relationship.

Laboratories must adhere to strict standards for chain of custody documents and reporting results that have forensic implications requiring Forensic Toxicology services must be accredited under ISO standards along with robust quality system management with continual proficiency testing.

When it comes to DOA testing laboratories are often

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caught at the intersection of public health objectives and individual rights. The expansion of drug testing in workplaces, schools and even prenatal-care have raised ethical questions about consent, privacy and potential discrimination. As addiction is increasingly recognized as a chronic medical condition rather than a moral failure, laboratories must ensure that testing policies align with principles of fairness, transparency and clinical necessity.

The above mentioned challenges require a multifaceted approach. It requires investment in advanced analytical technologies,[9] continuous assay developments and enhanced collaborations between laboratorians, toxicologists and clinicians. Moreover, interpretation guidelines are needed to be standardized to withstand legal challenges[10] along with education initiatives to ensure appropriate test ordering and their interpretation. We also need to safeguard patients interest while supporting public safety. The goal is not merely to detect drugs but to provide reliable information that supports sound clinical care, informed policy and compassionate responses to one of the most complex public heath challenges of our time.

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ORIGINAL ARTICLE

Molecular Subtypes of Breast Cancer in Quetta - A Hospital-Based Study

Muhammad Zubair[1], Javeria Faridi[2], Syed Salman Ali[3], Nabeel Khan Afridi[4], Akhter Ali Bajwa[5], Hamza Mansur[6]

ABSTRACT

Objective: This study aimed to determine the molecular subtypes of breast cancer using immunohistochemistry and to assess their distribution in the study population.

Study Design: It was a retrospective observational study.

Place and Duration of Study: The study was done at Combined Military Hospital, Quetta, from January 2022 to May 2025.

Materials and Methods: The study included 105 patients with complete histopathological data. The data was analysed using SPSS version 20, and employing chi-square tests to evaluate their associations. Statistical significance was determined at p-value < 0.05.

Results: Among the 105 cases, Invasive Ductal Carcinoma (IDC) was most common (89.5%, n=94), followed by Invasive Lobular Carcinoma (ILC) (4.8%, n=5) and Mucinous Carcinoma (3.8%, n=4). Rarer types included Metaplastic carcinoma and Medullary carcinomas. IHC-based molecular subtyping revealed Luminal A as the predominant subtype (40%, n=42), followed by Luminal B (24%, n=26), Triple-Negative Breast Cancers, TNBCs (19%, n=20), and HER2-enriched (16.2%, n=17). These subtypes were correlated with the patient's age, histological grade, and proliferation index.

Conclusion: Luminal A emerged as the most common molecular subtype, typically presenting with a lower histological grade than Luminal B, HER2-enriched, and TNBCs. Most lobular carcinomas were Luminal A type. TNBCs were high-grade, more frequent in younger patients, while other subtypes were common in older age groups. Utilizing IHC markers for molecular subtyping can enhance prognosis and facilitate targeted therapies for improved patient outcomes.

Key Words*: Breast Cancers, Molecular Subtypes, Triple-negative breast cancers.*

Introduction

Breast cancer continues to be a major health concern globally. In 2018, approximately 2.1 million new cases were reported worldwide, resulting in 627,000 deaths.[1] In Asia, the burden of breast cancer has been increasing, with Pakistan reporting the highest incidence rate among Asian countries. One in every nine Pakistani women faces a lifetime risk of being diagnosed with carcinoma breast.[1] According to recent projections, the age-standardized death rate (ASDR) for breast cancer in South Asia is expected to increase by approximately 35% from 13.4/100,000 in 1990 to 18.1/100,000 in 2030.[2] Pakistan, in particular, is predicted to experience the highest percent change in ASDR between 1990 and 2030, with a staggering 62% increase.[2] A recent study of 9,766 Pakistani women showed low breast cancer knowledge, with only 42.7% aware of risk factors and 41.8% familiar with symptoms.[3] This lack of awareness leads to delayed diagnosis and poorer outcomes.

Prognostic factors are integral to the management and treatment decision-making process in breast cancer. Traditionally, key elements influencing patient outcomes include tumor size, histological grade, lymph node status, and hormone receptor expression.[4] The status of hormone receptors—specifically estrogen receptor and progesterone receptor positivity—is linked to improved outcomes and is vital for guiding targeted therapeutic strategies.[5] Additionally, HER2 status has emerged as

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a crucial factor with both prognostic and predictive value. Notably, HER2-low status is associated with favorable outcomes in hormone receptor-positive breast cancers.[5] The proliferation marker Ki67 is associated with poor prognosis when expressed at elevated levels.[6]

Molecular subtyping of breast cancer using gene expression profiling (GEP) is crucial for prognostication and treatment planning. Immunohistochemical markers such as ER, PR, HER2, and Ki-67 act as reliable surrogate markers, allowing practical classification of tumors, prediction of therapeutic response, and risk stratification, especially in settings where gene expression profiling is not routinely available.[7] These subtypes include Luminal A (ER+/PR+/HER2-/Ki-67 low), Luminal B (ER+/PR+/HER2- with high Ki-67 or HER2+), HER2-enriched (ER-/PR-/HER2+), and Triple-Negative Breast Cancers (ER-/PR-/HER2-).[8] Each subtype exhibits distinct clinical outcomes and treatment responses. For instance, Luminal A is associated with the most favorable prognosis, whereas Triple-negative (TNBCs) and HER2-enriched subtypes are linked to higher risks of locoregional recurrence.[8] Immunohistochemistry markers serve as effective surrogates for molecular subtyping, offering a cost-efficient alternative to more complex gene expression profiling methods.

The study of ER, PR, HER2, and Ki67 in breast cancer has gained increasing importance in recent times. These biomarkers are crucial in determining breast cancer subtypes, guiding treatment decisions, and predicting patient outcomes.[9] In Pakistan, where breast cancer incidence is on the rise, accurate assessment of these biomarkers is essential for optimal patient care. Such studies are limited in Pakistan, particularly in remote areas like Quetta. Therefore, determining ER, PR, HER2, and Ki67 expression is expected to significantly contribute to improving treatment outcomes and providing valuable prognostic information for breast cancer patients across the country.

Materials and Methods

This was a retrospective observational study which was conducted at Combined Military Hospital Quetta, on patients who presented with breast lesions between 01 Jan 2022 and 05 May 2025 (CMH QTA-IERB/112/2025).

The study population included adults of both genders aged 22 years to 88 years who presented with breast lumps and were diagnosed with a malignant diagnosis following trucut biopsies, incisional biopsies, and mastectomies. Also, the patients for whom immunohistochemical markers for hormone receptors ER, PR, HER2/Neu, and Ki67 were applied were included. Patients with complete clinical and histopathological data were included.

Patients with incomplete biopsy data or inadequate tissue samples for histological evaluation were excluded. Patients with benign diagnoses and on whom no Immunohistochemical markers were applied were also excluded. Poorly fixed, inadequate, and nonrepresentative specimens were also excluded.

A sample size of 105 was determined using the WHO sample size calculator, incorporating a 95% confidence interval, an anticipated population proportion of 47.2%,[10] and an absolute precision of 10%. Data was collected from hospital electronic records and histopathology archives. Ethical approval was obtained from the Institutional Review Board (CMH QTA-IERB/112/2025), Combined Military Hospital, Quetta. Data confidentiality was maintained.

All surgical specimens, including trucut, incisional biopsies and mastectomies, were reported following the guidelines recommended by the RCPath. Tumor grade was systematically assessed using the modified Bloom–Richardson grading system. For hormone receptor evaluation, the Allred scoring method was employed to quantify both the presence and activity of these receptors. This assessment involved determining the percentage of positively stained tumor cells and calculating the average intensity of the staining.[11] HER2/Neu staining was evaluated on a scale ranging from 0 to 3+. The proliferation marker Ki-67 was quantified as the percentage of cells showing positive staining among the total malignant cell count, subsequently categorized into low (≤15%), intermediate (15–30%), and high (>30%) expression groups. For analytical purposes, patients were stratified into three distinct age groups: I (less than 30 years old), II (31 to 60 years old), and III (over 60 years old)

The study aimed to investigate the interrelationships among various parameters, including patient age,

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histologic type, histologic grade, and the expression levels of Estrogen Receptor, Progesterone Receptor, HER2/neu, and the Ki-67 index. Based on the expression profiles of these key immunohistochemical markers, the tumors were classified into four main molecular subtypes: Luminal A, Luminal B, Triple-Negative Breast Cancers, and HER2-positive categories. Statistical analyses were performed using SPSS version 20. Frequencies were calculated for all relevant variables, including age demographics, hormone receptor status, HER2 status, and the distribution of histological and molecular subtypes, alongside Ki-67 results. Chi-square tests were used to determine the statistical significance of the aforementioned variables, with findings considered significant if the p-value was less than 0.05.

Results

Patients in our study ranged from 22 to 88 years in age. Their mean age was 48.93 years ±14.09. Most of the cases were between 30 and 55 years of age. Females comprised the predominant group, representing 99.1% (n=104) of the sample, while only one male accounted for 0.9% (n=1). The samples primarily consisted of trucut biopsies, 52.4% (n=55), and incisional biopsies, 27.6% (n=29) followed by modified radical mastectomy (MRM) specimens, 17.1% (n=18), and 2.9% (n=3) cases of wide local excision. Among all breast cancer cases, 89.5% (n=94) were classified as invasive ductal carcinomas, no special type (IDC NST), 4.8% (n=5) as invasive lobular carcinomas (ILC), 3.8% (n=4) as mucinous carcinomas, 1% (n=1) medullary carcinoma and 1% (n=1) as metaplastic carcinoma. The results of immunohistochemical markers ER, PR, and HER2/Neu indicated that 66.7% (n=70) of cases were ER positive, while 33.3% (n=35) were ER negative. Additionally, 54% (n=84) of cases were PR positive, and 44.8% (n=47) were PR negative. Her2/Neu showed positivity in 22.9% (n=24) cases and was negative in 75.2% (n=79) of cases, while 1.9% (n=2) cases were equivocal and were sent for confirmation by fluorescence in situ hybridization, as shown in Table I.

Molecular subtyping was conducted utilizing immunohistochemical markers, which identified Luminal A as the most prevalent subtype, accounting for 40% (n=42) of cases, followed by Luminal B at 24% (N=26), triple-negative breast cancers (TNBCs) at 19% (n=20), and Her2-enriched at 16.2% (n=17), as illustrated in Figure 1. Most of the triple-negative cancers were high-grade invasive ductal carcinoma, comprising 19.1% (n=18) of cases. Additionally, both Medullary carcinoma and Metaplastic carcinoma were also classified as triple-negative.

The majority of cases were classified as grade II tumors (52.4%, n=55), followed by grade I (26.1%, n=27) and grade III (21%, n=22). According to the Ki-67 index, most cases were categorized as low grade (38.1%, n=40) and high grade (37.1%, n=39). Ductal carcinoma in situ (DCIS) was identified in 12.5% (n=13) of cases, while lymphovascular invasion (LVI) was identified in 11.4% (n=12) of cases.

ER, PR positivity was more prevalent in age groups II and III compared to age group I. HER2/Neu positivity was predominantly observed in perimenopausal females, 87.5% (n=21), and was mostly negative in postmenopausal females, 82.6% (n=19). Tumors that were ER and PR positive and HER2-negative exhibited low histological grade with a low Ki-67 index. ER and PR positive cases demonstrated a lower Ki-67 proliferation index than ER and PR negative cases. The results indicated the lowest proliferation rate in Luminal A tumors (97.6%, n=41). The majority of Luminal B tumors exhibited moderate to high Ki-67 (42.3% and 53.8%), suggesting a higher proliferation rate than Luminal A. TNBCs and HER2-enriched tumors are highly proliferative groups, underscoring their aggressive nature. In TNBCs, 70% have a Ki-67 index greater than 30%, indicating very high proliferation and high grade. The significant p-value (0.001) provides strong statistical evidence for differences in Ki-67 expression among these subtypes, as illustrated in Table II.

The majority of Luminal A (64.3%), Luminal B (80.8%), and HER2-enriched tumors (88.2%) were observed in age group II. The majority of Triple Negative Breast Cancers (TNBCs) were also found in age group II, accounting for 55% (n=11), followed by age group I at 25% (n=5). The data indicate that Luminal A is most prevalent in age group II (31-60 years), followed by age group III (>60 years).

TNBC is most prevalent in age group I (25%), which is significantly higher than in other subtypes, suggesting a higher frequency of TNBC in younger

patients. HER2-enriched tumors are predominantly found in age group II (31–60 years). These findings suggested a significant association between age groups and molecular subtype, with a p-value of 0.019, as presented in Table III.

The association between Ki-67 proliferation and age groups was not significant statistically (p=0.157). However, these findings indicated that a high Ki-67 level (>30%) was more prevalent in age group I (13.5%). Additionally, a single case of male breast carcinoma was observed, characterized by a triple-negative status and a low proliferative index (Ki-67 <15%).

Table I: ER, PR and Her2/Neu expression and its association with Ki67 (n=105)

IHC Markers	Ki67			Total	P-value
	<15%	15-30%	>30%		
ER Positive Negative	41 (58.6%) 1 (2.9%)	14 (20%) 12 (65.7%)	15 (21.4%) 22 (62.9%)	70 (66.7%) 35 (33.3%)	0.001
PR Positive Negative	39 (67.2%) 3 (6.4%)	11 (19%) 15 (31.9%)	8 (13.8%) 29 (61.7%)	58 (55.2%) 47 (44.8%)	0.001
Her2/Neu Positive Negative Equivocal	0(%) 42 (53.2%) 0	11 (45.8%) 13 (16.5%) 2	13 (54.2%) 24 (30.4%) 2 (100%)	24 (22.9%) 79 (75.2%) 2 (1.9%)	0.001

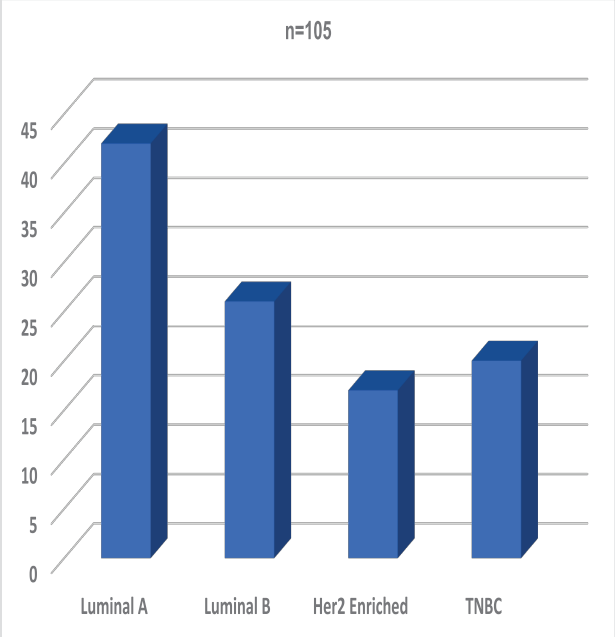

Figure-1: Molecular subtypes of breast cancer

Table II: Association of Molecular subtypes with Ki67 proliferation Index

IHC Markers	Ki67			Total	P-value
	<15%	15-30%	>30%		
Luminal A	41 (97.6%)	1 (2.4%)	0	42 (40%)	0.001
Luminal B	1 (2.5%)	11 (42.3%)	14 (53.8%)	26 (24.8%)	
Her2 Enriched	0	8 (47.1%)	9 (52.9%)	17 (16.2%)	
TNBC	0	6 (30%)	14 (70%)	20 (19%)	
Total	42 (40%)	26 (24.8%)	37 (35.2%)	105 (100%)	

Table III: Association of Molecular Subtypes with Age groups and Proliferation Index

IHC Markers	Age Groups			Total	P-value
	<30	31-60	>60		
Molecular Subtypes					
Luminal A	2 (4.8%)	27 (64.3%)	13 (31%)	42(40%)	0.019
Luminal B	1 (3.8%)	21 (80.8%)	4 (15.4%)	26(24.8%)	
Her2 Enriched	0	15 (88.2%)	2 (11.8%)	17(16.2%)	
TNBC	5 (25%)	11 (55%)	4 (20%)	20(19%)	
Total	8 (7.6%)	74 (70.5%)	23 (21.9%)	105 (100%)	
Ki67 Index					
Low grade (<15%)	2 (4.8%)	27(64.3%)	13(31%)	42 (40%%)	0.157
Intermediate grade (15-30%)	1(3.8%)	22 (84.6%)	3(11.5%)	26(24.8%)	
High grade (>30%)	5(13.5%)	25(67.6%)	7(18.9%)	37(35.2%)	
Total	8 (7.6%)	74 (70.5%)	23 (21.9%)	105(100%)	

Discussion

Breast cancer stands as the most frequently diagnosed malignancy globally, with over 2.26 million new cases reported in 2020.[12] This disease comprises various histological subtypes, each characterized by distinct clinical and pathological features. The most common form is invasive carcinoma of no special type, constituting approximately 80% of all breast cancer cases, followed by invasive lobular carcinoma at 10-15%.[13] Other less common subtypes include mucinous, tubular, medullary, metaplastic, and micropapillary carcinomas, each exhibiting unique characteristics concerning tumor size, lymph node involvement, and molecular subtypes.[14] In our study, invasive ductal carcinoma, NST (89.5%), emerged as the most prevalent subtype, accounting for the majority of cases, followed by invasive lobular carcinoma. These findings align with those of Mouabbi et al. and Jindal A et al., who reported IDC-NST in 80% and 83.09% of cases, respectively.[13,15] In our study Ductal carcinoma in situ (DCIS) was observed in 12.5% (n=13) of cases, and LVI was present in 11.2% (n=12) of cases.

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Immunohistochemical analysis in our cohort revealed estrogen receptor positivity in 66.7% (n=70) of cases, progesterone receptor positivity in 54% (n=84), and HER2/Neu positivity in 22.9% (n=24).

Molecular subtyping of breast cancer, typically determined through gene expression profiling, is vital for understanding disease heterogeneity and guiding personalized treatment strategies, offering insights into tumor behavior and therapeutic responses. Recent studies have shown prognostic significance of interferon-γ signatures in basal-like and luminal B breast cancers.[16] As gene expression profiling is not widely available, Immunohistochemistry (IHC) remains common for molecular subtyping due to its cost-effectiveness. A 2020 study found that IHC-based classifications for distinguishing between luminal A and B subtypes showed poor correlation with genomic subtyping by PAM50 assay, suggesting potential tumor misclassification.[17] However, a 2021 study proposed a deep learning framework for automatic molecular subtyping using IHC images, showing high concordance with pathologist assessment.[18]

Research consistently indicates that Luminal A and B tumors generally exhibit a lower histological grade, whereas HER2-positive and Triple-Negative Breast Cancers are often associated with higher grades. Our study corroborated this, showing ER positivity in 66.7% and PR positivity in 54% of cases, with HER2/Neu positive in 22.9%. Cases that were ER and PR positive exhibited a lower Ki67 index compared to those that were ER and PR negative. Utilizing IHC in our study, Luminal A was identified as the most common subtype at 40% (n=42), followed by Luminal B at 24% (n=26), TNBCs at 19% (n=20), and Her2 enriched at 16.2% (n=17). This pattern aligns with a study from KSA, which also found Luminal A to be the most prevalent (58.5%), followed by TNBCs (14.8%).[19] A study from India by Jindal et al. indicated that TNBCs and Luminal A were the most prevalent molecular subtypes.[15] The higher incidence of Luminal B and TNBCs in our population is likely attributable to low awareness, lack of screening, and inadequate healthcare facilities, resulting in the late presentation of patients with high-grade tumors. Despite both being hormone receptor-positive, Luminal A and Luminal B breast cancers possess distinct characteristics and clinical outcomes. Luminal A tumors, characterized by lower Ki67 expression, signify lower proliferation and a more favorable prognosis compared to Luminal B tumors.[17]

TNBCs account for 12-20% of all breast cancer cases. TNBC appears more common among South Asian women compared to Western populations, which may affect prognosis and treatment.[20] In India, TNBC rates have increased to 31% of breast cancer cases.[21] Our study found 19% (n=20) cases were TNBCs, correlating with international studies. Most TNBCs were high-grade Invasive ductal carcinoma, NST 19.1% (n=18), with 70% (n=14) showing Ki67 >30%. Our study showed one case of medullary carcinoma and one case of metaplastic carcinoma, which were both triple-negative. Triple-negative breast cancers are recognized for their aggressive nature, poor outcomes, and limited treatment options, with metastatic TNBCs having only a 12% five-year survival rate.[22] While chemotherapy was previously the only treatment, targeted therapies now include PARP inhibitors for BRCA1/2 mutations and immune checkpoint inhibitors with chemotherapy for PD-L1 positive cases.[23] Higher TNBC prevalence among our patients may be due to early onset age, diet, obesity, multiparity, socioeconomic status and screening behaviours.

In our study, the Luminal A subtype was most frequently observed in age group II (31-60 years), followed by age group III (>60 years). Conversely, TNBCs were most prevalent in age group I, a significantly higher proportion than other subtypes. This finding aligns with international studies, which also demonstrate a consistent association of TNBC with younger age groups compared to other breast cancer subtypes. Research conducted by Thakur et al. (2021) highlighted this pattern, revealing that TNBC represents about 12-24% of all breast cancer cases, with a higher prevalence among younger women.[24]

Molecular typing of breast cancer through immunohistochemistry (IHC) holds significant importance in remote regions like Balochistan, Pakistan. A study on the health poverty index indicates that Balochistan is the poorest province in Pakistan, with 62% of its population experiencing health deprivation.[25] This highlights the urgent need for efficient and cost-effective diagnostic tools in the area. IHC-based molecular subtyping offers essential

insights for the prognosis and targeted therapy of breast carcinoma, the most prevalent malignancy among women.[19] Additionally, large-scale, population-specific genomic studies from Pakistan and South Asia are also limited, emphasizing the necessity for regionally focused research to validate and potentially adapt molecular classifications developed in Western cohorts. This approach could expedite the subtyping process and reduce associated costs.

Conclusion

Immunohistochemistry (IHC) molecular typing of breast cancer is pivotal in precision oncology and personalized treatment strategies. The IHC-based classification, especially for ER, PR, HER2, and Ki67, remains the primary approach for identifying breast cancer subtypes and guiding therapeutic decisions. However, despite these advancements, the limitations of IHC-based subtyping underscore the necessity for ongoing research and the potential integration with more advanced genomic techniques to achieve accurate breast cancer classification and personalized treatment.

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CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

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DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon request.

ORIGINAL ARTICLE

Pattern of Coronary Artery Disease in Patients Under 50 Years of Age with Acute Coronary Syndrome

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ABSTRACT

Objective: To determine the angiographic patterns and severity of coronary artery disease (CAD) in patients aged ≤50 years presenting with acute coronary syndrome (ACS) at a tertiary care hospital.

Study Design: Hospital based cross sectional analytical study.

Place and Duration of Study: Department of Cardiology, PAEC General Hospital, Islamabad, from January 1 and June 30, 2025.

Materials and Methods: Consecutive patients aged 30–50 years presenting with STEMI, NSTEMI, or unstable angina who underwent coronary angiography were enrolled. Demographic characteristics, cardiovascular risk factors, and angiographic findings were recorded. Data were analyzed using SPSS version 26.0. Associations between risk factors and CAD severity were assessed using the chi-square test, with $p < 0.05$ considered statistically significant.

Results: Ninety patients were included (mean age 44.94 ± 3.94 years), with 67.8% males. STEMI was the most frequent presentation (74.4%), followed by unstable angina (16.7%) and NSTEMI (8.9%). After angiography single-vessel disease was observed in 37.8% of patients, double-vessel disease in 22.2%, triple-vessel disease in 11.1%, 28.9% had normal coronary arteries. Hypertension (55.6%) and smoking (40%) were the most prevalent risk factors.

