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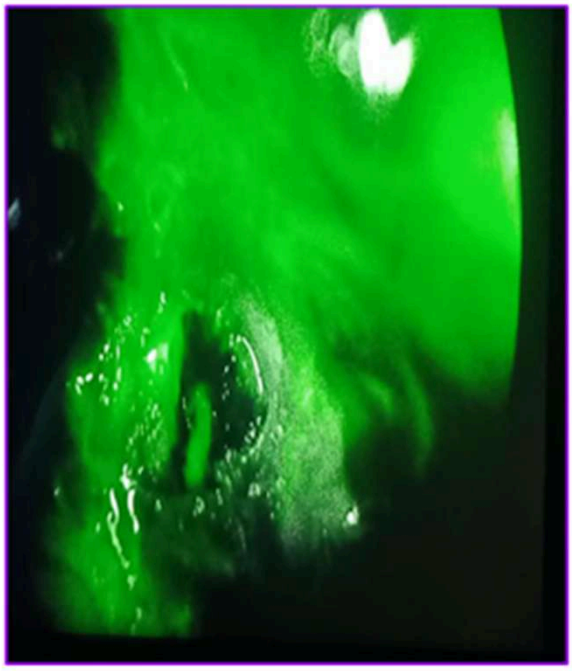
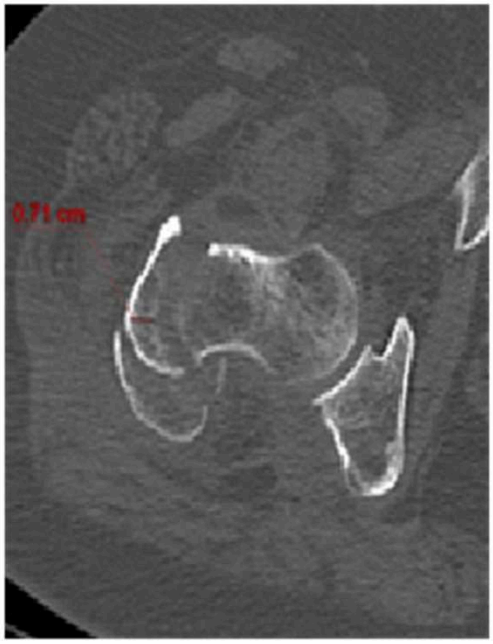
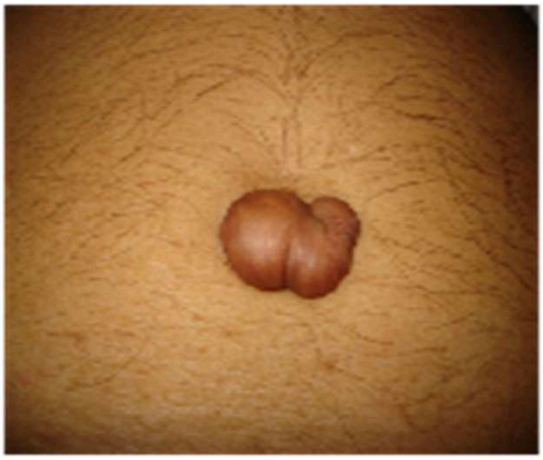
ICA near the lateral wall of Sella



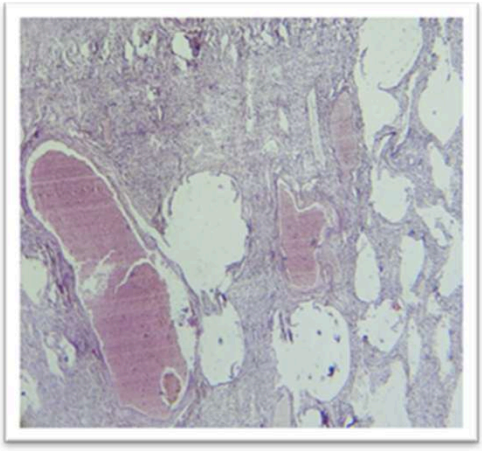
Axial - CT Scan image



Keloid over the umbilical port



Histopathology lung



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EDITORIAL

Need to Make Health Economics a Core Component of Postgraduate Medical Education (PGME)

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Health economics is the study of resource allocation in healthcare. There is a need to make it a core component of postgraduate medical education (PGME) to ensure sustainable and effective healthcare delivery

Modern healthcare systems face increasing challenges: including rising costs, limited resources, and growing demand for high-quality care. While postgraduate medical education (PGME) has traditionally emphasized clinical excellence, there is a pressing need to equip future physicians with the knowledge to navigate these economic challenges. **Integrating health economics into postgraduate medical education aims to equip future physicians with the knowledge and skills to make informed decisions about healthcare resource allocation, cost-effectiveness, and policy implications.**

- **Economic Decision-Making in Clinical Practice**

Health professionals frequently face decisions where costs and outcomes must be balanced—e.g., choosing between treatment modalities or designing care pathways. Familiarity with **cost-effectiveness**, **opportunity cost**, and **value-based care** enables them to make informed decisions that optimize both patient outcomes and resource utilization.

- **Sustainability of Health Systems**

In low- and middle-income countries, limited resources demand maximum efficiency. Health economics knowledge allows doctors to contribute to **rational resource allocation**, design **cost-conscious treatment plans**, and engage with **policy frameworks** that influence healthcare funding and delivery.

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- **Enhanced Policy Engagement**

Physicians trained in health economics can serve as informed contributors to policy debates, hospital administration, and public health planning, ensuring that clinical insights inform financial decisions and vice versa.

Postgraduate physicians are increasingly working in resource-constrained, complex health systems. Equipping them with health economics skills enables them to interpret system constraints and prioritize care effectively. This deeper system insight, in turn, improves their resource utilization and patient care. One study observes that "physicians and nurses with knowledge of health economics can enhance healthcare effectiveness through improved resource allocation and cost-effectiveness," as reported on ResearchGate. Health economics training also empowers doctors to contribute to policy and planning: lack of such training "hampers doctors' ability to contribute more effectively to healthcare policy and planning" pmc.ncbi.nlm.nih.gov, whereas applying economic methods helps clinicians translate clinical priorities into policy proposals (pmc.ncbi.nlm.nih.gov, researchgate.net).

Several advantages of teaching health economics to postgraduates are

- **Improved system understanding**

Physicians trained in economics better grasp how healthcare funding and insurance models work. For example, internal medicine residents in a health systems course (covering insurance, policy, and economics) reported that learning about the NHS and NICE decision-making helped them explain treatment availability to patients and appreciate the system's limitations. This means clinicians can manage patient expectations and navigate care pathways more effectively.

- **Enhanced resource use and patient care**

Economic reasoning guides clinicians toward more cost-effective interventions. By assessing costs versus benefits (opportunity costs) of treatments, doctors can choose therapies that yield the most significant health gain for a limited budget. One Saudi study concluded that health economics knowledge "ensures optimal clinical outcomes with consideration for financial implications," aligning care decisions with value researchgate.net. In practice, this leads to better patient outcomes on average, since resources are allocated to interventions with proven effectiveness.

- **Contribution to policy and leadership**

Clinicians with economics training are more effective advocates in policy discussions. They can critically evaluate evidence and economic models to inform the development of guidelines or funding debates. As one primer notes, economic analysis "will assist psychiatrists in translating their expertise and clinical priorities more effectively to policy-makers, governments, and insurers," pmc.ncbi.nlm.nih.gov. Similarly, knowing economics helps clinicians engage with bodies like NICE to shape coverage of new drugs. Thus, education in health economics enables physicians to influence healthcare policy and improve system sustainability.

Several effective methods for embedding health economics into

postgraduate training have been identified & include:

- Integration of dedicated economics topics into existing curricula (or electives). For instance, an internal medicine residency piloted a **week-long health systems course** including seminars on health economics, insurance, and policy. Residents rated these sessions highly and found them valuable for their clinical practice and development.
- Some programs offer certificate courses or online modules focused on health economics. For example, faculty developed a **massive open online course on health technology assessment**, providing clinicians with a practical introduction to cost-effectiveness methods. Continuing education workshops or certificate programs in health economics and outcomes research are also used to upskill trainees and faculty in decision-analytic methods.
- Experiential QI projects are a natural platform to apply economics. Postgraduate learners from multiple professions can collaborate on system-level improvement initiatives that incorporate cost or efficiency goals. For example, an **interprofessional quality improvement (QI) curriculum involving residents from medicine, nursing, pharmacy, and social work** led to measurable gains in QI knowledge and skills. pubmed.ncbi.nlm.nih.gov.
- Computerized simulations and case games can vividly illustrate economic concepts. A notable example is the *Clinical Health Economics System Simulation (CHESS)*: a computer-based, team competition where resident groups manage patient care under different payment models pubmed.ncbi.nlm.nih.gov. Simulation exercises like CHESS allow learners to experiment with budget constraints and cost-effectiveness in a risk-free setting, reinforcing economic reasoning in clinical decision-making.
- Training jointly with other health professionals amplifies learning. Because resource allocation and system navigation involve the whole care team, interprofessional sessions help trainees appreciate diverse perspectives (e.g., nursing, pharmacy, administration) on costs and value. Reviews note that IPE (often through simulation or shared QI projects) builds collaborative skills and has been linked to reduced errors and better outcomes. journals.lww.compubmed.ncbi.nlm.nih.gov.

Overall, a **multimodal approach**—blending lectures, seminars, practical projects, simulation games and team-based learning—appears most effective. Pilot programs emphasize active, case-based learning (not just lectures) to keep economics "relevant to clinical practice," researchgate.net, pmc.ncbi.nlm.nih.gov. By embedding health economics within routine postgraduate training and quality improvement (QI) initiatives, programs can help clinicians develop an "economic lens" for patient care, yielding better-informed doctors and more sustainable healthcare systems.

Sources

Recent educational studies and reviews have highlighted these points, researchgate.net, pmc. ncbi.nlm.nih.gov, pubmed. ncbi.nlm.nih.gov, pubmed. ncbi.nlm.nih.gov, researchgate.net, journals. lww.com, drawing on program evaluations and curricula from diverse settings. They consistently find that formal economics training enhances physician confidence and competence in system-level decision-making, ultimately benefiting both patients and policy.

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ORIGINAL ARTICLE

Intraoperative ICG Dye Monitoring for Identification of Pituitary Adenoma in Endoscopic Transsphenoidal Surgery: A Prospective Observational Study

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Abstract

Introduction: Histological and imaging studies have shown that pituitary adenomas possess a distinct capillary vascular density compared to adjacent anatomical structures. This has led to the hypothesis that intraoperative indocyanine green (ICG) fluorescence endoscopy may help visually differentiate tumors from surrounding normal tissues such as the pituitary gland and dura. Achieving accurate and complete tumor resection while preserving surrounding structures requires real-time intraoperative information on tumor location and margins. **Aim of the Study:** This study aimed to assess the utility of a novel intraoperative imaging technique—ICG fluorescence endoscopy—during transsphenoidal surgery (TSS) for pituitary tumors, with a focus on real-time visualization and differentiation of tumor tissue. **Methodology:** A conventional endoscopic endonasal approach was employed to access the sellar region. Following exposure of the sellar dura and tumor, a bolus of ICG (12.5–25 mg) was administered intravenously. Under near-infrared light, differences in fluorescence intensity between tumor tissue and adjacent normal structures were observed. These variations in intensity, temporal changes in fluorescence, and tissue-specific patterns allowed differentiation of tumor margins and identification of surrounding structures. Areas of dural invasion by tumor exhibited enhanced fluorescence compared to native dura. The fluorescence examination added approximately 15–20 minutes to the overall operative time under general anesthesia. No complications were noted due to ICG or the fluorescence imaging process. Patients were monitored postoperatively for up to three months, including follow-up MRI to assess for residual tumor or recurrence. **Results:** The use of ICG fluorescence provided valuable assistance in identifying tumor tissue, particularly in cases involving microadenomas. Among currently available fluorophores, ICG appears to be the most effective based on existing literature. However, the technique has certain limitations, such as blood pooling in the operative field and challenges in clearly distinguishing tumor from normal pituitary tissue. Further investigation is needed to better understand the fluorescence characteristics of various adenoma types and to refine the technique. **Conclusion:** ICG fluorescence endoscopy demonstrates potential as a real-time intraoperative tool for distinguishing pituitary tumors from surrounding tissues and for detecting dural invasion. This method may contribute to more complete tumor resections while reducing the risk of damage to adjacent normal structures.

Keywords: Pituitary adenoma, Endoscopic surgery, ICG endoscopy, Real time monitoring, Intra op ICG

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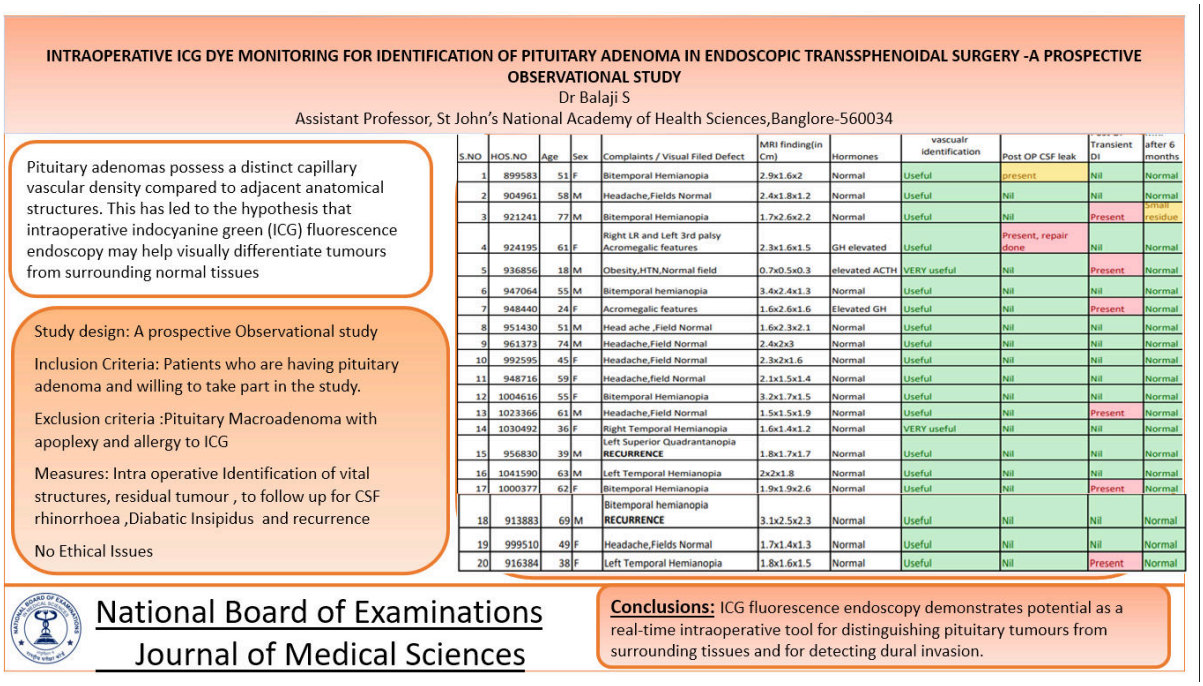
Graphical Abstract



Abbreviations

ICG: Indocyanin green
5-ALA: 5-Alpha leuvinic Acid
OLT 4: Folate receptor Agonist
PA: Pituitary Adenoma
DI: Diabetes Insipidus
MRI: Magnetic resonance Imaging
CT: Computer Tomography
Nm: Nano meter
ETSS: Endoscopic Trans Sphenoidal Surgery
ICA: internal Carotid Artery
CS: Cavernous Sinus
ICS: Inter Cavernous Sinus
iMRI: intra operative Magnetic Resonance Imaging
FDA: Food & Drug Administration
SWIG: Second Window Indo Cyanin Green
NIR: Near Infra Red
PPV: Positive Predictive Value
NPV: Negative Predictive Value

Introduction

In neurosurgery, indocyanine green (ICG) fluorescence has been widely utilized in the management of various conditions, including brain tumors, vascular anomalies, intracranial aneurysms, and spinal dural arteriovenous fistulas. The application of ICG in endoscopic pituitary surgery was first documented by Litvack et al. in 2012, who observed that pituitary adenomas exhibited reduced fluorescence compared to normal pituitary tissue under ICG imaging. Since then, studies have demonstrated that ICG endoscopy can aid in differentiating healthy pituitary gland from adenomatous tissue. These properties suggest that ICG fluorescence endoscopy could serve as a valuable adjunct to facilitate safer and more complete tumor resection during endoscopic transsphenoidal surgery (ETSS).

Despite these advantages, the optimal usage strategies and potential limitations of ICG fluorescence in ETSS are not fully established. In this study, we explored the utility of ICG endoscopy during ETSS for pituitary adenomas, focusing on its ability to distinguish tumors from critical structures such as the internal

carotid arteries (ICAs) and normal pituitary gland. We also examined practical considerations, including potential technical challenges and limitations, in using ICG as a real-time intraoperative imaging aid.

Typically, pituitary surgeries rely heavily on preoperative magnetic resonance imaging (MRI) for surgical planning. Intraoperatively, differentiation between tumor and normal tissue is usually based on subjective visual assessment of tissue characteristics, including color, consistency (e.g., soft, fibrous, or gelatinous), and capillary bleeding patterns. While techniques such as intraoperative frozen section diagnosis exist, they are technically demanding, time-intensive, and depend on additional personnel. As such, there remains a need for a straightforward, reliable, and real-time method for identifying tissue types during surgery that does not impede surgical visibility or instrument handling.

While intraoperative MRI has been introduced to improve the extent of tumor resection, its cost and procedural complexity limit widespread use. Fluorescent agents such as 5-aminolevulinic acid (5-ALA), ICG, and fluorescein have increasingly been adopted in neurosurgery as intraoperative contrast agents. Recently, their application in pituitary surgery has also been investigated. Various studies have evaluated the temporal fluorescence behavior of different anatomical and pathological structures, including the ICA, intercavernous sinus (ICS), pituitary gland, and tumors like adenomas, craniopharyngiomas, and meningiomas. Furthermore, ICG fluorescence has proven beneficial for assessing the patency of small vessels supplying the optic apparatus and pituitary stalk during and after tumor removal.

With endoscopic systems capable of delivering light sources directly into the sphenoid sinus and sella, the surgeon gains a wide-angle, high-resolution panoramic view. This enhanced visualization facilitates more extensive tumor resection compared to the narrower field and limited access provided by traditional microscopic approaches through sublabial or transnasal routes. Despite these advancements, no randomized controlled trials have yet compared outcomes of fully endoscopic versus microscopic approaches for pituitary tumor resection.

Materials and Methods

Study design: A prospective Observational study

Inclusion Criteria: Patients who are having pituitary adenoma and willing to take part in the study.

Exclusion criteria

1. Patient giving Negative consent
2. Pituitary Macroadenoma with apoplexy
3. Prior allergy to ICG dye

The ICG compound (25mg) {AUROGREEN}, was dissolved in 10ml of sterile water, and 5ml of the solution (12.5 mg of ICG) was injected into a peripheral vein as a bolus by the anesthetist (twice during the surgery), for flushing we used 10 ml of saline. The maximum absorption and emission wavelength of ICG in water are 780 nm and 805 nm, respectively; in plasma they are 800 nm and 825 nm.

Firstly, we will inject ICG (12.5mg) immediately after opening the dura, then we will inspect for the following

1. Identification of microadenoma
2. To identify the border between adenoma and normal pituitary
3. To identify the vital structures like ICA, cavernous sinus
4. To identify posterior pituitary

We do the dissection in white light only, we use NIR camera only if needed to identify the above mentioned structures and rest of the resection is done again carried out in white light only.

Second dose of ICG (12.5mg) is injected post resection before the skullbase reconstruction Post resection ICG is used to:

1. To identify the remnants those are left during the resection
2. To look for vasculature of Nasoseptal flap (But we didn't use ICG for this purpose)

AUROGREEN lyophilized powder (active ingredient indocyanine green ICG) i s a diagnostic dye used for ophthalmic angiography.

Results

We have done the study in 20 individuals who have undergone ETSS for Pituitary adenoma in the past two and half - three years in our Institute. The results are discussed here in the following headings

Age

Majority of the patients are in the age group between 50-60 years(n=6) and mean age is 52.25 years.

Sex

Out of the twenty subjects 10 were males and rest are females

Presenting complaints

Majority of the patients present with Headache (n=7), the next most common symptom is bitemporal field defect (n=6). Four patients had unilateral temporal field defects and three patients presented with hormonal disturbances.

Pre Operative MRI Findings

Majority of the patients had Pituitary macroadenoma and only one patient (Case no 5 in our master chart) had pituitary microadenoma (functional ACTH secreting adenoma causing Cushing's Disease).

Pre Op Hormonal Status of the Patient

Majority of the patients had normal preoperative hormonal status, two patients had Acromegaly (Case no 4 and 7 in our master chart) and one patient had Cushing's disease (case no 5)

Intra operative Identification of adenoma and other Vascular structures

Intra operative identification of pituitary adenoma and normal Pituitary gland is based on the Hypo fluorescence of adenoma when compared with normal pituitary, Though intra operatively adenoma shows hypofluorescence we could not identify the clear margin between Adenoma and normal pituitary gland due to following reasons (Figure 1)

A) Pooling of blood in the operative field: As there is pooling of blood in the operative field it obscures the margins of the tumor and the gland

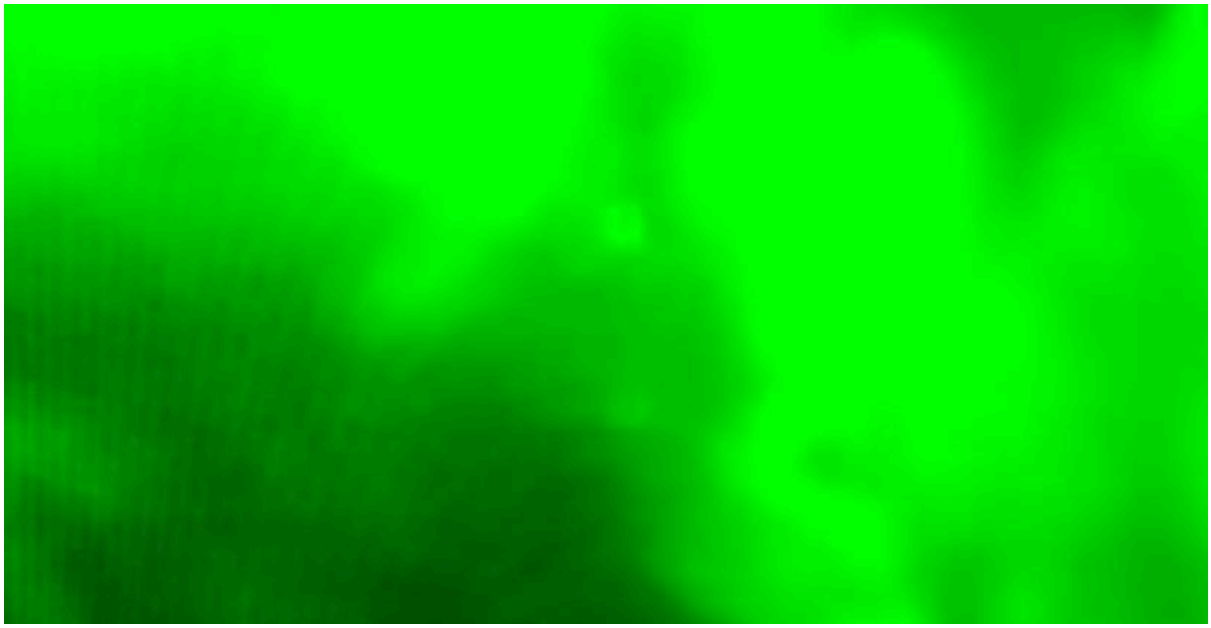


Figure 1. Image showing pooling of blood on operative field

B) Surrounding Vascular structures Obscuring the hypo fluorescence from the gland

Surrounding vascular structures like ICA and Cavernous sinus may obscure the hypofluorescence from gland and hence no distinct border could be made out between tumor and normal pituitary gland.

Identification of vascular structures

As mentioned earlier we can see the clear boundary and pulsation of ICA in ICG endoscopy and so it is very much useful in identification of vascular structures (Figure 2).

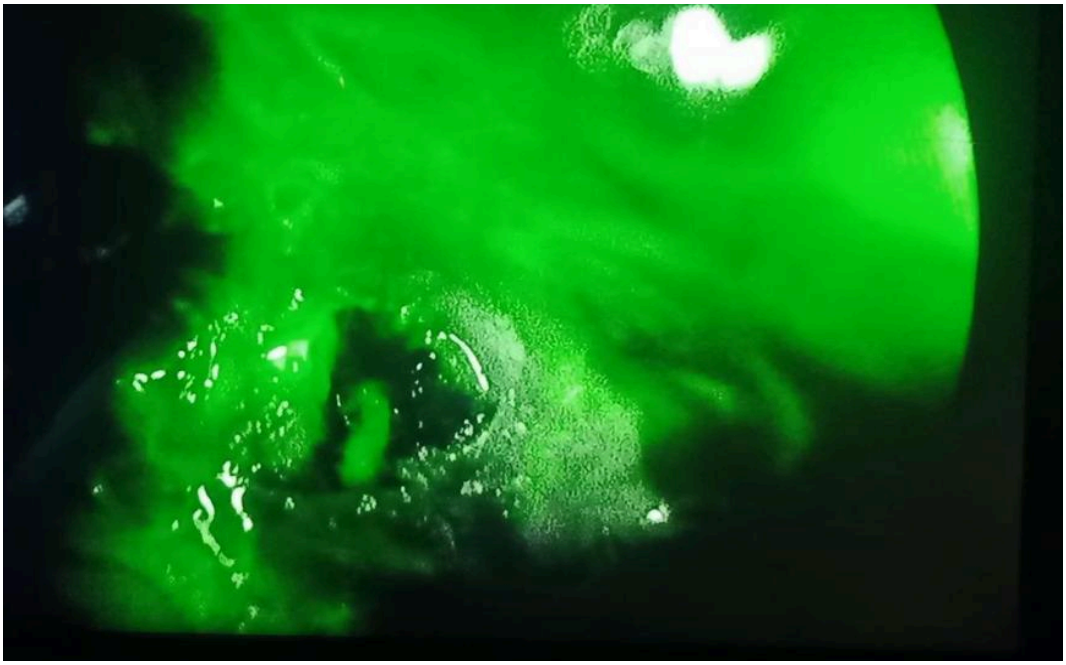


Figure 2. Image showing ICA near the lateral wall of Sella

ICA showing early hyper fluorescence immediately after ICG injection Identification of micro adenoma.

Postoperative CSF leak

Only Two patients had postOperative CSF leak, one patient (case no 1) managed conservatively with lumbar drain and other patient had undergone endoscopic CSF leak repair(Case no 4)

Postoperative Diabetes Insipidus

Out of 20 patients, 6 patients had postoperative transient diabetes insipidus. So with thus we conclude that the ICG is not useful in identifying the posterior pituitary (Table 1).

Table 1 Showing the observational finding and post op follow in patients who had undergone Intra Operative ICG endoscopy

S.NO	HOS.NO	Age	Sex	Complaints / Visual Filed Defect	MRI finding(in Cm)	Hormones	Tumour and vascualr identification	Post OP CSF leak	Post OP Transient DI	MRI after 6 months
1	899583	51	F	Bitemporal Hemianopia	2.9x1.6x2	Normal	Useful	present	Nil	Normal
2	904961	58	M	Headache,Fields Normal	2.4x1.8x1.2	Normal	Useful	Nil	Nil	Normal
3	921241	77	M	Bitemporal Hemianopia	1.7x2.6x2.2	Normal	Useful	Nil	Present	Small residue
4	924195	61	F	Right LR and Left 3rd palsy Acromegalic features	2.3x1.6x1.5	GH elevated	Useful	Present, repair done	Nil	Normal
5	936856	18	M	Obesity,HTN,Normal field	0.7x0.5x0.3	elevated ACTH	VERY useful	Nil	Present	Normal
6	947064	55	M	Bitemporal hemianopia	3.4x2.4x1.3	Normal	Useful	Nil	Nil	Normal
7	948440	24	F	Acromegalic features	1.6x2.6x1.6	Elevated GH	Useful	Nil	Present	Normal
8	951430	51	M	Head ache ,Field Normal	1.6x2.3x2.1	Normal	Useful	Nil	Nil	Normal
9	961373	74	M	Headache,Field Normal	2.4x2x3	Normal	Useful	Nil	Nil	Normal
10	992595	45	F	Headache,Field Normal	2.3x2x1.6	Normal	Useful	Nil	Nil	Normal
11	948716	59	F	Headache,field Normal	2.1x1.5x1.4	Normal	Useful	Nil	Nil	Normal
12	1004616	55	F	Bitemporal Hemianopia	3.2x1.7x1.5	Normal	Useful	Nil	Nil	Normal
13	1023366	61	M	Headache,Field Normal	1.5x1.5x1.9	Normal	Useful	Nil	Present	Normal
14	1030492	36	F	Right Temporal Hemianopia	1.6x1.4x1.2	Normal	VERY useful	Nil	Nil	Normal
15	956830	39	M	Left Superior Quadrantanopia **RECURRENCE**	1.8x1.7x1.7	Normal	Useful	Nil	Nil	Normal
16	1041590	63	M	Left Temporal Hemianopia	2x2x1.8	Normal	Useful	Nil	Nil	Normal
17	1000377	62	F	Bitemporal Hemianopia	1.9x1.9x2.6	Normal	Useful	Nil	Present	Normal
18	913883	69	M	Bitemporal hemianopia **RECURRENCE**	3.1x2.5x2.3	Normal	Useful	Nil	Nil	Normal
19	999510	49	F	Headache,Fields Normal	1.7x1.4x1.3	Normal	Useful	Nil	Nil	Normal
20	916384	38	F	Left Temporal Hemianopia	1.8x1.6x1.5	Normal	Useful	Nil	Present	Normal

Discussion

The introduction of endoscopic techniques into transsphenoidal surgery has significantly enhanced visualization by providing a wide-angle, panoramic view of the surgical field. The use of angled endoscopes offers multidirectional perspectives, allowing better understanding of the anatomical relationships between the sella and adjacent critical structures such as the internal carotid arteries (ICAs) and optic nerves. Despite these advancements, accurately distinguishing pituitary adenomas from surrounding tissues—particularly the normal pituitary gland and

vascular structures—remains challenging [1,2].

This distinction is especially vital in surgeries for functioning pituitary adenomas, where complete tumor removal is necessary to resolve hormonal imbalances and alleviate clinical symptoms. Achieving this requires real-time intraoperative tools capable of clearly identifying tumor boundaries while preserving normal tissues.

ICG fluorescence endoscopy has recently emerged as a valuable adjunct in this context. Endoscopes integrated with ICG video angiography help confirm the patency of vessels not readily visible with conventional microscopy or standard endoscopy. ICG is well-suited for vascular imaging due to its rapid hepatic clearance, strong binding to plasma proteins, and established safety profile. As noted in our study, ICG fluorescence enables intraoperative visualization of vascular and glandular structures in real time, supporting safer dissection and more complete resections [3].

However, optimal imaging with near-infrared (NIR) fluorescence requires a bloodless surgical field, as pooled blood can obscure fluorescence signals. Incomplete hemostasis or residual tumor burden can result in high background fluorescence, making it difficult to distinguish target structures. Additionally, repeated ICG administration within short intervals—less than 30 minutes—can interfere with tissue contrast, reducing imaging clarity. Thus, it is essential to determine in advance which structures are of most interest to the surgeon to maximize the diagnostic utility of ICG.

Although current ICG systems do not support simultaneous overlay of NIR and visible (white light) images, future developments in multimodal visualization—incorporating navigation systems and 3D imaging—may further enhance surgical precision and safety during ETSS [4].

Several technical and biological limitations also need to be considered. The current principle of ICG imaging relies on the delayed and reduced uptake of the dye by tumor tissue relative to normal pituitary gland. While this helps in identifying normal tissue, it would be even more effective if the tumor itself were selectively highlighted. The development of tumor-specific fluorescent tracers could improve the specificity of intraoperative visualization, allowing surgeons to resect only fluorescent, and therefore tumorous, tissue.

Additionally, the technique is prone to false-positive fluorescence in non-neoplastic tissues such as skin, nasal mucosa, and dura, possibly due to nonspecific binding of negatively charged ICG molecules. Moreover, endoscopic proximity to tissues can amplify fluorescence signals due to inverse-square intensity effects—bringing the scope too close can artificially enhance signal strength, leading to misinterpretation. Maintaining a consistent viewing distance is key to minimizing these errors [5].

A report by Sandow et al. highlighted a possible correlation between ICG signal patterns and clinical subtypes of pituitary adenomas. Notably, patients with Cushing's disease demonstrated early and distinct fluorescence, suggesting a possible link between tumor vascularity and fluorescence behavior. Previous studies have shown that the normal pituitary gland is highly vascularized, while adenomas typically display reduced microvascular

density (MVD), though this varies by tumor subtype [6].

The literature remains inconclusive on vascular differences among adenoma types. For instance, Niveiro et al. found higher MVD in thyrotroph adenomas compared to prolactinomas, and suggested that older patients may exhibit increased tumor vascularity. Conversely, Turner et al. reported lower MVD in ACTH-secreting tumors and microprolactinomas, while Jugenburg et al. found prolactinomas to have the highest MVD and GH-producing adenomas the lowest. To date, there are no studies directly comparing histological MVD assessments with intraoperative ICG imaging, which could provide valuable insights into adenoma angioarchitecture and the real-time applicability of ICG video angiography.

Interestingly, while Litvack et al. noted hypervascularity in cases of acromegaly and prolactinoma, and Sandow's series found hyperfluorescence in Cushing's disease, our findings differ. In our cohort, both acromegaly and Cushing's disease cases demonstrated hypofluorescence, even though the tumors were confirmed as corticotroph adenomas by a reputed national institution. These discrepancies suggest that additional research is necessary to elucidate how adenoma subtype, vascular characteristics, and tumor biology influence intraoperative fluorescence patterns [7,8].

Conclusion

Indocyanine green (ICG) fluorescence endoscopy holds significant potential as an intraoperative tool for distinguishing pituitary tumors from the normal gland and for identifying areas of dural invasion. With further refinement, ICG administration combined with endoscopic fluorescence-guided visualization could enhance tumor resection, ensuring better preservation of surrounding structures. This approach supports the development of fluorescence-guided resection techniques and encourages future prospective trials to confirm improved outcomes, such as the preservation of healthy tissue and more complete tumor removal. Given its promising capabilities, this technique could be applied to a variety of CNS tumors.

