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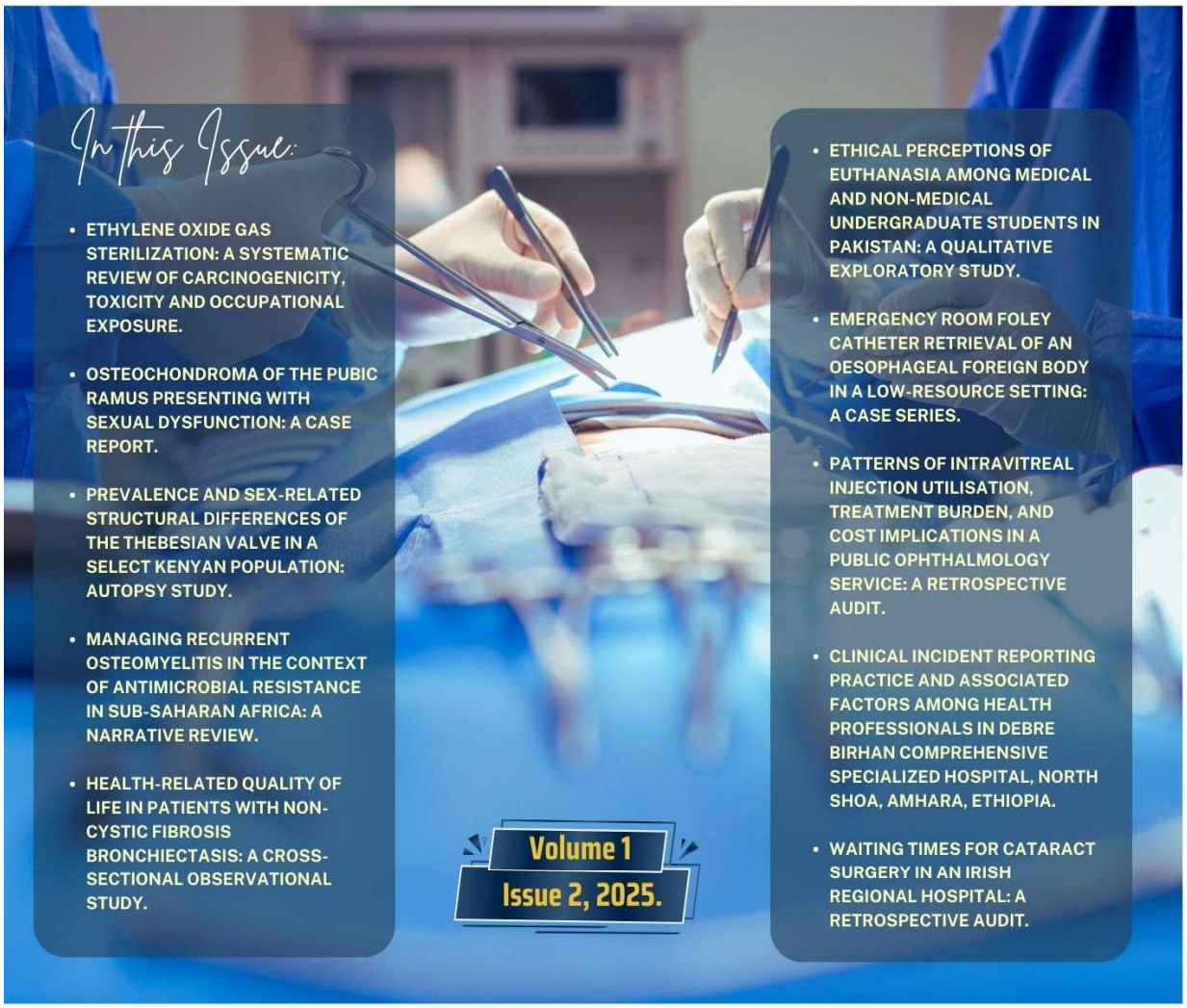
Theme: "Advancing Safe, Ethical, and Sustainable Patient-Centred Care Across Global Surgical and Perioperative Systems."



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Volume 1
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Aligned with the United Nations Sustainable Development Goals (SDGs):

- *SDG 3: Good Health and Well-Being.*
- *SDG 9: Industry, Innovation & Infrastructure.*
- *SDG 10: Reduced Inequalities.*
- *SDG 12: Responsible Consumption & Production.*
- *SDG 16: Peace, Justice & Strong Institutions.*

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LETTER FROM OUR **EDITOR-IN CHIEF**

As we present Volume 1, Issue 2 of The Operating Room Global Journal, I invite our readers to pause and reflect on a simple yet profound truth: at the heart of every surgical intervention lies a human life shaped by trust, vulnerability, and hope. This issue is dedicated to advancing care that is not only clinically sound, but deeply ethical, patient-centred, and sustainably embedded within health systems worldwide. Surgical and perioperative care across the globe is evolving rapidly. Innovation, data, and technology continue to transform how we diagnose, treat, and heal. Yet progress must be guided by purpose. Safety, ethical responsibility, equity, and sustainability must remain our compass, particularly as disparities in access, resources, and outcomes persist across regions and health systems. These priorities align closely with the United Nations Sustainable Development Goals (SDGs), especially SDG 3 (Good Health and Well-Being), SDG 9 (Industry, Innovation, and Infrastructure), SDG 10 (Reduced Inequalities), SDG 12 (Responsible Practices), and SDG 16 (Strong Institutions).

The scholarship featured in this issue reflects these realities with clarity and courage. From studies examining occupational exposure risks and antimicrobial resistance, to ethical perspectives on end-of-life decisions, patient-reported quality of life, and system audits addressing access, cost, and waiting times, the contributions collectively remind us that quality care is inseparable from the systems that sustain it. Several manuscripts emerge from resource-limited settings, offering grounded insights into resilience, innovation, and the pursuit of excellence despite constraint. These voices are essential in shaping a truly global and equitable conversation on surgical and perioperative care.

A recurring message throughout this issue is the need to strengthen cultures of safety, transparency, accountability, and learning. Improving incident reporting, reducing delays, addressing workforce and cost burdens, embedding ethical reflection into clinical practice, and promoting responsible use of resources are not merely administrative goals, they are moral and institutional imperatives that directly affect patient dignity, safety, and outcomes.

What gives me great optimism is the diversity and depth of perspectives represented here. Authors from different regions, disciplines, and clinical environments come together with a shared intention: to improve care for patients we may never meet, yet to whom we are collectively accountable. This spirit of shared responsibility across borders and systems defines both the vision of The Operating Room Global Journal and its contribution to sustainable global health development.

I extend my sincere gratitude to our authors, reviewers, and editorial team for their dedication and intellectual generosity. Their work strengthens not only this journal, but the broader global effort to deliver safer, fairer, ethically grounded, and more sustainable surgical care.

May the insights in this issue inspire reflection, dialogue, and action reminding us that progress in surgery is measured not only by technical success, but by the trust we earn, the systems we strengthen, and the lives we serve.

With warm regards,

Dr. Zakir Hussain Parray

EDITOR-IN-CHIEF,
THE OPERATING ROOM GLOBAL JOURNAL (TORGJ)

Dr. Zakir Hussain Parray
(Editor-in-Chief, TORGJ)

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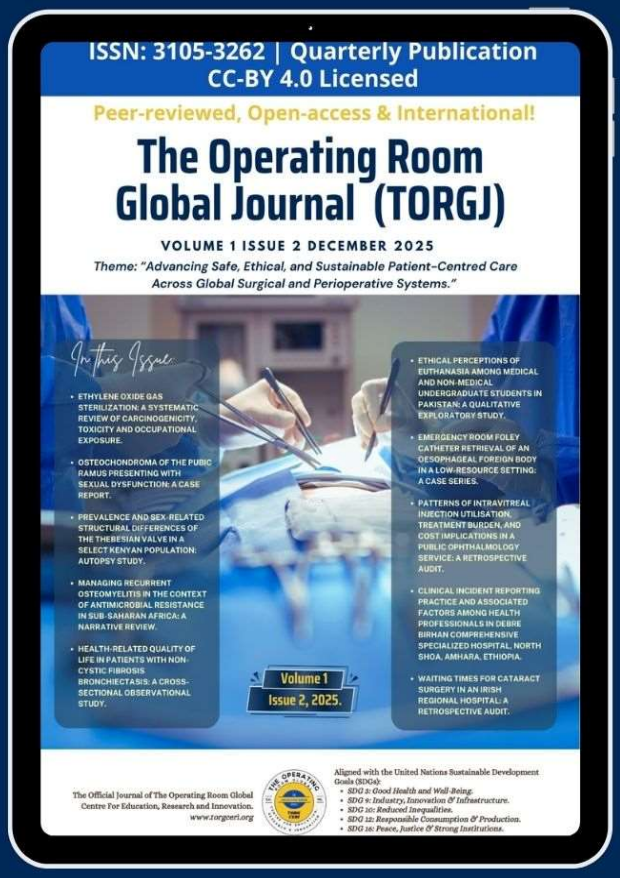

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Ethylene Oxide Gas Sterilization: A Systematic Review of Carcinogenicity, Toxicity and Occupational Exposure.

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ABSTRACT

Background: Ethylene oxide gas is a colorless gas that is used to sterilize all the items that are moisture, heat, and radiosensitive. 25ppm was the minimum amount of ethylene oxide gas that does not affect the patients and workers. Its overexposure has harmful effects on the human central nervous system, reproductive system, and peripheral nervous system.

Methodology: Web of Science, Science Direct, PubMed, Google Scholar, and Scopus websites are used to collect articles with relevant abbreviations.

Results: Firstly, 116 articles were selected, then after reviewing the title and the abstract, 15 articles were finalized. After this reading methodology, discussion, and conclusion finalized 10 articles were finalised that were completely relevant to the study.

Conclusion: This study showed that ethylene oxide gas sterilization was the best choice for sterilizing surgical instruments. Its high exposure can affect the central nervous system, reproductive system and in some cases, cancer and even death. Proper PPEs and attention are required while using ETO.

Key words: Ethylene oxide, Sterilization, Toxicity of ETO, Surgical instruments, Cancer, Neurogenic issues

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INTRODUCTION

Sterilization is a process that removes or deactivates all forms of life, such as bacteria, fungi, spores, eukaryotic organisms, and other biological agents, placed on any surface, fluid, or object [(1)]. It was a process of making something free from bacteria or other living organisms like unicellular eukaryotes, fungi spores, etc. It was also defined as the process where all the living microbes, including bacteria or spores, are killed. Sterilization has many applications in the industrial, medical, and surgical fields. Sterilization was carried out by a physical method or a chemical method. In the chemical method, sterilizing agents were known as chemisteriliants [(2)].

Nowadays, Ethylene oxide gas has gained more popularity in the medical and pharmaceutical fields. It was also a sterilizing agent and was used to sterilized the surgical items that are used during surgical procedures [(3)]. Its worldwide production was 5.5 million tonnes and in the United States, its production

was 3 million tonnes [4, 5]. Due to its reactive nature, ethylene oxide was a major industrial chemical. Its toxicity was comparable to ammonia. It was a colourless liquid and had a boiling point of 10.7 °C. It was an inflammable gas with the characteristics of the simplest epoxide compounds and a potent biocide. If the concentration of ethylene oxide is higher than 3% it becomes explosive and moderately toxic. The 12% mixture of ethylene oxide with carbon dioxide and freons was not inflammable [6]. Ethylene oxide was an alkylating agent potent biocide and an active epoxide agent. In the chemical industry, it was most widely used.

Ethylene oxide was a famous sterilizing agent that was used to carry out the sterilization process of all medical instruments and equipment that were resistant to heat, moisture, and radio waves [7]. It could kill bacteria, viruses, and spores. It was widely used due to its effective characteristics and compatibility with most materials. On the other hand, ethylene oxide has many disadvantages. It is carcinogenic and mutagenic in nature if it is not properly handled [8]. Ethylene oxide covalently and irreversibly binds to deoxyribonucleic acid and can cause mutations. Due to over-exposure and its alkylating ability, it can cause a spectrum of chromosomal damage. It was toxic to the reproductive system and could cause infertility in both males and females. EO can cause serious burns on the skin if it is used carelessly. The reaction of ethylene oxide was highly exothermic. The vapors of ethylene oxide can become explosive if the temperature is higher. At a temperature of 400 °C, the gaseous ethylene oxide starts to decompose into carbon monoxide and methane [9]. In the decomposition, the first step was the isomerization of ethylene oxide into acetaldehyde.

Amount of ethylene oxide gas near the working area

Annually, 75000 Healthcare workers are exposed to ethylene oxide in the United States. Exposure to ethylene oxide was high in healthcare facilities and hospitals as compared to the chemical industries. In 1978, the survey was conducted by the National Institute for Occupational Safety and Health in healthcare facilities (NIOSH). They concluded that ethylene oxide near the improperly designated equipment area was 100 ppm for a brief period. 50 ppm was the safe limit for breathing in the hospital [10].

The amount of ethylene oxide gas was 0.1ppm near the sterilizer before turning on and this amount was detected by the ethylene oxide gas monitor. Before opening the door of the sterilizer, the amount of gas in the sterilizer was in the range of 0.10- 2 4.56 ppm this amount was below the detection limit. After that, when the door of the sterilizer was opened for the placement of the instruments into the sterilizer for sterilization, the amount of ethylene oxide gas near the door was 1.71 ppm. After that, when the cycle started, no amount of ethylene oxide gas was detected in the unit. After completing this cycle, when the door was opened, the range was 2.10-2.73 ppm and when the door was closed, the residual amount was in the range of 0.5 - 0.57 ppm [11]. These values showed that the person near the sterilizer unit has a risk of exposure to ethylene oxide gas for 15 minutes during the instrumentation transfer. The 2-ppm residual amount of ethylene oxide gas was still present in sterilized instruments after 24 hours of aeration time. These findings showed that the person who used these instruments also has a risk of exposure [12].

Personal exposure limit

Exposure to ethylene oxide at the workplace was regulated by OSHA standards 29 CFR 1910. 1047. The International Standard Organization ISO 10993-7 (2008) gives a specific limit for ethylene oxide gas residual and its by-products [13]. It was formed by ethylene oxide gas reaction with Hydrochloric acid and Sulfuric acid aqueous solution. Ethylene oxide gas in this reaction was not produced only by water. If the residual amount of Ethylene oxide gas is not properly aerated, it can cause irritation to the skin and Eyes, and in severe cases, it can cause burns to the skin and mucosa. Ethylene gas toxicity was 10 times greater than ethylene chlorohydrin. 25ppm was the minimum amount that did not affect the patients and workers[14]. Acute exposure can cause irritation to the mucous membrane, depression in the central nervous system,

nasal discharge, and lacrimation [15]. 6 to 8 hours of exposure can cause diarrhea, nausea, lung edema, paralysis, and in some cases, it can cause even death.

MATERIALS AND METHODS

A systematic review was conducted according to PRISMA 2020 guidelines to ensure the originality of data. The aim of this systematic review was to find out the toxic effects of ethylene oxide gas in humans. All observational, case-control, Cohort, cross-sectional studies, case reports, and experimental studies were included in the study. Studies that included human subjects were included in the study. Animal-based studies, opinions, and those studies that lack qualitative and quantitative data on exposure to human health were also excluded from the study.

Five websites were used to collect relevant articles. Web of Science, Science Direct, PubMed, Google Scholar, and Scopus were used to fetch articles from sites. Key search terms that were used to collect articles were Ethylene oxide gas, sterilization techniques, EO sterilization techniques, toxicity of ethylene, toxic effects of ethylene oxide gas on humans, exposure limits of ethylene oxide gas, exposure limit of EO near the working area, benefits of ethylene oxide gas sterilization, disadvantages of ethylene oxide gas sterilization, mechanism of action of ethylene oxide gas sterilization, and usage of ethylene oxide gas in medical field. Firstly, I collected 116 articles from these websites. After these two independent observers reviewed and screened articles by reviewing the title, abstract, which showed the relevance of toxicity of ethylene oxide in humans, and its exposure limits in the working area, and finalized fifteen articles. Read these fifteen articles, thoroughly studied methodology, results, discussion, and conclusion sections, and finalized ten articles that were completely relevant to the study. After selecting articles, data was extracted from the articles and authors' names, study design, sample size, and key findings were noted, and a table was created based on the findings.

RESULTS

Table 1.1 Study Findings of Previous Literature

Name of Author	Study Design	Sample Size	Findings of The Study
Breuer et al	Case control study	12	Out of 8, 7 employees have allergic reactions to one percent epichlorohydrin
Bryant et al	Case series	165	Allergic reactions and neurological issues have been significantly associated with ethylene oxide gas exposure
Estrin et al	Case control study	20 (10 added into the exposed patient group and 10 added into the control group)	The exposed patient group has neurological symptoms with P value (P= 0.009)
Feitosa et al	Case report	1	The patient developed neurological symptoms

Gresie- Brusin et al	Cross-sectional study	98 (19 has higher exposure, while 79 has low exposure from ETO)	Pregnancy loss and spontaneous abortion risk increased with higher exposure to ETO
Kiran et al	Case control study	4810 cases, 2347 lymphoma cases and 2463 controls	Lymphoma cases increased to four times with higher to medium exposure of ethylene oxide gas sterilization (P= 0.003)
Lin et al	Case report	1	Patients develop neurological symptoms with exposure to ETO
Park et al	Cohort study	7185	Lung cancer and breast cancer are significantly associated with ethylene oxide gas exposure

A case-control study was conducted by Breuer et al. He took 12 patients for the study who had exposure to ethylene oxide gas. He noticed that out of eight, seven patients had allergic reactions. Another case series was reported by Bryan et al. He takes 165 patients and reports that allergic reactions and neurological issues have a significant association with ethylene oxide gas sterilization. Fstrin et al conducted a case-control study on 20 patients. He added ten patients to the control group and 10 to the exposed group. He noticed that neurological symptoms have a significant association with ethylene oxide gas exposure. A study was conducted by Park et al. He conducted a Cohort study on 7185 patients. He noticed that lung cancer and breast cancer have a significant association with ethylene oxide gas exposure. (Table 1.1)

DISCUSSION

This systematic review described details of the harmful effects of ethylene oxide gas in humans. Although it was a very useful gas for sterilization, it has very dangerous, long-lasting effects on the human population. It was a carcinogenic gas that has been found to have an association with the development of different types of cancer and many other long-lasting effects. All eight studies concluded that ethylene oxide has harmful effects on human health. Its normal exposure cannot pose a significant threat in humans, but its higher exposure can cause skin burn, bruises, skin irritation, leukemia, lymphoma, cytotoxicity, lung cancer, breast cancer, chromosomal damage, pregnancy issues, abortion, and in some cases, even death may occur.

Breuer et al and Bryant et concluded in their research that those workers who have exposure to ethylene oxide gas are more prone to allergic reactions as compared to others [16, 17]. A similar study was conducted by Cloth et al, which showed ethylene oxide has a significant association with skin irritation, itchy skin, and breathing difficulties. There was a very low chance of these issues; these studies are not like previous studies. Another study showed that high exposure to ETO can cause blisters, bruises, eye pain, and breathing difficulties [18]. These findings of previous literature showed that there is a strong association between ethylene oxide gas exposure and its toxic effects. Estrin [19], Bryan Lin, and Feitosa et al concluded in their research that overexposure to ethylene oxide can cause neurological symptoms[20]. A similar study concluded that neurological symptoms have a significant association with ethylene oxide gas sterilization [21]. Those workers who routinely worked near ethylene oxide gas are more prone to the risk of headaches, loss of memory, and unconsciousness. Another parallel study describes the issues of high exposure to ETO that showed that those workers who are more prone to exposure to ETO developed neurological symptoms as compared to those who have no exposure to ethylene oxide gas. A parallel study conducted by Jones et al showed that those workers who have prolonged exposure to ETO develop neurological issues [18]. These

comparable trends suggest that those workers who develop neurological symptoms have a high chance of ethylene oxide gas exposure.

A study conducted by Gresie-Brusin et al showed that loss of pregnancy and spontaneous abortion may increase with high exposure to ethylene oxide gas [22]. A parallel study showed that exposure to ethylene oxide gas can cause abortion and pregnancy issues in female workers. A similar study showed that ethylene oxide gas has a significant association with reproductive system impairment [15]. Kiran et al conducted a study on lymphoma patients, and they observed that the chances of lymphoma may be increased four times with high and moderate exposure to ethylene oxide gas [23]. Park et al conducted a cohort study. He concluded in his research that the chances of lungs and breast cancers increased with high exposure to ethylene oxide [24]. A similar study finding concluded that ETO caused mutations and suppressed genes that result in tumor formation [25].

A cross-sectional study was conducted in Egypt that showed gene mutations were detected in patients who had been exposed to ethylene oxide gas [25]. Another study showed that ethylene oxide has a significant correlation with breast cancer and lymphoma issues. Their chances increased with higher exposure [26]. Another study revealed that the risk of breast cancer increased with exposure to ethylene oxide but non-Hodgkin's lymphoma may not increase with exposure [27]. A parallel study showed that exposure to ethylene oxide gas has carcinogenic effects in humans [28]. A study was conducted by Park et al that concluded the chance of malignancies was increased with a higher dosage of exposure to ethylene oxide gas [15]. These research findings were consistent with previous literature that reported the same carcinogenic effects with exposure to ethylene oxide gas. That showed the reliability of these research findings.

A study was conducted in the USA that showed exposure to ethylene oxide gas was not associated with breast cancer and lymphoma. This study was not parallel to previous findings because they studied the mechanism of action of ethylene oxide gas effects in the body and stated the results. This study was conducted in the USA, so there might be a chance of bias due to the high standards of healthcare facilities. A study conducted by Jain et al showed that blood cancer has no significant association with ethylene exposure [29]. There might be a chance of biases or workers working in a state-of-the-art institution. Where proper guidelines are followed and aeration is done in a well-ventilated environment. So, the chances of ethylene oxide gas exposure are very low. The key findings of this systematic review give a brief detail that there was a strong association present between ethylene oxide gas exposure and carcinogenicity, genotoxicity, and toxic effects in humans. This result highlighted the importance of strict adherence to SOPs during usage and regulatory control measures are necessary to protect the environment and healthcare workers.

CONCLUSION

From all the above discussions, it was concluded that ethylene oxide gas sterilization was the best available sterilization method for all the sensitive and weird items. However, some precautions must be considered to reduce damage to healthcare providers. Clinically, all Healthcare workers, especially the sterilization supply department, must know ETO sterilization can be dangerous if precautions are not followed during its usage. 25 PPM was the normal range of exposure. If exposure increases from this limit, it can cause breathing difficulties, skin rashes, chromosomal damage, and cancer. So, during the usage of ethylene oxide gas, wearing PPEs and proper attention were required to minimize its effects.

RECOMMENDATIONS

Add more articles to conduct a more comprehensive study. Research on the health impacts of moderate and high exposure levels of ethylene oxide gas should be done separately. Examine the harmful consequences that ethylene oxide gas has on animals. Demographic variables that indicate which age group

and gender are more vulnerable to the harmful effects of ethylene oxide gas can be investigated further. The effects of ethylene oxide gas on the environment can be explored because there are currently few studies available in this area.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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Osteochondroma of the Pubic Ramus Presenting with Sexual Dysfunction: A Case Report.

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Authors' Contribution: Kidanemariam Abrha, Writing-review & editing. Writing-original draft, visualization, conceptualization; Seare Halefom Kahsay, writing-review & editing, Conceptualization; Zeamanuel Berihu Teshome, Investigation, conceptualization; Mezgebu aregawi, writing-review & editing, conceptualization.
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ABSTRACT

Background: Osteochondroma is the most common benign bone tumor, usually affecting long bones. While solitary osteochondromas are usually benign, they can occasionally cause complications such as compression of adjacent structures, vascular or neurological impingement, or, in rare cases, malignant transformation into secondary chondrosarcoma. Pelvic osteochondromas are rare but can sometimes lead to significant functional and psychosocial distress.

Observation: We present a 21-year-old female patient with a six-year history of progressively enlarging pelvic osteochondroma in the right groin. The tumor caused difficulty in wearing fit clothing, mechanical obstruction during sexual intercourse, and marital and social stigma. Despite its large size, there were no urinary or neurological symptoms. Surgical excision provided complete symptomatic relief and improved her quality of life.

Conclusion: This case highlights the atypical presentation and location of a benign bone tumor. Early surgical intervention should be considered in cases where the tumor leads to significant distress, even in the absence of pain or compression. This case reinforces the need to prioritize patient quality of life and highlights the significant role of surgical management in improving both functional and psychological well-being.

Key words: Osteochondroma, Pubic Ramus, Sexual Dysfunction.

INTRODUCTION

Osteochondromas constitute 35-40% of all benign bone tumors, commonly occurring in the metaphysis of long bones.[1] Pelvic osteochondromas are uncommon and can present mechanical compression, pain, or cosmetic concerns. In rare cases, they may affect social interactions, sexual function, and emotional well-

being.[2]This case report highlights a young female who's pelvic osteochondroma caused sexual dysfunction, marital distress, and social stigma, emphasizing the psychosocial implications of benign bone tumors.[3,4]

CASE REPORT

A 21-year-old female patient from a rural locale presented to our clinic with a 6-year history of a right inguinal mass. The mass exhibited an insidious onset, initially small but progressively increased in size, impeding her ability to wear clothing. She reported associated mild discomfort. Furthermore, it led to significant dyspareunia, contributing to marital discord, compounded by her husband's expressed concern regarding the lesion. Medical consultation was delayed due to limited health literacy. Further history revealed an absence of sensory or motor deficits. No analogous lesions were observed in other regions, nor was a familial history of the condition reported. Additionally, the patient's medical history was unremarkable for prior fractures, radiation exposure, or chronic systemic illnesses.

CLINICAL FINDINGS

On physical examination, a pertinent finding was observed in the right pubic region: a firm, bony mass, measuring approximately 4 x 7 cm, located at the right pubic tubercle.[Figure 1] The mass was non-tender and immobile, appearing fixed to the underlying pubic bone. The overlying skin was mobile, without evidence of discoloration or ulceration. The remainder of the physical examination was unremarkable.

DIAGNOSTIC ASSESSMENT

Imaging studies, including pelvic X-ray, CT, and MRI, were performed. The CT demonstrated a bony growth measuring 54 x 48 x 86 mm (transverse, craniocaudal, and anteroposterior dimensions) arising from the right superior pubic ramus and situated extrapelvically.[Figure 2] MRI further revealed a 4 mm thick cartilage cap, with no evidence of soft tissue, neurovascular or urinary tract involvement.