Conclusion: Among young adults presenting with ACS, STEMI is the predominant clinical presentation, and single-vessel CAD is the most frequent angiographic pattern. A considerable proportion had normal coronary arteries, highlighting the need for further evaluation of non-obstructive mechanisms in young ACS patients.

Key Words: *Acute Coronary Syndrome, Coronary Artery Disease, Hypertension, Myocardial Infarction, ST-Elevation.*

Introduction

Coronary artery disease (CAD) is one of the most common causes of morbidity and mortality in Pakistan and worldwide[1]. Despite traditionally being considered a disease of older adults, there has been a noticeable rise in the incidence of premature CAD over the past two decades, particularly in low- and middle-income countries like Pakistan. Among young adults, the increase in the frequency of cardiovascular disorders is associated with more aggressive outcomes.[2]

An increased involvement of the genetic component has been discussed in young-aged patients with CAD.[3] Men are much more likely than women to experience CAD in the younger age group, and the bulk of these cases are associated with lower-middle-class socioeconomic structure.[4]

Acute Coronary Syndrome (ACS) represents a critical spectrum of cardiovascular emergencies—encompassing ST-elevation myocardial infarction (STEMI), non-ST elevation myocardial infarction (NSTEMI), and unstable angina (UA). Its primary etiology involves the acute disruption of an atherosclerotic plaque through rupture or erosion, causing a localized thrombotic cascade, resulting in varying degrees of coronary arterial occlusion.[5,6,17]

This occlusion of arteries leads to Myocardial ischemia, while the tissue damage varies according to the extent and duration of obstruction.[7] Recent data indicates a rising incidence of Acute Coronary

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Syndrome (ACS) in young individuals, a demographic that typically presents with single-vessel disease and a higher prevalence of modifiable risk factors.[8,9,10]

Coronary artery disease (CAD) develops as a result of multiple interacting factors, including both modifiable and non-modifiable risk factors. Commonly recognized risk factors such as smoking, obesity, diabetes mellitus, dyslipidemia, and hypertension have been widely studied and are known to contribute significantly to the development of CAD.[11,12] In recent years, an increasing number of young adults in Pakistan have been presenting with premature CAD. Rapid urbanization reduced physical activity, unhealthy dietary habits, and rising tobacco use is considered important contributors to this growing burden of cardiovascular disease in younger populations.[18] Despite this trend, there is limited local evidence describing the angiographic patterns of coronary artery disease and associated risk factors among young patients presenting with acute coronary syndrome (ACS).

A better understanding of the angiographic characteristics and related risk factors in this age group is important for early identification of high-risk individuals and for improving preventive and management strategies. Therefore, the present study was conducted to determine the angiographic patterns and severity of coronary artery disease in patients aged less than 50 years presenting with acute coronary syndrome at a tertiary care hospital in Islamabad.

Materials and Methods

A Hospital based cross-sectional analytical study was conducted in the Cardiology Department of PAEC General Hospital, Islamabad between J*anuary 1, 2025, to June 30, 2025*. Ethical approval for the study was obtained from the Institutional Review Board of PAEC General Hospital (Approval No.: PGHI-IRB(DME)-RCD-06-041).

Consecutive patients aged ≤50 years, presenting with ACS (STEMI, NSTEMI, or unstable angina) and undergoing coronary angiography, were eligible for inclusion. This age group was selected to focus on premature CAD, as CAD occurring before 50 years is considered early onset[19].

Patients of 50 years and above, with a prior history of coronary artery bypass grafting (CABG), or who did not consent were excluded. All eligible patients were informed about the objective of study and verbally informed consent was obtained prior to enrolment as approved by the IRB while ensuring confidentiality.

Based on previous studies of premature CAD and recruitment feasibility, a minimum sample size of 80 patients was targeted. Ultimately, 90 eligible patients were enrolled during the study period.

A structured proforma was used to collect demographic data (age, sex), clinical presentation, along with each patient's clinical presentation, cardiovascular risk factors, and angiographic findings. The focused risk factors included hypertension, diabetes mellitus, smoking status, and family history of premature coronary artery disease (CAD). Hypertension was defined to have a systolic reading of 140 mmHg or higher and/or a diastolic reading of 90 mmHg or higher, or history of hypertension or taking antihypertensive medication. Diabetes Mellitus was defined as fasting blood glucose level of 126 mg/dL or more or ongoing treatment with anti-diabetic drugs.[20] Smoking was defined as either current or past use of cigarettes. A positive family history of premature CAD was noted if a first degree relative, such as a parent or sibling having CAD before the age of 55 in men or before 65 in women.[20]

Angiographic severity was classified into four categories: normal coronaries, single-vessel disease (SVD), double-vessel disease (DVD), and triple-vessel disease (TVD). For the purpose of this study, significant coronary artery disease was defined as ≥50% luminal stenosis in at least one major epicardial vessels(LAD, LCX or RCA). This threshold is widely used in angiographic studies and epidemiological research to define obstructive CAD and allows for consistent comparison with published literature.[1,21] Multi-vessel disease was defined when more than one artery met the stenosis criteria.

Data analysis was performed using SPSS version 26. Continuous variables are presented as mean ± SD, whereas categorical variables are presented as frequencies and percentages. The association between cardiovascular risk factors and CAD severity was evaluated by using the Chi-square test or Fisher's exact test, where appropriate.

To identify predictors of coronary artery disease,

binary logistic regression analysis was performed with the presence of CAD (≥50% stenosis) versus normal coronary arteries as the dependent variable. Independent variables included age, gender, smoking status, diabetes mellitus, and hypertension. Secondly, ordinal logistic regression analysis was conducted to evaluate predictors of increasing CAD severity, where angiographic severity was categorized as normal, single-vessel disease (SVD), double-vessel disease (DVD), and triple-vessel disease (TVD). The same variables entered into the regression model including age, gender, smoking, diabetes mellitus, and hypertension.

Model fit was assessed using the Hosmer–Lemeshow test, where a p-value >0.05 indicated adequate model calibration. For all other analyses, a p-value of <0.05 was considered statistically significant.

Results

A total of 90 patients aged less than 50 years presenting with acute coronary syndrome (ACS) were included in the analysis. The mean age was 44.94 ± 3.94 years. Males comprised 67.8% (n = 61) of the study population, while females accounted for 32.2% (n = 29).

Among ACS presentations, STEMI was most common (74.4%, n = 67), followed by unstable angina (16.7%, n = 15) and NSTEMI (8.9%, n = 8). Cardiovascular risk factors included hypertension (55.6%, n = 50), smoking (40%, n = 36), family history of premature CAD (26.7%, n = 24), and diabetes mellitus (17.8%, n = 16) (Table I). Angiographic patterns revealed: single-vessel disease (SVD) in 37.8% (n = 34), Double vessel disease (DVD) in 22.2% (n = 20), Triple vessel disease (TVD) in 11.1% (n = 10), and normal coronaries in 28.9% (n = 26).

Gender-specific patterns were as follows: **SVCAD**—males 24 (26.7%) vs. females 10 (11.1%); **DVD**—males 16 (17.8%) vs. females 4 (4.4%); **TVD**—males 8 (8.9%) vs. females 2 (2.2%); normal coronaries—males 13 (14.4%) vs. females 13 (14.4%). The association between gender and CAD severity was not statistically significant ($\chi^2 = 5.94$, df = 3, p = 0.115) (Table II). Chi-square analysis demonstrated a significant association between hypertension and CAD severity ($\chi^2 = 10.52$, df = 3, p = 0.0146), while smoking showed no statistically significant association ($\chi^2 = 6.34$, df = 3, p = 0.096), diabetes mellitus ($\chi^2 = 0.20$, df = 3, p = 0.977) and family history ($\chi^2 = 4.96$, df = 3, p = 0.178) were also not significantly associated with CAD severity (Table IV).

Binary logistic regression identified hypertension (OR = 9.51, p = 0.001) and male gender (OR = 6.55, p = 0.014) as significant independent predictors of CAD (Table V). Ordinal logistic regression confirmed that hypertension (OR = 5.04, p < 0.001) and male gender (OR = 2.83, p = 0.045) were associated with increasing CAD severity. Smoking showed increased odds but did not reach statistical significance (OR = 1.89, p = 0.183) (Table VI).

Table I: Socio-Demographic and Clinical Characteristics (N = 90)

Variables	Mean (SD)	n	%
Age (years)	44.94 (3.94)	–	–
Gender			
Male	–	61	67.8
Female	–	29	32.2
ACS Presentation			
STEMI	–	67	74.4
Unstable Angina	–	15	16.7
NSTEMI	–	8	8.9
Risk Factors			
Smoking	–	36	40.0
Hypertension	–	50	55.6
Diabetes Mellitus	–	16	17.8
Family History of CAD	–	24	26.7

Table II: Gender vs. CAD Severity (N = 90)

Gender	Normal	SVD	DVD	TVD	Total
Male	13	24	16	8	61 (67.8%)
Female	13	10	4	2	29 (32.2%)
Total	26	34	20	10	90 (100%)

Chi-square = 5.94; df = 3; p = 0.115

Table III: Distribution of Coronary Artery Involvement

Risk Factor	Chi-square (χ^2)	df	P-value
Smoking	6.335	3	0.0964
Diabetes Mellitus	0.204	3	0.9770
Hypertension	10.524	3	0.0146*
Family History	4.961	3	0.178

*Statistically significant at p < 0.05

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Table IV: Chi-Square Association Between Risk Factors and CAD Severity

Risk Factor	Chi-square (χ^2)	df	*P*-value
Smoking	6.335	3	0.0964
Diabetes Mellitus	0.204	3	0.9770
Hypertension	10.524	3	0.0146*
Family History	4.961	3	0.178

Table V: Binary Logistic Regression (Predictors of CAD)
(CAD = any stenosis ≥50% vs. normal)

Predictor	β Coefficient	P-value	Odds Ratio (OR)
Intercept	-0.3525	0.912	0.70
Age	-0.0260	0.710	0.97
Gender	1.8801	0.014	6.55
Smoking	0.1189	0.866	1.13
Diabetes Mellitus	0.8679	0.275	2.38
Hypertension	2.2521	0.0007	9.51

TABLE VI: Ordinal Logistic Regression (Normal → SVD → DVD → TVD)

Predictor	β Coefficient	p-value	Odds Ratio (OR)
Age	-0.0212	0.687	0.98
Gender	1.0413	0.045	2.83
Smoking	0.6366	0.183	1.89
Diabetes Mellitus	0.3763	0.474	1.46
Hypertension	1.6168	0.0002	5.04

Discussion

This study evaluated angiographic patterns and predictors of CAD among young adults (<50 years) presenting with ACS. The mean age was 44.9 years, and males predominated (67.8%). This was consistent with prior studies from Pakistan as well other South Asian populations, which have shown a higher prevalence of premature CAD in men due to hormonal, behavioral, and lifestyle differences.[1,2] Rehman et al. found a similar male-to-female ratio in their study in which men were affected more severely and earlier than women.[14]

Acute coronary syndrome presenting in the fourth decade reflects premature disease onset, a pattern increasingly seen in South Asian populations[5,10]. STEMI was the most common presentation in our study (74.4%), consistent with previous reports in young adults.[8,9] This likely reflects the tendency of younger patients to develop sudden plaque rupture rather than gradual erosion, often with fewer protective collateral vessels, leading to complete artery blockage. Delayed presentation to healthcare facilities may also contribute, as ischemia progresses to infarction before patients receive timely care. NSTEMI was less frequent in our cohort (8.9%), possibly due to referral or visit bias.

The high proportions of STEMI patients indicate the need for acute recognition and acute intervention among young adults as delays can lead to significant myocardial loss and early heart failure. Hypertension emerged as the most prevalent risk factor (55.6%), followed by smoking (40%), which is consistent with findings from previous studies from Pakistan and India.[8] Ashiq et al., emphasized blood pressure screening and anti-smoking campaigns as key prevention strategies.[11] Binary and ordinal regression confirmed hypertension and male gender were independently associated with CAD severity, consistent with Tabei et al. and Wang et al.[12,15]

Angiographic patterns showed SVD as the most common (37.8%), followed by DVD and TVD, with LAD involvement being predominant (54.4%), similar to Yagel et al.[10] The predominance of SVD suggests that young people typically present with atherosclerotic involvement limited to a single coronary artery, rather than the multivessel disease seen in older populations. Regardless, it has significant clinical implications to have even a single vessel occluded, which is the case typically with the LAD, as morbidity often occurs without timely interventional measures. Approximately 28.9% of patients had normal coronary angiography, likely reflecting coronary vasospasm, microvascular disease, or endothelial dysfunction, consistent with reports of ACS with non-obstructive CAD in young adults.[13,14]

Logistic regression showed that hypertension and male gender were independent predictors of CAD which is consistent with the global literature. The strength of association regarding hypertension (OR 9.51) in our dataset suggests a possible association that warrants further investigation in larger cohorts. Male gender (6.55), the second predictor, was significant in both binary and ordinal logistic regression reflecting both biological and behavioral risk differences between genders that require gender-specific management and preventive efforts on population health.

The findings from this present study can be

anticipated in the region, but also demonstrates a trend defining the Pakistani population where traditional risk factors like smoking, poor diet, and uncontrolled hypertension exist among patients with premature CAD.[3,9,15,16] With the disease developing at a younger age, this contributes to the burden of disease and preventable costs in the socioeconomic scope, as many patients are typically in their early career stage, where the disease is often experienced. Public health policy that includes preventative measures related to lifestyle modification, blood pressure monitoring, and community education are crucial to mitigating these effects.

Limitations include the single center design, small sample size, underrepresentation of NSTEMI, and absence of biochemical or genetic profiling. Future multicenter studies with larger cohorts and molecular analyses could validate and expand these findings.

Conclusion:

In young adults presenting with ACS, STEMI is the predominant clinical manifestation, with single-vessel CAD being the most common angiographic pattern. Hypertension and male gender appear to be associated with greater CAD severity in this population. Given the single-center design, larger multicenter studies are needed to confirm these findings and guide preventive strategies.

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CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

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DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon request.

ORIGINAL ARTICLE

Pseudothrombocytopenia Unveiled: Navigating Frequency and Causes in a Tertiary Care Hospital

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ABSTRACT

Objective: To determine the proportion and laboratory-identified mechanisms of pseudothrombocytopenia among patients with automated platelet counts <100 × 10^9/L in a tertiary care hospital.

Study Design: Descriptive Cross-sectional study

Place and Duration of Study: This study was conducted in the Department of Pathology, Fauji Foundation Hospital Rawalpindi, from January 01, 2025, to June 30, 2025.

Materials and Methods: All patients undergoing complete blood count analysis during the study period with an automated platelet count below 100 × 10^9/L were included. Peripheral blood smears were examined to classify the subtypes of thrombocytopenia into true thrombocytopenia and pseudothrombocytopenia, including platelet clumping, giant platelets, and abnormal platelet distribution. Data was analyzed using SPSS Statistics version 29.0. Chi-square test was applied for categorical variables, and p-value *< 0.05* which is considered statistically significant.

Results: Out of total 755 blood samples**,** morphologically consistent with true thrombocytopenia (absence of smear artefacts) accounted for the majority of cases (70.7%). Among the 221 cases of pseudo-thrombocytopenia (29.3%), platelet clumping was the most frequent cause (19.7%), followed by giant platelets (7.9%) and abnormal platelet distribution (1.6%).

Conclusion: Pseudothrombocytopenia remains a frequent laboratory artefact in patients with low automated platelet counts. Accurate classification through systematic peripheral blood smear evaluation is essential to differentiate pseudothrombocytopenia from true thrombocytopenia. Implementation of standardized laboratory verification practices supports reliable platelet count reporting and enhances patient safety.

Key Words*: Automated Hematology Analyzers, EDTA, Peripheral Blood Smear, Platelet Count, Pseudothrombocytopenia.*

Introduction

Pseudothrombocytopenia (PTCP) is well-known in vitro diagnostic artefact characterized by spuriously low automated platelet counts despite adequate in vivo levels. [1] Platelet clumping is most commonly observed in ethylenediaminetetraacetic acid (EDTA) anticoagulated samples, when cryptic glycoprotein epitopes are exposed and subsequently clumped by autoantibodies which cause in vitro platelet clumping and underestimation by automated analyzers, which fail to count as individual cells. Although EDTA induced clumping is common mechanism spuriously low automated platelet counts may also arise from additional analytical and pre-analytical factors, indicating that the phenomenon is multifactorial.[2]

This phenomenon poses a significant diagnostic challenge and laboratory reporting challenge. Failure to recognize PTCP cases might result in misdiagnosis, unnecessary delayed therapeutic interventions, additional costly testing, unnecessary transfusions, bone marrow examination, and patient anxiety. [3] According to recent data, the prevalence in routine laboratory practice is between 0.03 to 0.3%; however, hospitalized and hematology-oncology populations may have higher frequencies.[4]

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EDTA-induced platelet clumping is the most common cause of spuriously low automated platelet counts, while true thrombocytopenia may coexist with artefactual mechanisms, further complicating interpretation. [5] Furthermore, the presence of giant platelets can be misclassified by analyzers based on size thresholds, often being counted as other blood cells. A less common but notable cause is abnormal platelet distribution, often due to partial clotting or platelet satellitism around neutrophils, which also leads to erroneous underestimation.[6]

Although detection has been improved by advances in laboratory diagnostics, such as digital image analysis, alternate anticoagulant tubes (citrate, magnesium, or heparin), and improved analyzer flagging, standardization remains a concern due to variations in laboratory methods. [7] Recent reports have described transient PTCP associated with infections and immunologic stimuli, including SARS-CoV-2 infection and post-vaccination states, highlighting the dynamic nature of this artefact.[8]

The absence of systematic studies classifying PTCP according to its underlying mechanisms in tertiary care laboratories restricts evidence-based reporting practicesA comprehensive knowledge of the prevalence and implications of PTCP in our tertiary care setting would be possible via systematic study of the condition in a focus on its main causative categories: giant platelets, platelet clumping, genuine thrombocytopenia and abnormal distribution. Such studies are crucial to establish laboratory algorithms that ensure accurate reporting, avoid unnecessary treatments and enhance patient safety.[9] Given the diagnostic and clinical implications of pseudothrombocytopenia and the lack of standardized laboratory data; the objective of this study was to determine the proportion and laboratory-identified mechanisms of pseudothrombocytopenia among patients with automated platelet counts <100 × 10^9/L in a tertiary care hospital.

Materials and Methods

The study was designed as a descriptive cross-sectional observational study and was conducted in the Department of Pathology, Fauji Foundation Hospital, Rawalpindi, from January 01, 2025 to June 30, 2025. with ethical approval obtained from the Institutional Review Committee (Application Ref Number: 780/RC/FFH/RWP, dated January 4th, 2024). Patient confidentiality was maintained throughout the study. No additional blood sampling was performed other than specified in this study protocol. All eligible patients meeting the inclusion criteria during the study duration were consecutively included. Both outpatient and admitted patients were considered, and those with an automated platelet count below 100 ×10^9/L, with samples received in EDTA-anticoagulated tubes ensuring adequate sample volume and proper labeling were included. Patients were excluded if they had a platelet count above 150 × 10^9/L, known cause of thrombocytopenia(documented clinical diagnosis in hospital records (e.g., ITP, aplastic anemia, chemotherapy-induced thrombocytopenia) prior to current sample evaluation), who were taking drugs known to induce thrombocytopenia or had clotted and hemolyzed samples. Venous blood (2 mL) samples were collected by trained phlebotomy staff under aseptic conditions in tubes containing anticoagulant Ethylenediaminetetraacetic acid (EDTA) and analyzed within two hours using the Sysmex XN-1000 Automated Hematology Analyzer. All procedures adhered to the manufacturer's instructions and departmental standard operating procedures. underwent peripheral. Smears were prepared and stained with Leishman stain and manual platelet counts were performed on samples with platelet counts below 100 × 10^9/L. A third-year hematology resident examined the smears for giant platelets, platelet clumps, platelet satellitism and abnormal platelet distribution, with findings subsequently verified by senior consultant hematologists. Platelet clumping was defined by the presence of two or more discrete platelet aggregates per low-power field (10×) or readily visible clumps on smear scanning, associated with spuriously low automated platelet counts. Giant platelets were identified when platelet size equaled or exceeded that of a normal red blood cell (>7 µm), with individual platelets clearly recognizable on oil immersion. Abnormal platelet distribution was diagnosed when platelets showed uneven peripheral smear dispersion, including satellitism around leukocytes, in the absence of fibrin strands or widespread clot formation. Confirmatory testing with alternative anticoagulants was not routinely

performed. Data analysis was performed using SPSS version 29.0. Descriptive statistics were used to summarize continuous variables as mean ± standard deviation and categorical variables as frequencies and percentages. Cross tabulations were performed to examine the distribution of thrombocytopenia causes across gender, patient setting, age groups and hospital departments. Associations between categorical variables were assessed using the chi-square test. Data analysis was carried out using IBM SPSS Statistics version 29.0, with exact p-values and 95% confidence intervals calculated. The p-value was statistically significant (*P < 0.05)* and all percentages were reported together with their corresponding absolute numbers.

Results

A total of 755 patients were included in the final analysis. The findings were presented in sequential order, beginning with the demographic characteristics of the study population, followed by the distribution of thrombocytopenia causes. Cross tabulations were performed to explore the relationship of causes with gender, patient setting, age groups, and hospital departments. Chi-square tests were applied to assess statistical associations, and results were summarized in both descriptive and analytical tables.

As shown in Table I, the study population had a mean age of 46.3 ± 23.3 years. Females constituted (603/755; 79.9%) and the admitted patients (484/755; 64.1%).

The distribution of causes of thrombocytopenia is presented in Table II. Morphologically consistent with true thrombocytopenia accounted for most cases (70.7%). Among the 221 cases of pseudo-thrombocytopenia (29.3%), platelet clumping was the most frequent cause (19.7%), followed by giant platelets (7.9%) and abnormal platelet distribution (1.6%).

Table III. No statistically significant association was observed between thrombocytopenia cause and gender (p = 0.560). Statistically significant associations were identified with patient setting (p = 0.013), age group (p = 0.001), and department (p < 0.001).

The distribution of thrombocytopenia causes across demographic and clinical variables is shown in **Table IV**. True thrombocytopenia remained the most frequent finding across both genders and patient settings. A higher proportion of true thrombocytopenia was observed among inpatients compared with outpatients. Across age groups, true thrombocytopenia was most frequent in patients aged ≥61 years. Departmental distribution demonstrated variability in the pattern of causes, with pseudothrombocytopenia observed across multiple clinical services.

The results of chi-square analysis are presented in

Table I: Demographic characteristics of study population (n=755)

Variable	Category	n	%
Age (years)	Mean 46.3 ± 23.3; Range 1–101 years		–
Gender	Male	152	20.1
	Female	603	79.9
Setting	Outpatient	271	35.9
	Inpatient	484	64.1

n = 755

Table II: Laboratory-based distribution of causes of thrombocytopenia among the study population (n = 755)

Cause	n	%
True thrombocytopenia	534	70.73
Platelet clumps	149	19.74
Giant platelets	60	7.94
Abnormal platelet distribution	12	1.59

n = 755

Table III: Chi-square analysis of associations between thrombocytopenia causes and demographic and clinical variables (n = 755)

Variable	χ^2	Df	*p-value*
Gender	2.06	3	*0.560*
Setting	10.85	3	*0.013*
Age group	27.56	9	*0.001*
Department	132.12	57	*<0.001**

n = 755

A p-value of <0.05 was considered statistically significant.