ICG is considered one of the most effective fluorophores for real-time imaging, especially in pituitary tumor dissection, including microadenomas. However, as noted in the literature, challenges remain, such as blood pooling in the surgical field, which can obscure the fluorescence signal, making it difficult to clearly differentiate between the tumor and normal pituitary tissue. Moreover, as Sandow et al. highlighted, there is a lack of conclusive data on the fluorescence characteristics of different types of pituitary adenomas. Therefore, further research is necessary to determine whether ICG fluorescence is truly effective in identifying adenomas and understanding the fluorescence patterns specific to various adenoma subtypes.

The outcomes of our study are summarized as follows

1. Is the ICG dye helpful in identifying the margin between tumor and normal pituitary gland? No it is not very much helpful in identifying the distinct border between tumor and normal pituitary gland. Limitations a) Pooling of blood b) Presence of vascular structures which shows hyperfluorescence.

2. Whether it is helpful in identifying vascular structures?

   Yes it is really helpful in identifying vascular structures

3. Whether it is helpful in identifying posterior pituitary?

   No it is not helpful in identifying posterior pituitary gland, we had more patients with transient DI in the postoperative period

4. Whether it is helpful in identifying functional micro adenoma (Cushing's, acromegaly)?

   Yes it is very much helpful in identifying functional microadenoma, in our study functional microadenoma showed hypofluorescence and we confirmed the adenoma with HPE and ICH markers.

5. Whether it is helpful is decreasing postoperative CSF leak?

   To some extent it is helpful in reducing postoperative CSF leak, but it may vary among surgeons depending upon their experience.

6. Whether it is helpful in preventing recurrence of Pituitary adenoma?

It is very much helpful in preventing recurrence, out of the twenty patients operated on, only one patient had a small residue and the patient is asymptomatic for more than 3 years and he is on follow-up.

As mentioned earlier we used ICG endoscopy after the resection of adenoma to ensure the completion of excision, it is also useful in recurrent pituitary adenoma cases. So to conclude ICG endoscopy is very much useful in above mentioned scenarios for surgery of pituitary adenoma. Limitation of ICG dye is already mentioned and as it is a small study (n=20), we need larger study samples and clearly published data to talk about fluorescence patterns of different kinds of adenomas. The fluorescence pattern interpretation also has inter observer variations and it also depends upon the distance from which the endoscope is used. So I conclude that ICG is a good tool for pituitary adenoma excision but we need further study and research in this subject.

Statements and Declarations

Conflicts of interest

The authors declare that they do not have conflict of interest.

Funding

No funding was received for conducting this study.

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ORIGINAL ARTICLE

Correlation of Sarcopenia with Etiologies of Liver Cirrhosis and Its Association with Child-Pugh and MELD Scores

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Abstract

Background: Sarcopenia, defined by the progressive decline in muscle mass and strength, is a common yet often overlooked complication in individuals with liver cirrhosis. The extent of muscle loss varies based on the underlying cause of cirrhosis and may impact overall disease progression. While the Child-Pugh (CPS) and Model for End-Stage Liver Disease (MELD) scores are standard tools for assessing liver disease severity, their relationship with sarcopenia remains uncertain. **Aim:** This study aims to investigate the correlation between sarcopenia and various etiologies of liver cirrhosis and examine its association with CPS and MELD scores. **Discussion:** The prevalence of sarcopenia varies among different causes of cirrhosis, with alcohol-related and viral cirrhosis frequently linked to greater muscle depletion. A higher CPS and MELD score is often associated with severe sarcopenia, indicating poorer clinical outcomes and increased disease burden. **Conclusion:** Recognizing sarcopenia in cirrhotic patients can improve risk assessment and treatment strategies. Early identification and targeted interventions, including nutritional support and physical rehabilitation, may help mitigate its impact and improve patient outcomes.

Keywords: CPS, MELD, Sarcopenia, cirrhosis.

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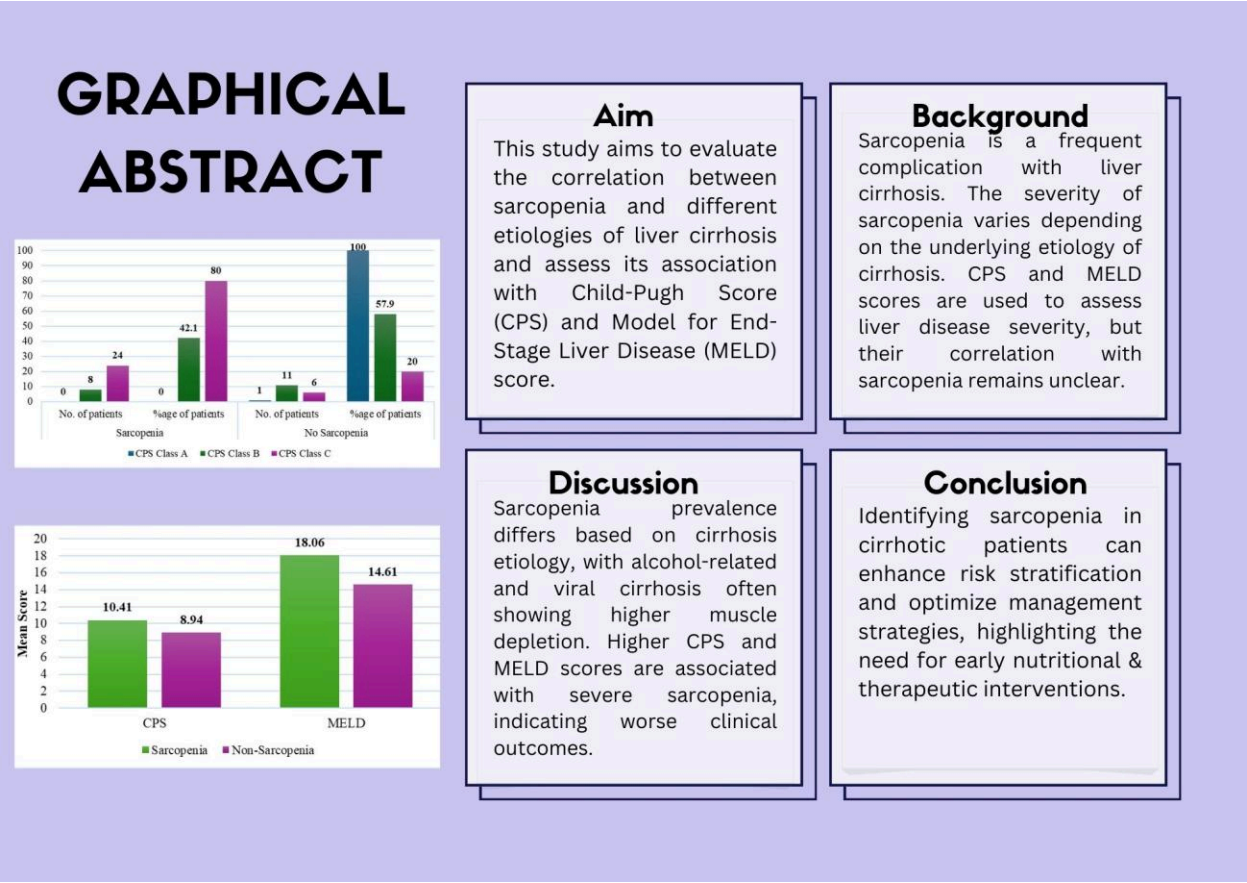
Abbreviations

ALD	:	Alcoholic Liver Disease
CPS	:	Child Pugh Score
NAFLD	:	Non-Alcoholic Fatty Liver Disease
HCV	:	Hepatitis C Virus
INR	:	International Normalized Ratio
HBV	:	Hepatitis B Virus
MELD	:	Model for End-Stage Liver Disease

Graphical Abstract



Introduction

Liver cirrhosis is a progressive condition leading to the result of fibrosis, hepatocellular dysfunction, and portal hypertension. Causative factors are like viral hepatitis, alcohol-related liver disease, autoimmune liver disorders and non-alcoholic fatty liver disease (NAFLD). Among the numerous complications of cirrhosis, sarcopenia—defined as the loss of skeletal muscle mass and strength—has emerged as a critical determinant of disease progression and patient outcomes. Sarcopenia not only contributes to increased morbidity and mortality but also influences

liver transplant eligibility and post-transplant prognosis [1].

The severity of cirrhosis is commonly assessed using Child-Pugh Score (CPS) and Model for End-Stage Liver Disease (MELD) Score, both of which help in predicting survival and guiding treatment decisions. However, their correlation with sarcopenia remains an area of growing clinical interest. Evidence suggests that sarcopenia is more prevalent in advanced liver disease, and its severity may vary depending on the underlying etiology of cirrhosis [2].

Understanding the relationship between sarcopenia, different causes of cirrhosis, and liver disease severity scores can aid in better risk stratification and management of cirrhotic patients. Early identification and intervention for sarcopenia could potentially improve functional status, reduce complications, and enhance overall survival in this vulnerable patient population.

Liver cirrhosis and Sarcopenia

Cirrhosis is the end-stage of liver damage characterized by progressive fibrosis, hepatocellular dysfunction, and altered hepatic architecture, leading to portal hypertension and liver failure. It occurs due to persistent liver injury caused by various etiologies, like viral infections (HBV and HCV), alcohol-related liver disease, NAFLD, autoimmune hepatitis, and metabolic disorders [3]. It disrupts metabolic processes, often leading to muscle wasting and malnutrition, which together contribute to sarcopenia [4]. Sarcopenia is characterized by a decline in skeletal muscle mass, strength, and function and is now recognized as a significant complication in patients with cirrhosis. Its presence is associated with poorer clinical outcomes, reduced quality of life, and increased mortality risk in affected individuals [5]. The prevalence of sarcopenia in cirrhosis is influenced by the underlying etiology. The pathogenesis of sarcopenia in cirrhosis is multifactorial. Chronic inflammation, hypermetabolism, impaired protein synthesis, and hormonal imbalances contribute to progressive muscle loss [6]. Additionally, insulin resistance, reduced physical activity, and malabsorption of essential nutrients exacerbate sarcopenia in these patients. The severity of cirrhosis, often assessed using CPS and MELD scores, correlates with worsening sarcopenia, as higher scores indicate more advanced liver dysfunction and nutritional deficits [7].

Identifying sarcopenia in cirrhotic patients is crucial, as it is associated with increased risk of infections, prolonged hospital stays, and higher mortality rates. Early nutritional interventions, physical therapy, and targeted therapies aimed at preserving muscle mass may help improve clinical outcomes and quality of life [8].

Methodology

This observational study was conducted on 50 patients diagnosed with liver cirrhosis, including both outpatients and inpatients admitted to the medical wards of the Department of Medicine at Adesh medical college and hospital. The selection of patients was made irrespective of the underlying cause of cirrhosis.

Inclusion Criteria:

- Age: 18-65 years
- Confirmed liver cirrhosis

- Written informed consent given

Exclusion Criteria:

- <18 years or >65 years
- Malignancy
- Thyroid disorders
- Retrovirus positive
- Malabsorption syndromes
- Advanced heart, lung, neuromuscular diseases or kidney failure

CPS and MELD scores

The CPS and MELD scores are widely used tools to assess the severity and prognosis of liver cirrhosis. These scoring systems help guide clinical decision-making, including treatment strategies, liver transplant eligibility, and risk stratification.

The Child-Pugh Score has five parameters:

- Presence of ascites
- Hepatic encephalopathy.
- Serum total bilirubin
- Serum albumin
- INR

Each parameter is scored between 1 to 3, and the total score categorizes patients into:

- Class A (score 5–6): **MILD**
- Class B (score 7–9): **MODERATE**
- Class C (score 10–15): **SEVERE**

with higher scores indicating worse liver function [9].

The MELD Score is a more objective tool used primarily for prioritizing liver transplant candidates. Higher MELD scores indicate a greater risk of mortality within three months, making it crucial for transplant allocation. While both scoring systems provide valuable prognostic information, MELD is more accurate for predicting short-term survival, whereas Child-Pugh helps in assessing overall liver function and clinical management [10].

MRI-Based Sarcopenia Assessment

Magnetic Resonance Imaging is a highly precise method for evaluating muscle mass in sarcopenia. Using a 1.5 Tesla Siemens Magnetom Aera, the third lumbar vertebral (L3) level is identified as the standard site for muscle mass measurement [11]. At this level, various muscles, including the psoas, paraspinals, transversus abdominis, rectus abdominis, and internal and external obliques, are assessed. The cross-sectional area of these muscles is measured and normalized to height squared to provide a standardized value. Sarcopenia is diagnosed when the L3 muscle area falls below 52.4 cm^2/m^2 in males and 38.5 cm^2/m^2 in females.

Handgrip Strength Based Sarcopenia Measurement

Handgrip strength is a functional measure of muscle strength, assessed using a mechanical handgrip dynamometer. Patients were seated comfortably, and the dynamometer handle was adjusted accordingly. They were instructed to hold the device away from their body and, using their non-dominant hand, squeeze the handle with maximum effort.

Three separate measurements were taken, with at least 30 seconds between each attempt, and the average value in kilograms is recorded [12].

Results

The age distribution of patients with liver cirrhosis is shown in Table 1**,** with ages ranging from 21 to 70 years**.** The highest prevalence was in the 41–50 years group (40%)**,** followed by 31–40 years (22%) and 51–60 years (18%)**.** The 21–30 years group had the lowest prevalence (6%).

The mean age was 47.22 ± 10.845 years, indicating that middle-aged individuals are most affected**,** highlighting the need for targeted screening and preventive measures in this population.

Table 1. Age distribution

Age Group	No. of patients	%age
21 – 30 years	3	6
31 – 40 years	11	22
41 – 50 years	20	40
51 – 60 years	9	18
61 – 70 years	7	14

Table 2. Association of Alcoholic liver disease with sarcopenia

Alcoholic liver disease	Total	Sarcopenia		No Sarcopenia		p-value
	No. of patients	No. of patients	%age of patients	No. of patients	%age of patients	
ALD	32	23	71.9%	9	28.1%	0.007
No ALD	18	9	50%	9	50%	
Total	50	32	64%	18	36%	

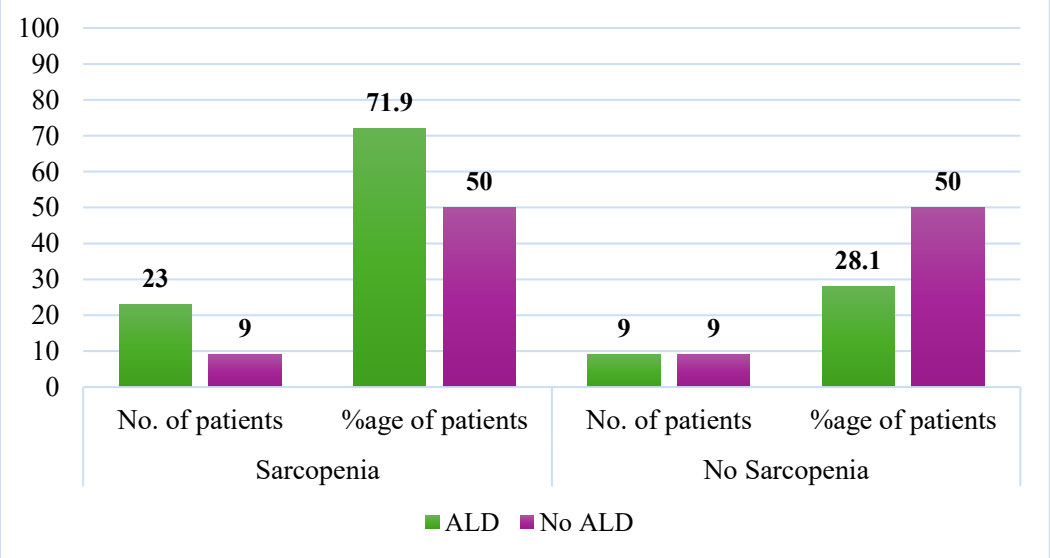


Figure 1. Bar chart showing prevalence of sarcopenia in alcoholic liver disease

Table 2 and Figure 1 presents data on the prevalence of sarcopenia among patients with liver cirrhosis, categorized based on the presence or absence of ALD. A total of 50 patients, 32 diagnosed with ALD and 18 without ALD were included. Among the ALD group (n=32), 23 patients (71.9%) were found to have sarcopenia, while 9 patients (28.1%) did not exhibit sarcopenia. In contrast, among the non-ALD group (n=18),

sarcopenia was observed in 9 patients (50%), while the remaining 9 patients (50%) did not have sarcopenia. The overall prevalence of sarcopenia in the study population was 64% (32 out of 50 patients), whereas 36% (18 out of 50 patients) did not have sarcopenia. The p-value (0.007) indicates a statistically significant association.

Table 3. Association of HBV with sarcopenia

HBV	Total	Sarcopenia		No Sarcopenia		p-value
	No. of patients	No. of patients	%age of patients	No. of patients	%age of patients	
Non-reactive	46	31	67.4%	15	32.6%	0.09
Reactive	4	1	25%	3	75%	
Total	50	32	64%	18	36%	

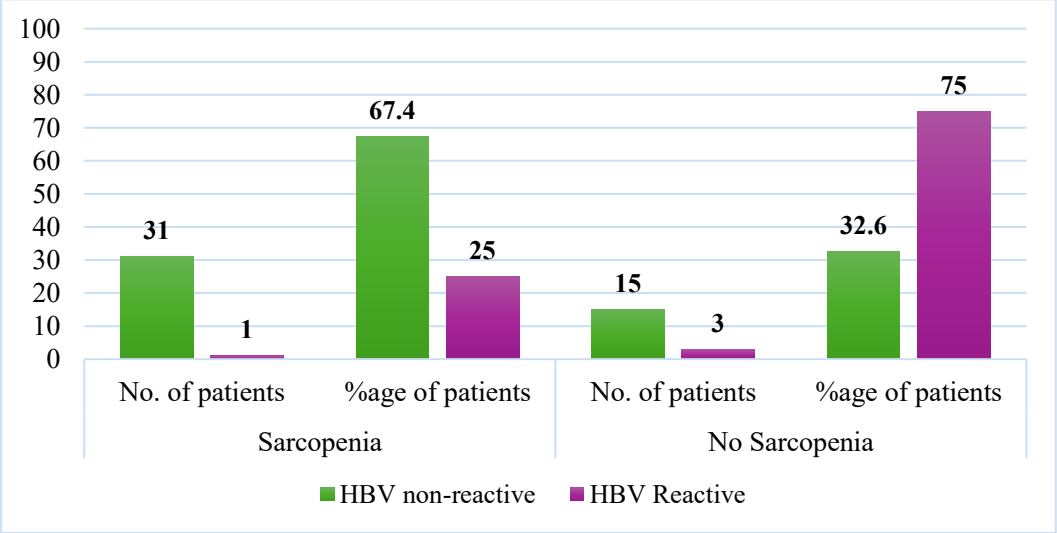


Figure 2. Bar chart showing prevalence of sarcopenia in chronic HBV infection

Table 3 and figure 2 presents the correlation between HBV status and sarcopenia in patients with liver cirrhosis. The study categorized patients based on their HBV reactivity. Among 46 non-reactive patients, 31 (67.4%) had sarcopenia, while 15 (32.6%) did not. In contrast, among the 4 HBV-reactive patients, only 1 (25%) had sarcopenia, whereas 3 (75%) did not. The statistical analysis revealed a p-value of 0.03, indicating a significant association.

Table 4. Distribution of patients according to HCV reactivity

HCV	Total	Sarcopenia		No Sarcopenia		p-value
	No. of patients	No. of patients	%age of patients	No. of patients	%age of patients	
Non-reactive	36	24	66.7%	12	33.3%	0.02
Reactive	14	9	64.3%	5	35.7%	
Total	50	33	66%	17	34%	

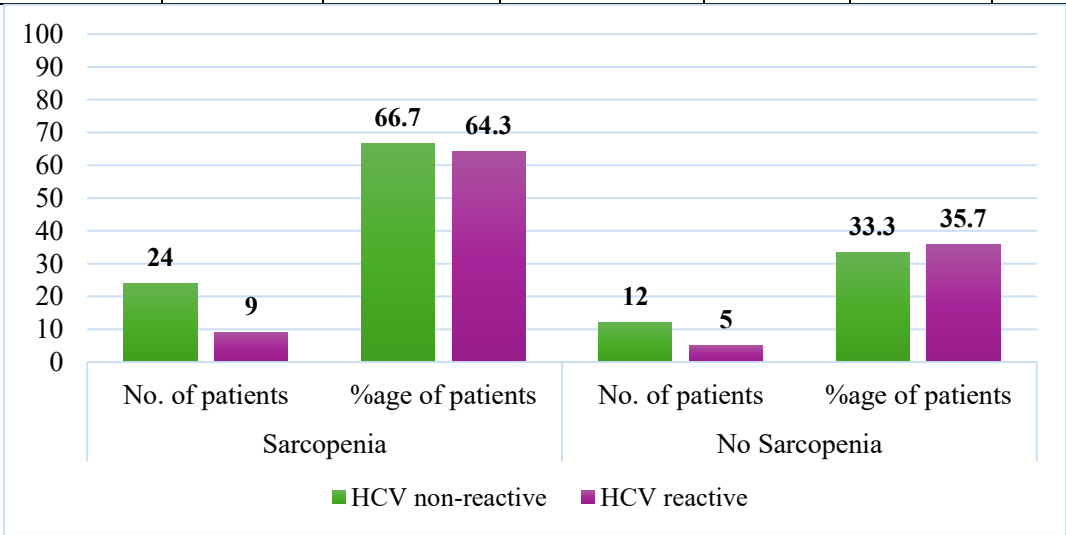


Figure 3. Bar chart showing prevalence of sarcopenia in chronic HCV infection

Table 4 and figure 3 present the correlation between HCV status and sarcopenia among with liver cirrhosis. The cohort was divided into HCV reactive and non-reactive groups, with their respective sarcopenia prevalence analyzed. Among 36 HCV non-reactive patients, 24 (66.7%) had sarcopenia, while 12 (33.3%) did not. In contrast, out of 14 HCV reactive patients, 9 (64.3%) were sarcopenic, and 5 (35.7%) were not. The overall sarcopenia prevalence in the study population was 66% (33 patients), while 34% (17 patients) did not have sarcopenia. The p-value of 0.02 suggests a statistically significant association, indicating that HCV may contribute to muscle loss in cirrhotic patients.

Table 5: Association of Sarcopenia with Child Pugh score

Child Pugh Score	Total	Sarcopenia		No Sarcopenia		p-value
	No. of patients	No. of patients	%age of patients	No. of patients	%age of patients	
Class A	1	0	.0%	1	100%	0.01
Class B	19	8	42.1%	11	57.9%	
Class C	30	24	80%	6	20%	

Total	50	32	64%	18	36%	

Table 5 and figure 4 presents the distribution of sarcopenia among patients with different Child-Pugh classifications. Out of 50 cirrhotic patients, 32 (64%) had sarcopenia, while 18 (36%) did not. The prevalence of sarcopenia increased with worsening liver function.

- In Class A (mild cirrhosis), only one patient was included, who did not have sarcopenia (0% prevalence).
- In Class B (moderate cirrhosis), 19 patients were analyzed, with 8 (42.1%) having sarcopenia, while 11 (57.9%) did not.
- In Class C (severe cirrhosis), 30 patients were assessed, with 24 (80%) diagnosed with sarcopenia, and only 6 (20%) without it.

A statistically significant association (p-value = 0.01) was observed, indicating that sarcopenia is more prevalent in advanced cirrhosis (Class C) compared to milder forms.

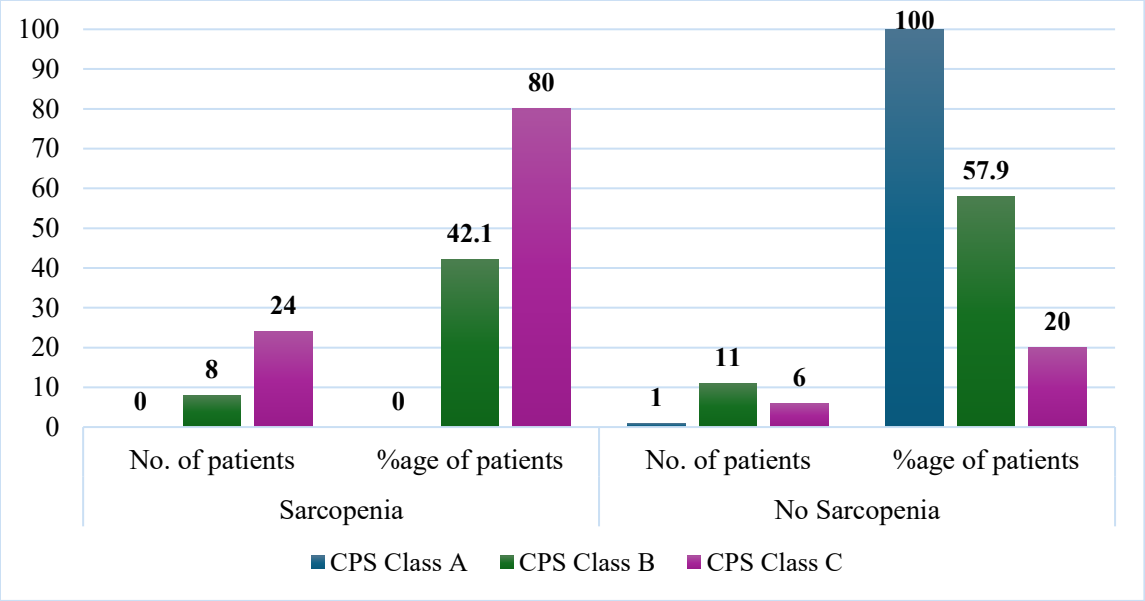


Figure 4. Bar chart showing correlation of sarcopenia with Child-Pugh score

Table 6: Comparing CPS and MELD scores with sarcopenia

	Total	Sarcopenia	Non-Sarcopenia	p-value
CPS	9.88±1.7	10.41±1.58	8.94±1.69	0.004
MELD	16.82±6.19	18.06±5.358	14.61±7.08	0.05

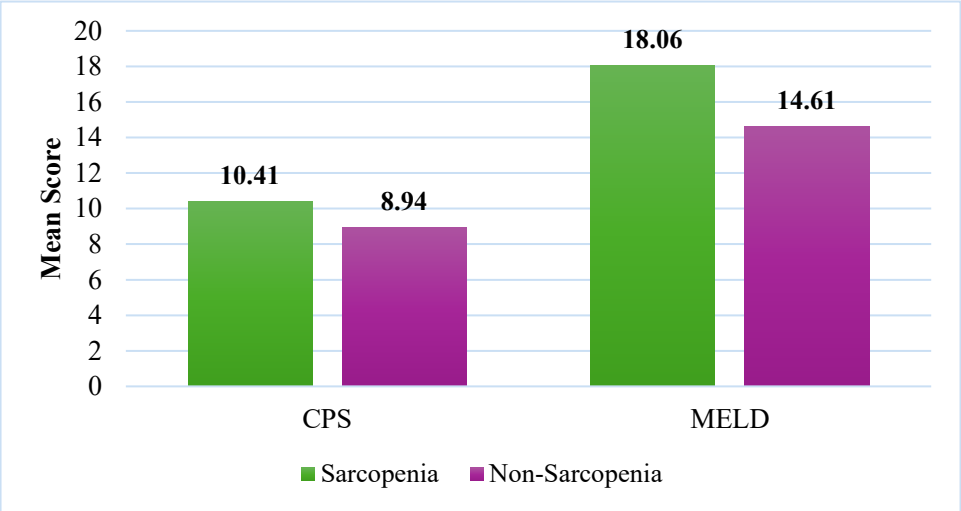


Figure 5. Bar chart showing correlation of mean CPS and MELD scores with sarcopenia

Table 6 and figure 5 compares CPS and MELD scores between patients with and without sarcopenia.

- The mean CPS was higher in sarcopenic patients (10.41 ± 1.58) compared to non-sarcopenic patients (8.94 ± 1.69), with a statistically significant p-value of 0.004, indicating a strong correlation between worsening liver function and sarcopenia.
- Similarly, the mean MELD score was higher in the sarcopenia group (18.06 ± 5.358) compared to the non-sarcopenia group (14.61 ± 7.08), with a p-value of 0.05, suggesting a significant association.

Discussion

This study highlights a strong correlation between sarcopenia and liver cirrhosis severity. The highest prevalence was seen in middle-aged individuals (41–50 years), emphasizing the need for early screening.

Alcoholic liver disease (ALD) showed a significant association with sarcopenia (71.9% vs. 50%, p = 0.007), consistent with studies linking ALD to malnutrition and muscle loss. HCV-reactive patients also had a higher prevalence of sarcopenia (64.3%), with a significant p-value (0.02), while HBV showed a weaker correlation (p = 0.09).

Sarcopenia's prevalence increased with worsening CPS class, from 0% in Class A to 80% in Class C (p = 0.01), reflecting disease progression. Higher CPS (10.41 vs.

8.94, p = 0.004) and MELD scores (18.06 vs. 14.61, p = 0.05) in sarcopenic patients further confirm this trend.

Conclusion

This study highlights a significant correlation between sarcopenia and liver cirrhosis, with its prevalence increasing as liver function deteriorates. Patients with higher Child-Pugh and MELD scores showed a greater incidence of sarcopenia, emphasizing the role of liver dysfunction in muscle loss. The findings suggest that early identification and management of sarcopenia in cirrhotic patients could improve clinical outcomes and quality of life.

Strengths and limitations

This study highlights the clinically significant association between sarcopenia and the severity of liver cirrhosis, as evaluated through Child-Pugh and MELD scores, and further explores its correlation with different etiologies. A major strength of the study lies in its use of objective tools for sarcopenia assessment, allowing for more accurate stratification. Additionally, the inclusion of multiple cirrhotic etiologies adds depth to the findings. However, the study is limited by its relatively small sample size and cross-sectional design, which restrict causal inferences. Moreover, potential confounding factors such as dietary intake, physical activity, and comorbid conditions were not fully controlled.

Future Scope

Further research is needed to explore the underlying mechanisms linking sarcopenia and liver disease across different etiologies. Future longitudinal studies exploring the effects of nutritional strategies, physical rehabilitation, and pharmacological treatments on muscle preservation and liver disease progression could offer significant insights. Furthermore, incorporating advanced imaging modalities for muscle mass evaluation and establishing standardized screening protocols may facilitate early identification and targeted management of sarcopenia in patients with liver cirrhosis.

Statements and Declarations

Conflicts of interest

The authors declare that they do not have conflict of interest.

Funding

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ORIGINAL ARTICLE

Comparative Study of Traditional and Molecular Methods of Diagnosis and Resistance Determination in Paediatric Pulmonary Tuberculosis Samples

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Abstract

Background: The burden of childhood tuberculosis provides the measure of tuberculosis control in a community as it reflects recent transmission. The paucibacillary nature of the disease and the inability to produce sufficient volumes of sputum severely hamper accurate diagnosis of tuberculosis in children. It is also equally important to address drug-resistant tuberculosis. Cartridge-Based Nucleic Acid Amplification Test (CBNAAT) is one such test that aids in the rapid detection of Mycobacterium tuberculosis and also rifampicin resistance simultaneously. Very limited studies are available in pediatric cases of pulmonary tuberculosis on the efficacy of CBNAAT compared to other conventional and molecular methods. **Material & Methods:** 50 children less than 15 years of age suspected to have pulmonary tuberculosis according to National TB Guidelines 2012 were included in the study. Pulmonary samples such as sputum samples (n = 30) and gastric aspirates (n = 20) were collected and sent for testing. **Results**: Among the 50 subjects, 78% were Tuberculin skin test (TST) positive, 14% were positive for AFB microscopy, CBNAAT was positive in 80%, liquid culture was positive in 40%, and PCR was positive in 52%. Using CBNAAT, n = 34 patients were rifampicin sensitive, and n = 6 were rifampicin resistant. Conventional DST (n = 20) showed RR pattern (resistance to both INH and Rifampicin) in n = 3 and SS pattern (sensitivity to both INH and Rifampicin) in n = 17. LPA (n = 22) showed RR pattern in n = 3, SR pattern (INH sensitive/Rifampicin resistance) in n = 1, and SS pattern in n = 18. **Conclusion**: CBNAAT results are quite promising for the diagnosis of pulmonary TB in paediatric patients residing in highly TB-endemic countries compared to other tests. It is the least time-consuming test and has the extra benefit of simultaneous Rifampicin resistance detection, which will be a great aid for treatment planning.

Keywords: Children, Tuberculosis, CBNAAT, rifampicin resistance

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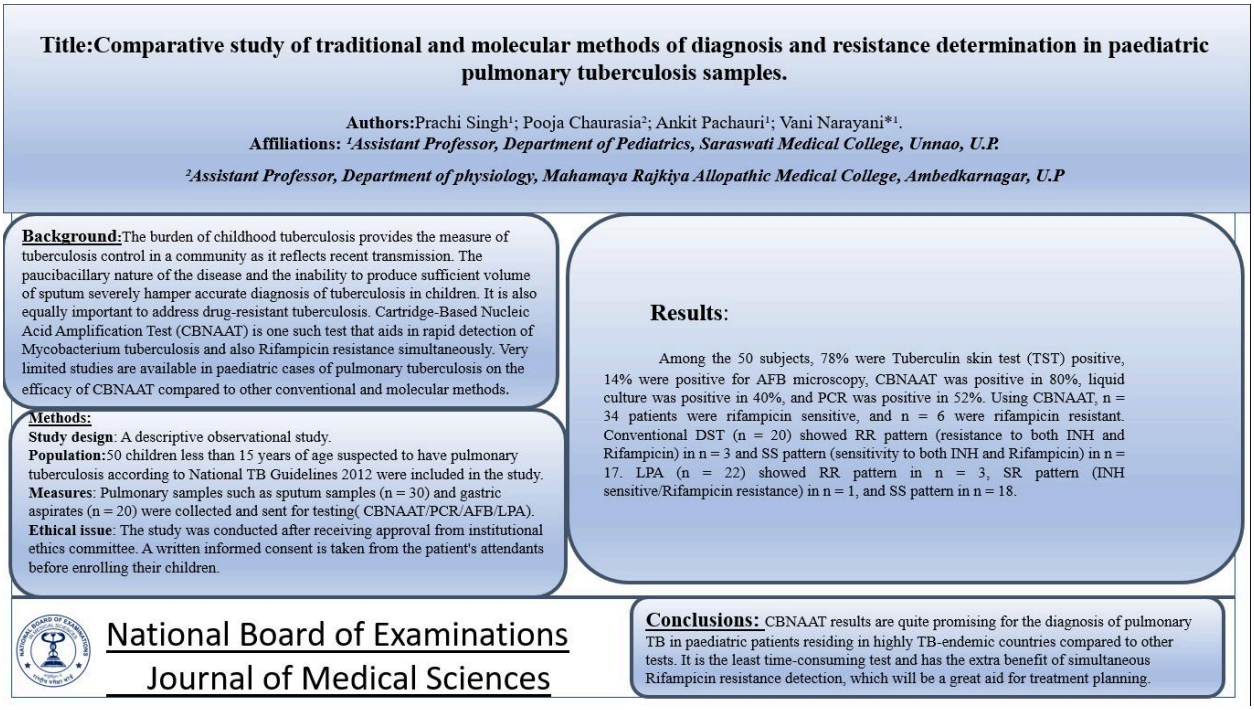
Graphical Abstract



Introduction

Mycobacterium tuberculosis is the pathogenic organism that causes tuberculosis. Roughly 6–8% of tuberculosis patients are under the age of fifteen. The burden of childhood tuberculosis indicates the measure of tuberculosis control in a community as it reflects recent transmission.