THERAPEUTIC INTERVENTION

Following preoperative optimization, the patient underwent surgical excision of the mass. Under regional anesthesia, the patient was positioned supine on the operating table. A transverse suprapubic skin incision was made, and careful dissection of the soft tissue exposed the mass.[Figure 3] The mass was meticulously excised from its bony attachment using an osteotome. Subsequently, the wound was closed in anatomical layers [Figure 4]. The excised specimen was submitted for histopathological evaluation, which showed mature bony trabeculae covered by hyaline cartilage, confirming the clinical diagnosis of benign osteochondroma [Figure 5].

FOLLOW-UP AND OUTCOMES

The patient experienced an uneventful postoperative recovery. Home discharge occurred on postoperative day three, followed by a one-year monitoring period during which no new growth or recurrence was seen. Following the surgical procedure, the patient reported a resumption of normal daily activities and indicated improvements in both self-esteem and marital relations.

DISCUSSION

Osteochondromas constitute the most prevalent benign bone tumors, accounting for approximately 35% to 40% of all benign osseous neoplasms.[1,2,4,5] These typically originate from the metaphyses of long bones, with the femur and tibia being the most commonly affected sites. Nevertheless, pelvic Osteochondromas are

exceptionally rare, representing a minor proportion of reported cases. Our presented case exemplifies one such infrequent pelvic osteochondroma. Osteochondromas result from aberrant cartilage growth at the growth plate, forming an exophytic lesion composed of mature bone covered by a hyaline cartilage cap. These lesions are typically slow-growing and stop enlarging once skeletal maturity is reached.[2,3,4] While solitary osteochondromas are usually benign, they can occasionally cause complications such as compression of adjacent structures, vascular or neurological impingement, or, in rare cases, malignant transformation into secondary chondrosarcoma. The risk of malignant transformation is generally low (<1%) in solitary osteochondromas but is higher in cases of multiple hereditary exostoses.[3,4,5,6]

These benign tumors often remain asymptomatic but can lead to mechanical discomfort, restricted movement, and cosmetic concerns when they grow significantly in size.[1,3] While cosmetic concerns were present for the patient, her principal reason for seeking medical attention was sexual dysfunction and the resultant marital discord. She reported significant sexual discomfort and subsequent relational strain, contributing to profound psycho-social distress. In conservative societies, many patients delay seeking medical care due to fear of surgery or social stigma associated with visible deformities.[7]

Imaging modalities, such as X-ray, CT and MRI, are crucial for evaluating tumor characteristics and guiding surgical planning.[8] In the present case, preoperative imaging utilizing these modalities affirmed the presence of a well-defined, pedunculated osteochondroma lacking aggressive features, thus facilitating a direct surgical approach. The decision to proceed with surgical excision was based on the patient's discomfort, functional limitations, and emotional distress. Given its large size and significant impact on the patient's quality of life, surgical excision was indicated.

Owing to the superficial anatomical position of the tumor, the surgical procedure was relatively straightforward, involving exposure, meticulous dissection, and complete excision. Subsequent histopathological evaluation confirmed a benign osteochondroma, with no evidence of malignant transformation, thereby precluding the need for further oncological intervention. Consistent with findings in similar cases, the postoperative outcome was excellent, characterized by complete symptomatic relief, enhanced self-confidence, and an overall improvement in quality of life.[4-8]

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CONFLICT OF INTEREST

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INFORMED CONSENT

Written informed consent was obtained from the patient for publication of this case report and accompanying images. We extend our gratitude to the patient for consenting to publish her clinical information.

FIGURES

Figure 1

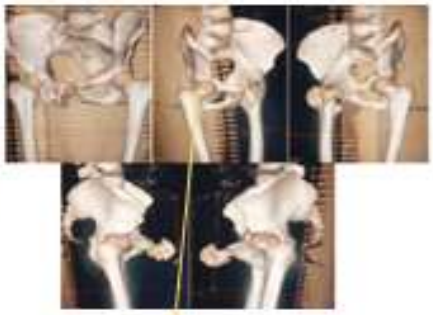

Figure 2

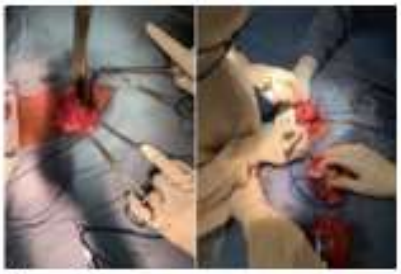

Figure 3

Figure 4

Figure 5

AUTHORS CONTRIBUTION

Kidanemariam Abrha - Writing – review & editing. Writing-original draft, visualization, conceptualization
Seare Halefom Kahsay -writing – review & editing, Conceptualization
Zeamanuel Berihu Teshome – Investigation, conceptualization.
Mezgebu aregawi– writing – review & editing, Conceptualization

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LEGENDS TO FIGURES

Figure 1: A clinical image showing a firm, bony mass, measuring approximately 4 x 7 cm, located at the right pubic tubercle.
Figure 2: 3-D CT scan image shows an anteriorly projecting bony mass attached to the right pubic tubercle
Figure 3: The in situ visualization of the mass was achieved subsequent to the dissection of the adjacent soft tissue.
Figure 4: This image depicts the post-excision appearance of the closed surgical wound.
Figure 5: This picture shows excised mass that was sent for histopathologic evaluation.

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Prevalence And Sex-Related Structural Differences Of The Thebesian Valve In A Select Kenyan Population: Autopsy Study.

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ABSTRACT

Background
The coronary sinus is increasingly being used for cardiovascular interventional procedures. Thebesian valve, an endocardial remnant located at the coronary sinus opening into the right atrium, can hinder catheterization of the coronary sinus. The valve morphology varies between individuals. Despite its clinical relevance, data on its prevalence and morphology, particularly by sex, especially in African population, remain limited. Therefore, this study aimed to investigate the prevalence and sex-related structural differences in the Thebesian valves.

Methods
A total of 100 post-mortem hearts (63 males, 37 females) were examined. The coronary sinus and Thebesian valve were measured, photographed, and classified by morphology. Data were analyzed using appropriate statistical tests, including Mann-Whitney U and Spearman's correlation.

Results
The Thebesian valve was present in 73% of hearts and showed varied morphologies. Absence of the valve was associated with a larger coronary sinus opening. Percentage occlusion of the coronary sinus opening was higher in males, though sex-related structural differences were not statistically significant. Age showed no influence on valve morphology. Positive correlations were observed between heart size and coronary sinus dimensions.

In conclusion, the study highlights anatomical variations that may impact interventional procedures involving the coronary sinus.

Keywords: Thebesian valve, coronary sinus, prevalence, variations.

INTRODUCTION

The heart is a tissue organ that has both arterial supply and venous drainage(1). The coronary sinus (CS) is the central vein that runs in the coronary groove as a continuation of the great cardiac vein after the Valve of Viussens(2). The coronary sinus opening is frequently covered by a fold of endocardial remnant known as the Thebesian valve(3). This valve, which bears the name Adam Christian Thebesius in honour of the early anatomist, has drawn more attention due to its possible involvement in controlling heart function and blood flow dynamics(3). The function of this valve is believed to prevent the retrograde blood flow into

the coronary sinus during atrial systole[4]. The valve is characterised by a wide diversity of shapes and various studies have grouped them into various classifications[2]. This valve has been studied and classified into various shapes and morphologies including fibrous, fibromuscular, muscular composition, and fenestrations which have different compositions and histological structures[4]. The coronary sinus (CS) is a commonly cannulated structure in patients undergoing electrophysiology studies, catheter ablation of arrhythmias, implantation of resynchronization therapy devices and, more recently, percutaneous mitral valve repair[5]. The advent of these procedures has led to a renewed interest in the anatomy of the coronary venous system including its various components[6]. To improve our understanding of this structure, we studied the anatomy of the human CS, including the valve that guards its ostium, the Thebesian valve[7]. This valve covers the coronary sinus at varying percentages making it potentially complicating during coronary sinus catheterization[8].

Age-related changes have been linked to heart valves, most especially to the tricuspid and bicuspid valves[9]. Thebesian valve may differ with age, just like other valves of the heart, which would influence its function[10]. Calcium deposition and fibrosis might be structural changes that affect valve performance[11]. Moreover, variations in the mechanical properties of the tissue might be ascribed to age-related modifications in the extracellular matrix re-modelling and collagen composition of the valve tissue[9]. These developments could have a significant effect on the C.S. catheterization during invasive cardiac operations, therefore causing ineffective coronary sinus catheterization[12]. Studies have shown that variations in the height of the valve might block the coronary sinus opening (CSO), therefore causing ostium to be obstructed[13].

Recent advances in treating heart failure and valvular heart disease, particularly with cardiac resynchronization therapy and percutaneous mitral valve repair, have renewed interest in the anatomy of the coronary venous system, especially the coronary sinus[4]. The CS is crucial for accessing the left atrial and ventricular epicardium during invasive procedures. Although the transvenous left ventricular (LV) lead placement success rate is high (88-95%), it fails in 5-12% of patients, often due to obstructive Thebesian valve[2,4,14]. Despite the increased use of the CS in procedures, its anatomy and variations, particularly in Black African populations, remain underexplored. Therefore, the study aims to investigate the prevalence, age and sex-related structural differences of the Thebesian valve in a select Kenyan population.

Broad Objectives

To determine the prevalence and sex-related structural differences of Thebesian valve in a select Kenyan population.

Specific Objectives

To describe the prevalence of morphologies and variations of coronary sinus opening and Thebesian valve in a select Kenyan population.

To determine the sex-related structural differences of the Thebesian valve.

To correlate coronary sinus length with coronary sinus dimensions.

METHODS

The study was a descriptive cross-sectional study. The hearts used in the study were obtained from the Kenyatta National Hospital Funeral Home, Nairobi City Mortuary and the Chiromo Funeral Parlor. The examination and data analysis were conducted at the Department of Human Anatomy, University of Nairobi. Cochran's formula[15] was used to determine the number of hearts to be harvested, which was estimated to be 100. For ethical approval, the Kenyatta National Hospital-University of Nairobi Ethics and Research Committee (KNH-UoN ERC) provided ethical approval number UP53/02/2024. The management of the individual mortuaries provided permission and the necessary authorities. The families of the deceased were contacted to get their informed consent before using any autopsy material. Kenyan laws, the Human Anatomy Act (Cap 249, 1976) and the Human Tissues Act (Cap 252, 1968), were followed to

allow for the use of cadaveric materials. No unnecessary details were disclosed during data dissemination in the dissertation.

Inclusion Criteria

Specimens from all hearts of both sexes without any cardiac pathology were included in this study.

Exclusion Criteria

Subjects with a history of heart surgery or heart grafts, cardiomegaly i.e., hearts that weighed more than 450 grams, heart damage with macroscopic symptoms of decomposition, or any discernible congenital heart defects were excluded from the study. Moreover, autopsy specimens that had been retained for longer than 48 hours after death were excluded from the study.

Sampling method

Before the selection of the specimen used, available post-mortem specimens from the target population in each mortuary were stratified into different age groups. Systematic random sampling was used to select the subjects within different age groups from which samples were collected. The samples obtained were classified into sex.

Dissections and measurements

The chest cavity was opened through 'Y' incisions made on the costal cartilages that were just medial to the costochondral junction and cut through the capsular ligament to disarticulate the sternoclavicular joint and extend to the sternum. The heart was subsequently exposed by removing the sternum and making a longitudinal incision through the pericardium. Then, by cutting the proximal parts of the major vessels at the ligamentum arteriosus level, the heart was removed together with the base of the ascending aorta, pulmonary trunk, superior vena cava (SVC), inferior vena cava (IVC), and all of the pulmonary veins. The hearts were then weighed in grams using an electronic weighing balance SF-400c, and data were recorded on data sheets. The macroscopic features of the heart were examined. The height of the heart was measured from the apex of the heart to the base of great vessels and the width of the heart as the widest section of the heart. The measurements were taken using an electronic Vernier Callipers version CVU 200m(zero error = +0.02). An incision was made on the right atrium from the SVC orifice to the IVC orifice. If necessary, additional incisions were made on the right border of the RV to expose the T.V. better. Situated between the tricuspid valve and the inferior caval orifice, the coronary sinus ostium was located on the posterior wall of the right atrium. The target structures of the study, i.e., coronary sinus ostium and Thebesian valve were kept intact and then inspected in each specimen as shown in *Figure 1*. The length of the coronary sinus was measured as a continuation of the Great Cardiac vein at the Valve of Viuessens up to the opening of CSO at the Thebesian valve using an electronic vernier calliper. Images of the coronary sinus opening and Thebesian valve were taken while the heart was in anatomical position for the classification of the valves into various morphologies as described in *Table 1*. The valves were classified as per the classification by Slawet et al.,(2021)[2].

Transverse and craniocaudal(longitudinal) diameters of the CSO were measured as shown in *Figure 3* and the CSO percentage occlusion was calculated according to the commonly used Mehra's formula for the surface area of an ellipse ($\pi \times$ half the vertical dimension $\times$ half the transverse diameter)[16]. The presence of Thebesian was noted and if present, the height of the TV was measured from the posterior or inferior side. Its shape was observed and recorded in the data collection sheet. All the measurements were made using electronic vernier callipers while the heart was anatomically positioned relative to the live body. Measurements were repeated thrice and the average was calculated and recorded as the measurement. The images to classify the valve into various morphologies were taken by the research assistant while the principal investigator was holding the heart and the valve in its anatomical position.

Statistical analysis

All values were standardized to the heart weight of the specimens by deriving indexes as follows: $Standardized\ value = \frac{X\ value}{Heart\ weigh} \times 100\%$. After being coded, the morphometric data were loaded into SPSS (version 27.0 for Windows 11, Chicago, Illinois, USA) for statistical analysis. The normality of the

data was tested using Kolmogorov- Smirnov test where normal data was expressed in means and standard deviation. Data which were not normally distributed were analyzed using median and interquartile ranges for descriptive statistics. Morphometric results were statistically analyzed for independent variables. Kruskal–Wallis was used to compare the structural differences of Thebesian valves among various age groups. Mann – Whitney U test was used to compare structural differences of the Thebesian valve between males and females. Spearman's Rank-Order correlation test was used for the correlation between gross morphometry parameters of the hearts with the diameter of the coronary sinus. A p-value of <0.05 was considered significant. Photographs and tables were used.

RESULTS

Out of the 100 hearts studied, 63 were males and 37 were females. The median age for the specimen was 37 years ranging from the minimum age of 17 years to maximum age of 88 years. The interquartile range was from 28 to 49. The median weight for the hearts was 289.00 grams in males and 284.16 grams in females.

Morphology of Thebesian valve

The coronary sinus was located on the inferior aspect of the left atrium course on the left atrioventricular groove in all the 100 heart specimens. The majority of Thebesian Valves were observed to originate from either the inferior (67%) or posterior (33%) aspect of the coronary sinus opening. The mean length of the coronary sinus was 38.61mm in males and 36.27 mm in females. The coronary sinus opening was located on the right atrium lateral to the opening of the Inferior Vena Cava.

Heart specimens with absent Thebesian valves for both males and females tended to have larger CS Ostia as shown in *Table 2*. The transverse and craniocaudal dimensions of the CS ostia in hearts with Thebesian valves were 8.16±2.34 mm and 8.24±2.33 mm in males and 7.91 ± 1.48 and 8.07 ± 1.55 mm in females respectively. The transverse and craniocaudal diameters of hearts with TV were significantly smaller when compared with those specimens with no Thebesian valve as shown in *table 2* below. The maximum diameter of the CS ostium tended to vary inversely with the extent of the height of the Thebesian valve.

A wide variety of Thebesian valve morphologies were seen as seen in *Figure 9*, including remnant fold valves (covering <10% of the ostium) and valves that almost completely occluded the CS ostium as shown in *Figure 2*.

The Thebesian valve was absent in 27 of the 100 hearts examined (27%) 17/27(63%) in males and 10/27(37%) in females. A typical example of a coronary sinus opening with an absent Thebesian valve is shown in *Figure 3*. In 12/73 hearts (16.4%)of hearts with a Thebesian valve, the valve was large and covered at least 75% of the CS ostium, whereas the valve covered <10% of the ostium in 25/73 hearts (34.24%).

Various morphologies of the Thebesian valve were noted as shown in *figure 5.* Most T.V. were semilunar in shape (42/73-57.5% of heart specimens, males- 28/42 -, females 14/42). In a minority of specimens, the valve was a fused strand (5/73—6.8% males - 3/5, females – 2/5) or chord strand (9/73-12.3% males – 5/9, females 4/5) as shown in *Table 3* below. We also noted a Y-shaped valve which was a subtype of fused strands Thebesian valve as shown in Figure 4.

Sex-related structural differences on of Thebesian valve

There were similarities and slight differences between males and females across various structural parameters of the heart parameters and Thebesian valve as shown in *table 4* below. The median ages for males and females were 36 and 27 respectively. The interquartile range for both genders showed a similar range from 27 to 54 years. In terms of morphometric measurements, such as height and width of the heart,

females exhibit median values of 105.30 mm and 95.73 mm, respectively, compared to males with nearly identical median values of 106.42 mm and 95.84 mm. The length of the coronary sinus ranges from 33.66 mm to 41.43 mm for both males and females, indicating consistency across genders. However, there are notable differences in certain aspects, such as the percentage occlusion of the Thebesian valve, where

females have a median of 32.00% compared to males with 65.42. The mean percentage occlusion in males was higher in males than in females ie 50.76% and 44.39% respectively.
Table 5 summarizes the variables with their corresponding p-values from the Mann-Whitney U tests comparing males and females for various structural parameters of the Thebesian valve
The p-values indicate that for every structural characteristic of the Thebesian valve examined between males and females, all of them are above 0.05, implying that there are no statistically significant variations between males and females for the data present.

Correlation between CS parameters and gross heart parameters
The coronary sinus (CS) parameters showed a positive significant correlation with gross heart parameters as shown in table 6. The weight of the hearts showed a strong positive correlation with the CS length ($p < 0.001$), and CSO transverse diameter ($p = 0.028$) Additionally, the CS length was positively correlated with the CSO transverse diameter ($rho = 0.414$, $p < 0.001$) and CSO craniocaudal diameter ($rho = 0.262$, $p = 0.009$). The table below summarizes the findings.

DISCUSSION

Our study showed the Thebesian valve (TV) was present in 73% of the hearts examined. Similar findings were obtained in previous studies as shown in *Table 7*. The valve types were either semilunar, chord, fused strands, remnant fold and fenestrated in both males and females and across the various age groups. Two fenestrated valves that covered >75% of the coronary sinus opening(CSO) were found. It has been noted that fenestrated valves could potentially occlude cannulation of the CS(17). 16.4% of hearts that had TV as 'potentially complicating', was in cross range with Gami et al, Anh et al and Ghosh et al as shown in ***Table 9***(17–19). These potentially occlusive TV may require the cardiologist to use the appropriate size of catheter to prevent fatal injuries to the CS or inside the right atrium(7).
The TV exhibits variations in its occurrence, size, shape, and extent of coverage(20). According to the literature, the occurrence of TV varies across different studies from 65% to 95% as shown in table 8(4,7,17–24). Contrary to our study, imaging studies record a lower prevalence of TV which records 36% due to the coronary sinus dynamic nature in a live body, especially during atrial systole(25). Imaging studies record a lower prevalence of TV due to failure of fiberoptic technique to visualize remnant valves and the CS may be dilated(18).
In this study, the classification suggested by Holda et al. was considered(20). Five types of TV have been described, with the most common type being type II (semilunar). While fold, cord/band, fenestrated, and mesh types which have ostial coverage <75% might cause difficulty in cannulation due to the possibility of entanglement of CS catheter, the fibrous type with ostial coverage >75% might obstruct CS cannulation leading to failure of interventional cardiac procedures. According to Hill et al, endoscope visualization might help for successful cannulation of such valves(14).
The attachment TV in the current study from the inferior margin (63%) or posterior margin (27%) of the CSO was a similar finding by Mak et al who found that 33% of the posterior margin and 61% from the inferior margin of the coronary sinus opening(4).

In this study, 5 hearts showed the TV closing 90-100% of the CSO. Valves that cover the CSO completely have been recorded and shown to cause obstruction of CSO(2,26). This implies that visualization of CSO before the catheterization is important as there may be a valve that may occlude the CSO. A recent study from Turkey showed that 8% of examined hearts had TV that 'would result in low probability for CS cannulation due to obstruction by TV. They defined TV characteristics as being 'worst for cannulation' if

the TV is fenestrated or band-shaped(23). Most cardiologists, especially those familiar with the CS catheterization technique, would disagree with the definition as imaging can be used and avoid obstruction. Similar to our findings, Silver and Rowley found potentially complicating TV (covering >75% of the CS ostium) in 12% of the hearts examined(27).

Sex-related structural differences of Thebesian valve

There were no significant differences between males and females in the length of the CS, transverse diameter, and craniocaudal diameter of the CSO. Similar findings were found by Verenna et al., (2015) who also did not find sex differences in CS parameters and heights of TV(13). The difference found in the standard deviation of the parameters of the heart might be due to hormonal differences between males and females (28). This indicates that gender does not significantly influence these heart morphometric parameters in the population studied(29).

Percentage occlusion which was significantly higher in males than in females may have been caused by higher means of TV height in males than in females which may have been caused by hormonal and genetic differences (29). Similar findings of percentage occlusion of CSO where males had higher occlusion than females were recorded by Verenna et al (13). This highlights the need for imaging that during CS catheterization for successful procedures.

Correlation between heart morphometry and coronary sinus parameters

The size of the coronary sinus ostium (CSO) is important during the catheterization of the CS (2).The weight of the hearts showed a strong positive correlation with the CS length, and CSO transverse diameter but no significant correlation with the CSO craniocaudal diameter which were similar to Kucybala et al.(30). Additionally, the CS length was positively correlated with the CSO transverse diameter and craniocaudal diameter. This is in line with a study done in the Kenyan population which correlated CS length with gross parameters of the heart and right atrium size (31).This suggests that longer CS tend to have wider transverse and craniocaudal diameters at the CSO. Similar positive correlations between gross heart parameters and CS parameters have been noted in a previous study(2).

Awareness of the length of the CS may facilitate the pre-procedural planning and selection of appropriate size, thickness, length and angulation of catheter and reduce the procedure time and the risk of potential complications during left ventricular lead placement(2).

LIMITATIONS

The study was based on heart specimens from autopsies, lacking physiological in vivo haemodynamic conditions, which might have introduced measurement bias. Additionally, the dynamic nature of the TV and CSO couldn't be observed, as these dimensions may vary during the cardiac cycle in living hearts. The study focused solely on anatomical evaluation without microscopic correlations.

STRENGTHS

TV and CS were obtained within 48 hours after death to minimize autolysis and tissue shrinkage unlike most of the studies on coronary sinus and its Thebesian valve which used cadaveric specimens fixed with formalin. All heart measurements were taken in its anatomical position to mimic the position of the heart in a live body.

RECOMMENDATION

The study recommends further microscopic study of the TV where variations to check on collagen density on the various valve types. In addition, the study recommends multicentred study from various regions with a larger sample size to investigate the structural differences of TV in various age groups.

CONCLUSION

The study highlights the morphological variation of the Thebesian valves between males and females and its potential implications in unsuccessful CS cannulation and failure of invasive cardiac procedures. We identified 5 main types of TV. Only 16.4% of the TVs in our sample could potentially occlude the CSO.This study provides unique insight into the anatomy of the CS, which might facilitate successful CS catheterization. The findings can contribute to a better understanding of cardiovascular anatomy and may have implications for clinical practices involving the CS.Thus, detailed anatomical knowledge about the morphology of the TV is pivotal to planning and adapting procedural strategies during various invasive cardiac procedures.

CONFLICT OF INTEREST

There was no conflict of interest in the study

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TABLES AND FIGURES

Table 1 shows the description of Thebesian valve morphologies.

Type	Name	Description
I	Remnant fold	Residual endocardial flap around the perimeter, that covers <10% of the total CSO area
II	Semilunar	The crescentic endocardial flap covering the CSO in variable degree
III	Fenestrated	Cribriform, net-like valve mostly semi-lunar shaped
IV	Chord strand	A simple endocardial band mostly in the midline of the CSO.
V	Fused strands	Connected in different manners endocardial strands localized mostly in the midline

Table 2 shows the mean of the transverse and craniocaudal diameter of the coronary sinus opening of hearts with Thebesian valves.

Parameter	Sex	With Thebesian valve (mean ±SD)	Without Thebesian valve (Mean ±SD)	p-value
Transverse diameter(mm)	Male	8.16±2.34	8.38±0.95	0.009
	Female	7.91±1.48	8.25±1.78	0.005
Craniocaudal diameter(mm)	Male	8.24±2.33	8.42±1.64	0.036
	Female	8.07±1.55	8.43±1.32	0.045

Table 3 shows frequencies and percentages of various morphologies of the valve

Type of Valve	Name	**Frequency**	Percentage(x/73 ×100%)
I	Fused strands	5	6.8
II	Semilunar	42	57.5
III	Remnant fold	6	8.2
IV	Chord strand	9	12.3
V	Fenestrated	11	15.1

Table 4 shows a summary of variables of gross heart parameters.

Variable	Median		25th Percentile		75th Percentile		p-value.
	Median males	Median females	25th Males	25th Females	75th Males	75th Females	
Weight	0.285	0.265	0.323	0.285	0.265	0.323	0.015
Height	105.30	99.61	112.13	105.30	99.61	112.13	<0.001
Width	95.73	92.01	99.80	95.73	92.02	99.80	<0.001
Length of CS	38.54	33.66	41.43	38.54	33.66	41.43	<0.001

Table 5 summarizes the variables with their corresponding p-values from the Mann-Whitney U tests comparing males and females for various structural parameters of the Thebesian valve.

Table 6 below shows Mann-Whitney U tests comparing males and females for various structural parameters of the Thebesian valve.

Variable	Median differences (Mann-Whitney U)	P - value
Length of Coronary Sinus (mm)	1142.50	0.164
Transverse diameter of CSO (mm)	1107.00	0.418
Craniocaudal diameter of CSO (mm)	1150.00	0.111
Height of Thebesian valve	1054.50	0.800
Percentage Occlusion of TV	1054.00	0.128

The p-values indicate that for every structural characteristic of the Thebesian valve examined between males and females, all of them are above 0.05, implying that there are no statistically significant variations between males and females for the data present.

