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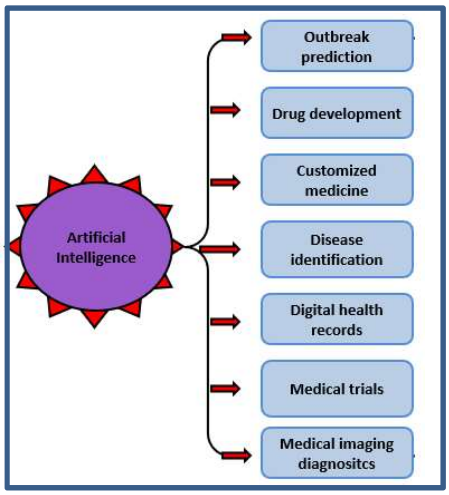

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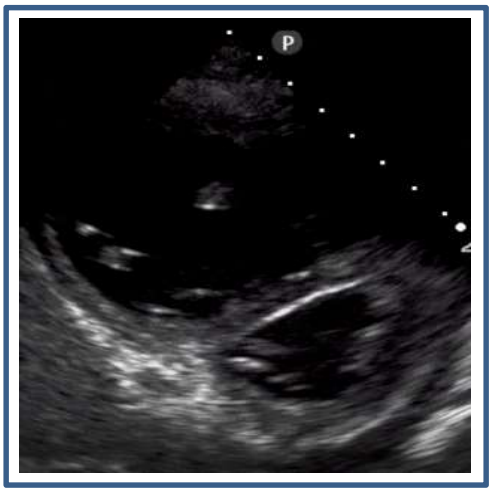

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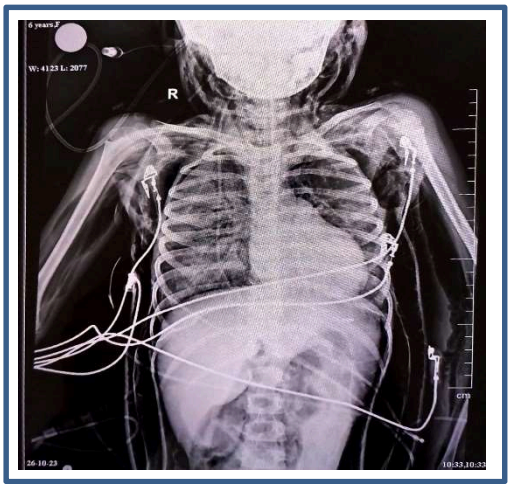

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(Contents Continued)

National Board of Examinations - Journal of Medical Sciences
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ACKNOWLEDGEMENT TO REFEREES

Acknowledgement to Referees

Dear Reader,

Welcome to the first issue of *National Board of Examinations – Journal of Medical Sciences (NBEJMS)* for 2025.

We would like to start by thanking the authors of the articles published in *National Board of Examinations – Journal of Medical Sciences (NBEJMS)* over the course of 2024. The skill and dedication of these experts is critical to the continued success of the journal.

The quality of published articles is also testament to the significant efforts of the peer reviewers, whose commitment ensures that the journal's content is held to the highest possible standard. We would like to thank the following individuals who acted as reviewers for *National Board of Examinations – Journal of Medical Sciences (NBEJMS)* in the last 12 months:

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We are also extremely grateful to the members of the journal's Honorary Editorial Board, who provided guidance on journal content.

The editorial program for 2025 is well under way, and we are looking forward to continuing to bring you many high-quality and authoritative articles in the field of Medical Sciences over the coming year. Print has become much less important in publishing, hence our publication mode always will be E-Only.

Best wishes

Minu Bajpai and Abhijat Sheth

Editors-in-Chief, *National Board of Examinations – Journal of Medical Sciences (NBEJMS)*

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EDITORIAL

Federated Learning: The Monobloc of Artificial Intelligence & Machine Learning (AI-ML) Applications in Health Care

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In this current issue, the article by Khanna et al. [1], highlights the role of AI-ML in healthcare. A significant bottleneck in realizing this nature of data mining, viz., patient related sensitive information, is data security concern. The latter pertains to the hospitals from where this information is to be procured. Federated learning has the necessary mechanism to overcome this significantly - M. Bajpai and A. Sheth

Recent breakthroughs in **Deep Learning (DL)** have been used in current medical data processes, which **include automatic disease diagnosis, classification, biomedical data analysis, Question Answering in the medical domain, and segmentation.**

AI-ML utilizes datasets distributed across data centers such as hospitals, clinical research labs, and mobile devices. In order for AI models to be effective, they often require large amounts of data to be trained on. Transmission & usage of information and the usage of stored medical data & its transmission are central to patient rights. Training AI models on a broader range of data (across different hospitals, regions, or countries) helps improve **model generalization.**

The **EHR (Electronic Health Records)** in hospitals are sensitive and widespread in nature. If learning from individual datasets could be utilized without exposure to the seat of data generation, the privacy issue could be circumvented. Federated learning allows institutions to share model parameters without compromising data privacy, making the resulting models more **robust** and **generalizable** to real-world scenarios. This exclusiveness becomes the boon of Federated Learning (FL).

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The General Data Protection Regulation (GDPR) and the **Health Insurance Portability and Accountability Act (HIPAA)**, have passed new laws that control data shared while preserving user security and privacy.