After HIV/AIDS, tuberculosis (TB) is the leading cause of death from a single infectious agent and the ninth most common cause of death globally. 10.4 million new cases of tuberculosis (TB) were reported worldwide in 2016, of which 10% were individuals living with HIV. An estimated one million children also became ill with TB. Ninety percent were adults, of whom 65% were male. Seven nations—India, Indonesia, China, the Philippines, Pakistan, Nigeria, and South Africa—accounted for sixty-four percent of the total [1]. Globally, there were 6 lakh cases of MDR-TB in 2016, including 1.1 lakh R-R cases. 47% of all MDR/RR-TB cases overall originated in China, India, and the Russian Federation. India and China accounted for 39% of the global gap. For not notified the DR-TB, it is estimated XDRTB is of 6.2% of MDR cases. It is now believed that TB is a major or contributory cause of many deaths in children under five years old [2]. As per the Global TB Report 2017, the estimated incidence of TB in India was around 2,800,000 accounting for about a quarter of the world's TB cases. Out of them, 423,000 die due to TB [3]. The burden of childhood TB in India was little known; however, according to WHO regional data, 0.6%–3.6% of all cases reported were sputum microscopy smear-positive in children under the age of 14. However, these results underestimate the true burden of childhood tuberculosis (TB) because the majority of

children were sputum microscopy smear negative. According to estimates, 8–20% of TB-related deaths occur in high-burden countries, where childhood TB accounts for 10–20% of all cases of TB [4].

According to the WHO, detection of TB disease in children is often unnoticed because it has non-specific symptoms and is difficult to diagnose. In India, sputum smear microscopy remained the mainstay for diagnosing pulmonary TB. However, because the disease is paucibacillary, there are insufficient bacteria in sputum and stomach aspirate samples for microscopy to detect the bacilli [5].

253 pulmonary and 176 extrapulmonary specimens were collected and tested in the MTB/RIF assay in a study conducted by Zeka et al. Sensitivities for smear-positive and smear-negative lung specimens were 100% (27/27) and 68.6% (24/35) respectively. In extrapulmonary specimens, its sensitivity was reduced to 100% in smear-positive specimens (4/4) and 47.7% in smear-negative specimens (21/44). The GeneXpert test has a very high specificity (97–100%) when it comes to diagnosing pulmonary tuberculosis, according to Nicol et al.

Although pulmonary TB is the most prevalent in children, extra pulmonary TB accounts for 20–30% of all paediatric cases. Among paediatric patients with pulmonary tuberculosis, the prevalence of drug resistance is also on the rise (6). This shows how important diagnosis of TB in children is, the purpose of this study was to compare CBNAAT against all other conventional and molecular methods that our centre offers.

Aims and objectives

The study aimed to detect *Mycobacterium tuberculosis* in pulmonary clinical specimens (sputum/gastric aspirates) using Gene Xpert testing (CBNAAT), PCR targeting IS6110, liquid culture MGIT 960, and conventional methods like CXR, TST, and AFB smears. To detect drug resistance to *Mycobacterium tuberculosis* using Gene Xpert CBNAAT, conventional DST, and LPA and compare the results. We have made an attempt to compare the CBNAAT results with both conventional and molecular methods of diagnosis and resistance detection in paediatric pulmonary TB samples. Also, the results of all studies with respect to age and sample type (sputum/gastric aspirate) have been compared.

Material and Methods

The study included children (0–15 years) of either sex who were suspected to have Pulmonary tuberculosis, according to the National TB Guidelines 2012, was selected for the study. Those patients who were already on anti-tubercular drugs were excluded from the study. A written informed consent is taken from the patient's attendants before enrolling their children. All the cases were subject to detailed clinical history, contact history with tuberculosis patients, immunisation history, socioeconomic classification according to the modified Kupuswamy scale, and history of previous chemotherapy. A thorough clinical examination was done, and anthropometry measurements were recorded to assess the nutritional status. TST testing and chest X-rays were done in all cases. Gastric aspirate/sputum collected from the study

subject was subjected to AFB microscopy using Ziehl Neelson staining, CBNAAT (cartridge-based nucleic acid amplification test also known as GeneXpert test), PCR IS6110 (polymerase chain reaction targeting insertion sequence 6110), line probe assay, culture on the BACTEC MGIT 960 TB system, and conventional DST. A 10 ml sample (sputum/gastric aspirate) was collected from each subject. 5 ml was sent to the state TB training and demonstration centre, and a 5 ml sample was sent to the National JALMA Institute. TRANSPORT-Specified samples were collected in sterile vials under aseptic conditions and stored at 2-8°C. The samples were then transported to the laboratory at <8° maintaining the cold chain.

Analysis: All the data were collected and compiled in an MS Excel spreadsheet. Data were analysed using SPSS software version 20.0. Descriptive data was expressed in the form of frequency and percentages. Sensitivity (Sn), specificity (Sp), positive predictive value (PPV), and negative predictive value (NPV) of different tests were also calculated. Applying the chi-square test, P values were obtained.

Results

In the current study, 50 children suspected to have pulmonary TB were included. 56% of the patients were males (n = 28), and 44% (n = 22) were females. The majority (40%) of the patients were 15 years old, followed by 11–15 years (26%), 6–10 years (24%), and less than one year (10%). Among male patients (n = 28), the majority of the patients were 1–5 years old (42.9%), while among female patients (n = 22), the majority of the patients were 11–15 years old (40.9%). More than half (52%) of the patients in the current study belonged to the middle class. 40 patients (80%) had history of contact with TB patients.

In our study, 98% of cases were malnourished. According to the WHO classification, 42% of cases were in moderate malnutrition and 18% were severely malnourished. Chest roentgenography was abnormal in the majority of cases in our study, showing hilar lymphadenopathy in 46% of cases. Other findings were patchy opacities in the lung parenchyma (34%),, pleural effusion (2%), miliary shadows (2%), consolidation (2%), hydropneumothorax (2%), and hyperinflated lung fields with nonspecific shadows (2%). Among the samples collected, 60% of the samples were sputum, and the rest, 40%, were gastric aspirates. CBNAAT was positive in 40 patients (80%). Among sputum samples (n = 30), 76.7% (n = 23) were CBNAAT positive, while among gastric aspirate samples (n = 20), 85% (n = 17) were CBNAAT positive. TST performed gave a positive reading in 78% patients (n=39). Among CBNAAT-positive patients (n = 40), the majority of the patients (85%) were positive for TST. While in CBNAAT-negative patients (n = 10), 50% of patients were positive for TST. Odds of tuberculosis positivity in TST were 17.6% lower compared to Odds of tuberculosis positivity in CBNAAT, and this was found to be statistically significant ($p<0.05$). For tuberculosis diagnosis, sensitivity of the TST test was 85%, specificity was 50%, PPV was 87.2%, and NPV was 45.5%. 70% of CBNAAT-positive patients were unimmunized for the BCG vaccine. While in

CBNAAT-negative patients, 90% of patients were immunised for the BCG vaccine. Odds of positivity in CBNAAT were 48% lower in those who immunised with BCG vaccine, and this was found to be statistically significant ($p<0.05$). Among the sputum or gastric aspirate samples checked for AFB microscopy, 14% (n = 7) were positive. All the samples positive for AFB smear microscopy were sputum, and the AFB smear was negative in all gastric aspirate samples. Among the CBNAAT positive cases, 17.5% of patients were positive for AFB microscopy. Among CBNAAT-positive patients (n = 40) and none-positive for AFB microscopy among CBNAAT-negative patients. For tuberculosis diagnosis: sensitivity (Sn), Specificity (Sp), positive predictive value (PPV), and negative predictive value (NPV) of AFB microscopy compared to CBNAAT were 17.5%, 100%, 100%, and 23.3%, respectively. By applying the chi square test, the relation between CBNAAT and AFB microscopy findings was found to be statistically non-significant ($p > 0.05$) (Table 1).

Table 1. Age wise Positive findings of different test:

Age wise Positive findings of different test									
Type of test	**Age groups (Years)**						**Total**	**Sensitivity Compared to CBNAAT (n=40)positive cases**	**P value applying chi square test**
AGE	**< 1 yr**	**1 – 5yrs**	**6 – 10yrs**	**11 – 15 yrs**	**SPUTUM N=30**	**GA N=20**	**N=50**		
AFB	0	0	1 (14.3)	6 (85.7)	7	0	7 (100)	17.5%	(p>0.05)
CB NAAT	5 (12.5)	18 (45.0)	6 (15.0)	11 (27.5)	23	17	40 (100)	100%	(p<0.05)
PCR	4 (15.4)	11 (42.3)	4 (15.4)	7 (26.9)	17	9	26 (100)	65%	(p<0.05)
Culture	2 (10.0)	9 (45.0)	4 (20.0)	5 (25.0)	13	7	20 (100)	50%	(p<0.05)

Liquid culture was positive in 40% (n = 20) samples. Among sputum samples (n = 30), 43.3% (n = 13) were culture positive, and among gastric aspirates (n = 20), 35% (n = 7) were culture positive (Table 1). Among the CBNAAT positive cases, 20 cases were liquid culture positive, i.e., 50%, but none of the CBNAAT negative samples were culture positive. For TB diagnosis, Sn, Sp, PPV, and NPV of liquid culture compared to CBNAAT were 50%, 100%, 100%, and 33.3%. By applying the chi square test, the difference of results between CBNAAT and liquid culture was found to be statistically significant ($p<0.05$). PCR targeting IS6110 was positive in 52% (n = 26) patients. Among the sputum samples (n = 30), 56.7% (n = 17) were PCR IS6110 positive, and among the gastric aspirates (n = 20), 45% (n = 9) were positive for PCR IS6110. Among the CBNAAT positive cases, 26 cases were PCR IS6110 positive. i.e., 65%, but none of the CBNAAT negative samples were culture positive. For TB diagnosis, Sn, Sp, PPV, and NPV of liquid culture compared to CBNAAT were 65%, 100%, 100%, and 41.7%. By applying the chi square test, the relation between CBNAAT and PCR test findings was found to be statistically significant ($p<0.05$) (Table 2).

Table 2. Comparison of Rifampicin sensitivity with different test

Type of test	**Rifampicin sensitivity**		
	Sensitive	**Resistance**	**Total**
***LPA* (%)**	18 (81.8)	4 (18.1)	22 (100)
***DST* (%)**	17 (85)	3 (15)	20 (100)
CBNAAT	34(85)	6(15)	40(100)

Among CBNAAT-positive patients, 85% (n = 34) patients were rifampicin-sensitive, and 15% (n = 6) patients were rifampicin-resistant. DST was done in all culture-positive samples and showed the SS pattern (i.e., isoniazid-rifampicin sensitive) in 17 samples and the RR pattern (i.e., isoniazid resistance-rifampicin resistance). LPA was done in all culture and smear-positive samples. (n = 22), and the SS pattern (i.e., Isoniazid sensitive-rifampicin sensitive) was obtained in 18 samples; the SR pattern (i.e., Isoniazid sensitive-rifampicin resistance) was found in 1 sample; and the RR pattern (i.e., Isoniazid resistance-rifampicin resistance) was seen in 4 samples. DST and LPA results were in concordance with the resistant pattern obtained in CBNAAT (Table 2).

Discussion

For the past several years, Xpert MTB/RIF, also known as GeneXpert or cartridge-based nucleic acid amplification testing (CBNAAT), has been used more frequently in the diagnosis of pulmonary tuberculosis in highly endemic and poorly resourced countries like India. Limited studies have been conducted regarding the diagnostic use of this newer technique in a highly endemic country like India. Though there are sufficient studies in adult TB cases, there are very limited studies in the paediatric population. Also, comparative studies on resistance detection by means of conventional and molecular methods in samples of the paediatric population are very few. In gastric aspirate and sputum samples that were smear and culture positive, the sensitivity of CBNAAT was 95.6%, which was similar to that reported in fresh clinical samples. As expected, the sensitivity of CBNAAT was superior to that of smear microscopy ($p = 0.0001$). Performance of CBNAAT has been previously evaluated mostly on sputum samples collected from adult TB patients (7–10).

Of the 50 children in the current study, 50% were between the ages of 0-5, 26% were between the ages of 11-15, and 24% were between the ages of 6-10 years. Similarly, Anshu et al. [11] noted 47.6% of patients under the age of five, while Raizada et al. (12) reported 28.9% of patients in the 0–4 age range.

A study by Singh et al. [13] included 403 children under the age of 14, with a median age of 10. Males (56%) dominated the current study with a male-female ratio of 1.2:1. Similarly, male patient predominance was present in the study conducted by Anshu et al. (11) (67% male, M:F ratio 2.1:1) and Raizada et al. (12) (54.7%). However, in the study of 403 children, Singh et al. [13] observed a female (58.2%) predominance.

According to the current study, 80% of patients had a positive contact history, and 98% of patients were malnourished. In the Anshu et al.(11) study, however, only 18.4% of the patients had a contact history. Of the drug-resistant TB patients, Raizada et al. [12] observed that 79.6% had a positive contact history with TB or DR-TB.

The CBNAAT machine is easy to operate, however, and is a little dependent on the user's skills. Though a one- to two-day training program can easily train technicians or routine users to handle CBNAAT. This method yields results within 90 minutes. Concerns about contamination and biosafety are also minimised as compared to AFB microscopy and culture techniques. RIF resistance and M. tuberculosis can be detected simultaneously by CBNAAT in less than two hours, giving it a quick turnaround time. In the current investigation, the Mantoux test turned positive in 78% of the patients, AFB microscopy found MTB in 14% of the patients, liquid culture gave positive results in 40% of the patients, and CBNAAT detected MTB complex in 80% of the patients. Anshu et al. [11], however, reported that 13% of patients had positive mantoux tests, 27.7% were culture positive, 18.9% of patients had MTB detected by AFB microscopy, and 26.4% of the samples only had positive CBNAAT results. In 144 out of 205 lung specimens, Swojanya et al. [14] detected MTB in CBNAAT, while sputum

AFB was able to detect only 108 cases (52.68%), as opposed to 144 (70.24%).

Of the 109 sputum smear-positive patients, CBNAAT confirmed MTB in 108 of them and in 36 of the 96 sputum smear-negative cases. Among 8,370 paediatric presumptive TB and presumptive DR-TB cases between April and November 2014, Raizada et al. [12] discovered that TB detection rates were twofold greater with CBNAAT as opposed to smear microscopy. Out of 30 patients, 58.8% tested positive for Xpert MTB, 63.3% tested positive for MGIT culture, and 29.4% tested positive for AFB microscopy, according to research by Shah and Gupta [16].

In this study, gastric aspirate samples (85%) had more pulmonary TB-positive CBNAAT results than sputum samples (76.7%). Similarly, a study by Anshu et al. [11] found that a sample of gastric aspirate/lavage showed higher positive pulmonary TB by CBNAAT (33%) than a sample of sputum (21.4%). According to Singh et al. [13], 24.4% of the samples tested positive for CBNAAT. 34 samples (85%) of the 40 CBNAAT-positive samples in our study were rifampicin sensitive, while 6 samples (15%) were rifampicin resistant. The CBNAAT results also showed concordance with the LPA and conventional DST results. Anshu et al. [11] reported that out of 105 CBNAAT-positive individuals, 5.7% of them were rifampicin resistant and 94.3% were rifampicin sensitive. Among the 677 MTB-positive CBNAAT samples, Raizada et al. [12] reported 11% of samples were resistant to rifampicin. Rifampicin resistance was detected in 55% of patients among positive Xpert MTB samples, according to research by Shah and Gupta [16].

In the current study, the Sn, Sp, PPV, and NPV values of AFB microscopy were 17.5%, 100%, 100%, and 23.3%, respectively, for tuberculosis diagnosis when compared to CBNAAT. Nonetheless, Anshu et al. [11] reported that the ZN smear's Sn, Sp, PPV, and NPV values in reference to culture were, respectively, 39.09%, 88.85%, 57.33%, and 79.19%. It was clearly evident that Sn, Sp, PPV, and NPV values of AFB microscopy were very poor for diagnosing MTB in a sputum/gastric aspirate sample. CBNAAT would divert treatment burden away from “false cases” to “true” smear-negative TB cases, thereby reducing treatment costs and toxicity in individuals who do not actually have TB while improving treatment accuracy and cost-effectiveness. It also helps identify true TB-negative patients, thus contributing to cost savings by avoiding unnecessary treatment.

52% of the cases in the current study tested positive for the IS6110 gene by PCR, while 48% tested negative. When it came to PCR targeting IS6110, none of the CBNAAT-negative subjects tested positive. In the current study, the sensitivity of PCR targeting the IS6110 gene for tuberculosis diagnosis was 65%, specificity was 100%, PPV was 100%, and NPV was 41.7%. Among the patients sputum sample (n = 30), 56.7% of them had positive PCR results, while 43.3% had negative results. While among the gastric aspirate samples (n = 20), 45% of patients turned PCR positive and 55% PCR negative. Thus, the PCR result yield was higher in the sputum sample than gastric aspirate. There

are no studies yet comparing PCR IS6110 and CBNAAT in paediatric pulmonary samples.

One patient in the current study was positive for HIV. ATT was initiated for the samples that turned positive on CBNAAT. CBNAAT negative cases were considered for alternate diagnosis; one had bronchiectasis, one had bronchial asthma, and three others had latent TB infection. In this study, patchy opacities in the lung parenchyma were observed in 34% of cases and hilar lymphadenopathy in 46% of cases on chest roentography. In a study by Boloursaz et al., hilar lymphadenopathy, with or without lung parenchymal involvement, was the most common finding (15).

Conclusion

Around 17.5% were positive on AFB Ziehl Neelson staining among the n = 40 CBNAAT-positive patients; however, the AFB smear was negative in all CBNAAT-negative cases.

Merely 20 cases, or 50%, had liquid culture positive results out of the CBNAAT negative samples; none showed culture positive results.

Among the 22 samples in which LPA was done and TB bacilli detected, CBNAAT was also positive.

DST and LPA results were in concordance with the resistant pattern identified on CBNAAT.

In 52% of CBNAAT-positive samples, PCR IS6110 was positive; in all CBNAAT-negative cases, it was negative. Clinically, among the patients who were negative on CBNAAT, five responded well to antibiotics, two had an alternate diagnosis, and the remaining three were given INH prophylaxis. On follow-up, none of them developed active tuberculosis.

Accordingly, the results strongly suggest that CBNAAT of sputum/gastric aspirate is 100% specific and very sensitive for diagnosing paediatric pulmonary tuberculosis cases and detecting resistance.

Conflict of interest

The authors declare that they do not have conflict of interest.

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ORIGINAL ARTICLE

A Study on Awareness and Willingness for Eye Donation Among Health Care Professionals in a Tertiary Care Teaching Hospital

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Abstract

Background: According to WHO Globally at least 2.2 billion people have a near or distant vision impairment. In at least 1 billion or almost half of these cases, vision impairment could have been prevented or has yet to be addressed. Corneal opacity is the major cause of vision loss and blindness after Cataract and glaucoma. By donating eyes after death, a corneal blind person can see again through Corneal transplantation. The objective of the study is to assess medical, paramedical and allied health science students' knowledge willingness and perceived obstacles regarding eye donation, aiming to raise awareness and underscore the significance of promoting the cause. **Materials and Methods:** This study is a cross sectional hospital based study conducted in Chengalpattu Medical college and hospital, Chengalpattu. The study population includes all the health care professionals. The total sample size calculated from the previous study was 400 based on a Venkatapathy Narendran et al. The study was conducted for a period of 6 months. A convenient sampling technique was used in our study. In this study we had included all the Doctors, Paramedical students, MBBS students, Post graduates, Nursing students in Chengalpattu medical college and hospital. **Results:** The majority of respondents (41.25%) are aged 20–30, with 65% being male. Students dominate the study (92%), mainly undergraduate medical (43.5%), while faculty represents only 8%. 73.75% knew eye donation is possible, and 77.5% were aware it occurs only after death. Consent awareness varied, with 87.25% believing friends could consent, while only 15.5% thought children could. Eligibility perceptions differed, with 60.5% considering diabetics eligible, 44.5% believing those with glasses could donate, and 72.5% recognizing the need for HIV/hepatitis screening. **Conclusion:** The study found that 56.75% were willing to donate eyes, 35.75% were not, and 7.5% had already pledged. While 84.9% knew corneas restore vision, 78.3% cited family objections as a major barrier.

Keywords: Eye Donation, corneas restore vision, Awareness

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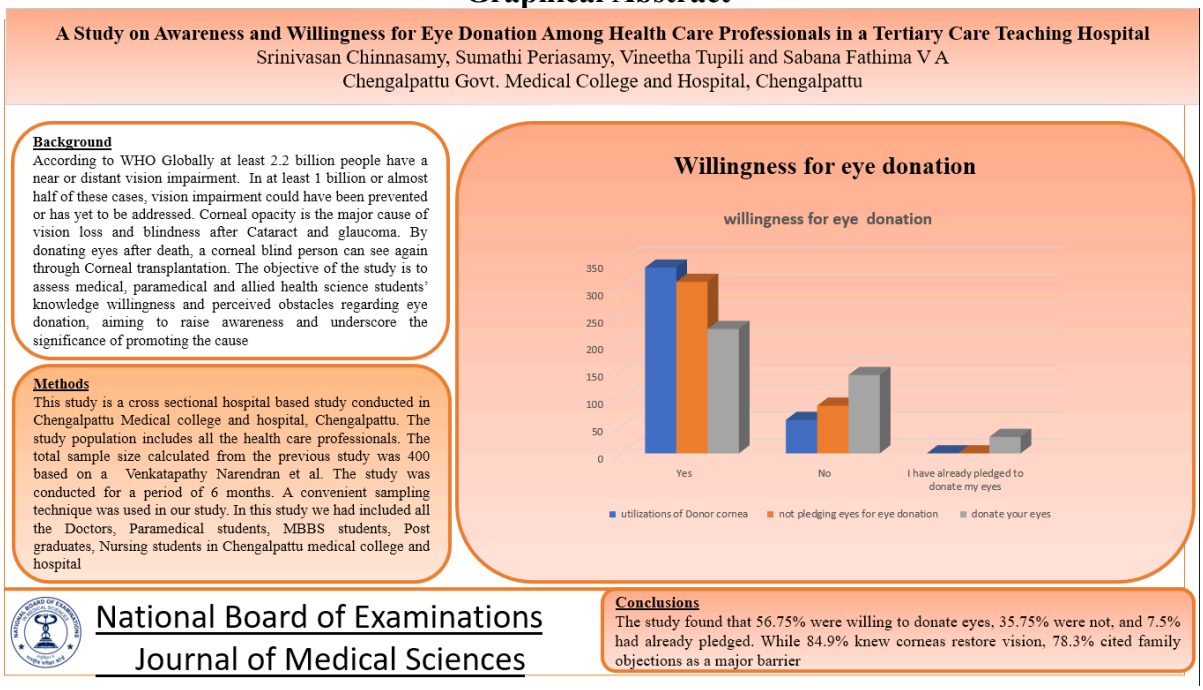
Graphical Abstract



Introduction

Eye donation refers to the process of collecting, preparing, and distributing donated eyes for corneal transplants and research purposes. In underdeveloped nations like India, corneal illness is one of the main causes of blindness. Approximately one million Indians are bilaterally blind, while almost 6.8 million are blind in at least one eye. The only way to lessen corneal blindness is through corneal transplantation. The corneal transplant comes from a willing or driven member of the public. However, corneal donation is dependent on both the willingness of individuals to donate their eyes and the agreement of family members to do so [1]. In India, the annual corneal procurement rate is now a pitiful 22,000. India needs at least two lakh eye donations a year, compared to an average of 45,000. The government has launched a number of initiatives to raise public awareness of the value of eye donation and to promote pledges. One such effort is the Hospital Cornea Recovery effort (HCRP), which aims to recover corneal tissues from voluntary and eligible donors after they pass away in a hospital [2]. Visual impairment or blindness, ranging from partial to total with different visual acuity, occurs from any decline in vision, which is the capacity to comprehend the environment utilising light in the visible spectrum reflected by the objects in the environment.

The World Health Organisation (WHO) estimates that one person becomes blind every five seconds, which is particularly concerning considering that 80% of known vision impairments are either avoidable or treatable. It is projected that 39 million of the 2.2 million visually impaired persons in the globe are classified as blind. Eighty percent of blind people worldwide live in developing nations [3]. It is estimated that the annual global expenses of lost productivity owing to visual impairment from untreated myopia and presbyopia alone are $244 billion and $25.4 billion, respectively. There is only one cornea available for every 70 corneal

recipients globally, according to a new global assessment on eye banking and corneal transplantation. This indicates that there is a significant mismatch between the availability and demand for donor corneas worldwide [4]. The most effective treatment for vision rehabilitation is still corneal transplantation. It is estimated that 2,70,000 donor eyes will be required to perform 1,00,000 corneal transplants annually in India, a fourfold increase over the existing supply of donor eyes, given the accessibility of donor eyes and their consumption rates [5]. A three-tiered community system called eye donation centres, eye banks, and eye bank training centres has been proposed for India in order to address the lack of eye donors. These institutions are in charge of gathering, processing, and distributing tissue, raising public awareness, and providing training and skill development for eye banking staff. EDC is in responsibility for raising professional and public awareness of eye banks. In order to encourage eye donation and harvest corneal tissues, it works with donor families and medical facilities. Additionally, it encourages safe procedures for eye transplants and draws blood for serology [6].

Numerous studies have already been conducted on the general public's knowledge of eye donation. The paramedical and allied health science students at a tertiary care teaching hospital are the subject of this study. They were selected because they are young, highly qualified professionals who have complete access to newspapers, digital media, and other literary sources. They should be more knowledgeable about eye donation than the general population as they will be working as healthcare professionals in the future. Through patient counselling, they will be a viable source for boosting the number of eye donors among patients while they work towards their medical degrees. In order to raise awareness of the significance of supporting this endeavour, the study aims to assess the knowledge, willingness, and challenges surrounding eye donation among students studying paramedical and allied health sciences.

Aims and objective

The aim of the study is to assess medical, paramedical and allied health science students knowledge willingness and perceived obstacles regarding eye donation, aiming to raise awareness and underscore the significance of promoting the cause

Objectives

- To assess the awareness on eye donation
- To find out the willingness for eye donation
- To explore the factors responsible for unwillingness

Materials and Methods

This study is a cross sectional hospital based study conducted in Chengalpattu Medical college and hospital, Chengalpattu. The study population includes all the health care professionals including Doctors, MBBS students, Post graduates, allied health students and nursing students. The total sample size calculated from the previous study was 400. The study was conducted for a period of 6 months. A convenient sampling technique was used in our study. In this study we had included all the Doctors, Paramedical students, MBBS students, Post graduates, Nursing students in Chengalpattu medical college and hospital. Health care

professionals who are not willing to participate in the study or give consent for the study were excluded from our study.

Once the ethical approval obtained from the institutional ethical committee, a detailed self-directed questionnaire pertaining to eye donation was given to medical and paramedical students, post graduates and doctors and asked to mark the appropriate option. The Questionnaire will be made available in both google form or physical copy for convenience. All the data was entered in MS excel sheet and statical analysis will be done using SPSS. Multivariate logistic regression analysis was done.

Results

Table 1. Distribution of study participants as per Demographic profile

	No of participants	%
Age		
Below 20	62	15.5
20 -30	165	41.25
30-40	112	28
40-50	30	7.5
Above 50	31	7.75
Total	400	100
Sex		
Male	260	65
Female	140	35
Total	400	100
Designation		
Faculty		
Professor	4	1
Associate Professor	6	1.5
Assistant Professor	10	2.5
Senior residents	12	3
Total	32	8
Student- domain		
UG Medical-I/II/III/IV/CRMI	174	43.5
PG Medical-I/II/III	28	7
Allied Health Science-I/II/III	84	21
Nursing-I/II/III	82	20.5
Total	368	92

The demographic information of 400 participants in the eye donation awareness research is shown in Table 1. According to the age distribution, 41.25% of respondents are between the ages of 20 and 30, followed by 28% who are between the ages of 30 and 40, and 7.75% who are over 50. In terms of gender, there is a greater representation of men in the study, with men making up 65% of the participants and women 35%. Faculty members make up a minor percentage (8%), with the following professional roles: professors (1%), associate professors (1.5%), assistant professors (2.5%), and senior residents (3%). On the other hand, the study is dominated by students (92%), with undergraduate medical students making up the biggest group (43.5%), followed by nursing (20.5%), allied health science (21%), and postgraduate medical students (7%).

Table 2. Awareness of eye donation

S. No.	Questions	Yes	%	No	%	total
1.	**Is it possible to donate eyes?**	295	73.75	105	26.25	400
2.	**Eyes can be donated only after the donor's death?**	310	77.5	90	22.5	400
3.	**Does your hospital have an eye bank?**	258	64.5	142	35.5	400
4.	**Who has the right to give consent for eye donation?**					
	Parents	253	63.25	147	36.75	400
	Spouse	242	60.5	158	39.5	400
	Children	62	15.5	338	84.5	400
	Relative	276	69	124	31	400
	Friend	349	87.25	51	12.75	400
5.	**Who is eligible for eye donation?**					
	Any age and sex are eligible for eye donation	228	57	172	43	400
	Only above 18 years of age are eligible for eye donation	175	43.75	225	56.25	400
	Can patients who have undergone cataract surgery or other eye surgeries donate eyes	189	47.25	211	52.75	400
	Can a person having diabetes/hypertension donate eyes	242	60.5	158	39.5	400
	Can a person wearing glasses/lens donate eyes	178	44.5	222	55.5	400
	Can a person with corneal diseases donate eyes	184	46	216	54	400
	Can a person with intraocular tumors donate eyes	256	64	144	36	400
	Can a person with glaucoma donate eyes	193	48.25	207	51.75	400

6.	**Is screening of donor blood for HIV and Hepatitis necessary for eye donation?**	290	72.5	110	27.5	400
7.	**Have you counselled anyone for eye donation?**	125	31.25	275	68.75	400

The Table 2 shows awareness of eye donation, 73.75% of participants knew that eye donation is possible, and 77.5% were aware that it can only occur after the donor's death. About 64.5% knew that their hospital had an eye bank. In terms of consent for eye donation, 87.25% believed that a friend could give consent, while 69% identified a relative, 63.25% a parent, and 60.5% a spouse. However, only 15.5% believed that children could give consent. When asked about eligibility, 57% agreed that anyone of any age or sex could donate, whereas 43.75% believed only those above 18 years could donate. Awareness about donation eligibility in certain conditions was varied: 47.25% thought patients who underwent eye surgery could donate, 60.5% believed diabetics and hypertensives were eligible, 44.5% thought individuals wearing glasses or lenses could donate, while 64% thought individuals with intraocular tumors were eligible. Furthermore, 72.5% of participants recognized the necessity of screening donor blood for HIV and hepatitis. However, only 31.25% had counseled someone regarding eye donation.

Table 3. Timeframe for Eyeball removal following death

Knowledge regarding timeframe for Eyeball removal following death	Frequency	Percent
Don't know	60	15
Immediately after death	19	4.8
Within 2 days of death	18	4.5
Within 6 hours of death	303	75.8
Total	400	100

Concerning the timeframe for eyeball removal post-death, 75.8% correctly identified that removal should occur within six hours, whereas 15% did not know the timeframe.

Table 4. Knowledge regarding Eye bank

Knowledge regarding "eye bank"	Frequency	Percent
All of the above	200	50
Place where eyes are collected and stored	184	46
Place where eyes are pledged	12	3
Place where eyes are removed	4	1
Total	400	100

The Table 4 shows the awareness of eye banks was high, with 50% recognizing them as institutions that collect, store, and distribute donated eyes, and 46% identifying them as storage facilities. About 3% knows where eyes are pledged and 1% where eyes are removed.

Table 5. Knowledge regarding Eye Transplantation

Knowledge regarding eye transplantation	Frequency	Percent
I don’t know	58	14.5
Only Sclera	18	4.5
Only the cornea (layer in front of black portion of eye) is used for transplantation	300	75
Whole eyeball is transplanted	24	6
Total	400	100

From Table 5, Knowledge of eye transplantation showed that 75% correctly stated that only the cornea is used for transplantation, whereas 14.5% admitted to not knowing, and 6% mistakenly believed that the entire eyeball is transplanted.

Table 6. Knowledge regarding problems encountered during counselling anyone for eye donation

Knowledge regarding problems encountered during counselling anyone for eye donation	Frequency	Percent
Disfigurement	115	28.8
Infections	35	8.8
Objections by family members	250	62.5
Total	400	100

From Table 6 it had been found that the major barriers to counseling others for eye donation included objections from family members (62.5%), fear of disfigurement (28.8%), and concerns about infections (8.8%).

Table 7. Source of awareness on eye

Source of awareness on eye	Frequency	Percent
Books	8	2
College	20	5
Family and Friends	96	24
Hospital	2	0.5
Internet	190	47.5
Knowledge acquired by education	7	1.75
Magazine	12	3
Medical student	3	0.75

My study	3	0.75
Newspaper	23	5.75
Ophthalmologist	2	0.5
Studies	4	1
Television	27	6.75
Textbook	3	0.75
Total	400	100

The Table 7 shows that awareness of eye donation primarily came from the internet (47.5%), followed by family and friends (24%), television (6.75%), and newspapers (5.75%), with minimal contribution from books, colleges, or ophthalmologists (Figure 1).