Table 6 shows correlations between CS parameters and gross heart parameters

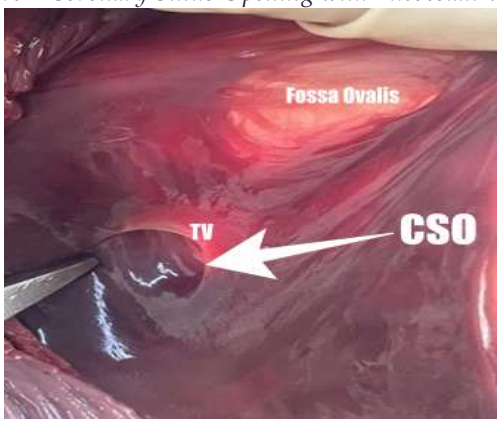
Characteristic variables	CS length	CSO Transverse diameter	CSO Craniocaudal diameter

	rho	p-value	rho	p-value	rho	p-value
Weight of the hearts	0.465	<0.001	0.219	0.028	0.143	0.155
Height of the hearts	0.260	<0.001	0.360	<0.001	0.195	0.052
Width of the hearts	0.467	<0.001	0.400	<0.001	0.220	0.028
CS length	-	-	0.414	<0.001	0.262	0.009

Table 7 shows the comparison between the present study and those conducted previously

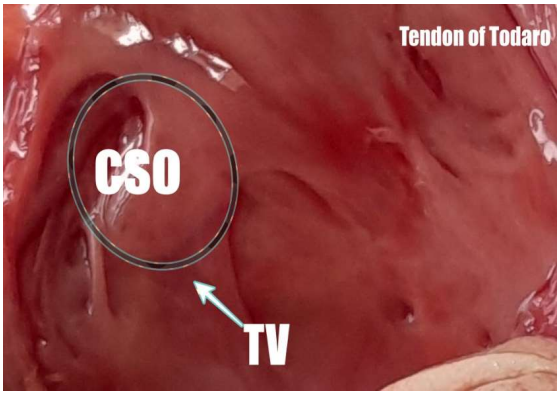
Name of author	Sample population	Type of specimen used	Number of hearts with TV	Number of hearts with occlusive TV
Present study	100	Autopsy	73(73%)	12(16.4%)
Holda et al	273	Cadaveric	224(82%)	39(14.3%)
Gami et al	560	Cadaveric	348(82%)	71(12.5%)
Mlynarski et al	150	Multislice computed tomography	69(46%)	-
Ghosh et al	150	Cadaveric	118(79%)	27(18%)
Hellerstein and Orbison	150	Cadaveric	128(85)	37(24.7%)
Anh et al	98	In vivo	53(54%)	11(11%)
Mak et al	75	Cadaveric	55(73%)	12(16%)
Keraca et al	52	Cadaveric	35(67%)	4(8%)
Katti and Patil	50	Cadaveric	44(80%)	10(20%)
Randhawa et al.	50	Cadaveric	32(64%)	8(16%)

Figure 1 Coronary Sinus Opening with Thebesian Valve



Legend: The figure above shows an intact Coronary Sinus Opening(CSO) with a Thebesian Valve(TV) located in the right atrium of the heart.

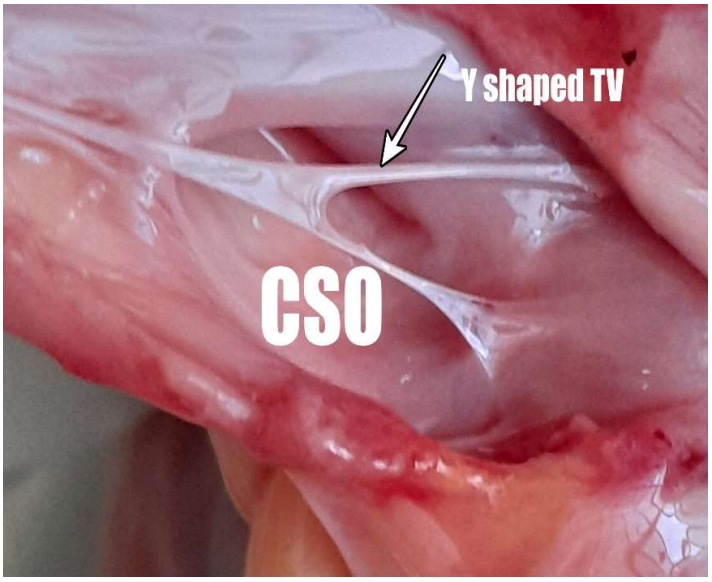
Figure 2 shows the coronary sinus opening completely occluded by the Thebesian valve.



Legend: The figure above shows a coronary sinus opening(CSO) that is fully occluded by the Thebesian valve. Note that the free margin of the valve is covering even the periphery of the coronary sinus opening. TV – Thebesian valve, CSO – coronary sinus opening

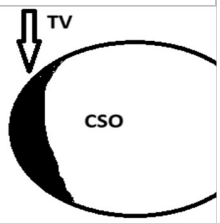
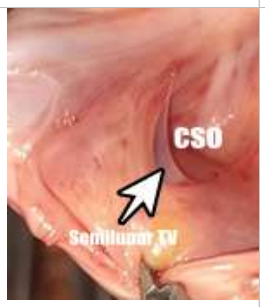
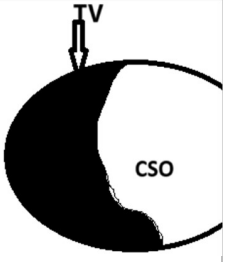
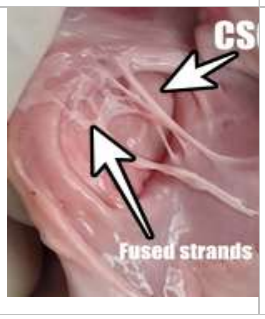
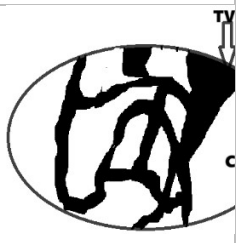
Figure 3 shows a coronary sinus opening without a Thebesian valve

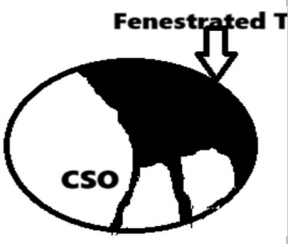
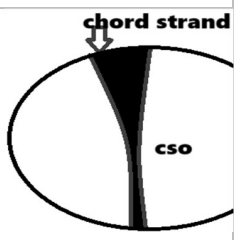
Legend: Figure above shows Coronary sinus Ostia with absent Thebesian valves. CSO – coronary sinus opening.
Figure 4 shows a Y-shaped fused type of Thebesian valve.



Legend: The figure above shows a Y-shaped Thebesian valve which is a subtype of fused strands subtype. CSO- coronary sinus opening. TV – Thebesian valve.

Figure 5 Various morphologies of Thebesian valve.

Type	Sample 1	Sample 2	Drawing
I Remnant fold			
II – Semilunar			
III- Fused strands			

IV- Fenestrated				
V – Chord strand				

Legend: The table above shows various morphologies of the Thebesian Valve. CSO - Coronary Sinus Opening, TV - Thebesian Valve Type I -Remnant fold, Type II – Semilunar valve, Type III – fused strands, Type IV- fenestrated valve, Type V – chord strand. Using the images taken, we outlined the various types of valves as shown above.

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Managing Recurrent Osteomyelitis in the Context of Antimicrobial Resistance in Sub-Saharan Africa: A Narrative Review.

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ABSTRACT

Background: Chronic osteomyelitis (COM) persists globally as a challenging surgical infection, with recurrence rates remaining high, especially in resource-constrained Sub-Saharan Africa (SSA). The rise of antimicrobial resistance (AMR) further complicates effective management, necessitating practical and scalable solutions.
Methods: We conducted a narrative review using studies published between 2000 and 2025 from PubMed, AJOL, Google Scholar, and WHO resources, with terms such as "chronic osteomyelitis," "recurrent osteomyelitis," "AMR," and "Sub-Saharan Africa." Inclusion criteria encompassed recurrence rates, AMR profiles, treatment strategies, simulation-based training (SBT), and low-cost interventions in SSA.
Results: The recurrence rates of COM in SSA range from 2.8% to 16.7%, with adolescents and young adults being the predominant affected group. High burdens of Staphylococcus aureus (including methicillin-resistant Staphylococcus aureus) and extended-spectrum β-lactamase-producing Gram-negative bacteria complicate treatment in settings with limited microbiology and surgical infrastructure. Low-cost innovations, such as locally produced antibiotic-impregnated beads and biodegradable carriers, have demonstrated improved outcomes; however, systematic evidence of scalability remains limited. Simulation-based training (SBT) and context-specific antimicrobial stewardship are underutilized despite their potential to improve infection prevention.
Conclusions: Practical solutions such as low-cost antibiotic delivery, SBT integration, and tailored stewardship should be prioritized to reduce recurrence and improve outcomes.
Keywords: Chronic Osteomyelitis, Recurrent Osteomyelitis, Antimicrobial Resistance, Sub-Saharan Africa, Simulation-Based Training.

INTRODUCTION

Osteomyelitis, first described by Hippocrates, is an ancient disease with evidence of similar bone infections in prehistoric fossils. It currently affects approximately 13 per 100,000 people annually worldwide, with higher rates in settings with increased trauma and limited healthcare access.[1] It is characterized by progressive bone inflammation, necrosis, and sequestrum formation resulting from disrupted blood

supply and biofilm formation, which protects pathogens from host immunity and antibiotics.[1,2] Despite standard treatment combining surgical debridement and prolonged antibiotic therapy, recurrence rates remain high, particularly in low-resource environments like Sub-Saharan Africa (SSA).[3]

The rising threat of antimicrobial resistance (AMR) complicates treatment further, as Staphylococcus aureus acquires resistance to beta-lactam antibiotics, thereby increasing the prevalence of methicillin-resistant Staphylococcus aureus (MRSA), and multidrug-resistant Gram-negative bacteria add complexity to management.[4,5] SSA faces additional challenges due to inadequate diagnostics, surgical capacity, and infection prevention practices, necessitating the exploration of low-cost, scalable interventions and context-adapted antimicrobial stewardship.

This review synthesizes evidence on recurrent Chronic osteomyelitis (COM) within the AMR context in SSA, highlighting pathogen profiles, recurrence rates, barriers to effective care, and low-cost innovations while identifying critical gaps to guide policy, practice, and research priorities.

METHODS

A narrative review approach was adopted, targeting English-language publications from 2000 to 2025, using PubMed, AJOL, Google Scholar, and WHO resources. Search terms included "chronic osteomyelitis," "recurrent osteomyelitis," "antimicrobial resistance," and "Sub-Saharan Africa." Grey literature and WHO reports were also reviewed.

Inclusion criteria:

- Studies reporting prevalence and recurrence rates of COM in SSA.
- Articles discussing pathogen profiles and AMR patterns.
- Studies detailing treatment strategies, low-resource innovations, and SBT in orthopedic infections.

Exclusion criteria:

- Studies unrelated to osteomyelitis or antimicrobial resistance in orthopedic infections.
- Studies outside Sub-Saharan Africa unless they provide insights which can be applied to SSA countries.
- Case reports without broader epidemiological or treatment strategy insights.
- Editorials, commentaries, and opinion pieces lacking empirical data or policy analysis.
- Studies focusing exclusively on acute osteomyelitis without discussion of chronic or recurrent aspects.

Selection process

1. Identification: 120 identified records from databases and grey literature.
2. Screening: 20 duplicates removed; 100 titles/abstracts screened; 50 excluded
3. Eligibility: 50 Full-text articles reviewed; 25 excluded.
4. Included: 25 publications

The findings were narratively synthesized to align with SSA's context, emphasizing practical insights for clinicians and policymakers. Two reviewers (PB and WOF) independently assessed the methodological quality of included studies. For randomized controlled trials we used the Cochrane Risk of Bias tool; for non-randomized cohort and case-control studies we used the Newcastle–Ottawa Scale (NOS); for cross-sectional and case series we used the Joanna Briggs Institute (JBI) critical appraisal checklists; and for qualitative or implementation studies we used the CASP qualitative checklist.

Disagreements were resolved by discussion and, if needed, by arbitration with a third reviewer (EAO). Each study was assigned a certainty rating (High / Moderate / Low / Very low) adapted from GRADE principles for narrative synthesis: randomized trial evidence was rated higher than observational evidence, and risk of bias downgraded certainty where appropriate. Results of the critical appraisal are summarized in Supplementary Table S1.

Table 1: Summary of Studies on Recurrent Osteomyelitis in Sub-Saharan Africa

AUTHORS	STUDY DESIGN	SAMPLE SIZE	FINDINGS
Achor MT, Aaron FE, Obene TA (2025, Nigeria)	Hospital-based retrospective study	Not specified	Reported recurrence rate ~16.7%, identified S. aureus, Pseudomonas, Klebsiella; highlighted AMR challenges.
Tesfaye Bizuneh B, Kassahun Tarekegn T, et al. (2023, Ethiopia)	Retrospective study	Hospital records (2018–2021)	Prevalence of acute and chronic osteomyelitis; recurrence rate 2.89%; pathogens mainly S. aureus.
Mantero E, Carbone M, Calevo MG, Boero S (2011, Kenya)	Prospective study	96 pediatric patients	Diagnosis and treatment of pediatric chronic osteomyelitis; recurrence rate ~12.2%; S. aureus predominant.
Ouedraogo S, Zida M, Walla A, Tall M (2017, Burkina Faso)	Epidemiological, bacteriological and therapeutic study	Not specified	Reported recurrence rate 5.3%; common pathogens included ceftriaxone-resistant Salmonella and Staphylococcus.
Nacoulma SI, Ouédraogo DD, et al. (2007, Burkina Faso)	Retrospective study	102 cases (1996–2000)	Chronic osteomyelitis cases described; resistant pathogens noted.
Ikpeme IA, Oku EO, Ngim NE, Ilori IU, Abang IE (2013, Nigeria)	Comparative study (with/without local antibiotic delivery)	Not specified	Antibiotic beads improved outcomes (77.8% cure) compared to debridement alone (57.7%).
Salawu ON, Babalola OM, et al. (2017, Nigeria)	Comparative clinical study	Not specified	Better outcomes with antibiotic beads vs gentamicin-saline after sequestrectomy.
Alonge TO, Ogunlade SO, et al. (2002, Nigeria)	Clinical trial (initial study)	Not specified	Ceftriaxone–PMMA beads were effective in management of chronic osteomyelitis.
Fonkoue L, Tissingh EK, et al. (2024, Cameroon)	Cohort study	Not specified	66% Gram-negative fracture-related infections; high resistance to fluoroquinolones/rifampicin, carbapenems moderately effective.

Alamarat ZI, Babic J, et al. (2020, Nigeria case)	Case report (compassionate drug use)	Single pediatric case	Cefiderocol successfully used for resistant Pseudomonas and Klebsiella osteomyelitis.
Venter RG, Tanwar YS, et al. (2020, South Africa)	Retrospective cohort study	80 patients	Debridement and dead space management used. 6% recurrence successfully treated with bio-glass

RESULTS

RECURRENCE RATES AND EPIDEMIOLOGY

Chronic osteomyelitis (COM) recurrence rates in Sub-Saharan Africa (SSA) vary across regions:

- Nigeria: 16.7%[6]
- Ethiopia: 2.89%[7]
- Burkina Faso: 5.3%[8]
- Kenya: 12.2%[9]
- South Africa: 6%[26,27]

Adolescent and young adult males are commonly affected due to open fractures and hematogenous spread, with the tibia and femur frequently involved.[10,11]

Table 2: Recurrent Osteomyelitis: Recurrence Rates, Pathogen Profiles, and Innovations in Sub-Saharan Africa

Country	Recurrence Rate (%)	Common Pathogens	AMR Challenges	Innovations
Nigeria	16.7	*Staphylococcus aureus* (MRSA, MSSA), *Pseudomonas*, *Klebsiella*	MRSA, extended-spectrum β-lactamase-producing Gram-negatives	Antibiotic-impregnated polymethylmethacrylate (PMMA) beads, biodegradable carriers
Ethiopia	2.89	Likely *Staphylococcus aureus*	Likely AMR (details not specified)	N/A
Burkina Faso	5.3	*Salmonella spp.* (ceftriaxone-resistant), *Staphylococcus*	Ceftriaxone-resistant *Salmonella*	N/A
Kenya	12.2	*Staphylococcus aureus*	MRSA, limited AMR data	N/A

Cameroon	N/A	Gram-negative (66%)	High resistance to fluoroquinolones and rifampicin; moderate efficacy of carbapenems	Limited stewardship; local antibiotic delivery challenges
Zaire	N/A	N/A	N/A	Plaster-of-Paris antibiotic systems, collagen fleece
South Africa	6%	Klebsiella Pneumoniae (70%), Staphylococccus aureus (17%)	High resistance to cephalosporins carbapenems; 17% Staphylococcus aureus infections are non-susceptible to cloxacillin (MRSA)	Bioactive glass (S53P4)

PATHOGEN PROFILES AND AMR CHALLENGES

Staphylococcus aureus (including methicillin-sensitive *Staphylococcus aureus*[MSSA] and methicillin-resistant *Staphylococcus aureus*[MRSA]) remain the leading pathogen in bone and joint infections, accounting for up to 75% of cases worldwide. In SSA, the emergence of MRSA and ESBL-producing Gram-negative bacteria significantly complicates treatment options.[12] In Cameroon, Gram-negative pathogens accounted for 66% of fracture-related infections, exhibiting high resistance (>60%) to fluoroquinolones and rifampicin, with only carbapenems, amikacin, and vancomycin showing moderate efficacy. A study in Nigeria also showed an adolescent male with chronic osteomyelitis caused by a resistant Pseudomonas aeruginosa and a Klebsiella pneumoniae strain, which was treated using Cefiderecol.[13] A case of osteomyelitis caused by ceftriaxone-resistant Salmonella was reported in a study in Burkina Faso.[14]

Barriers to effective antimicrobial stewardship include:

- Limited microbiology capacity and diagnostics[15]
- Bacteria evolving into minor colony variants (SCV) or forming biofilm[16–18]
- Unregulated antibiotic sales[15,19]
- Outpatient poor adherence to the antibiotic regimen[20]
- Weak prescribing oversight and inadequate healthcare training[12]

TREATMENT STRATEGIES AND INNOVATIONS

Standard Management

Standard treatment for chronic osteomyelitis (COM) typically involves surgical debridement and prolonged parenteral antibiotic therapy, often hindered by limited surgical resources and inadequate sterile conditions in SSA.[21] A systematic review reported no significant differences in recurrence rates between single-stage and two-stage surgeries for long-bone COM.[22] Oral versus parenteral antibiotic

effectiveness shows no significant differences if pathogens are sensitive; however, limitations in oral formulations remain in availability and spectrum.[2]

Low-Resource Innovations
Clinically Tested in SSA:

- Locally produced antibiotic-impregnated polymethylmethacrylate (PMMA) beads: Studies in Nigeria demonstrated a 77.8% cure rate with antibiotic beads versus 57.7% with debridement alone.[21,23]

Experimental/Limited to Case Series:

- Biodegradable carriers (e.g., plaster-of-Paris antibiotic systems): Plaster-of-Paris antibiotic systems in Zaire achieved wound healing in 16 of 18 patients with radiographic bone regeneration within six weeks.[24]
- Collagen fleece filled with antibiotics: Emerging reports suggest higher antibiotic dispersion rates than PMMA beads, but current data are largely observational and not yet supported by large-scale clinical trials.[25]

These innovations reduce recurrence while minimizing hospital stays and systemic antibiotic use; however, they lack evidence of region-wide scalability, standardization, and long-term safety.

SIMULATION-BASED TRAINING (SBT)

SBT is underutilized in SSA but offers a promising adjunct to infection prevention education. A study revealed that SBT improved infection prevention compliance, reduced healthcare-associated infections, and enhanced learners' confidence and competence in infection control measures[28].

Simulation-based training (SBT) has demonstrable effects on improving infection-prevention knowledge, adherence to practices (including hand hygiene and aseptic technique), and learner confidence; several systematic reviews and meta-analyses report improved compliance and reductions in healthcare-associated infection rates after institution-wide SBT programmes[29]. In low-resource and SSA settings, pilot simulation modules (e.g., hand-hygiene scenarios and PPE donning/doffing training) have shown feasibility, increased adherence and improved skills scores, though larger scale effectiveness studies with patient-level outcomes remain limited[28,29]. Given this evidence, SBT is a promising adjunct to stewardship and surgical training but should be implemented alongside robust monitoring and outcome measurement. Similar SBT adaptation in SSA could address infection prevention deficits and reduce the recurrence of COM.

IDENTIFIED GAPS IN SSA CONTEXT

Despite available insights, critical gaps persist:

- Lack of systematic synthesis on recurrence rates, treatment outcomes, and AMR patterns across SSA, hindering informed policy development.
- The underexplored scalability of low-cost interventions like local antibiotic delivery systems across diverse SSA contexts[15]
- Minimal SBT integration in orthopedic infection prevention within SSA despite demonstrated effectiveness elsewhere
- Limited antimicrobial stewardship models tailored to recurrent COM in SSA's low-resource orthopedic settings.[20]
- Absence of patient-centered outcome measures (quality of life, functional recovery, financial burden) in studies, limiting comprehensive disease impact assessment.[15]

DISCUSSION

COM recurrence remains a significant burden in SSA, driven by high AMR prevalence and limited healthcare resources. Local innovations, such as PMMA beads and biodegradable carriers, offer cost-effective solutions; however, a systematic evaluation across diverse SSA contexts is necessary to determine their effectiveness and applicability.

Addressing these challenges requires:

1. Expand local antibiotic delivery systems (PMMA beads / biodegradable carriers) - Evidence: Moderate (observational comparative studies in Nigeria reported improved cure rates). Implementation: surgical training on bead implantation, local production protocols, hospital infection control review[6]. (Responsible: Hospital surgical departments, national orthopedic societies).
2. Strengthen microbiology capacity and local antibiograms - Evidence: Strong indirect (surveillance data indicate variable resistance). Implementation: standardize specimen transport, subsidize basic AST panels, connect sentinel labs to NICD/GERMS networks. (Responsible: Ministries of Health, NHLS/NICD)[27].
3. Integrate context-appropriate SBT into surgical/IPC training - Evidence: Moderate (SBT improves IPC practices; SSA pilots feasible). Implementation: start with low-cost scenarios (hand hygiene, aseptic technique), evaluate impact on IPC metrics, scale iteratively[28].
4. Implement antimicrobial stewardship tailored to orthopedic services - Evidence: Low to Moderate; implementation studies show feasibility. Implementation: develop standard empiric protocols updated by local hospital antibiograms, audit prescribing, provide targeted education. (Responsible: Hospital stewardship teams).
5. These strategies will improve patient outcomes, reduce recurrence, and support AMR containment.

LIMITATIONS

The inherent constraints of narrative synthesis limit this narrative review, as it lacks quantitative meta-analysis and a formal risk of bias assessment. The review may have missed unpublished data or region-specific reports not indexed in major databases. Additionally, antimicrobial resistance patterns can vary significantly across local contexts within Sub-Saharan Africa, potentially affecting the generalizability of the findings.

CONCLUSION

This narrative review synthesizes published evidence on recurrent chronic osteomyelitis in Sub-Saharan Africa and highlights the interaction between recurrence and antimicrobial resistance. Observational studies and local innovations (e.g., locally produced antibiotic-impregnated beads) suggest potential benefits in reducing recurrence, but the overall evidence base is limited by heterogeneity and moderate to high risk of bias. Surveillance data from regional programs indicate a persistent burden of resistant *S. aureus* and resistant Gram-negative pathogens that should inform empiric therapy and stewardship[2]. Consequently, we recommend prioritizing strengthening microbiology capacity and local antibiograms, pragmatic local antibiotic delivery strategies evaluated in prospective studies, and integration of simulation-based infection prevention training with monitoring of clinical outcomes. Future research should include multicentre prospective studies with standardized outcome measures and implementation research to test scalability.

ETHICS STATEMENT

This study is a narrative review of published data and did not require institutional ethics approval.

DATA AVAILABILITY STATEMENT

Data sharing does not apply to this article as no new data were created or analyzed in this study.

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

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Ethical Perceptions of Euthanasia Among Medical and Non-Medical Undergraduate Students in Pakistan: A Qualitative Exploratory Study.

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ABSTRACT

Background: Euthanasia remains one of the most ethically complex and socially contested issues in contemporary healthcare, particularly in societies where religious beliefs and cultural traditions strongly shape moral decision-making. While global debates on euthanasia often emphasize patient autonomy, quality of life, and medical responsibility, perspectives from religiously conservative contexts remain underrepresented in empirical literature.

Objective: This qualitative study explored the awareness, ethical perceptions, and sociocultural interpretations of euthanasia among medical and non-medical undergraduate students in Pakistan.

Methods: An exploratory qualitative design was employed using semi-structured interviews to capture participants' personal understanding and moral reasoning. Thirty undergraduate students aged 18-24 years were recruited from medical disciplines, including Pharmacy and Allied Health Sciences, and non-medical disciplines such as Social Sciences, Business, Engineering, and Arts. Interviews were conducted face-to-face, audio-recorded with consent, and transcribed verbatim. Data were analyzed using thematic analysis to identify recurring patterns and underlying meanings within participants' narratives.

Results: The findings revealed that most students had limited prior awareness of euthanasia, with many encountering the concept for the first time during the interview. Ethical perceptions were strongly influenced by religious beliefs, with euthanasia predominantly viewed as morally impermissible and inconsistent with the belief that life and death are governed by divine authority. Cultural norms further reinforced opposition, as euthanasia was widely regarded as a taboo subject that contradicts family values and societal expectations. Medical students demonstrated relatively greater conceptual clarity and analytical reasoning, often acknowledging patient suffering and clinical realities; however, they remained ethically conflicted and largely unwilling to support or perform euthanasia due to religious, moral, and professional constraints. In contrast, non-medical students relied more on emotional and moral reasoning, frequently equating euthanasia with killing or wrongdoing.

Conclusion: Overall, the study highlights that perceptions of euthanasia among Pakistani university students are shaped more by faith, culture, and collective social values than by academic background alone. These findings emphasize the need for structured bioethics education and culturally sensitive dialogue to promote informed and balanced understanding of end-of-life issues.

Keywords: Euthanasia; Bioethics; Ethical Perceptions; Undergraduate Students; Religion and Culture; End-of-Life Care

INTRODUCTION

Euthanasia has long occupied a central and contentious position in debates surrounding medical ethics, law, and human rights, as it directly challenges fundamental notions about the sanctity of life, the limits of medical intervention, and the moral authority to decide the timing and manner of death [1]. Broadly understood as the intentional act of ending a person's life to relieve suffering, euthanasia raises profound ethical questions that extend beyond clinical practice into religious doctrine, cultural values, and social norms [2]. As advances in medical technology continue to prolong life even in cases of severe, irreversible illness, societies across the world are increasingly confronted with difficult questions about quality of life, dignity, and the ethical boundaries of end-of-life care [3].