Discussion

Several factors contribute to pseudothrombocytopenia; however, EDTA, the most commonly used anticoagulant for complete blood count analysis, remains the leading cause of spuriously low platelet counts. The EDTA dependent phenomenon is largely reversible using alternative anticoagulants such as citrate, oxalate, or heparin, which prevent antibody-mediated platelet agglutination. [10,11] In our study the most common cause of PTCP was EDTA

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Table IV: Distribution of laboratory-identified causes of thrombocytopenia across demographic and clinical variables (n = 755)

	Category	True thrombocytopenia n (%)	Platelet clumping n (%)	Giant platelets n (%)	Abnormal platelet distribution n (%)	Total (n)
Gender	Male	113 (74.34)	26 (17.11)	12 (7.89)	1 (0.66)	152
	Female	421 (69.8)	123 (20.4)	48 (8)	11 (1.8)	603
Patient setting	Outpatient	173 (63.8)	64 (23.6)	27 (10.0)	7 (2.6)	271
	Inpatient	361 (74.6)	85 (17.6)	33 (6.8)	5 (1.0)	484
Age group (years)	≤20	105 (74)	29 (20.4)	8 (5.6)	0 (0.0)	142
	21–40	82 (63.57)	21 (16.28)	22 (17.05)	4 (3.1)	129
	41–60	170 (68.55)	58 (23.39)	14 (5.64)	6 (2.42)	248
	≥61	177 (75.0)	41 (17.4)	16 (6.8)	2 (0.8)	236
Department	Medicine	245 (76.1)	63 (19.6)	11 (3.4)	3 (0.9)	322
	Pediatrics	69 (75.8)	18 (19.8)	4 (4.4)	0 (0.0)	91
	Gynecology	23 (50.0)	9 (19.6)	12 (26.1)	2 (4.3)	46
	General Surgery	21 (55.3)	14 (36.8)	2 (5.3)	1 (2.6)	38
	ICU	55 (85.9)	7 (10.9)	1 (1.6)	1 (1.6)	64
	Emergency Dept.	49 (76.56)	10 (15.63)	4 (6.25)	1 (1.56)	64
	Oncology	42 (93.3)	1 (2.2)	2 (4.4)	0 (0.0)	45
	Nephrology	7 (50)	3 (21.43)	3 (21.43)	1 (7.14)	14
	Others	23 (32.4)	28 (39.4)	20 (28.2)	0 (0.0)	71

n = 755

induced PTCP (which accounts for approximately 29% of total cases). Gowland et. al first reported PTCP induced by EDTA establishing its antibody-mediated in-vitro nature. [7]. Lixia Zhang et al reported the rate of EDTA induced PTCP to be 49.1% which is closely in accordance with our study findings. [9] Incidence of EDTA dependent PTCP is approximately between 0.07% and 0.20% in general hospital practice. [12] A recent national study conducted by Noureen A found that the incidence of EDTA induced psuedothrombocyopenia to be around 45% which is in strong agreement to our study.[13]

Kausar F reported the incidence of EDTA PTCP to be approximately 75%. This frequency of EDTA PTCP was quite high compared to our study. which may reflect differences in study population, laboratory protocols, or inclusion criteria. [14]

In our current study, the satellitism pattern of platelets resulting from platelet adherence to leukocytes in anticoagulated blood samples are also a cause of pseudo thrombocytopenia. Naureen A reported platelet satellitism to be around 09% while kausar F reported platelet satellitism to be approximately around 10.9% which are comparable to our study. [13,14]

Bizzaro N et al showed platelet satellitisms around polymorphonuclears. Suri et al observed Spurious thrombocytopenia due to platelet satellitisms around neutrophils, with platelet phagocytosis. [15] Platelet satellitism was also reported around eosinophils and rarely basophils. Seven patients had pseudo thrombocytopenia due to clumps around neutrophils which make it a total of (8%). This in vitro phenomenon involves platelets adhering to the plasma membrane of white blood cells in anticoagulated blood. In our study, the occurrence of

platelet satellitism was the lowest. It was observed in only one patient among PTCP. Tangella et al. has a similar finding of a very low occurrence of platelet satellitism, which was 0.1% for PTCP due to platelet satellitism describing its rare occurrence.[8]

Electronic counters may underestimate platelet counts in patients with large or giant platelets because they are not recognized as such due to their size (1.5-3 µm diameter) due to size-based misclassification, resulting in falsely low automated counts compared with manual estimation. [2] Consequently, manual counts often show higher values than automated counts in these cases. In our study, giant platelets were another cause of PTCP, Gogoi G et al reported giant platelets as a cause of PTCP around 11.5% [16] while Naureen A reported to be around 18% which is slightly higher[13].

Management of PTP involves all three steps including identification, confirmation and prevention. [17,18] Automated counters tend to miss psuedothrombocytopenia. [19] Due to inconsistent flagging of automated counters it is sometimes hard to identify PTCP.[20] Confirmation and prevention are two further crucial steps in the management of PTCP which when applied in routine blood complete picture reporting will ascertain accurate reporting.[21, 22]

This study was conducted at a single tertiary care center, which may limit the wide applicability of the findings. The analysis was restricted to patients with platelet counts below 100×10^9/L, and confirmatory testing using alternative anticoagulants or advanced platelet counting methods could not be performed in all cases due to limited resources; therefore, definitive resolution of pseudo thrombocytopenia was not possible in every patient. Future multicenter studies with larger sample sizes are recommended to better define the true burden of pseudo thrombocytopenia. The use of repeat sampling with non-EDTA anticoagulants, standardized peripheral smear review protocols and advanced platelet counting techniques should be incorporated in future studies to allow complete resolution and improve diagnostic accuracy.[17] Considering the diagnostic challenges and associated clinical risks of pseudothrombocytopenia, a structured evaluation of its prevalence and causative mechanisms in a tertiary care laboratory was undertaken. This study was conducted to support evidence-based laboratory algorithms that improve platelet count interpretation, prevent misdiagnosis, enhance patient safety.

Conclusion

Pseudothrombocytopenia represents a considerable proportion among patients with low platelet counts and requires systematic recognition in routine hematology practice to prevent misinterpretation and inappropriate clinical decisions. Automated analyzers may underestimate platelet counts; therefore, manual verification with peripheral blood smear examination is essential for accurate diagnosis. Accurate identification and classification of its underlying causes are essential to distinguish spurious thrombocytopenia from true thrombocytopenia. A structured laboratory approach incorporating peripheral blood smear review and appropriate verification strategies, supports reliable platelet count reporting. Standardization of diagnostic algorithms in tertiary care laboratories contributes to improved result interpretation and patient safety.

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CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

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DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon request.

ORIGINAL ARTICLE

Comparison of Surgical Site Infections in Emergency Laparotomy and Elective Laparotomy

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ABSTRACT

Objective: This study aimed to find out the frequency, microbiological profile, pattern and predictors of wound site infections comparing emergency and elective midline laparotomy.

Study Design: Prospective comparative observational study.

Place and Duration of Study: was conducted in Department of General Surgery Hayatabad Medical Complex, Peshawar from 1 February 2024 to 30 September 2025.

Materials and Methods: The complete data was collected on a standardized proforma. Patients were operated and post-operative data was collected during follow-up for one months.

Results: Among 328 patients, 200 (60.9%) underwent emergency and 128 (39.1%) elective laparotomies. Baseline demographics, ASA class, and comorbidities were comparable between groups. Emergency surgeries had longer operative duration ($p < 0.001$), higher peritoneal contamination (63% vs. 3.1%) ($p < 0.001$), more contaminated/dirty wounds ($p < 0.001$), and greater ICU admission (37.5% vs. 17.1%) ($p < 0.001$). Surgical site infection (SSI) was significantly higher after emergency surgery (17.0% vs. 7.8%), with more superficial and deeper or organ-space infections ($p < 0.001$). Emergency cases also showed higher rates of reoperation, readmission, 30-day mortality (5.5%), and longer hospital stay (8.7 ± 4.7 vs. 6.9 ± 1.9 days).

Conclusion: Surgical site infections were frequently higher in emergency laparotomy than in elective laparotomy, driven by contamination, wound class, and operative complexity. Several risk factors in emergency signify risk of SSI, like contamination, prolonged operative duration and intra-abdominal sepsis.

Key Words*: Emergency Laparotomy, Laparotomy, Midline Incision, Wound Site Infections, Wound Complications.*

Introduction

A surgical wound is an incision or cut made through the skin with a scalpel or device during a surgical procedure. [1,2] Surgical Site Infection (SSI), as defined by the Centers for Disease Control and Prevention (CDC), is an infection at the surgical incision or deeper tissues/organs within 30 days of surgery (or up to 90 days/1 year if an implant is involved). [2] SSI is one of the most common complications in abdominal surgeries contributing to increase in morbidity, mortality and costs of hospitalization.[3,4] Emergency laparotomies carry a higher risk of infections compared to elective surgeries, due to multiple factors including the emergency patients' burden, the poor conditions of patients which are the cause of surgery, and contaminations from complex surgical conditions.[5–7] Surgical classification of wounds is a crucial tool to predict the future rate of SSI, complications, and reoperations in patients undergoing laparotomy.[5,8] In emergency versus elective laparotomies, risk factors for SSI include prior presence of infectious disease, malnutrition, extremes of age, high BMI, smoking, and known comorbidities. [1] Surgical factors such as prolonged operation time, inadequate scrubbing, poor skin preparation, and complex tissue handling further increase infection risk, especially in emergency cases with contamination and poor patient condition.[7,9] signs and symptoms of SSI include painful, red, hot, and tender swelling, purulent discharge from the wound, presence of microorganisms on culture, and delayed healing. [2,8] Microorganisms which are already present in patients' body as natural flora can enter the body from different routes depending on the type of surgery (elective or emergency) and the healthcare setting.[4,7] Despite implementation of

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infection prevention strategies, challenges remain due to limited resources and variable training of healthcare workers. [7,10] This study is essential to know the effective and preventive strategies of improvement in outcomes of emergency and elective surgical procedures. Although several studies from tertiary care centers in Pakistan have reported limited prospective comparative data with microbiological profiles, multivariable risk analysis and predictors of SSI in these two surgical contexts remain insufficiently characterized. [5,11] This study aimed to find out the frequency, microbiological profile, pattern and predictors of wound site infections comparing emergency and elective midline laparotomies.

Materials and Methods

This prospective comparative observational cohort study was conducted in Department of General Surgery Hayatabad Medical Complex, Peshawar during period of 1 February 2024 to 30 September 2025. The sample was calculated using Cochran's formula for estimation of a single proportion with a 95% confidence level (Z = 1.96), a precision (margin of error) of 5% (d = 0.05), and an expected surgical site infection (SSI) proportion of 20.8% (p = 0.208), based on the local study by Nawab et al. [10] Using Cochran's formula $n = (Z^2\ p\ (1-p)) / d^2$, the required sample size was

$$n = \frac{1.96^2 \times 0.208 \times 0.792}{0.05^2} = \frac{(3.8416 \times 0.164736)}{0.0025} = 0.632 / 0.0025 \approx 253.$$

To account for an anticipated 10% loss to follow-up, the final target sample size was increased to 278 patients. However, we include 328 cases into the study for increasing the study power and precision of the estimates. The study population was categorized into elective (128) and emergency groups (200). Those patients are encompassed in this study who aged 18-70 years, undergoing elective or emergency midline laparotomy, Complete perioperative and 30-day follow-up data could be recorded. However, patients <18 years, non-laparotomy procedures, pre-existing wound infection, implant-only procedures, incomplete follow-up data or loss of follow-up, those who refuse to provide consent are excluded from the study.

Elective laparotomy was planned surgical procedure with preoperative optimization, whereas emergency laparotomy is an urgent unplanned surgery performed due to acute abdominal pathology. Data were collected in a standardized proforma after securing an informed consent in Urdu from every patient, after taking ethical approval from ethical board of our Institution with (HMC-QAD-F-00-IREB NO. 1740**).** This observational study was conducted and reported in accordance with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines.[12] A single prophylactic dose of Cefuroxime Sodium 1.5 grams was administered intravenously at the time of induction of anesthesia and redosing was considered if the duration of surgery exceeded 4 hours, in accordance with standard surgical prophylaxis guidelines. The patients were monitored during hospital stay subsequently followed for 30 days after discharge. Post-discharge follow-up was conducted through scheduled outpatient clinic visits, during which surgical wounds were examined and wound swabs were obtained in aseptic conditions. In addition, telephonic follow-up was performed to confirm culture reports and identify any wound-related complications for 30 days. Data were collected using a structured proforma that included both demographic and clinical variables like group classification (elective or emergency laparotomy), age, gender, ASA class (I-VI), and comorbidities such as diabetes mellitus, hypertension, chronic obstructive pulmonary disease and cardiovascular disease. Surgical data included the indication for surgery, procedure performed, duration of operation, peritoneal contamination status, wound class according to CDC classification (I-IV), and whether ICU care was required or not. Postoperative outcomes were documented for 30 days and included SSI classified according to the Centers for Disease Control and Prevention (CDC) criteria into (superficial, deep or organ space), type of microorganism isolated at first and second follow-up, need for reoperation, readmission within 30 days, mortality within 30 days, and length of hospital stay. A total of 342 patients were initially enrolled, of whom 14 were lost to follow-up during the 30-day postoperative period.

Data collected were entered into SPSS version 23.0 and statistical analysis was conducted. Mean and standard deviations were calculated for normally distributed variables, while medians and

interquartile (IQR) ranges were used for non-normal distributions. Frequency and percentages for both groups were computed for qualitative variables. Multivariable binary logistic regression analysis was performed to identify independent predictors of surgical site infection, variables including emergency versus elective surgery, age, gender, ASA class, diabetes mellitus, duration of operation, peritoneal contamination, and ICU requirement, with results expressed as odds ratios, 95% confidence intervals, and p-values. Model fitness was assessed using the Hosmer-Lemeshow goodness-of-fit test, and multicollinearity was evaluated prior to regression analysis. A p-value of ≤ 0.05 was considered statistically significant according to the normal theory method.

Results

A total of 328, 128 (39.1%) patients underwent elective laparotomy and 200 (60.9%) underwent emergency surgery. In table I; showing baseline and clinical features, overall, 200 (60.9%) of patients underwent emergency laparotomy compared to 128 (39.1%) electives, with 146 (44.5%) male (58 elective, 88 emergency) and 182 (55.5%) were female (70 elective, 112 emergency). Females constituted a slightly higher proportion of the study population. The mean age was 40.8 ± 13.5 years, with no significant difference between elective and emergency group. Table I also shows that, ASA class I and II were frequently involved with no significant differences in distribution between two groups. Additionally, Table I show comparable co-morbidity profiles including the prevalence of diabetes mellitus, hypertension, chronic obstructive pulmonary disease, cardiovascular disease with no statistical significance.

Table II; surgical features, showing elective laparotomies were frequently indicated for biliary tract disease, malignancy, and other planned procedures whereas emergency laparotomies were performed for broader spectrum of acute pathologies, including hollow viscus perforations, abdominal abscesses, peritonitis, and trauma. The indication for surgery differed significantly between the two groups. The mean duration of surgery was 155.3 ± 44.5 minutes longer significantly in emergency compare to 146.1 ± 41.3 minutes in elective surgery. It was also noted that in emergency cases there was significantly high level of peritoneal contamination 126 (63%), compare to the only 4 (3.1%) in elective cases. Similarly in table II, results show that contaminated and dirty wound classes (CDC III–IV) were significantly more frequent in emergency surgeries, whereas elective procedures were predominantly clean-contaminated. Postoperative ICU admission was also significantly higher among emergency patients 75 vs 22 (37.5% vs. 17.1%) shown in Table II.

Figure 1, show that SSI occurred more frequently in emergency group 34 (17.0%) compared to 10(7.8%) elective group. Loss to follow-up or death occurred in 14 (4.2%) of patients, predominantly in the emergency group in which SSI could not be documented in 30 days assessment and excluded from final analysis. Microbiological profile and wound healing assessed in 1 month follow-up and wounds cultures were noted. Among patients with SSI, at **first follow-up**, where normal wound healing was observed in 121 (95.7%) of elective cases compared to 145 (72.5%) of emergency cases. Gram-negative organisms *Escherichia coli* 15 (5.3%) being the most frequently isolated pathogen, followed by *Streptococcus pyogenes 8(2.4%)*, *Enterococcus* species {E. faecalis 6 (1.8%) and E. Faecium 1 (0.3%)}, *Pseudomonas spp. 1(0.3%)*, and *Staphylococcus aureus 4 (1.2%). Other isolates included Acinetobacter 2 (0.6%) and Klebsiella pneumoniae 2 (0.6%).* At the **second follow-up**, most wounds assessment shows normal wound healing in 125 (97.7%) of elective and 145 (72.5%) of emergency cases. A marked reduction in positive culture results was observed. The organisms isolated included Escherichia coli 3 (0.9%), Mycobacterium tuberculosis 1 (0.3%), Pseudomonas spp. 3 (0.9%), Staphylococcus aureus 1 (0.3%), and Streptococcus pyogenes 1 (0.3%). The majority of emergency cases showed no microbial growth 35 (10.7%), indicating resolution of infection following appropriate management.

Table III and **Figure 2** shows post operative outcomes; that reoperation 55 (27.5%), readmission 55(27.5%) and mortality within 30days 11(5.5%), were most frequently associated with emergency cases compared to elective cases. Additionally, the length of hospital stay was significantly longer among emergency patients (8.7 ± 4.7 days)

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compared to elective patients (6.9 ± 1.9 days).

In Table IV predictors of SSI are analyzed through logistic regression. This show that peritoneal contamination and duration of operation emerged as the strongest independent predictors of SSI (OR = 7.19; 95% CI: 3.58–14.45; p < 0.001) and (OR = 11.00; 95% CI: 0.99 – 13.01; p < 0.001) respectively. Age, gender, ASA class, diabetes mellitus and ICU requirement were not independently associated with SSI development.

Table I: Baseline Demographic and Clinical Characteristics

Variable	Subgroup	Elective (n=128/328)	Emergency (n=200/328)	Total (N=328)	p-value
Age	(mean ± SD)	41± 13.1	40.6 ±13.7	40.8 ±13.5	0.111
Gender	Male Female	58 (17.7%) 70 (21.3%)	88(26.8%) 112(34.1%)	146 (44.5%) 182 (55.5%)	0.816
ASA Class	I II III IV	82(64.0%) 38(29.6%) 8(6.2%) 0	139(69.5%) 43(21.5%) 13(6.5%) 5(2.5%) 0	221(67.37%) 81(24.6%) 21(6.4%) 5(1.5%) 0	0.129
Diabetes Mellitus (%)	Yes No	11(8.5%) 117(91.4%)	16(8%) 184(92 %)	27(8.2% 301(91.7%)	0.849
Hypertension (%)	Yes No	20(15.6%) 108(84.3%)	29 (14.5%) 170(85%)	49(14.9%) 278(84.7%)	0.069
COPD (%)	Yes No	3(2.3%) 125(97.6%)	1(0.5%) 199(99.5%)	4(1.21%) 324(98.7%)	0.139
Cardiovascular Disease (%)	Yes No	1(0.78%) 127(99.2%)	4(2%) 196(98%)	5(1.5%) 323(98.4%)	0.772
Independent t-test: age **Chi-square test: gender, ASA class, comorbidities.**					

Table II: Surgical Features

Variable	Subgroup	Elective (n=128) n (%)	Emergency (n=200) n (%)	Total (N=328) n (%)	p-value
Indication of Surgery					
Hepatobiliary	Biliary Tract	19 (14.8)	35 (17.5)	54 (16.5)	
	Liver	17 (13.3)	9 (4.5)	26 (7.9)	
	Spleen	3 (2.3)	3 (1.5)	6 (1.8)	
Renal / Urinary	Kidney/Ureter/Bladder	13 (10.2)	6 (3.0)	19 (5.8)	
Perforation	Small Bowel Perforation	0 (0.0)	30 (15.0)	30 (9.1)	0.000
	Stomach Perforation	0 (0.0)	26 (13.0)	26 (7.9)	
	Perforated Duodenal Ulcer	0 (0.0)	65 (32.5)	65 (19.8)	
	Abdominal Abscess	0 (0.0)	10 (5.0)	10 (3.0)	
Trauma	Blunt or stab trauma	0 (0.0)	13 (6.5)	13 (4.0)	
Malignancy	Malignancy	0 (0.0)	3 (1.5)	3 (0.9)	
Other Pathology	Other	41 (32.0)	16 (8.0)	57 (15.5)	
Duration of Operation (min)	Mean ± SD	146.1 ± 41.3	155.3 ± 44.5	149 ± 42.2	0.000
Level of Peritoneal Contamination	No peritonitis / aseptic ascites	103 (80.4)	17 (8.5)	120 (39.6)	
	Localized Peritonitis	21 (16.4)	57 (28.5)	78 (23.8)	0.000
	Contaminated / Dirty Peritoneum	4 (3.1)	126 (63.0)	130 (39.6)	

Wound Class (CDC I–IV)	I	0 (0.0)	0 (0.0)	0 (0.0)	0.000
	II	125 (97.7)	54 (27.0)	179 (54.6)	
	III	3 (2.3)	99 (49.5)	102 (31.1)	
	IV	0 (0.0)	47 (23.5)	47 (14.3)	
ICU Requirement	Yes	22 (17.2)	75 (37.5)	97 (29.6)	0.000
	No	106 (82.8)	125 (62.5)	231 (70.4)	
T-test: duration of operation **Chi-square test/Fisher's exact: indications of surgery, peritoneal contamination, wound class, ICU requirement.**					

Table III: Postoperative Outcomes

Variable	Sub groups	Elective (n=128)	Emergency (n=200)	Total (N=328)	p-value (chi square test)
Re-operation (%)	Yes No	8 (6.2%) 120 (93.75%)	55 (27.5%) 145 (72.5%)	63 (19.2%) 265 (80.8%)	0.000
Readmission within 30 days (%)	Yes No	8 (6.2%) 120 (93.75%)	55 (27.5%) 145 (72.5%)	63(19.2%) 265 (80.8%)	0.000
Mortality within 30 days (%)	Yes No	3 (3.2%) 125 (97.85%)	11(5.5%) 189 (94.5%)	14 (4.2%) 314 (95.8%)	0.000
Length of Stay (mean ± SD)	days	6.9 ± 1.9	8.7±4.7	8.0±4.0	
All patients who underwent re-operation were also readmitted within 30 days; overlap explains identical values.					

Table IV: Predictors of SSI

Variable	Odds Ratio (OR)	95% CI	p-value (Logistic Regression)
Age	0.99	0.97 – 1.02	0.875
Gender	0.95	0.47 – 1.91	0.888
ASA Class	1.37	0.82 – 2.30	0.234
Diabetes Mellitus	2.29	0.45 – 11.60	0.316
Duration of Operation	11.00	1.99 – 13.01	0.000
Peritoneal Contamination	7.19	3.58 – 14.45	0.000
ICU Required	1.12	0.44 – 2.84	0.814
Duration of operation and peritoneal contamination were identified as significant predictors of surgical site infection ($p < 0.001$).			

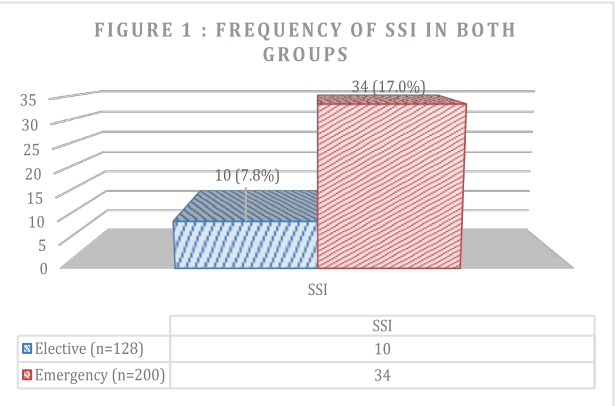

Figure 1:Frequency of SSI in both Groups.