Healthcare data often resides in **isolated silos**, such as individual hospitals, clinics, and research institutions, making it difficult to create comprehensive models. Federated learning helps unify these fragmented datasets by allowing institutions to train their local models and only share updates (like gradients or model weights). This **decentralized approach** fosters collaboration across institutions while maintaining each institution's data privacy. With federated learning, it becomes feasible to scale AI/ML models for precision medicine. Models trained using federated learning can take into account diverse, multi-institutional data to make more **personalized and equitable predictions**, minimizing biases that might arise when training models with data from only a single institution. This scalability is especially crucial in healthcare, where **rare diseases** and **patient heterogeneity** require models that can generalize across various populations.

Federated learning doesn't just benefit one subset of healthcare (e.g., radiology, genomics, or pathology). Instead, it enables the development of **cross-disciplinary models** that leverage data across specialties. For example, models that combine radiology, genomics, and patient history could deliver more comprehensive clinical insights, improving diagnosis and treatment recommendations. By keeping data within the institution's firewall, federated learning can help address healthcare's stringent regulatory and ethical standards. **Patients and regulators** can trust that their sensitive medical data is not being shared indiscriminately, while still benefiting from the advancements in AI/ML that improve patient outcomes.

Precision Medicine at Scale

- Federated learning can enable **precision medicine** by leveraging data from multiple institutions to train models that account for individual patient variations (e.g., genomics, medical history, lifestyle factors). This ensures that AI-driven solutions are tailored to the specific needs of patients, offering more **personalized treatment options** and improving patient outcomes.
- By facilitating access to a broader range of data without compromising privacy, FL creates an **opportunity for large-scale precision medicine** that can serve diverse populations and rare conditions.

Supporting a Wide Range of Healthcare Applications

- Federated learning enables **AI/ML applications** across a broad range of healthcare areas, such as:
  - **Medical imaging (radiology, pathology)**
  - **Genomic data analysis**
  - **Clinical decision support systems**

    - **Predictive models for patient outcomes (e.g., sepsis, COVID-19 risk)**
    - **Drug discovery**
- FL supports these applications by providing a platform for collaborative, cross-disciplinary efforts where data privacy and compliance are non-negotiable. This collaborative ecosystem nurtures continuous innovation in healthcare AI.

Thus, **FL** is the process of developing machine learning models over datasets distributed across data centers such as hospitals, clinical research labs, and mobile devices while preventing data leakage. FL is used to train other machine learning algorithms, thereby allowing companies to create a 'shared global model' without having to centralize data. As healthcare data becomes increasingly important for machine learning models, federated learning acts as the **fundamental building block** (the "monobloc") to enable secure, large-scale, and collaborative AI-driven innovations in the healthcare industry. Through FL, healthcare AI can evolve, scale, and provide more accurate, equitable, and personalized solutions across a wide range of applications—from medical imaging to precision medicine—ultimately improving patient care globally.

Reference

1. Khanna S, Siddiqui MH, Bhushan S, Saxena R. Deciphering the Role of Artificial Intelligence in Medical Sciences: An Update. Natl. Board Exam. J. Med. Sci. 2025;3(1):56-66. doi: 10.61770/NBEJMS.2025.v03.i01.008

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ORIGINAL ARTICLE

Neuropathic Pain Management: Prescription Strategies in a Tertiary Care Setting

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Abstract

Background: Neuropathic pain, resulting from nerve damage, presents a complex challenge in clinical management due to its multifaceted nature and varied patient responses to treatment. Understanding prescription patterns in a tertiary care setting can provide insights into current clinical practices and highlight areas for improvement. **Objective:** prospective study of prescription pattern among neuropathic pain and its management. **Methods:** A prospective study was carried out with collecting patent data from a tertiary care Father muller medical college hospital, Mangalore, Karnataka. Where the data were collected from May 2023 to October 2023 and included patient demographic, diagnosis of neuropathic pain and prescription information. Statistical analysis of prescribing trends correlated to patient demographics was done using SPSS software. **Results:** The study analyzed 363 medical records, with a higher prevalence of male patients (56%) compared to female patients. Diabetic neuropathy was the most frequently observed condition, accounting for 49.04% of cases. The treatment and prescription patterns were based on the severity of pain, current condition, and age group of the patients. The age group most affected by neuropathic pain was 39-50 years. Monotherapy was administered to 40.77% of patients (148/363), with anticonvulsants being the most commonly prescribed drug class (76.2%). **Conclusion:** These findings demonstrate marked dependence on combination therapy and polypharmacy in managing neuropathic pain. While these strategies align with clinical guidelines, they also underscore the need for careful management to minimize the risks associated with multiple drug regimens. Future research should focus on optimizing treatment protocols and integrating non-pharmacological interventions to improve patient outcomes.

Keywords: Neuropathic pain, Diabetic Neuropathic pain, In-patients, Out-patients, Chronic inflammatory demyelinating polyneuropathy, Wong Baker Scale, Tricyclic Antidepressants, Serotonin-Norepinephrine Reuptake Inhibitors