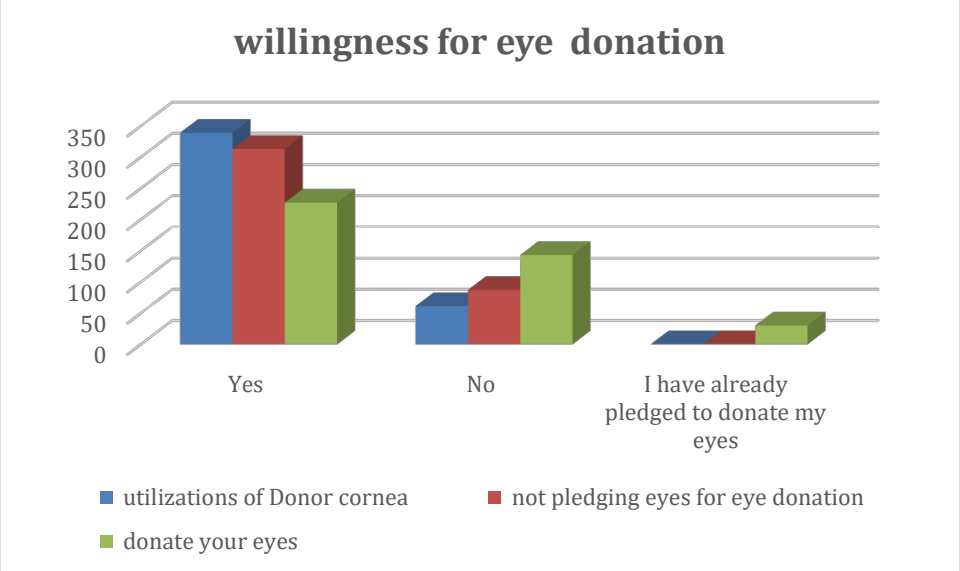


Figure 1. Willingness for eye donation

The findings reveal that 56.75% of respondents expressed willingness to donate their eyes, while 35.75% were not willing, and 7.5% had already pledged their eyes for donation. Regarding the utilization of donor corneas, a significant 84.9% were aware that corneas are primarily used for optical purposes to restore vision, whereas 15.2% were unaware of this application. A key barrier to eye donation was objection from family members, reported by 78.3% of participants, while 21.8% did not face such objections. This highlights the crucial role of family attitudes in influencing

individuals' decisions to pledge for eye donation. Overall, the results indicate that while a majority are open to eye donation, awareness initiatives and family counselling could play an essential role in addressing concerns and increasing the actual rate of eye donation pledges.

The study investigated the participants' awareness and understanding of several facets of eye donation. Regarding the steps that must be taken before the eyeball is removed, 28% of respondents correctly indicated that the donor's eyelids must be closed, and 24% said that the donor's head must be flat. Furthermore, 21.75% of respondents said that calling the closest eye bank should come first, while 15.5% recommended using a cushion to elevate the donor's head a little and 10.75% thought that turning off the fan while using an air conditioner was an essential precaution. Participants' knowledge about National Eye Donation Fortnight varied. The majority of those surveyed (55.25%) accurately recognised that it is observed from August 25 to September 8. Though 17.75% of individuals thought it was celebrated from July 10 to July 24, 17% selected January 26 to February 9, and 10% selected October 22 to November 4, a sizable minority of participants were mistaken. This implies a lack of knowledge on national initiatives encouraging eye donation. About 48% of respondents knew that family members might give a deceased person's eyes without making a previous commitment, but 24.5% had the false belief that this was not permitted. Furthermore, 27.5% expressed uncertainty, suggesting that the public needs to be better informed on the moral and legal implications of eye donation.

Discussion

The study's findings shed light on the current state of awareness, attitudes, and practices regarding eye donation among healthcare professionals and students. A significant majority (73.75%) were aware that eye donation is possible, and 77.5% correctly understood that it can only occur posthumously. However, only 64.5% knew about the existence of an eye bank in their hospital. This suggests that while general awareness is relatively high, specific institutional knowledge may be lacking. Similarly, a study by Parija et al. [7]. reported a 95.6% awareness rate among participants, though only 51.5% had pledged to donate their eyes, indicating a gap between awareness and actionable commitment.

When considering consent for eye donation, 87.25% believed that a friend could provide consent, followed by relatives (69%), parents (63.25%), and spouses (60.5%). Only 15.5% thought children could give consent. This reflects some uncertainty about consent protocols, underscoring the need for clearer guidelines and education. Regarding donor eligibility, 57% agreed that individuals of any age or sex could donate, while 43.75% believed only those above 18 years were eligible. This misconception aligns with findings from a study done by Kacheri et al. [6] where 66.67% of students were unaware that there is no age limit restricting eye donation.

Knowledge about the utilization of donor corneas was high, with 84.9% aware that corneas are primarily used for optical purposes to restore vision. However, misconceptions persist, as evidenced by a study by Kacheri et al. [6] where 9% of students incorrectly believed that the entire eye was transplanted.

Barriers to eye donation were predominantly due to objections from family members (62.5%), followed by fears of disfigurement (28.8%) and concerns about infections (8.8%). This is consistent with other study by Acharya et al. [8] highlighting that misinformation and concerns about proper utilization of donated tissue are significant impediments to eye donation.

Sources of awareness about eye donation were primarily the internet (47.5%), followed by family and friends (24%), television (6.75%), and newspapers (5.75%). This indicates a shift towards digital platforms as the main channels for disseminating information. Similarly, a study by Pooja et al. [9] found that media was the primary source of awareness among medical students.

Conclusion

While the study participants demonstrated a reasonable level of awareness regarding eye donation, significant gaps and misconceptions persist, particularly concerning consent procedures and donor eligibility criteria. Addressing these issues through targeted educational programs within medical curricula and public awareness campaigns is essential. Emphasizing the role of family discussions and consent, clarifying eligibility misconceptions, and promoting the importance of eye donation can collectively contribute to increased donation rates and help alleviate the burden of corneal blindness. The level of awareness regarding eye donation communicated by ophthalmologists and hospitals to healthcare professionals is below 1%, indicating a critical need for improvement.

Statements and Declarations

Conflicts of interest

The authors declare that they do not have conflict of interest.

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ORIGINAL ARTICLE

Usefulness of Pre-operative CT Scan to Assess Lateral Wall Instability in Trochanteric Fractures

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Abstract

Background: Intertrochanteric (IT) femur fractures are increasingly prevalent, especially in the aging population, necessitating precise diagnostic tools for optimal surgical management. Conventional classification systems using plain radiographs have limitations in accurately assessing unstable fracture patterns, particularly those involving lateral wall deficiency. **Methods:** This prospective, single-centre study (September 2023–November 2024) evaluated the role of preoperative computed tomography (CT) in managing IT fractures with lateral wall involvement. The study included 33 patients (aged ≥55) with unstable lateral wall fractures treated with Proximal Femoral Nail (PFN). Preoperative CT parameters, including lateral wall thickness and fracture morphology, were assessed and correlated with intraoperative findings. **Results:** CT scans significantly altered fracture classification compared to radiographs alone. While 85.7% of fractures were classified as AO 2 on X-ray, CT reclassification revealed 63.6% as AO 2 and 36.4% as AO 3. The addition of CT led to a classification upgrade in 45.5% of cases, enhancing the detection of complex fractures. However, statistical analysis showed a weak agreement between X-ray and CT (Kappa = 0.012, p = 0.854), suggesting that while CT provides additional details, its impact on classification significance remains debatable. **Conclusion:** CT imaging enhances the assessment of intertrochanteric fractures, particularly in evaluating lateral wall integrity and comminution. While its statistical significance remains inconclusive, CT remains a valuable adjunct for improving surgical planning, optimizing fixation strategies, and potentially reducing failure rates in IT fractures.

Keywords: Intertrochanteric fractures, pre-operative CT scan, Lateral wall fractures

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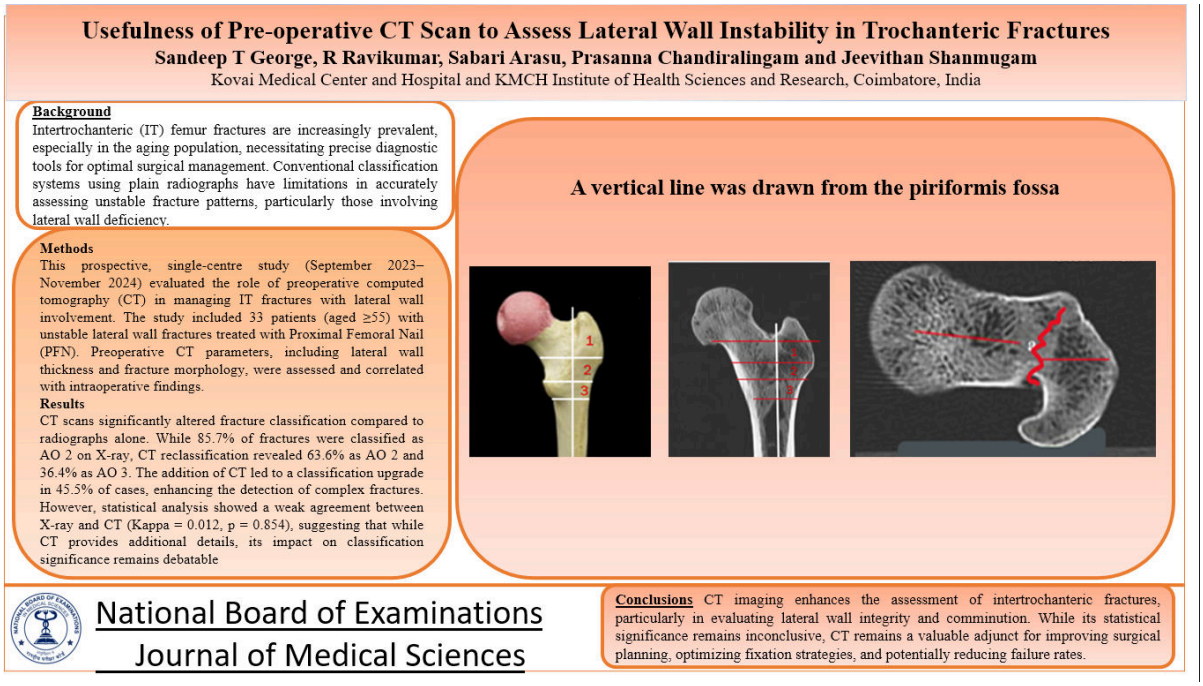
Graphical Abstract



Introduction

Intertrochanteric (IT) femur fractures are becoming an increasingly significant challenge in healthcare, particularly due to the growing aging population [1]. These fractures predominantly affect elderly individuals and necessitate accurate diagnostic tools for effective surgical treatment [2-4].

Traditional classification systems, such as Evans, Jensen, Boyd-Griffin, and AO/OTA, have been used to assess fracture patterns and stability [3,4]. However, these systems often have limitations, particularly regarding the challenges posed by plain radiographs, which may struggle to accurately capture the complex morphology of unstable fractures, especially those with oblique fragments or significant comminution [4-7].

Recent advancements in imaging technologies, particularly computed tomography (CT) and three-dimensional CT, address these challenges. These modalities provide detailed visualization of fracture patterns, enhancing diagnostic accuracy, improving surgical planning, and increasing agreement among observers [8-10]. CT is particularly valuable for assessing crucial aspects such as lateral wall integrity, which is a key factor in determining fracture stability and guiding implant selection [9].

This study emphasizes the benefits of CT imaging in the clinical management of unstable trochanteric fractures, particularly in cases involving lateral wall deficiency. We will analyse the correlation between pre-operative CT findings and intraoperative observations, focusing on comminution and stability. Additionally, we aim to assess the predictive value of CT-based lateral wall measurements on fixation outcomes and introduce a novel approach to fracture mapping. Our ultimate objective is to improve the understanding of intertrochanteric fracture patterns and morphology. By utilizing CT scans, we hope to facilitate more informed surgical

strategies, reduce fixation failures, and enhance outcomes for elderly patients.

Materials and Methods

This prospective single-center study assessed the effectiveness of preoperative CT scans in managing intertrochanteric (IT) fractures with lateral wall involvement. Conducted between September 2023 and November 2024, the study included patients aged 55 and older who underwent intramedullary nailing for IT fractures. To be included in the study, patients needed radiographically confirmed lateral wall fractures within one week of their injury. Patients with pathological fractures, neglected fractures, associated shaft fractures, polytrauma, or those who lost follow-up were excluded from the study.

A total of 51 patients with IT fractures were initially enrolled, of which 33 patients with unstable lateral wall fractures treated with Proximal Femoral Nail (PFN) were included in the final analysis. Upon admission, all patients underwent standardized imaging, including anteroposterior (AP) and lateral radiographs and preoperative CT scans with GE-Optima, 16 Slice.

Parameters assessed in CT scan:

1. In the CT scan, the proximal femur was marked using a vertical line drawn from the piriformis to the Centre of the medullary cavity. Lateral to this line, three horizontal markings were made, one at the level of the innominate tubercle (a), second from the proximal level of the lesser trochanter (b), and third at the distal level of the lesser trochanter (c). This divides the lateral proximal femur into three segments: the greater tuberosity marked as 1, the upper lateral wall segment marked as 2, and the lower lateral wall segment marked as 3. (Figure 1).
2. Lateral wall thickness was assessed in both axial and coronal sections with the above-mentioned lines b and c in their respective sections (Figure 1).
3. Sagittal sections to assess comminution, coronal split, and displacement of the fracture fragment (Figure 1).

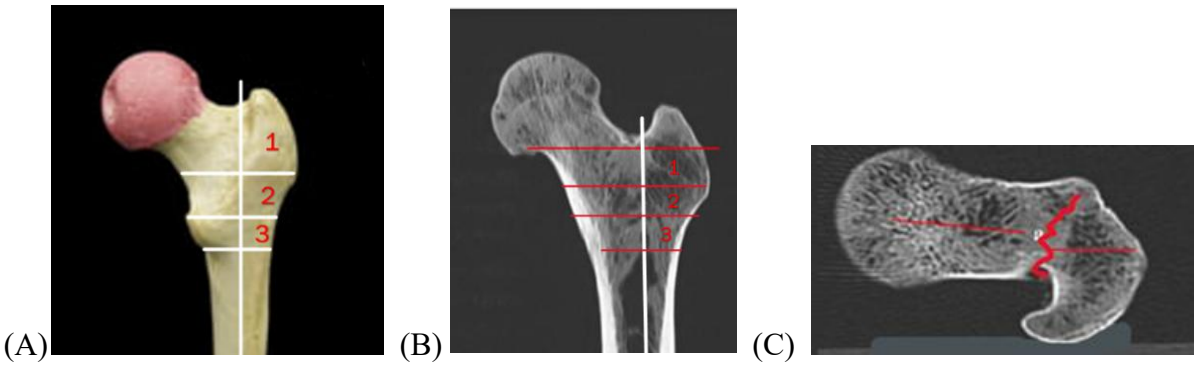


Figure 1. (A), (B) A vertical line was drawn from the piriformis fossa to the centre of the medullary cavity, Lateral to this line, three horizontal markings were made. These markings divided the lateral proximal femur into three segments: **Segment 1:** Greater tuberosity, **2:** Upper lateral wall, **3:** Lower lateral wall. (C) Lateral wall thickness was assessed in both axial and coronal sections with the above mentioned lines b and c in their respective sections.

A musculoskeletal radiologist reviewed CT images, including axial, sagittal, and coronal reconstructions (Figure 2 and 3). Intraoperatively, the operating surgeon assessed the fractures, focusing on lateral wall comminution and fracture morphology. Comminution was defined as fractures with three or more fragments [11].

Anteroposterior (AP) and lateral radiographs obtained were classified using AO/OTA classification, including 31A1 to 31A3. The preoperative CT findings were compared to intraoperative observations to assess fracture stability and lateral wall integrity.

The institutional review board granted ethical approval, and informed consent was obtained from all participants. Data analysis evaluated the concordance between CT imaging and intraoperative findings, particularly regarding lateral wall integrity and its impact on surgical planning and fixation outcomes.

Figure 2. A 59-year-old male patient with AO Type 31 A3.3 left intertrochanteric fracture. (A) pre-operative radiograph, (B) A 3D-CT scan shows a fracture extending into the greater trochanter and neck, along with a multi-fragmented lateral wall fracture. (C) Sagittal sections to assess comminution and coronal split.

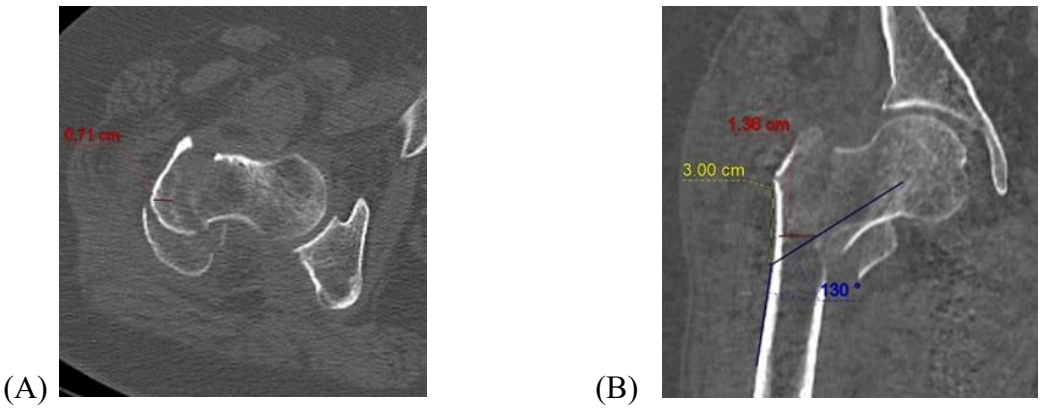


Figure 3. (A) Axial - CT Scan image measuring the lateral wall thickness at the central quadrant as 0.71cm. (B) Coronal - CT Scan image measuring lateral wall thickness, 3cm below lateral ridge along 130-degree neck shaft angle as 1.36cm

Results

When only using X-ray, most of the fractures were classified as AO Classification 2 (85.7%), with a smaller portion being classified as AO Classification 1 (15.2%). No fractures were classified as AO Classification 3 using X-ray alone (Tables 1 and 2).

Table 1. Distribution of study population according to AO fracture and study type

	AO Classification					
Modality	**1**		**2**		**3**	
	F	**%**	**F**	**%**	**F**	**%**
Only X-RAY	5	15.2	28	84.8	-	-
Xray + CT	-	-	21	63.6	12	36.4

Table 2. Distribution of study population according to grade

	FREQUENCY	**PERCENTAGE**
No change	18	54.5
One level upgrade	13	39.4
Two level upgrade	2	6.1

In contrast, when using X-ray combined with CT, 63.6% of fractures were classified as AO Classification 2, and 36.4% were classified as AO Classification 3. This shows that the addition of CT identified fractures that were not captured with X-ray alone (i.e., AO Classification 3).The majority of cases (54.5%) showed no change in the AO classification between X-ray and X-ray + CT, suggesting that CT did not alter the fracture classification in many cases compared to X-ray. A substantial number of cases (39.4%) experienced a level upgrade, meaning that CT provided a more detailed view of the fracture, potentially leading to a more accurate or higher classification. A small proportion (6.1%) experienced a two-level upgrade, indicating that CT contributed significantly in some cases by identifying more severe fractures (Table 3).

Table 3. Association between AO fracture X-ray and AO fracture CT

AO FRACTURE X-RAY	AO FRACTURE CT				KAPPA	P VALUE
	2		3			
	F	%	F	%		
1	3	14.3	2	16.7	0.012	0.854
2	18	85.7	10	83.3		

Kappa Value: A Kappa value of 0.012 suggests an inferior agreement between the X-ray and CT regarding fracture classification. This implies that the results from X-ray and CT are not in substantial agreement, indicating that CT may reveal additional details or a different classification than X-ray alone. P-Value: The p-value of 0.854 is well above the conventional significance threshold (0.05), suggesting that the difference in AO classification between X-ray and CT is not statistically significant. This implies that despite the poor agreement (as indicated by Kappa), the observed differences could be due to random variation rather than a substantial systematic difference (Table4).

Table 4. Association between AO fracture X-ray and AO fracture CT

AO FRACTURE X-RAY	AO FRACTURE CT				KAPPA	P VALUE
	2		3			
	F	%	F	%		
1	3	14.3	2	16.7	0.012	0.854
2	18	85.7	10	83.3		

Discussion

In today's orthopaedic practice, the rising incidence of intertrochanteric fractures has become a significant public health concern [1-4]. Proper management of these fractures during the initial surgical intervention is crucial for minimizing the risk of future revision surgeries, which are often associated with higher morbidity, mortality, increased healthcare costs, and

poorer functional outcomes [4-7]. Therefore, it is essential to thoroughly understand the characteristics of the fracture and to select an appropriate implant for osteosynthesis [7,8].

The failure of treated intertrochanteric fractures depends on various factors, including fracture type, the quality of reduction, fixation stability, the degree of osteoporosis, patient compliance, and existing comorbidities [11-13]. A comprehensive assessment of fracture patterns and geometry is vital for ensuring adequate fixation. In many cases, standard radiographs alone may not provide sufficient detail about the fracture [16-18]. A CT scan can provide a more detailed overview, including the degree of comminution and accurate measurements of various parameters [19].

The recent AO Compendium (2018) has been updated to include an additional variable: lateral wall thickness [17-19]. According to this classification, fractures with a lateral wall thickness of less than 20.5 mm are categorized as A2, while those thicker than 20.5 mm are classified as A1. This classification of fractures is based on both radiographs and CT scans [17]. Variations in different subtypes compared to other studies may arise from previous AO classification codes, which did not consider lateral wall thickness, as well as the involvement of a younger population that experiences higher energy trauma [17-19].

When using dynamic hip screws, both Gottfried and Palm emphasized the critical importance of the lateral wall [1,2]. Hsu et al. cautioned that intertrochanteric fractures with a lateral wall thickness of less than 20.5 mm should not be treated solely with a sliding hip screw [3]. Tan et al. identified superolateral support as a key factor in successful treatment, highlighting its priority over the medial calcar buttress [11]. They also recommended that a CT scan is essential for preoperative planning.

The definition of lateral wall thickness can be somewhat controversial, and its measurement may not be consistent across all radiographs, particularly since rotational angles can influence the values obtained [2-6]. Therefore, measuring lateral wall thickness on 2D CT axial images is recommended, as this method is more reliable than plain radiographs [9-11]. Fixation failure and revision rates in intertrochanteric fractures are often linked to the integrity of the lateral femoral wall, making it a vital consideration for biomechanical decision-making regarding further management. Another significant predictor of surgical success is the presence of coronal fragments [12-14,20,21].

Cho et al. were the first to define coronal fragments in intertrochanteric fractures based on a 3D CT scan study [21]. The impact of CT on fracture classification is notable; the addition of CT imaging has allowed for the detection of AO Classification 3 fractures that were not visible on X-rays. This highlights the additional diagnostic value that CT provides, especially in cases where X-rays might overlook more complex fractures.

Effectiveness of CT in Upgrading Classifications: When CT was added, there was a noticeable shift in fracture classification, with 39.4% of cases being upgraded by one level and 6.1% being upgraded by two levels. This highlights CT's ability to identify fractures in more detail, leading to more accurate treatment planning.

Agreement between X-ray and CT: Despite the differences in classifications between X-ray and CT, the Kappa value

and p-value suggest that the association between X-ray and CT fracture classifications is not strong, meaning that CT provides more detailed and possibly more accurate information. However, the lack of statistical significance ($p = 0.854$) indicates that the differences between the modalities might not be large enough to be considered definitively significant in a clinical setting.

Conclusion

While CT provides additional insights into fracture classification and has the potential to detect fractures that X-ray cannot, the statistical analysis suggests that these differences are not substantial enough to suggest a significant improvement in diagnostic accuracy. However, CT still appears to offer a valuable supplement to X-rays, especially when the classification is unclear or more detailed information is needed.

Statements and Declarations

Conflicts of interest

The authors declare that they do not have conflict of interest.

Funding

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ORIGINAL ARTICLE

Morbidity Pattern Among Elderly in the Village Adopted Under Family Adoption Survey

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Abstract

Background: The world's life expectancy has improved due to new developments in clinical interventions and public health advancements. Morbidity is becoming a bigger problem, especially in developing Asian nations where the population is aging quickly. In a village adopted for survey via a family adoption program in a tertiary care hospital field practice area, we sought to ascertain the prevalence of illness and investigate its relationship with demographic and socioeconomic variables among the older population. **Material & Methods**: The prevalence of morbidities, their types, and their relationships to demographic and socioeconomic factors, a community-based cross-sectional study was carried out with 300 senior citizens selected from a survey on family adoption. Using a systematic pro forma interview, sociodemographic information, blood pressure, diabetes, vision impairment, and other reported diagnosed morbidities were evaluated. The Statistical Package for Social Sciences was used to enter and evaluate the collected data (SPSS). **Results:** The largest percentage (32.9%) of the 300 senior people were in the 60–64 age range. A total of 783 specific morbid disorders were noted among the 300 study participants. Some of the individuals complained more than one morbid condition which is multiple morbidity. the prevalence of cataract and eye related disorders was highest among the older population (63.6%) followed by Hypertension (45%), Stress and psychological illnesses were around 29.3% followed by hearing impairment (23.6%) and musculoskeletal disorders like low back ache and generalized myalgia were around 21.6% among the elderly. **Conclusion:** Researchers and physicians should focus especially on diagnosing morbidity in the elderly due to its high frequency and the population's increasing aging.

Keywords: Morbidity, Family adoption, elderly, quality of life in elderly

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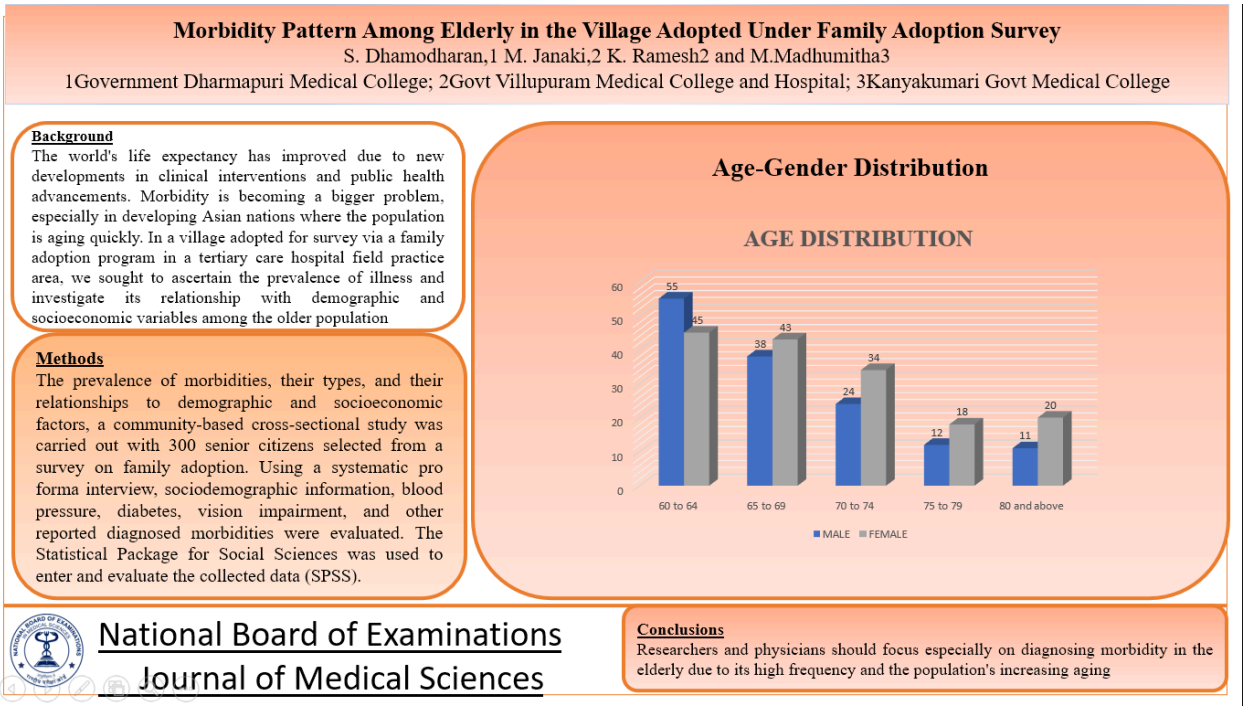
Graphical Abstract



Introduction

The WHO was invited to spearhead the UN Decade of Healthy Ageing, which was announced by the UN General Assembly in 2021–2030. For ten years, governments, civil society, international agencies, professionals, academia, the media, and the corporate sector will work together as part of the UN Decade of Healthy Ageing to promote longer and healthier lives [1].

Globally, the number of adults aged 60 and above is expected to roughly double between 2015 and 2050, reaching around 2.1 billion people [2]. Chronic illness prevalence has become a public health concern in low- and middle-income countries, with major implications for primary and secondary care physicians [3]. The burden of morbidity is rapidly increasing in India due to longer lifespans and increased exposure to risk factors for chronic diseases [4]. Many people refer to India's current health situation as "dismal" or "disturbing." The condition in the majority of the country is concerning, with the exception of a few states that have fared reasonably well, such as Kerala, Goa, and Tamil Nadu. India faces the risk of falling short of the Millennium Development Goals' health targets if current trends continue [5]. The unresolved agenda of infectious diseases, emerging lifestyle-related non-communicable diseases, and unfinished communicable diseases are all part of India's "Triple burden of diseases," which is a result of industrialization and the persistent health status disparity between and within States and Union Territories (due to various economic, social, and political factors) [6].

All countries have tremendous hurdles in ensuring their health and social systems are ready to take advantage of this demographic shift. By 2050, 80 percent of

older people will live in low- and middle-income countries. Compared to earlier times, the population is aging much more fast presently. Between 2015 and 2050, the proportion of adults over 60 will nearly double, rising from 12% to 22% [7].

Common conditions in older adults include diabetes, depression, dementia, chronic obstructive pulmonary disease, chronic neck and back pain, osteoarthritis, cataracts, hearing loss, and refractive errors. As people age, they are more likely to experience several conditions at once. Another feature of older age is the emergence of a variety of complex health conditions called geriatric syndromes. Conditions like frailty, stumbles, dementia, pressure ulcers, and urine incontinence are often caused by a variety of underlying factors.

Material and methods:

In the field practice area of Govt. Dharmapuri Medical College Hospital, 300 elderly people aged 60 and over participated in family adoption survey camps over the course of three months, from June 2024 to August 2024, in the village of Athagapadi in the Dharmapuri district of Tamil Nadu, a state in south India.

Sample size: $n = \frac{Z_{1-\alpha}^2 pq}{d^2}$ N= 266
10% non-responding error 266+26.6 =292.6
So round off 300

The sample size 300 was calculated based a similar study Pathak et al. the expected proportion of elderly 46 with precision of 6 % the level of significance was taken as 5%

The study was cross-sectional. There were 8457 people living in this village as of the 2021 census, 4871 of them were men and 3586 of whom were women. Approximately four Family Adoption survey medical camps were held in order to enhance the village residents' health care. During the study period, the camps were held, offering health education and promotion services in addition to health screening and referral services.

All participants who attended the Health camp and completed the family adoption survey and were 60 years of age or older were included in the study after providing their informed consent. In every instance, anthropometric measurements (height and weight), clinical examination (including blood pressure, eye examination using Snellen chart for refractive error, cataract screening, hearing impairment, and blood sugar examination), and demographic data were documented. To gather demographic data, a personal interview was conducted with each participant in the study. Trained researchers used an electronic weighing scale with a ±100 gram inaccuracy to weigh each patient.

A portable stadiometer was used to measure the height using a traditional method, with an accuracy of 0.1 cm. The body mass index was calculated as weight in kilos divided by height in meters squared. BMIs of ≥ 23 and ≥ 25 were considered overweight and obesity, respectively. Obesity: >25 kg/m^2, Overweight: 23.0-24.9 kg/m2, Normal BMI: 18.0-22.9 kg/m2) [8].

Statistical analysis

A Microsoft Excel spreadsheet was used to enter the acquired data. IBM SPSS

Version V.27 was utilized to describe the distribution of morbidity profiles among the study population, and descriptive tables were created to further explain the findings. Using descriptive analysis, the prevalence and pattern of morbidity among older adults with different background characteristics were reported. The significance of the relationships between sociodemographic factors and morbidity was investigated using the chi-square test and percentages.

Ethical and financial consideration:

This study involved all camp attendees, who were informed of the goal of data collection and gave their signed informed consent. The Institutional Ethics Committee gave their approval to the project. As part of the logistics support, the Institution supplied all the supplies, labor, and other resources required to run the camps (Table 1).

Results:

Table 1. The Study Population's Age-Gender Distribution

Age groups (in years)	Male		Female		Total	
	No.	%	No.	%	No.	%
60- 64	55	38.5	45	27.8	100	32.9
65 - 69	38	27.3	43	27.2	81	27.0
70 -74	24	16.8	34	21.0	58	19.1
75 - 79	12	8.4	18	11.1	30	9.8
Above 80	11	9.1	20	13	31	11.0
Total	140	100	160	100	300	100

Three-quarters (32.9%) of the 300 elderly participants in this study were in the 60–64 age range. A significant percentage of the elderly (11.0%) were 80 years of age or older. There were 160 females (53.1%) compared to 140 males (46.9%) (Figure 1 and Table 2).

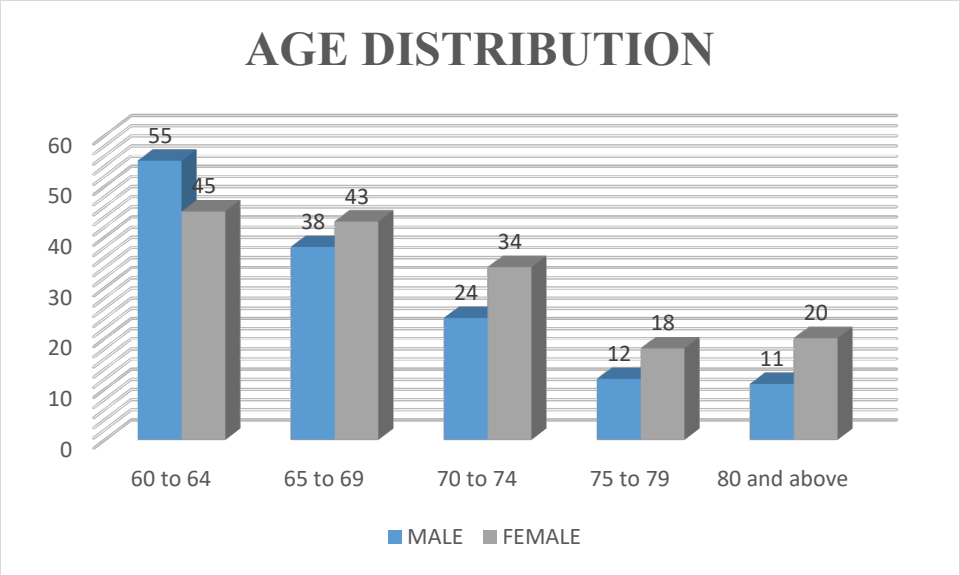


Figure 1: Age-gender distribution

Table 2. Elderly people's educational status

Category	Male		Female		Total	
	No.	%	No.	%	No.	%
Illiterate	69	49.2	134	83.7	203	67.6
Literate (No formal schooling)	29	21	10	6.2	40	13.2
Primary school	30	21.7	14	9.3	44	15.2
High school and above	12	8.4	2	1.9	14	4.9
Total	140	100	160	100	300	100

The survey found that 203 (67.6%) of the elderly were illiterate, 40 (13.1%) were literate but had not attended formal school, and 44 (15.2%) had completed primary school. Just 14 people (4.9%) had completed high school or above. The female illiteracy rate was higher than the male illiteracy rate, which was approximately 83.7% and 49.2%, respectively (Figure 2 and Table 3).