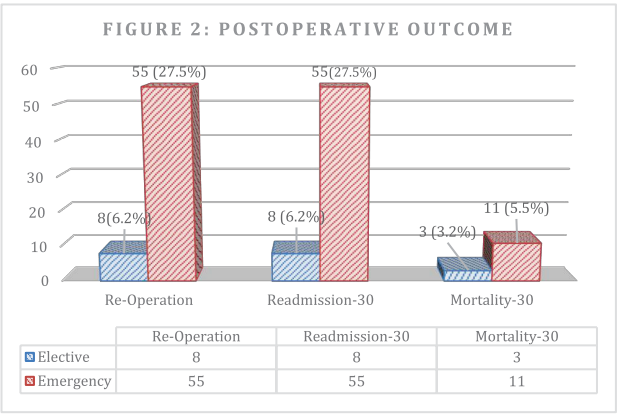

Figure 2: Postoperative Outcomes of Cohort

Discussion

The study revealed that surgical site infections (SSI) occurred more frequently and with greater postoperative morbidity in emergency procedures compared to elective procedures.[5] This increased risk in emergency cases is likely due to delayed presentation, higher level of contamination, longer operative durations and inadequate preoperative optimization.[5,13] The improved outcomes of our cohort highlighted the protective role of planned surgery and controlled operative conditions in elective surgery.

Age was not an independent predictor of SSI in our cohort, suggesting that rather than chronological

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age alone, physiological status and comorbid burden determine postoperative infection.[14] Similarly, the prevalence of comorbidities and higher ASA class did not independently predict SSI, consistently reported by Mukagendaneza et al. and Shamail Zahra et al.[5,14] Gender did not significantly affect SSI rates following emergency surgery, consistent with reporting negligible differences. [5]

Although operative duration independently predict SSI, the longer duration of emergency surgeries likely reflects greater procedural complexity, severity of disease and elevated infection risk.[5,15] Megahed et al. and Ansari et al. reported a disparity that strongly explains the higher SSI rates observed in emergency surgeries and corroborates our microbiological findings in patients predominantly with contaminated and dirty wound classes. [7,15] It emphasizes the need for good source control and antimicrobial stewardship in emergency cases. The association between higher wound class and infection risk is well documented and corroborated by microbiological profiles observed in Magehed et al. and Akter et al. [7,16] There was reduction in positive culture at the second follow-up indicating good infection control and antibiotic therapy in elective cases claiming similarity with reports by Megahed et al. and Ortega et al.[7,17] The elective cases had near normal wound healing at both follow-ups, whereas emergency cases demonstrated delayed healing and persistent infection in a subset of patients. This might be due to cumulative effect of contamination, emergency pathology and systemic stress on wound recovery and it might reinforce the importance of early intervention and standardized postoperative wound care protocols. [7] Emergency procedures were reported with higher rates of reoperation, and prolonged hospital stay, necessity of readmission and higher morbidity and mortality. [13,18] In conclusion this study demonstrated that emergency laparotomy is associated with significantly higher SSI rate and worse postoperative outcomes compared to elective laparotomy. The most critical modifiable predictor of SSI is adherent to peritoneal contamination, which highlight the need for prompt diagnosis, timely surgical intervention, optimization and infection prevention measures in emergency settings.

Being a single-center observational study, the findings may have limited generalizability with other institutions and populations. Despite these limitations, the study highlights important and clinically relevant differences between emergency and elective laparotomy. We recommend that future studies that are multicenter, detailed perioperative antibiotic protocols and stratification by wound contamination level to better define modifiable risk factors.

Conclusion

This study demonstrates that surgical site infections occur significantly more frequent and severe in emergency laparotomy compared to elective laparotomy. Peritoneal contamination, prolonged operative duration and intra-abdominal sepsis were strong predictors of SSI. Strategies aimed at early surgical intervention, effective contamination control, and optimized perioperative care may reduce infection rates and improve postoperative outcomes.

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DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon request.

ORIGINAL ARTICLE

Hospital-Based Descriptive Analysis of Surgically Treated Malignancies: A Single Center Four-Year Experience

Muhammad Imran[1], Muhammad Farhan[2], Muhammad Murad[3], Filza Usman[4], Habib Ahmed[5], Ejaz Ahmed[6]

ABSTRACT

Objective: To describe the institutional pattern of histologically confirmed malignancies managed surgically at a tertiary care hospital in Gilgit-Baltistan (GB), Pakistan, and to identify the need for structured cancer surveillance in the region.

Study Design: Retrospective record-based descriptive analysis.

Place and Duration of Study: Department of General Surgery, Shaheed Saif ur Rehman Government Teaching Hospital, Gilgit, 1st January 2021 – 31st December 2024.

Materials and Methods: Records of patients with confirmed malignant tumors treated surgically during the study period were reviewed. Tumor sites were classified using ICD-10 codes and histological diagnoses verified from pathology reports. Descriptive statistics were applied to summarize demographic and tumor characteristics. Association between gender and tumor site was analyzed using the Chi-square test.

Results: One hundred twenty-one surgically managed malignancies were included (mean age 52.4 ± 14.8 years; male-to-female ratio 1.05:1). The most frequent tumor sites were stomach (18.1%), skin (15.7%), retroperitoneum/peritoneum (15.7%), colorectal (9%), breast (9%), and ovary (8.2%). Gastrointestinal malignancies collectively constituted 35.3% of cases. Adenocarcinoma was the predominant histological subtype in gastrointestinal cancers. The annual number of cases treated increased over the four-year period, reflecting expanding surgical capacity.

Conclusion: These findings represent hospital-based case distribution rather than population-level incidence. Establishment of a regional cancer registry is essential to generate reliable epidemiological data for health planning in Gilgit-Baltistan.

Key Words: *Breast Neoplasms, Colorectal Neoplasms, Epidemiology, Surgical Oncology.*

Introduction

With an estimated mortality rate of 10.0 million deaths worldwide, Cancer is the second leading cause of death among non-communicable diseases.[1] A total of 19.9 million new cancer cases occurred in 2022, and health experts project a 43% growth by 2040.[2] Countries with poor socioeconomic status, otherwise termed as low and middle-income countries (LMICs), lack basic diagnostic centers and treatment facilities, therefore, the disease burden can rise up to 57%.[3] Global and local data in Pakistan indicate that this life-threatening condition is growing exponentially, evident by the fact that 148,000 new cases were reported between 2015 to 2016, whereas 100,000 individuals succumb to this disease annually, as reported in the WHO country cancer profile.[4] Being an LMIC with an estimated population of 241.4 million, Pakistan cannot devote adequate resources to improving health infrastructure.[5] The Karachi Cancer Registry (KCR) and Punjab Cancer Registry (PCR) are currently the only major operational cancer registries in Pakistan. However, their ability to accurately reflect national trends in cancer incidence and epidemiology remains limited due to non-uniform data collection practices and inadequate financial support for large-scale epidemiological studies. This lack of standardized methodology and resource allocation in major metropolitan registries consequently extends to the underserved and remote regions such

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as Gilgit-Baltistan (GB), further compounding the gaps in national cancer surveillance.

Due to its rugged mountainous terrain, Gilgit-Baltistan, a small province with only 1.8 million inhabitants, faces a shortage of healthcare facilities.[6] Earlier, almost all patients were referred to other provinces for cancer treatment. Nowadays, many surgical procedures are being performed at local centers to meet regional healthcare needs. The aim of the study was to assess the incidence and patterns of cancer in Gilgit-Baltistan to inform evidence-based policy, optimize resource allocation, and support the establishment of a regional cancer registry, as cancer treatment is supported through the government endowment fund.

Materials and Methods

This retrospective hospital-based descriptive study was conducted at the Department of General Surgery, Shaheed Saif ur Rehman Government Teaching Hospital (SSGTH), Gilgit, Gilgit-Baltistan, Pakistan. Ethical approval was obtained from the Institutional Ethical Review Board (Ref No. 04/IRB/2025). The study was conducted in accordance with the Declaration of Helsinki.

All consecutive patients with **histologically confirmed malignant neoplasms** managed surgically between 1st January 2021 and 31st December 2024 were eligible for inclusion. Patients with incomplete medical records and those referred to other centers before definitive surgical management were excluded. The study population, therefore, represents surgically treated malignancies at this institution and does not reflect population-based incidence.

Data were extracted from surgical registers and verified against histopathology records. Variables collected included age, gender, anatomical site of tumor (classified according to ICD-10), and histological subtype. Tumors coded under benign classifications were excluded from the final analysis.

Continuous variables (e.g., age) were summarized as mean ± standard deviation, while categorical variables (tumor site, gender, histological type) were presented as frequencies and percentages. Missing data were documented but not imputed. No population denominator was available; therefore, incidence rates were not calculated.

Associations between tumor site and gender were evaluated using appropriate categorical statistical tests after verification of assumptions. All analyses were conducted using SPSS version 26, and a two-sided p-value < 0.05 was considered statistically significant. This study is reported in accordance with the STROBE guidelines for observational studies.

Results

A total of 121 patients with histologically confirmed malignancies were managed surgically during the study period. The mean age was 52.4 ± 14.8 years. Of these, 62 (51.2%) were male and 59 (48.8%) were female. The largest proportion of cases was observed in the 31–40-year age group (n = 39; 32.2%), followed by the 41–50-year and 51–60-year groups (each n = 21; 17.4%) (Table I).

The most frequently managed tumor sites overall were stomach (n = 22; 18.1%), skin (n = 19; 15.7%), retroperitoneum/peritoneum (n = 19; 15.7%), colorectal region (n = 11; 9%), breast (n = 11; 9%), and ovary (n = 10; 8.2%) (Table II). Gastrointestinal malignancies (stomach, esophagus, colorectal, and appendix) collectively accounted for 35.3% of cases.

Tumor distribution differed between genders. Among males, the most common malignancies were stomach (n = 16; 25.8%) and skin (n = 15; 24.1%), followed by retroperitoneum/peritoneum (n = 11; 17.7%) and esophagus (n = 7; 11.2%). In females, breast cancer was the most frequent site (n = 11; 18.6%), followed by the ovary (n = 10; 16.9%), the colorectal (n = 8; 13.5%), and the retroperitoneum/peritoneum (n = 8; 13.3%) (Table III). The retroperitoneal masses include only primary malignant tumors of the retroperitoneum. After regrouping tumor categories to satisfy statistical test assumptions, a statistically significant difference in tumor distribution between male and female patients was observed (Chi-square test, $p < 0.001$). This finding reflects variation in tumor site distribution within this hospital cohort.

Histologically, adenocarcinoma was the predominant subtype in stomach (n = 19; 86.4%), colorectal (n = 10; 90.9%), esophageal (n = 6; 75%), and gallbladder cancers (n = 4; 100%). Skin malignancies were distributed between squamous cell carcinoma (n = 10; 52.6%) and basal cell carcinoma (n = 9; 47.4%). Breast cancers were primarily invasive ductal carcinoma (n = 9; 81.8%), while ovarian tumors were predominantly epithelial

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in origin (n = 7; 63.6%). Retroperitoneal/peritoneal tumors were mainly leiomyosarcoma (n = 9; 47.4%) and liposarcoma (n = 7; 36.8%) (Table IV).

An increase in the annual number of surgically treated malignancies was observed over the four-year period, with the highest number recorded in 2024 (n = 40), as illustrated in Figure 1.

Table I: Age- and Gender-Wise Distribution of Patients (n = 121)

Age Group (years)	Total n (%)	Male n (%)	Female n (%)
1–10	0 (0.0%)	0 (0.0%)	0 (0.0%)
11–20	4 (3.3%)	0 (0.0%)	4 (3.3%)
21–30	23 (19.0%)	9 (7.4%)	14 (11.6%)
31–40	39 (32.2%)	15 (12.4%)	24 (19.8%)
41–50	21 (17.4%)	11 (9.1%)	10 (8.3%)
51–60	21 (17.4%)	16 (13.2%)	5 (4.1%)
61–70	8 (6.6%)	7 (5.8%)	1 (0.8%)
71–80	5 (4.1%)	4 (3.3%)	1 (0.8%)
>80	0 (0.0%)	0 (0.0%)	0 (0.0%)
Total	**121 (100%)**	**62 (51.2%)**	**59 (48.8%)**

Table II: Leading Cancer Sites Overall (According to ICD-10 coding)

S.No	Site (ICD-10)	Number of Cases (n)	Percentage (%)
1	Stomach (C16)	22	18.1
2	Skin (C44)	19	15.7
3	Retroperitoneum / Peritoneum (C48)	19	15.7
4	Breast (C50)	11	9.0
5	Colorectal (C18)	11	9.0
6	Ovary (C56)	10	8.2
7	Esophagus (C15)	8	6.6
8	Salivary Gland (C07, C08)	7	5.7
9	Thyroid (C73)	4	3.3
10	Gall Bladder (C23)	4	3.3
11	Soft Tissue / Subcutaneous Lesion (C49)	4	3.3
12	Appendix (C18.1)	2	1.6
Total		**121**	**100**

Table III: Gender-Wise Distribution of Cancer Sites with Overall P-Value

S.No	Site (ICD-10)	Male (n)	% within Males (n = 62)	Female (n)	% within Females (n = 59)	Male % within Site	Female % within Site	Overall Significance (p-value)
1	**Stomach**	16	25.8 %	6	10.1 %	**72.7 %**	**27.3 %**	<0.01 *
2	**Skin**	15	24.1 %	4	6.7 %	**78.9 %**	**21.1 %**	—
3	**Retroperitoneum / Peritoneum**	11	17.7 %	8	13.3 %	**57.9 %**	**42.1 %**	—
4	**Breast**	0	0 %	11	18.6 %	**0 %**	**100 %**	—
5	**Colorectal**	3	4.8 %	8	13.5 %	**27.3 %**	**72.7 %**	—
6	**Ovary**	0	0 %	10	16.9 %	**0 %**	**100 %**	—
7	**Esophagus**	7	11.2 %	1	1.6 %	**87.5 %**	**12.5 %**	—
8	**Salivary Gland**	4	6.4 %	3	5.0 %	**57.1 %**	**42.9 %**	—
9	**Thyroid**	1	1.6 %	3	5.0 %	**25.0 %**	**75.0 %**	—
10	**Gall Bladder**	2	3.2 %	2	3.3 %	**50.0 %**	**50.0 %**	—
11	**Soft Tissue / Subcutaneous**	2	3.2 %	2	3.3 %	**50.0 %**	**50.0 %**	—
12	**Appendix**	1	1.6 %	1	1.6 %	**50.0 %**	**50.0 %**	—
Total		62	100 %	59	100 %	**51.2 %**	**48.8 %**	—

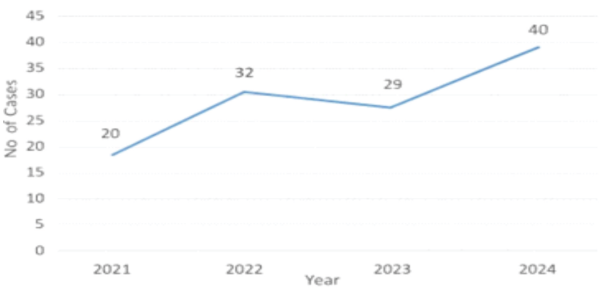

Figure 1: Surgically Treated Malignancies Over 4 Years at the Department of General Surgery, Shaheed Saif ur Rehman Government Teaching Hospital, Gilgit

Discussion

This four-year retrospective analysis describes the distribution of histologically confirmed malignancies managed surgically at a tertiary care hospital in Gilgit-Baltistan (GB). In the absence of a regional cancer registry, these institutional data provide an initial overview of the types of malignancies presenting for surgical management in this setting.

The mean age of patients was 52.4 years, with a nearly equal male-to-female distribution. The highest frequency of cases occurred in the 31–40-year age group. While this appears younger

Table IV: Distribution Of Histological Variants of Different Cancers

S.No	Site (ICD-10)	Histological Subtype	Count	% within Site
1	Stomach (C16)	Adenocarcinoma	19	86.4%
		Squamous Cell Carcinoma	2	9.1%
		GIST	1	4.5%
2	Skin (C44)	Squamous Cell Carcinoma	10	52.6%
		Basal Cell Carcinoma	9	47.4%
3	Retroperitoneum / Peritoneum (C48)	Leiomyosarcoma	9	47.4%
		Liposarcoma	7	36.8%
		Ewing Sarcoma	2	10.5%
		Synovial Sarcoma	1	5.3%
4	Breast (C50)	Invasive Ductal Carcinoma	9	81.8%
		Invasive Lobular Carcinoma	1	9.1%
		Malignant Phyllodes Tumor	1	9.1%
5	Colorectal (C18)	Adenocarcinoma	10	90.9%
		Myofibroblastic Tumor	1	9.1%
6	Ovary (C56)	Epithelial Tumors	7	63.6%
		Germ Cell Tumors	3	27.3%
		Sex Cord Stromal Tumor	1	9.1%
7	Esophagus (C15)	Adenocarcinoma	6	75.0%
		Squamous Cell Carcinoma	2	25.0%
8	Thyroid (C73)	Papillary Carcinoma	3	75.0%
		Hurthle Cell Carcinoma	1	25.0%
9	Gall Bladder (C23)	Adenocarcinoma	4	100%
10	Soft Tissue / Subcutaneous (C49)	Dermatofibrosarcoma Protuberans	2	50%
		Extraskeletal Ewing Sarcoma	2	50%
11	Salivary Gland (C07, C08)	Mucoepidermoid Carcinoma	5	71.4%
		Adenocarcinoma	2	28.5%
12	Appendix (C18.1)	Mucinous Neoplasm	2	100%

compared to national registry data, this observation likely reflects referral patterns, surgical selection bias, and the exclusion of non-surgical cases rather than true age-specific population incidence. Without age-standardized rates or population denominators, comparisons with national or global incidence trends should be interpreted cautiously.

Gastrointestinal malignancies collectively constituted the largest group (35.3%) of surgically managed cases, with stomach cancer being the most frequent single site (18.1%). Adenocarcinoma was the predominant histological subtype in stomach, colorectal, and esophageal tumors, consistent with established pathological patterns. These findings align with hospital-based reports from certain regions of Pakistan, where gastrointestinal malignancies contribute substantially to the surgical oncology workload[7] while national studies reported breast malignancies to be the most common overall [8,9]. However, this distribution reflects cases managed at this institution rather than population-based cancer epidemiology.

Non-melanoma skin cancers accounted for 15.7% of cases and represented the second most frequent category overall. Both squamous cell carcinoma and basal cell carcinoma were observed in comparable proportions. Although high-altitude ultraviolet exposure has been described as a potential risk factor in mountainous regions, the current study was not designed to assess environmental or etiological associations.[10,11] Therefore, causal inferences cannot be drawn from these findings.

Among female patients, breast cancer was the most commonly managed malignancy, followed by ovarian cancer. These findings are consistent with national and global trends, where breast cancer remains the leading malignancy among women.[12,13] Due to late-stage diagnoses, often stemming from cultural taboos and limited awareness about available surgical treatments, Pakistan records one of the highest breast cancer mortality rates in the world.[7,13] Breast cancer continues to be the most common malignancy among women across all four provinces and Azad Jammu & Kashmir (AJK), exerting a profound emotional, physical, and financial toll on affected individuals and their families.[7] However, only surgically treated cases were included in our analysis; patients managed primarily with chemotherapy, radiotherapy, or referred to higher centers were not captured in this dataset.

Colorectal cancer emerged as a significant malignancy in both sexes, accounting for 4.8% of male and 13.5% of female cancer cases. These results are consistent with several national studies identifying colorectal cancer as a leading malignancy in Pakistan.[14,15] To enhance prognosis and mitigate the emotional and economic burden associated with its management, early detection through screening is essential for identifying precancerous lesions. Therefore, strengthening and expanding colonoscopy facilities at major hospitals across Gilgit-Baltistan is imperative for improving early diagnosis and patient outcomes

The observed increase in the number of surgically treated cases over the four-year period likely reflects

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improved institutional surgical capacity, diagnostic services, and patient access rather than a quantified rise in cancer incidence. The limitations of this study included a small sample size, and It is a single-center, hospital-based analysis. It includes only surgically managed malignancies, thereby excluding hematological cancers, advanced inoperable tumors, and patients referred elsewhere. Data on tumor staging, grading, and long-term outcomes were unavailable. Consequently, these findings should not be interpreted as representing the overall cancer burden or incidence in Gilgit-Baltistan.

Despite these limitations, this study provides baseline institutional data from a geographically remote and underserved region. The findings underscore the need for systematic cancer surveillance through the establishment of a regional cancer registry. Such a registry would enable accurate estimation of incidence, facilitate resource planning, and support future population-based epidemiological research in Gilgit-Baltistan.

Conclusion

This single-center, hospital-based study describes the distribution of surgically managed malignancies in Gilgit-Baltistan over a four-year period. Gastrointestinal and skin cancers constituted a substantial proportion of cases, with gender-specific differences in tumor distribution. However, these findings reflect institutional surgical data and should not be interpreted as population-based cancer incidence or regional burden.

The observed increase in treated cases likely represents improved local surgical capacity and patient access rather than a quantified rise in disease occurrence. The absence of comprehensive population-based data highlights a critical gap in cancer surveillance in the region. Establishment of a structured regional cancer registry is essential to determine true incidence, guide preventive strategies, facilitate resource allocation, and support future epidemiological research in Gilgit-Baltistan.

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CONFLICT OF INTEREST

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ORIGINAL ARTICLE

Prevalence and Multi-Faceted Effects of Unintended Pregnancy on Women's Psychology, Physical Health, and Socioeconomic Status in Saudi Arabia

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ABSTRACT

Objective: To determine the prevalence of unintended pregnancy among women in Saudi Arabia and assess its psychological, physical, and socioeconomic impact.

Study Design: Descriptive cross-sectional.

Place and Duration of Study: The study data were retrieved from all the provinces of Saudi Arabia from October 2024 to April 2025.

Materials and Methods: A cross-sectional study was conducted on women aged 18-49 who had experienced an unintended pregnancy in the last five years across all provinces of Saudi Arabia. Most of the participants of the study were recruited via social media platforms using online structured questionnaires.

Results: This study included 587 women from across Saudi Arabia who had experienced an unintended pregnancy. Most of the participants were Saudi nationals (93.9%) with a bachelor's degree (61.7%). Unintended pregnancies were predominantly reported once in the past five years (83.6%), with singleton pregnancies being most common (94.2%). Over half of the pregnancies were not protected by any contraception (54.7%). Financial strain was reported by 23.7% of participants and was significantly associated with nationality (p=0.027) and age (p=0.016), with greater impact among non-Saudis and less financial disruption in women aged ≥36 years. Mental health was notably affected post-pregnancy, especially in those with multiple unintended pregnancies (p=0.020). Educational impacts were significant among those with only elementary to middle education (p<0.001).

Conclusion: Unintended pregnancies significantly impact Saudi women's financial, mental, and educational domains. Notably, the lack of contraceptive use is widespread, contributing to high rates of unintended pregnancies. Targeted educational programs and improved access to family planning services are critical for alleviating significant societal consequences

Key Words: *Contraception, Mental Health, Saudi Arabia, Socioeconomic Impact, Unintended Pregnancy, Women's Health.*

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Introduction

Unintended pregnancy is a multifaceted issue with profound implications for individuals, families, and societies at large. Beyond its immediate ramifications on reproductive health, unintended pregnancy carries significant socioeconomic, physical health, and mental health consequences that ripple through communities and impact life trajectories, particularly in adolescent early marriage.[1] Unplanned pregnancies can lead to lower educational and employment opportunities, which result in a substantial economic burden.[2] In a situation like the COVID-19 pandemic, unplanned pregnancy incidence increased to 33.6% which further exacerbated the socioeconomic stress.[3] Beyond economic and social dimensions, the

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consequences of unintended pregnancies extend, leading to an increased rate of induced abortion, delayed initiation, and fewer visits for antenatal care, and risky and careless behaviors during pregnancy. These factors may further contribute to adverse birth outcomes and neonatal health issues, and impaired psychophysical maternal health.[4] Notably, the rate of abortion induced following unplanned pregnancies did not vary between countries where abortion was legal and restricted. However, in recent data in countries with restrictive abortion laws, induced abortions following unintended pregnancies increased from 2015 to 2019 compared to the period between 1990 and 1994.[5]

Globally, the prevalence of unintended pregnancies varies widely, reflecting disparities in access to family planning services, education, and healthcare infrastructure. [4,12.] Across the world from 2015 to 2019, the unplanned pregnancy rate constituted 121 million, while 61% ended up in abortion.[6] In North Africa and the Middle East, this rate varies significantly, ranging from 15% to 58%. Yemen reports the highest rate at 58%, followed by Palestine at 38%, Morocco at 32%, and both Syria and Algeria at 31%. In Egypt, the rate was estimated to be around 23%. [7] Research data in Saudi Arabia on the prevalence of unintended pregnancies and their effects is very scarce.[8] Improvement in health education, counseling, motivation, and access to modern contraceptives is essential to counteract unplanned pregnancy and its impact on physical and mental health, as well as socioeconomic stress. [9,10.] Moreover, family planning and maternal healthcare services should be promoted to encourage women with unintended pregnancies to utilize maternal healthcare services. An approach that would not only reduce the incidence but also prevent undesirable maternal and fetal consequences. [11-13.]