Within biomedical ethics, euthanasia is often discussed in relation to core ethical principles such as autonomy, beneficence, non-maleficence, and justice [4]. Proponents frequently emphasize respect for patient autonomy and the moral obligation to alleviate unbearable suffering, particularly in cases of terminal illness where curative treatment is no longer possible [5]. Opponents, however, argue that intentionally ending life fundamentally violates the ethical duty of healthcare professionals to preserve life and avoid harm, and may erode trust in the medical profession [6]. These opposing viewpoints have **resulted** in polarized legal frameworks worldwide, with some countries permitting certain forms of euthanasia or physician-assisted dying under strict regulations, while others prohibit it entirely [7].

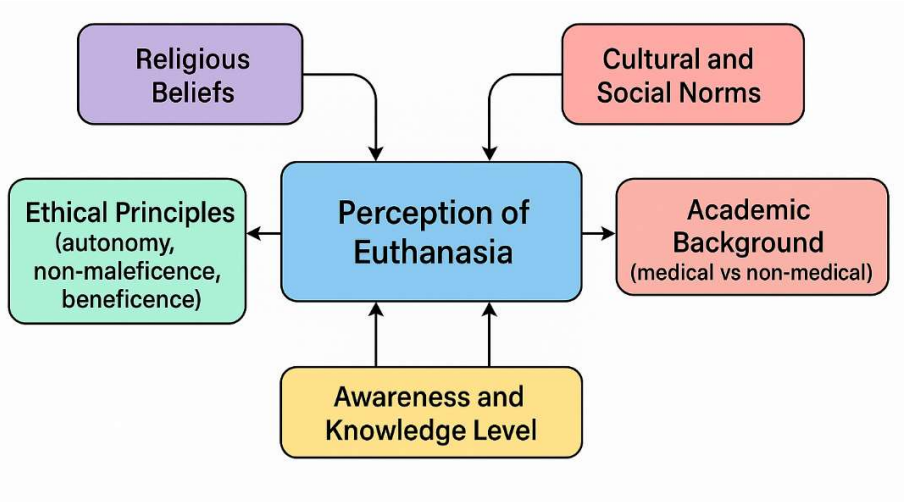

Figure 1. Conceptual Framework of Factors Influencing Perceptions of Euthanasia

Attitudes toward euthanasia are not formed in isolation but are deeply influenced by sociocultural context, religious beliefs, and moral worldviews [8]. Empirical studies consistently demonstrate that acceptance of euthanasia varies significantly across regions, with higher acceptance reported in secular societies and stronger opposition observed in countries where religion plays a central role in public and private life [9]. In many religious traditions, life is regarded as sacred and divinely ordained, and human intervention to hasten death is viewed as morally impermissible [10]. These beliefs often extend beyond individual faith to shape collective cultural norms, social expectations, and legal systems.

Religion has been identified as one of the strongest predictors of negative attitudes toward euthanasia, frequently outweighing demographic variables such as age, gender, or educational level [11]. In Islamic ethical thought, for example, life is considered an amanah, or trust, bestowed by God, and both suicide and euthanasia are generally prohibited on the grounds that only divine authority determines life and death [12]. Similar moral reservations are found in Christian, Sikh, and other religious traditions, where suffering may be interpreted as spiritually meaningful or as a test of faith rather than a justification for ending life [13]. As a result, individuals raised in religiously conservative societies often internalize moral frameworks that strongly oppose euthanasia, regardless of exposure to medical knowledge or ethical theory [14].
Cultural values further reinforce these religious perspectives, particularly in collectivist societies where family and community play a central role in decision-making [9]. In such contexts, end-of-life decisions are rarely viewed as purely individual choices, and personal autonomy may be subordinated to familial obligations, social expectations, and cultural ideals of patience, endurance, and respect for elders [15]. Discussions about death and dying may also be considered taboo, limiting public discourse and awareness about end-of-life care options, including palliative care and ethical decision-making [16].

University students represent a particularly important population for examining attitudes toward euthanasia, as they are in a formative phase of moral development and professional identity formation [17]. During this period, individuals begin to critically engage with ethical dilemmas, societal values, and professional norms that may influence their future roles as healthcare providers, policymakers, or informed citizens [18]. Research suggests that exposure to higher education can both challenge and reinforce pre-existing moral beliefs, depending on the academic discipline and cultural environment in which learning occurs [19].

Differences between medical and non-medical students are especially relevant in the context of euthanasia [20]. Medical students are exposed to clinical settings, patient suffering, and formal instruction in medical ethics, which may foster more nuanced or pragmatic views on end-of-life care [21]. Several studies have reported that medical students demonstrate greater awareness of euthanasia and are more likely to consider its ethical complexity compared to their non-medical counterparts [22]. However, other research indicates that even among medical students, strong religious and cultural beliefs can limit acceptance of euthanasia and generate ethical conflict between professional responsibilities and personal values [23].

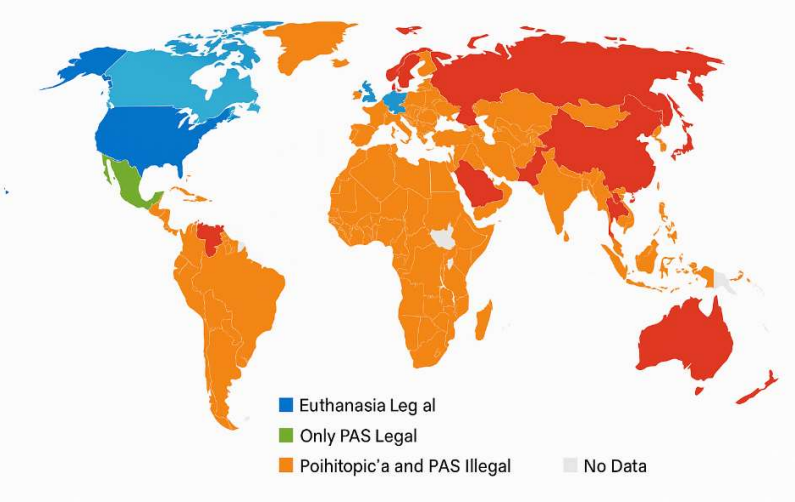

Figure 2. Contextualizing Euthanasia: Global to Pakistani Perspective

Non-medical students, by contrast, often rely more heavily on societal teachings, moral intuitions, and emotional reasoning when evaluating ethically sensitive issues such as euthanasia [24]. Limited exposure to clinical realities and bioethical frameworks may result in simplified interpretations, with euthanasia frequently equated with murder, suicide, or moral wrongdoing [25]. Understanding these differences is essential, as both groups contribute to future societal discourse and policymaking related to healthcare ethics [26].

In Pakistan, discussions surrounding euthanasia are particularly sensitive due to the country's strong religious identity and deeply rooted cultural traditions [27]. Euthanasia is illegal, socially stigmatized, and rarely ssed openly, even within academic or healthcare gs [28]. Existing research in Pakistan has largely ed on medical professionals or medical students, with limited attention given to non-medical populations or comparative perspectives [29]. Furthermore, qualitative research capturing students lived experiences, moral reasoning, and personal narratives remains scarce.

Given these gaps, the present study aimed to explore the ethical perceptions of euthanasia among medical and non-medical undergraduate students in Pakistan using a qualitative approach. By examining levels of awareness, religious and ethical interpretations, cultural influences, and disciplinary differences, this study seeks to provide a deeper understanding of how young adults in a religious and culturally conservative society engage with one of the most complex ethical issues in modern medicine [30]. Such insights are essential for informing bioethics education, promoting culturally sensitive dialogue, and supporting ethical decision-making in end-of-life care.

METHODOLOGY

tudy employed a qualitative exploratory design to gain an in-depth understanding of undergraduate students' ptions of euthanasia, as qualitative inquiry is particularly suitable for exploring sensitive ethical issues shaped by nal beliefs, cultural norms, and moral reasoning. The study was conducted at a university in Pakistan and included l of thirty undergraduate students aged between 18 and 24 years. Participants were drawn from both medical lines, including Pharmacy and Allied Health Sciences, and non-medical disciplines such as Social Sciences, ess, Engineering, and Arts. A purposive sampling strategy was used following initial convenience recruitment s different departments to ensure variation in academic background, gender, and sociocultural perspectives. nts with prior professional experience in end-of-life care or those not currently enrolled in an undergraduate am were excluded to maintain a consistent student-based perspective.

Data was collected between October and November 2025 through face-to-face semi-structured interviews conducted in a private setting within the university. An interview guide was developed based on existing literature on euthanasia and medical ethics to facilitate open discussion while allowing flexibility for participants to express their views in their own words. Each interview lasted approximately 10–15 minutes and was audio-recorded with participants' informed consent. Interviews were conducted until thematic saturation was reached, indicated by the absence of new themes in successive interviews.

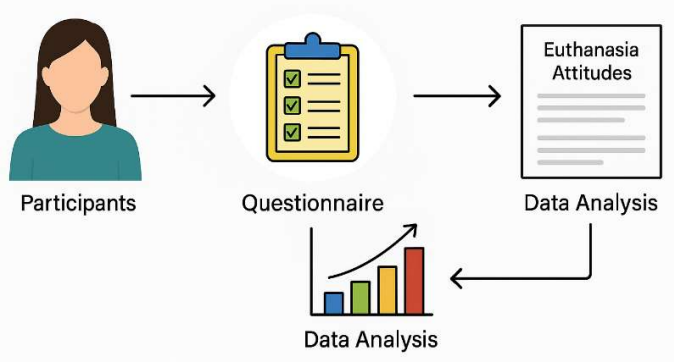

Figure 3. Flowchart of the Qualitative Research Process

All recordings were transcribed verbatim and anonymized prior to analysis. The data were analyzed using thematic analysis following Braun and Clarke's six-phase approach, which involved familiarization with the data, generation of initial codes, identification and review of themes, and development of a coherent analytical narrative [31]. Ethical approval for the study was obtained from the departmental Ethics Review Board, and all participants provided written informed consent. Confidentiality, voluntary participation, and the right to withdraw at any stage were ensured throughout the research process.

RESULTS

Analysis of the interview data produced a rich and nuanced understanding of how undergraduate students perceive euthanasia within the Pakistani sociocultural context. Four interconnected themes emerged from the narratives: awareness and basic understanding of euthanasia, ethical and religious interpretations, cultural and social influences, and differences between medical and non-medical perspectives. These themes collectively illustrate how limited knowledge, strong religious beliefs, cultural expectations, and academic background interact to shape students' ethical reasoning.

Table 1. Themes, Sub-Themes, Codes, and Representative Quotations

Theme	Sub Theme	Codes	Short Direct Quotations
Awareness & Basic Understanding	Limited Prior Knowledge	Never heard the term, Confusion with "killing", Understanding only after explanation	"Nahi suna kabhi." "No idea, jab aap ne bataya tab samjha."
	Conceptual Understanding (Medical vs Non-Medical)	Medical students clearer, Link with terminal illness, Non-medical emotional framing	"Patient ki zindagi intentionally end karna." "Isko tou qatal karna keheingy."

	Perceived Purpose of Euthanasia	Relief from suffering, Ending pain, Misinterpreted as murder	"Usko takleef me rakhne sy behtar hy, khatam kr dia jaye." "Killing word hi bohot heavy hai."
Ethical & Cultural Perspective	Religious Objections	Haram / forbidden, Life is sacred, Death is God's domain, Sabar & prayer emphasized	"Deen hamy sabar karne ka hukum deta hy." "Allah bardasht se zyada bojh nahi dalta."
	Ethical Moral Dilemma	Mercy vs murder, Fear of misuse, Ethical conflict in medical roles	"Ethically wrong, but watching a patient suffer also feels wrong." "Agar patient khud consent de raha hy tou kar dena chahiye."
	Minority Religious Perspective	Spiritual meaning of suffering, Doctors must preserve life	"Bible sikhaati hai ke suffering ka spiritual purpose hota hai." "God life deta hai."
Cultural & Social Influence	Cultural Taboos	Topic never discussed, Seen as dishonor or sin, Considered culturally "impossible"	"Hamare culture me yeh hota hi nahi." "Log isay gunah samajhte hain."
	Role of Family & Society	Family decisions dominate, Emotional attachment, Social disapproval	"Kon chahay ga k uska pyara door jaye, beshak takleef me hi kiu na ho."
Medical vs Non-Medical Perspective	Cognitive Differences	Medical = logical reasoning, Non-medical = emotional responses	"Medical wale logically sochte hain." "Rehm kar ke mar dena chahiye."
	Differences in Awareness	Medical students familiar with terminal illness, Non-medical low awareness	"Agar mera medical background hota, opinion different hota."
	Professional Boundaries	Medical students refuse to perform euthanasia, Preference for continued care, Need for professional oversight	"As a doctor, me yeh kabhi perform na karti." "Akhir tak koshish karni chahiye."
	Mental Health Interpretation	Some see euthanasia request as psychological distress	"Yeh aik mental health disorder hy, unki counselling karni chahiye."

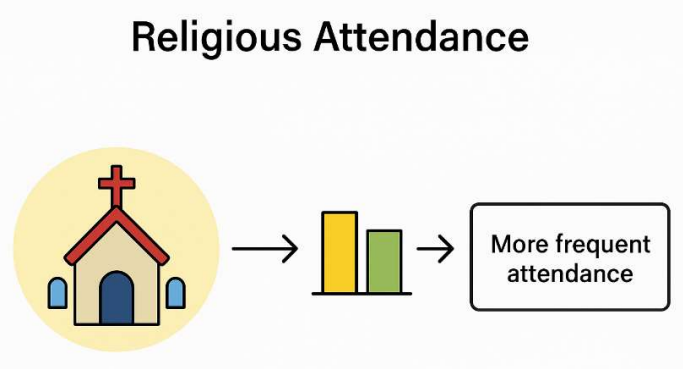

Figure 4. Awareness and Understanding of Euthanasia

A striking finding across interviews was the limited awareness and understanding of euthanasia, particularly among non-medical students. Many participants reported that they had never encountered the term before and were initially confused about its meaning. Several students explained that their understanding developed only after the interviewer provided an explanation. One participant stated, *"Honestly, maine yeh term pehle kabhi nahi suna tha. Jab aap ne explain kiya tab samajh aayi ke yeh kis cheez ke baare mein hai"* (P6). Another participant similarly remarked, *"Mujhe sirf itna lagta tha ke shayad yeh kisi ko maar dena hota hai, detail nahi pata thi"* (P19).

Medical students, in contrast, generally demonstrated greater conceptual clarity and were more familiar with the term. They often linked euthanasia to terminal illness, irreversible conditions, and uncontrolled pain. One medical student explained, *"Euthanasia ka concept usually end-stage patients ke liye hota hai jahan treatment ka koi faida nahi hota aur patient extreme pain mein hota hai"* (P1). Despite this clearer understanding, even medical students expressed uncertainty and discomfort when discussing the concept, suggesting that awareness did not necessarily translate into acceptance. A participant reflected, *"Concept samajh aata hai, lekin accept karna mushkil lagta hai"* (P14).

Participants' interpretations of euthanasia were frequently emotionally charged. Non-medical students, in particular, tended to equate euthanasia with killing or murder, using strong moral language. One participant stated, *"Isko mercy killing ka naam de dein, lekin asal mein yeh qatal hi hai"* (P27). Another remarked, *"Kisi ki zindagi intentionally end karna ghalat lagta hai, chahe reason kuch bhi ho"* (P30). At the same time, a small number of participants acknowledged the idea of euthanasia as a means of relieving unbearable suffering, expressing ambivalence rather than outright rejection. As one student noted, *"Agar patient bohat takleef mein ho aur koi umeed na ho, toh dil mein khayal aata hai ke shayad yeh reham ho sakta hai"* (P22).

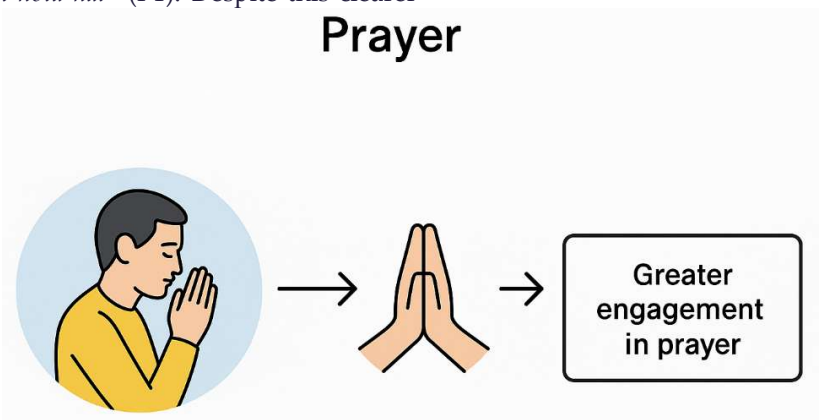

Figure 5. Ethical and Religious Interpretations of Euthanasia

Ethical and religious interpretations emerged as the most dominant influence shaping attitudes toward euthanasia. The majority of participants viewed euthanasia as morally impermissible due to religious beliefs, particularly within Islamic teachings. Life was consistently described as a sacred trust from God, and ending it intentionally was perceived as

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a violation of divine authority. One participant stated, *"Life Allah ki amanat hai, aur insan ko yeh haq nahi diya gaya ke woh kisi ki zindagi khatam kare"* (P23). Another explained, *"Deen humein sabar sikhata hai, takleef Allah ki taraf se azmaish hoti hai"* (P18).

Several participants emphasized the role of faith-based coping mechanisms, such as prayer and patience, as alternatives to euthanasia. One student remarked, *"Bemari ka matlab yeh nahi ke zindagi bekaar ho gayi, Quran aur dua se shifa mil sakti hai"* (P26). Even when acknowledging severe suffering, many participants insisted that endurance was morally superior to ending life. A participant explained, *"Takleef jitni bhi ho, akhir tak sabar karna chahiye, kyun ke har cheez ka ajar hota hai"* (P17).

Medical students frequently expressed ethical conflict in this domain. While they recognized the intensity of patient suffering and the limitations of medical treatment in terminal cases, they felt constrained by both religious beliefs and professional responsibilities. One medical student stated, *"Ethically mujhe patient ka dard samajh aata hai, lekin doctor hone ke nate meri zimmedari hai ke life protect karoon"* (P1). Another shared, *"Agar patient khud bhi request kare, tab bhi mujhe lagta hai ke yeh meri boundaries se bahar hai"* (P15). This internal struggle was a recurring feature of medical students' narratives, reflecting tension between empathy and moral obligation.

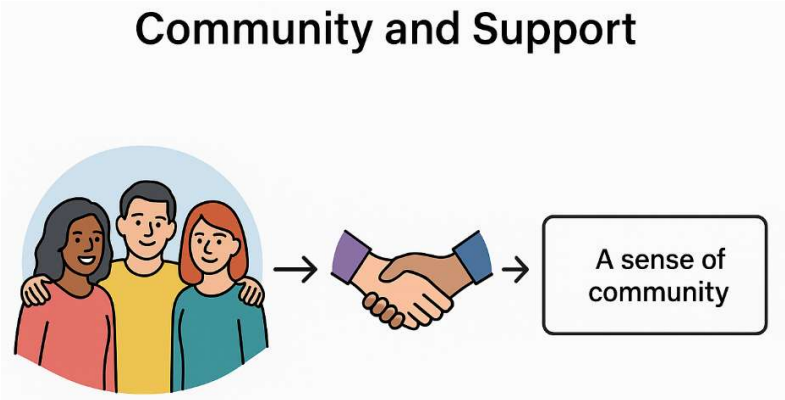

Figure 6. Cultural and Social Influences on Attitudes Toward Euthanasia

Participants belonging to minority religious backgrounds also expressed opposition to euthanasia, though their reasoning differed slightly in emphasis. Rather than referencing Islamic teachings, these students highlighted spiritual meanings attached to suffering and the moral duty of healthcare providers. One participant stated, *"Christian belief ke mutabiq suffering ka apna spiritual purpose hota hai, isliye life ko khud end karna theek nahi"* (P11). Another explained, *"God life deta hai aur God hi wapas leta hai, doctor ka kaam sirf care dena hai"* (P10). These perspectives suggest that rejection of euthanasia extended beyond a single religious framework and was rooted in broader moral worldviews.

Cultural and social influences strongly reinforced religious objections to euthanasia. Almost all participants described euthanasia as a taboo topic within Pakistani society, rarely discussed openly and often associated with sin, shame, or dishonor. One participant remarked, *"Hamare culture mein yeh baat openly discuss hi nahi hoti, log foran gunah keh dete hain"* (P25). Another added, *"Yeh cheez society mein accept hi nahi hai, chahe koi kitni bhi padhai kar le"* (P21).

Family influence was repeatedly highlighted as a decisive factor in end-of-life decision-making. Many participants emphasized that decisions about life and death are viewed as collective family matters rather than individual choices. Emotional attachment to loved ones was seen as a major barrier to accepting euthanasia. One student explained, *"Koi bhi apne maa baap ya bhai behen ke liye yeh faisla nahi kar sakta, chahe woh kitni takleef mein hi kyun na ho"* (P24). Another noted, *"Family pressure itna hota hai ke doctor bhi kuch aur soch hi nahi sakta"* (P9).

A small number of participants suggested that cultural traditions should not interfere with modern medical decisions, but such views were expressed cautiously and often met with hesitation. One participant stated, *"Kabhi kabhi lagta hai ke culture humein peeche rok leta hai, lekin phir society ka dar bhi hota hai"* (P4). Overall, cultural norms were perceived as a powerful force discouraging any acceptance of euthanasia.

Figure 7. Comparison of Medical and Non-Medical Student Perspectives

Clear differences emerged between medical and non-medical students in terms of reasoning patterns and ethical framing. Medical students tended to adopt a more analytical approach, drawing on their exposure to illness, patient care, and medical training. One participant remarked, *"Medical wale thora logically sochte hain, sirf emotions nahi balkay patient ki condition bhi dekhte hain"* (P22). They were more likely to discuss concepts such as prognosis, quality of life, and treatment futility.

Despite this analytical orientation, most medical students firmly stated that they would refuse to perform euthanasia themselves. One participant stated clearly, *"As a doctor, main yeh kabhi perform nahi karungi, chahe situation kitni bhi extreme ho"* (P15). Several medical students interpreted requests for euthanasia as signs of psychological distress rather than genuine desire to die. One explained, *"Mujhe lagta hai ke aise patients ko counselling ki zarurat hoti hai, na ke life end karne ki"* (P28).

Non-medical students, on the other hand, relied more heavily on emotional, moral, and religious reasoning. Their responses were often immediate and categorical, with euthanasia labeled as wrong, sinful, or equivalent to murder. One participant stated, *"Reham ke naam par kisi ko mar dena bhi ghalat hi hota hai"* (P30). Another remarked, *"Agar main doctor hota bhi, toh main yeh kaam kabhi na karta"* (P2). These narratives reflected limited engagement with clinical or ethical complexities and greater reliance on societal teachings.

Taken together, the results demonstrate that students' perceptions of euthanasia are shaped by a complex interaction of limited awareness, strong religious convictions, cultural expectations, and academic exposure. While medical education contributed to greater conceptual understanding and analytical reasoning, it did not override deeply held moral and religious beliefs. Across both groups, euthanasia was viewed as ethically sensitive, socially unacceptable, and morally troubling, highlighting the powerful role of faith and culture in shaping end-of-life perspectives among Pakistani undergraduate students.

DISCUSSION

This study explored ethical perceptions of euthanasia among medical and non-medical undergraduate students in Pakistan and revealed that attitudes toward end-of-life decisions are shaped predominantly by religious beliefs, cultural norms, and collective social values rather than academic background alone. The findings contribute to the growing body of recent literature indicating that perceptions of euthanasia in religiously conservative societies remain largely oppositional, even among populations with exposure to medical education and ethical discourse [32].

A key finding of this study was the limited baseline awareness of euthanasia, particularly among non-medical students. Many participants reported encountering the concept for the first time during the interview and initially interpreted it as synonymous with killing or murder. Similar gaps in awareness have been reported in recent studies conducted among university students in South Asia and the Middle East, where euthanasia is rarely discussed publicly and remains legally

prohibited [33]. These findings suggest that lack of exposure to structured discussions on end-of-life ethics contributes to simplified and emotionally driven interpretations of euthanasia among young adults.

Medical students in the present study demonstrated comparatively greater conceptual clarity, often associating euthanasia with terminal illness, irreversible suffering, and treatment futility. This aligns with recent international research showing that medical students tend to possess higher awareness and more nuanced understanding of euthanasia due to their exposure to clinical education and patient narratives [34]. However, despite this greater understanding, most medical students in the present study remained unwilling to support or perform euthanasia, highlighting a persistent ethical conflict between clinical reasoning and moral or religious obligations. Similar internal conflicts have been documented in recent studies among medical students in Turkey, Lebanon, and India, where empathy for patient suffering coexists with strong moral resistance to life-ending practices [35].

Religious beliefs emerged as the most dominant influence shaping attitudes toward euthanasia across both medical and non-medical groups. Participants overwhelmingly described life as sacred and divinely ordained, viewing euthanasia as a violation of God's authority over life and death. These findings are consistent with recent empirical studies demonstrating that religiosity is one of the strongest predictors of opposition to euthanasia, often outweighing factors such as education level or professional training [36]. In Islamic contexts in particular, euthanasia is frequently equated with suicide and is considered morally impermissible, a perspective that has been widely reported in contemporary bioethics literature from Muslim-majority countries [37].

Interestingly, minority religious participants in this study also opposed euthanasia, although their reasoning emphasized spiritual meanings of suffering and moral duty rather than Islamic doctrine. Recent comparative studies suggest that opposition to euthanasia among religious minorities is often rooted in broader theological beliefs about the sanctity of life and the moral role of suffering, rather than specific legal or cultural frameworks [38]. This indicates that resistance to euthanasia in Pakistan is not exclusively tied to Islam but reflects a shared moral orientation across religious traditions.
Cultural and social norms further reinforced religious objections to euthanasia. Participants consistently described euthanasia as a taboo subject that is socially unacceptable and rarely discussed within families or communities. This finding aligns with recent qualitative studies from collectivist societies, which highlight the central role of family authority, emotional attachment, and social judgment in end-of-life decision-making [39]. In such contexts, individual autonomy is often subordinated to collective values, making acceptance of euthanasia particularly difficult even when patient suffering is acknowledged.
The strong influence of family expectations observed in this study mirrors recent research showing that end-of-life decisions in South Asian cultures are commonly viewed as shared family responsibilities rather than personal choices [40]. Participants' emphasis on emotional bonds and fear of social condemnation suggests that cultural pressures may discourage open discussion of euthanasia and limit consideration of alternative end-of-life options, such as palliative care.
Differences between medical and non-medical students in this study were evident primarily in reasoning style rather than overall attitude. Medical students tended to adopt a more analytical and condition-based approach, while non-medical students relied more heavily on emotional and moral judgments. Recent studies similarly report that medical education fosters greater engagement with ethical complexity, though it does not necessarily lead to increased acceptance of euthanasia in conservative settings [41]. The tendency of some medical students to interpret euthanasia requests as indicators of psychological distress is also supported by recent literature emphasizing the overlap between end-of-life suffering, depression, and the need for mental health support [42].