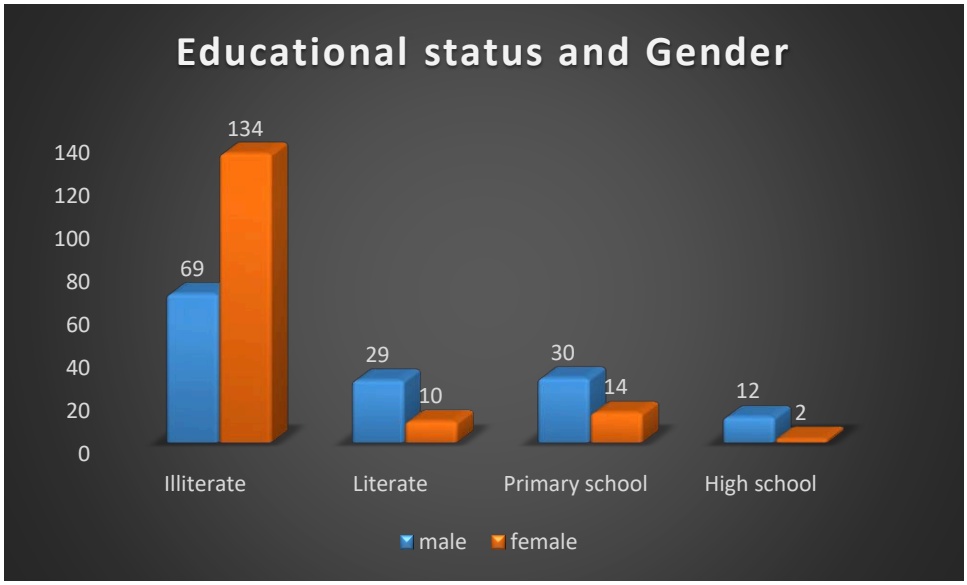


Figure 2. Educational status and gender wise distribution

Table 3. Morbidity Profile and Gender Among the Elderly

S.No	MORBIDITY	Male (n=140) No. (%)	Female (n=160) No. (%)	Total (n=300) No. (%)
1	**Cataract and Refractive error**	88 (61.5)	103(63.6)	191 (63.6)
2	**Hypertension**	72(50.3)	63 (38.9)	135 (45)

3	**Respiratory illnesses**	48(33.6)	55(34.6)	103 (34.3)
4	**Stress and insomnia**	37(26.6)	51(31.5)	88 (29.3)
5	**Hearing Impairment**	24(16.8)	48 (29.6)	72 (23.6)
6	**Low back ache and Myalgia**	34(24.5)	31 (19.1)	65 (21.6)
7	**Diabetes mellitus**	22 (15.4)	18 (11.7)	40 (13.3)
8	**GERD and Loss of appetite**	25 (17.5)	14(8.6)	39(12.8)
9	**Anemia**	14 (10.5)	18 (11.1)	32 (10.6)
10	**Genitourinary disorders**	6 (4.1)	12 (7.4)	18 (5.9)

Amongst 300 study participants total 783 specified morbid conditions were recorded. Some of the individuals complained more than one morbid condition which is Multiple morbidity. The pattern of specific health issues among the elderly population is displayed in the table. It was found that the older population had the highest prevalence of cataract and eye-related disorders (63.6%), followed by hypertension (45%), stress and psychological illnesses (about 29.3%), hearing impairment (23.6%), and musculoskeletal disorders (such as generalized myalgia and low back pain) (about 21.6%). Men were 15.4% more likely than women to have diabetes mellitus (11.7%), with the prevalence being slightly greater among study participants who were female. This study found that women were much more likely than men to have hearing impairment (29.6% vs. 16.8%).

Discussion

The most important health care issue is probably morbidity, which has many negative effects. This study assessed the frequency and correlates of morbidity and disease-specific multiple morbidity in older individuals in India. This study's prevalence of morbidity differs from that of other nations; this could be due to differences in socioeconomic status, the age pyramid, how cases of morbidity are reported, and the health care system. Previous research carried out in different regions of India demonstrated that the prevalence of morbidity varied by state.

One study in South India found that one-third of the population had morbidity [9], while another in Odisha found that fewer than one third of the population had multiple morbidity, with one-third of women and one-fourth of men having multiple morbidities [10]. In Germany, for example, a prior study found that 62% of older adults over 65 had multiple morbidity [11], and in Sweden, 55%

of adults over 77 had multiple morbidity [12]. A study conducted in Ghana revealed that 38.8% of outpatients had several morbidities [14], while a study conducted in Brazil reported that 29% of older individuals had morbidity [13].

Conclusion

This study among elderly has highlighted a high prevalence of morbidity and identified common existing medical problems like cataract, hypertension, respiratory illnesses, insomnia, deafness, hearing impairment, diabetes, anemia and Genito urinary problems. As there is a rapid expansion of elderly population, there is an urgent need to develop and promote geriatric health care services in the developing countries like India and to provide training to health care providers to manage the commonly existing health problems among geriatric in the country.

Statements and Declarations

Conflicts of interest

The authors declare that they do not have conflict of interest.

Funding

No funding was received for conducting this study.

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ORIGINAL ARTICLE

Watch-Antibiotic: Teicoplanin: Usage Practices in Various Departments of a Tertiary Care Hospital, Coimbatore, Western Tamil Nadu

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Abstract

Background: Watch - antibiotics have high potential to develop resistance. Teicoplanin is one of the antibiotics given under Watch classification in Access, Watch and Reserve (AWaRe), 2023 classification. Aim of this study is to evaluate the usage pattern of Teicoplanin in various departments and the cost of Teicoplanin therapy. **Methods:** Retrospective study was conducted and medical records prescribed with Teicoplanin from Jan 2021 to Dec 2023 were evaluated for their usage pattern. **Results:** Totally 84 case records were prescribed with Teicoplanin during the study period. It was prescribed mostly in Nephrology department (28.57%) followed by General medicine (22.62%) and for genitourinary system (17.9%) infections. Teicoplanin was frequently used for *Staphylococcus aureus* (44 cases & 52.38%) infection. Out of 44 cases of *Staphylococcus aureus*, 36 cases were MRSA. Teicoplanin was used in 100mg, 200mg, 400mg and 600mg doses. Average days of Teicoplanin therapy was 5.95 days. Two different brands of Teicoplanin were used. Among them, cost of brand-1 is 11955.38 INR per patient and brand-2 is 10190.77 INR per patient. Nil adverse drug reactions were reported during the study period. **Conclusion:** Using Teicoplanin as Empirical therapy is not advised. Judicious monitoring is advised to prevent the overuse and misuse of Teicoplanin.

Keywords: Teicoplanin, Drug utilization, Cost analysis

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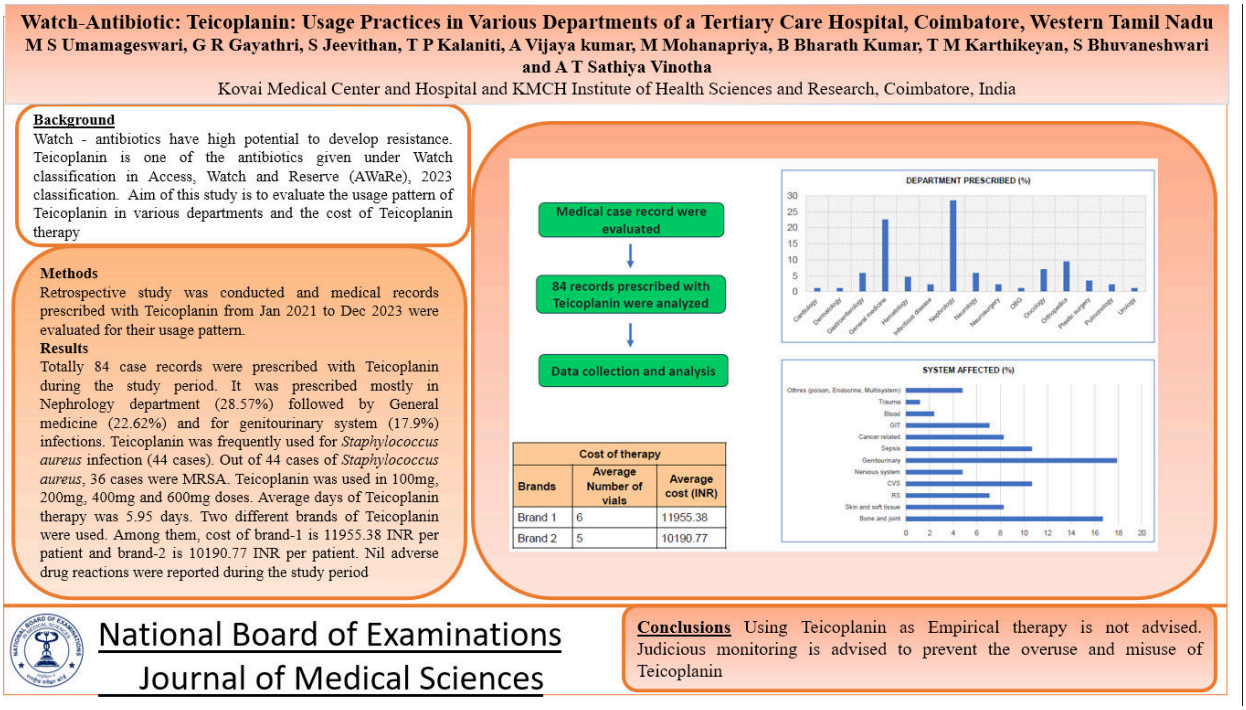
Graphical Abstract



Introduction

As mentioned by National Ambulatory Medical Care, antibiotics are the second leading drugs prescribed by the health care professionals. Antimicrobials are used for the purpose of prevention and treatment. Criteria for selecting an optimal antibiotic for the specific patient include clinical condition, safety, efficacy, contraindications, and cost of therapy. Overuse or inappropriate use of antibiotics may lead to drug interactions, financial burden, drug resistance, and poor treatment outcomes which include loss of life [1].

The World Health Organization classified antibiotics into Access, Watch, and Reserve (AWaRe) in the year 2017 with the intention of increasing the consumption of 'access' antibiotics and reducing the utilization of 'watch' and 'reserve' antibiotics. Watch antibiotics have a broad spectrum of action and have a higher antibiotic resistance potential. As per the 'AWaRe' classification of antibiotics for evaluation and monitoring of use guidelines, Teicoplanin is one of the antibiotics listed under the watch list by WHO in the year 2023 [2,3].

Teicoplanin is isolated from the fermentation broth of a strain of *Actinoplanes teichomyceticus*. It is one of the glycopeptide antibiotics. Teicoplanin is the mixture of five glycopeptide analogues that are closely related. It has a heptapeptide structure consisting of seven aromatic amino acids, distinct carbohydrates d-mannose and d-glucosamine, and an acyl residue that carries various fatty acids [4,5].

It exhibits the advantages of more activity against *Enterococcus,* bears less renal toxicity, and less histamine release than Vancomycin, which is another antibiotic

from the same class. Vancomycin-resistant enterococci (VRE) are also susceptible to Teicoplanin. Teicoplanin is active against gram-positive organisms including Methicillin-resistant *Staphylococcus aureus* (MRSA) and penicillin resistant *Streptococcal* infections. It is used for osteomyelitis, alternative to Vancomycin for surgical prophylaxis, and for multidrug resistant infections [6,7]. It is also active against *Clostridium* species like *Clostridium difficile, Clostridium perfringens, Corynebacterium jeikeium, and* resistant species of *Corynebacterium* group *D2, Peptostreptococcus species, Propionibacterium acnes, and Listeria monocytogenes [8-10]*. Teicoplanin acts by inhibiting cell wall synthesis by binding to the D-ala-D-ala sequence and interfering with the trans-glycosylation reaction [11].

Irrational prescription of Teicoplanin leads to an increase in the incidence of Glycopeptide antibiotic-resistant MRSA, prolonged hospitalization, treatment failure, and higher cost of therapy [12]. This necessitates conducting this study with the aim of evaluating the usage pattern of Teicoplanin among various departments and the cost of therapy of Teicoplanin in a tertiary care hospital, Coimbatore.

Materials and Methods

Materials

A Retrospective cross-sectional study was carried out at Kovai Medical Center and Hospitals, Coimbatore. The study was conducted for 6 months after getting approval from the Scientific Research Committee (SRC/374/2024) and the Institutional Human Ethics Committee (EC/AP/1138/03/2024). Medical records of patients admitted under various departments who were treated with Teicoplanin from Jan 2021 to Dec 2023 were included in the study. Complete enumeration method was used for the selection of medical records.

Inclusion and Exclusion Criteria

The inclusion criteria were medical records of all age groups, either gender, with or without concomitant diseases and who were treated with Teicoplanin. The exclusion criteria were medical records which were not legible and incomplete.

Methods

Anonymized data from the medical records were entered in the Microsoft Excel Worksheet 2019. The data collection proforma contained the sections for demographic profile, history, diagnosis, departments under which the patient was admitted, primary system affected, empirical antibiotics used, culture sensitivity report, resistance pattern, brands of Teicoplanin used, dose, frequency, duration of Teicoplanin treatment, number of vials used, its cost, adverse drug reactions encountered (if any) and treatment outcome. The data collection tool was validated by pilot testing and refinement with few case records and modified according to the feedback obtained from the coinvestigators for its completeness.

Statistical analysis

The data was analyzed using SPSS version 27.0. The numerical variables were represented by mean ± standard error of mean (Mean ± SEM). The categorical variables

were expressed by frequency and percentage [13].

Results

A total of 84 medical records were found to be prescribed with Teicoplanin during the study period. All the medical records fulfilled the inclusion criteria. None of the case sheets were excluded. Demographic characters, medical history, past history, empirical antibiotic usage, sensitivity pattern of microorganisms, usage pattern of Teicoplanin therapy, and outcome were evaluated.

Out of 84 patient medical records, 62 were males (73.8%) and 22 were females (26.2%). 79 patients were from Tamil Nadu (94%), and 5 patients were outside Tamil Nadu (6%). Table 1 explains the age distribution, comorbid conditions, various departments that prescribed Teicoplanin, and specimens collected for microbiological analysis. Figure 1 explains the system affected.

Table 1. Demographic information

Variables (N=84)	Frequency	Percent (%)
Age		
Below 18	2	2.38
18 to 60	46	54.76
Above 60	36	42.86
Comorbidity (Multiple response)		
Diabetes mellitus	39	46.43
Hypertension	29	34.52
Chronic Kidney Disease	10	11.90
Coronary Artery Disease	9	10.71
Nil	17	12.24
Departments		
Nephrology & Urology	25	29.76
General medicine	19	22.62

Orthopedics	8	9.52
Oncology	6	7.14
Gastroenterology	5	5.95
Neurology	5	5.95
Hematology	4	4.76
Plastic surgery	3	3.57
Other departments	9	10.71
Specimen (multiple response)		
Blood	38	45.2
Urine	25	29.8
Pus	24	28.6
ET	1	1.2
Multiple specimen	4	4.8

Other departments:
Neurology, Infectious disease, and Pulmonology – 2 patients each (2.38% each)
Cardiology, Dermatology, and Obstetrics & Gynecology – 1 patient each (1.19% each)

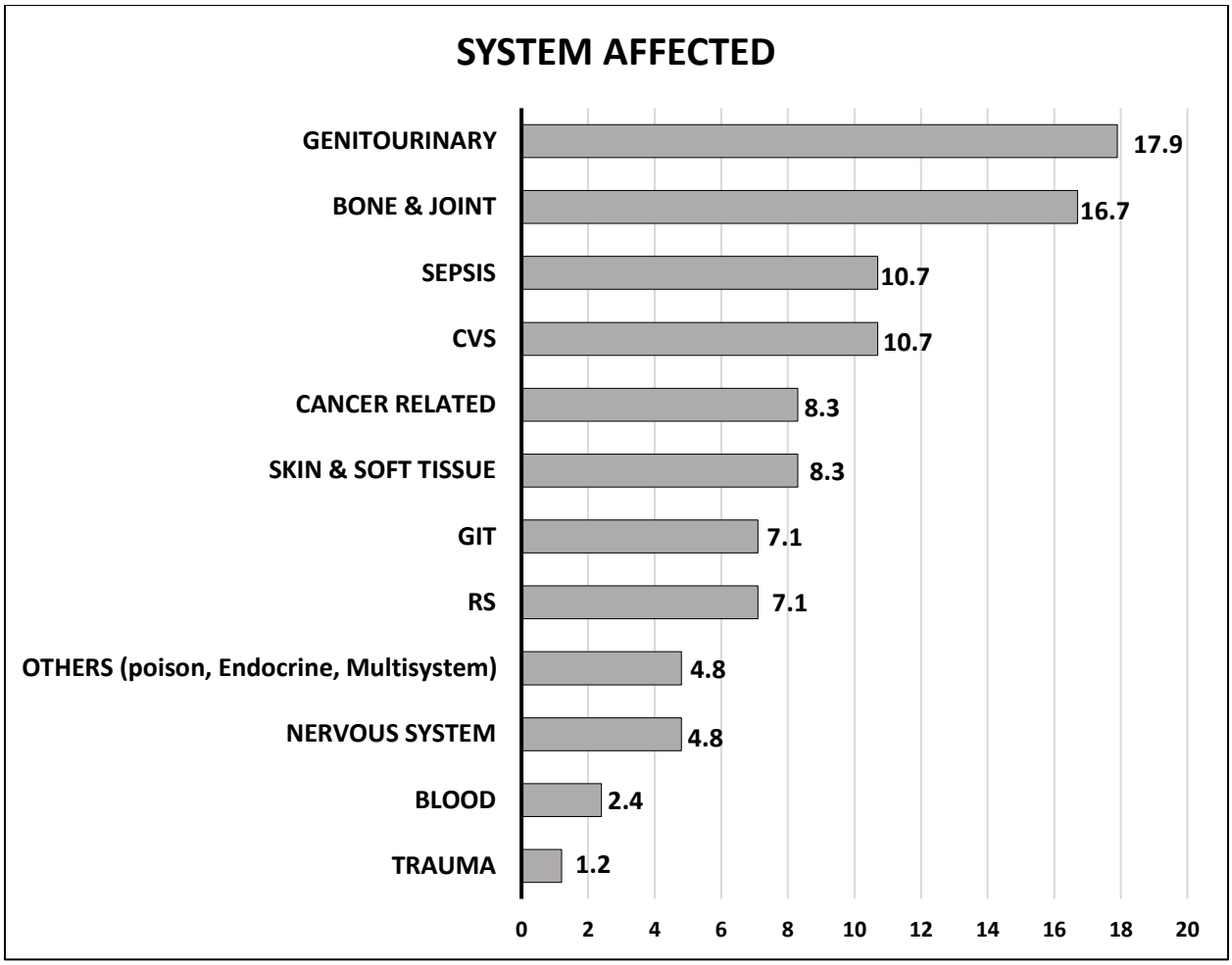


Figure 1. System affected (in percentage)

First Empirical antibiotic was used at the time of admission for those who were suspected of having high-risk bacterial infections and Second Empirical antibiotic was used when patients did not show any response to the first empirical antibiotic before the culture report. After the availability of the culture report and the resistance pattern, Teicoplanin was administered. For 61 patient first empirical antibiotic was administered, and for 12 patients second empirical antibiotic was administered. The percentages of usage of empirical antibiotics are given in Figures 2 and 3. Empirical antibiotics were not prescribed for 23 patients (27.4%). This early antibiotic treatment was chosen based on diagnosis, site of infection, severity of infection, and immune status of the patient. It contributed to the improvement of the disease condition before the identification of specific bacteria and culture-sensitivity testing results.

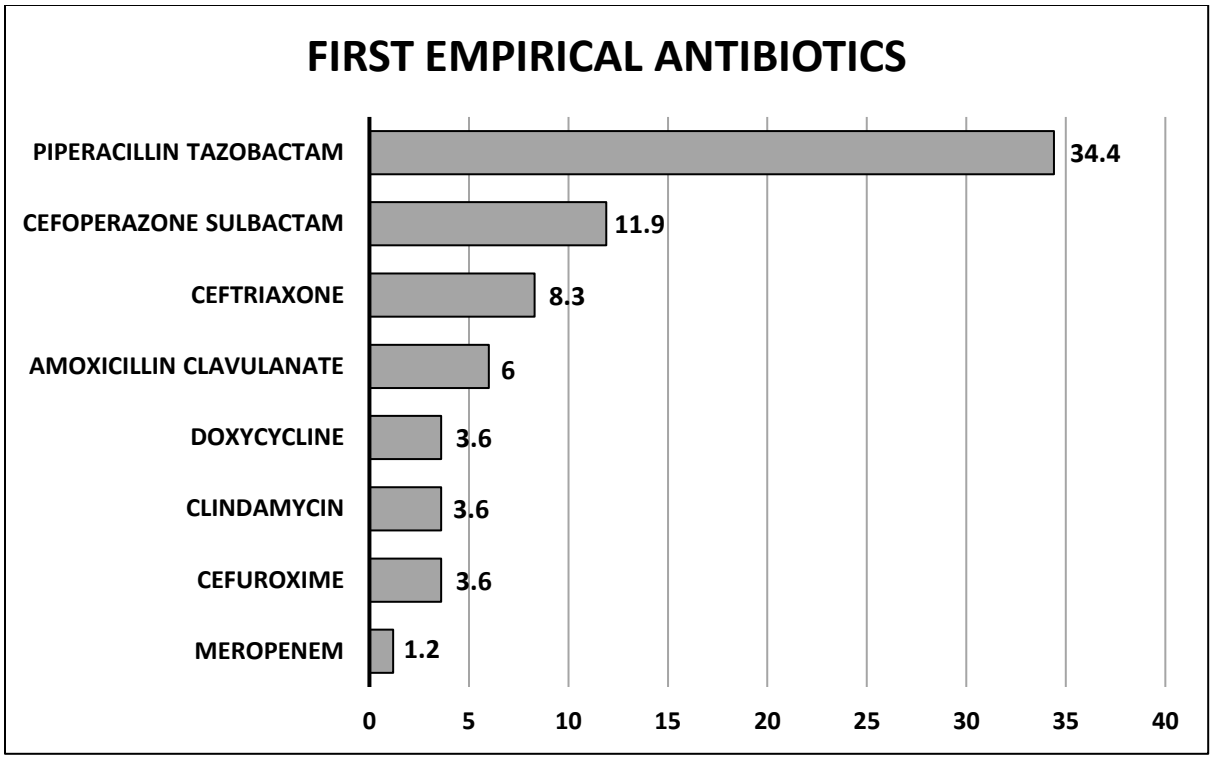


Figure 2. Usage of First Empirical antibiotics (%)

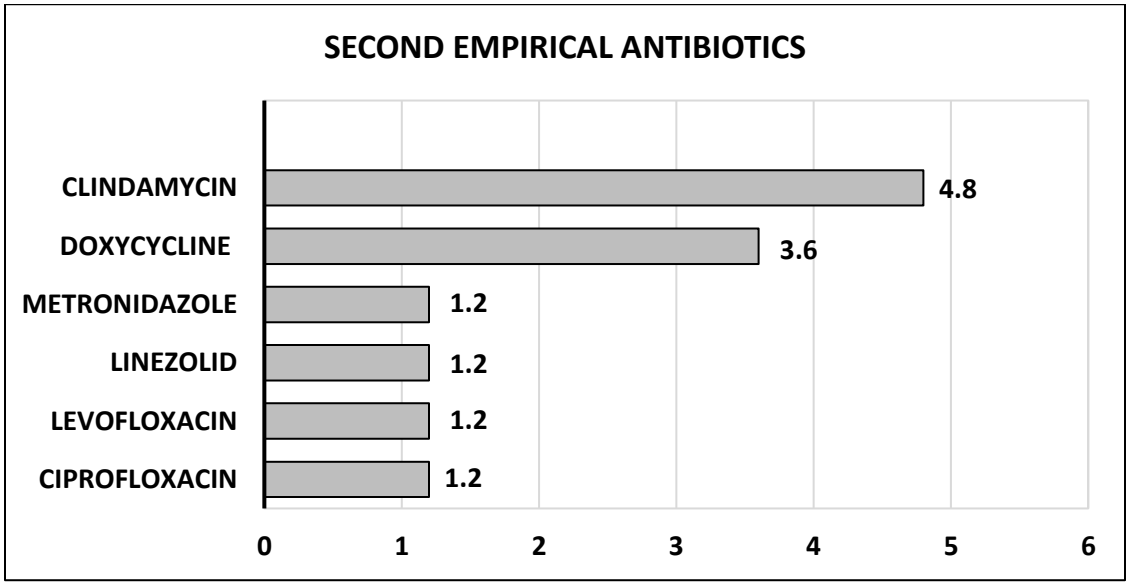


Figure 3. Usage of Second Empirical antibiotics (%)

The first culture specimen was collected from all 84 patients. Second culture specimen was taken for 6 patients and multiples specimens were collected (blood 3.6% and urine 4.8%). Table 2 explains various organisms isolated from culture and their resistant pattern.

Table 3 explains the dose of Teicoplanin therapy and dosing frequency. Two different brands of Teicoplanin were used. The average number of vials of Brand-1 was 6.45±0.36, and Brand-2 was 5±0.82. The average cost of each vial of Brand -1 was INR 1886.74±64.79 and the average total cost of Brand-1 was INR 11955.4±854.35 per patient. The average cost of each vial of Brand-2 was INR 1800.19±391.40, and the average of total cost of Brand-2 was INR 10190.77 ±3734.35 per patient. The average days of therapy with Teicoplanin was 5.95±0.412 days (results are expressed in Mean ± SEM). Daily Defined Dose (DDD) was calculated based on World Health Organization Anatomical Therapeutic Chemical/DDD [14]. Department wise, the DDD of Teicoplanin was 6.47.

Table 2. Organism isolated and Resistant pattern

First culture specimen			
Organisms-1	**Number of cases**	**Resistant pattern**	**Number of resistant cases**
Staphylococcus aureus	44	MRSA	36
		MSSA	8
Enterococcus faecalis	12	MDS	3
Enterococcus faecium	12	MDR	1
		VRE	1
		MRE	1
E coli	1	MDS	1
Elizabethkingia meningoseptica	1	MDR	1
Enterococcus gallinarium	1	VRE	1
Klebsiella pneumoniae	1	PCP	1
Nocardiosis	1	Nil	0

Providencia sps	1	Nil	0
Pseudomonas aeruginosa	2	MDS	2
Culture negative	8	Not applicable	Not applicable
Second culture specimen			
Organisms 2	**Number of cases**	**Resistant pattern**	**Number of resistant cases**
Klebsiella pneumoniae	3	PCP	2
Culture negative	3	Not applicable	Not applicable

MDS – Multi Drug Sensitive, MDR- Multi Drug Resistant, VRE - Vancomycin-Resistant *Enterococci*, MRE- Multidrug-Resistant *Enterococci*, PCP - Potential Carbapenemase Producer, MRSA - Methicillin-Resistant *Staphylococcus aureus*, MSSA - Methicillin- Susceptible *Staphylococcus aureus*

Table 3. Teicoplanin dose and frequency:

Dose of therapy			**Dosing frequency**		
Dose of Teicoplanin	**Frequency**	**Percentage**	**Dosing Frequency**	**Frequency**	**Percentage**
100mg	1	1.2	OD	1	1.190476
200mg	1	1.2	OD	1	1.190476
400mg	77	91.7	OD/Q48H/Q72H	66/10/1	78.5/11.9/1.19
600mg	5	6.0	OD/Q48H	4/1	4.8/1.2

OD – Once daily administration, Q48H - Every 48 hours administration, Q72H - Every 72 hours administration

67 patients received Teicoplanin as monotherapy. In 17 patients, Teicoplanin was used as combination therapy with another antibiotic, which is given in Table 4. Teicoplanin as monotherapy or combination therapy: among 84 patients, 72 patients were discharged alive (85.71%), and 2 patients were discharged against medical advice (2.38%) and 10 patients were declared dead (11.90%). Teicoplanin mono/combination therapy showed an 85.71% cure rate. Nil adverse drug reactions were reported among all 84 medical records.

Table 4. Antibiotics combined with Teicoplanin

Antibiotics combined with Teicoplanin	Dose	Frequency	Percent
Polymyxin-B	7.2 Lakhs unit BD	1	1.2
Amoxicillin+Clavulanate	1.2g TID	1	1.2
Ceftazidime avibactam + aztreonam	2.5g/2g TID	1	1.2
Ceftriaxone	1g BD	1	1.2
Fosfomycin	4g TID	1	1.2
Meropenem	1g TID/500mg TID	6/1 (Total 7)	8.3
Piperacillin and Tazobactam	400mg OD	6	7.2

OD - Once daily administration, BD – Twice daily administration, TID – Three times a day administration

Discussion

Teicoplanin is one of the Watch-group of antibiotics as per the 2023 WHO AWaRe classification. Rational use of antibiotics is an important measure to prevent antibiotic resistance. Usage patterns of antibiotics help the clinicians to foster the rational use of antibiotics at the correct dosage and duration and at less cost [15].

This study showed Teicoplanin was mostly prescribed in the Nephrology department (28.57%), followed by General Medicine department (22.62%). The common system affected was genitourinary (17.9%), followed by bone and joint (16.7%), then CVS (10.7%), and sepsis (10.7%). Piperacillin+Tazobactam (34.5%) was the commonly used empirical antibiotic, followed by Cefoperazone+Sulbactam (11.9%). Masoud Hajialigol et al. studied the irrational prescription of Teicoplanin in a lage academic hospital in Isfahan, Iran. 64% of

Teicoplanin usage was found to be in medical wards, followed by ICU and surgical wards. In 240 cases, Teicoplanin was administered as empirical therapy out of 256 cases [16]. In our study Teicoplanin was administered only after the culture sensitivity report.

Out of 84 cases, common organisms isolated were *Staphylococcus aureus* (44 cases 52.38%), *Enterococcus faecium, and Enterococcus faecalis* (12 cases each, 14.28% each). Out of 44 cases of *Stap. aureus,* 36 cases were MRSA. Teicoplanin was also used for Nocardiosis and *Providencia* infection. Eun A Kim et al. did a study in a university hospital in Seoul, Korea in the years 1999 to 2000. It showed that Teicoplanin was used mostly for surgical wound infection, followed by lower respiratory tract infection. In 69% of cases, MRSA was the organism detected [17]. In our study, 42.9% cases of MRSA was detected.

Sophiya TV et al. evaluated the utilization pattern of Colistin, Teicoplanin, and Tigecycline in a tertiary care hospital in Tamil Nadu. According to their study, Teicoplanin was prescribed for *Staphylococcus* infection, followed by *Enterococcus* and *Streptococcus* infections. It was also prescribed for *Shewanella* infection, *E. coli, Klebsiella*, Methicillin-resistant coagulase-negative *Staphylococci* (MR Cons), *Citrobacter*. In that study, Teicoplanin was mostly used for sepsis, followed by renal diseases, and respiratory tract infections [18]. The results of this study support the part of our work.

Our study found out Teicoplanin was used in 100mg, 200mg, 400mg, and 600mg. 100mg and 200mg were used in the age group of 18 and below and used as once-daily frequency. The frequently used dose was 400mg (91.7%) in above 18 years of age with the dosing frequency of once daily at 78.5%, Q48H at 11.9% and Q72H at 1.2%. The dose frequency was followed according to the status of the renal condition. The average number of days of Teicoplanin therapy administered in our study was 5.95 days. Bahram FF et al. studied utilization evaluation of Carbapenems, Linezolid, and Teicoplanin in a teaching hospital in Tehran, Iran. In their study Among all the drugs compared, 21.6 % of cases received Teicoplanin. The consumed vial/patient was 7.7, the average dose was 394.4, the ratio of prescribed daily dose to DDD was 0.98, and the average duration of treatment was 7.84 days. Teicoplanin was mostly used for respiratory infection (20.68%), followed by skin infection (13.79) and then sepsis (10.34). It was also used for abdominal infection, chest infection, and neutropenic patient (3.44 each) [19].

In 17 patients, Teicoplanin was combined with other antibiotics. In that 8.3% cases used meropenem, 7.2% cases used Piperacillin+Tazobactam. Other drugs combined were Polymyxin-B, Amoxicillin+clavulanate, Ceftazidime avibactam + Aztreonam combination, Ceftriaxone, and Fosfomycin (each 1.2%). According to Eun A Kim et al. study, the mean duration of Teicoplanin usage was 16.5 days, and Teicoplanin was combined mostly with aminoglycosides [17].

Subin et al. studied the incidence of Teicoplanin in non-susceptible *Staphylococcus epidermidis* strains in South Korea between 2016 and 2021. Authors found out that the minimum inhibitory

concentration (MIC) of Teicoplainin was increased from 4mg/L to 8mg/L in 2021. The incidence of Teicoplanin non-susceptible (MIC>16mg/L) is increased in the same year. They concluded that the increased incidence of *S. epidermidis* with Teicoplanin nonsusceptibility (elevated MIC) over the six-year period of study duration [20]. In our study, no *Staph. epidermidis* is isolated in culture.

Christine et al. studied pharmacokinetics of Teicoplanin in renal failure patients. They have compared the pharmacokinetics in healthy volunteers with moderate and severe renal failure patients. They found out that renal failure did not affect the distribution but decreased the renal clearance. They advised that Teicoplanin can be administered every two and three days in patients suffering from moderate and severe renal failure [21]. Our study showed the usage pattern as once in Q48H (11 patients) and Q72H (1 patient) administration in patients with renal diseases.

Two different brands of Teicoplanin were used at our hospital. The average vial count of Brand-1 is 6, and Brand-2 is 5. The average cost of Brand-1 is 11955.38 INR per patient and for Brand-2 is 10190.77 INR per patient. Vázquez et al. compared the cost-effectiveness of Teicoplanin vs Vancomycin as 2nd line empirical therapy in neutropenia patients in 1999. The average cost per patient was $450±180 for the Teicoplanin group and $473±347 for the Vancomycin group. They concluded that there is no statistical difference between Vancomycin and Teicoplanin therapy in the cost-effectiveness of therapy [22].

Simoens et al. studied the cost of therapy for catheter related infection in patients treated with Teicoplanin and Vancomycin in the year 2006 at University Hospitals Leuven. Mean treatment cost was 1,272€ for Teicoplanin and 1,041€ for Vancomycin. They found out that Teicoplanin acquisition cost is higher than Vancomycin. But laboratory monitoring of the therapeutic plasma level of Vancomycin is costlier than Teicoplanin [23]. In their study, the cost of therapy with Teicoplanin is approximately 120907.42 INR, according to the conversion of Euro to INR in Mar 2025. In our study, Combined Brand-1 & Brand-2, the average cost of therapy was 11073 INR.