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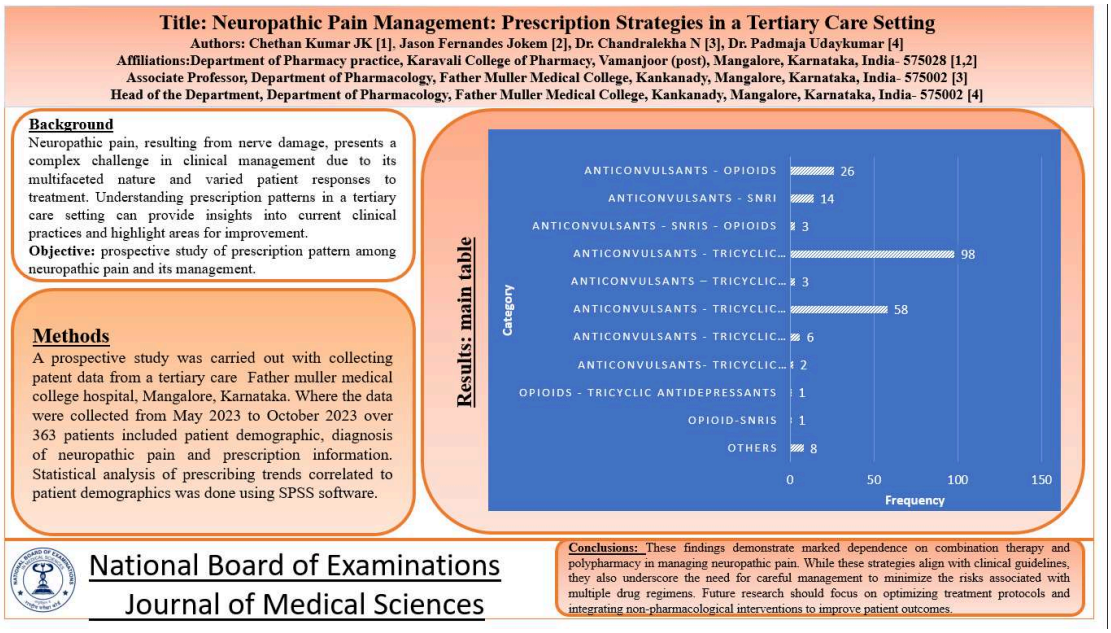
Graphical Abstract



Introduction

Neuropathic pain is a complex, chronic pain condition resulting from damage to the nervous system, either peripheral or central. Unlike nociceptive pain, which arises from actual tissue damage, neuropathic pain is caused by abnormal neural activity and can be particularly challenging to manage. This condition is characterized by symptoms such as burning, tingling, shooting pain, and allodynia (pain from stimuli that do not normally provoke pain), which significantly impair a patient's quality of life and daily functioning [1,10].

The pathophysiology of neuropathic pain involves several mechanisms, including peripheral sensitization, central sensitization, and altered pain modulation. These mechanisms can be influenced by various factors such as metabolic diseases (e.g., diabetes), infections (e.g., herpes zoster), traumatic injuries, and neurodegenerative diseases. Given this complexity, the management of neuropathic pain often requires a multifaceted therapeutic approach [4,9].

Current clinical guidelines for the management of neuropathic pain recommend several pharmacological treatments as first-line options, including anticonvulsants (e.g., gabapentin and pregabalin) and antidepressants (e.g., amitriptyline and duloxetine). These medications work by modulating pain pathways and reducing the transmission of pain signals. Despite the availability of these guidelines, the optimal management of neuropathic pain remains elusive for many clinicians, as patient responses to treatment can vary widely, and side effects are common [5,7,8,16].

Polypharmacy, the use of multiple medications, is a common strategy employed to enhance pain control in patients with neuropathic pain. This approach aims to target different pain mechanisms simultaneously, potentially improving therapeutic outcomes.

However, polypharmacy also increases the risk of adverse drug reactions and interactions, necessitating careful monitoring and individualized treatment plans.

The management of neuropathic pain in a tertiary care setting often reflects the complexity and challenges of treating this condition in real-world clinical practice. Understanding prescribing patterns in such settings can provide valuable insights into current practices and areas for improvement. This study aims to analyse the prescribing patterns for neuropathic pain at a tertiary care hospital, focusing on the prevalence and nature of polypharmacy and combination therapy [12,14,17].

Specifically, the objectives of this study are to:

1. Identify the most commonly prescribed medications for neuropathic pain.
2. Assess the prevalence and types of polypharmacy and combination therapies used.
3. Evaluate differences in prescribing patterns based on the specific type of neuropathic pain, such as diabetic neuropathy and post-herpetic neuralgia.

By examining these aspects, this study seeks to contribute to the optimization of pharmacological management strategies for neuropathic pain, enhancing both efficacy and safety for patients. The findings can inform clinical guidelines and support the development of more personalized treatment plans, ultimately improving patient outcomes in neuropathic pain management [11,13,15].

Methods

Study Design

This study is a prospective observational analysis carried out over a six-month period at Father Muller Medical College and Hospital, Mangalore, India.

Data Source

Data were sourced from the hospital's inpatient and outpatient departments, focusing on medical records, including patient case sheets, laboratory reports, and medication charts.

Sample Selection

The study included 363 patients diagnosed with neuropathic pain. The sample size was determined using a 95% confidence interval and a 1% allowable error margin.

Inclusion and Exclusion Criteria

Inclusion Criteria

- Patients aged between 10 and 90 years.
- Both male and female patients.
- Diagnosed with neuropathic pain conditions, such as diabetic neuropathy, CIDP, post-herpetic neuralgia, and phantom limb pain.

Exclusion Criteria

- Pregnant and lactating women.
- Patients admitted for psychiatric conditions or due to poisoning and accidents.

Data Collection

Comprehensive data collection was performed, encompassing demographic information, medical history, detailed medication records like IP/OP no, age, gender, diagnosis, treatment, discharge medications and other data related to study was collected.

Statistical Analysis

Descriptive statistics were applied using MS Excel and SPSS software to determine the frequency, percentage, mean, standard deviation, and chi-square tests for analyzing the data.

A detailed statistical analysis was performed, yielding a z-value of 1.96 and a two-tailed p-value of 0.05 (exact value: 0.05076), with a sample size of 363.