Overall, the findings suggest that academic exposure alone is insufficient to alter deeply held moral beliefs regarding euthanasia in religious and culturally conservative societies. Recent scholarship emphasizes the importance of integrating culturally sensitive bioethics education that acknowledges religious values while encouraging critical reflection and ethical dialogue [43]. Without such approaches, students may continue to experience ethical confusion or rely on emotionally driven interpretations when confronted with complex end-of-life dilemmas.

In summary, this study's findings are consistent with recent international literature demonstrating that opposition to euthanasia among university students in conservative societies is shaped by a powerful intersection of religion, culture, and collective moral values. While medical education enhances awareness and ethical reasoning, it does not override the influence of faith and societal expectations. These insights underscore the need for interdisciplinary and culturally grounded bioethics education to support informed and reflective engagement with end-of-life issues in Pakistan and similar contexts.

RECOMMENDATIONS

The findings of this study indicate a clear need for structured and contextually appropriate bioethics education within higher education institutions in Pakistan. Integrating formal instruction on end-of-life care, medical ethics, and moral decision-making into both medical and non-medical curricula may help improve students' conceptual understanding of euthanasia and related ethical dilemmas. Creating safe academic spaces for open discussion, such as seminars, workshops, and interdisciplinary dialogues, may reduce stigma and encourage reflective engagement with ethically sensitive topics. Given that some participants interpreted requests for euthanasia as indicators of psychological distress, greater emphasis on mental health awareness and counseling services within universities is also warranted. Importantly, educational initiatives should remain culturally and religiously sensitive, acknowledging prevailing belief systems while fostering critical ethical reflection rather than confrontation.

LIMITATIONS

This study has several limitations that should be considered when interpreting the findings. The sample size was relatively small and drawn from a single institution, which limits the generalizability of the results to broader student populations across Pakistan. The sensitive nature of euthanasia may have led to social desirability bias, with participants expressing views aligned with dominant religious or cultural norms. Additionally, cross-sectional design captured perceptions at a single point in time and does not account for how students' ethical views may evolve with increased academic exposure or clinical experience.

CONCLUSION

This qualitative study provides valuable insight into how medical and non-medical undergraduate students in Pakistan perceive euthanasia within a deeply religious and culturally conservative context. The findings demonstrate that attitudes toward euthanasia are shaped predominantly by religious beliefs, cultural values, and societal expectations, while academic background plays a secondary role. Although medical students exhibited greater awareness and analytical reasoning related to end-of-life care, they remained ethically conflicted and largely opposed to euthanasia due to moral and professional constraints. Non-medical students relied more heavily on emotional and moral reasoning, often equating euthanasia with wrongdoing or sin. Overall, the study underscores the need for culturally sensitive bioethics education and open dialogue to promote informed, reflective, and ethically grounded engagement with end-of-life issues among university students.

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CONFLICT OF INTEREST

The authors declare no conflict of interest related to the content, data sources, or affiliations presented in this paper.

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Health-Related Quality of Life in Patients with Non-Cystic Fibrosis Bronchiectasis: A Cross-Sectional Observational Study.

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ABSTRACT

Background: Bronchiectasis is a chronic, progressive lung disease causing irreversible bronchial dilatation, impaired mucociliary clearance, and recurrent infections, leading to physical and psychosocial limitations. Assessing health-related quality of life (HRQoL) is crucial for understanding the disease burden.

Methods: A cross-sectional study was conducted on 100 HRCT-confirmed non-cystic fibrosis bronchiectasis patients aged 45–80 years at Gulab Devi Educational Complex, Lahore. HRQoL was assessed using the SF-36 questionnaire, and data were analyzed in SPSS 26 using descriptive statistics and chi-square tests.

Results: The mean age was 58.10 ± 8.86 years; 54% were male. Overall, 92% reported poor general health, and 64% reported deterioration compared to the previous year. Physical limitations were common, with 97% unable to perform vigorous or moderate activities, 95% limited in work, and 93% having difficulty performing daily tasks. Social activities were restricted in 62%, and 89% reported significant emotional distress. Most (99%) could not walk more than a mile, with substantial limitations in climbing stairs, carrying groceries, and self-care. No significant associations were observed between gender and HRQoL domains ($p > 0.05$).

Conclusion: Bronchiectasis markedly reduces HRQoL across physical, social, and emotional domains, irrespective of gender. These findings highlight the need for multidisciplinary interventions to improve functional status and well-being.

Keywords: Bronchiectasis, Health-related quality of life, Physical limitations, Emotional health, and Short Form-36.

INTRODUCTION

Bronchiectasis is a chronic, progressive respiratory disease characterized by irreversible bronchial dilatation and impaired mucociliary clearance resulting from a process of alternating infection and inflammation (1). The underlying etiology in bronchiectasis could involve cystic fibrosis (CF), alpha-1-antitrypsin deficiency, primary ciliary dyskinesia, allergic bronchopulmonary aspergillus, connective tissue disorders, inflammatory bowel diseases, congenital malformations, aspiration, humoral immunodeficiency, post-infectious, and idiopathic causes (2).

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CF and non-CF bronchiectasis (NCFB), both interlinked between inflammation and infection, sustains pro-inflammatory vicious cycle that increases the production of bronchiectasis and pulmonary structural destruction (3). Inflammatory immune cells (essentially activated macrophages and neutrophils) are the predominant infiltrating cell population in a disease state complicated by bronchiectasis and a significant cause of tissue damage and bronchiectasis production via discharge of their cytotoxic cellular contents (4). Specifically, proteases derived from cells and reactive oxygen species are crucial mediators of the degradation and destruction of extracellular pulmonary tissue that results in the development of bronchiectasis. The exact early immune-mediated processes of initiating and sustaining the development of bronchiectasis are still poorly understood (5). Regulated immune homeostasis appears to be critical, as both immune deficiencies and hyper-reactive immune responses are linked to bronchiectasis (6).
NCFB patients were estimated to be chronically colonized with Pseudomonas aeruginosa in about 25% of cases (7). Along with Pseudomonas, Haemophilus, Streptococcus, Staphylococcus, Veillonella, Prevotella, and Achromobacter make up the core of the bronchiectasis microbiota (8). Interestingly, Pseudomonas aeruginosa and Haemophilus influenzae are known to inhibit each other and so alter the core microbiota in the airway of NCFB patients. Another significant group of pathogens colonizing CF and non-CF airways is Tuberculous Mycobacterium (NTM). With CF, Mycobacterium avium complex and Mycobacterium abscessus are the most frequently isolated and these organisms have high rates of multidrug resistance, which makes treatment incredibly difficult (9).

Colonization by Pseudomonas aeruginosa was correlated with unfavorable outcomes in patients with bronchiectasis, which included more extensive and severe bronchiectatic changes on imaging, a decline in lung function, and increased hospitalization stay. The severity of NCFB was classified using two validated scores: the age, forced expiratory volume in 1 second (FEV1), colonization, extension, dyspnea (FACED) score, and the bronchiectasis severity index (BSI) (10).

Pseudomonas aeruginosa Colonization is also a component of BSI and FACED scores, which are predictive of future prognosis and hospitalization. BSI is made up of the clinical history of hospitalization and exacerbation, body mass index (BMI), and Medical Research Council Dyspnea Scale score (MMRC). The FACED score used to measure mortality prediction involves FEV1, age, Pseudomonas aeruginosa colonization, radiological extension, and dyspnea. Pseudomonas aeruginosa colonization is a valuable predictive factor for adverse prognosis, additionally helping to increase the risk of hospitalization and increased mortality rate (11).

Repeated chronic inflammatory damage to the airways leads to tissue breakdown, dilation of affected airways, mucociliary clearance inefficiency, and endogenous antimicrobial immunity, allowing survival of bacteria within the airways. The presence of bacteria causing continuously damages the airway structure, and the key clinical symptoms are chronic productive cough and shortness of breath (12). Bronchiectasis is characterized by an incessant and excessive discharge of purulent sputum. Dyspnea is variable and depends on the extent of involvement and the underlying disease. Mild hemoptysis is common; however, more severe forms are also possible. These symptoms impact HRQL (2, 13).

Bronchiectasis has three major anatomical patterns. In cylindrical bronchiectasis, the airway wall is regularly and uniformly dilated. In varicose bronchiectasis, there is irregular pattern with alternating areas of constriction and dilation. In cystic bronchiectasis, there is progressive, distal enlargement of the airways that results in saclike dilation. Bronchial dilation progresses and results in ballooning of bronchi that end in fluid or mucus-filled sacs (14). Radiographic studies confirm the diagnosis by showing airway dilation. A chest radiograph may show cystic spaces. The gold standard for

confirming the diagnosis is a high-resolution computed tomography scan (HRCT) of the chest, ideally done when the patient is clinically stable (15). HRCT is the diagnostic standard. Bronchoscopy is sometimes required to evaluate the cause of hemoptysis (16).

The worldwide prevalence has continued to rise over the years. The effect could be at least partly attributed to rising awareness of disease and improvements in imaging modalities. When we look at bronchiectasis on a global scale, it turns out that women are more affected, with reports showing a prevalence rate between 51.6% and 68.0%. Additionally, this condition tends to become more common as people age, jumping from 4.2 to 43.4 cases per 100,000 individuals in the 18 to 34 age group, all the way up to 153 to 1,365 cases per 100,000 for those aged 65 to 75 and older (17).

Bronchiectasis is a distinct, heterogeneous condition. Quality of life is deeply personal and specific to an individual. For patients, their quality of life is not just about the number of physical symptoms they experience or how often they occur; it's also shaped by social, psychological, and other individual factors. Some of the significant ways bronchiectasis influences patients' quality of life includes feelings of social embarrassment, disruptions in sleep, changes to daily routines, alterations in holiday plans, and anxiety regarding flare-ups (18).

Due to symptoms, the patient is unable to go out as the patient has severe hemoptysis and breathlessness, and he or she is restricted at home. Nighttime symptoms interfere with sleep significantly. Uncertainty of an exacerbation is a major cause of anxiety and depression for the patient and his or her family, especially around organizing travel and family activities. Anxiety and fear of exacerbation greatly affect the quality of life, as patients have no objective measurements of their symptoms (19).

HRQoL is a more inclusive, patient-focused evaluation; however, there is limited data available in South Asian populations where healthcare and cultural factors could impact the outcome. This study intends to evaluate HRQoL in patients of NCFB and investigate its correlation with demographic, clinical, and functional parameters, thus informing evidence-based, targeted interventions and enhancing patient-focused care.

METHODOLOGY

An Observational cross-sectional study conducted at the Pulmonology Department of Gulab Devi Educational Complex, Lahore, from February 10, 2025, to August 9, 2025, A total of 100 patients diagnosed with NCFB were included in the study.

sample size= $\boldsymbol{n} = \frac{Z^2\frac{\alpha}{2}pq}{\rho^2}$ (Cochrane-equation)

Where n = required sample size
Z = standard normal variate at 95% confidence level (Z = 1.96)
p = estimated prevalence of the attribute (assumed as 0.50 due to lack of prior local data)
q = 1 − p (0.50)
d = margin of error (0.10)

$$n = \frac{(1.96)^2 \times 0.50 \times 0.50}{(0.10)^2} = 96$$

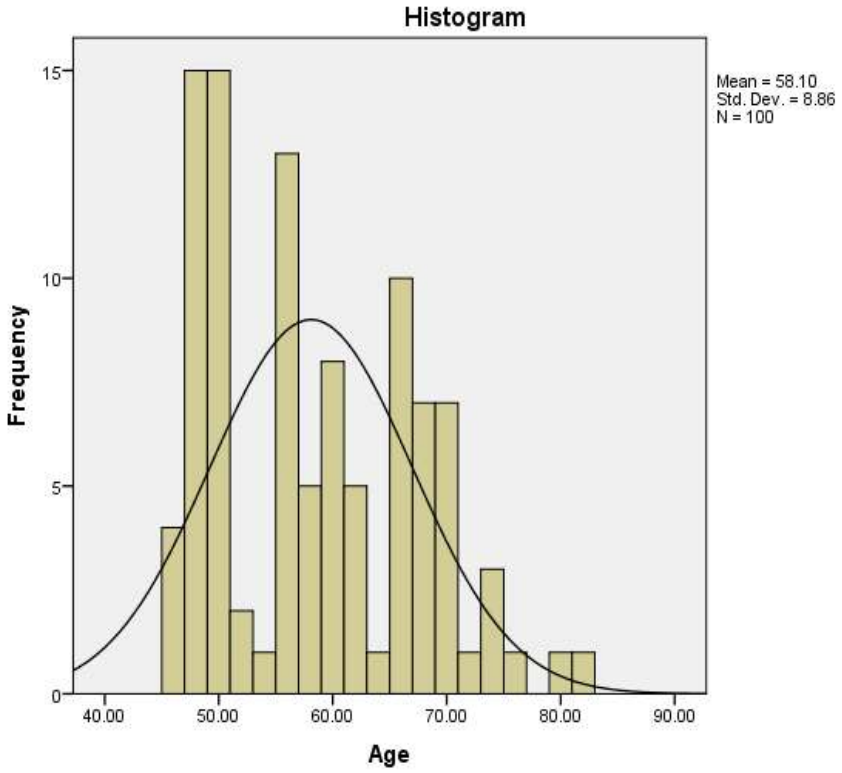
Participants were recruited using a **non-probability purposive sampling technique** over a six-month period. Ethical approval was obtained prior to data collection, and all patient information was handled confidentially.

Inclusion criteria:

1. Either gender of Age **45-80 years (20)**.
2. Confirmed diagnosis of bronchiectasis by **HRCT** and clinical assessment.
3. Clinically stable (no exacerbations in the last 4 weeks).

Exclusion criteria:

1. Acute exacerbation at the time of recruitment.
2. Bronchiectasis patients with significant co-morbidities such as Cardiovascular diseases, Cystic fibrosis, Malignancy, Asthma, Chronic obstructive pulmonary disease.
3. Significant cognitive impairment affecting questionnaire response.



Data Collection

Data was collected through **face-to-face interviews**, anthropometric and clinical measurements (weight, height, BMI, vital signs, and pulmonary function test parameters), and review of patient medical records. Health-related quality of life was assessed using the **SF-36 questionnaire.** Study variables included age, gender, cough, dyspnea, physical limitation, and anxiety.

Statistical Analysis

Data were analyzed using **SPSS version 26**. Descriptive statistics were applied, with means and standard deviations calculated for continuous variables (age, BMI, and SF-36 domain scores), while frequencies and percentages were used for categorical variables (gender, cough, dyspnea, and physical limitations). The **Chi-square test** was employed to assess differences in physical functioning, emotional health, and social activity across gender categories. Results were presented using tables, graphs, and charts. A **p-value < 0.05** was considered statistically significant.

FIGURE 1: FREQUENCY DISTRIBUTION OF AGE

In this study, 54(54%) were male and 46(46%) were female.

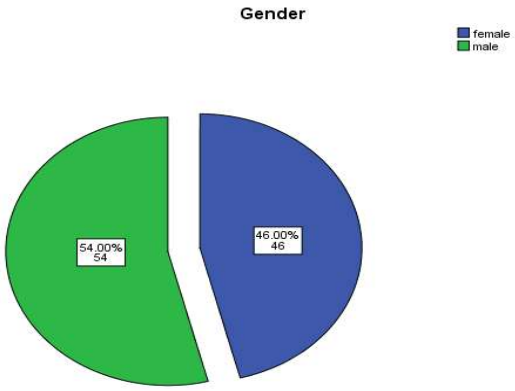


Figure 2: Frequency distribution of gender

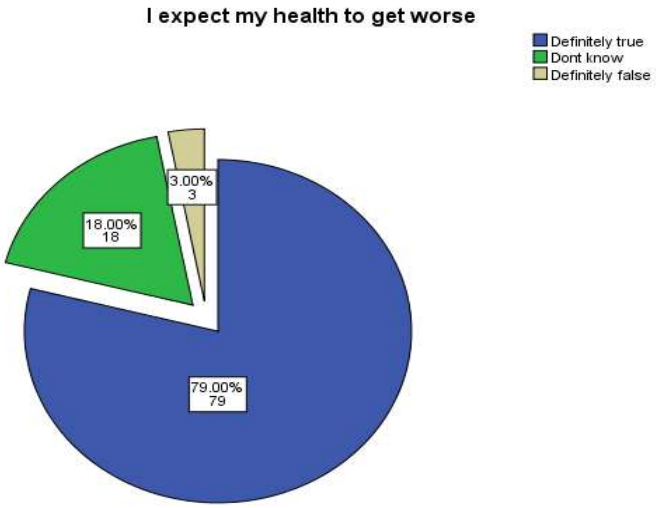


Figure 3: Frequency distribution of health worsening

In this study, most patients, 79 (79%), perceived worsening health status, whereas 18 (18%) were unsure about their health status, and 3 (3%) reported good health.

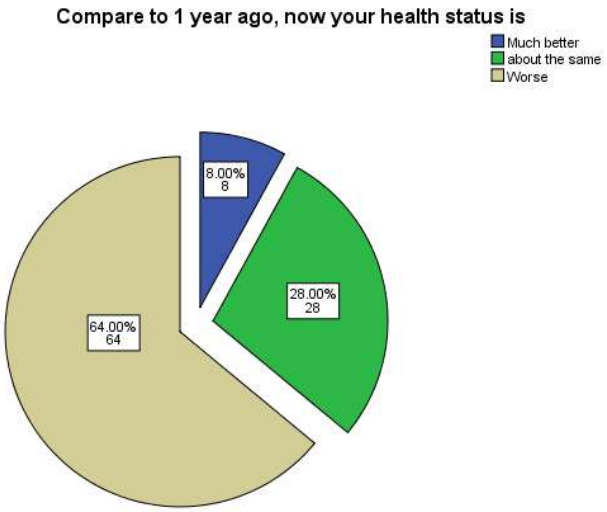


Figure 4: Frequency distribution of health status comparison

Relative to one year prior, health status had worsened in 64 (64%) patients, remained unchanged in 28 (28%), and improved in 8 (8%).

Table 1: Association between Gender and Perceived Future Health Status in Patients with NCFB

Gender		I expect my health to get worse			P-value
		Definitely true	Don't know	Definitely false	
	Female	37	8	1	0.861
	Male	44	8	2	
Total		81	16	3	

The chi-square test revealed no statistically significant association between gender and the response to the statement "I expect my health to get worse" $p > 0.05$ (Table 1).

The chi-square test showed that there was no statistically significant correlation between gender and the feeling of worsening health ($p = 0.861$, > 0.05). It indicates that male and female study participants gave the same response when questioned about whether they would experience worsening health in the future. A high percentage of both males (81.5%) and females (80.4%) responded with "Definitely true," showing a pessimistic attitude toward future health for most participants, irrespective of sex. Few participants chose "Definitely false" (2.2% of females and 3.7% of males), possibly indicating a lack of optimism concerning preserving health in this population. The comparatively high proportion of "Don't know" answers (17.4% among females and 14.8% among males) indicates an extent of uncertainty in predicting personal health outcomes, which may be caused by disease progression, treatment history, or poor health awareness.

In general, findings indicate that in this sample of NCFB patients, negative health expectations are prevalent and are not determined by gender. This emphasizes the necessity for patient education and psychological support to challenge negative health expectations among both men and women.

Table 1.1: Association between Gender and Limitation in Work or Other Activities in Patients with NCFB

Gender		Were limited in the kind of work or other activities		P-value
		No	Yes	
	Female	1	45	0.65
	Male	2	52	
Total		3	97	

Physical functioning was more affected in males than in females, but the association with gender was not statistically significant ($p > 0.05$) (Table 1.1).

Table 1.2: Association between Gender and Limitation in Social Activities among NCFB Patients

Gender		Social activities like visiting with friends		P-value
		Limited a lot	Limited a little	
	Female	26	20	0.298
	Male	36	18	
Total		62	38	

Social activities were more often "limited a lot" in males than females, but the association between gender and social activity limitation was not statistically significant ($p > 0.05$) (Table 1.2).

Out of 100 patients with NCFB, 62% said they had their social activities, like going out to see friends, "limited a lot," and 38% had only "limited a little". Among the females, 26 (56.5%) were "limited a lot" and 20 (43.5%) were "limited a little." For males, there was a higher percentage of "limited a lot" at 36 (66.7%), with 18 (33.3%) reporting "limited a little." The chi-square test identified no statistically significant gender-limitation association in social activities ($p = 0.298$, $p > 0.05$), suggesting that while the males seemed to be slightly more limited in social activity, the difference was not large enough to be statistically significant.

Table 1.3: Association between Gender and Emotional Well-being among NCFB

Gender		Have you felt so down that nothing could cheer you up		P-value
		No	Yes	
	Female	7	39	0.213
	Male	4	50	

Total	11	89	

Emotional well-being impairment was common in both genders, with no significant association found ($p > 0.05$) (Table 1.3).

In this study, cross-tabulation of gender with emotional health shows male mental health is more affected than female. (P>0.05), hence result shows that emotional health of bronchiectasis patients has no significant association with gender.

DISCUSSION

This study demonstrates that patients with NCFB experience substantial impairments across multiple domains of HRQoL, with physical, social, and emotional limitations being highly prevalent. The overwhelming majority reported poor general health, severe restrictions in daily functioning, and reduced social participation. These findings are consistent with previous studies, which have shown that bronchiectasis imposes a high burden and functional disability due to chronic respiratory symptoms, recurrent infections, and progressive lung damage.

Quality-of-life measures in clinical trials and practices assess the impact of disease and the response to treatment. All questionnaires have their strengths and limitations. By comparing them, we have been able to derive a template for the "ideal" quality-of-life measure for bronchiectasis patients. We found that the Short Form-36 (SF-36) was the most used quality-of-life questionnaire for bronchiectasis patients (21). HRQoL is greatly diminished in bronchiectasis, but there are few standardized and disease-specific instruments available for frequent use. The Bronchiectasis Health Questionnaire (BHQ), however, was developed and validated by Spinou et al. (2017) and is a straightforward 10-item scale that produces a single composite score. It had excellent internal consistency (Cronbach's α=0.85), high validity against the St George's Respiratory Questionnaire (r = -0.82), and marked correlations with clinically significant outcomes such as exacerbations, hospitalizations, bacterial colonization, and radiological disease extent. Its reliability, intra-class correlation coefficients (ICC) = 0.89, also makes it suitable for both clinical monitoring and research. In comparison to the generic measures SF-36, which evaluates general health domains but is insensitive to bronchiectasis-related changes, the BHQ is more sensitive and patient-focused. Likewise, although the Quality of Life - Bronchiectasis (QOL-B) survey is exhaustive, its 37 items constrain utility in busy clinics. The BHQ, with just 10 items, provides a quick, valid, and internationally applicable measurement, and thus represents a useful contribution for assessing HRQoL in bronchiectasis patients. SF-36 is a self-report questionnaire made up of 36 statements in 8 health domains, namely general health, physical functioning, limitation of activities, bodily pain, vitality, social functioning, emotional health problems, and mental health. We chiefly focus on 4 domains, having 21 statements, i.e., general health, physical functioning, limitations of activities, and emotional health problems. It results from a variety of underlying disorders occurring in all ages and with a very variable clinical course (22).

Our study included 100 patients with bronchiectasis, with a mean age of 58.10 ± 8.86 years; 54% were male and 46% female. Overall, 92% patients had poor health status, while 8% patients had good health status. In comparison to 1 year ago, 64% of the patients had worsened health, 28% had the same, and 8% had much better health. 94% patients became ill a little bit more easily than other individuals, while 6% patients did not. 79% patients feel that their health has been worsening, 18% did not know, and 3% patients feel their condition would improve. 93% patients did not feel as healthy as anyone they know, and 7% did not know. Gender has no significant correlation with general health (P>0.05). These results are consistent with more recent literature indicating that bronchiectasis patients have severely compromised quality of life, especially in physical, role, vitality, emotion, and social aspects, especially in patients with poorer dyspnea scores, frequent exacerbations, and greater disease extent. Compared to literature, our results confirm that bronchiectasis

has a strong negative impact on overall health perception. While some studies suggest that specialized care can improve certain quality-of-life domains, most patients still experience poor health status. This highlights the importance of regular quality-of-life assessments, such as the BHQ, in managing the disease effectively (23).
94% patients at that time, they used to work had lessened, while 6% did work normally. 97% were unable to finish work on time, less than they wanted, while 3% did work normally. Bronchiectasis patients had much physical limitations. 95% patients were restricted in work, while 5% were not restricted in work. 93% were unable to do the work, while 7% patients were unaffected. There is no significant gender association with physical activities (P>0.05). These trends are consistent with recent evidence demonstrating that bronchiectasis results in significant impairment in physical function and daily activity. For example, such patients have significantly lower activity levels and daily steps compared to healthy people, and impaired exercise tolerance is strongly correlated with dyspnea and poor lung function. This emphasizes the profound influence of bronchiectasis on work and activity performance by patients (24).

Physical limitations, particularly in activities requiring endurance or strength, were reported by nearly all participants. This aligns with earlier work indicating that reduced exercise tolerance in bronchiectasis is linked to airflow obstruction, muscle deconditioning, and fatigue. Most patients experienced marked limitations in daily functioning. Specifically, 97% were unable to perform vigorous or moderate activities, and 93% could not climb several flights of stairs, while 87% had major difficulty with one flight of stairs. Walking long distances was highly restricted, with 99% limited in walking more than a mile, 97% in walking several blocks, and 80% in walking a single block. Similarly, 80% reported severe limitations in carrying groceries and in bathing/dressing, while 62% faced major restrictions in social activities. In contrast, 1–20% of patients reported only minimal limitations. No significant association was observed between gender and social activities (P>0.05). Bronchiectasis patients showed substantially lower pulmonary function, muscle strength, exercise capacity, step count, and Physical Activity duration compared with controls ($p < 0.05$). International Physical Activity Questionnaire (IPAQ) underestimated physical activity compared with Sense Wear Armband, and this suggests a requirement for disease-specific Physical Activity assessment tools (25).