Batoul et al. did a randomized controlled trial comparing the therapeutic effects of Teicoplanin & Vancomycin among patients who underwent cardiac surgery due to MRSA infective endocarditis. Among 28 patients in the Teicoplanin arm, eight patients developed acute kidney injury and one patient developed thrombocytopenia [24]. In our study, no adverse drug reaction was reported during the study period. The dose was selected depending upon the renal status of the patient may be the reason behind this. Out of 84 patients who received Teicoplanin therapy, 72 patients (85.71%) were discharged alive, 10 patients (11.90%) showed negative outcomes, and 2 patients (2.38%) were discharged against medical advice.

In this retrospective study time taken for the microbial eradication and normalization of infectious markers were not analyzed, and it was a single-centric study. A prospective multicentric study in a larger

population is warranted to evaluate the effective usage pattern.

Conclusion

This study concludes that Teicoplanin was frequently used in the Nephrology department. It is used for MRSA, *Enterococcus faecalis, and Enterococcus faecium* (VRE) infections. The frequently used dose was 400mg OD and the dose was decided depending on the renal status of the patients. The average cost of Teicoplanin therapy was INR 11073, and the average duration of therapy was 5.97 days, with 85.71% successful outcome. Usage patterns of broad-spectrum antibiotics like Teicoplanin must be watched carefully to prevent the development of resistance. Using Teicoplanin as Empirical therapy is not advised. It is mandatory to study antibiotic sensitivity and resistance pattern to prescribe antibiotics like Teicoplanin. Judicious use of antibiotics is mandatory for the reduction of overuse and misuse.

Authors contributions

All authors involved and contributed in study design, data collection, analysis and interpretation of data. They took part in manuscript writing, revising, and gave final approval for publication.

Funding

No funding was received for conducting this study.

Conflicts of Interest

The authors declare that they do not have conflict of interest.

Ethical Approval

This study is approved by the Institutional Human Ethics Committee of Kovai Medical Center and Hospital Ltd. (EC/AP/1138/03/2024).

Data availability

Raw data is available with the corresponding author and provided upon request

Informed Consent Statement

This study did not involve human participants, and therefore, informed consent was not required.

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ORIGINAL ARTICLE

Post COVID-19 Stress and Anxiety Levels Among Undergraduates at a Tertiary Care Hospital, Pondicherry

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Abstract

Background: Stress, Anxiety and Depression are threat indicators which debilitates an individual's life span. These stressors are often undiagnosed or misdiagnosed due to which the person does not know the prevalence of them in his / her own life. **Materials & Methods:** The study was conducted with total of 379 medical students participated in the Department of Forensic Medicine and Toxicology, Mahatma Gandhi Medical College and Research Institute, Puducherry with a self – designed questionnaire mailed as Google Form. The study tool used in this study Peritraumatic Distress Inventory (PDI) and Zung Self - rating Anxiety Scale. The data analyzed and the results were automated accordingly. **Results:** A total of 205 MBBS students participated in the study. Nearly half of the sample had undergone self-quarantine (51.2%). Most of the students had relatives quarantined during the pandemic (68.8%) and were treated for COVID symptoms (68.8%). Peri-traumatic distress was greater among students with self-quarantine history or relative being quarantined, and history of treatment for self or relative for COVID symptoms than students without such history. **Conclusion:** The findings of this study underscore the significant psychological impact of the COVID-19 pandemic on medical undergraduate students, particularly in those who experienced personal or familial exposure to treatment or quarantine.

Keywords: Stress; Anxiety; Pandemic; Mental Health; Depression; Psychological

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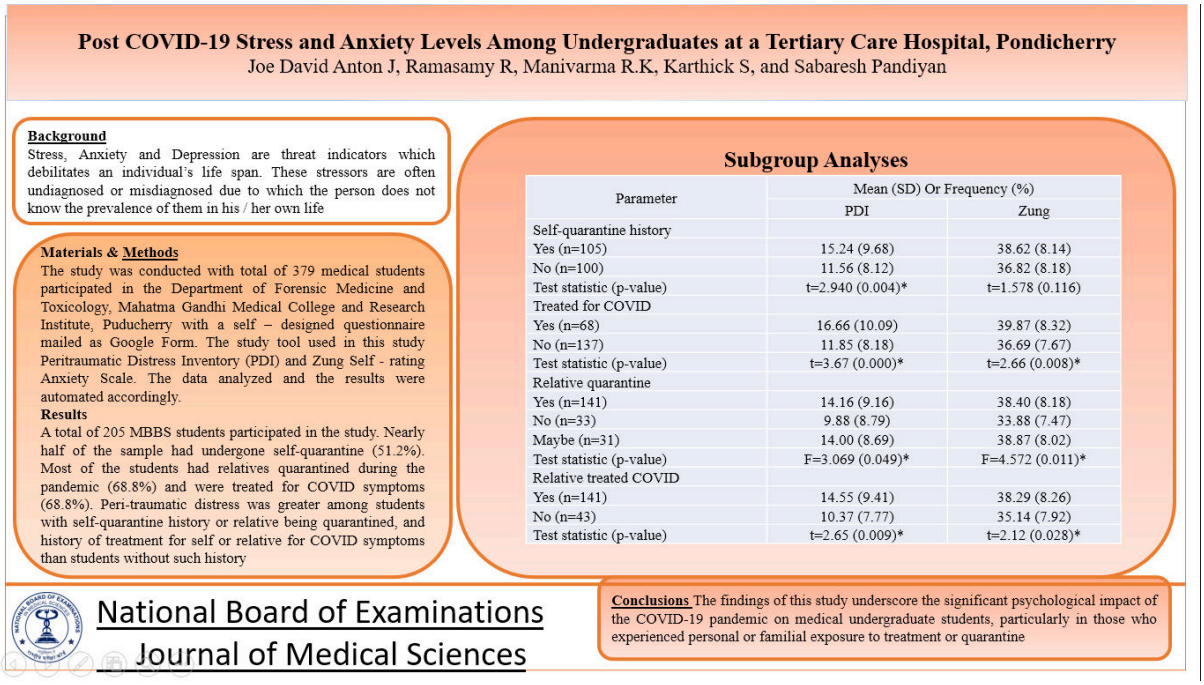
Graphical Abstract



Background

Stressors have become a part of day-to-day lifestyle. The most common is the academic stress. The extent of the stress is directly proportion to a student's performance and health [1]. Research professionals stated, medical education is considered to be more stressful with the highest degree of psychological morbidity [2-7]. With varying stressor's each day and continuous stress responses, the effect of coping mechanisms by an individual are in doubt [8].

These stressors and stress responses creates an imbalance during adolescence, thus affecting the academic, personnel and social life [9]. Failure is adaptation to the environment leads to increased stressors, causing the student to engage in violent activities [10] as a result the students become law breakers at a very young age. This hinders the student to achieve the goals and objectives set by the NMC to be a competent medical profession [10].

Stress, Depression and Anxiety were terms confined to mental illness in old age reported by patients in psychiatric department, but in recent past, it prevails in all ages. Recent statistics on % of Stress, Depression and Anxiety globally and India increased within 5 years. Though some stressors are considered to be unfavorable (inhibition and suppression) for medical students, some are seen to be favorable (promotion and facilitation) in the process of medical education [11]. The process of managing stress and anxiety levels by a medical undergraduate, depends upon how he / she, perceives, responds and copes the stressors.

COVID 19 has surpassed its predecessors from its start in becoming a global threat [12]. The recent pandemic has placed a greater impact on the society by installing fear in everyone's mind. The pandemic (COVID'19) lockdown has made the medical profession to face a new dimension in terms of education and health of the students and the people. Fear has

escalated the stressors affecting the adolescence in their professional carrier each day.[8]

Considering to be a post pandemic (COVID'19) phase, with the rejoining of medical students, this study is conducted to assess the stress and anxiety levels currently experienced by the medical students post lockdown.

Aim and Objectives

- To estimate the burden of post-pandemic distress among medical undergraduate students.
- To estimate the burden of post-pandemic anxiety among medical undergraduate students.
- To identify the psychosocial factors contributing to post-pandemic distress and anxiety among medical undergraduate students.

Materials and Methods

The Institutional Ethical Committee clearance was obtained from the study centre's human ethics committee. The present study was conducted with Medical Students of Health Care Profession by the department of Forensic Medicine and Toxicology in collaboration with department of Psychiatry. It was a hospital-based cross-sectional study with convenient sampling method of 350 study participants (Male – 209 and Female – 141).

Based on the inclusion criteria, undergraduate medical, who were above 18 years, males and females, who were willing to participate were selected. Students who are not willing to participate were excluded. The purpose of the study was informed to the study participants and their participation was approved after receiving the written informed consent. Google Form questionnaire regarding the study was prepared and emailed to the study participants. The filled in answers were requested to send back on said date and time for evaluation.

Study Tool

The study tools used in the study are as follows. 1) Peritraumatic Distress Inventory (PDI) [13] is used for the variable Pandemic-associated distress with 13 items which are self reported and the rating scales are 0 – Not at All True; 1 – Slightly True; 2 – Somewhat True; 3 – Very True and 4 – Extremely True. 2) Zung Self - rating Anxiety Scale [14] used for the variable Anxiety with 20 items which are self reported and the rating scales are 0 – None or a little of the time; 1 – Some of the time; 2 – Good part of the time and 3 – Most or all of the time.

Statistical Analyses

The distribution of continuous variables was depicted using means and standard deviation, and that of categorical variables using frequency and percentages. Subgroup analyses were done within the sample based on gender, domicile, living with parents, quarantine history of self or relative, COVID-treatment history for self or relative, and exposure to social media. Comparison of means of normally distributed continuous variables was done using independent sample t-test and One-way ANOVA. The differences between categorical variables were computed using the Chi-Square test. Data analysis was performed using Statistical Package for Social Sciences (SPSS for Windows, Version 17.0). Statistical significance was set at $p \leq 0.05$.

Results

Socio-demographic, Family, and COVID characteristics

A total of 205 MBBS students participated in the study. Nearly half of the sample were females (52.2%), with majority of the sample hailed from urban domicile (82.4%) and belonged to nuclear families (73.2%). During the pandemic period, a significant majority of the students reported that they lived with parents (94.6%) and had steady income (92.7%). Nearly half of the sample had undergone self-quarantine (51.2%) and revealed that they had not required any treatment for COVID symptoms (66.8%). Most of the students had relatives quarantined during the pandemic (68.8%) and were treated for COVID symptoms (68.8%). Social media (37.6%) was the major source of information regarding COVID during the pandemic (Table 1).

Table 1. Socio-demographic, Family and COVID characteristics of the study sample (N=205)

Parameter	Mean (± SD) Or Frequency (%)
Age (in years)	19.91 (± 1.12)
Gender	
Male	98 (47.8%)
Female	107 (52.2%)
Domicile	
Rural	36 (17.6%)
Urban	169 (82.4%)
Family type	
Nuclear	150 (73.2%)
Joint	43 (21%)
Three generation	12 (5.9%)
Living with parents	
Yes	194 (94.6%)
No	11 (5.4%)
Steady income	
Yes	190 (92.7%)
No	15 (7.3%)
Self-quarantine history	
Yes	105 (51.2%)
No	100 (48.8%)
Treated for COVID	
Yes	68 (33.2%)
No	137 (66.8%)
Relative quarantine	
Yes	141 (68.8%)
No	33 (16.1%)
Maybe	31 (15.1%)

Relative treated COVID	
Yes	141 (68.8%)
No	43 (21%)
Maybe	21 (10.2%)
COVID source information	
Social media	77 (37.6%)
Internet	65 (31.7%)
TV	52 (25.4%)
Print media	3 (1.5%)
Others	8 (3.9%)
PDI Total	13.44 (±9.12)
ZungSelf-rated anxiety scale	37.74 (±8.19)

Subgroup Analyses

The group of MBBS students (N=205) were divided into various subgroups to assess the influence of various socio-demographic and COVID-related characteristics on peri-traumatic distress and anxiety. The analyses revealed that peri-traumatic distress was greater among students with self-quarantine history or relative being quarantined, and history of treatment for self or relative for COVID symptoms than students without such history. Age and gender did not have any effect on peritraumatic distress and anxiety (Table 2).

Table 2. Subgroup Analyses

Parameter	Mean (SD) Or Frequency (%)	
	PDI	Zung
Self-quarantine history		
Yes (n=105)	15.24 (9.68)	38.62 (8.14)
No (n=100)	11.56 (8.12)	36.82 (8.18)
Test statistic (p-value)	t=2.940 (0.004)*	t=1.578 (0.116)
Treated for COVID		
Yes (n=68)	16.66 (10.09)	39.87 (8.32)
No (n=137)	11.85 (8.18)	36.69 (7.67)
Test statistic (p-value)	t=3.67 (0.000)*	t=2.66 (0.008)*
Relative quarantine		
Yes (n=141)	14.16 (9.16)	38.40 (8.18)
No (n=33)	9.88 (8.79)	33.88 (7.47)
Maybe (n=31)	14.00 (8.69)	38.87 (8.02)
Test statistic (p-value)	F=3.069 (0.049)*	F=4.572 (0.011)*
Relative treated COVID		
Yes (n=141)	14.55 (9.41)	38.29 (8.26)
No (n=43)	10.37 (7.77)	35.14 (7.92)
Test statistic (p-value)	t=2.65 (0.009)*	t=2.12 (0.028)*

Discussion

Stress, anxiety and depression among medical students have been reported across the globe. It has been observed that stress levels in preclinical medical students vary widely depending on the context, ranging from 20.9% to over 90% [15]. Various factors such as the academic curriculum, high expectation of the parents, teachers and patients along with time constraints for exploring personal interests have been the most common causes for the psychological morbidity [16]. Meanwhile during COVID 19 pandemic, review of various studies has shown that even in general population, the prevalence of depression was around 20%, anxiety 35%, stress 53%, which was relatively higher [17]. It was also seen that younger age-groups were particularly more vulnerable during COVID 19 reporting greater stress, anxiety and distress compared to middle and older age groups due to loneliness, financial distress and poor resilience [18]. While COVID 19 pandemic led to significant changes in the medical education, including curricular restructuring, examination modifications, and shifts to online learning, all of which likely impacted medical students' health. Given that medical students already experience higher stress levels than general population, the pandemic exacerbated this issue [19]. Various studies have observed that the increase in stress levels among medical students specifically during COVID 19 was due to abrupt academic changes [20], anxiety related to asymptomatic transmission in the community [21].

The present study was done to assess the presence of stress and anxiety among medical undergraduate students during COVID 19 particularly in those who themselves or their close family members were treated or quarantined in view of COVID 19 and the role of psychosocial factors related to the same. The findings indicate that distress levels were notably higher among students who were quarantined or treated for COVID-19 or had relatives undergoing quarantine or treatment. Additionally, anxiety levels were observed to be elevated in students when they themselves were treated for COVID-19 or when their relatives were quarantined or treated.

These findings also align with recent study by Son et al. 2020 [22], which highlighted in 71 % of the students had increase in depressive thoughts, stress and anxiety levels, the most significant effects of the pandemic identified were concerns about personal health and the health of loved ones, followed by problems in concentration, sleep disturbances and decrease in social interaction due to social distancing and concerns about their academic performance. Difficulty concentrating, frequently reported by participants, has been previously linked to reduced self-confidence in students, a factor known to correlate with heightened stress and adverse mental health outcomes. In contrast, review by Lasheras et al. (2020) [23] suggested that anxiety levels among medical students did not rise significantly during the pandemic, possibly due to resilience, effective coping mechanisms, reduced academic pressures, and supportive family environments. So, the impact of COVID-19 pandemic on the prevalence of anxiety and depression remains a debated issue. The extend of psychological distress would depend on an individual's adaptive or maladaptive coping strategy [24]. In our current study, the coping strategies of students has not

been evaluated, but it is observed that medical students who engage in active coping strategies, such as planning and accepting reality, tend to achieve more favourable outcomes compared to those who rely on avoidance based approaches like denial, disengagement or substance use [25]. In short, adaptive coping methods supports better mental health, whereas maladaptive strategies are associated with a higher risk of depression in young adults. Individuals employ various coping mechanisms when faced with challenging situations, and medical students, often unprepared for such demands, may find stress management particularly difficult. Previous studies also highlight the critical role of coping strategies in managing stress, particularly when supported by social factors such as family support and emotional resilience [26]. This would explain the increased levels of anxiety and distress observed in the current student population may, in part, be attributed to disruptions in these supportive factors.

Conclusion

The findings of this study underscore the significant psychological impact of the COVID-19 pandemic on medical undergraduate students, particularly in those who experienced personal or familial exposure to treatment or quarantine. Elevated levels of stress and anxiety were notably prevalent, consistent with global trends observed during the pandemic. Key contributors include concerns about personal and familial health, academic disruptions, and decreased social interactions, all compounded by pre-existing stressors inherent to medical education.

Statements and Declarations

Conflicts of interest

The authors declare that they do not have conflict of interest.

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REVIEW ARTICLE

Global Regulatory Perspectives on Clinical Data Management: A Comparative Review of Various Regulatory Agencies

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Abstract

Background: Clinical trials are conducted with a set of ethical standards, patient safety measures, and scientific scrutiny. Clinical Data Management Systems have evolved over time, shaped by historical milestones, technological advancement, and international harmonization. **Objective:** This paper aims to analyze real-world evidence and data protection approaches provided by Health Canada, Food and Drug Administration and the European Medicines Agency, and their impact on regulating clinical data. It also discusses modernization of regulatory frameworks. **Methods:** This study is based on empirical legislative documents from international regulatory bodies. Literature from PubMed Central, ScienceDirect, and Google Scholar was consulted to analyze Good Clinical Practice, data integrity, and global data synchronization. **Results:** All agencies reviewed have robust frameworks ensuring data quality, safety, and transparency. Developments include GCP guidelines, electronic data standards (e.g., FDA 21 CFR Part 11), public release policies (e.g., PRCI), and harmonization via ICH guidelines. Real-world evidence (RWE) has expanded post-marketing surveillance and regulatory paradigms. **Conclusion:** Despite regional differences, convergence around international standards and digital systems has strengthened global clinical trial ecosystems. Continuous evolution is needed to adapt to new data sources and safeguard patient welfare.

Keywords: Clinical Trial, Data Management, Drug Approval, Good Clinical Practice, Electronic Health Records

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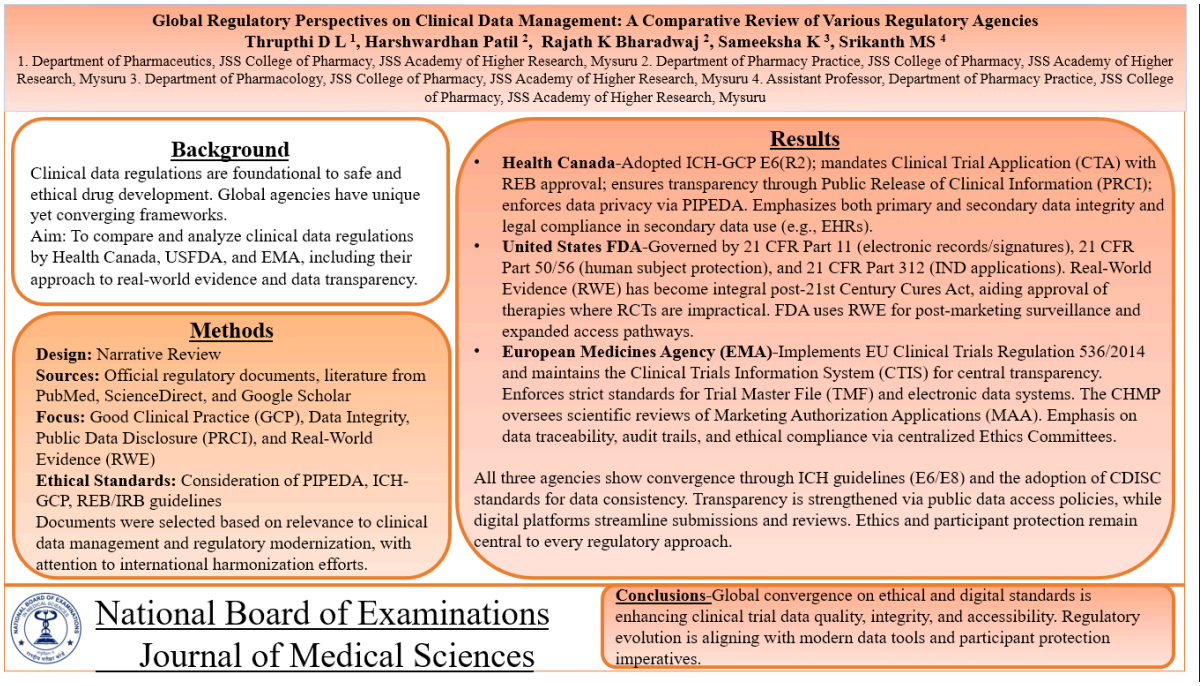
Graphical Abstract



Abbreviations

21 CFR Part 11 – Title 21 of the Code of Federal Regulations Part 11
ADaM – Analysis Data Model
CDISC – Clinical Data Interchange Standards Consortium
CDM – Clinical Data Management
CDMS – Clinical Data Management System
CDSCO – Central Drugs Standard Control Organization
CHMP – Committee for Medicinal Products for Human Use
CTA – Clinical Trial Application
CTIS – Clinical Trials Information System
EDC – Electronic Data Capture
EMA – European Medicines Agency
FDA – Food and Drug Administration
GCP – Good Clinical Practice
ICH – International Council for Harmonisation
IRB – Institutional Review Board
MAA – Marketing Authorization Application
PII – Personally Identifiable Information
PIPEDA – Personal Information Protection and Electronic Documents Act
PRCI – Public Release of Clinical Information
RCT – Randomized Controlled Trial
REB – Research Ethics Board
RWE – Real-World Evidence
SDTM – Study Data Tabulation Model
TMF – Trial Master File
TGA – Therapeutic Goods Administration
USFDA – United States Food and Drug Administration

Introduction

Any approach to encouraging drug development in humans must begin with an understanding of the regulatory conditions governing clinical trials [1]. A clinical trial is designed to produce data to answer a research question, providing evidence to support or refute a hypothesis [2]. Regulatory frameworks extend beyond Good Clinical Practice (GCP); they also provide safeguards that ensure the meaningful and ethical development of new medicines [1].

Clinical Data Management (CDM) is the backbone of modern clinical research, guaranteeing that trial data are complete, reliable, and accurate. Effective CDM goes beyond mere tick-box regulatory compliance; it is essential for ensuring patient safety and maintaining the credibility of trial outcomes.

Lessons from past tragedies, such as the Thalidomide scandal of the 1960s, revealed critical flaws in drug safety protocols. These events reinforced the need for rigorous data oversight throughout drug development [3].

Initially, data were captured using handwritten forms and paper records. In the 1970s, Electronic Data Capture (EDC) systems began automating data entry and reducing clerical errors. By the 1980s and 1990s, standardized digital systems emerged. Organizations like the Clinical Data Interchange Standards Consortium (CDISC) and the International Council for Harmonisation (ICH) were formed to support interoperability and data format standardization.

Modern Clinical Data Management Systems (CDMS) introduced secure storage, audit trails, and automated validation features [4]. Regulatory agencies like CDSCO (Central Drugs Standard Control Organization India), EMA (European Medicines Agency, Europe), and the FDA (Food and Drug Administration United States) now enforce exacting standards for scientific and ethical rigor in trials. Harmonization efforts through the ICH promote global alignment in clinical regulations [5].

1. Health Canada

Evolution of Clinical Data Management Regulations at Health Canada

Health Canada's history with CDM began in the mid-20th century when clinical trials started to take on greater importance. Data management in the early years was unofficial and on paper, with no standardized processes at that point. However, by the late 20th century, regulatory changes were implemented in an effort to strengthen patient safety and improve the quality of data being collected during clinical trials [4]. In Canada, distribution and importation of drugs for human clinical trials are regulated by the Food and Drugs Act and the associated Food and Drug Regulations [6]. In 2001, Health Canada established federal standards for medications used in clinical trials, including adherence to Good Clinical Practice (GCP) guidelines, using Part C, Division 5 of the Food and Drug Regulations under the Food and Drugs Act. Health Canada had already reaffirmed its commitment to participant welfare and clinical trial data quality in 1997 when it adopted the ICH GCP guideline E6(R1) [7].

In order to promote greater effectiveness and calibre of conduct in clinical trials, the ICH guideline was revised to E6 (R2) in 2016. In 2019, Health Canada fully complied with this updated version [7].

Current Regulations and Example Situations

Sponsors must file a Clinical Trial Application (CTA) with Health Canada prior to initiating any clinical trial in Canada. Information about the trial protocol, a risk management strategy, and the qualifications of the participating investigators should all be included in such an application. Every trial must adhere to Division 5 guidelines, Good Clinical Practices (GCP), labelling, and Research Ethics Board (REB) approval. Additionally, sponsors should register trials in WHO-approved registries that are open to the public, such as ClinicalTrials.gov and the Current Controlled Trials Register [8]. Human research is ethically evaluated by the REB, which is required by Health Canada and the Public Health Agency of Canada. It protects research participants by reviewing studies involving biological samples, human subjects, or information pertaining to them [9].

Study Data in Clinical Trials: Regulatory Considerations for Health Canada

Along with the continuous development of clinical trials according to guidelines issued by the regulator, study data are now a part of the regulatory scheme. Study data encompass all the information collected or created in clinical trials, including primary data (specifically collected for the study) and secondary data (derived from external databases or previous studies).

Health Canada's regulatory needs place foremost the collection, processing, and storage of clinical trial data under the Food and Drugs Act and according to Good Clinical Practice guidelines for both data integrity and participant safety.

Sponsors are accountable for high standards of quality, consistency, and completeness for primary and secondary data. Health Canada requires meticulous analysis of each data source to ensure they are accurate, up-to-date, and relevant prior to synthesizing into a study. Additionally, secondary use of data i.e., electronic health records or historical clinical trials—requires extensive analysis to meet the study's individual needs. In cases where secondary data proves insufficient, sponsors must gather primary data to fill in the gaps. Importantly, the use of secondary data must adhere to all legal requirements, particularly those pertaining to participant privacy as specified by the Personal Information Protection and Electronic Documents Act (PIPEDA) [10]. If the research does include referencing external data sources like health records or databases those references must also meet PIPEDA's requirements to keep participant information treated ethically, by law, and in a way demonstrating their rights are respected to their fullest potential [10]. Transparency Through the Public Release of Clinical Information (PRCI).

The responsibility of maintaining clinical data integrity and confidentiality is not only at the process and collection stage but also entails transparency regarding disclosure of this information to the public and the regulatory organizations.

Health Canada openness is reflected in moves like Public Release of Clinical Information (PRCI) that was introduced in March 2019. The move facilitates proactive disclosure of data on approved, unapproved, and withdrawn drug and biologic submissions and Class III and IV medical device applications [11]. Through opening up clinical trial information to the public at time of market authorization,

Health Canada aims to spur public trust, facilitate informed practice by healthcare practitioners and patients, and foster scientific progress. During review, even though the data is maintained under confidentiality, some information can be exempted with a request, so transparency will be maintained under intellectual data protection [12].

2. United States Food and Drug Administration

Key Milestones in FDA Regulatory History

The development of the FDA role during the management of clinical data goes back to early communities that employed medical observation to determine what worked.During the early 20th century, it was trendy to make use of the term "well-controlled" drug trials, which involved the union of clinical and laboratory science. The Federal Food, Drug, and Cosmetic Act of 1938 initially mandated the testing of new drugs for safety prior to sale, enabling the FDA to review pre-clinical and clinical information prior to approval. The law also provided the FDA with the right to delay or prevent the marketing of a drug when additional data were required. After the 1961 international drug debacle, the 1962 Drug Amendments ensured that not just safety, but also "substantial evidence" of efficacy under clinical tests would be required for drug approval. The FDA took on the role of determining what standards were to be employed in drug testing, which fortified the need for "adequate and well-controlled" studies to gain approval [13].

Present Day Food and Drug Administration Regulations

Existing guidelines established by the FDA concentrate on safety, effectiveness, and integrity of clinical information, responsive to evolution in clinical trial design, technology, and international standards. The guidelines provide new guidance on conduct of clinical research with protecting the participants and ensuring integrity of the data.

GCP prescribes internationally agreed standards for the design, conduct, and reporting of trials in relation to the ethical considerations. It is focused on data quality and ethical adherence. With advancements in technology, the FDA published the Electronic Records and Electronic Signatures regulation (21 CFR Part 11) in an effort to provide standards for reliable and valid electronic records and signatures. This was due to the growing application of electronic systems in FDA-regulated activities. Part 11 was enacted on August 20, 1997, and it makes electronic technologies available to use while protecting public heal [14]. It provides the guidelines for the application of controls like audits, system verifications, audit trails, and electronic signatures. In 2003, the FDA issued guidelines, and in 2007, an authoritative version was published to help provide clarification to the use and application of Part 11. These are applicable to most industries like the drug firms, medical device firms, and biotechnology firms [15].

Protection of Human Subjects (21 CFR Part 50) mandates that human subjects provide informed consent, being aware of the risks and benefits of active involvement. The regulation prioritizes participants' rights and welfare in the research process. Institutional Review Boards (21 CFR Part 56) govern the ethical aspects of the clinical trial. They evaluate and approve study protocols to ascertain that the research is

carried out ethically and risks to participants are kept at a minimum. In America, the Investigational New Drug (IND) Application, which is regulated by 21 CFR Part 312, sets forth the procedure for filing clinical trial results on new drugs [16].

Use of Real-World Evidence (RWE) in USFDA Approvals

Real-World Evidence (RWE) originates from traditional registry-based research, which has been around for many decades. However, the term "real-world evidence" only gained widespread popularity in the early 2000s. In 2004, the first important practical example of RWE could be found in the study of lamotrigine for bipolar disorder treatment, which indicated a significant milestone towards RWE potentially being a meaningful contributor to clinical research. In 2016, the passage of the 21st Century Cures Act prompted a major shift indicating the U.S. FDA intended to actively incorporate RWE into its regulatory decision-making processes. This was a tipping point and officially solidified RWE in the chronicles of history as an integral mechanism by which new health care policies and avenues of clinical practice are developed. [17] RWE has since gained traction as an evolving and evolving viable body of knowledge with insights on how effective interventions work in routine clinical use as opposed to tightly-controlled clinical trial settings. RWE facilitates questions about how effective treatments are prescribed, how effective they are billed in routine clinical practice, and ad adverse effects could emerge over time. RWE can be gathered from various types of sources including observational studies, pragmatic trials, electronic health data, and even claims data to provide a full and richer impression of treatment experiences [18].

Where conventional randomized controlled trials (RCTs) are not possible based on ethical or practical limitations, the FDA has increasingly relied on RWE to inform its regulatory actions. Indeed, between 2017 and 2022, RWE was involved in a broad variety of assessments—demonstrating its growing role in the regulatory science [19] ecosystem.

In total, RWE has become a critical resource for the FDA, enabling meaningful alternatives to conventional trials and expanding patient access to cutting-edge therapies—particularly where there is great unmet medical need [20].

3. European Agency Regulation of Clinical Trials

Clinical trials are critical to the creation of new therapies and the continuous advancement of healthcare. In Europe, the regulation of these trials has undergone significant change through the years, all directed at establishing a more harmonized system among EU member states—yet maintaining participant safety and the validity of clinical data. This article examines the historical milestones, current regulatory practices, mechanisms of oversight, and data management procedures employed by European regulatory authorities [19].

Historical Context

The sequence of tragic and dramatic incidents that caused Europe to start thinking about the regulation of clinical trials, is impacted by the thalidomide incident in the 1960s where thousands of babies were born with birth defects due to the absence of rigorous safety testing [20].

In 1965, the countries of the European Union implemented their pharmaceutical law with the adoption of Directive 65/65/EEC. For the first time, it was written that no drug could be offered to the public prior to the approval of the national authority of that country. This was the watershed legislation that cemented public health control by creating regulations that all drugs must be proven safe and efficacious before being approved [21]. Prior to 2001, each EU Member country had its own regulatory and approval process for clinical trials resulting in a fragmented environment that made multinational research difficult to organize and even more difficult to implement. In 2001, the European Commission addressed these problems with the European Clinical Trials Directive (Directive 2001/20/EC) [23].

Clinical Data Regulation and Management

Regulatory control in clinical trials has been shaped by critical historical, ethical, and technological milestones. The global efforts, though fragmented, have worked collectively to catalyze developments in data integrity, transparency, and harmonization of clinical data standards. Such milestones from legislative reformations to electronic innovations are enumerated in Table 1 that presents an integrated overview of regulatory transformations which influenced Clinical Data Management practices globally. Good clinical data management is crucial in order to ensure a credible and dependable result from a clinical trial. To assist with this, the European Medicines Agency (EMA) published the "Guideline on Computerised Systems and Electronic Data in Clinical Trials" specifying detailed guidelines about the following topics:

- The use of computerised systems in the clinical trial process
- The data collection and processing of electronic data
- Data quality, accuracy, and reliability measures
- Provisions meant to protect the rights, dignity, safety, and well-being of trial subjects.

The guideline gives considerable emphasis to data integrity during each step of a clinical trial process from the initial collection of first-hand data to final long-term storage [24].

Additionally, it lays out precise specifications for system validation, accurate data entry, and audit trails to monitor data modifications. These rules are meant to support the integrity of the trial data and participant safety by guaranteeing that electronic records are always accurate, comprehensive, and secure. Furthermore, the European Medicines Agency (EMA) has released final guidelines regarding the structure, administration, and preservation of the Trial Master File (TMF), a crucial part of clinical trial documentation.

According to the guidelines, the TMF must contain all the documentation needed to demonstrate how the trial was carried out and how the data were handled, and it should be easily available for regulators to review. The TMF needs to have a thorough version history, good document identification, and traceability of any updates or modifications, regardless of whether it is stored electronically or on paper. These procedures support the clinical trial process's accountability and transparency [25]. Current Regulations and

the Most Important Laws in European Clinical Trials To safeguard the rights and welfare of those who take part in clinical trials, the European Union (EU) has established a strong regulatory framework [25]. The ICH E6 Good Clinical Practice (GCP) guideline, as implemented by the European Medicines Agency (EMA), gives clear and comprehensive guidance to ensure the protection of human subjects during clinical trials. It sets forth sponsors', investigators', and Ethics Committees' specific responsibilities and makes sure that trial subjects' rights, safety, and well-being are afforded maximum attention at every stage of research [26].

Ethics Committees (Institutional Review Boards)

Within the EU, Ethics Committees have a significant role to play in guiding clinical trials. A trial, prior to commencement, will need to have a favorable opinion from an Ethics Committee regarding whether the ethical issues of a trial are deemed acceptable, i.e., evaluating the informed consent process for adequacy, the risk-benefit and human participant right safeguard. The Clinical Trial Regulation harmonizes the function of and the duties of Ethics Committees in member states and provides consistency in the ethical assessment process [27].

New Drug Application (Marketing Authorization Application)

In the EU, the parallel procedure to the New Drug Application (NDA) in the US is the Marketing Authorization Application (MAA). Pharmaceutical firms are required to file an MAA with the EMA in order to be authorized to market a new drug product.