Results

Patient Demographics

The study cohort consisted of 363 patients diagnosed with neuropathic pain, comprising 192 outpatients (52.89%) and 171 inpatients (47.1%). The gender distribution was 202 males (56%) and 161 females (44%). The mean age of the patients was 55 years, with a standard deviation of 15 years, highlighting a wide age range affected by neuropathic pain.

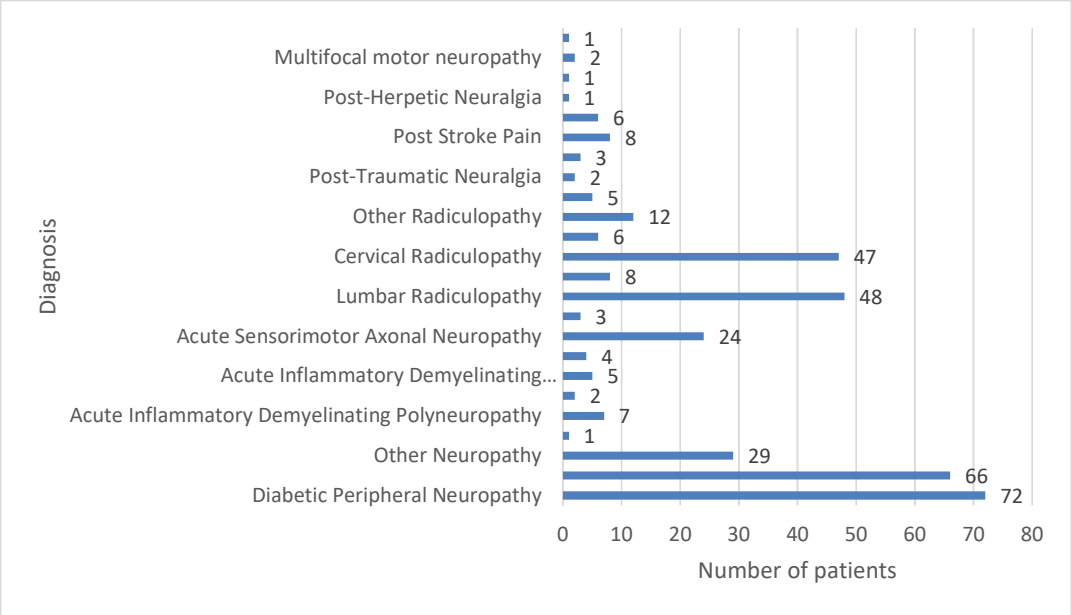
The patients presented with various types of neuropathic pain, out of 363 patients, Diabetic Peripheral Neuropathy emerged as the most common neuropathic condition, affecting 72 patients (19.83%). Peripheral Neuropathy followed closely, diagnosed in 66 patients (18.18%). Less frequent conditions included Other Neuropathy in 29 patients (7.99%) and Acute Sensorimotor Axonal Neuropathy in 24 patients (6.61%).

Rare conditions, such as Chronic Inflammatory Demyelinating Polyneuropathy and Acute Inflammatory Demyelinating Polyneuropathy, affected 1 (0.28%) and 7 patients (1.93%), respectively. Additionally, conditions like Guillain-Barré Syndrome (GBS) and Post-Herpetic Neuralgia were only seen in 1 to 3 patients.

Lumbar and Cervical Radiculopathy were relatively common, diagnosed in 48 (13.22%) and 47 patients (12.95%), while Lumbosacral and Thoracic Radiculopathy were rarer, with 8 (2.20%) and 6 patients (1.65%) affected.

Other neuropathic conditions, including Multiple Sclerosis, Trigeminal Neuralgia, Post Stroke Pain, and Cancer Chemotherapy-Induced Neuropathic Pain, occurred at various frequencies, with the lowest being 0.28%.

Table 1. Distribution of Neuropathic Pain Conditions



Pain Scale Assessment

Pain severity was assessed using the **Wong-Baker Scale** for severity assessment provides a quantitative measure of the pain experience, offering valuable insights into the patient's subjective perception. The emphasis on pain severity is crucial for tailoring effective treatment plans, considering individual tolerance levels, potential side effects, and the impact on daily functioning. The Wong-Baker Scale to quantitatively assess pain severity, revealing that a majority of patients (53.16%) reported experiencing moderate pain, with a rating of 2 on the scale. This finding aligns with existing literature, which frequently characterizes pain severity using scales with variable thresholds for mild, moderate, and severe pain. The congruence in the prevalence of moderate pain is significant, resonating with the chronic and debilitating nature commonly associated with neuropathic pain. The Wong Baker Scale (WBS), with scores ranging from 0 (no pain) to 10 (worst possible pain). The distribution of pain scores among patients is presented in Table 2.

Table 2. Pain Scale Assessment

WBS Score	Frequency	Percentage (%)
0	41	4.9
2	193	53.16
4	116	31.9
8	13	3.5

- **WBS Score 0**: Mild pain, reported by 4.9% of patients.
- **WBS Score 2**: Moderate pain, experienced by 53.16% of patients.
- **WBS Score 4**: Severe pain, reported by 31.9% of patients.
- **WBS Score 8**: Very severe pain, experienced by 3.5% of patients.

1. **Combination Therapy Preference**: A significant preference for combination therapy was observed, with 59.22% of prescriptions involving multiple drugs. This reflects the complexity of neuropathic pain management and the need to address multiple pain pathways.
2. **Anticonvulsants Dominance**: Anticonvulsants were the most commonly prescribed drugs, both in monotherapy and multitherapy, highlighting their central role in neuropathic pain management.
3. **Pain Severity**: The majority of patients (85.06%) reported moderate to sever (WBS scores 2-4), underscoring the challenging nature of managing neuropathic pain.
4. **Gender and Age Distribution**: The study found a slight male predominance and a wide age range of patients, with a mean age of 45.6 years, indicating the broad impact of neuropathic pain across different demographics.