89% patients did not do work as carefully as usual, and nothing could cheer them up, whereas 11% patients did not have any effect. There is no significant association of gender with emotional health (P>0.05). A previous study showed 103 patients were enrolled (52.4% male, mean age 49.1 ± 14.4 years). Prior pulmonary tuberculosis was the most common cause (49.5%). Chronic productive cough (95.1%) was the most common symptom, followed by dyspnea (86.4%) and exacerbations (79.6%); half had been hospitalized in the previous year. Anxiety (22.3%) and depression (31.1%) were prevalent and strongly related to severe disease. HRQoL scores were low in all areas and showed a strong negative effect for psychological distress, with anxiety and social interaction being the exceptions (26). Emotional distress was common in our Study, with patients indicating a severe feeling of "being so down that nothing could cheer them up," and gender played no significant role (P>0.05) in impairments in emotion or body, implicating that disease burden, for HRQoL decline in bronchiectasis. Anxiety and emotional stress are independent predictors of health-related quality of life in patients with bronchiectasis. This evidence demonstrating that psychological symptoms like depression and anxiety are very common among bronchiectasis patients and predict poorer HRQoL independently of age, gender, and lung function parameters. In combination, these results attest to the necessity for an integrated, multidisciplinary model of medical management, pulmonary rehabilitation, and psychosocial intervention to treat the wide-ranging and long-term influence of bronchiectasis on patients' lives (24).

CONCLUSION

Patients with bronchiectasis had lower HRQoL scores. As the disease progresses, impairments in physical functioning worsen, leading to a decline in the ability to perform even routine activities. This not only restricts social participation but also has a considerable negative impact on mental health. The disease burden was high in all aspects and did not vary significantly by gender, indicating that the effect is largely explained by disease severity. These results emphasize the need for comprehensive care, including medical treatment, pulmonary rehabilitation, and psychosocial support, to improve the quality of life in bronchiectasis patients.

RECOMMENDATIONS

Regular follow-up and personalized care strategies might be beneficial in reducing disease-related problems and increasing functional ability in these patients. Moreover, future research should focus on longitudinal and multicenter studies using disease-specific quality-of-life to better evaluate treatment outcomes and disease progression.

LIMITATIONS

This study also has some limitations that need to be mentioned because it is a cross-sectional study in nature; it is not possible to establish causal relationships or identify changes in health-related quality of life. Since it is non-probability purposive sample and it is centred in a single organization, it may affect its generalizability. It did not use disease severity and did not conduct long-term follow-ups; it is limited in terms of interpreting its results.

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CONFLICT OF INTEREST

The authors declare no conflict of interest related to the content, data sources, or affiliations presented in this paper.

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Emergency Room Foley Catheter Retrieval of an Oesophageal Foreign Body In A Low-Resource Setting: A Case Series.

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ABSTRACT

Introduction: Infants are the most vulnerable population to oesophageal foreign bodies(EFB). They explore their environment with reflex hand-to-mouth gestures, putting them at even more risk. The presentation may be obvious and symptomatic, such as airway compromise, or silent, with subtle signs like drooling or refusal to feed. Therefore, the vigilance and awareness of parents and guardians are crucial for rapid diagnosis and management.

Case Series: We present two infants, a 12-month-old male and a 9-month-old male, with no relevant medical histories, brought in by their mothers with similar complaints of drooling and suspicion of ingestion of a coin at two different hospitals. A thorough clinical examination ruled out any signs of respiratory compromise; consequently, a chest X-ray was performed for both patients, revealing a coin at the thoracic inlet. Physicians trained in the concept of retrieval of EFB under mild sedation with a Foley catheter resulted in the successful retrieval of approximately 24mm coins with accompanying symptom resolution.

Intervention: While endoscopy remains the gold standard for EFB removal, alternative methods like Foley catheter extraction can be effective in selected cases. These cases highlight the usefulness of the Foley catheter method as a cost-effective, minimally invasive alternative for EFB removal in resource-limited settings. Proper patient selection, imaging confirmation, and procedural expertise are essential to minimize risks.

Conclusion: This technique is particularly suitable for blunt, radiopaque objects located in the upper oesophagus and for cooperative patients. These cases emphasise the importance of adaptable clinical strategies in emergency care, especially where endoscopic resources are limited.

Keywords: Childproofing, Esophageal Foreign Body, ENT, Emergency, Cameroon, Case Series

INTRODUCTION

Children frequently ingest foreign objects due to exploratory hand-to-mouth behaviour (1), with oesophagal foreign bodies (EFBs) being common in emergency settings, especially among children and the elderly. In Sokoto, Nigeria, EFBs accounted for 12.2% of ENT cases in 2019, with coins being the most frequent item (35%), and a male predominance (ratio 1.75) (2). Most foreign bodies are found in the upper esophagus. Endoscopy is the gold standard for removal, but limited access in low-resource areas necessitates alternatives (3).

The Foley catheter technique, first described in the mid-20th century, offers a cost-effective solution for retrieving blunt, radiopaque objects from the proximal oesophagus (1,4). It is suitable when the patient is stable and there are no

contraindications, such as sharp edges or caustic injury. Though primarily used in children, it has shown success in adults (2). This technique has, however, been sparsely used in our current dispensation, probably due to advancements in technology and the presence of safer and more efficient methods of retrieval. To present a cost-effective method of retrieval of EFBs, this case series presents two successful Foley catheter extractions, emphasising their clinical value, safety, and ethical relevance in resource-limited emergency care.

Case 1

A 12-month-old male infant was brought to the emergency department at Presbyterian Health Complex Nsimeyong Yaounde with symptoms of drooling, mouth opening, and refusal to feed. He appeared distressed, with neck hyperextension and a mildly altered general status. Vital signs were stable, and no cyanosis or abdominal distension was noted. Chest wall movements were age-appropriate, and abdominal findings were benign. A lateral and AP chest X-ray revealed a circular radiopaque object, likely a coin lodged at the thoracic inlet in the proximal oesophagus (Figure 1).

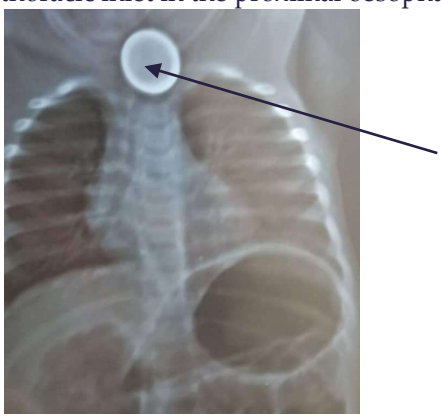

Figure 1: Chest X-ray in AP view of a 12-month-old known to have ingested a coin.

After obtaining informed consent and confirming the absence of contraindications, the team prepared for Foley catheter retrieval. The child was placed in dorsal decubitus with slight head flexion. Following an 8-hour fast, mild sedation with IV diazepam was administered to relax voluntary muscles while preserving the gag reflex. A 12 Fr Foley catheter was lubricated and gently inserted through the mouth. External anatomical landmarks guided insertion depth, and aspiration confirmed esophageal placement. The balloon was inflated with air, and with controlled traction and upward neck massage, the coin was successfully extracted (Figure 2).

Figure 2: 12-month-old post extraction of coin using a foley catheter.

Post-procedure care included airway reassessment and monitoring in the recovery room. A stat dose of dexamethasone was given to reduce potential edema. The infant remained stable, with no signs of bleeding or respiratory compromise. At a one-week follow-up, he showed no evidence of dysphagia or complications, confirming the safety and effectiveness of the Foley catheter technique in a resource-limited setting. This case highlights a practical, low-cost alternative to endoscopy for esophageal foreign body removal.

Case 2

A 9-month-old infant was urgently brought to the Regional Hospital Annex Nkambe after ingesting a 100 FCFA coin. The mother reported immediate gagging, persistent fussiness, refusal to feed, and excessive drooling. Within an hour, the child developed intermittent coughing and noisy breathing, though there were no signs of infection or prior choking episodes. On examination, the infant appeared distressed with neck hyperextension, profuse drooling, inspiratory stridor, and mild intercostal retractions, indicating upper airway compromise. Vital signs were stable, and no cyanosis or abdominal issues were noted.

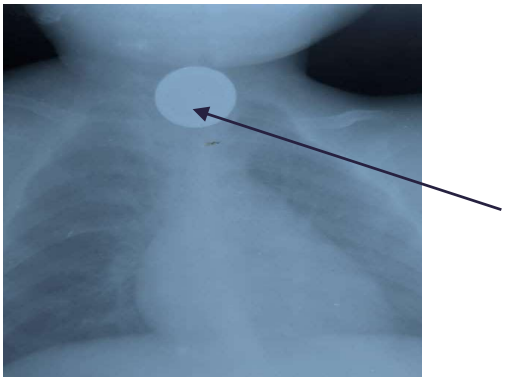

Figure 3: Chest X ray of 9-month-old known to have ingested a coin

Radiographic imaging (Figure 3) confirmed the presence of a circular radiopaque object lodged in the proximal esophagus at the thoracic inlet. Given the risk of aspiration and potential esophageal damage, an urgent extraction was performed under general anaesthesia. Direct laryngoscopy revealed the coin, and a Foley catheter was inserted past it. The balloon was inflated and gently pulled back, successfully retrieving the coin without complications (Figure 4). The esophagus was inspected for perforation, and the infant was extubated without incident.

Figure 4: Tail surface of Coin retrieved from esophagus of 9-month-old using a foley catheter

DISCUSSION

This paper describes the procedure of retrieving an EFB using an uncommon but practical technique. Whilst the primary treatment for lodged foreign bodies in the esophagus in children and adults remains endoscopic removal (4,5) and surgical removal in the event of failure (1), this technique sheds light on the possibility of having a similar result, in a shorter time frame with very little or mild sedation. In a setting where expert critical care is not easily reachable, with a notion of the high cost accompanying such elaborate procedures, innovative cost cost-effective, and rapid procedures such as these are pivotal in providing critical care to selected cases.

The Foley catheter balloon technique is an effective alternative for extracting blunt, smooth, radiopaque objects (e.g., coins, buttons) lodged in the upper or mid-esophagus of stable, cooperative pediatric or adult patients. This method applies only when no perforation, strictures, or corrosive materials are present and the object fits within the esophageal diameter. The procedure should be performed by experienced practitioners with sedation, emergency endoscopy backup, and is especially useful in resource-limited settings. Sharp objects, batteries, magnets, airway compromise, bleeding, and objects lodged beyond 24 hours are contraindications.

Historical data report high success rates when strict inclusion criteria are followed. Hawkins et al. demonstrated effective coin removal within 24 hours using this technique, emphasizing its simplicity, low cost, and minimal infrastructure requirements. However, risks such as balloon dislodgement into the airway, mucosal injury, and incomplete retrieval necessitate careful procedural safeguards. While rigid endoscopy remains the gold standard for esophageal foreign bodies, the Foley catheter method represents a valuable adjunct in low-resource environments when timely endoscopic intervention is unavailable, demonstrating the importance of contextual decision-making and medical improvisation.

CONCLUSION

EFBs could pose significant risks if not identified and treated accordingly. While endoscopy remains the gold standard, most rural areas are still deprived of this luxury. As such, adapting clinical practice to this context will involve the use of this technique. Strict observation and application of exclusion criteria is primordial to the success and applicability of this technique.

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Patterns of Intravitreal Injection Utilisation, Treatment Burden, and Cost Implications in a Public Ophthalmology Service: A Retrospective Audit.

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ABSTRACT

Background: The global rise of intravitreal treatment has impacted ophthalmic service delivery, workforce demands, and healthcare cost. Public ophthalmology services must strike a balance between increasing clinical demand and sustainable resource usage. The aim of this study was to assess intravitreal injection patterns, temporal trends, as well as associated drug procurement costs in a public ophthalmology service.

Methods: A retrospective clinical audit was undertaken to analyze all intravitreal injections administered between June 2023 & September 2025. The data were taken from intravitreal therapy registers & comprised injection volume, agent selection, laterality, & monthly utilization trends. Drug procurement costs were determined using institutional pharmacy records. The data were anonymized & analyzed descriptively. Formal ethical approval was not necessary because this was a service evaluation audit.

Results: A total of 1,446 intravitreal injections were delivered during the audit period. Anti-VEGF therapy accounted for most of the activity, with aflibercept formulations representing 55.2% of all injections. Introduction of high dose aflibercept (8 mg) was associated with rapid adoption and displacement of alternative agents. The total drug acquisition cost was €697,504.90, with aflibercept contributing the greatest proportion of expenditure. Lower-cost agents accounted for a smaller proportion of injections.

Conclusion: Intravitreal therapy represents a substantial and growing clinical and economic burden within public ophthalmology services. Clinical effectiveness and treatment durability appear to be more important than cost when determining prescribing trends. Continuous auditing and service-level evaluation are required to guide sustainable service delivery, workforce planning, and policy development.

Keywords: *Intravitreal injections, Anti-VEGF therapy, Ophthalmology services, Health economics, Clinical audit.*

INTRODUCTION

Intravitreal injection therapy has become one of the most frequently performed ophthalmic procedures globally. The introduction of anti-vascular endothelial growth factor, also known as anti-VEGF medicines, has improved results for individuals with neovascular age-related macular degeneration (nAMD), diabetic macular edema (DMO), retinal vein occlusion, and inflammatory retinal diseases.[1-3] As treatment indications have expanded, so too has the procedural workload placed on ophthalmology services.

In many healthcare systems, intravitreal injections are delivered in high-throughput injection suites that function at the interface of outpatient care & procedural medicine.[4] These treatments involve substantial collaboration between clinical professionals, theatre-related institutions, pharmaceutical assistance, & infection prevention methods. The cumulative operational & financial burden of intravitreal therapy is increasingly viewed as a key issue to ophthalmic care sustainability.[5]

Intravitreal therapy aligns closely with broader themes in global surgery & perioperative care, including efficiency, access, workforce optimisation, & cost containment, from a health systems perspective.[6] Despite this, real-world audit data examining utilisation patterns & expenditure within public services remain limited. Audit and service evaluation provide an essential mechanism for understanding evolving practice & informing local & national policy.[7]
This study aimed to examine intravitreal injection activity over a 27-month period within a public ophthalmology service, focusing on agent utilisation, temporal trends, laterality, and drug-related costs. By contextualising findings within existing clinical and health systems literature, this audit seeks to inform sustainable service planning and innovation in intravitreal therapy delivery.

METHODS

Study Design and Rationale

This study was conducted as a retrospective clinical audit and service evaluation. Audit methodology was selected to assess real-world practice against emerging clinical and operational considerations, rather than to test a predefined hypothesis.[8] The audit timeframe was chosen to capture changes in prescribing behaviour associated with the introduction of newer intravitreal agents.

The 27-month audit period was chosen to capture baseline prescribing patterns as well as changes related with the introduction of newer intravitreal drugs, such as high-dose aflibercept (8 mg), allowing for the examination of temporal trends as well as service adaptability across time.

Setting and Scope

The audit was undertaken at a public ophthalmology service that provided routine intravitreal treatment. The program provides a specialized intravitreal injection pathway, which is supported by interdisciplinary teams.

Data Collection

Intravitreal therapy registers were reviewed for the period June 2023 to September 2025. Variables extracted included: Total number of injections administered, Intravitreal agent used, Injection laterality and Monthly injection volume.
Drug acquisition costs were obtained from institutional pharmacy procurement records and reflected direct costs to the ophthalmology service. Injections were counted per eye & administration episode. Bilateral shots administered at the same appointment were documented as two injections and priced accordingly. Repeat injections in the same patient were classified as separate events, reflecting service workload rather than patient-specific long-term outcomes.

Analytical Framework

The Donabedian paradigm for medical care quality evaluation supervised data collection, analysis, & interpretation while conceptualizing service performance in three interconnected domains: structure, procedure, & outcomes. Structured elements of this audit included the availability of intravitreal agents & procurement costs; process elements included dosage patterns, injection volume, and laterality distribution; & outcome-related considerations focused on service workload, treatment burden, and cost implications rather than patient-level clinical outcomes. Structural factors consisted of intravitreal agent availability and acquisition costs; process variables involved agent selection, injection quantity, laterality, and spatial utilisation patterns; and outcome-related service indicators included treatment burden, workload, and total drug costs. These mappings directly influenced data extraction, processing, and interpretation.

Data analysis

The data was anonymized and compiled using Microsoft Excel. Descriptive statistics were employed to summarize utilization patterns. Temporal trends were analyzed using a graphical representation of monthly injection volumes.

Cost Analysis

The cost analysis was restricted to direct drug procurement expenses derived from institutional pharmacy records. Reported costs are list procurement prices exclusive of VAT, and do not include confidential rebates or bargained discounts. Staffing, equipment, consumables, and operating expenses were excluded. This method was chosen to provide a transparent and reproducible assessment of pharmaceutical-related financial burden, while noting that total service costs are likely underestimated.

Ethical and Governance Considerations

This study was classed as a service evaluation audit that included a retrospective analysis of anonymized data. Formal ethical approval and informed consent were not necessary, as stated in institutional governance principles and international recommendations.[9] Data handling conformed with GDPR regulations.

Although this study was carried out as a clinical audit/service evaluation, it fits the journal's unique Research requirements by producing original, thoroughly analyzed real-world evidence on service delivery, treatment burden, and cost implications of intravitreal therapy. The audit did not compare current practices to predetermined norms but rather sought to characterize them to enhance service planning, policy, and sustainability, in line with observational health services research.

RESULTS

The total number of intravitreal injections administered throughout the audit period was 1,446. Injection activity was constantly high, indicating a continued demand for retinal care.

The laterality patterns of the total injections showed that 32.9% were given to the left eye, 30.7% to the right eye, and 18.3% were bilateral. Most left-eye injections were not clinically significant, but it did reflect the variability inherent in in-service activities.

Table 1: Distribution Of Intravitreal Injections by Agent During the Audit Period, June 2023 to September 2025.

Intravitreal Agent	Number of Injections	Percentage (%)
Aflibercept 2 mg	518	35.8
Aflibercept 8 mg	281	19.4
Lucentis (Ranibizumab)	328	22.7
Avastin (Bevacizumab)	197	13.6
Dexamethasone implant (Ozurdex)	95	6.6
Faricimab	13	0.9
Triamcinolone	14	1.0
Total	1,446	100

Percentages may not total exactly 100 due to rounding.

Table 1 presents the distribution of intravitreal injections by agent across the audit timeframe. Aflibercept formulations accounted for more than half of all injections, with lower-cost and corticosteroid-based medications being utilized more selectively. Bilateral injections are operationally significant because they increase chair time, personnel demand, and operational workload per clinic session. Intravitreal agent distribution Anti-VEGF therapy constituted many injections.

Table 2: Drug Acquisition Costs by Intravitreal Agent During the Audit Period.

Intravitreal Agent	Unit Cost (€)	Number of Injections	Total Cost (€)
Aflibercept 2 mg	721.60	518	373,788.80
Aflibercept 8 mg	721.60	281	202,769.60
Ranibizumab	741.00	328	243,048.00
Bevacizumab	245.51	197	48,366.47
Dexamethasone implant (Ozurdex)	1,217.00	95	115,615.00
Faricimab	800.00	13	10,400.00
Triamcinolone	180.51	14	2,527.14
Total	-	1,446	697,504.90

Costs represent direct drug acquisition costs only and exclude VAT, staffing, infrastructure, consumables, and overheads.

Table 2 shows the unit and total drug acquisition expenses by intravitreal agent. Anti-VEGF therapy accounted for most of the total expenditure, demonstrating high utilization and higher unit prices when compared to other agents.

Figure 1: Total cost per intravitreal agent over the audit period

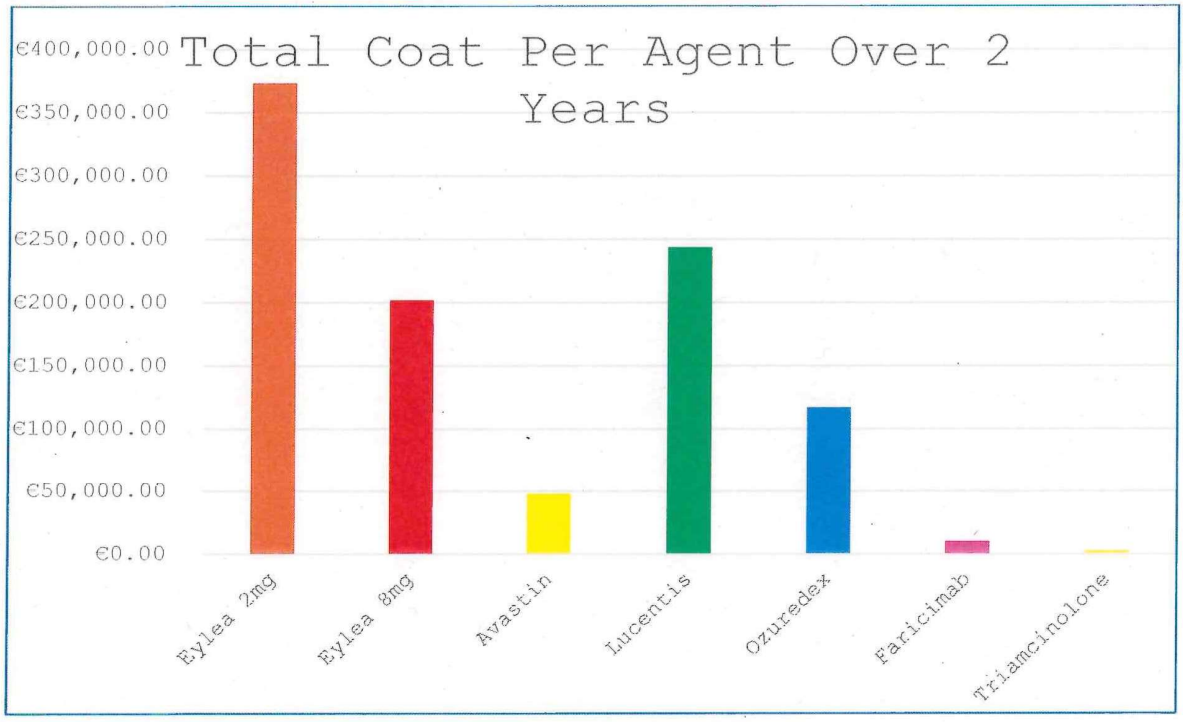

Figure 1 depicts the aggregate drug purchase cost per intravitreal agent over the audit period. Aflibercept preparations accounted for most total expense, indicating their high utilisation, while corticosteroid-based and lower-cost medicines contributed less.

Table 3: Comparison of Intravitreal Agent Use Before and After the Implementation of High-Dose Aflibercept (8 Mg).

Agent	Pre-Introduction*	Post-Introduction*	Direction of Change
Aflibercept (2 mg)	High	Moderate	↓
Aflibercept (8 mg)	0	High	↑↑
Ranibizumab	Moderate	Low	↓↓
Bevacizumab	Low	Low	↔
Corticosteroids	Low	Low	↔

**Pre-introduction, June 2023 - August 2024*
**Post-introduction, September 2024 - September 2025*

Table 3 shows changes in intravitreal agent use before and following the debut of high dose aflibercept (8 mg), indicating a shift in prescribing trends over time rather than an exclusive static pattern.

Temporal trends

Temporal analysis revealed a shift in intravitreal agent use over time, particularly after the introduction of a high dose aflibercept (8 mg) in late 2024 (Figure 2). Within four months, it had become the most administered agent. Meanwhile, Faricimab use fell dramatically.

Figure 2: Monthly Utilisation Trends of Intravitreal Agents Over the Audit Period, June 2023 - September 2025.

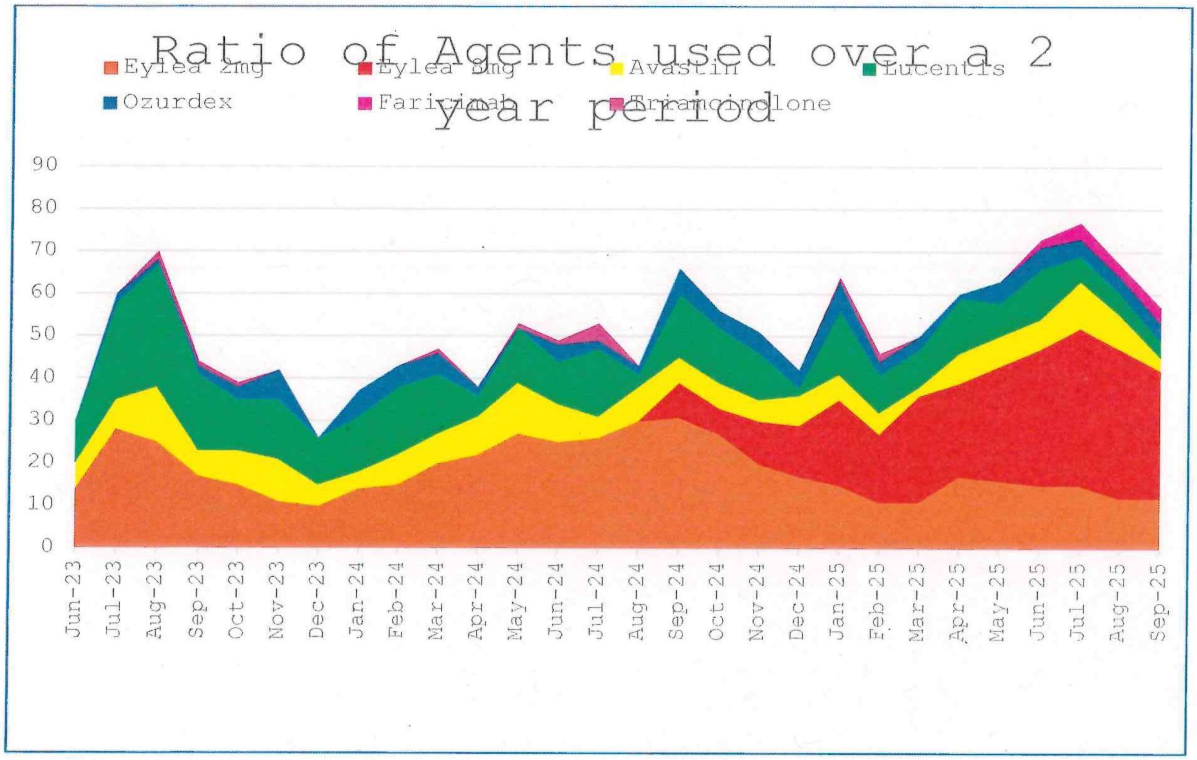

Figure 2 demonstrates dynamic changes in intravitreal agent utilisation over time. Use of aflibercept 2 mg predominated during the early audit period, with a gradual increase in aflibercept 8 mg following its introduction in September 2024. Concurrently, utilisation of Avastin and Lucentis declines while corticosteroid-based therapies remained relatively stable at lower volumes. The overall medicine acquisition cost throughout the audit period was €697,504.90. Anti-VEGF medications accounted for most of the spending. Despite lower unit costs, bevacizumab accounted for a relatively small share of total injections.