The filing must contain extensive clinical trial data that confirm the quality, safety, and effectiveness of the product. The EMA's Committee for Medicinal Products for Human Use (CHMP) reviews the filing on a scientific basis and makes a recommendation regarding whether or not the drug should be approved [22].

Principal Legislative Regulations

1. Clinical Trials Regulation (EU) No 536/2014

This directive is a significant move toward harmonizing the way clinical trials are evaluated and regulated across the EU. Its primary aim is to simplify the approval process among member states while maintaining maximum transparency and the highest level of safety standards for trial participants. Perhaps its most prominent feature is the establishment of a centralized EU portal and database, which will make trial information more readily available to regulators and the public.

2. Directive 2001/20/EC – The Clinical Trials Directive

Enacted in 2001, this was the initial EU-wide legislative package specifically aimed at clinical trials. Although most of its provisions have since been updated by the new Regulation (EU) No 536/2014, certain aspects continue to be in place throughout the transitional period. Accordingly, it continues to influence clinical trial practice in some situations, especially for those trials initiated prior to the coming into effect of the new regulation.

3. ICH E6(R2) – Good Clinical Practice (GCP) Guideline

This internationally accepted guideline sets out both scientific and ethical requirements for designing, conducting, recording, and reporting clinical trials in human subjects. Adherence to GCP

guidelines ensures that the rights, safety, and well-being of participants are safeguarded at all times, and assists in ensuring the credibility and integrity of the data produced [26].

These rules and regulations collectively ensure that clinical trials in the EU are conducted ethically, with robust human subject protections, and under stringent scientific standards for the approval of new medicinal products.

Conclusion

The development of European clinical trial regulation reflects a bias towards harmonization of procedure, increased transparency, and protection of participants' safety and rights.

The adoption of the Clinical Trials Regulation (EU) No 536/2014 and launch of the CTIS mark an important step toward a more efficient and harmonized system.

In parallel, the EMA computerized system and data management rules put the role of data integrity and safeguarding participant safety in the era of electronic technology in stark relief.

As the environment of clinical research continues to change, European regulatory authorities remain devoted to promoting an environment conducive to scientific progress alongside the strictest ethical and quality standards.

Table 1. Chronology of Global Regulatory Milestones in Clinical Data Management. This table presents a chronological summary of key global events and regulatory initiatives that have significantly shaped the evolution of Clinical Data Management (CDM). It includes the respective regulatory bodies and the major outcomes associated with each milestone.

Year	Event	Regulatory Body	Impact on CDM
1962	Kefauver–Harris Amendment	U.S. FDA	Required drug manufacturers to demonstrate the effectiveness and safety of their drugs prior to approval [28].
1996	ICH-GCP (E6) Guidelines Adoption	U.S. FDA, EMA, TGA, Health Canada	Established unified standards for designing, conducting, recording, and reporting clinical trials [29].
1997	21 CFR Part 11 Implementation	U.S. FDA	The U.S. FDA Set criteria for electronic records and electronic signatures, ensuring their reliability and equivalence to paper records [30]

2001	EU Clinical Trials Directive (2001/20/EC)	EMA	Harmonized the regulation of clinical trials across EU member states, emphasizing the protection of clinical trial participants [31].
2003	Adoption of CDISC Standards	U.S. FDA, EMA, TGA, Health Canada	Promoted the use of standardized data formats (e.g., SDTM, ADaM) for the submission of clinical trial data [32].
2004	Guidance on Electronic Records and Signatures (21 CFR Part 11)	U.S. FDA	This guidance provided a framework for the use of electronic records and signatures in clinical trials [33].
2014	EU Clinical Trials Regulation (536/2014) Approval	EMA	Aimed to streamline and harmonize the assessment and supervision processes for clinical trials throughout the EU [34].
2019	TGA's Priority Review Process Implementation	TGA	Established an expedited pathway for the evaluation of certain prescription medicines, reducing approval times [35].
2020	Health Canada's Public Release of Clinical Information Initiative	Health Canada	Launched a policy to increase transparency by making clinical information from drug submissions and medical device applications publicly accessible [35].

Abbreviation: FDA: Food and Drug Administration (USA), EMA: European Medicines Agency, TGA: Therapeutic Goods Administration (Australia), CDISC: Clinical Data Interchange Standards Consortium, ICH: International Council for Harmonisation, GCP: Good Clinical Practice PRCI: Public Release of Clinical Information.

Statements and Declarations

Conflicts of interest

The authors declare that they do not have conflict of interest.

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REVIEW ARTICLE

Artificial Intelligence in Gastroenterology: A Comprehensive Review

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Abstract

Artificial Intelligence (AI) is revolutionizing gastroenterology by enhancing diagnostic accuracy and streamlining endoscopic procedures in response to the growing prevalence of gastrointestinal diseases. This comprehensive review explores AI's transformative applications, particularly in gastrointestinal endoscopy, where it addresses critical challenges such as diagnostic 'miss rates' and the overwhelming volume of medical images. Through advanced technologies like Computer-Aided detection (CADe) and Computer-Aided diagnosis (CADx) using deep learning models, AI significantly improves polyp detection rates and reduces miss rates, with reported performances of 95% detection and 50% miss rate reduction. In capsule endoscopy, AI can significantly reduce reading time with improved algorithms to increase sensitivity and specificity in identifying gastrointestinal abnormalities. Additionally, AI plays a vital role in early oesophagal cancer detection by analyzing endoscopic images and distinguishing between dysplastic and non-dysplastic tissues. This review highlights AI's multifaceted benefits to Gastroenterology while noting limitations and future perspectives. As AI continues to evolve and integrate into clinical practice, it can enhance patient outcomes and significantly revolutionize diagnostic approaches in Gastroenterology.

Keywords: Artificial Intelligence, Gastroenterology, Endoscopy, Colorectal Cancer, Diagnostic Imaging

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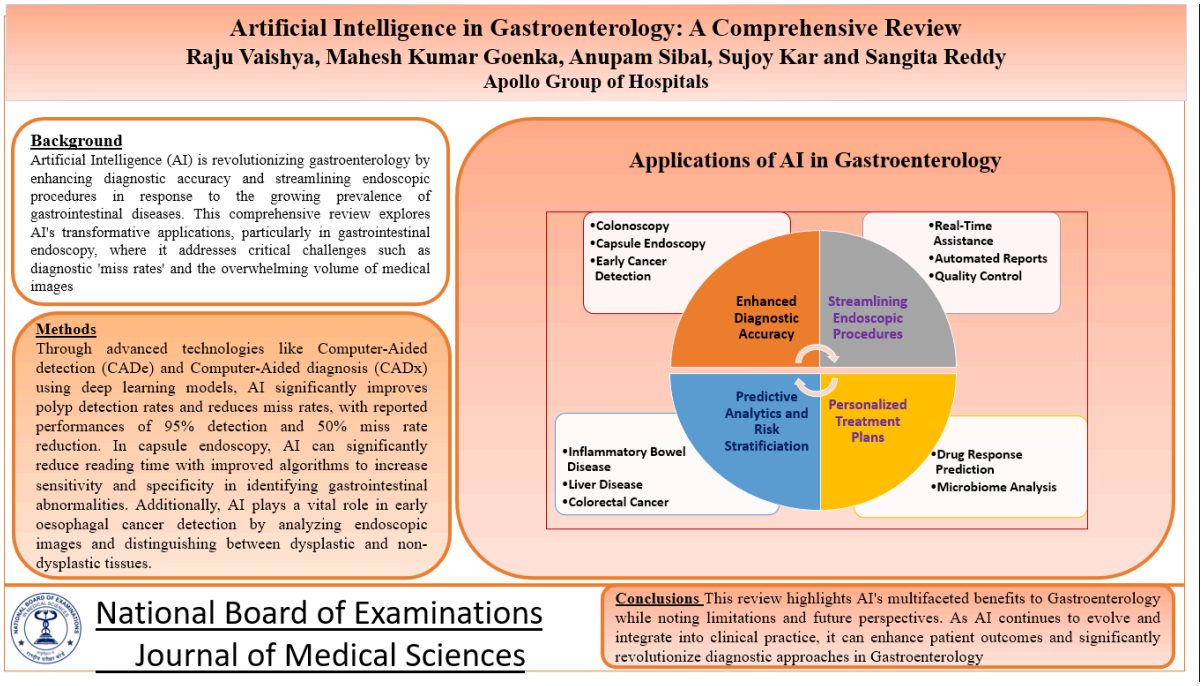
Graphical Abstract



Key Highlights

- AI technologies can enhance diagnostic accuracy and reduce miss rates
- AI automates the review of capsule endoscopy images effectively
- AI plays a pivotal role in the early detection of various cancers and premalignant conditions
- AI-based algorithms can change the approach to a clinical dilemma

Introduction

Gastroenterology has seen significant advancements over the years. With an increasing prevalence of gastrointestinal (GI) diseases, encompassing conditions like inflammatory bowel disease (IBD), colorectal cancer (CRC), and various functional GI disorders, there is a pressing need for practical diagnostic tools and personalized treatment strategies [1]. The barriers to efficient care include complex diagnostic procedures, variations in clinical practice, and errors stemming from human cognition limitations.

In this context, Artificial Intelligence (AI), particularly its branches, machine learning (ML) and deep learning (DL), have surfaced as a transformative tool aimed at addressing these challenges. AI technologies are reshaping how healthcare providers approach diagnostics, treatment planning, and patient management in gastroenterology. By automating routine tasks, providing advanced data analytics, and enhancing diagnostic accuracy, AI is paving the way for its integration into everyday practice [2].

AI is rapidly transforming GI endoscopy, offering significant advancements in detecting, diagnosing, and managing various conditions. As extensively reviewed by Kröner et al. [3] and El Hajjar and Rey [4], current applications leverage AI's capabilities to enhance image analysis. Specifically, AI-powered systems can aid in automating the detection of abnormalities such as bleeding,

ulcers, and tumours, as highlighted by Pannala et al. [5]. While offering immense promise, the widespread integration of AI in colonoscopy still faces challenges and limitations, which have been thoroughly discussed by Hann et al. [6]. Despite these hurdles, a recent consensus by the ASGE AI Task Force, led by Parasa, Berzin et al. (2025), outlines the evolving landscape of AI applications in endoscopy, addresses existing roadblocks, and sets a clear path for further advancing AI's role in gastroenterology, ultimately aiming to improve diagnostic accuracy and patient outcomes [7].

This review provides an update on the role of AI in gastroenterology, highlighting its clinical utility, advantages, and limitations. It concludes with insights into future research opportunities and clinical applications of AI in the field.

Methodology

This review article evaluated the applications of AI within gastroenterology on 20th March 2025; a comprehensive literature search was conducted across multiple databases, including PubMed, Scopus, and Web of Science. Keywords related to "AI," "gastroenterology," "endoscopy," and "diagnostic imaging" were utilized to identify relevant research articles, clinical trials, and systematic reviews. The selected studies were assessed for their methodologies, findings, and implications regarding AI's role in diagnostic accuracy and efficiency in gastroenterological practices. Key themes were extracted, including advancements in Computer-Aided Detection (CADe), deep learning applications in capsule endoscopy, and early cancer detection methods. This synthesis of existing literature provides a nuanced understanding of the current landscape of AI in gastroenterology, highlighting its benefits and limitations.

Results and Discussion

Applications of AI in Gastroenterology (Figure 1)

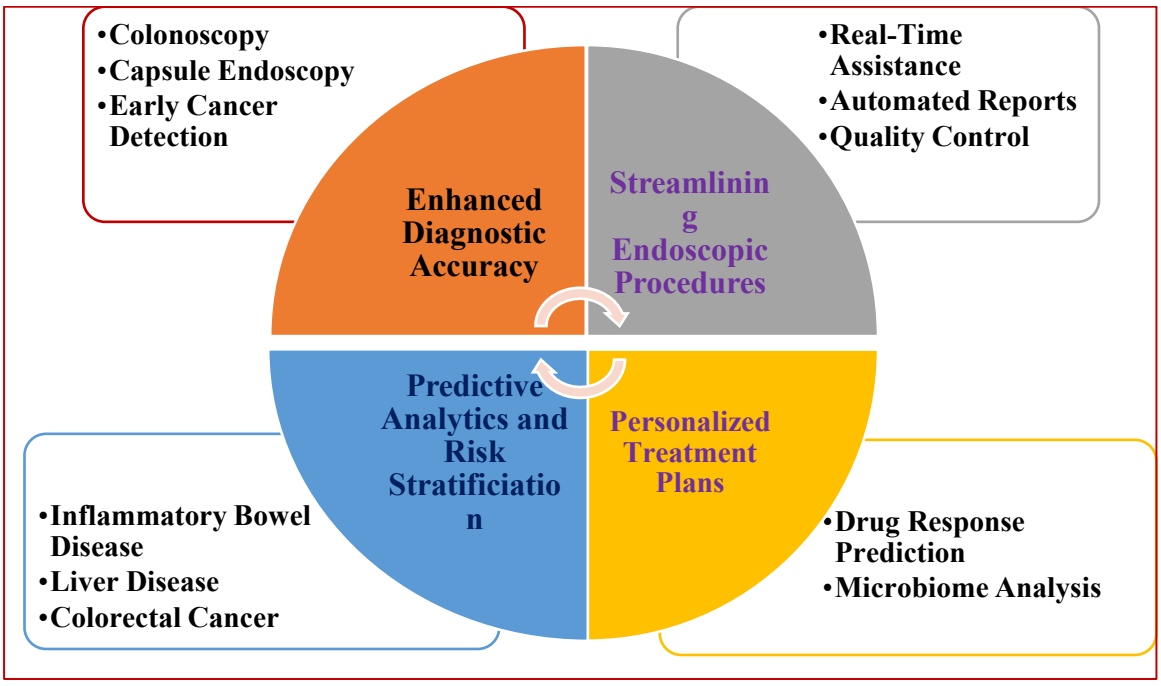


Figure 1. Main applications of Artificial Intelligence in Gastroenterology

Enhanced Diagnostic Accuracy

AI has significantly enhanced gastroenterology diagnostic accuracy, particularly in colon and capsule endoscopy procedures. In the critical area of CRC screening, where timely detection of precancerous lesions is paramount, AI addresses the well-documented issue of endoscopic 'miss rates' (20-30% of significant lesions) through innovative CAD systems. This transformative impact of AI instils optimism about the future of gastroenterology, where diagnostic accuracy is significantly improved [8,9].

AI helps improve adenoma detection rates in a large, asymptomatic screening population across multiple centres [10]. A network meta-analysis of randomized Control Trials (RCTs) compared and found AI to improve adenoma detection compared to other interventions [11]. A recent multicenter (RCT) confirmed the clinical utility of AI for polyp detection during colonoscopy [12]. Furthermore, a multicenter diagnostic study found improved accuracy of AI in upper GI cancer detection, especially for non-expert endoscopists [14].

Colonoscopy

The rapid accumulation of GI endoscopy data, including millions of images and videos annually, presents a unique opportunity for advancing healthcare but poses a significant challenge in managing and utilizing this massive dataset. The sheer volume of data, with 27,000 images from a single 15-minute procedure, highlights the potential for AI and machine learning to extract valuable insights for diagnosis, treatment, and research. The increasing volume of data, while beneficial for AI/ML advancements, poses a challenge to human analytical capabilities, as it is impossible for individuals to process and interpret vast quantities of information effectively. This data deluge creates a bottleneck for researchers and analysts, making extracting meaningful insights and patterns challenging without automated tools. Consequently, gastroenterologists must navigate complex ethical and legal data privacy and ownership issues as AI/ML transforms the field [14].

AI utilizing CADe systems is being investigated to enhance polyp detection during colonoscopy, addressing the issue of missed polyps attributed to human error. Misawa et al. demonstrated CADe's ability to improve polyp detection rates to 95% while reducing miss rates by 50% [15]. These systems shift diagnostics from reliance on human observation alone to a collaborative human-AI approach. Further refining this process, Computer-Aided Diagnosis (CADx) systems classify detected polyps as benign or malignant, with Wang et al. reporting 92% detection accuracy and a 45% reduction in miss rates [16]. Furthermore, DL models, specifically convolutional neural networks (CNNs), have achieved a 94% cross-validation accuracy and an Area Under the Curve (AUC) of 0.991 in real-time polyp detection and localization [17]. The main findings of these studies are summarized in Table 1, highlighting AI's consistent performance in improving endoscopic outcomes.

Table 1. Performance of Artificial Intelligence (AI) Systems in Polyp Detection

Study	Artificial Intelligence System	Polyp Detection Rate	Miss Rate Reduction
Misawa et al. (2021) [15]	Computer-Aided Detection	95%	50%
Wang et al. (2020) [16]	Computer-Aided Diagnosis	92%	45%
Urban et al. (2018) [17]	Deep Learning	94%	48%

Hassan et al., in a systematic review and meta-analysis, reported the good performance of AI in colonoscopy for polyp detection [18]. Byrne et al. also demonstrated the real-time capabilities of deep learning in polyp differentiation during colonoscopy [19].

Capsule Endoscopy

Beyond colonoscopy, AI streamlines *capsule endoscopy,* where the high volume of images traditionally challenges thorough review. Capsule endoscopy presents a unique challenge due to its non-invasive nature and the substantial volume of images it produces, making the review process cumbersome and susceptible to human error. AI technologies can significantly streamline this process, enhancing efficiency and accuracy in detecting GI abnormalities. A significant advancement in the field of AI in capsule endoscopy has been AI's ability to reduce image reading time from 96 minutes to less than 10 minutes [20]. CNNs automate the detection of abnormalities like bleeding, ulcers, and tumours, achieving 96% sensitivity and 94% specificity in identifying GI bleeding (Table 2) [21,22]. This reduces diagnostic delays and alleviates clinician workload, underscoring AI's role in optimizing accuracy and efficiency across gastroenterological diagnostics.

Table 2. Artificial Intelligence (AI) Performance in Capsule Endoscopy

Application	AI Model	Sensitivity	Specificity
Bleeding Detection	CNN	96%	94%
Tumor Identification	ResNet	92%	90%
Ulcer Detection	InceptionV3	89%	91%

CNN-Convolutional Neural Network; ResNet-Residual Network

Early Cancer Detection

AI is also helpful in early cancer detection. Barrett's oesophagus, a precursor to oesophagal adenocarcinoma, necessitates diligent monitoring through endoscopic evaluations. AI systems have been developed to analyze endoscopic images, identifying morphological changes that signify dysplasia or early malignancy [23]. AI algorithms can distinguish between dysplastic and non-dysplastic tissues, guiding clinicians in biopsy procedures and subsequent management [24]. These systems contribute to earlier oesophagal cancer detection, positively impacting treatment outcomes [25]. Cai et al. (2019) developed and validated a deep neural network (DNN) CADe system for early esophageal squamous cell carcinoma (ESCC) screening using white-light endoscopy. The DNN-CAD, trained on over 2,400 images, achieved an AUC above 96% and, in validation, demonstrated high sensitivity (97.8%) and accuracy (91.4%). Notably, when used as an aid, the CAD system outperformed endoscopists, particularly junior ones, and improved diagnostic accuracy across all experience levels. The study concludes that the DNN-CAD system effectively detects early ESCC lesions, potentially reducing missed diagnoses during routine endoscopy [19].

Streamlining Endoscopic Procedures

Real-Time Assistance in Endoscopic Procedures

AI not only aids in diagnostics but also enhances the quality and efficiency of endoscopic procedures. Goenka et al. (2023), in a pilot study, assessed the completeness of esophagogastroduodenoscopy (EGD) using AI analysis of 277 procedures (114 by trainees, 163 by experienced endoscopists). While common areas like the greater curvature of the antrum (97.47%) and the second part of the duodenum (96.75%) were well-visualized, critical areas like the vocal cords (99.28% missed) and epiglottis (93.14% missed) were frequently overlooked. The incisura also showed significant misses (posterior 78.70%, anterior 73.65%, lateral 73.53%). Experienced endoscopists (category B) performed significantly more complete procedures (88.68% vs. 11.32%, $p < 0.00001$). The study concludes that AI effectively evaluates EGD quality and could be valuable in endoscopy training [**26**]. Real-time feedback mechanisms allow the detection of abnormalities instantaneously, improving procedural outcomes. AI systems can guide endoscopic procedures by highlighting areas requiring attention, such as regions with inflammation or bleeding, ensuring that critical findings are not overlooked**.** This emphasis on the role of AI in streamlining procedures reassures the audience about the quality and efficiency of patient care in gastroenterology.

Automated Reporting and Quality Control

Clinicians often face the challenge of time-consuming documentation. AI can mitigate this with automated reporting solutions that synthesize findings from endoscopic evaluations into structured reports, thus reducing administrative workload while enhancing report accuracy [27]. These tools can also facilitate quality control by evaluating colonoscopy metrics, ensuring procedures meet established standards, and reducing the chance of missed lesions [28]. AI can also monitor bowel preparation during colonoscopy, an essential quality parameter for

colonoscopic quality that can impact the diagnosis [29].

Predictive Analytics and Risk Stratification

AI excels at analyzing large datasets to predict disease outcomes and stratify patient risk. Below are some key applications:

Inflammatory Bowel Disease

AI is revolutionizing predictive analytics in gastroenterology by analyzing vast datasets to forecast disease progression and optimize patient risk stratification. A key application lies in *IBD*. AI models demonstrate strong potential in predicting disease flares, which is critical for a condition marked by unpredictable exacerbations and remission periods [30]. AI can categorize patients by risk level by integrating clinical data, biomarkers, and genetic information, facilitating personalized treatment plans. Advanced ML algorithms can process medical history, dietary patterns, medication adherence, and lab results to anticipate impending flares. This enables early, proactive interventions that may prevent hospitalizations and reduce the need for aggressive therapies, ultimately improving outcomes while lowering healthcare costs.

There is considerable interobserver variation in scoring the severity of IBD at endoscopy. Abadir et al. (2020) have demonstrated AI's ability to differentiate different severity grades [28]. Furthermore, it is sometimes challenging to differentiate ulcerative colitis from Crohn's disease in the pediatric population. Mossotto et al. (2017) explored the use of ML to improve the diagnosis of pediatric IBD, specifically Crohn's disease, ulcerative colitis, and IBD-unclassified, in 287 children. Unsupervised ML models showed overlapping disease patterns, but hierarchical clustering identified four novel subgroups based on colonic involvement. Using endoscopic, histological, and combined data, supervised ML models achieved classification accuracies of 71.0%, 76.9%, and 82.7%, respectively. The combined model, validated on an independent cohort of 48 patients, correctly classified 83.3% [31].

Liver Disease

AI algorithms help analyze imaging, laboratory results, and patient history to predict the progression of liver fibrosis, cirrhosis, and hepatocellular carcinoma (HCC). This enables early intervention and improves patient outcomes [32]. Thus, as discussed ahead, AI plays a significant role in liver disease diagnosis, prognosis, and treatment.

A) Diagnosis and Imaging: AI can analyze medical images like CT scans and MRIs to detect subtle changes in the liver that the human eye might miss. Furthermore, AI models are being developed to assist in the diagnosis of various liver diseases, including non-alcoholic fatty liver disease (NAFLD), cirrhosis, and HCC. AI can also help classify and segment liver masses, improving diagnostic accuracy [33,34]. Beyond current applications, AI's role in identifying new biomarkers and pathways involved in liver diseases is crucial, leading to the development of new diagnostic tools that can be incorporated into imaging analysis.

B) Prognosis and Prediction: AI models can predict the progression of liver fibrosis and cirrhosis, helping to identify patients at higher risk of developing complications. AI can also be used to predict the response to

treatment and the risk of recurrence of HCC. It can also help prioritize patients for liver transplants by predicting one-year mortality and post-transplant survival [35,36]. This predictive power is constantly being refined through AI's ability to identify new biomarkers and pathways relevant to disease progression and patient outcomes, enhancing the accuracy and scope of prognostic models.

C) Treatment and Management: AI can help select the optimal treatment strategy for different liver diseases, considering individual patient characteristics and helping personalize treatment plans and predict treatment outcomes. Furthermore, AI tools can assist in monitoring patients after liver transplantation, helping to identify risk factors for disease recurrence and other complications [37,38]. AI also plays a vital role in accelerating drug discovery and development for liver diseases, leading to new therapeutic options that can then be optimized and managed with AI-driven strategies.

Colorectal Cancer (CRC)

AI also enhances CRC *screening* through sophisticated risk stratification models [39]. AI refines individual risk assessments by analyzing family history, lifestyle factors, and comorbidities, allowing physicians to tailor screening recommendations more precisely. This ensures that high-risk patients receive timely colonoscopies or other interventions, improving early detection rates and survival outcomes. Through these applications, AI is transforming gastroenterology into a more proactive, data-driven field that is shifting from reactive treatment to predictive, precision-based care.

Table 3. Artificial Intelligence Applications in Predictive Analytics

Disease	AI Model	Prediction Task	Accuracy
Inflammatory Bowel Disease	Random Forest	Disease Flare Prediction	88%
Liver Fibrosis	SVM	Fibrosis Progression Prediction	90%
Colorectal Cancer	Neural Network	Risk Stratification	85%

SVM- Support Vector Machines; AI- Artificial Intelligence

Table 3 presents some AI applications in predictive analytics in IBD, Liver Fibrosis, and CRC. AI's prowess extends to predictive analytics, where large datasets are analyzed to effectively forecast disease outcomes and stratify patient risks. This potential of AI in predicting disease outcomes instils hope about the future of patient care in gastroenterology, where proactive interventions can be made to prevent hospitalizations and reduce the need for aggressive therapies.

Personalized Treatment Plans

AI is revolutionizing precision medicine in gastroenterology by facilitating

personalized treatment strategies tailored to individual patient profiles.

Drug Response Prediction

AI models can process genetic, clinical, and lifestyle data to forecast patient-specific therapeutic outcomes. For instance, ML algorithms can predict the effectiveness of biological therapies in Crohn's disease patients or estimate the probability of achieving sustained virologic response in hepatitis C treatment regimens [40].

AI-driven microbiome analysis

AI-driven microbiome analysis deciphers complex gut microbiota patterns to guide customized dietary and probiotic interventions for conditions like irritable bowel syndrome (IBS) and IBD. Advanced AI systems can pinpoint specific bacterial signatures linked to disease progression and recommend precision-targeted therapeutic approaches [41]. These innovations demonstrate AI's transformative potential in shifting gastroenterology from generalized protocols to genuinely personalized, data-driven patient care.

Commercially available Computer-Aided Diagnosis systems

Several commercial CAD systems are now available, with key developments in both diagnostic (CADx) and detection (CADe) capabilities for endoscopy (Table 4). The pioneering CADx system, EndoBRAIN, developed by Kudo and Mori et al. with Cybernet Systems Co., uses ultra-high-magnification endoscopy and a machine learning algorithm. Initial studies showed its diagnostic accuracy for differentiating neoplastic from non-neoplastic lesions (89%), comparable to that of a specialist clinician (91%). Following successful multicenter trials, it significantly outperformed non-specialist clinicians (97% sensitivity, 98% accuracy vs. 71% sensitivity, 69% accuracy). An extensive prospective study further confirmed its utility in real-time clinical practice, achieving 92.7% sensitivity and 89.8% specificity for distinguishing neoplastic lesions. In the realm of CADe, the EndoBRAIN-EYE, designed for automatic colorectal lesion detection, demonstrated strong performance with 90.5% sensitivity and 93.7% specificity in a frame-based analysis of over 150,000 images. Extending beyond basic lesion differentiation, the new EndoBRAIN-Plus system, using ultra-high magnification endo-cystoscopy, achieved high diagnostic reliability for invasive cancer (89.4% sensitivity, 98.9% specificity). Furthermore, the EndoBRAIN-UC, designed to assess inflammatory activity in ulcerative colitis, has also been approved, expanding AI's application to inflammatory bowel disorders [42].

Table 4. Commercially available Computer-Aided Diagnosis/Detection Systems

PRODUCT NAME	COMPANY	CAD NAME
EndoBRAIN	Cybernet Systems Co. (Tokyo, Japan)	CADx
EndoBRAIN-EYE	Cybernet Systems Co. (Tokyo, Japan)	CADe
EndoBRAIN-Plus	Cybernet Systems Co. (Tokyo, Japan)	CADx
EndoBRAIN-UC	Cybernet Systems Co. (Tokyo, Japan)	CADx
GI Genius	Medtronics Co. (Dublin, Ireland)	CADe
DISCOVERY	Pentax Medical Co. (Tokyo, Japan)	CADe
ENDO-AID	Olympus Co. (Tokyo, Japan)	CADe
CAD EYE	Fujifilm (Tokyo, Japan)	CADe, CADx
EndoScreener	Shanghani Wision AI Co. (Shanghai, China)	CADe
WISE VISION	NEC Co. (Tokyo, Japan)	CADe

CADx: Computer-Aided Diagnosis; CADe: Computer-Aided Detection.
Adapted from Kamitani and Isomoto, 2022 [42]

Challenges and Limitations of AI in Gastroenterology

Despite AI's significant advantages in gastroenterology, several challenges and limitations must be addressed to ensure its effective and ethical implementation. One primary concern is data quality and availability, as the performance of AI models depends heavily on the volume and consistency of training data [43]. In gastroenterology, imaging technique variations and data collection discrepancies can negatively impact model accuracy. Additionally, ensuring diverse and representative datasets is crucial to minimizing biases and improving the generalizability of AI tools across different populations. Since AI training requires the collection of vast amounts of data, the issue of data privacy remains paramount.

Another challenge is the integration of AI into clinical workflows. Adopting AI solutions may disrupt established practices, and clinicians' reluctance to embrace new technologies can hinder implementation [44]. Financial barriers, particularly in low-resource settings, further complicate developing and deploying AI-driven tools in GE. Hassan et al. (2024), reviewing 50 studies from a pool of 2,514 articles, identified 18 categories of barriers and facilitators, emphasizing that trust is a critical catalyst for AI adoption, necessitating robust governance and regulatory frameworks [45]. This need for trust is echoed by Esteva et al. [46], who highlight that clinician and patient trust is essential for successful AI implementation. Clinician trust requires rigorous validation through real-world trials and interpretable AI algorithms, while patient trust hinges on stringent privacy measures and advanced data handling techniques like federated learning. Both reviews conclude that

overcoming these trust-related obstacles is crucial to realizing AI's potential to create a more accessible and equitable healthcare system.

Ethical considerations also play a critical role regarding accountability and transparency in AI-assisted decision-making [47]. Clinicians must be able to interpret AI-generated recommendations confidently to maintain patient trust, which requires clear explanations of how these systems arrive at their conclusions. Regulatory and legal challenges present ongoing hurdles as the AI landscape in healthcare evolves [48]. One important area is how to divide accountability between machines and men while doing root cause analyses in cases of improper diagnosis. Compliance with medical and technological standards demands a thorough understanding of both fields [49-51], and establishing clear guidelines for responsible AI deployment in gastroenterology remains a priority for policymakers and practitioners alike (Figure 2).

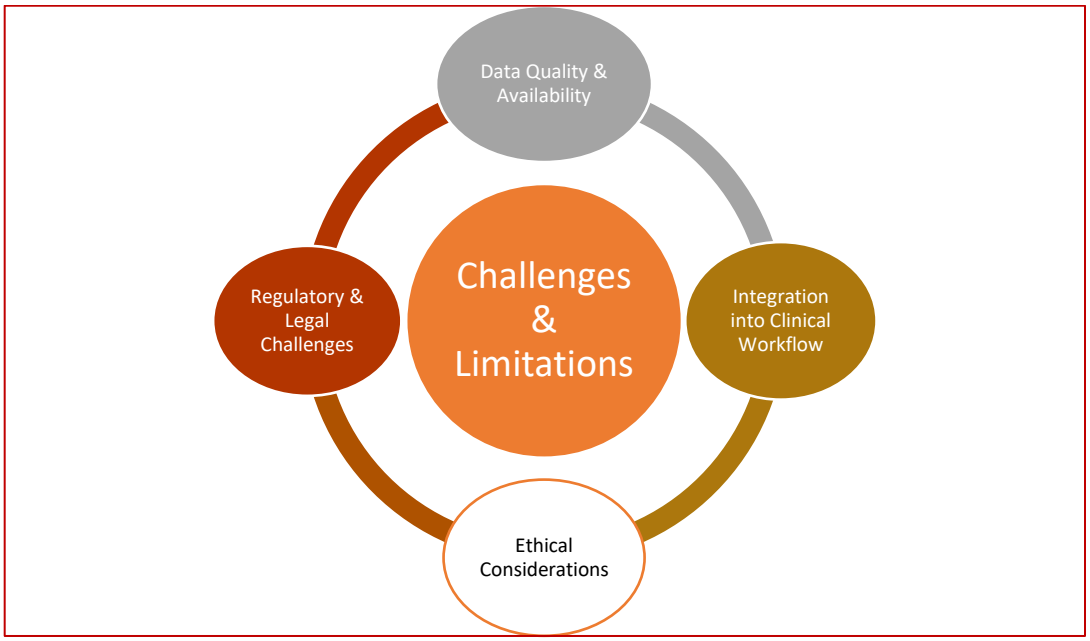


Figure 2. Challenges and Limitations of Artificial Intelligence in Gastroenterology

Future Directions

The future of AI in gastroenterology holds significant promise, with several key areas poised for advancement (Figure 3). Natural Language Processing (NLP) technologies are expected to play a crucial role by automating the analysis of unstructured clinical narratives, streamlining documentation, and synthesizing data from diverse sources to enhance the diagnosis and management of GI disorders. Additionally, utilizing real-world data from electronic health records (EHRs) and patient registries will provide valuable insights into the effectiveness of AI applications across diverse populations, helping refine predictive models and treatment protocols [52]. Collaboration among healthcare professionals, data scientists, and industry stakeholders will be essential to drive innovation and develop clinically relevant AI tools that prioritize safety and efficacy [53]. To ensure

successful integration, healthcare providers will need targeted education and training to build competency in AI technologies to augment diagnostic and clinical decision-making [54].

Figure 3. Future of Artificial Intelligence in Gastroenterology

Further advancements include the development of multimodal AI, which integrates imaging, genomic, and clinical data for a more comprehensive disease assessment [52]. AI-driven robotic endoscopy systems may also enhance precision in complex endoscopic procedures [55,56]. Additionally, patient-centric AI applications, such as wearable devices and mobile apps, could enable continuous GI health monitoring, empowering patients to take a proactive role in their care [57,58].

Conclusion

The review highlights the transformative impact of Artificial Intelligence (AI) on gastroenterology, particularly in enhancing diagnostic accuracy and optimizing endoscopic procedures. AI technologies, including Computer-Aided Detection (CADe), significantly improve polyp detection rates and reduce miss rates during colonoscopy. In capsule endoscopy, AI efficiently analyzes large volumes of images, facilitating the timely identification of gastrointestinal abnormalities with high sensitivity and specificity. Additionally, AI contributes to the early detection of oesophagal adenocarcinoma by effectively distinguishing between dysplastic and non-dysplastic tissues through advanced image analysis and overall, integrating AI in gastroenterology promises to improve patient outcomes by addressing existing diagnostic challenges and streamlining clinical workflows.