The gap in the knowledge of prevalence and effects of unwanted pregnancy on psychology, physical health, and economic status limits the development of targeted interventions and policies to address the multifaceted effects of unintended pregnancies. Hence, this study aims to cover this gap in all provinces of Saudi Arabia.

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Material and Methods

This descriptive cross-sectional study was conducted across all provinces of Saudi Arabia from October 2024 to April 2025. The ethical approval was obtained from the Deanship of Research, King Faisal University. (Reference Approval No.: [KFU-REC-2024-APR-ETHICS2236]).

The minimum sample size of 390 participants was calculated from the sample size calculator with the Confidence interval of 95%, and a 5% margin of error. The responses received were 630 while 587 were found eligible for inclusion in the study. The study population comprised women of reproductive age (18-49 years) residing in Saudi Arabia (both Saudis & non-Saudis) who had experienced an unintended pregnancy in the last five years. The participants were recruited through a convenience sampling method, where women who met the inclusion criteria were invited to participate through all social media platforms (including WhatsApp, Twitter, and Instagram). The questionnaire was also administered in person, through email, and via telephone on the personal preference and feasibility of the participant.

The questionnaire contained demographic data, contraceptive use (including methods, frequency, and reasons for discontinuation), experiences with unintended pregnancies (number, reasons, and outcomes), psychological effects (such as anxiety, depression, regret, and postpartum distress), economic impact (financial strain and effects on work and education), and health behaviors before, during, and after an unintended pregnancy. The questionnaire, designed in both Arabic and English, was intended to enhance accessibility for a broad participant demographic. The questionnaire was tested in a pilot study of 20 married eligible females to assess its validity and feasibility (Cronbach's alpha 0.76 for both questionnaires). The respondents were required to actively confirm that they were 18 years of age or older and had read, understood, and voluntarily agreed to participate based on the provided information. They were fully informed about the purpose of research, confidentiality measures, and the voluntary nature of participation, with clear assurance that they could withdraw at any time without penalty. All collected variables were coded and analyzed using SPSS version 29.0. The

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categorical variables included demographic parameters (nationality, education, region), pregnancy-related features (frequency of unintended pregnancy, age group at pregnancy, number of fetuses, pregnancy outcome, contraception use), and outcome-related parameters (financial impact, career/study impact, post-natal mental health status). Descriptive statistics were expressed as frequencies and percentages for categorical variables. Chi-square tests (χ^2) were applied to assess associations between categorical variables, while Fisher's Exact Test was employed when any expected cell count was <5. A p-value <0.05 was considered statistically significant.

Results

Our study assessed the unintended pregnancy and its parameters among females in Saudi Arabia (Table I*)*. Data were collected from participants across all provinces of Saudi Arabia, ensuring nationwide representation. Therefore, Saudi nationals were predominant participants, with varying education level where most (61.7%) had a bachelor's degree. Most reported one unintended pregnancy in the last five years (83.6%), primarily between the ages of 26-35 years. More than half were not using any method of contraception at the time of conception, while some of the participants used a protective method, but it was inappropriate to be effective against pregnancy.

Table I: Sociodemographic Parameters of Participants and Features of Unintended Pregnancy

		Frequency N (%)
Nationality	Non-Saudi	36 (6.1%)
	Saudi	551 (93.9%)
Educational Level	Elementary to Middle Education	17 (2.9%)
	Secondary Education	115 (19.6%)
	Diploma	65 (11.1%)
	Bachelor's Education	362 (61.7%)
	Master's/PhD	28 (4.8%)
Region	Western Region	167 (28.4%)
	Eastern Region	160 (27.3%)
	Central Region	108 (18.4%)
	Southern Region	101 (17.2%)
	Northern Region	51 (8.7%)
Parameters of Unintended Pregnancy		
No. of times "Unintended Pregnancy" occurred in the last five years (between 2018 and 2024)?	Once	491 (83.6%)
	2-4 Times	87 (14.8%)
	>4 Times	9 (1.5%)
Age at the Time of that Unintended Pregnancy?	18-25 Years	219 (37.3%)
	26-35 Years	273 (46.5%)
	36-49 Years	95 (16.2%)
No. of Fetuses in the Unintended Pregnancy?	Singleton Pregnancy (One Fetus)	553 (94.2%)
	Multiple Pregnancy (Twins or More)	34 (5.8%)
Outcome of That Pregnancy	Born Prematurely Before 37th Week of Pregnancy	67 (11.4%)
	Born Term/After 37th Week of Pregnancy	312 (53.2%)
	Miscarriage	172 (29.3%)
	Stillborn/ Dead Baby	31 (5.3%)
	Healthy Outcome	5 (0.9%)
In the month that I became pregnant: My partner and I	Not Using Contraception	321 (54.7%)
	Occasionally Use Contraception	144 (24.5%)

	Always Used Contraception	66 (11.2%)
	Always Used Contraception (but Method had Failed (i.e. broke, moved, came off, came out, not worked etc.) at Least Once)	56 (9.5%)
I feel like my pregnancy was	At Right Time	153 (26.1%)
	Ok (But Not Quite Right Time)	270 (46.0%)
	Wrong Time	164 (27.9%)
Just before I became pregnant	Didn't Intend to get Pregnant	285 (48.6%)
	Intended to get Pregnant	108 (18.4%)
	My Intentions kept on Changing	194 (33.0%)
Before I became pregnant	Never Discussed about Children	178 (30.3%)
	My Partner and I agreed to get me Pregnant	130 (22.1%)
	My Partner and I Discussed Having Children Together (But hadn't agreed to me to get Pregnant)	279 (47.5%)

Figure 1 shows the awareness and practices of various contraceptive methods used by participants to avoid unintended pregnancy. The withdrawal method was the most used by 47%, followed by condom (44.4%) and birth control pills by 38%.

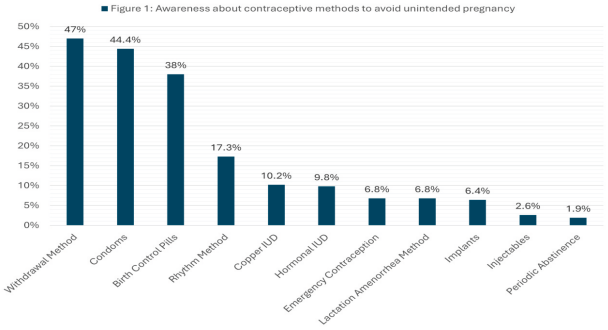

Figure 1: Awareness about Contraceptive Methods to Avoid Unintended Pregnancy

This study also examined physical, financial, and emotional outcomes following unintended pregnancy. While most participants (66.3%) made no preconception health efforts, the majority adopted healthier behaviors post-conception, including folic acid use (80.2%) and regular antenatal care (87%). Economically, although 85.3% reported sufficient income before pregnancy, 23% faced financial constraints and 21.8% struggled to meet family needs afterward. Career and education were negatively impacted by 21.1% of respondents. Socially, nearly half reported giving up luxuries (50.9%) or experiencing strained relationships (44.6%). Emotionally, 72.2% experienced negative feelings during pregnancy, persisting in 60.8% after childbirth, highlighting the profound multidimensional impact of unintended pregnancies.

A spectrum of negative emotions was retrieved for the psychological impact that constituted a significant stressor for both maternal health and fetal development, illustrated in ***Figure 2***. The most frequently reported emotion was anxiety, followed by feeling lethargic, and some were unable to do anything, indicating significant levels of distress affecting physical motivation.

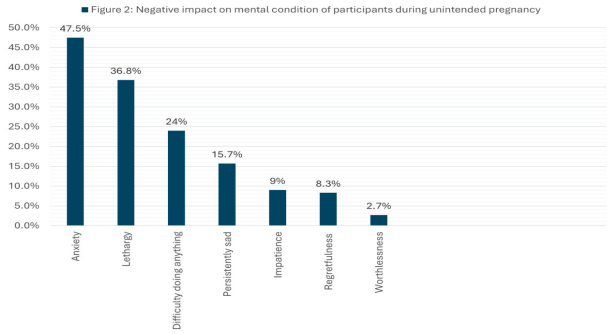

Figure 2: Negative Impact on Mental Condition of Participants during Unintended Pregnancy

Mental health challenges persisted postpartum, with anxiety remaining the most prevalent emotion, likely due to unwanted responsibility. Many participants reported difficulty with daily activities and persistent lethargy. Notably, 21.1% experienced persistent sadness, while some participants also expressed regret, underscoring the persistent psychological burden of unintended pregnancy.

Table II presents the associations between sociodemographic factors, unintended pregnancy characteristics, and financial implications for participants. Non-Saudi participants experienced a higher financial impact compared to other nationals (38.9% vs 22.7%), with statistically significance (p=0.027). Age played a significant role (p=0.016), with older women (36-49 years) reporting the least financial disruption (12.6%) compared to younger age groups (24.2% and 27.1%). No other variables showed significant associations.

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Table II: ***Association between Sociodemographic and Unintended Pregnancy-related Features with their impact on Financial Condition***

		Impact on Financial Condition		Chi-Square/ Fisher Test	*p-value*
		No N (%)	**Yes N (%)**		
Nationality	Non-Saudi	22 (61.1%)	14 (38.9%)	***4.89***	***0.027*** [a]
	Saudi	426 (77.3%)	125 (22.7%)		
Educational Background	Elementary to Middle Education	13 (76.5%)	4 (23.5%)	0.41	0.929 [b]
	Secondary Education	91 (79.1%)	24 (20.9%)		
	Diploma	48 (73.8%)	17 (26.2%)		
	Bachelor's Education	274 (75.7%)	88 (24.3%)		
	Master's/PhD	22 (78.6%)	6 (21.4%)		
Residential Area	Western Region	118 (70.7%)	49 (29.3%)	0.57	0.237 [a]
	Eastern Region	122 (76.3%)	38 (23.8%)		
	Central Region	86 (79.6%)	22 (20.4%)		
	Southern Region	83 (82.2%)	18 (17.8%)		
	Northern Region	39 (76.5%)	12 (23.5%)		
Unintended Pregnancy Frequency During Past 5 Years (2018-2024)	Once	379 (77.2%)	112 (22.8%)	1.73	0.421 [a]
	2-4 Times	63 (72.4%)	24 (27.6%)		
	>4 Times	6 (66.7%)	3 (33.3%)		
Age at Unintended Pregnancy	18-25 Years	166 (75.8%)	53 (24.2%)	***8.25***	***0.016*** [a]
	26-35 Years	199 (72.9%)	74 (27.1%)		
	36-49 Years	83 (87.4%)	12 (12.6%)		
Fetuses in Unintended Pregnancy	Singleton	421 (76.1%)	132 (23.9%)	0.19	0.662 [a]
	Multiple	27 (79.4%)	7 (20.6%)		

(a) Chi-Square Test, (b) Fisher's Exact Test

Table III outlines the sociodemographic factors influencing work and academic disruption. Education level showed a highly significant association (p<0.001): while 100% of women with elementary to middle education reported no impact, 26.2% of those with a bachelor's degree experienced disruption.

Table III: Association between Sociodemographic and Unintended Pregnancy-related Features with their impact on Work and Study

		Impact on Study/Work/Job		Chi-Square/ Fisher Test	*P-value*
		No/Not Planned N (%)	**Yes N (%)**		
Nationality	Non-Saudi	28 (77.8%)	8 (22.2%)	0.03	0.868 [a]
	Saudi	435 (78.9%)	116 (21.1%)		
Educational Background	Elementary to Middle Education	17 (100.0%)	0 (0.0%)	***14.21***	***<0.001*** [b]
	Secondary Education	99 (86.1%)	16 (13.9%)		
	Diploma	58 (89.2%)	7 (10.8%)		
	Bachelor's Education	267 (73.8%)	95 (26.2%)		
	Master's/PhD	22 (78.6%)	6 (21.4%)		

Residential Area	Western Region	123 (73.7%)	44 (26.3%)	6.15	0.210 [a]
	Eastern Region	128 (80.0%)	32 (20.0%)		
	Central Region	85 (78.7%)	23 (21.3%)		
	Southern Region	82 (81.2%)	19 (18.8%)		
	Northern Region	45 (88.2%)	6 (11.8%)		
Unintended Pregnancy Frequency During Past 5 Years (2018-2024)	Once	390 (79.4%)	101 (20.6%)	1.41	0.495b [a]
	2-4 Times	67 (77.0%)	20 (23.0%)		
	>4 Times	6 (66.7%)	3 (33.3%)		
Age at Unintended Pregnancy	18-25 Years	172 (78.5%)	47 (21.5%)	0.72	0.695 [a]
	26-35 Years	213 (78.0%)	60 (22.0%)		
	36-49 Years	78 (82.1%)	17 (17.9%)		
Fetuses in Unintended Pregnancy	Singleton	437 (79.0%)	116 (21.0%)	0.12	0.723 [a]
	Multiple	26 (76.5%)	8 (23.5%)		

(a) Chi-Square Test, (b) Fisher's Exact Test

Table IV displays significant associations between several factors and postnatal mental health. Participants from the Eastern Region reported the highest negative impact (68.8%, p=0.010). Those with more than four unintended pregnancies experienced a 100% negative impact on mental health (p=0.020). Pregnancy with multiple fetuses also showed a trend toward greater psychological burden (p=0.054). No other sociodemographic variables reached statistical significance.

Table IV: Association between Sociodemographic and Unintended Pregnancy-related Features with their impact on Work and Study

		Negative Impact on Post-Natal Mental Health		*Chi-Square/ Fisher Test*	P-value
		No N (%)	**Yes N (%)**		
Nationality	Non-Saudi	10 (27.8%)	26 (72.2%)	2.09	0.148 [a]
	Saudi	220 (39.9%)	331 (60.1%)		
Educational Background	Elementary to Middle Education	8 (47.1%)	9 (52.9%)	3.51	0.468 [a]
	Secondary Education	42 (36.5%)	73 (63.5%)		
	Diploma	21 (32.3%)	44 (67.7%)		
	Bachelor's Education	145 (40.1%)	217 (59.9%)		
	Master's/PhD	14 (50.0%)	14 (50.0%)		
Residential Area	Western Region	65 (38.9%)	102 (61.1%)	***13.27***	***0.010 [a]***
	Eastern Region	50 (31.3%)	110 (68.8%)		
	Central Region	54 (50.0%)	54 (50.0%)		
	Southern Region	35 (34.7%)	66 (65.3%)		
	Northern Region	26 (51.0%)	25 (49.0%)		
Unintended Pregnancy Frequency During Past 5 Years (2018-2024)	Once	200 (40.7%)	291 (59.3%)	***7.90***	***0.020 [b]***
	2-4 Times	30 (34.5%)	57 (65.5%)		
	>4 Times	0 (0.0%)	9 (100.0%)		
Age at Unintended Pregnancy	18-25 Years	76 (34.7%)	143 (65.3%)	2.98	0.226 [a]
	26-35 Years	115 (42.1%)	158 (57.9%)		
	36-49 Years	39 (41.1%)	56 (58.9%)		
Fetuses in Unintended Pregnancy	Singleton	222 (40.1%)	331 (59.9%)	3.72	0.054[a]
	Multiple	8 (23.5%)	26 (76.5%)		

(a) Chi-Square Test, (b) Fisher's Exact Tes

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Discussion

This study provides the first known assessment of unintended pregnancy across all provinces of Saudi Arabia, revealing significant intersections with women's mental, physical, and socioeconomic well-being. Notably**,** a significant finding from our study is the high proportions of unintended pregnancies among Saudi nationals, which is in line with regional demographic patterns where larger segments of the population are Saudi nationals. According to a study by Sarder et al. (2021), about 29% of pregnancies were found to be unintended, with a higher rate among older women. [9] Interestingly, most of our respondents had a bachelor's degree, indicating a good educational background among the participants. This observation supports earlier research that suggests having a higher education level does not always lead to fewer unintended pregnancies. Additionally, a study by Alsafar et al. (2022) stated that the rate of unintended pregnancies varies with education levels; specifically, 25% of individuals with education below high school experienced unplanned pregnancies, while the rate was 23.6% for those with higher education. [8]

Moreover, the contraceptive usage patterns revealed in our study indicated a reliance on traditional methods like withdrawal and condoms, with a lower uptake of more reliable long-term contraceptives such as IUDs or implants. This preference may reflect accessibility issues, cultural attitudes, or knowledge gaps regarding contraceptive options. However, findings from other Middle Eastern studies highlight some variations in these trends. Ashoor et al. (2023) showed that the most practiced method was contraceptive pills (55.6%) followed by intrauterine devices (17.6%). [14] Another study by Aladham et al. (2020) showed that the most used methods were oral contraceptive pills, male condoms, and intrauterine devices (69%, 34%, 22%, respectively). [15] Most of the participants' reliance was on less effective methods in our study the withdrawal method could be contributing to the high rates of unintended pregnancies observed. [16, 17.]

Notably, our study findings reveal that most women did not proactively seek to improve their health before pregnancy but took substantial steps during pregnancy. This reactive approach to health during pregnancy emphasizes a need for more robust preconception health promotion and education. Similar concepts were observed in previous studies, as indicated by Chivers et al. (2020), showing that women who are actively planning a pregnancy optimize their health behavior and lifestyle in preparation for pregnancy to improve alignment with current preconception care recommendations.[18] Financially, unintended pregnancies significantly strained family resources, particularly among non-Saudi families, which may reflect differential socio-economic conditions or support systems available to non-nationals. Similarly, Maghalian et al. (2024) show that unintended pregnancy, along with the consequent unsafe abortions, can impose significant financial and social burdens.[19]

Comparatively, literature from other regions, such as Southeast Asia, shows a similar pattern where unintended pregnancies often lead to financial strain due to the direct and indirect costs associated with prenatal care, childbirth, and postnatal care (Sharma et al. 2023).[20] The economic impact is profound, often exacerbating existing inequalities and impacting women's ability to return to work or continue education, which aligns with our findings, where over 20% of participants reported negative impacts on their career or study. Similarly, Asrat et al. (2024) showed that unplanned pregnancies can hinder women's financial independence by limiting educational and career opportunities, thus impacting their economic empowerment and long-term financial stability. [21]

Moreover, the psychological impact of unintentional pregnancies is one of the most significant findings of our study, with high levels of anxiety, lethargy, and difficulty in carrying out daily activities reported. Beumer et al. (2023) showed that those who carried a more unplanned pregnancy to term reported more symptoms of psychological distress at postpartum.[22] With persistently high levels of worry and other negative emotions like regret and feelings of worthlessness, postpartum statistics were especially worrisome. These results are in line with international research showing a clear correlation between unintended pregnancies and negative mental health consequences, such as increased risk of anxiety and postpartum depression.[23]

Interestingly, the emotional responses varied widely with demographic factors such as age and frequency of unintended pregnancies. Older participants and those who had experienced multiple unintended pregnancies reported less financial and psychological stress, which might indicate an increased resilience or access to better support systems over time.

Unintended pregnancy in Saudi Arabia underscores the need for comprehensive public health strategies, emphasizing enhanced contraceptive education and accessibility, especially promoting long-acting reversible contraceptives. It highlights the importance of integrating preconceptions and antenatal care into routine services and incorporating mental health supports within maternity care. Policymakers are urged to develop community engagement initiatives and tailored interventions for different demographics to address specific needs. A multidisciplinary approach is essential to reduce unintended pregnancies and improve overall outcomes for women in Saudi Arabia.

The limitations of our study include the reliance on self-reported data that may lead to underreporting or bias in reporting sensitive information, such as contraceptive use and psychological impacts. Additionally, the cross-sectional nature of the study limits our ability to draw causal inferences about the impacts of unintended pregnancies.

Conclusion

Our study showed the pervasive and multifaceted impact of unintended pregnancies on women in Saudi Arabia, emphasizing the urgent need for enhanced contraceptive education and access. The findings reveal significant disparities in the use of effective contraceptive methods, the sufficiency of prenatal care, and the substantial financial and emotional toll on affected women. This study underlines the critical necessity for targeted public health interventions that address these gaps, specifically advocating for improved reproductive health services and broader educational initiatives. Ultimately, a more informed and supported female population will lead to better health outcomes and reduced rates of unintended pregnancies.

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CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

GRANT SUPPORT AND FINANCIAL DISCLOSURE

Authors have declared no specific grant for this research from any funding agency in public, commercial or nonprofit sector.

DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon request.

ORIGINAL ARTICLE

Evaluation of Thrombophilia Profile in Northern Pakistan: Frequency and Presentation

Omama Abbasi, Ayesha Junaid.

ABSTRACT

Objective: This study aims to ascertain the prevalence of thrombotic disorders and thrombophilia profile among patients in Northern Pakistan.

Study Design: Cross sectional descriptive study.

Place and Duration of Study: This study was conducted at the department of hematology, Shifa International Hospital, Islamabad, Pakistan from 1st June 2024 to 31st July 2025.

Materials and Methods: Ethical approval was obtained from the Institutional Review Board (IRB) prior to commencement of the study. The sample size was calculated using the WHO sample size calculator, considering a confidence level of 95% and anticipated prevalence of 2.5%. Non- probability consecutive sampling technique was employed. Data were collected using a structured proforma and analysed using SPSS version.

Results: Out of the 926 patients, there were 256 patients with portal vein thrombosis (PVT) (27.6%), 192 with stroke (20.7%), 160 with Deep vein thrombosis (DVT) (17.2%), mesenteric thrombosis 124 (13.3%) and 94 with Pulmonary embolism (PE) (10.1%) remaining 100 were presented with minor thrombotic episodes. Thrombophilia profiles revealed that 368 patients had protein S deficiency, 298 had anti-thrombin deficiency, 146 had protein C deficiency, and 114 patients had an activated protein C resistance. A total of 50 thrombotic disorders patients underwent molecular testing, out of which 10% were heterozygous for the Factor V Leiden mutation. 2% were homozygous for the Prothrombin (Factor II) mutation, and 88% did not exhibit any mutation.

Conclusion: According to this study, Protein S and anti-thrombin deficiencies are the most common deficiencies among thrombotic disorders patients in northern Pakistan. The prevalence of undetected site thrombosis, such as PVT, was higher than reported globally.

Key Words*: Anti-Thrombin, Factor V Leiden, Protein C Deficiency, Protein S Deficiency, Thrombotic Disorders.*

Introduction

Blockage of a vein caused by a thrombus (blood clot), is termed as Thrombotic disorders. It primarily presents as deep vein thrombosis (DVT), stroke, pulmonary embolism (PE), and portal vein thrombosis. Thrombotic disorders are acknowledged as a leading cause of morbidity and mortality on a global scale. It is placing a heavy strain on healthcare systems. In addition to contributing to acute patient care more difficult, the illness can have long-term effects such recurrent thromboembolism, persistent pulmonary hypertension and post-thrombotic syndrome.[1,7,9]

The pathogenesis of thromboembolism encompasses a complex interaction of three primary components, referred to as Virchow's triad: venous stasis, hypercoagulability, and endothelial damage. Under normal circumstances, naturally occurring inhibitors like anti-thrombin (AT), protein S (PS), and protein C (PC) effectively regulate haemostasis. These inhibitors have an essential role in preventing excessive thrombus formation by inhibiting the function of clotting factors. Together with protein S, activated protein C deactivates clotting factors VIII(a) and V(a), which inhibits the coagulation cascade[1,7,8]. Anti-thrombin also limits the pro-coagulant activity of thrombin by forming complexes with it and other serine proteases such factors IX(a), XI(a), and XII(a). Any genetic or acquired deficiency in these natural inhibitors exposes patients at risk for thrombophilia, a condition in which they are hypercoagulable[8,9,14].