Prescription Patterns

A variety of medications were prescribed for neuropathic pain management, with a notable trend towards polypharmacy. The prescription patterns for neuropathic pain management were

categorized into monotherapy and multitherapy (combination therapy).

Monotherapy

Monotherapy, where a single drug is used, was prescribed to 148 patients, accounting for 40.77% of the total study population. The distribution of drugs prescribed as monotherapy is detailed below:

Table 3. Monotherapy Prescriptions

Drug Class	**Frequency**	**Percentage (%)**
Anticonvulsants	109	76.2
Tricyclic Antidepressants	4	2.7
Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)	3	2.09
Opioids	14	9.7
Other Medications	18	12.16

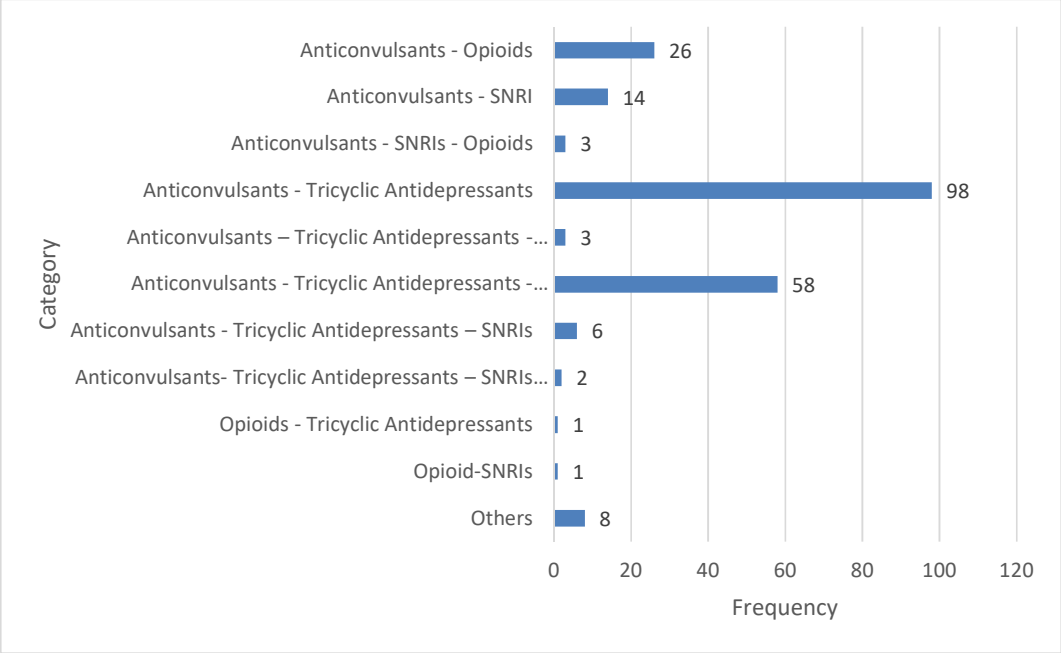
Distribution of Monotherapy Prescriptions

- **Anticonvulsants**: These were the most commonly prescribed drugs in monotherapy, with 76.2% of patients receiving drugs such as gabapentin and pregabalin. These drugs are favoured for their efficacy in modulating nerve pain.
- **Tricyclic Antidepressants (TCAs)**: Prescribed to 2.7% of patients, TCAs such as amitriptyline were less commonly used alone.
- **Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)**: Medications like duloxetine were prescribed to 2.09% of patients.
- **Opioids**: Used in 9.7% of monotherapy cases, primarily for severe pain.
- **Other Medications**: This category included various other drugs like muscle relaxants and topical agents, prescribed to 12.16% of patients.
- The average number of medications prescribed per patient was 3.4, with a range from 1 to 7 drugs.

Multitherapy

Multitherapy, involving the use of two or more drugs, was prescribed to 215 patients, making up 59.22% of the study population. The distribution of drug combinations in multitherapy is detailed below:

Table 4. Multitherapy Combinations



Distribution of Multitherapy Combinations

- **Anticonvulsants + Tricyclic Antidepressants**: This combination was the most prevalent, prescribed to 44.5% of patients receiving multitherapy. The combination leverages the synergistic effects of anticonvulsants and TCAs to manage complex neuropathic pain.
- **Anticonvulsants + Tricyclic Antidepressants + Opioids**: Prescribed to 26.3% of patients, this combination was used in more severe cases where additional pain control was necessary.
- **Anticonvulsants + Opioids**: This combination was prescribed to 11.8% of patients, providing a balanced approach for moderate to severe pain management.
- **Anticonvulsants + SNRIs**: This combination, prescribed to 6.3% of patients, utilized the efficacy of SNRIs in pain modulation alongside anticonvulsants.
- **Other Combinations**: Various other drug combinations, including those with muscle relaxants, topical agents, and other analgesics, were prescribed to 11.1% of patients.

Duration and Dosage Patterns

The study also examined the duration of therapy and dosage patterns. The average duration of neuropathic pain treatment was 12 weeks, with some patients requiring longer-term management. Gabapentin was typically initiated at a dose of 300 mg per day and titrated up to a maximum of 1800 mg per day, depending on the patient's response and tolerance. Pregabalin was usually started at 75 mg per day, with the dose gradually increased to 300 mg per day.