DISCUSSION

This audit illustrates the significant clinical and cost burden involved with administering intravitreal treatment in a public ophthalmology service. The prevalence of aflibercept-based therapy is due to evolving research supporting longer dose intervals & a lower treatment burden.[10–12] The data were evaluated using the Donabedian model, which conceptualizes healthcare quality as structural, process, & outcome dimensions. This audit's fundamental characteristics covered the availability & purchasing expenses of intravitreal agents, which indicate resource inputs to service delivery.[26] Process metrics included prescribing patterns, injection volume, laterality distribution, and temporal variations in agent use, which captured how care was delivered in practice. Outcome-related considerations were centred on service workload, treatment burden, and financial effect rather than patient-level clinical results, which is consistent with the objective of the service review. Using this approach allowed for a more structured understanding of intravitreal treatment delivery as a complicated, high-volume procedural service, highlighting the interrelationship of resource availability, clinical decision-making, & care sustainability.[26]

While this audit did not explicitly examine drivers of prescribing behavior, the observed trends indicate that outcomes, treatment duration, and service capacity concerns may have influenced agent selection more than purchase cost. Existing data supports this interpretation, emphasizing the relevance of reducing treatment burden and using extended dose intervals in real-world anti-VEGF use. Alternative explanations, such as local clinical preferences, formulary decisions, and purchasing practices should be examined.[13,14]

The vast volume of intravitreal injections highlights the importance of efficient injection pathways and interdisciplinary team support. Optimal workflow and task allocation may help to reduce procedural bottlenecks and increase patient throughput.[15] Relevance for Global Surgery and Innovation: Intravitreal treatment services represent the convergence of high-volume procedural care and outpatient medicine. Lessons from this audit can be used to broader concerns about surgical system strengthening, care delivery innovation, and sustainable resource utilization.[16]

LIMITATIONS

The retrospective nature of this audit and its focus on a single service limited its scope. Clinical results, patient demographics, and indirect expenses were not analyzed. Future research that combines outcome & cost-effectiveness data would provide additional insight.

IMPLICATIONS FOR PRACTICE AND POLICY

Regular audits of intravitreal treatment use can help influence procurement strategies, staff planning, & service redesign. Integrating audit findings into quality improvement activities could help sustain ophthalmic care.

CONCLUSION

Intravitreal injection therapy is a significant and growing component of ophthalmic service delivery. This audit reveals changed prescribing practices, increased dependence on newer medications, and significant financial implications. Continuous auditing & innovation are essential to deliver safe, effective, and long-lasting treatment.

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Original draft and formal analysis: Thomas Ahern (T.A.)
Review, editing and data curation: Adebusola Adenike Owokole (A.A.O.)
Supervision: Conall Hurley (C.H.)

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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Clinical Incidents Reporting Practice and Associated Factors Among Health Professionals in Debre Birhan Comprehensive Specialized Hospital, North Shoa, Amhara, Ethiopia.

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ABSTRACT

Background: Clinical incident reporting is crucial means of the continuous learning system in improving patient safety. The patient safety incident reporting system is low and has not fully adhered to standard guidelines, particularly in the study area. The study assessed clinical incident reporting practice and associated factors among health care professionals in the area.

Methods and materials: A facility-based cross-sectional study design was conducted, and study units were selected using the systematic random sampling technique. Statistical Package for Social Science version 21 was used for data analysis.

Result: Around 240 healthcare workers participated in the study with a 100% response rate. The prevalence of incident reporting practice was 16% (with 95% CI (12%, 21%)). Work experience (AOR=1.15, with 95% CI (1.06, 1.26)), orientation about clinical incidents (AOR=0.09, with 95% CI (0.01, 0.56)), incident monitoring and evaluation (AOR=0.09, with 95% CI (0.01, 0.69)), and uncertainties on organizational plan about the consequence of reported clinical incident (AOR=12.9, with 95% CI (2.88, 57.99)) were found to be significant predictors of incident reporting practice among health care professionals in the study area.

Conclusion: The study revealed low incident reporting practice in the area. Integrating structure with the process for a better patient safety incident outcome is vital.

Keywords: Patient Safety, Incident Reporting, Healthcare Professionals, Safety Culture, Quality Improvement

INTRODUCTION

A patient safety incident refers to any unintended or unexpected event that could have, or did, result in harm (such as injury or disability due to acquired infections, medication errors, or procedural mistakes) for one or more patients receiving healthcare, as well as for the staff involved. Prevention of patient safety incidents involves several key steps: identifying the incident, reporting it initially, conducting a risk assessment, engaging in discussions for learning, and submitting an incident report to enhance patient care [1,2].

However, many medical practices and risks associated with health care are emerging as major challenges for patient safety, which contribute significantly to the burden of harm due to unsafe care. The actions stemming from the investigation would result in a redesign of policies, care processes, products, and procedures. Additionally, there would be changes to clinical care practices and the working styles of practitioners. Agreed-upon processes would be established to aggregate data and conduct analyses that reveal systemic weaknesses and facilitate the development of solutions. [2-4]. Here the reporting of incidents and near misses has been seen as a crucial means of improving patient safety [5].

A survey done at the Royal College of General Practitioners on patient safety culture emphasizes patient safety and incident reporting as essential tools to improve patient safety. High levels of reporting will facilitate lesson-drawing, with information from the reports being disseminated both within and across service areas. Critical incident reporting systems (CIRS) can be an important tool for the identification of organizational safety needs. Incident reporting systems are believed to fulfil one or more of the following purposes: public accountability, responding to patients and families involved, providing a communication alert route, assessing the weight of risk within health care, and serving as a foundation for learning and improvement [5,6].
Most countries have experienced incidents and adverse events that show failures in their health care systems. Studies have highlighted the burden of accidents caused by adverse events within the health and social care settings, which significantly impacted patients, families, and the health care system [7]. Patients die unnecessarily because of injury, fall accidents, missed diagnoses or poor clinical management of their acute illnesses, pressure ulcers, faulty or misused equipment, or incompetent staff [3,8].

Incident reporting by health care providers who first discover, witness, or have familiarity with details of an incident or unsafe condition is fundamental to error prevention. Through incident reporting, various kinds of errors can be traced and discussed among health professionals, and preventive mechanisms can be designed. The present results indicate that there are still hindrances keeping errors from being reported. We advocate that besides clear reporting routines, there is a need for a complementary system that can identify and prevent near misses. A reporting system of incidents like near misses, such as a valid short and easy-to-use questionnaire or observational protocol, might be a solution to reduce the burden on personnel and to increase the possibility of error prevention. Reporting incidents can be improved by fostering a non-blaming safety culture [9,10].

Improving patient safety requires understanding the work conditions and processes that contribute to incidents. This understanding is optimally achieved through continuous clinical incident reporting and learning systems; however, these systems have generally not been implemented according to standards. Global studies show that clinical incident reporting rates remain low. While critical incident reporting systems exist in many countries, national-level reporting and learning systems have not yet been established, especially in low- and middle-income countries. Literature reviews indicate that although e-reporting systems were established to simplify reporting, they remain in an immature stage. Furthermore, while some studies have focused on types of incidents and others on identifying the causes behind them were focused on types of incidents and some of them focused on identifying the causes behind these incidents, significant gaps in system implementation persist [11-13].

In the USA, a study on primary health care showed that 69% of staff reported that they had never filed an incident report regarding venous blood sampling[11]. A study done in South Africa on incident reporting reviewed that the vast majority had never reported adverse drug reactions (ADR). Only 2.3% knew how many incidents were reported; from these, 6.1% were discussed by a committee, and internal feedback was given [14].

Few cross-sectional and mixed-type studies done in Ethiopia perceived that the percentage of clinical incident reporting practice of the health professionals was very low. A study done in Amhara region public hospitals, the proportion of reported incidents was 31.9% [15]. Another study conducted in GUSH found that the proportion of nurses who reported incidents was 25.4%. Similar studies in Dessie and Addis Ababa hospitals showed that the reported incidents were 12.4% and 30.4%, respectively [8,10,16,17]. There was a gap because earlier studies didn't involve the qualified clinical staff who are directly involved in reporting incidents, analyzing them, and providing feedback. Also, there were factors that needed to be considered but couldn't be concluded due to differences in facility setups.

As incidents or mistakes are not reported, it affects patient safety. Clinical incident disclosing allows the healthcare systems to adjusted themselves. Incidents reporting provides valuable insights for preventing mistakes by identifying ongoing issues

in the system that could put patients at risk for medical problems. If done right in healthcare settings, it can help spot issues that could be avoided, but a lot of these cases either go unreported or simply go unnoticed
As per the Ethiopian guidelines for hospital reform, each facility should have an incident officer responsible for gathering and analyzing incidents [18]. According to the 2022 annual report of Debre Birhan Hospital, there were just three clinical incidents reported. It's normal for clinical incidents to happen, not just in our hospital but also in more developed countries. So, doing this study can help highlight the real situation regarding incident reporting at the hospital and pinpoint factors that might influence it, either positively or negatively.

METHODS

Study area, Design, and period

The study was conducted in Debre Birhan Comprehensive Specialized Hospital which is located 130km from the capital city of Ethiopia. The hospital has 670 staff of which 140 non-clinical and 530 clinical staff. An institution-based cross-sectional study was conducted from April 1 to 15 /2023. With the protocol number IRB 051/2022, Asrat Woldeyes Health Science Campus, Debre Berhan University, granted ethical clearance.

Population

All Debre Birhan Comprehensive Specialized Hospital staffs were the source population for the study. Randomly selected clinical staffs (Nurses, Midwives, Pharmacists, Medical doctors, laboratory technicians, infection prevention staff, patient safety officers, public health emergency managers, and Anaesthesia) working in Debre Birhan comprehensive specialized hospital were the study populations.

Inclusion Criteria

All clinical staff in Debre Birhan comprehensive specialized hospital who are engaged in clinical practice participated in the study.

Exclusion criteria

Clinical staff on long-term training and maternity and annual leave are excluded.

Sample size estimation

The sample size was determined using the double population proportion formula by using Epi info version 7. Power 80%, and confidence interval 95% were assumed, by taking the variable fear of prestige among colleagues which was a significantly associated factor with incident reporting in a study conducted at public hospitals of Addis Ababa [16]. The final sample size was 240 health professionals.

Sampling procedure

Systematic random sampling was used. Since there is a homogenous staff regarding incident exposure and reporting, since we have human resource roster and to avoid bias. The participants were selected systematically from the human resource registration from each category. The first participant was selected using the lottery method and the rest participants were included at every Kth value until the given quota was satisfied. The clinical staffs were nurses, midwives, medical doctors, pharmacists, laboratory professionals, and others. Major departments where clinical staffs incorporated were inpatient, outpatient, laboratory and pharmacy, obstetric, and emergency departments. Other healthcare professionals included quality officers, infection prevention officers, porters, public health emergency managers, incident officers or patient safety officers, and cleaners. The total sample size is 240. The Kth value is 2.

Data Collection Methods

Data were collected by using a structured self-administered English version of the Google Forms questionnaire adapted from studies done at Gondar University and Dessie and Addis Ababa hospitals [8,16,17]. The tool was composed of three parts, which were sociodemographic characteristics of clinical staff, institutional factors, and perceived barriers of clinical staff to incident reporting. The completeness of each recording format was checked before collecting the data.
Questionnaires were reviewed and checked for completeness, accuracy, and consistency by the principal investigator every day during the data collection period. A reasonable amount of time to fill out the questionnaire was agreed upon between the research assistant and the respondent's Android phone and tablet. Two experienced BSc nurses (from another hospital) were collecting the data, and the researcher as well as the external supervisor supervised during the data collection period. The aim of the study was clearly explained to the study participants before they filled out the

questionnaire. The data collectors were trained for half a day on how to facilitate the data collection process and prevent errors.

Table 1. Study variables, DBCSH, Debre Birhan, Ethiopia 2023, (n=240).

Sociodemographic	Institutional	Perceived barriers	Independent variable
Age Sex Educational level Marital status Profession Years of service	Training Orientation Availability of guideline/policy reporting formats	Supportive environment (culture of shame and blame) Loss of prestige among colleagues Fear of legal or financial penalties Fear of administrative sanction Lack of incident analysis and feedback Believe on incedent reporting	clinical incident reporting practice

Operational Definition

1. Incident: Any deviation from usual medical care that either causes an injury to the patient or poses a risk of harm, including errors, preventable adverse events, and hazards
2. Incident reporting: is the process of recording worksite events, including near misses, injuries, and accidents. It can be measured by comparing the global and national research findings of clinical incidents that occurred
3. Sentinel event: an unexpected occurrence involving death or serious physical or psychological injury, or the risk thereof
4. Adverse event: an incident that results in preventable harm to a patient. a health care facility
5. Patient safety: a framework of organized activities that creates cultures, processes and procedures, behaviours, technologies, and environments in health care that consistently and sustainably
6. Near miss: an incident that did not reach the patient but narrowly avoided.

Data Quality Management

For quality assurance purpose, pre-test on 5% of the sample size was done one week before the actual data collection time at Debre Sina Primary Hospital. A total of 12(5%) participants were involved and of these 5(42%) were females. The Cronbach's Alpha value was 0.78 and most important amendments done on the tool. Variable, like whether incident encountered or not, categories and respondent options included. Educational levels subspecialities and must require also incorporated. The order of the questionnaires also rearranged and appropriate. Data collectors were trained and close field supervision by the researcher and a careful data validation at the point of entry and analysis done. The principal investigator checked completeness of each data collection tool, and its consistency of the entered data were crosschecked in a daily basis.

Data processing and Analysis

The Google form collected data were checked for completeness and exported to SPSS version 21 for cleaning and analysis. Bivariable logistic regressions used to evaluate the effects of each independent variable on the dependent variable. From the analysis variables with P-value≤ 0.05 used as statistically significance and the degree of association described using adjusted odds ratio (AOR) with 95% confidence interval (CI). All variable with P-value ≤ 0.25 in bivariable regression entered a multivariable regression. The sociodemographic variables and prevalence of incident report was presented in terms of frequency, mean and percentage using tables. Multicollinearity was checked among selected independent variable using variance inflation factor which is less than five. Additionally, the necessary assumption of logistic regression was also checked using Hosmer and Lemeshow goodness-of-fit-test (Pseudo-R^2 =0.000).

Ethical Considerations

Ethical clearance obtained from the Ethical Committee of Institute review board (IRB) of AWHSC, school of public health, department of public health, Debre Birhan University before conducting the study. Letter of cooperation was written to DBCSH for permission and support and permission letter obtained from the hospitals. Informed written consent was taken from each participant, and confidentiality was assured. Participation of the respondents was purely voluntary. Respondents were free to pull out of the study, for whatever reason(s) and their decisions to do so were highly respected.

RESULT

Sociodemographic characteristics of the respondents

A total of 240 study participants participated in the study with a 100% response rate. About 151(63%) of the respondents were male. The mean age of the participants was 34 (SD=6.04) years, and their mean work experience was 10 (SD=6.12) years. Of all the participants, 41 (17%) responded that clinical incidents are being reported, while 199 (83%) thought there was no clinical incident reporting procedure at the facility level. All the respondents know and believe in clinical risk and incidents. Only 39 (16%) respondents out of a total of 240 had a clinical incident reporting practice, with a 95% confidence interval of 12–21(Table 2).

Table 2: Sociodemographic characteristics of the respondents, DBCSH, Debre Birhan, Ethiopia 2023, (n=240).

Variable categories		Frequency	Percent (%)
Sex	Female	89	37.1
	Male	151	62.9
Age	21-30	71	71 30
	31-40	136	36 57
	41-55	30	30 13
	56-70	3	3 1
Total work experience	<5	23	9.6
	5 to 10	16	6.7
	11 to 15	25	10.4
	>15	176	73.3
Work experience in this facility	5	111	46
	6 to 10	100	42
	11 to 15	17	7
	>15	12	5
Marital status	Divorced	7	2.9
	Married	165	68.8
	Single	68	28.3
Educational level	Diploma	22	9.2
	Degree level	176	73.3
	Master level	30	12.5
	Specialist	12	5.0
Profession	Anesthetist	9	3.8
	Biomedical	4	1.7
	EMT	5	2.1
	Environmental health	6	2.5
	Health officer	6	2.5
	Laboratory	27	11.3
	Medical Doctor	50	20.8
	Midwife	20	8.3
	Nurse	90	37.5
	Pharmacist	21	8.8
	Physiotherapy	2	0.8

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Institutional factors

One hundred sixty-six respondents (66%) indicated that there was no clinical incident guideline in the facility, while 8 (34%) reported about the existence. Twenty-two respondents (9%) reported the existence of a continuous learning system in the study area. Six respondents noted that there was administrative support for facilitating incident reporting. Among all participants, 50 (21%) indicated that a reporting format is available in their service area. From the total of 240 respondents, only 18 (8%) reported receiving orientation on incident reporting. In terms of workload, 94 (39%) expressed concerns about the high demands in their clinical practice area. Additionally, only 17 (7%) indicated that monitoring and evaluation for clinical incidents were in place(Table 3).

Table 3: Summary of institutional factors, DBCSH, Debre Birhan, Ethiopia 2023, (n=240).

Variables categories		Frequency	Percent (%)
Believe on incident reporting practice	Yes No	41 199	17 83
Incident guideline	Yes No	8 160	34 66
Reporting format	Yes No	50 190	21 79
Incident monitoring and evaluation	No Yes	223 17	93 7
Incident analysis	No Yes	235 5	98.6 2
Orientation	No Yes	222 18	92 8
Training	No Yes	232 8	97 3
Continuous learning	No Yes	218 22	91 9
Workload	No Yes	144 94	61 39
Administrative support	No Yes	234 6	97 3

Perceived barriers

A possible perceived barrier for low incident reporting practice may be due to the possibility that clinical practitioners may not encounter clinical incidents. However, in this study, 207 respondents (86%) acknowledged that the low reporting practice is not solely due to a lack of clinical incidents encountered. But in this study 207(86%) respondents did not deny that low reporting practice is not because they did not encounter clinical incidents. But in this study 207 (86%) respondents did not deny that low reporting practice is not since they did not encounter clinical incidents. Only 33 (14%) of them responded that they did not encounter clinical incidents in their life. The reporting practice of the clinical practitioner can be affected due to feelings of personal failure and loss of prestige with their staff whereas 206(86%), 175(73%) and 34(14%), 64(27%) disagree with this idea respectively. Uncertainties about the organizational plan and fear of legal punishment also affect the incident reporting practice; 192 (80%), 197 (82%), 48 (20%), and 43 (18%) of the participants were against this, respectively. Workload and low-priority stress also affect clinical incident reporting [182 (76%)]. Lack of feedback and departmental cooperation, 193 (80%) and 184 (77%), also affect incident reporting practice, respectively. Two hundred six (86%) of the participants replied that the type of incident can affect the reporting practice. (Table 4).

Table 4: Summary of perceived barriers, DBCSH, Debre Birhan, Ethiopia 2023, (n=240).

Variable categories		Frequency	Percent (%)
Do you know the incidents and risks	Yes No	235 5	98 2
No Incident encounter	No Yes	207 33	86 14
Feelings of personal failure	No Yes	34 206	14 86
Uncertainties on organizational plan	Yes No	192 48	80 20
Workload and low priority Stress	Yes No	182 58	76 24
Need for support	Yes No	197 43	82 18

Fear of legal punishment	Yes No	197 43	82 18
Loss of prestige with collegues	Yes No	176 64	73 27
Lack of departmental cooperation	Yes No	184 56	77 23
Lack of feedback	Yes No	193 47	80 20
Type of incident affects reporting	Yes No	206 34	86 14

Factors Associated with incident reporting practice

The variables associated with the bivariable analysis included work experience, uncertainties regarding the organization's plan, orientation about clinical incidents, fear of legal repercussions, incident monitoring and evaluation, the type of incident impacting reporting practices, and a lack of interdepartmental cooperation. These variables were further analyzed using multiple logistic regression.

For health professionals, each additional year of work experience correlates with 1.15 times decrease in the practice of reporting clinical incidents (AOR = 1.15, with a 95% confidence interval of (1.06 to 1.26)). As health professionals are oriented about clinical incidents, their incident reporting practice is enhanced by 91% when compared to those without orientation (AOR = 0.09, with 95% CI (0.01, 0.56)). Incident monitoring and evaluation could also increase incident report practice by 91% with AOR=0.09 and 95% CI (0.01, 0.69). Uncertainties about the organizational plan also negatively affected clinical incident reporting practice by 13 times (AOR=12.9, with 95% CI (2.88, 57.99)) (Table 5).

Table 5: Multivariable analysis of factors associated with incident reporting practice,(n=240).

Variable category		IRP		COR(95%CI)	AOR (95% C.I.)	Sig.
		No	Yes			
Incident monitoring and evaluation						
	Yes	7	10		1	
	No	194	29	**0.11 (0.04, 0.30)**	**0.09 (0.01, 0.69)**	0.021
Type of incident affecting reporting practice						
	No	20	14		1	
	Yes	181	25	5.06 (2.20, 11.28)	2.51 (0.63, 9.96)	0.190
Orientation on clinical incidents						
	Yes	7	11		1	
	No	194	28	**0.07 (0.02, 0.23)**	**0.09 (0.01, 0.56)**	0.011
Fear of legal punishment						
	No	15	28		1	
	Yes	186	11	**44.8 (17.6, 113.5)**	2.72 (0.76 , 9.75)	0.124
Uncertainties on organizational plan						
	No	19	29		**1**	
	Yes	182	10	**27.70 (11.75, 65.6)**	**12.90 (2.88, 57.99)**	0.001
Lack of interdepartmental cooperation						
	No	26	30		1	
	Yes	175	9	22.43(9.57, 52.5)	3.80 (0.95, 15.00)	0.057
Work experience				**1.16 (1.10, 1.23)**	**1.15 (1.06, 1.26)**	0.001

AOR: adjusted odd ration; COR: crude odd ration.

DISCUSSION

Clinical incident reporting, along with analysis and feedback, as well as the implementation of a continuous learning system within the facility, contributes to the prevention of error recurrence and ultimately enhances patient safety[19]. The incident reporting practice in the study area was 16%, which aligns with a study conducted at Dessie Hospital (12.4%). Additionally, other studies in Australia and Ethiopia indicate that incident reporting and analysis behaviors among healthcare professionals remain low [3,8,10,9]. Although incident reporting and analysis began over a decade ago, a study conducted in Indonesia revealed that the patient safety incident reporting system has not fully complied with the WHO guidelines [20]. The reporting rate is currently low compared to prospective studies, indicating an issue of underreporting [21]. A study done in Rwanda suggested that only 35% of nurses have incident reporting practice [22]. Health care providers reported 30.4% of events in Addis Ababa hospitals, 31.9% in Northwest Amhara hospitals, and 25.4% in Gondar Hospital, according to a study [8,10,16,17].

An Australian study comparing two hospitals discovered variations in the risks they faced and the organizational structures they established. These variations may have resulted from the two institutions' differing perspectives on reporting incidents [10,16,23,24]. In this case, MOH has set up a procedure or system whereby an incident officer is assigned to each hospital to receive and investigate all incident reports, evaluate them, and provide input to the clinical area. [18].

Generally, healthcare professionals tend to become more sensitive to risks, accidents, and dangers, leading to improve incident tracking and reporting practices. However, in this study, in contrary to this general trend, the practice of incident reporting practice decreases as work experience increases. This may be due to work experience leading to desensitization regarding incidents and a subsequent disregard for established policies and procedures. These individuals become more knowledgeable about patient safety and infection prevention and control, focusing on specific incidents rather than reporting all occurrences.

Orientation about clinical incidents for health care professionals is believed to increase incident reporting practice. Similar studies done in Europe, Indonesia, and Africa assured us that, as healthcare professionals are oriented about clinical incidents, there would be an increment in incident reporting practice [19,25-29]. Availability of clinical incident guidelines and reporting formats also plays a significant role in the clinical incident reporting practice of health care professionals. The clinical incident reporting practice of trained staff was higher than those who had no training. Research also showed that teaching professionals how to report incidents and fostering strong, positive personal sentiments to enhance safety continue to be the main elements that facilitate clinical incident reporting. The reports also don't follow accepted guidelines. Healthcare workers who had received medical incident reporting training were more cooperative than those who had not[28, 30]. Higher officials should be aware of the reporting system at all levels, and CIRP is impacted by supportive environments and administrative assistance in all areas [10,16,23].

The study confirms that low incident reporting practice is also strongly linked to clinical incident reporting barriers such as ambiguity about the organizational plan. This is typically caused by a lack of clarity in the organizational strategy on the destination of reported incidents and the purpose of reporting. This finding is supported by the study done in Addis Ababa, Dessie, and other Amhara hospitals. It identified barriers like hospital management support, non-punitive response to errors, or lack of feedback. Other identified barriers in the above areas are communication openness, supervisors' actions, safety promotion, feedback on reported errors, fear of administrative and legal sanctions or penalties, non-supportive environment, and feeling that reporting to colleagues was easier [10,16,23]. A study conducted in Indonesia that highlighted confusion because of the system's lack of feedback and confidentiality mechanisms supported this study. The clinical incident reporting procedure was also impacted by the lack of a policy that protects the healthcare provider from any punitive actions taken in response to reported clinical occurrences. On the other hand, a study done in Uganda revealed that reporting behaviour was unaffected by fear of the consequences. Studies showed that incident monitoring was efficacious as a quality tool in identifying incident contributing factors. Incident monitoring allowed for greater systems evaluation. Further evaluation of this quality tool within different disaster settings is required. It was concluded that incident monitoring may be a suitable technique for improving patient safety in intensive care [28,30].

STRENGTH OF THE STUDY

The study was done by the clinicians who had direct day-to-day life experience with the clinical incidents. It was done in one health facility that could avoid variation of clinical incident occurrence due to variation in structure, process and outcome as variables due to these differences were controlled.

LIMITATIONS

This study finding is lower than in most study findings in Ethiopia except Dessie Hospital, this might be due to the difference in infrastructure setup, variables selection, and health facility clinical and administrative process differences.

CONCLUSION AND RECOMMENDATIONS

Even though patient safety incident reporting mainly helps as the foundation for learning and improvement, this study reveals that clinical incident reporting practice is low in the study area. Finally, this study signified that monitoring and evaluation, work experience, and uncertainties in organizational plans about the consequence of reported clinical incidents are important predictors for regular incident reporting. The health facility better establishes a clear organizational clinical incident reporting plan and creates awareness about the purpose of incident collection and analysis. Incidents will be collected centrally, analyzed, and entered a feedback loop to create a continuous learning system in the facility. It is advisable to initiate a sequential observational confirmatory qualitative study in the area to address the safety culture of health care professionals.