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The prothrombin gene mutation, such as the G20210A variant, or Factor V Leiden (FVL) mutation is one of the most extensively studied genetic causes of thrombophilia. The mutation causes Factor V to become resistant to cleavage by activated protein C, extending its pro-coagulant activity. It involves the substitution of glutamine for arginine at position 506 (FVR506Q).[2,3,7,9,15] Similarly, insufficient inhibition of clotting factors and an increased risk of VTE are caused by deficits in PC, PS, or AT. The presence of lupus anticoagulant and mutations in the prothrombin gene are other noteworthy contributions. These inherited or acquired abnormalities disrupt the natural balance of coagulation, leading to a predisposition for thrombosis[7,9,16,17].

Depending on the location and degree of thrombosis, thromboembolism can manifest with a wide range of clinical symptoms. Pain, swelling, redness, and dilated superficial veins are the usual symptoms of deep vein thrombosis, which usually affects the major veins of the lower limbs. A potentially fatal consequence, pulmonary embolism presents as abrupt dyspnoea, chest discomfort, tachypnoea, and occasionally circulatory collapse. In contrast to portal vein thrombosis, which frequently results in stomach pain, ascites, or splenomegaly, cerebral venous thrombosis or stroke caused by thrombophilia can manifest as disorientation, speech abnormalities, or focal neurological disability. Clinical suspicion, laboratory testing, and radiographic confirmation are all necessary for an accurate and prompt diagnosis of various presentations.[3,7,9,15,17]

Geographical and ethnic factors affect the frequency of hereditary thrombophilia worldwide. Factor V Leiden mutations are reported to be 4–5% common in Western populations, although PC, PS, and AT deficits are quite uncommon, affecting less than 1% of the general population. Data is scant in South Asian nations, such as India and Pakistan, but recent studies point to regional differences in prevalence that may be caused by consanguinity, genetic origins, and a lack of knowledge about thrombophilia testing. Studies from Pakistan, show comparatively higher rates of FVL (4.9%) and AT deficiency (10.9%) than the global average. These results highlight how crucial population-specific research is for establishing treatment and diagnosis plans.[5,7,11,12]

Despite thrombophilia's clinical significance, there is limited research occurring in Pakistan. Only a handful of studies have attempted to correlate laboratory results with clinical manifestations, and even fewer have reported the prevalence of familial thrombophilia in VTE patients. Therefore, there is not enough information to support evidence-based practice regarding how long anticoagulant therapy should be administered, whether family members should be screened, or genetic counselling should be provided to high-risk groups. Regional epidemiological statistics are also essential for developing public health plans, enhancing provider awareness, and tailoring diagnostic procedures to fulfil local requirements.[6,9,15,18,19]

Long-term or even lifetime anticoagulation medication is frequently necessary for patients with thrombophilia, particularly those who have recurring episodes, were young when they first had the condition, have uncommon site thrombosis, or have a strong family history. However, determining underlying risk factors, especially genetic predispositions, is crucial in determining the duration of therapy. Lack of data makes it difficult to diagnose patients quickly and provide the best care possible, which results in unavoidable morbidity and mortality in areas like northern Pakistan where healthcare access and awareness are varied.[7,9,18,19]

Therefore, by assessing the prevalence of thrombophilia profile and clinical manifestations of thromboembolism in patients from northern Pakistan, this study seeks to fill this critically important gap. The goal of the study is to improve knowledge of hereditary thrombophilia in the local context by methodically evaluating genetic and laboratory risk factors in addition to clinical manifestations. In addition to adding to the body of scientific literature, the results will facilitate the development of regional guidelines, educate preventive measures, and enhance patient outcomes in this clinically significant but little-studied field.

Materials and Methods

This cross-sectional study was conducted in the Department of Haematology, Shifa International Hospital, Islamabad, from 1st June 2024 to 31st July 2025, following STROBE guidelines. Ethical approval

was obtained from the Institutional Review Board (IRB#0433-25, approval date 16-Nov-2023). A total of 926 patients with proven thrombotic disorders diagnosed through radiological imaging (Doppler ultrasonography, CT pulmonary angiography, MRI/MRV) and D-dimer testing, between the ages of 18-45, were included, as the prevalence of Thrombotic disorders are significantly higher in this age group. Patients who were already receiving anticoagulant medication or who had tested within two weeks of a thrombotic incident, to minimise the effect of laboratory variability on measured levels of protein C, protein S, and antithrombin, patients were excluded if testing was performed during an episode of acute thrombosis or while on anticoagulation therapy. The medical records of every patient whose blood sample was sent to the institute laboratory for thrombophilia screening were reviewed in order to collect demographic and clinical data.

To maintain the optimal anticoagulant-to-blood ratio, peripheral venous blood samples were collected in EDTA vacutainers for molecular studies and in 3.2% trisodium citrate tubes for serological assays, in accordance with standard laboratory protocols. To obtain platelet-poor plasma for serological testing, the samples were centrifuged for 15 minutes at 4000 rpm. This plasma was then used for thrombophilia screening, including protein S, protein C, anti-thrombin and Activated Protein C resistance (APCR). using a Sysmex 2500 automated coagulation analyser. A functional chromogenic assay based on the PROTAC activation method was used to evaluate protein C deficiency; 70–140% activity was accepted as normal. Using a clotting-based assay, protein S activity was assessed and reference values ranged from 60 to 130%. Using chromogenic functional test, anti-thrombin levels were assessed, with 75–125% being considered normal.

For Factor APCR, the patient's plasma was mixed with Factor V–deficient plasma in a 1:4 ratio and activated protein C resistance was assessed using the Pro C Global kit, with ratios of 0.86–1.10 regarded as normal.

Blood samples were subjected to molecular testing; an SNP Genotyping Assay (a Multiplex end-point Allelic Discrimination Assay) was used to evaluate mutations in Factor V Leiden (FVL) and Prothrombin (PT). These tests are relatively expensive and not routinely covered in our resource-limited healthcare settings. Therefore, testing was restricted to patients who gave consent, has no affordability issues and with strong clinical suspicion of inherited thrombophilia, such as those with unprovoked or recurrent thrombotic events, young age at presentation, or positive family history. Only 50 patients out of 926 fulfilled the criteria and were successfully underwent molecular testing.

Strict internal and external quality controls were put in place to guarantee quality assurance. Internal QC with 2 levels per batch and external proficiency testing via CAP thrice yearly were employed. SPSS version 26 was used to analyse the data. While categorical variables (gender, clinical presentation, and thrombophilia profile) are expressed as frequencies and percentages.

Results

The study comprised 926 patients, of whom 432 (46.8%) were female and 494 (53.2%) were male. In terms of clinical presentation, 256 patients (27.6%) had portal vein thrombosis (PVT), 192 patients (20.7%) had stroke, 160 patients (17.2%) had DVT, 124 patients (13.4%) had mesenteric thrombosis, and 94 patients (10.1%) had PE. Minor occurrences of thrombosis were observed in the remaining 100 patients (10.8%).

Overall, DVT predominated in both genders, with a slightly higher frequency in males.

Figure 1 Illustrates the distribution of thrombotic disorders clinical presentations.

Among 926 patients, Protein S deficiency was found in 368 patients (39.7%), antithrombin deficiency in 298 (32.2%), protein C deficiency in 146 (15.8%), and activated protein C resistance in 114 (12.3%) from thrombophilia screening.

Figure 2 Demonstrates the prevalence of thrombophilia profiles.

Fifty patients with a known history of thrombotic disorders were subjected to molecular testing; of these, 88% had no detectable mutations in both gene, 10% were heterozygous for the Factor V Leiden mutation, and 2% were homozygous for the Prothrombin (Factor II, G20210A) mutation.

Overall, the study shows that this group has a significant prevalence of hereditary deficits, especially those related to Protein S and anti-

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thrombin. Higher than anticipated rates of unusual site thrombosis, particularly portal vein thrombosis and stroke, were noted in comparison to global statistics.

Table I: Primer Sequences Used for Detection of Factor V Leiden and Prothrombin Mutations

FVL F	GGG CTA ATA GGA CTA CTT CTA ATC TGT AAG A
FVL R	TTC TGA AAG GTT ACT TCA AGG AA
FVL	1691G/A
PMT F	TGT GTT TCT AAA ACT ATG GTT CCC AT
PMT R	CCA TGA ATA GCA CTG GGA GCA T

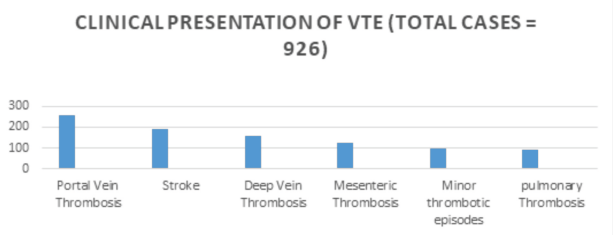

Figure 1: Illustrates the distribution of thrombotic disorders clinical presentations.

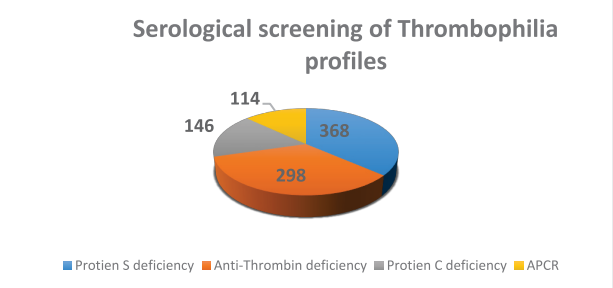

Figure 2: Demonstrates The Prevalence of Thrombophilia Profiles

Discussion

This study provides a current assessment of the clinical manifestations and thrombophilia profiles of patients with thrombotic disorders from northern Pakistan. In light of earlier research, the results are significant, especially the study by Khan et al. (2021), which found that in a smaller cohort, heritable thrombophilia rates were 3.2% for protein C deficiency, 2.5% for protein S deficiency, 10.9% for anti-thrombin deficiency, and 4.9% for Factor V Leiden mutation. According to the study's findings, thrombophilia-related abnormalities are quite common among thrombotic disorders patients in our area. Significant of our population (34.3%) had protein S deficit, which was closely followed by protein C deficiency (15.7%) and antithrombin deficiency (32.2%). 12.3% of cases had activated protein C resistance, which is significantly higher than the rates of ~4–5% found in previous Pakistani and Western-based investigations.[6]

Our thrombotic disorders subgroup's molecular test results confirmed the genetic component of thrombophilia. Among 50 tested patients, 10% were heterozygous for the Factor V Leiden (FVL) mutation and 2% homozygous for the Prothrombin (Factor II, G20210A) mutation; the remaining 88% had no detectable mutations. Although skewed by sample selection, these mutation rates are on par with or marginally greater than those observed in some recent studies conducted in Pakistan.[2,6,15,18]

These mutation rates are comparable to or slightly higher than those seen in some recent Pakistan-based studies, though skewed by sample selection. According to Maria Khan et al. (2021) in "Heritable Thrombophilia in Venous Thromboembolism in Northern Pakistan," of 182 VTE patients, ~4.9% had a Factor V Leiden mutation and ~10.9% had antithrombin deficiency[1,6,20].

Our cohort's clinical presentation also differed from several international findings. The prevalence of deep vein thrombosis (DVT) remained high (17.8%), consistent with global research showing that DVT is the most prevalent kind of thromboembolism. In contrast to previous local and Western cohorts, portal vein thrombosis (28.5%) and stroke (20.8%) were disproportionately common.[21] These results imply that inherited thrombophilia is more likely to cause "unusual site" thrombosis in our demographic, that individuals in our area may appear later in the course of the disease, or that referral patterns may favour more severe or uncommon presentations. Particularly for younger patients or those with recurrent thromboses, the significant prevalence of thrombophilia in this group supports the need for routine screening in northern Pakistani thromboembolic patients[5,11,12].

Decisions on prolonged or even lifetime anticoagulation therapy may be influenced by the early identification of deficiencies in protein C, protein S, or antithrombin as well as Factor V Leiden or Prothrombin mutations.[4,7,8,13,17] Furthermore, in high-risk circumstances like surgery, pregnancy, or extended immobility, bearers of mutations may benefit from genetic counselling and preventive measures. Our results highlight the necessity of raising awareness and increasing access to thrombophilia testing in Pakistan from a perspective

of public health. Before major problems arise, many patients remain undiagnosed.[10,21] Morbidity and mortality may be decreased by implementing cost-effective screening procedures, particularly in tertiary care settings, and perhaps by employing cutting-edge molecular tools for mutation identification. According to a recent article titled "Revisiting thrombophilia testing: leveraging next-generation sequencing for precision in VTE management" (Youssry & Ayad, 2025), patients with unprovoked or atypical VTE presentations should be given more opportunities to use broader genetic panels than just FVL and Prothrombin G20210A.[9,14,19] Finally, further research is needed to determine whether the unexpectedly high rates of protein deficiencies are caused by methodological factors, such as laboratory standards and cutoff values. It is also important to investigate the potential influence of demographic or environmental variables, including nutrition and illnesses.

Limitations: Some patients had incomplete clinical and molecular data, which may have influenced prevalence estimates. Functional levels of protein C, protein S and antithrombin may be influenced by acute thrombosis and inflammatory states; therefore, some deficiencies observed may represent transient reductions rather than hereditary thrombophilia.

Only 5.4% (50 out of 926 patients) of cohort underwent genetic testing due to cost constraints.

Despite these limitations, the study represents one of the largest cohorts reported from northern Pakistan evaluating comprehensive thrombophilia profiles. It provides valuable regional data, help to bridge an important knowledge gap and inform future diagnostic and management strategies.

Conclusion

According to this study, protein S and anti-thrombin deficiencies are the most prevalent among thrombotic disorders patients in northern Pakistan, highlighting a significant occurrence of hereditary thrombophilia within this group. Although the most frequent clinical manifestation noted was portal vein thrombosis which is abnormally high, while globally it is DVT. Therefore, our findings indicate a greater prevalence of thrombophilia in this region than previously reported.

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CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

GRANT SUPPORT AND FINANCIAL DISCLOSURE

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DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon request.

ORIGINAL ARTICLE

A Comparative Assessment of Clinical and Pathological Staging in Patients Undergoing Surgery for Oral Squamous Cell Carcinoma in Pakistan

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ABSTRACT

Objective: To compare the radiological and histopathological staging of Oral Squamous cell carcinoma and to measure the concordance between clinical and histopathological staging in patients visiting a tertiary care hospital in Pakistan.

Study Design: Retrospective cross-sectional study.

Place and Duration of Study: Foundation University College of Dentistry, September 2019-November 2023.

Materials and Methods: Thirty-two histopathologically confirmed cases of OSCC who underwent tumor resection with neck dissection were included. Clinical and radiological records were reviewed for clinical staging (cT, cN), and histopathological reports for pathological staging (pT, pN). Concordance was assessed using Chi-square, Kendall's tau-b, Cohen's Kappa, and Cramer's V, with $p < 0.05$ considered significant.

Results: Concordance between clinical tumor size (cT) and pathological tumor size (pT) was 46.9%, The Chi-square test was not significant ($p = .232$), but Kendall's tau-b showed a significant positive correlation, Cramer's V indicated a moderate effect size ($V = 0.349$), and Cohen's Kappa demonstrated fair agreement ($\kappa = 0.271$, $p = .005$). Nodal staging showed marked discordance (84.4%) between cN and pN, with no significant association ($p > 0.05$), weak correlation ($\tau b = 0.124$, $p = .433$), moderate but non-significant effect size ($V = 0.408$, $p = .192$), and negligible agreement ($\kappa = 0.002$, $p = .968$).

Conclusion: Assessment of OSCC staging showed fair agreement for tumor size but negligible correlation for nodal status. These findings highlight the limitations of clinical staging and stress the role of pathological confirmation in guiding treatment.

Key Words*: Concordance, Lymph Node, OSCC, Pathological Staging.*

Introduction

Oral squamous cell carcinoma (OSCC) represents a significant burden of disease globally, with most patients reported in South East Asia[1]. Among the various factors influencing the prognosis and treatment outcomes in OSCC, lymph node metastasis plays a pivotal role. Lymph node involvement is a critical determinant of disease staging, treatment planning, and overall survival in OSCC patients[2].

Accurate evaluation of lymph nodes is essential for guiding therapeutic decisions and predicting patient outcomes in OSCC. Traditionally, clinical examination reinforced with radiological imaging were utilized for preoperative lymph node assessment. Clinical examination involves palpation of cervical lymph nodes to detect any enlargement or abnormality. However, its sensitivity and specificity are limited, particularly for subclinical nodal disease. [3]

Radiological imaging modalities, including ultrasound, computed tomography (CT), magnetic resonance imaging (MRI), offer non-invasive means to assess lymph node status in OSCC patients [4]. These imaging techniques provide detailed anatomical information and enable visualization of nodal size, morphology, and the presence of necrosis or extracapsular spread. Based on CT scan findings and the presence or absence of lymph node metastasis, critical decisions regarding the type and extent of neck dissection are made. The primary objective, along with wide local excision of the tumor, is to clear the lymphatic channels in order to reduce the risk of recurrence and improve the survival rate of patients undergoing treatment[2].

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Histopathological analysis of resected lymph nodes remains the gold standard for diagnosing metastatic disease in OSCC [5]. It provides definitive information on tumor burden, extracapsular spread, and lymph node ratio, which are crucial for determining disease stage and informing further treatment decisions like post op radiotherapy/chemotherapy[6].

It has been reported that the tumor size clinically, radiologically and histopathologically doesn't show much variation but lymph node involvement despite using the sensitive radiological tools may show discrepancy when compared with histopathological results. Clinical staging encompasses both clinical and radiological data. There is a trend of clinical overstaging of the disease which may lead to extensive surgery resulting in increased morbidity in the patient[7]. Keeping in mind in OSCC complete eradication of diseases and potential channels are the hallmarks of treatment planning.

This study was carried out to compare the clinical and histopathological staging of OSCC and to measure the concordance between clinical and histopathological staging. Clinical staging encompasses both clinical and radiological data. Numerous research on the link between the clinical and histological findings of neck nodes in OSCC patients have recently been reported in worldwide literature[8,9]. To the best of our knowledge, Pakistan has not yet made any such comparisons, though. Thus, this study's goal is to assess the aforementioned contrast at a Pakistani tertiary care facility.

Materials and Methods

The retrospective analysis involved 32 newly diagnosed patients with biopsy-confirmed Oral Squamous Cell Carcinoma (OSCC), all managed with curative intent at the Department of Oral and Maxillofacial Surgery, Foundation University College of Dentistry and Hospital (FUCD&H), between 2019 and 2023. Sample size of 32 was calculated using Raosoft online calculator, keeping confidence level at 95%, anticipated population proportion was kept at 4.17 with margin of error at 7%.[10] Ethical review was obtained from institute review committee letter no. FF/FUMC/215-265 Phy22. Patients included in this study were those who had complete clinical, radiological, and histopathological records and had undergone surgical management for oral squamous cell carcinoma with wide local excision and neck dissection. Patients were excluded if they had surgery for tumors other than oral squamous cell carcinoma, had recurrent disease, distant metastasis, or incomplete clinical and radiological information. Initially, 38 cases were reviewed; however, 6 cases were excluded due to incomplete documentation, resulting in a final sample of 32 patients. Follow-up information was not available for this retrospective dataset and, therefore, was not evaluated in the present study.

Clinical and histopathologic staging was conducted according to the 7th edition of the American Joint Committee on Cancer (AJCC) for oral squamous cell carcinoma. Although the 8th edition incorporates additional parameters such as depth of invasion and extranodal extension, these variables were inconsistently reported in the retrieved archival histopathological records. As this was a retrospective study based on pre-existing pathology reports, several essential components required for accurate 8th edition staging were unavailable. Therefore, the use of the 7th edition AJCC staging system was methodologically justified to ensure consistency, completeness, and accuracy of staging within the constraints of the available data[10].

Preoperative Variables

Initial assessment of biopsy proven OSCC cases was done at OMFS Department, FUCD&H. where clinical findings along with demographic details were recorded followed by referral to Radiology Department, Fauji Foundation Hospital (FFH) for preoperative radiological assessment. CT-scan with contrast of the head and neck region was performed on all patients using Puffed-cheek technique, Toshiba Aquilon 16 slice. Axial, coronal and sagittal sections of 5mm thickness along with neck sections of 2mm thickness were obtained. Overall Ct head and neck effective dose was 1.2mSv. For a more comprehensive assessment, findings across different imaging planes were also correlated. To rule out distant metastasis, ultrasound abdomen and chest x-ray were also done. All the CT scans were reviewed by a consultant Radiologist ensuring uniformity and minimizing variability.

Based on CT scan reports the clinical variables considered were; tumor site, clinical tumor size (cT), clinical node stage (cN), bone and submandibular

gland involvement. Positive indicators for clinical node stage (cN) were node size (lymph nodes diameter > 1cm), round shape, central necrosis, perinodal stranding and laterality. [11]

Operative Variable

After initial assessment, all cases were discussed in Multi-disciplinary team meeting comprising of OMFS surgeons, radiation oncologists, medical oncologists, radiologists, pathologists and plastic surgeons to determine the detailed treatment plan for each case including the indications for adjuvant treatment individually. All individuals underwent treatment through radical surgical intervention, the type of neck dissection was decided considering radiological assessment. Modified radical neck dissection or supra omohyoid neck dissection either ipsilateral or bilateral was done keeping in mind the nodal and clinical staging.

Post op Variables

Pathological staging data was gathered from post-operative histopathology reports taken from Histopathology Department, Foundation University Medical College. The pathological variables considered were tumor grade, tumor size (pT), tumor margins, pathological node stage (pN), submandibular gland in addition bone invasion. Pathological node stage (pN) was based on presence of metastatic deposits, extra nodal extension and laterality of positive neck nodes. The patients with positive neck nodes, positive margins and perineural/ perivascular invasion were referred to Oncology department FFH for further adjuvant treatment.

Data were analyzed using SPSS version 24. Normality was assessed using the Shapiro–Wilk test. Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. Concordance between clinical and pathological staging of T and N classifications was determined. The Chi-square test was applied for categorical variables, while Kendall's tau-b was used to evaluate correlations between cT/pT and cN/pN. A p-value < 0.05 was considered statistically significant.

Cohen's Kappa was used to assess agreement (<0.20 = slight, 0.21–0.40 = fair, 0.41–0.60 = moderate, >0.60 = strong). Cramer's V was applied to estimate effect size (0.10 = small, 0.30 = moderate, ≥0.50 = large).

Results

Thirty-two cases, who underwent neck dissection for oral squamous cell carcinoma. Mean age of patients was 60.57 years (Age range 39-79) with 90.6% females. Rest of our data characteristics are shown in Table I Tests of normality indicated that age was normally distributed with p-value of greater 0.05.

On correlating the location with pT and pN, lesions on lower alveolar ridge showed comparatively advanced stage. (Figure 1)

Concordance between clinical tumor size (cT) and pathological tumor size (pT) was found to be 46.9%. 53.1% cases showed discordance primarily due to clinical over staging.