Statements and Disclosures

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SHORT COMMUNICATION

Toxico-Epidemiological Profile of Fatal Poisonings at a Tertiary Care Hospital in Visakhapatnam, India (2023): A Brief Report

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Abstract
Suicide is a global issue in modern society, with people from different cultures exhibiting distinct behavioural patterns and methods. In recent times, suicide by pesticide poisoning has become a common occurrence in India. Generating data on the toxico-epidemiology of poisoning in each region is critical for implementing targeted interventions to restrict access to these substances and, in turn, prevent self-harm. The present study was conducted on fatal poisoning cases autopsied at a tertiary care hospital in Visakhapatnam during the year 2023. The study included 195 fatal poisoning cases, with 74.4% of the victims being male, and the majority falling within the 31–40 years age group. Pesticide consumption was responsible for 80% of all deaths, and 94.87% of the cases were intentional poisoning. The herbicide paraquat alone accounted for 39.4% of the deaths in the study population. Financial issues, familial disputes, and drug addiction were the primary reasons for suicides, and the survival period varied, with most individuals dying within 24 hours. Several Highly Hazardous Pesticides (HHPs) were used for these intentional self-harm cases, emphasizing the urgent need to restrict access to these substances to save lives as envisaged by the WHO.

Keywords: Poisoning, Suicide, Pesticide, Autopsy, Mental health, HHPs

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Introduction

Poisoning is a prevalent cause of death frequently encountered in medico-legal autopsy practice across India, as it remains a common method of suicide in the country [1]. The misuse of pesticides for self-harm has been a persistent issue not only in India but also in several other Southeast Asian nations [2]. Recognizing the gravity of the problem, the WHO has consistently emphasized the need to restrict access [3] to such toxic substances as a practical and effective strategy for suicide prevention. Sadly, fatal self-poisoning with pesticides remains a widespread issue in many low- and middle-income countries (LMICs) due to limited political commitment, insufficient public dialogue around the problem, administrative challenges, and gaps in the technical infrastructure needed to ensure safe management and regulation of highly hazardous pesticides.

India currently lacks a formal poison incident reporting system to track cases of suicidal, accidental, or homicidal poisonings [4,5]. In the absence of such surveillance, multi-centre toxicoepidemiology studies become essential to understand the true scale of the problem of both fatal and non-fatal poisoning instances. Gathering this evidence is extremely necessary to identify which agrochemicals and/or other substances are commonly abused for self-harm. Furthermore, such data can help plan proper practical strategies to restrict access to these toxic substances and inform public health systems to be prepared for handling poisoning cases.

This study aims to examine the toxicoepidemiology of all fatal poisoning cases autopsied at a tertiary healthcare facility in Visakhapatnam, Andhra Pradesh. The objectives include studying the sociodemographic profile of poisoning victims, the reasons for consumption, the specific substances involved, the period of survival, and other related factors.

Methodology

This retrospective study was conducted in the Department of Forensic Medicine at Andhra Medical College, Visakhapatnam, Andhra Pradesh. The data on poisoning deaths were collected from police inquest reports, autopsy findings, toxicological analysis reports, and any available medical records. The study included all poisoning cases autopsied during the calendar year 2023, while autopsies conducted for envenomation (snake bite, bee sting, scorpion sting) were excluded. In all 195 cases included the toxicological substance identification was solely based on forensic science laboratory reports. In some cases, the generic nature of the compound was established (e.g., Organophosphate, etc.), while in others, the exact substance was identified (e.g., Chlorpyriphos, Paraquat, etc.).

As this was a record-based study involving manual data extraction from available documents, the authors acknowledge the possibility of missing a few cases of poisoning due to oversight. On average, around 2,000 autopsies (for the year 2023, n= 2010) are performed annually at Andhra Medical College/King George Hospital, Visakhapatnam, with poisoning deaths accounting for approximately 10–15% of the total cases. In general, about 25% (for the year 2023 total suicide cases n= 557) of cases involve suicide by poisoning, with other common means of taking one's life including hanging, falls from height, and railway fatalities.

Results

A total of 195 poisoning cases were included for analysis, of which 145 were male (74.4%) and 50 were female (25.6%). The age distribution of the cases is shown in Figure 1, with the highest number of victims (49 cases, 25.1%) belonging to the age group of 31–40 years.

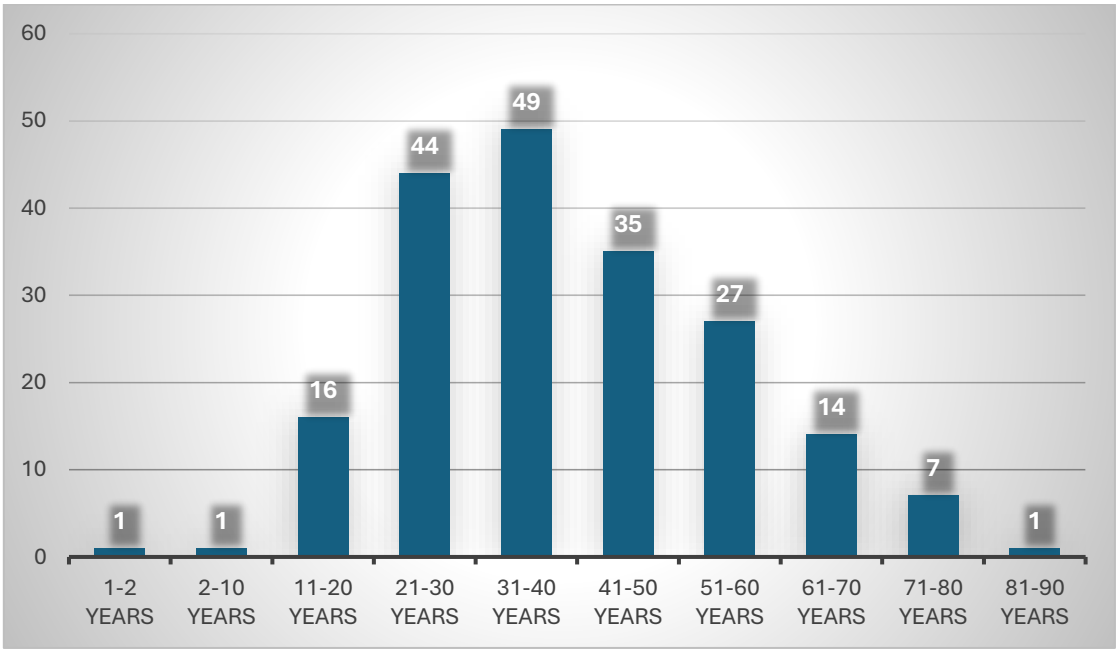

Figure 1. Age distribution of fatal poisoning cases

The occupations of the decedents due to poisoning showed a wide spectrum. The most affected were those engaged in agriculture and farming, with 36 cases. Self-employed individuals accounted for 32 cases, daily wage workers for 24 cases, housewives for 20 cases, and students for 12 cases. There were also 4 cases each among watchmen and unemployed individuals, and 3 cases involving salespersons. In addition, there were 2 software engineering professionals among the decedents. In 23 cases, the occupation was not known**.** Lastly, 35 cases were categorised as "others," that included skilled and unskilled professionals across blue-collar and white-collar backgrounds, such as technicians, plumbers, university teachers, bank managers, and other highly educated individuals. It was difficult to ascertain the economic status of the study population from available sources, hence, it was not done.

Out of the total of 195 cases, 98 were from rural areas, 95 from urban areas, and 2 from tribal areas. In terms of seasonal distribution, 71 cases occurred during the summer, 45 during the winter, and 79 during the rainy season. In terms of marital status, 146 individuals were married, and 49 were unmarried.

Out of the total 195 cases, 150 individuals consumed poison at home, 17 in agricultural fields, 23 away from home, and 5 in other locations not specified. The total number of poisoning cases in the study was 195, of which 185 were suicidal. The remaining 10 cases included 1 homicidal case involving paraquat poisoning and 9 accidental poisoning cases. These accidental cases comprised 2 instances of paraquat poisoning, 2 cases of corrosive

(hydrochloric acid) poisoning, 1 case of drug overdose (metformin), 1 case involving chlorhexidine and cetrimide antiseptic, 1 case of propoxur poisoning, 1 case of transfluthrin poisoning, and 1 case of uncategorized organophosphate poisoning.

The reasons for attempting suicide in the study population were manifold. Debts and financial liabilities were reported in 43 cases. Familial disputes, relationship issues, and marital discord accounted for a total of 47 cases (38 involving familial disputes and relationship issues, and 9 involving marital discord). Drug addiction and substance abuse were identified in 34 cases. Chronic illnesses were reported as the reason in 17 cases. Other psychiatric conditions and feelings of being vexed with life contributed to 35 cases (26 with psychiatric conditions and 9 feeling vexed with life). In 19 cases, the reason remained unknown.

The survival periods of the poisoning cases also showed a wide variation. In 37 cases, the survival period was less than 12 hours, while 48 cases had a survival period between 12 and 24 hours. In 35 cases, the survival period ranged from 1 to 2 days, and in 24 cases, it was between 3 to 4 days. There were 21 cases where the survival period was between 5 to 7 days, 11 cases where it was between 8 to 10 days, and 13 cases where the survival period ranged from 11 to 15 days. In 3 cases, the survival period was between 16 to 31 days, and in 1 case, it lasted 1 to 2 months. The survival period was unknown in 2 cases.

Herbicides and insecticides were the most common substances involved in poisoning cases, each being reported in 78 cases. A breakdown of the substances is provided in Table 1.

Table 1. Profile of substances involved in fatal poisoning cases

S. No	Type Of Poison	No. of cases
1.	Herbicide	78
2.	Insecticide	78
3.	Corrosives	11
4.	Drug Overdose	9
5.	Undetermined Poisoning	6
6.	Rodenticide (Phosphide)	5
7.	Ethyl Alcohol	3
8.	Fungicide (Hexaconazole)	2
9.	Antiseptic (Chlorhexidine + Cetrimide)	1
10.	Engine Oil	1
11.	Oleander Seeds	1
	Total	195

Among the 78 cases of herbicide poisoning, 77 resulted from paraquat, while one was due to pretilachlor. The profile of insecticide poisoning is shown in Table 2, with organophosphate compounds being the most abused.

Table 2. Profile of Insecticides in fatal poisoning cases

S. No	Insecticide	No. of cases
1.	Uncategorised Organophosphate Compound (OPC)	32
2.	Chlorpyriphos (OPC)	15
3.	Profenophos (OPC) & Cypermethrin (Pyrethroid)	6
4.	Profenophos (OPC)	4
5.	Propoxur (Carbamate)	3
6.	Monocrotophos (OPC)	3
7.	Dimethoate (OPC)	3
8.	Chlorpyriphos (OPC) & Cypermethrin (Pyrethroid)	2
9.	Cyhalothrin (Pyrethroid)	2
10.	Emamectin Benzoate (Avermectin)	1
11.	Chlorfenapyr (Pyrrole)	1
12.	Ethion (OPC) & Cypermethrin (Pyrethroid)	1
13.	Permethrin (Pyrethroid)	1
14.	Phenyl Pyrazole	1
15.	Phorate (Nematicide)	1
16.	Imidacloprid (Neonicotinoid)	1
17.	Transfluthrin (Pyrethroid)	1
	Total	78

Discussion

This study is the first of its kind in the Visakhapatnam region and was conducted at King George Hospital. The hospital serves the healthcare needs of three North Coastal Andhra Pradesh districts, and the study population is representative of Visakhapatnam, Vizianagaram, and Srikakulam districts to some extent.

Middle-aged (31-40 years, 25.12%) males (74.4%) were the most common victims of fatal poisonings in our study, which is concordant with several studies in India [6,7]. Our study shows a changing trend of preference of herbicides like paraquat for self-harm alongside the traditional organophosphate compounds as reported by several researchers in India [8,9].

Pesticide poisoning has traditionally been more prevalent in rural areas [10]. However, in the present study, it is also increasingly observed in urban areas (95 cases, 48.7%) and among non-agrarian communities. This trend was also noted in our earlier empirical observations [11]. 94.87% of cases are intentional poisonings, indicating this as an important means of suicide alongside hanging, self-immolation, etc., in the Indian subcontinent [12].

Financial and familial issues (46.1%) were responsible for most individuals resorting to the extreme step of suicide by poisoning, a trend that aligns with the prevailing conditions observed in the general suicide trends of the country [13]. Most of the victims in the present study died within 2 days of poison consumption, indicating extreme acute toxicity of the substances consumed.

The Highly Hazardous Pesticides (HHPs) identified in the study include paraquat (herbicide), chlorpyrifos (organophosphate), dimethoate (organophosphate), ethion (organophosphate), monochrotophos (organophosphate), phorate (nematicide),

prophenophos (organophosphate), and profenophos and cypermethrin (organophosphate/pyrethroid combination). They fall within categories 1 and 2 as per WHO criteria, though classifications can sometimes vary slightly depending on the specific formulations.

As of March 1, 2021, India has registered a total of 293 pesticides for use. In the 2019–2020 period, the total annual consumption of technical-grade chemical pesticides amounted to 61,703 MT. Of these, nearly 80% of the pesticides consumed in India fall under the category of extremely or highly hazardous pesticides [14].

A systematic review of lethal poisonings in India from 1999 to 2018 found that 94.5% of deaths were attributed to pesticide poisoning, with aluminum phosphide and organophosphates being the most common culprits. The review also highlighted paraquat as an emerging concern. In contrast, our study from 2023 shows a surge in paraquat-related deaths, while fatalities from rodenticides like aluminum phosphide have decreased [15]. It is worth mentioning that the choice of pesticide for self-harm is greatly influenced by word of mouth regarding the toxicity of various substances. Lately, paraquat has been ruling the roost, as it has no antidote and almost always leads to death.

Our findings indicate a higher incidence of paraquat poisoning compared to other studies, as previously discussed, which may be attributed to the elevated usage of this herbicide in coastal regions. Of the 77 cases, all except three—two accidental and one homicidal—were suicides. The choice of paraquat for suicide is primarily due to its severe acute toxicity and the absence of a specific antidote, making management purely supportive. There are also several reasons for high mortality apart from the lethality of the substance. Since organophosphate compound (OPC) abuse for suicide was quite common for a while, many primary care physicians confuse paraquat with OP compounds and atropinize the patient, which can sometimes be harmful. Similarly, the point-of-care test for paraquat (dithionate test) is generally not available in public hospitals, adding to the challenge of diagnosis. The clinical pattern of toxic manifestations is complex, sometimes causing acute renal failure and sometimes leading to toxic hepatitis or paraquat lung if patient survives a few days [11]. A weight-of-evidence approach like GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) should be used to develop clinical guidelines for paraquat poisoning management in an effective manner.

Limiting access to means of suicide, such as Highly Hazardous Pesticides (HHPs), has proven effective in reducing suicide rates in some countries [16]. It is now time for a thorough review of the availability of pesticides, balancing the needs of agriculture with the imperative to prevent suicides.

The results of this study highlight that pesticide poisoning is no longer confined to agricultural workers. Easy accessibility and socioeconomic stressors have contributed to a rising number of cases among urban populations, including low-income communities, migrant workers, and youth [17,18]. This shift strengthens the urgent need for a multi-sectoral approach to prevention, moving beyond traditional agricultural safety measures. Effective interventions must include strict regulations on the sale and distribution of highly hazardous pesticides, improved

enforcement of safe storage practices, and public awareness campaigns to educate communities on the risks associated with pesticide exposure [19]. By the same token, integrating pesticide control measures with broader suicide prevention strategies—such as mental health support services, crisis helplines, and community-based interventions—can help address the underlying drivers of self-harm and poisoning incidents [20,21].

Drawing on successful international models, India can implement policies similar to Sri Lanka's pesticide bans, which led to a decline in suicide rates [22], or the European Union's stringent pesticide regulations [23]. A phased approach to restricting access to highly toxic pesticides and promoting safer alternatives like large-scale adoption and monitoring of integrated pest management (IPM) could substantially reduce poisoning cases. Government-led initiatives should prioritize farmer support programs to ensure that economic pressures do not push agricultural workers toward hazardous pesticide use or self-harm [24]. More to that, providing financial incentives and training for adopting mandatory IPM practices could accelerate the transition to safer pest control methods.

Strengthening healthcare systems to improve poisoning management, investing in early warning systems to identify at-risk individuals, and fostering collaborations between public health, agriculture, and regulatory bodies will address this growing crisis [25-27]. Implementing robust surveillance systems to track poisoning trends and identify high-risk regions can enable targeted interventions, ensuring that prevention efforts are data-driven and directed where they are most needed. Real-time monitoring of pesticide poisoning cases could also help policymakers adapt regulations and intervention strategies effectively.

It is important to note that paraquat herbicide has recently been abused for homicidal purposes in India on multiple occasions, further strengthening the argument for its ban in the country [28-30]. Sadly, a male child (aged 18 months) who was criminally poisoned to death with paraquat was also part of the study population in our research.

This study has some limitations. The exact percentage of consumed compounds/lethal substances (formulations) is unavailable, and the toxicological analysis is only qualitative. Also, since data extraction was performed manually, there may be minor errors in substance categorization.

Conclusion

This toxicoepidemiology study of fatal poisonings in the Visakhapatnam region during the year 2023 revealed the widespread abuse of paraquat, a herbicide, for committing suicide. Furthermore, pesticide poisoning is no longer limited to rural areas; it is becoming a common means of suicide in urban areas and among individuals from non-agrarian backgrounds. Middle-aged males were the most common victims of poisoning, and the decedents ingested several highly hazardous pesticides to take away their lives. This raises concerns about the availability of such substances in the market since restricting their access is a modifiable risk factor for preventing suicide.

Statements and Declarations

Conflicts of interest

The authors declare that they do not have conflict of interest.

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Ethical considerations

All ethical concerns should be addressed by the authors.

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IMAGES IN SURGERY

Umbilical Keloid Formation in the Port Site Post Laparoscopy

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Abstract
A rare entity of keloid formation in the umbilical port site after undergoing laparoscopic cholecystectomy is being highlighted.

Keywords: Keloid, laparoscopy, transposition flap

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A 45-year-old man presented with an umbilical port site ovoid-shaped keloid formation after three years of laparoscopic cholecystectomy (Figure 1). The patient was advised to undergo surgery followed by radiotherapy. Being an extremely rare complication of laparoscopy with very few isolated case reports being available on this issue, most of the treatment protocols are also vague or incomplete. In view of the fear of recurrence, it is recommended for umbilical keloids to ideally undergo appropriate surgical modalities (including umbilicoplasty, if required) with transpositional flap followed by postoperative radiotherapy (15 Gy/2 fractions/2 days), and wound/scar self-management with silicone tape and steroid plaster [1]. Other additional treatment is corticosteroid injection which has the anti-inflammatory properties and inhibit the production of fibroblasts by reducing collagen and synthesizing glycosaminoglycans into the lesion site. Even autologous platelet-rich plasma, bleomycin, or verapamil has been applied as adjuvant therapies to prevent recurrence of keloid after surgery [2,3].

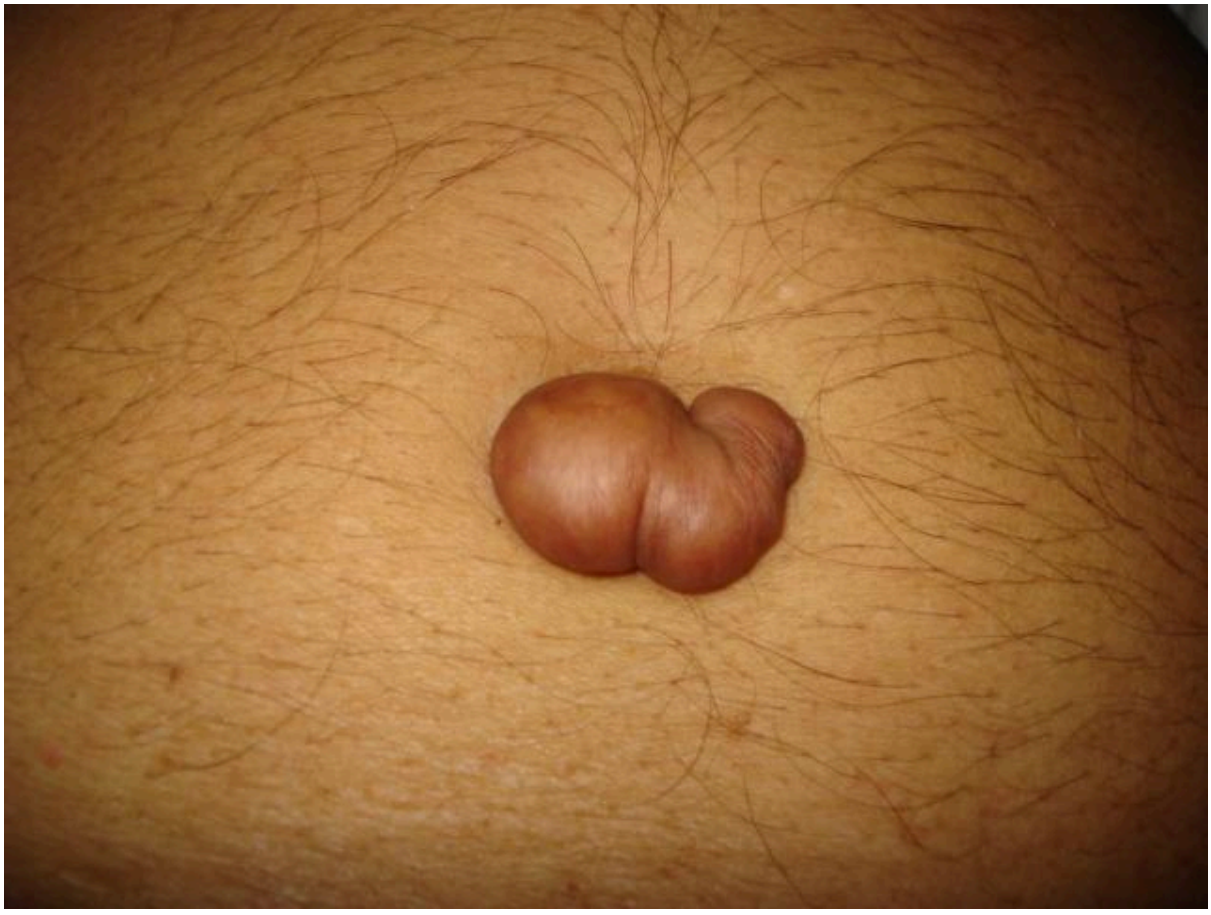

Figure 1. Keloid over the umbilical port site

This condition remains important as the umbilicus is a very important place for cosmesis and all attempts should be made to give a normal look to the umbilicus after any surgical intervention or its sequalae. A close long term follow up is recommended for all laparoscopy cases (Figure 2).

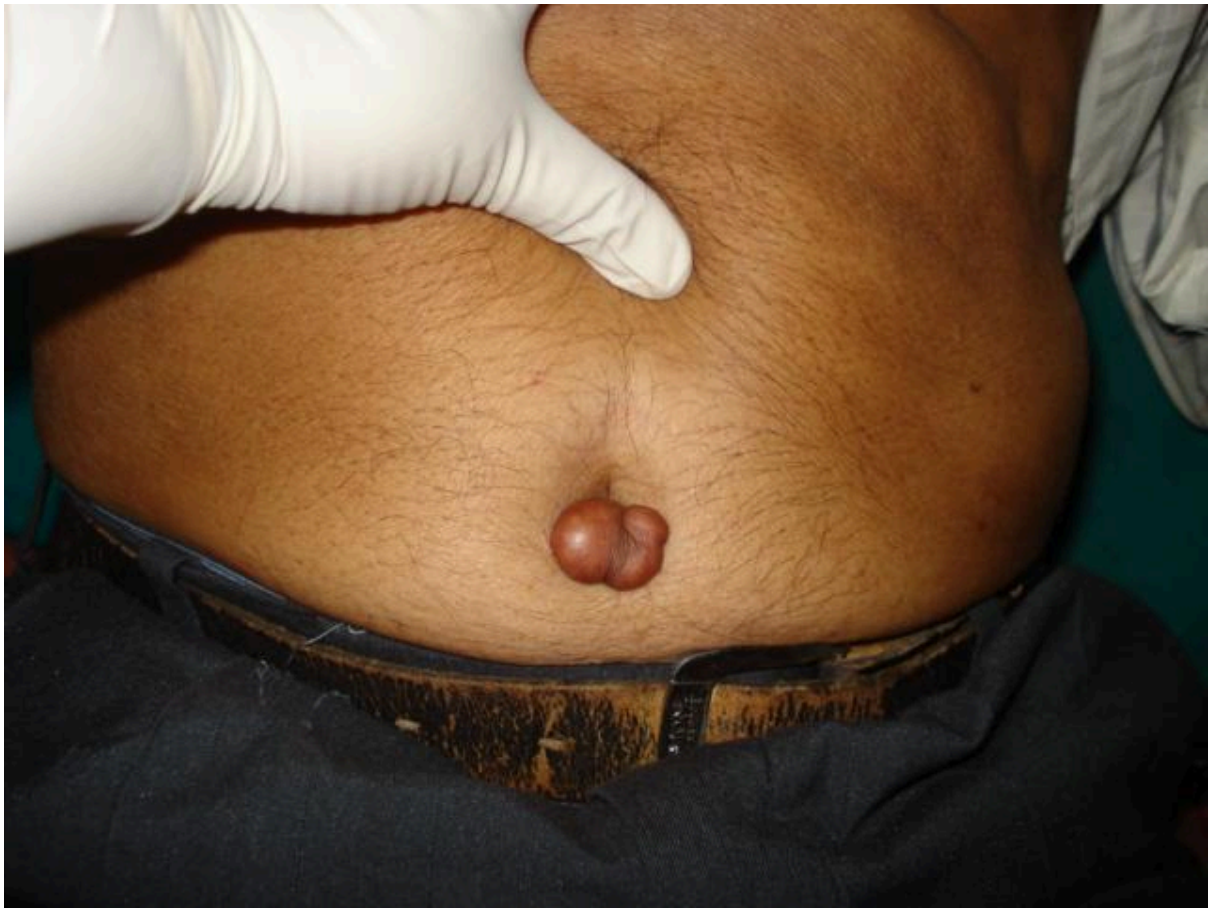

Figure 2. Keloid in the supine position

Statements and Declarations

Conflicts of interest

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CASE REPORT

Tracheostomy-Assisted Retrival of Bullet from Right Main Bronchus: A Case Report

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Abstract

Background: Foreign body aspiration is a serious pediatric emergency that can cause severe morbidity and mortality. Early diagnosis and immediate are necessary to avoid complications. **Case Presentation:** A 5 years old boy presented with history of dyspnea, fever, cough and chest pain since 2 weeks after the ingestion of a bullet while playing. Clinical features were dyspnea, stridor and markedly reduced air entry on the right. A chest X ray revealed radio-opaque foreign body in the right main bronchus. An Emergency rigid bronchoscopy under general anaesthesia was not successful in the removal of the foreign body despite repeated attempts. Subsequently, a tracheostomy was performed and bullet removal was successful. Post-operatively, improvement was impressive, and on the 4th day, the patient was discharged in good condition. **Conclusion:** The case report describes about a difficult extraction of a foreign body from Right main bronchus, needing a tracheostomy at the end to retrieve the same in view of failure of extraction via rigid bronchoscope. Early diagnosis, appropriate imaging and a multidisciplinary strategy are important for effective management of foreign body aspiration in children. This case also highlights the limitation of rigid bronchoscopy and reminds us to be prepared for tracheostomy if required.

Keywords: Foreign body, Bronchus, Rigid Laryngoscopy, Tracheostomy-assisted

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Introduction

Foreign body aspiration (FBA) is a potentially life-threatening pediatric emergency that typically happens in children below the age of 5. FBA is accidental insertion of some foreign object like food, small object, toy or debris, into the airway, causing major respiratory distress and other serious complications if left untreated. Specifically, aspiration of foreign bodies into bronchial tree can result to life threatening conditions including airway obstruction, infection, atelectasis, pneumonia, obstructive emphysema and even death if left untreated [1,7].

One of the less common but potentially fatal foreign body aspirations is the aspiration of a bullet or other metal object, while rare, offers a distinct diagnostic and management challenge. The right main bronchus is especially susceptible secondary to its direct course from trachea and slightly larger diameter than that of the left main bronchus, thus more likely to accommodate a foreign body [2]. This case report discusses the treatment of a pediatric patient who aspirated a bullet into the right main bronchus, necessitating the treatment by tracheostomy-assisted retrieval. The prompt and efficient retrieval of such an object is paramount to maintain minimal morbidity and mortality, and its highlights the significance of a multidisciplinary approach to the management of complex pediatric airway emergencies. This Case report emphasizes the clinical dilemmas and decision-making processes involved with foreign body aspiration, especially in the setting of unusual and dangerous objects such as bullets.

Case Presentation

A 5-year-old male child was referred to our hospital with a history of respiratory distress, fever, cough, and chest pain for 14 days. The child had reportedly aspirated a bullet while playing. On examination, he presented with dyspnea, audible stridor, and a productive cough. Auscultation revealed markedly reduced air entry on the right side and crepitations on the left. Oxygen saturation (SPO2) was maintained on room air. A chest X-ray (poster anterior view) revealed radio-opaque shadow consistent with a bullet lodged in the right main bronchus (Fig1.A). Preoperative work up was completed in the emergency department and the patient was taken for an emergency rigid bronchoscopy under general anesthesia**.**

Anesthesia was administered via a port in the pediatric bronchoscope. The rigid bronchoscope was advanced to the carina, where the bullet was visualized in the right main bronchus surrounded by mucus and slough. The smooth cylindrical bullet posed significant challenges in securing a firm grasp. Multiple attempts to extract the foreign body through the vocal cords were unsuccessful, as it repeatedly slipped back into the bronchus.

To facilitate safe retrieval of the bullet, a tracheostomy was performed due to difficulty encountered in retrieving the bullet through the laryngeal inlet. The foreign body was successfully extracted through the tracheal opening. The bullet measured 2x 1.5x 1 cm (Fig. 1B). Post-procedure, the patient was transferred to the pediatric ICU for observation. The stridor resolved, and air entry to the right lung improved. On the 2nd post-operative day, mild subcutaneous

emphysema was noted and managed conservatively. A chest X-ray on the same day confirmed the clearance of lung parenchyma. The tracheostomy tube was decannulated on the 4th day and the patient was discharged in stable condition.

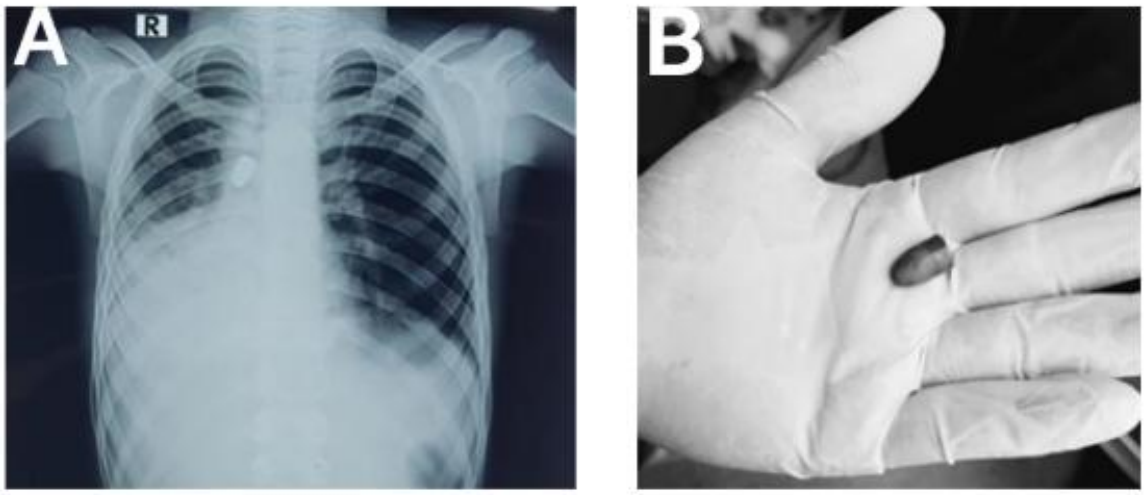

Figure 1. (A) X-ray Chest PA view showing a radio-opaque shadow consistent with a bullet lodged in the right main bronchus (B) Showing the retrieved bullet.

Discussion

Foreign body aspiration in children is typically non- radio-opaque, with the majority of objects being located in the right main bronchus [3,8]. However, the aspiration of metallic objects such as bullets is rare as it poses significant challenges due to their smooth surface. Common presenting symptoms include cough, wheezing and respiratory distress, and if these symptoms are not promptly addressed, can lead to serious complications [4].

Thorough history, physical examination, radiographic imaging and rigid bronchoscopy are gold standard in diagnosing and treating foreign body aspiration [5]. In this case too, a thorough history and physical examination was conducted and the chest X ray clearly identified the location of the bullet in the right main bronchus. The rigid bronchoscope is typically the first line tool for foreign body removal in pediatric patients due to its large lumen and better visualization capabilities compared to the flexible bronchoscope. In our case, removal of the foreign body required a novel approach, as the bullet could not be extracted through the laryngeal inlet. A tracheostomy was performed to successfully retrieve the bullet. However, other potential retrieval techniques, such as a flexible bronchoscopy with dormia baskets or suction catheters were not explored for this case.

Despite an exhaustive literature search, we found no previously published reports of bullet or metallic foreign body retrieval via tracheostomy in pediatric patients except for one case series where 7 cases of non- metallic foreign body aspirations required tracheostomy out of which 5 cases were in sub glottis and 2 cases

in the right main bronchus [6].

This case also emphasizes the importance of a multidisciplinary approach involving pediatricians, radiologists, anesthesiologists, surgeons to manage complex foreign body aspirations effectively. Prompt recognition and intervention are crucial to prevent complications such as atelectasis, pneumonia, obstructive emphysema and even death [7]. Certainly, there is a need for case series on this technique to provide a generalizable conclusions or evidence for best practice.

Conclusion

This case report presents a unique case of bullet aspiration in a child, which was removed successfully by tracheostomy following a series of unsuccessful attempts with rigid bronchoscopy. The positive outcome of the patient underscores the need for adaptable treatment options and the preparedness to utilize surgical measures when and where needed. Early diagnosis, appropriate imaging, and multidisciplinary management are essential for effective treatment of foreign body aspirations in pediatric patients.

Author Contribution

TL: Design, Patient history taking, Case management and writing manuscript of the case report. LV: Writing the manuscript of the case report. CM: Case management and review of manuscript.

Conflict of Interest

The authors declares that they don't have conflict of interest.

Ethics approval and Consent to Participate

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