Amitriptyline was often prescribed at a starting dose of 10 mg per day, with incremental increases up to 75 mg per day. Duloxetine was started at 30 mg per day,

increasing to 60 mg per day. The dosing schedules were individualized based on the severity of pain, patient response, and occurrence of side effects.

Patient Outcomes

The study assessed patient outcomes in terms of pain relief and improvement in quality of life. The majority of patients reported moderate to significant pain relief with their prescribed medication regimens. About 65% of patients on gabapentin and 60% on pregabalin reported a reduction in pain intensity by at least 50%. Antidepressants like Amitriptyline and Duloxetine also contributed to improved mood and sleep, enhancing overall quality of life.

Patients receiving combination therapy often reported better outcomes compared to those on monotherapy, highlighting the effectiveness of multimodal treatment approaches. However, a small subset of patients (10%) reported minimal improvement, indicating the need for alternative therapeutic strategies for these individuals.

Table 5. Patient Outcomes

Outcome Measure	Gabapentin (%)	Pregabalin (%)	Amitriptyline (%)	Duloxetine (%)	Combination Therapy (%)
Pain Reduction (≥50%)	65	60	55	50	70
Improvement in Quality of Life	60	55	50	45	65
Minimal Improvement	10	12	15	20	5

Discussion

Study Findings

This study provides an in-depth analysis of the prescribing patterns for managing neuropathic pain at a tertiary care hospital. Our findings highlight the intricate nature of treating neuropathic pain, often necessitating a combination of medications. On average, patients were prescribed 3-4 different medications, reflecting the complexity of effective pain management strategies.

The predominant medications were anticonvulsants and antidepressants. Specifically, gabapentin and pregabalin emerged as the leading anticonvulsants, while amitriptyline and duloxetine were the most used antidepressants. These results align with current clinical guidelines, which recommend these drug classes as first-line treatments for neuropathic pain due to their efficacy in targeting different pain pathways. The frequent use of combination therapies in our study underscores the clinical strategy of utilizing multiple mechanisms to enhance pain control and improve patient outcomes.

Our study revealed distinct differences in medication use based on the type of neuropathic pain. Patients with diabetic neuropathy were more frequently prescribed gabapentin and amitriptyline, which are effective in alleviating diabetic

nerve pain. Gabapentin helps modulate neuronal excitability and reduce neuropathic symptoms, while amitriptyline, a tricyclic antidepressant, works by inhibiting the reuptake of serotonin and norepinephrine, thus enhancing pain inhibition and addressing associated depressive symptoms. For patients with post-herpetic neuralgia, pregabalin and duloxetine were more commonly prescribed. Pregabalin is known for reducing pain and improving sleep quality, whereas duloxetine, a serotonin-norepinephrine reuptake inhibitor, provides pain relief and addresses mood disorders. These tailored prescribing patterns suggest that clinicians customize treatment plans based on the specific type of neuropathic pain, aiming to optimize therapeutic outcomes.

Combination therapy was employed in 45% of cases, often involving an anticonvulsant paired with an antidepressant. This approach leverages the synergistic effects of different drug classes to achieve superior pain control. For instance, combining gabapentin with amitriptyline has demonstrated enhanced pain relief and functional improvement compared to monotherapy. However, the study also highlighted a high prevalence of polypharmacy, with patients averaging 3-4 medications each. This finding underscores the need for careful management to mitigate the risks associated with multiple drug use, such as adverse drug reactions and interactions.

Although less common, monotherapy was still utilized in many cases, especially where pain severity was moderate or where patients had a higher risk of adverse reactions. Gabapentin monotherapy, for example, is often the first-line treatment for mild to moderate diabetic neuropathy, providing effective pain relief with a lower risk profile compared to multi-drug regimens.

The comprehensive analysis of neuropathic pain management underscores the intricate and multifaceted nature of treating this chronic condition. Neuropathic pain, characterized by a complex interplay of sensory, motor, and autonomic dysfunction, poses significant challenges that necessitate a patient-centric approach to care. This study integrates diverse demographic characteristics, etiological factors, and management strategies, providing a nuanced understanding of neuropathic pain epidemiology, diagnosis, treatment patterns, and safety considerations.

The demographic insights gleaned from this study reveal varied profiles of individuals affected by neuropathic pain, with a predominance of males (56%) over females (44%). This gender distribution prompts a closer examination of gender-specific considerations in the assessment and management of neuropathic pain. Emerging evidence suggests that gender differences may influence pain perception and response to treatment, emphasizing the importance of personalized approaches that considers both biological and psychosocial factors. Comparative studies in Nepal, India, and Lebanon show different gender distributions, further underscoring the need for region-specific strategies. For instance, Shrestha et al. (2016) [2] reported a majority of females (69%) in their Kathmandu study, while Jena et al. (2014) [6] found 62.9% females in their Indian cohort, highlighting regional variations that may impact clinical approaches.

Examining the age-wise distribution, the peak incidence of

neuropathic pain in the 50-59 age group, as revealed in this study, aligns with the broader understanding of neuropathic pain epidemiology. This consistency signifies a regional trend or specific factors influencing the age-related prevalence of neuropathic pain. The literature reviews indicate global variations in peak incidence across different age groups, adding complexity to our understanding. For instance, Bahia et al. (2021) [18] reported a mean age of 50.2 years among patients in Lebanon, with cervical or lumbar radiculopathy being the most prevalent condition.