However, clinical (cN) and pathological (pN) nodal staging showed huge disconcordance of 84.4%. Figure 2

According to AJCC 7th edition staging criteria for OSCC, 10 of 32 neck dissection specimens showed regional lymph node metastasis. Only three cases showed concordant clinical (cN) and pathological (pN) stage and were labelled as true positive. Similarly, three cases were clinically under staged and were marked false negative and two cases were true negatives as both were cN0 and pN0. However, 24 cases were clinically over staged and were labelled as false positive. While correlating cN & pN using chi-square, P-value was found to be p>0.05 and was considered insignificant as shown in table 2. Measures of association further supported these findings. Cramer's V suggested a moderate effect size (V = 0.408), but this association was not statistically significant (p = .192). Kendall's tau-b indicated only a weak positive relationship (τb = 0.124, p = .433), and Cohen's Kappa demonstrated almost no agreement between the variables (κ = 0.002, p = .968).

Taken together, these results suggest/demonstrated that there is no statistically significant relationship between the two ordinal variables under study, despite a moderate effect size indicated by Cramer's V.

Similarly, the disconcordance between clinical tumor size (cT) and pathological tumor size (pT) was 53%. There were 15 true positives, zero true negatives, 15 false positives (that were clinically over staged) and 2 false negatives (clinically under staged). The Chi-Square test did not show a statistically significant

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association between cT and pT (p = .232), Similarly, Cramer's V suggested a moderate effect size (V = 0.349), though this was not statistically significant. Kendall's Tau-b revealed a significant positive relationship. Additionally, Cohen's Kappa indicated a fair but significant level of agreement (κ = 0.271, p = .005). Table III. While the overall Chi-Square test was not significant, that no association between the two variables while the specific tests demonstrate a meaningful, moderate, and statistically significant positive association and agreement between cT and pT.

We also correlated clinical tumor size (cT) with pathological node stage (pN) and statistically insignificant relationship (p=0.804) was found as shown in table IV.

Table I: Patients and Tumor Characteristic of Study Participants (n= 32)

Age		**Localization**		**Age**
Younger half of median	16 (50%)	Buccal Mucosa	7 (21.9%)	Younger half of median
Older half of median	16 (50%)	Lip	4 (12.5%)	Older half of median
Sex		Lower Alveolar Ridge	12 (37.5%)	**Sex**
Male	3 (9.4%)	Upper Alveolar Ridge	1 (13.1)	Male
Female	29 (90.6%)	Tongue	8 (25%)	Female
Neck Dissection Type		**Treatment**		**Neck Dissection Type**
		Surgery	11 (34.4%)	
Supra omohyoid	3 (9.4%)	Surgery + RT	13 (40.6%)	Supra omohyoid
Modified Radical	25 (78.1%)	Surgery + CT	1 (3.1%)	Modified Radical
Bilateral	4 (12.5 %)	Surgery + RT + CT	3 (9.4%)	Bilateral
Histological Grade		**Histological Positive Margin**		**Histological Grade**
Well Differentiated	28 (87.5%)	Yes	8 (25%)	Well Differentiated
Moderate	3 (9.4%)	No	24 (75%)	Moderate
Poor	1 (3.1%)			Poor
Clinical Tumor Size (cT)		**Pathological Tumor Size (pT)**		**Clinical Tumor Size (cT)**
cT1	5 (15.6%)	pT1	9 (28.1%)	cT1
cT2	7 (21.9%)	pT2	15 (46.9%)	cT2
cT3	2 (6.3%)	pT3	1 (3.1%)	cT3
cT4	18 (56.3%)	pT4	7 (21.9%)	cT4
Clinical Node Stage (cN)		**Histological Node Stage (pN)**		**Clinical Node Stage (cN)**
cN0	3 (9.4%)	pN0	22 (68.8%)	cN0
cN1	4 (12.5%)	pN1	5 (15.6%)	cN1
cN2a	4 (12.5%)	pN2a	0 (0%)	cN2a
cN2b	17 (53.1%)	pN2b	4 (12.5%)	cN2b
cN2c	4 (12.5%)	pN2c	1 (3.1%)	cN2c

Table II: Concordance of cN and pN staging

		Histological Node Stage					Total	Chi-square P – value	Kendall ’s tau - b		
		pN0	pN1	pN2a	pN2b	pN2c				Cramers ’ V	Kappa (K)
Clinical Node stage	cN0	2	1	0	0	0	3	0.192	r=0.124 p=0.433	V= 0.408	0.002 P=0.968
	cN1	4	0	0	0	0	4				
	cN2a	2	0	0	2	0	4				
	cN2b	12	3	0	2	0	17				
	cN2c	2	1	0	0	1	4				
Total		22	5	0	4	1	32				

Table I: Patients and Tumor Characteristic of Study Participants (n= 32)

		Pathological Tumor Size (pT)				Total	Chi-square p- value	Kendall's tau b	Cramer' V	Kappa (K)
		pT1	pT2	pT3	pT4					
Clinical Tumor Size (cT)	cT1	3	2	0	0	5	0.232	r=0.394 p= 0.006	0.349	K=0.271 P=0.005
	cT2	2	5	0	0	7				
	cT3	0	2	0	0	2				
	cT4	4	6	1	7	18				
Total		9	15	1	7	32				

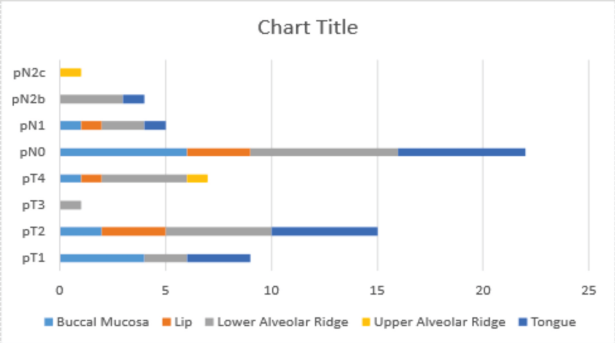

Figure 1: Occult Metastasis in Oral Subsites

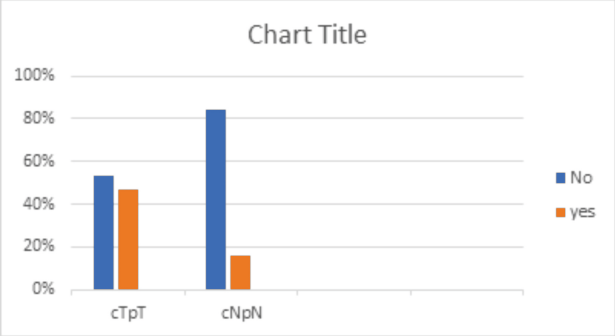

Figure 2: Bar Graph Showing Concordance Of cT/pT and cN/pN

Discussion

The assessment of primary tumor characteristics and lymph node involvement in Head and Neck Cancer holds significant importance. Variations may arise in the clinical and pathological T and N stages of Head and Neck Cancer[12]. This discrepancy is primarily attributed to inaccuracies in interpreting preoperative imaging, the diverse methods employed for identifying finding, and the impact of malignant lymph node biology on contrast agent uptake[13].

The present retrospective study showed a strikingly high percentage (90%) of female patients, reason being administrative policy as till the time of data collection FFH use to cater for private patients (both male and female) and only the families of retired army personnels spouse and children under 10yrs). Thus this contrasting finding does not require any comparison with local or worldwide studies.

The most common sub site of oral cavity cancer observed was lower alveolar ridge. Similar finding is observed in multiple national studies reporting buccal mucosa and lower alveolar ridge to be most frequent sites for OSCC[14, 15]. This is particularly attributed to a common habit in South Asian population particularly Indians and Pakistani who not only chew but also place the known etiological agents of OSCC like tobacco, pan (beetle quid), gutka (areca nut), naswar (powdered tobacco) in the buccal vestibule area[16]. Interestingly, in our study occult metastasis (pN+) in relation to oral subsites showed lower alveolar ridge to be the most frequent site. The finding was in accordance to a study held in South Korea who also reported the mandibular and maxillary posterior areas as the predominant subsites[17]. Another study however reported that tongue cancer metastasizes more often than alveolar ridge and floor-of-the-mouth cancer[18].

Accurate preoperative prediction of lymph node (LN) status via contrast enhanced CT scan plays a pivotal role in determining the extension of neck dissection required for patients with OSCC[18]. As per the guidelines for OSCC management, three supraomohyoid neck dissection were carried out for patients with cN0 as a prophylactic neck dissection[19], rest were treated with radical neck dissection unilateral or bilateral.

Since 87% of our cases were well differentiated, out of these 64% cases had pN0, running comparison between histological grade and nodal metastasis didn't produce statistically significant results. However, comparing our results with a Korean study somewhat similar findings were seen who observed 67% cases of well differentiated OSCC also had pN0 status[17]. While comparing relation between neck node metastasis and clinical tumor size in present study, a statistically insignificant relation was found

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(p=0.804). This in contrast to a study held in South Korea who found a statistically significant relationship (p=0.04) among clinical tumor size, neck node metastasis[17].

In order to make comparison of cT/pT and cN/pN results of our study with worldwide studies comparable results were seen. In a prospective multicenter study encompassing a substantial patient cohort of 560 patients diagnosed with oral squamous cell carcinoma, the agreement rate between clinical and pathological staging was found to be 52.2% for T staging**,** which is better than our concordance rate of 47%. For N staging they reported 53.5%, however a strikingly huge discrepancy as seen in our study with a value of 84%[20].

In a separate study conducted in Poland, almost 50% cases showed agreement between the pathologic stages and their parallel clinical stages. The accuracy of clinical diagnoses for pN stages varied between 66.67% and nearly 90%, with the greatest consistency seen in severe cases.[21]

Another study involving patients with tongue malignancy, the agreement between clinical and pathological T stage was assessed to be 60.6%, and for the N stage, it was determined to be 54.5%.[22]

Biron et al. emphasized that most T staging discrepancies resulted in upstaging of the disease (from early to advanced stage) in an attempt to ensure that patients were not undertreated[23]. For the same reason somewhat, similar findings were observed in our study where among disconcordant cases (53%), 46.7% cases were clinically overstaged.

Another study conducted by Choi et al. on oral cancer cases reported a concordance amount of 87.3% among clinical and pathological tumor staging, and 82.5% among clinical and pathological nodal staging[24]. The higher concordance they assumed is due to use of CT along with highly sensitive PET scans for clinical staging. This is in contrast to our study where only CT scans were used as a tool for clinical staging. From a risk benefit perspective, over-staging let the surgeon to adopt a more aggressive therapeutic approach which potentially improves the oncological outcomes by reducing the risk of recurrence or metastasis especially in a third world country like Pakistan.

Kreppel et al. observed a reasonable alignment of 62% for T stage assessment and 59% for N stage evaluation in a similar patient cohort. In instances where discrepancies occurred, the primary tumors were frequently overestimated. Additionally, they analyzed survival outcomes through univariate analysis, which showed that cT, cN, and pT categories had a notable effect on overall survival. Nevertheless, multivariate analysis identified only the pT and pN classifications as having a significant influence on overall survival.[11]

Another study analyzed 54 patients with oral squamous cell carcinoma (OSCC), focusing on the agreement between clinical and pathological staging, T2 tumors were frequently upstaged, while T4a tumors were often downstaged when comparing clinical to pathological staging. The highest concordance was observed in T4a stage tumors, followed by T2, T3, and T1. In nodal status, N1 showed the most variation, with the highest concordance observed in N0 and N1 stages.[25]

Additional Polish study carried out comparison between overall TNM staging with cT/pT and cN/pN. Approximately one-third of individuals classified as stage pN1 were clinically over staged. Their results indicated that T upstaging occurred frequently during the initial phases of head and neck cancer, whereas underestimating tumor dimensions was more prevalent in advanced stages of the disease (53.3%) [21]. This is in contrast to our study, in which most patients were diagnosed in advanced stage of disease.

Overall, most studies agree that clinical staging often diverges from pathological findings, with T categories commonly overestimated to minimize undertreatment. Concordance for T staging generally falls around 50–65%, improving when advanced imaging such as PET is used. N staging shows greater variability, with both moderate agreement and marked discrepancies reported. Consensus exists on the tendency to upstage early tumors and underestimate advanced ones, though the extent of concordance remains inconsistent across populations and methodologies.

Limitations

Among the few limitations of the current study, most prominent was a low sample size attributed to the fact that we had to exclude quite a good number of cases because of unavailability of complete data.

Another limitation which may have resulted in over

staging of disease was use of only CT scans as a preoperative radiological assessment tool.

Conclusion

This study revealed substantial discrepancies between clinical and pathological staging of OSCC, particularly in nodal assessment, where agreement was negligible. In contrast, clinical evaluation of tumor size showed moderate but statistically significant agreement with pathological findings. These results emphasize that reliance on clinical staging alone. Incorporating histopathological confirmation and, where possible, advanced imaging modalities is essential for accurate staging, appropriate treatment decisions, and improved patient outcomes.

Recommendations

Being a low-income country but wherever applicable, more sensitive radiological techniques like MRI or PET scans could be used for pre-operative clinical staging of OSCC patients in order to reduce the number of false positive cases.

Furthermore, in future studies use of AJCC 8th edition for cancer staging should be used allowing inclusion of more advanced histopathological variables like depth of invasion (DOI).

Moreover prospective, Multi center studies with larger cohorts should also be considered.

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CONFLICT OF INTEREST

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DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon request.

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ORIGINAL ARTICLE

Adapting to Change: Undergraduate Dental Students' Learning Experiences and Perceived Enablers and Barriers During the Post-COVID-19 Transition From Online to Onsite Education

Galvin Sim Siang Lin[1], Jessica Grace Cockburn[2], Vinod Pallath[3]

ABSTRACT

Objective: The present study aimed to explore final-year undergraduate dental students' learning experiences and their perceived enablers and barriers during the post-COVID-19 transitional phase from online to onsite education.

Study Design: A qualitative case study design using focus group discussions was employed in accordance with the Consolidated Guidelines for Reporting Qualitative Research (COREQ) checklist.

Place and Duration of Study: Faculty of Dentistry, Asian Institute of Medicine, Science and Technology (AIMST) University, from April 2022 to June 2023.

Materials and Methods: Homogeneous convenience sampling was used to identify final-year undergraduate dental students currently enrolled at AIMST University Malaysia. Eighteen dental students were recruited and randomly assigned to three groups. They were invited for an online discussion through the recorded Zoom platform. The focus group discussions were audio-recorded and transcribed verbatim. Thematic analysis was performed using an inductive approach.

Results: Three major themes were discovered: (1) Perception of learning facilitating experiences, (2) Perceptions of learning impeding experiences, and (3) Factors influencing learning during transition. The first major theme is divided into five sub-themes: clinical hands-on, treating 'real' patients, knowledge acquisition and understanding, teaching quality, and social interaction. Meanwhile, two sub-themes emerged from the second major theme: expectation and challenging schedule. Finally, the third major theme is divided into six sub-themes: adaptability, confidence and readiness; changes in availability of support; lifestyle; communication; and technical.

Conclusion: Undergraduate final-year dental students reported both facilitating and impeding learning experiences during the COVID-19 transitional period. Dental educators should tailor the current dental education and pedagogical structures to suit the needs and demands of dental students when the country has fully entered the endemic phase.

Key Words: *Dental Student, Health Profession, Online Learning, Post-COVID-19, Undergraduate.*

Introduction

Dentistry is a challenging discipline for students as they are faced with a demanding curriculum, precise skill training, extensive patient interaction, and continuous clinical assessment.[1] This is generally approached through a large devotion of time in patient and instructor-facing environments. However, due to the widespread transmission of the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus, also known as COVID-19, education systems throughout the world have been pushed to explore alternatives to onsite and face-to-face teaching and learning. Distance learning activities were introduced as a remedy during the pandemic.[2] Consequently, dental students had limited hands-on training exposure. In addition, it is remarkably difficult to simulate dental clinical training through home-based online

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platforms, and a lack of practical training was identified as a serious challenge faced by dental students during their clinical years as a consequence of the COVID-19 pandemic.[3]

Malaysia was largely impacted by the global COVID-19 pandemic, and as a result of the Malaysian government's efforts to mitigate the effects through stringent lockdown regulations, there was a conversion of face-to-face to virtual educational programs, and limited clinical teaching among medical and health science students from April 2020 to mid-2022.[4] In October 2021, the Malaysian government took the initiative to transition the country from a COVID-19 pandemic response to a sustained endemic phase. Following this declaration, higher education institutions were being restored, allowing students to gradually resume physical classes and face-to-face activities from fully online learning. Thus, it becomes imperative to assess and understand undergraduate dental students' perceptions of their learning during the transitional phase after two years of facing pandemic-related challenges. This allows dental educators, curriculum creators, and stakeholders to gain valuable insights that can be used as evidence for future curriculum improvements and ensure readiness for sudden and unexpected changes.

Virtual learning, online learning, or e-learning has evolved as a method to improve the learning process during the outbreak of the COVID-19 pandemic. Although unpleasant, the abrupt shutdown of universities around the world owing to the pandemic provided a massive potential and opportunity for a cultural revolution in higher education.[5] Nevertheless, the shift from face-to-face learning to distance e-learning during the pandemic has proven to change students' learning perceptions as well as the use of educational technology and pedagogy practices.[6] Hence, the transition from pandemic to endemic or post-pandemic phase may be viewed as a critical step in discovering and investing in the learning innovation required to provide the most effective education to our future dentists. To date, studies on the learning perceptions of undergraduate dental students during the transitional period are still scarce in the literature, and no such research has been undertaken among Malaysian dental students. Therefore, the purpose of the present study was to explore undergraduate dental students' learning experiences and perceived enablers and barriers during the post-COVID-19 transition from online to onsite education.

Materials and Methods

An exploratory qualitative case study was carried out at the Asian Institute of Medicine, Science and Technology (AIMST) University from April 2022 to June 2023, in accordance with the Consolidated Guidelines for Reporting Qualitative Research (COREQ) checklist.[7] The ethical approval was obtained from the AIMST University Human Ethics Committee with ethical approval code AUHEC/FOD/2022/04. Both written and verbal consent were obtained from the participants, and all information from the participants was kept confidential and anonymous by the investigators. A focus group approach was used and facilitated by an academic staff member who has prior experience in conducting education-based dental research. Final-year undergraduate dental students currently enrolled in the undergraduate dental program at AIMST University, Malaysia, were included in the present study. Participants were eligible if they had experienced both online learning during the COVID-19 pandemic and the subsequent transition back to onsite training. Students who were on academic leave or who had not resumed onsite learning activities at the time of data collection were excluded.

They were approached via WhatsApp and were invited for an online discussion through the recorded Zoom platform once verbal and written consent was obtained. Students were also informed regarding the purpose of the study. No obligation or dependency was identified between the students and any of the investigators of the present study. Participation was voluntary, and pseudonyms were used to maintain the confidentiality of participants' identities. Sixty-eight final-year undergraduate dental students were invited for the focus group interview, and 18 agreed to participate in the study. These students were divided randomly into three different focus groups, comprising six students per group. Homogeneous focus groups were formed to facilitate open discussion among peers with similar academic exposure, and participants were randomly assigned to groups to minimise potential selection bias.

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A topic guide was developed by the research team following a review of the literature on online learning, disruption to clinical education, and student adaptation during the COVID-19 pandemic. The questions were designed to elicit students' learning experiences, perceived challenges, and facilitating factors, and their adaptation during the transition phase from online to onsite education. Content validity was established through internal review by two senior faculty members with prior experience in instrument development and validation, and minor revisions were made to enhance clarity and relevance before data collection. No formal theoretical framework was imposed, allowing for an inductive exploration of participants' perspectives. The validated topic guide was subsequently used to conduct the focus group discussions. Each session began with a brief introduction by the facilitator, followed by an informal conversation to establish rapport and ensure participants were comfortable before proceeding with the guided questions (Appendix 1). The focus group interviews were conducted without any other third-party involvement to safeguard student participants' confidentiality. The discussions were audio-recorded, and the facilitator took the field notes during and after each focus group session. At the time of data collection, teaching and learning were in an active transition phase during the post-COVID-19 period, with a combination of resumed onsite clinical sessions and selected online lectures, requiring students to continuously adapt to changing educational modalities.

Analysis and Findings

Thematic analysis was performed in which the audio recordings were transcribed verbatim and evaluated. Subsequently, the participants received the transcribed manuscripts to cross-check for accuracy. An inductive approach was used to allocate a code to each key sentence and then arrange similar codes into sub-themes, as reported in a previous study.[8] Under a major theme, related sub-themes were grouped together, and these sub-themes were examined again to ensure no missing data. The data were then reviewed by all investigators, followed by contemplation and refinement until a consensus was obtained.

Results

All the investigators agreed that saturation had been reached and that adding more participants to the focus group discussion would not be necessary. Three major themes were discovered and divided into sub-themes, which are listed below with representative quotes from the participants (Figure 1). The following three major themes were: (1) Perception of learning facilitating experiences, (2) Perceptions of learning impeding experiences, and (3) Factors influencing the learning during transition. These themes reflect students' experiences while adapting to resumed onsite learning during the post-COVID-19 transition phase, rather than a completed post-transition state.

Theme 1: Perception of Learning Facilitating Experiences

The positive perceptions of undergraduate final year dental students towards their academic learning during the transitional period can be divided into five sub-themes, including (1) Clinical hands-on; (2) Treating 'real' patients; (3) Knowledge acquisition and understanding; (4) Teaching quality; and (5) Social interaction.

Sub-theme 1: Clinical Hands-On

Students were satisfied with the transition from online back to onsite as they claimed that they could have more hands-on practical sessions, which enhanced their academic learning rather than online classes during the pandemic.

"When we transit back to face to face, we were allowed to practice clinical and lab works, it improves our hands-on practical skills." [P4]

"I learned more (transition period), especially doing more hands-on work." [P8]

"My learning greatly improved. I learnt a lot through face-to-face clinical sessions instead of online lectures." [P9]

Sub-theme 2: Treating 'Real' Patients

Students felt that they learned better on-site as they could observe and treat real patients during the transitional period.

"Onsite learning and look at humans (patients) again, it felt very lively." [P5]

"I felt that our learning is improving because we treat real patients." [P14]

"I started to see real practical cases which is on the benefit side." [P15]

"During the transitional period, we can treat real patients which enhanced our learning." [P16]

Sub-theme 3: Knowledge acquisition and understanding

Students preferred onsite learning because they found it difficult to focus and understand the content delivered during online classes, and they claimed online learning mode was not conducive, which did not help in their learning progress. Students also felt that they could apply and retain their knowledge better during the transition from online to onsite learning.

"I cannot pay attention online. It is not conducive, not helping in my learning progress." [P1]

"I can't focus 100% during online class." [P2]

"Onsite learning tends to retain the knowledge better." [P8]

"I did not learn much and I did not understand what the teachers are trying to teach on Zoom." [P13]

"I would prefer more face-to-face sessions so I can apply the knowledge and brush up my clinical skills." [P17]

Sub-theme 4: Teaching quality

Students felt that the teaching quality was inferior during the COVID-19 pandemic, as the teachers were unable to show them the clinical dental procedures during online lessons, but this gradually improved during the transition to onsite learning.

"Teachers can show us the procedure on patient, and we can clearly see it during the transition phase." [P1]

"Lecturer is able to answer you better face-to-face compared to online." [P8]

"The lecturer never shows us how to do it during the pandemic. During the COVID, we must watch YouTube and learn by ourselves." [P9]

Sub-theme 5: Social interaction

The shift from online to onsite learning was perceived by students as improving their ability to communicate with their teachers and patients, rather than just looking at the screen during online classes and being unable to get their doubts cleared by their teachers via online learning.

"There are less interactions during online class." [P1]

"When we are back to face-to-face session, we get to learn the communication part too." [P2]

"This (transition period) benefits us from our communication skills and also interactions with people." [P6]

"Face-to-face interaction is better, as we're going to learn how to communicate with people." [P11]

Theme 2: Perceptions of Learning Impeding Experiences

Some students demonstrated negative perceptions of their academic learning during the transitional period, and they preferred their learning to be delivered online mode with the sub-themes that emerged as (1) Expectation and (2) Challenging schedule.