ABBREVIATIONS

ARHB: Amhara Regional Health Bureau, AWHSC: Asrat Woldeyes Health Science Campus, DBCSH: Debre Birhan Comprehensive Specialized Hospital, CIRS: Critical Incident Reporting Systems, CIRP: Clinical incident reporting practice, DCSH: Dessie Comprehensive Specialized Hospital, EMT: Emergency Medical Technician, FMOH: Federal Ministry of Health, PSI: Patient safety incident, PSIR: Patient safety incident reporting, GCSH: Gondar University Comprehensive Specialized Hospital, IPC: Infection Prevention and Control, PHEM: Public Health Emergency Management.

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AUTHOR CONTRIBUTIONS (CRediT)

All authors participated in proposal development, data collection, data entry and analysis, results write-up and interpretation, and manuscript preparation. All authors read and approved the final manuscript.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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AVAILABILITY OF DATA AND MATERIALS

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

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

With the protocol number IRB 051/2022, Asrat Woldeyes Health Science Campus, Debre Berhan University, granted ethical clearance. A written informed consent form outlining the study's goals and participants' rights was given to every study participant. The questionnaires were securely handled after completion, and all access to the results was strictly controlled. Participants were all chosen at random without any bias.

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Waiting Times for Cataract Surgery in a Dedicated Cataract Clinic: A Retrospective Audit.

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ABSTRACT

Background: Cataract surgery is a popular & cost-effective solution that helps to prevent needless vision impairment & maintain functional independence. As a result, timely access to cataract surgery is an important indication of surgical system performance & healthcare fairness. Despite the introduction of Dedicated Cataract Clinics (DCCs) to improve efficiency & throughput, elective ophthalmic services continue to face rising capacity constraints.

Aim: To assess waiting times for cataract surgery in a Dedicated Cataract Clinic & analyze improvements in access over two years.

Methods: A retrospective clinical audit of cataract surgery waiting list data was performed for patients who had surgery in March-April 2024 & March-April 2025. Waiting times for all eyes, first-eye surgeries, & second-eye surgeries were investigated using descriptive data & non-parametric comparisons.

Results: A total of 233 cataract surgeries were examined (114 in 2024, 119 in 2025). The median waiting time for all eyes increased dramatically, from 113.5 days in 2024 to 194.0 days in 2025 ($p = 0.0002$). The wait time for first-eye surgery rose from 109.0 to 171.0 days ($p = 0.0175$). The biggest significant increase was seen in second-eye procedures, with median waiting times rising from 134.5 to 322.0 days ($p = 0.0008$).

Conclusion: Waiting times for cataract surgery rose significantly over a 12-month period, showing rising service pressure & insufficient capacity to fulfil demand, even in a dedicated service paradigm. Continuous auditing, capacity optimization, & targeted system-level interventions are necessary to restore timely & equitable access to cataract surgery.

Keywords: *Cataract surgery; audit; surgical access; ophthalmology services; waiting times.*

INTRODUCTION

Cataract is the biggest cause of reversible blindness worldwide, & it continues to be a substantial contributor to visual impairment, particularly in older adults[1]. As populations age & life expectancy rises, the prevalence of cataracts rises, resulting in increased demand for surgical intervention & ongoing strain on publicly supported health systems. Cataract surgery is largely regarded as one of the most effective & cost-effective surgical procedures available, providing significant gains in visual acuity, functional independence, & overall quality of life[2,3]. In addition to vision restoration, prompt cataract surgery has broader societal & health-system benefits, such as lower risk of accident, more mobility, decreased reliance on social care, & lower long-term healthcare utilization.

Given these advantages, timely access to cataract surgery is viewed as an important indicator of surgical effectiveness, equity, & responsiveness. Prolonged waiting periods have been consistently linked to vision impairment, an increased risk of falls, decreased involvement in daily activities, & negative mental health outcomes such as anxiety & depression[4]. These

repercussions are more obvious in older persons, for whom visual impairment can jeopardize independence, safety, & quality of life, putting additional strain on health & social care systems.

Second-eye cataract surgery delays need to be considered. Data indicates that long-term binocular vision impairment following unilateral surgery has a detrimental effect on depth perception, balance, and mobility5, even though first-eye surgery is often prioritized in resource-constrained settings. Long-term postponements of second-eye surgery have been associated with a higher risk of harmful falls and inadequate functional recovery, highlighting the importance of equitable access to both eyes rather than viewing second-eye surgeries as optional or low priority.

Dedicated Cataract Clinics (DCCs) are a service delivery innovation that many health systems have implemented in response to growing demand and backlogs in elective surgery. By using streamlined referral channels, standardized pre-operative evaluations, protocol-driven care, and high-volume surgical lists, these clinics aim to increase efficiency and throughput. Elective ophthalmology services still face severe capacity issues, even though DCCs have been helpful in maximizing theatre utilization and removing needless variation in care delivery. Rising referral rates, personnel difficulties, limited operating theatre availability, & system-wide elective care backlogs have all posed challenges to the models' long-term viability[6].

Within this context, routine audit of cataract surgery waiting times is essential to monitor service performance, identify emerging access challenges, & inform targeted quality improvement initiatives. Clinical audit provides a pragmatic mechanism for evaluating real-world service delivery, benchmarking performance against access standards, & guiding data-driven system redesign. To produce actionable service-level evidence to support prompt, equitable, and sustainable access to care, this audit assesses changes in waiting times for cataract surgery within a Dedicated Cataract Clinic over the course of two consecutive years.

AIM & OBJECTIVES

Aim

To assess waiting times for cataract surgery in a Dedicated Cataract Clinic & analyze improvements in access over two years.

Objectives

1. To quantify cataract surgery waiting times in March-April 2024 & March-April 2025.
2. To compare wait times for all eyes, first- & second-eye procedures.
3. To determine whether waiting times have drastically increased over time.
4. To identify the consequences for service capacity & quality improvement.

METHODS

Study Design

This study was carried out as a retrospective clinical audit to assess service performance & promote quality improvement, rather than to test hypotheses or generate generalizable research findings.

Setting

The audit was carried out in a Dedicated Cataract Clinic at a publicly financed regional hospital. The hospital was anonymized in accordance with best practices for audit distribution & service evaluation.

Data Source & Population

We evaluated surgical waiting list data for individuals who received cataract surgery in March-April 2024 & March-April 2025. Both first- & second-eye cataract surgeries were included to account for differences in prioritization & access.

Outcome Measure

Waiting time was defined as the number of days between being placed on the surgical waiting list & having surgery.

Data Analysis

The data were analyzed using GraphPad Prism version 10. Descriptive statistics were created; normality tests were run, & non-parametric statistical tests were used due to skewed waiting-time distributions. Median differences & Hodges-Lehmann estimators were computed. Statistical significance was determined at $p < 0.05$.

Ethical Considerations

Ethical approval was not requested because this study was a clinical audit of routinely gathered service data undertaken for quality improvement. There was no usage of patient-identifiable information, & conventional clinical treatment was followed exactly.

Analytical Framework

An analytical framework based on service evaluation & quality improvement concepts was used to guide data analysis & interpretation. Waiting time was used as the major performance criterion to assess access to elective surgical care & system capacity. The analyses were designed to look at variations in waiting times over two consecutive audit periods, as well as to distinguish between all cataract surgeries, first-eye procedures, & second-eye procedures, considering differences in clinical prioritisation & functional impact. Due to the non-normal distribution of waiting time data, a non-parametric analytical method was used to ensure robust comparison of medians & distributional shifts over time. The findings were interpreted in respect to published access criteria & service-level standards for elective ophthalmic care[6,7,8], allowing for an assessment of system performance & identification of areas that require focused quality improvement. This paradigm promotes a pragmatic, systems-based assessment of access rather than causal inference, which is congruent with the goals of a clinical audit.

RESULTS

A total of 233 cataract surgeries were studied, 114 in 2024 & 119 in 2025.

Surgical Activity

Table 1. Cataract surgical activity by year & eye status.

Y	Total proced	First-eye surge	Second-eye surge
2024	114	90	24
2025	119	91	28

Table 1 illustrates that overall surgical throughput remained consistent during both audit periods. Increased demand and/or system capacity limits rather than lower productivity are indicated by the observed increase in waiting times, which happened despite equivalent operating volume.

Wait Times for All Eyes

The median wait time for all eyes increased from 113.5 days in 2024 to 194.0 days in 2025 (p=0.0002).

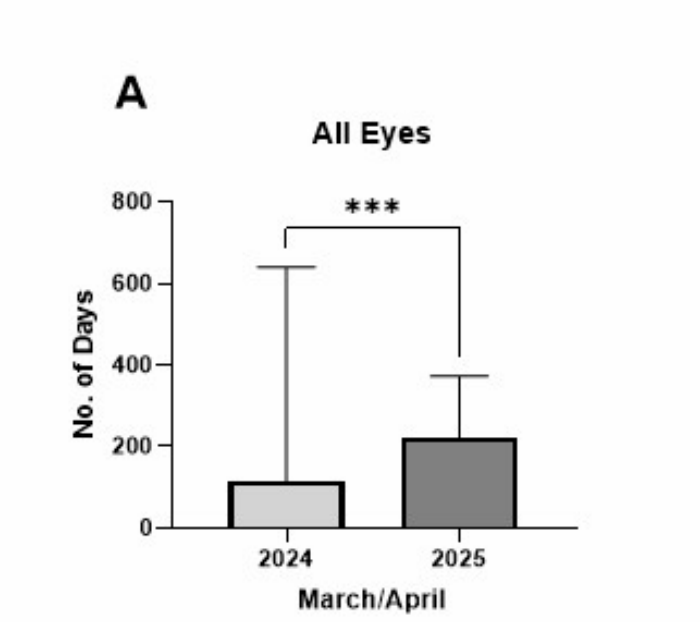

Figure 1A: Median waiting times for all cataract surgeries (2024 vs 2025)

Figure 1A shows a noticeable rightward shift in waiting time distribution in 2025, indicating a statistically significant delay in operation.

First Eye Surgery Waiting Times

The median wait time for first-eye procedures has grown from 109.0 days in 2024 to 171.0 days in 2025 (p = 0.0175).

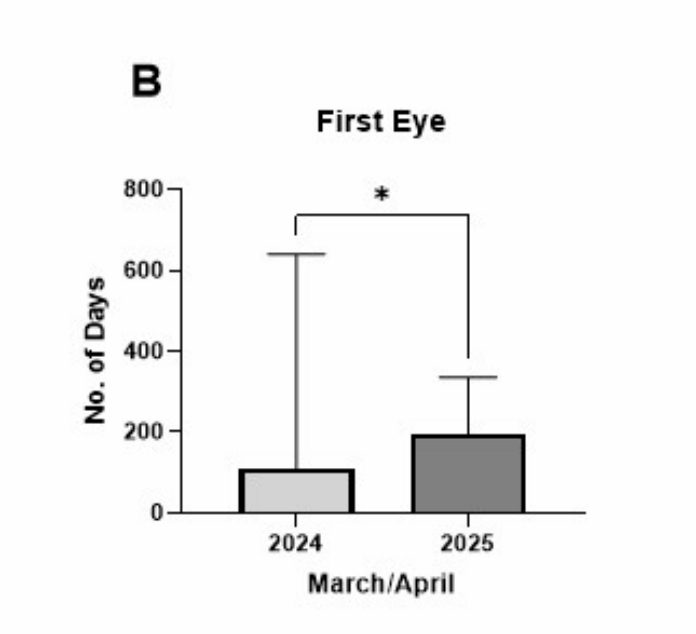

Figure 1B. Median waiting times for first-eye cataract surgeries

Figure 1B shows a considerable drop in access to first cataract surgery, with possible consequences for long-term vision impairment & functional decline.

Second-Eye Surgery Waiting Times

Second-eye procedures saw the highest rise in wait time, from 134.5 days in 2024 to 322.0 days in 2025 (p=0.0008).

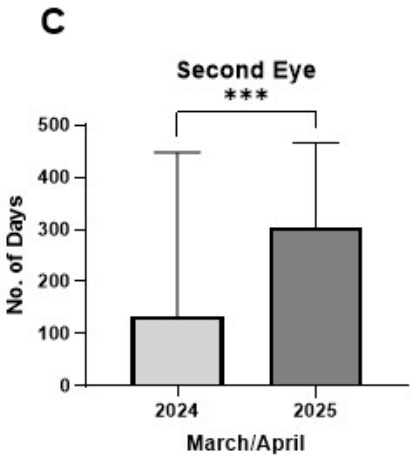

Figure 1C. Median waiting times for second-eye cataract surgeries

Figure 1C shows a significant increase in delays for second-eye treatments, indicating reprioritization due to capacity constraints & raising concerns about binocular vision, fall risk, & patient safety.

Service-Level Access Standards

Category	Benchmark sourc	Recommended standa	Median 2025
First-eye surgery	NHS Referral-to-Treatme	≤18 weeks (126 days)	171 days

Second-eye surgery	Royal College of Ophthalmologists	≤6 months where indicated	322 days
All cataract surgery	OECD benchmarks	≤4 months	194 days

Table 2. Observed waiting times compared with published access benchmarks

Table 2 showed that waiting times in 2025 surpassed specified access targets in all categories, with the most dramatic breach reported for second-eye operation.

DISCUSSION

This audit shows a dramatic decline in availability to cataract surgery over a 12-month period at a Dedicated Cataract Clinic, with waiting times increasing across all surgical categories. Importantly, these delays occurred despite steady surgical throughput across the two audit periods, implying that the observed rise in waiting times was caused by rising demand & limited system capacity, rather than decreased productivity. This research demonstrates a growing disparity between service provision & population need, even within a care paradigm designed to maximise efficiency.
Waiting periods for second-eye cataract surgery have increased significantly. In resource-constrained systems, first-eye surgery is frequently prioritized to maximize population-level benefit by restoring functional vision to as many patients as feasible.

However, the results of this audit indicate that such prioritizing processes may have unforeseen repercussions. Prolonged delays in second-eye surgery are linked to compromised binocular vision, decreased depth perception, an increased risk of falls, & insufficient functional recovery after first-eye surgery[4,5]. As a result, long wait times for second-eye surgeries pose serious issues about patient safety, equity of access, & quality of care.

From an equality standpoint, lengthy delays in second-eye surgery may disproportionately affect older persons & those with pre-existing mobility or balance problems, aggravating health disparities. The significant difference in waiting times seen between first & second-eye procedures shows that second-eye surgery may be progressively deprioritised due to capacity constraints, despite its well-documented importance to functional independence & quality of life. These findings highlight the need of including both eyes in access planning frameworks, rather than treating second-eye surgery as elective or deferrable.

The findings of this audit are consistent with national & international research demonstrating that ophthalmology has been one of the most impacted specialties in elective surgery backlog. According to reports from professional bodies & international organisations, waiting lists for cataract surgery have been steadily increasing due to rising demand, personnel shortages, limited operating theatre capacity, & system-wide elective care demands following the COVID-19 pandemic[6,7]. The congruence of local audit findings with these broader trends implies that the reported difficulties are not isolated but represent systemic pressures affecting elective ophthalmology services more broadly.

When combined, these results highlight the difficulties of meeting growing demand solely through service reconfiguration models, like Dedicated Cataract Clinics, without also investing in labor capacity, theater availability, and system-wide planning. DCCs are vulnerable to outside demands that surpass available resources, even though they can improve care efficiency and consistency. Therefore, regular waiting time audits are essential for identifying early signs of deteriorating access and motivating targeted quality improvement projects.In this context, the current audit's results highlight the need for a balanced approach to cataract service planning that safeguards access to both first & second-eye surgery, includes transparent prioritisation criteria, & involves continuous performance monitoring. Without such controls, lengthy waiting periods risk compromising the therapeutic & societal benefits of cataract surgery & may contribute to preventable injury.

QUALITY IMPROVEMENT FRAMEWORK

We propose a four-domain Cataract Access Improvement Framework:
1. Optimize capacity with protected high-volume lists, prolonged sessions, & workforce optimisation.
2. Improved efficiency through streamlined pre-operative assessments & eliminated duplication.
3. Ensuring transparency & equity in prioritizing & protecting capacity for second-eye surgeries.
4. Performance monitoring includes periodical audit cycles & waiting-time dashboards.
This strategy outlines a systematic way to restoring timely access while maintaining service quality.

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IMPLICATIONS FOR PRACTICE & POLICY

This audit's results have significant consequences for clinical practice & health system policy. The observed increase in cataract surgery waiting times, despite consistent surgical throughput, suggests that present service capacity is insufficient to meet demand, even under a Dedicated Cataract Clinic paradigm. This emphasizes the importance of proactive capacity planning, which goes beyond service reconfiguration & includes workforce expansion, protected theatre time, & flexible scheduling to cope with increased referral volumes.

From a clinical practice standpoint, the unequal delays found for second-eye cataract surgery underline the importance of transparent & equitable prioritization systems. While first-eye surgery frequently provides the greatest immediate functional benefit, delaying second-eye surgeries increases the risk of falling, impairs binocular vision, & lowers quality of life[4,5]. Services should therefore guarantee that second-eye surgery is expressly considered into access planning & not routinely deprioritised due to capacity constraints.

On a policy level, these findings justify the routine use of waiting time parameters as key performance indicators for elective ophthalmic services. Regular audit cycles & continual tracking dashboards can aid in the early detection of access deterioration & prompt remediation. Furthermore, aligning local service delivery with published access criteria can help to improve accountability & guide resource allocation decisions at the organizational & system levels[6, 7].

Lastly, the findings highlight the need of including continual audits into elective surgery paths. Clinical audits provide actionable, locally relevant evidence that can help lead service improvement, inform data-driven legislative choices, & contribute to more equitable & long-term access to surgery for cataracts.

LIMITATIONS

This audit was confined to a single service & two specific time periods. Patient-reported outcomes, referral patterns, & workforce indicators were not investigated. Nonetheless, the findings provide strong service-level data to help guide quality enhancements.

CONCLUSION

Over a 12-month period, wait times for cataract surgery climbed dramatically, with second-eye treatments seeing the most pronounced delays. These findings show increased service demand & underscore the importance of targeted capacity building, pathway optimization, & continual auditing to ensure timely & impartial access to cataract surgery.

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The authors also recognize the value of clinical audit as a tool for improving surgical system performance & ensuring fair access to care.

AUTHOR CONTRIBUTIONS (CRediT)

Original draft & formal analysis: Emma Hennessy (E.H.) & Emily Greenan (E.G.)
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Supervision: Conall Hurley (C.H.)

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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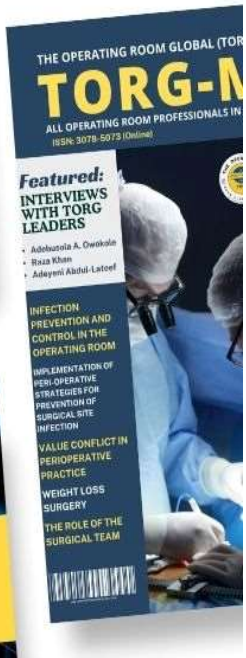

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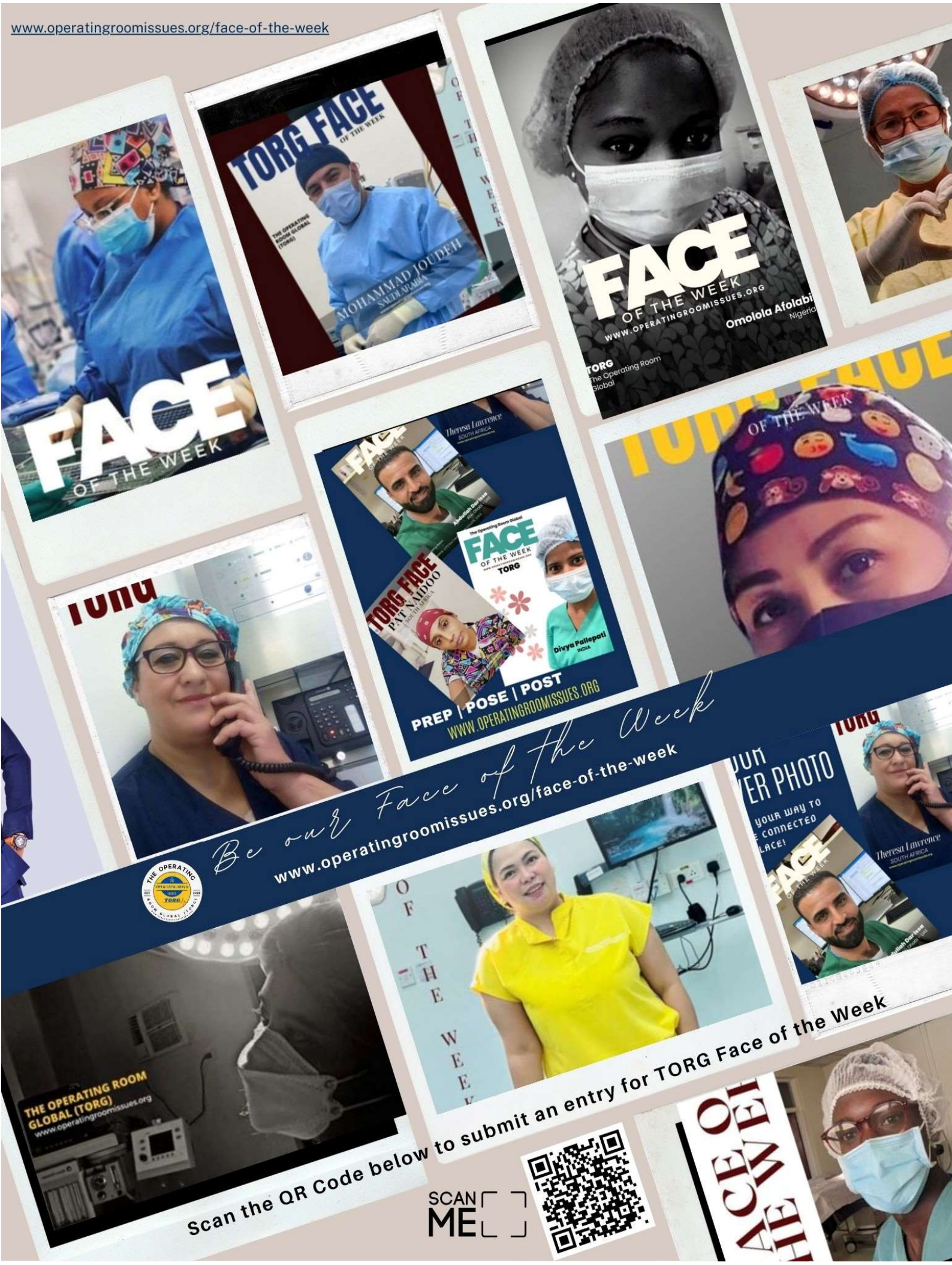

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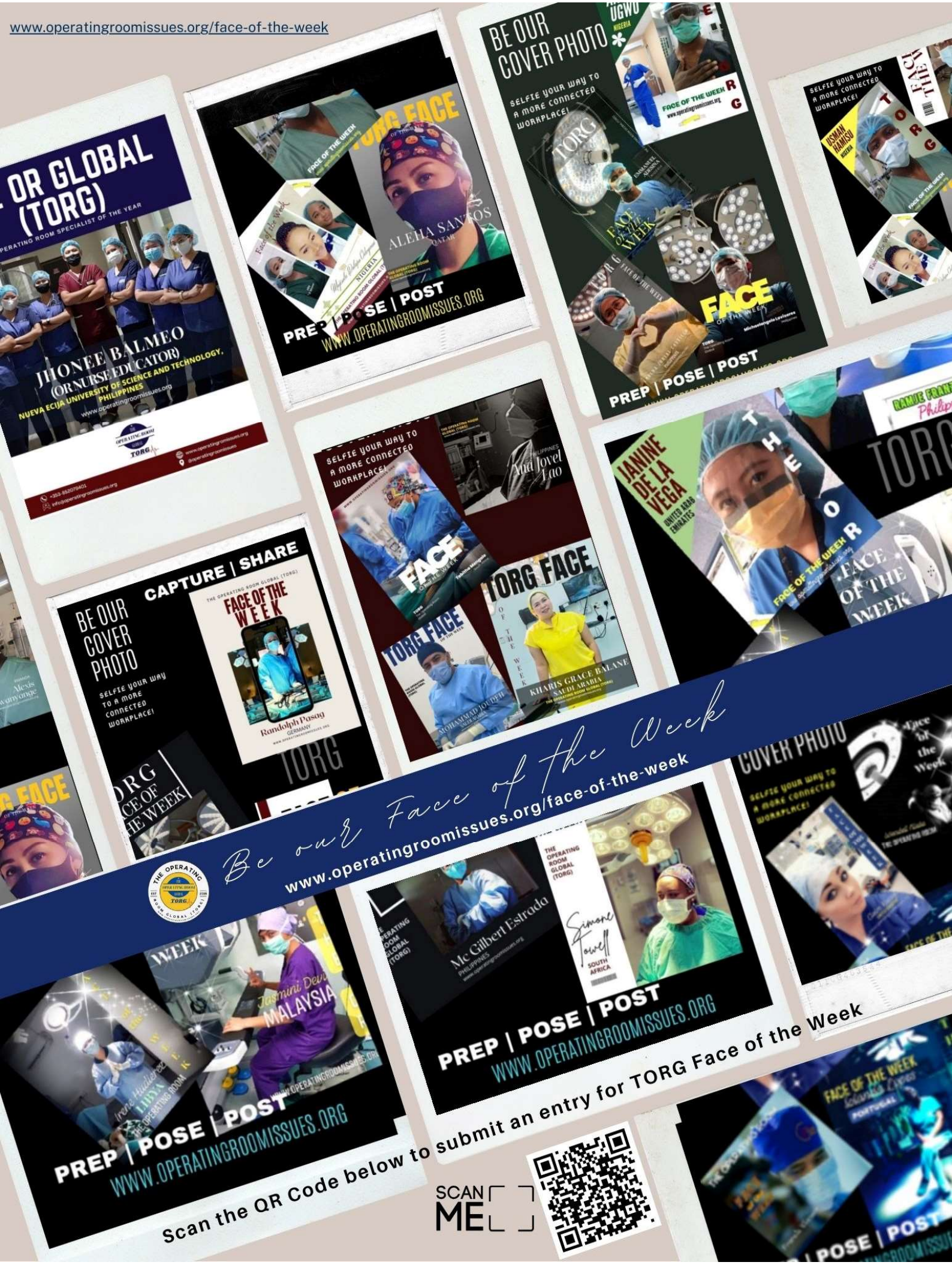

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