Utilizing the Wong-Baker Scale for severity assessment provides a quantitative measure of the pain experience, offering valuable insights into the patient's subjective perception. The emphasis on pain severity is crucial for tailoring effective treatment plans, considering individual tolerance levels, potential side effects, and the impact on daily functioning. In this study, a majority of patients (53.16%) reported moderate pain, with a significant reduction in pain levels post-treatment. This finding aligns with existing literature, frequently characterizing pain severity using similar scales, underscoring the chronic and debilitating nature of neuropathic pain. The study identified Diabetic Peripheral Neuropathy as the most prevalent condition (19.83%), closely followed by Peripheral Neuropathy (18.18%). These findings are consistent with global trends, emphasizing diabetes as a leading cause of neuropathic pain. However, the relative frequencies of other neuropathic conditions may vary based on regional prevalence and healthcare practices. This diversity necessitates individualized treatment approaches, recognizing that different conditions may respond differentially to specific interventions. The prescription patterns revealed that 40.77% of patients received monotherapy, predominantly involving anticonvulsants (76.2%). In contrast, 59.22% of patients were prescribed combination therapy, with the most common regimen being anticonvulsants and tricyclic antidepressants (44.5%). This approach aligns with international guidelines advocating for multidrug strategies to address the diverse underlying pathophysiological mechanisms of neuropathic pain.

Combination therapy leverages the synergistic effects of different drug classes to achieve superior pain control. For example, combining gabapentin with amitriptyline has demonstrated enhanced pain relief and functional improvement compared to monotherapy. However, the high prevalence of polypharmacy, with patients averaging 3-4 medications each, underscores the need for careful management to mitigate the risks associated with multiple drug use, such as adverse drug reactions and interactions.

Comparative analysis of studies conducted in different geographical regions provides valuable insights into the global landscape of neuropathic pain management. Shrestha et al. (2016) [2] focused on the Nepalese population, linking manual work to pain aggravation, highlighting the need for targeted interventions that consider occupational challenges. Jena et al. (2014) [6] and Bahia et al. (2021) [18] emphasized the prevalence of neuropathic pain and the importance of pharmacological interventions across different settings. This finding underscores the significance of managing polypharmacy to prevent

adverse outcomes. Regular medication reviews and decision-support tools are recommended to enhance patient safety and therapeutic efficacy. The study's findings are consistent with existing literature but also highlight regional and healthcare setting variations. For instance, Dworkin et al. (2010) [7] found a higher prevalence of opioid prescriptions for neuropathic pain in European countries compared to this study, underscoring regional differences in prescribing habits and clinical guidelines. This suggests that local practices and regulations significantly influence medication choices.

Our findings are consistent with several other studies but also highlight notable differences. For instance, Shrestha et al. (2016) [2] reported that anticonvulsants and antidepressants are the most frequently prescribed drugs for neuropathic pain, with gabapentin and amitriptyline being preferred choices, corroborating our observations [2]. Similarly, Gore et al. noted the frequent use of these drug classes due to their proven efficacy in managing neuropathic pain, aligning with our findings [3]. However, regional and healthcare setting variations exist. For example, Dworkin et al. (2010) [7] found a higher prevalence of opioid prescriptions for neuropathic pain in European countries compared to our findings, underscoring regional differences in prescribing habits and clinical guidelines. This suggests that local practices and regulations significantly influence medication choices [7]. Jena et al. (2014) [6] also identified polypharmacy as a common issue in neuropathic pain management, emphasizing the potential risks such as increased chances of adverse drug reactions and interactions. These concerns align with our findings and underscore the need for careful management of patients receiving multiple medications [6].

The high rate of polypharmacy observed in this study has significant clinical implications. While combination therapy can enhance pain relief by targeting multiple pain pathways, it also increases the risk of adverse drug reactions and interactions. This necessitates careful management and monitoring, including regular medication reviews and the use of clinical decision-support tools to help clinicians make informed prescribing decisions. Personalized treatment plans tailored to the individual patient's pain profile, comorbidities, and response to therapy are crucial for optimizing outcomes. Educating patients about their medications, potential side effects, and the importance of adherence is essential to maximize the benefits of treatment and minimize risks. Additionally, integrating non-pharmacological interventions, such as physical therapy and cognitive-behavioural therapy, could provide a holistic approach to managing neuropathic pain and reduce reliance on medications. The differentiation in prescribing patterns based on the specific type of neuropathic pain, as observed in our study, emphasizes the importance of personalized medicine. Clinicians need to consider the underlying cause of neuropathic pain and tailor treatment strategies accordingly. For instance, gabapentin and amitriptyline are more suitable for diabetic neuropathy, while pregabalin and duloxetine are preferred for post-herpetic neuralgia. This approach ensures that patients receive the most effective treatment for their specific condition, improving overall outcomes.

This study highlights several areas for future research and clinical practice

improvement. Optimizing pharmacotherapy protocols and integrating decision-support tools can enhance clinical decision-making and patient outcomes. Future research should also explore the long-term effects of different treatment strategies, especially the impact of polypharmacy on patient health and quality of life. Continuous patient education and regular medication reviews are vital for improving patient outcomes and minimizing the risks associated with polypharmacy. Addressing these areas will help healthcare providers better manage the complexities of neuropathic pain, ultimately enhancing the quality of life for patients suffering from this challenging condition.

Additionally, future studies should investigate the effectiveness of non-pharmacological interventions in combination with pharmacotherapy. Integrating treatments such as physical therapy, cognitive-behavioural therapy, and lifestyle modifications could offer a more comprehensive approach to managing neuropathic pain. This holistic strategy may reduce the reliance on medications and their associated risks, leading to improved patient outcomes and quality of life.

By providing a detailed analysis of current prescribing practices and comparing them with other studies, our research highlights both the commonalities and unique aspects of neuropathic pain management in different settings. This comprehensive approach will inform future efforts to refine treatment protocols and improve patient care in neuropathic pain management.