Sub-theme 1: Expectations

Students felt that teachers had high expectations of their academic knowledge and clinical performance during the transition from online back to onsite.

"Our lecturers expect us to know everything in final year and it was a very difficult time." [P8]

"Some lecturers have high expectation on us." [P16]

Sub-theme 2: Challenging schedule

Students felt that their timetable was packed and that they were rushing with their schedule during the transitional period from online to onsite learning.

"The timetable and schedule are too packed, we have brush up all the things in short period." [P2]

"We started our final year very rushed." [P3]

"Tt's a shock to me that there were a lot of things to learn and do when we entered year five clinic." [P4]

"We do not have that much time to practice" [P13]

Theme 3: Factors influencing learning during transition

Students faced several difficulties or challenges during the transitional period from online back to onsite face-to-face learning, with sub-themes that emerged as: (1) Adaptability, (2) Confidence and readiness, (3) Changes in availability of support, (4) Lifestyle, (5) Communication, and (6) Technical.

Sub-theme 1: Adaptability

Students found it difficult as they needed to adapt to the new transition educational system and environment.

"When we started to enter the clinics, it was very difficult for us to adapt." [P8]

"The transition was something very new for me and I find it very difficult to adapt to it." [P14]

"We need to keep adapting ourselves to a whole new system. It's a whole jumbled up." [P17]

Sub-theme 2: Confidence and readiness

Students felt that they were not confident and not

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ready as final-year students. Some of them also felt stress with their clinical skills during the transition period, as they had limited practical experience during the COVID-19 pandemic.

"I feel nervous and afraid of what's going to happen next because I lost all my confidence during COVID." [P2]

"We do not have adequate hands-on, and it makes me feel stress and not confident." [P10]

"I feel stress and not ready to transit back to face-to-face." [P13]

Sub-theme 3: Changes in the availability of support

Students felt stressed and depressed as they found it difficult to seek family support during the transition back from online to onsite learning.

"I do not get the support emotionally when I am stressed." [P7]

"It has been depressing for me for the past six months... I need my family here." [P11]

Sub-theme 4: Lifestyle

Students find it challenging to wake up early for physical class sessions, unlike online classes during the COVID-19 pandemic, as they can wake up late.

"That change (from online to onsite) was a little unsatisfied for me, because I had to wake up early for class." [P7]

"The difficulty that I faced is to wake up early for the class." [P12]

"Since we are used to online classes, I feel very tired to wake up early in the morning." [P14]

Sub-theme 5: Communication

Students felt that communication was a challenge for them during the transition from online to onsite learning.

"I felt my communication skill was very bad." [P6]

"I feel stress when I come back because I am not used to meet new people." [P18]

Sub-theme 6: Technical

Students claimed that internet connectivity was an issue during the transitional period, as some lectures were still conducted online.

"There are always connectivity issues." [P8]

"The main problem is Wi-Fi interruptions or any slow internet connectivity problems." [P11]

"Our lectures that are still conducted online always face internet problems." [P13]

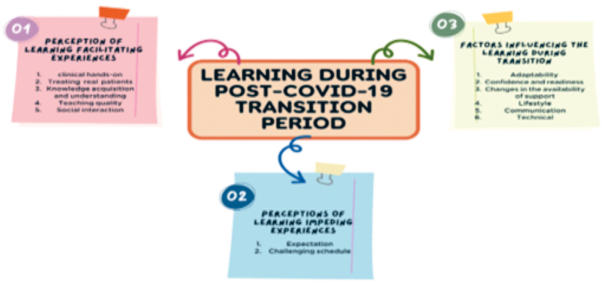

Figure 1: Themes and sub-themes of the present findings

Discussion

The present study explored the perceptions of final-year undergraduate dental students regarding their academic learning during the transition from online to onsite face-to-face learning. The first theme reveals that these students are satisfied with the transitional period because it allows them to engage in more hands-on practical learning during onsite sessions. This aligns with previous research, which also indicates that online classes do not significantly enhance clinical performance in dental education.[9-12] This may be due to the nature of the curriculum in dentistry requiring extensive clinical exposure to master high levels of psychomotor skills.[13] It should also be highlighted that dental training simulations using online manikins are not exclusively feasible as they are highly expensive, difficult to use, hard to get in educational settings, and do not cover all aspects of dental specialties.[14]

Undergraduate dental students in the present study found that their learning experience improved when they could directly observe and treat actual patients. While preclinical didactic case-based exercises or virtual simulations can be effectively delivered online, these teaching methods may not adequately replicate real patient experiences, especially for clinical year students.[12] Moreover, without demonstration on live patients, it might be challenging for students to put the practical applications of the conceptual knowledge they have learnt into practice and correlate them. The absence of essential psychomotor learning opportunities during their final year could have adverse effects, as graduate dentists require substantial exposure to real patients and clinical practice, which were limited on online platforms during the pandemic.[12]

Students in the current study reported improved satisfaction with teaching quality when transitioning from the pandemic's online learning to face-to-face instruction. This can be attributed to the challenges faced by teachers during the COVID-19 outbreak, as

they had to quickly adapt to online or virtual learning technologies and provide comprehensive instruction in dental education through online platforms.[12] Developing effective online learning content was also time-consuming and required proper training.[15] To sustain online or remote learning during the ongoing COVID-19 endemic phase, teachers may need to better organise their lesson plans and make use of readily available teaching resources. In addition, students found that transitioning from online to onsite learning improved their ability to interact with teachers and fellow students. Previous studies indicate that online learning hinders effective communication with teachers and peers.[10, 11] They also highlighted that social networks cannot replace in-person interactions.[10]

On the other hand, students perceived that their teachers had high expectations for their clinical performance and academic success as they transitioned from online to onsite learning. There may be additional factors at play during the COVID-19 transitioning phase, such as stress among teachers, that contribute to the climate of a "high expectations" learning environment. Furthermore, students experienced a packed schedule and rushed during the transition from online to onsite learning. Monitoring the psychological well-being of dental students and faculty members is crucial during this period.[3] It is essential to emphasise strategies for managing a demanding schedule and establish mutual understanding between the dental school and students to ensure the timely completion of clinical requirements and graduation.[16]

In the present study, students encountered challenges in adapting to the new educational system and environment, which is consistent with previous similar studies.[3, 10] Students must figure out how to adjust to the current environment, given the considerable transition from online to onsite learning during the transitional period. Lack of confidence and preparation when transitioning from online to on-site learning is one of the factors influencing learning during transition among final-year undergraduate students in the present study. Therefore, more clinical sessions or simulated practical are needed to reinforce their clinical skills and boost their confidence, and mentoring is crucial during the transitional period. Moreover, students experienced stress and depression as they struggled to seek family support during the transition from online to onsite learning. To support student well-being during the COVID-19 transitional period, dental schools should establish a student support system and implement policies for health-promoting measures.[17]

Undergraduate dental students expressed that their lifestyle has changed ever since teaching and learning have gradually reverted to face-to-face, as they need to wake up early for physical class. Unquestionably, any modifications to the educational system will result in alterations to students' personal lifestyles.[10] This underscores the need for additional counselling and behavioural support during this transitional phase. Moreover, communication challenges have emerged during the transition from online to onsite learning, though it is plausible that dental students' communication skills may improve as they enter their professional careers. Several students also cited internet connectivity issues as a challenge during this transition, a concern supported by previous research.[10, 11] The success of online learning systems relies on high-quality internet access and responsive technical support teams.[18] Hence, educators must consider integrating diverse educational resources and programs that align with contemporary technology within the existing curriculum.[19] Dental schools should seize the opportunity presented by students' pandemic learning experiences to reconfigure their teaching and learning approaches. If dental schools plan to continue offering e-learning or distance education beyond the COVID-19 pandemic, they must contemplate redesigning their pedagogical structures.

One limitation of the current cross-sectional study is its restriction to a single dental school. Students' perceptions may have been influenced by various factors, such as concerns related to the endemic situation, isolation in their homes or hostels, and the time spent with family during the transitional period. The study was conducted during the early stages of the COVID-19 transitional period, when dental students experienced a sudden shift to a new educational setting and new regulations following nearly two years of a national lockdown. As the country's recommendations and guidelines may

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change with the nation's progress into the endemic phase, it is advisable to conduct future longitudinal studies.[20] It should encompass both public and private dental schools, along with students from other health professions, to comprehensively assess the general academic learning perceptions during the transition from pandemic to endemic. Nonetheless, the findings from this study can serve as a foundational basis for future research, particularly on a larger sample size covering multiple dental schools in Malaysia.

Conclusion

Within the limitations, the present study has addressed undergraduate final-year dental students' perceptions of their academic learning during the post-COVID-19 transitional period and explored the challenges and concerns they faced when online learning was reverted to face-to-face. Although different students would perceive their academic learning differently, it is imperative for dental educators to investigate this matter and tailor the current dental education and pedagogical structures to suit the needs and demands of dental students when the country has fully entered the endemic phase.

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CONFLICT OF INTEREST

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DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon request.

CASE REPORT

Anaesthetic Management of An Adult Patient with Homocystinuria and Dystonia Undergoing Orthopaedic Surgery: A Case Report

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ABSTRACT

Homocystinuria is a rare inherited metabolic disorder associated with increased perioperative risk due to hypercoagulability and metabolic stress. Anaesthetic management in adult patients undergoing non-ocular surgery has rarely been reported. We describe the anaesthetic management of a 29-year-old man with homocystinuria, marfanoid features, and dystonia who underwent elective orthopaedic foot surgery. Perioperative care focused on minimizing thromboembolic and metabolic risks through reduced fasting duration, maintenance of normothermia and adequate hydration, avoidance of nitrous oxide, and use of mechanical thromboprophylaxis. General anaesthesia was administered using a laryngeal mask airway with sevoflurane and atracurium. The intraoperative and postoperative courses were uneventful, and the patient was discharged on the same day of the surgery.

This case highlights that with careful, physiologically guided planning, safe anaesthesia can be achieved in adult patients with homocystinuria, even in resource-limited settings.

Key Words*: Anaesthetic Management; Case Report; Homocystinuria; Hypercoagulability; Orthopaedic Surgery.*

Introduction

Homocystinuria is a rare autosomal recessive disorder of methionine metabolism associated with multisystem involvement, including ocular, skeletal, neurological, and vascular abnormalities, and an increased perioperative anaesthetic risk due to hypercoagulability and endothelial dysfunction[1,2]. From an anaesthetic perspective, elevated homocysteine levels are linked to an increased risk of thromboembolism, metabolic instability, and adverse neurological outcomes, particularly during general anesthesia[3]. Anaesthetic management is further complicated by skeletal abnormalities, neurological manifestations, and the need to avoid nitrous oxide, which can exacerbate hyperhomocysteinemia[3]. The published literature on anaesthesia in homocystinuria is limited and largely confined to paediatric ophthalmic procedures, with few reports addressing adult patients undergoing non-ocular surgery. We report the anaesthetic management of a 29-year-old man with homocystinuria and dystonia who underwent elective orthopaedic foot surgery.

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Case Presentation

A 29-year-old man with a known diagnosis of homocystinuria presented for the elective correction of left foot hammer toes (Figure 1). His medical history was notable for dystonia with intermittent left-sided limb tremors, resulting in a progressive functional impairment. He had previously undergone nasal surgery under general anaesthesia in adulthood and ophthalmic surgery in childhood, both without any perioperative complications. There was no history of thromboembolic events, seizures, fractures, or allergies to drugs.

On examination, the patient had a marfanoid habitus and mild intellectual developmental delay, with intermittent tremors in the left upper and lower limbs. Airway assessment revealed a Mallampati class III view with upper dental cap. Cardiovascular and respiratory examinations were unremarkable, and the baseline vital signs were within normal limits.

Laboratory investigations were within normal limits, except for a markedly elevated plasma homocysteine level of 31.7 µmol/L (5.46-16.2

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µmol/L). The patient was under regular metabolic follow-up for homocystinuria and was receiving vitamin supplementation as part of his long-term management. Standard metabolic therapy includes pyridoxine (vitamin B6), folate supplementation, and dietary modification to reduce homocysteine levels. Perioperatively, continuation of metabolic therapy and avoidance of factors that could increase homocysteine levels were emphasized. Adequate hydration and minimization of fasting were also implemented to reduce metabolic stress. Electrocardiography and chest radiography showed no abnormalities. (Table I)

The patient was scheduled for a left second-to-fourth metatarsal tenotomy with distal interphalangeal joint excision and K-wire arthrodesis. To minimize fasting-related metabolic stress, the procedure was scheduled first on the operating list and planned as a day-case surgery. Preoperative fasting followed ASA guidelines, permitting clear fluids up to 2 h and solids up to 6 h before anaesthesia. Intravenous access was established upon admission, and maintenance hydration was initiated with Ringer's lactate at 70 mL/h.

Standard ASA monitoring was performed before anaesthesia induction. Following preoxygenation, general anaesthesia was induced with nalbuphine, midazolam, propofol, and atracurium. A laryngeal mask airway was used for airway management, and anaesthesia was maintained with sevoflurane in an oxygen–air mixture, avoiding nitrous oxide. Normothermia was maintained using forced air warming, and mechanical thromboprophylaxis was applied throughout the procedure. The hemodynamic parameters remained stable, and blood loss was minimal. Warmed intravenous fluid was administered intraoperatively.

Neuromuscular blockade was reversed at the conclusion of the surgery, and the patient was transferred to the recovery area in a stable condition. Postoperatively, early mobilization and oral hydration were encouraged in this patient. The postoperative course was uneventful, and the patient was discharged on the same day with analgesics, vitamin supplementation, and follow-up instructions provided. Postoperative radiographs confirmed satisfactory alignment following K-wire fixation of the lesser toes (Figure 1)

Table I: Baseline Laboratory Investigations

Investigation	Result	Reference range
Hemoglobin	14.8 g/dL	13.0–17.0 g/dL
Total leukocyte count	11,290 /µL	4,000–11,000 /µL
Platelet count	214,000 /µL	150,000–450,000 /µL
Serum sodium	137 mEq/L	135–145 mEq/L
Serum potassium	4.3 mEq/L	3.5–5.0 mEq/L
Serum chloride	99 mEq/L	98–107 mEq/L
Serum bicarbonate	20 mEq/L	22–29 mEq/L
Blood urea nitrogen	12 mg/dL	6–20 mg/dL
Serum creatinine	0.73 mg/dL	0.72–1.25 mg/dL
Estimated GFR (CKD-EPI)	143 mL/min/1.73 m²	>60 mL/min/1.73 m²
Prothrombin time	10.2 s	9.5–11.7 s
INR	0.95	0.8–1.3
Activated partial thromboplastin time	25.0 s	24.8–36.2 s
AST (SGOT)	33 U/L	≤50 U/L
ALT (SGPT)	19 U/L	≤50 U/L
Alkaline phosphatase	64 U/L	40–130 U/L
Total bilirubin	0.56 mg/dL	0.2–1.2 mg/dL
Direct bilirubin	0.23 mg/dL	≤0.30 mg/dL
Gamma-GT	13 U/L	≤60 U/L
Plasma homocysteine (fasting)	31.7 µmol/L	5.46–16.2 µmol/L

Figure 1: Postoperative radiographs of the left foot (lateral and dorsoplantarviews) demonstrating K-wire fixation following corrective surgery for hammer toe deformities.

Discussion

Homocystinuria poses significant anaesthetic challenges due to hypercoagulability, metabolic vulnerability, and multisystem involvement.[4,5] Most published anaesthetic reports involve paediatric patients undergoing ophthalmic procedures, while adult patients requiring non-ocular surgery, particularly orthopaedic procedures associated with venous stasis, are rarely described.[6] This case highlights the safe perioperative management of an

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adult patient with homocystinuria who underwent elective foot surgery.

In addition to metabolic considerations, our patient had dystonia and limb tremors, which influenced perioperative communication, positioning, and postoperative mobilization efforts. Neurological manifestations are less frequently emphasized in anaesthetic reports of homocystinuria but are clinically relevant, particularly in adult patients, and warrant individualized perioperative planning.

Thromboembolism remains the principal cause of perioperative morbidity in patients with homocystinuria.[5] In this case, risk mitigation focused on nonpharmacological strategies, including minimization of fasting, maintenance of adequate hydration and normothermia, application of mechanical thromboprophylaxis, and early postoperative mobilization. These measures have been consistently recommended in previous reports and were effective in our patient despite the absence of pharmacological anticoagulation.[7] Given the patient's lack of prior thrombotic events, normal cardiac evaluation, and moderate duration of surgery, a non-pharmacological approach was considered appropriate. In addition to thromboembolic complications, several other systemic features of homocystinuria may influence anaesthetic management. Connective-tissue abnormalities such as marfanoid habitus, osteoporosis, and joint laxity increase the risk of fractures and positioning injuries during surgery, necessitating careful handling and padding[8]. Skeletal abnormalities and dental issues may also contribute to airway management challenges, particularly in patients with kyphoscoliosis or limited cervical mobility. Neurological manifestations including developmental delay, tremors, dystonia, and seizures can complicate perioperative communication, positioning, and postoperative recovery. Awareness of these multisystem features is therefore essential for anaesthesiologists when planning individualized perioperative care in patients with homocystinuria.

Avoidance of nitrous oxide was a key anaesthetic decision, as nitrous oxide inhibits methionine synthase, a vitamin B12 dependent enzyme involved in homocysteine metabolism, leading to further accumulation of homocysteine and potential neurological and cardiovascular complications.[3] The sevoflurane-based anaesthetic technique allowed for stable intraoperative conditions without metabolic disturbance.

Airway management can be challenging in patients with marfanoid features; however, for this short orthopaedic procedure, a laryngeal mask airway provided a safe and effective alternative to endotracheal intubation. Overall, this case demonstrates that with careful physiologically guided planning, anaesthesia can be safely administered to adult patients with homocystinuria, even in resource-limited settings such as ours.

Conclusion

This case demonstrates that adult patients with homocystinuria can safely undergo non-ocular orthopaedic surgery when perioperative management is guided by the physiological principles. Key strategies include the avoidance of nitrous oxide, minimization of fasting, maintenance of normothermia and hydration, and use of mechanical thromboprophylaxis. Careful anaesthetic planning is essential to reduce thromboembolic and metabolic risks in this population.

Consent statement: Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

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CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

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Authors have declared no specific grant for this research from any funding agency in public, commercial or nonprofit sector.

DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon request.

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SUBJECT AREA: JIIMC is a multi-disciplinary medical journal that publishes scientific research articles related to biomedical sciences.

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  A clinical trial is any research study that prospectively assigns human participants or groups to one or more health-related interventions to assess their effects on health outcomes. These interventions can include drugs, surgical procedures, devices, behavioral treatments, dietary changes, and modifications in care processes. Health outcomes encompass any biomedical or health-related measures collected from patients or participants, including pharmacokinetic data and adverse events. Purely observational studies (those in which the assignment of the medical intervention is not at the discretion of the investigator) do not require registration.

GENERAL ARCHIVAL INSTRUCTIONS

The manuscript should be typed in MS Word. Each manuscript should include a title page (containing email address, cell numbers, institution, and postal address of the corresponding author), abstract, key words, text, acknowledgements (if any), references, tables (each table, complete with title and footnotes) and legends for illustrations and photographs. Each component should begin on a new page. Sub-headings should not be used in any section of the script except in the abstract.

TEXT ORGANIZATION

All manuscripts except Short Communication and Letter to the Editor should be divided into the following sections.

ABSTRACT

Abstracts of original article should be in structured with following sub-headings:

- Objective
- Study Design
- Place & Duration of Study
- Materials & Methods
- Results
- Conclusion

Four elements should be addressed: "why did you

start?", "what did you do?", "what did you find?" and "what does it mean? “.” Why did you start?" is addressed in the objective. "What did you do?" constitutes the methodology and could include design, setting, patients or other participants, interventions, and outcome measures. "What did you find?" is the 'results', and "what does it mean?" would constitute the conclusions. Please label each section clearly with the appropriate sub-headings. Structured abstract for an original article, should not be more than 250 words. At least 3 key words should be written at the end of the abstract. Review articles, case reports and others require a short, unstructured abstract. Commentaries do not require an abstract.

INTRODUCTION

Write this section with references as per following instructions:

1. Give background information about the subject matter and the issues your study intends to address. Only strictly pertinent references should be cited, and the subject should not be extensively reviewed.
2. Describe what is known (in the literature) and what is not clear about the subject with reference to relevant literature thus identifying the literature gap.
3. You write the rationale (justification) of your study.
4. Finally, you mention the objective of your study

MATERIALS AND METHODS

Methodology is written in past tense.

Follow this sequence **without headings:**

- Study design
- Place and Duration of Study
- Sample size
- Sampling technique
- Mention about permission of the ethical review board and other ethical issues addressed.
- Inclusion and Exclusion Criteria
- Data collection procedure-
- Type of data: parametric or nonparametric
- Data analysis: including Statistical Software used, and statistical test applied for the calculation of p value and to determine the statistical significance. Exact p-values and 95% confidence interval (CI) limits must be mentioned instead of only stating greater or less than level of significance. All percentages must be accompanied with actual numbers.

RESULTS

These should be presented in logical sequence in the text, tables, and illustrations. All the data in the tables or illustrations should not be repeated in the text; only important observations should be emphasized or summarized. No opinion should be given in this portion of the text.

DISCUSSION

This section should include the author's comments on the results. Write in present tense, active voice except for results, which are written in past tense. It should be written in following sequence:

- First, very briefly summarize, Interpret and discuss main results and don't merely repeat the results.
- Discuss key studies relevant to your study.
- Compare your work with other's work.
- Describe limitations of your study.
- Suggest future work if necessary.

CONCLUSION

Conclusion should be provided under a separate heading. It should be in congruence with the objective. No recommendations are needed under this heading.

REFERENCES

References must be written in Roman Number and in the Vancouver Style only. References should be numbered in the order in which they are superscripted in the text. At the end of the article, the full list of references should give the names and initials of all authors (unless there are more than six when only the first six should be given followed by et al). The author's names are followed by the title of the article; title of the journal abbreviated according to the style of the Index Medicus (see “List of Journals Indexed”, printed yearly in the January issue of Index Medicus); year, volume, and page number, e.g., Hall, RR. The healing of tissues by C02 laser. Br J. Surg: 1970; 58:222-225. References to books should give the names of editors, place of publication, publisher, and year. The author must verify the references against the original documents before the article. References to papers accepted but not yet published should be designated as “in press” or “forthcoming”; authors should obtain written permission to cite such papers as well as verification that they have been accepted for publication.

TABLES AND ILLUSTRATIONS

Tables and illustrations should be merged within the text of the paper, maximum number of tables and illustrations should not exceed four, and legends to illustrations should be typed on the same sheet. Tables should be simple and should supplement rather than duplicate information in the text; tables repeating information will be omitted. Each table should have a title and be typed in double space without horizontal and vertical lines on an 8 ½" x 11' paper. Tables should be numbered consecutively with Roman numerals in the order they are mentioned in the text. Page number should be in the upper right corner. If abbreviations are used, they should be explained in footnotes and when they first appear in text. When graphs, scattergrams, or histograms are submitted, the numerical data on which they are based should be supplied. All graphs should be made with MS Excel and be sent as a separate Excel file even if merged in the manuscript. For scanned photographs the highest resolution should be used.

S.I.UNITS

System International (SI) Unit measurements should be used. All drugs must be mentioned in their generic form. The commercial name may however be mentioned within brackets, if necessary.

PHOTOGRAPHS AND FIGURES

Figures and Photographs should only be included when data cannot be expressed in any other form. Figures and photographs must be cited in the text in consecutive order. Legends must be typed on the same paper. Legends for photomicrographs should indicate the magnifications, internal scale, and method of staining. Figures should be numbered in Arabic numbers.

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2. Have been involved in drafting the work or

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