Ultimately, the goal is to develop more effective, personalized treatment plans that consider the individual patient's needs, preferences, and overall health. This will involve ongoing education for healthcare providers on the latest clinical guidelines and best practices, as well as continued research into new and innovative treatment options. Through these efforts, we can enhance the management of neuropathic pain and improve the lives of those affected by this debilitating condition.

Study Limitations

1. **Observational Study Design:** The reliance on existing patient records may not capture all relevant clinical details.
2. **Single Centre Study:** Conducted at a single tertiary care hospital, which may limit the generalizability of the results.
3. **Sample Size and Duration:** Limited sample size and study duration may not reflect long-term prescribing trends and outcomes.
4. **Data Completeness:** Potential gaps in data recording and reporting could influence the findings.
5. **Adverse Effects and Interactions**: While focusing on prescription patterns, the study did not analyse drug interactions and adverse effects in detail, which are critical for comprehensive understanding.

Conclusion

This study provides a comprehensive overview of the prescribing patterns for neuropathic pain management in a tertiary care hospital, emphasizing the complexities and challenges of treating this condition. By conducting a prospective observational study, we examined the medical records of 363 patients diagnosed with neuropathic pain. The analysis focused on the types of

medications prescribed, the prevalence of polypharmacy, and the use of monotherapy and combination therapies. Our methods involved required detailed data collection from patient records, including demographics, specific diagnoses, and prescription details, followed by statistical analysis to identify trends and significant differences in prescribing practices based on the type of neuropathic pain.

Our results revealed that anticonvulsants and antidepressants were the most commonly prescribed medications, with gabapentin and pregabalin being the predominant anticonvulsants, and amitriptyline and duloxetine the primary antidepressants. Combination therapy, involving an anticonvulsant and an antidepressant, was used in nearly half of the cases. This approach reflects an effort to enhance pain relief by targeting multiple pain pathways simultaneously. Polypharmacy was prevalent, with patients receiving an average of 3.4 medications, indicating the multifaceted approach required for effective neuropathic pain management. Significant differences in prescribing patterns were observed based on the type of neuropathic pain, such as diabetic neuropathy and post-herpetic neuralgia, underscoring the need for tailored treatment strategies.

The study's discussion highlighted the complexity of neuropathic pain management in a tertiary care setting. The high rates of polypharmacy and combination therapy align with current clinical guidelines but also emphasize the necessity for careful and individualized treatment planning to balance efficacy and safety. Comparing our findings with other studies, we noted similar trends in prescribing practices, although regional variations, such as the more frequent use of opioids in European studies, suggest that local clinical practices and guidelines significantly influence treatment strategies.

Our findings underscore the importance of regular medication reviews and the use of decision-support tools to aid clinicians in managing polypharmacy effectively. Personalized treatment plans tailored to individual patient profiles and regular monitoring of therapy efficacy and safety are crucial. Additionally, educating patients about their treatment regimens, potential side effects, and the importance of adherence is vital to optimize therapeutic outcomes.

Our study highlights the prevalent use of polypharmacy and combination therapy in managing neuropathic pain at a tertiary care hospital. These findings emphasize the need for careful and judicious prescribing to balance the benefits and risks associated with polypharmacy. Future research should focus on optimizing pharmacotherapy for neuropathic pain, including the development of decision-support tools and patient education programs to enhance clinical decision-making. By addressing these aspects, we can move towards more effective and safer management of neuropathic pain, ultimately improving the quality of life for affected patients.

Statements and Declarations

Conflicts of interest

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

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ORIGINAL ARTICLE

Comparative Analysis of Percutaneous Nephrostomy and Double J Stenting in Upper Urinary Tract Obstruction with Acute Kidney Injury: A Tertiary Hospital Based Prospective Study

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Abstract

Background: Upper urinary tract obstruction is a serious condition that can lead to significant renal impairment if not managed promptly. Emergency urinary diversion is crucial for alleviating obstruction and preserving renal function. This study investigates various emergency urinary diversion techniques, compares their outcomes, and evaluates factors influencing recovery. **Methods:** We conducted a prospective study involving 106 patients diagnosed with obstructive uropathy at Jawaharlal Nehru Medical College, Aligarh Muslim University. Patients were classified into upper urinary tract obstruction and lower urinary tract obstruction. 70 patients of the upper urinary tract obstruction cases were further managed by either percutaneous nephrostomy (PCN) or double-J (DJ) ureteral stenting diversion procedures. 68 out of 70 upper urinary tract obstruction underwent either of the two procedures. Clinical, demographic, and laboratory parameters were analysed in such patients, and their outcomes were assessed at one and three months. **Results:** The study included 68 out of 106 patients with a mean age of 48 years. Most patients presented with acute kidney injury (AKI) and had symptoms of loin pain and haematuria. Both PCN and DJ stenting were equally effective in managing upper tract obstruction, with no significant differences in improvement of the laboratory parameters (e.g. Hemoglobin, Serum Creatinine, estimated Glomerular Filtration Rate, Blood Urea Nitrogen) between the two techniques at one and three months. Associated factor like age was associated with unfavourable outcomes. **Conclusion:** Emergency urinary diversion via PCN or DJ stenting effectively manages upper urinary tract obstruction, with comparable outcomes. Early intervention and management of underlying conditions are critical for optimal renal recovery and prevent irreversible kidney damage.

Keywords: per cutaneous nephrostomy (PCN), double J (DJ) stent, Acute Kidney Injury (AKI), Chronic Kidney Disease (CKD)

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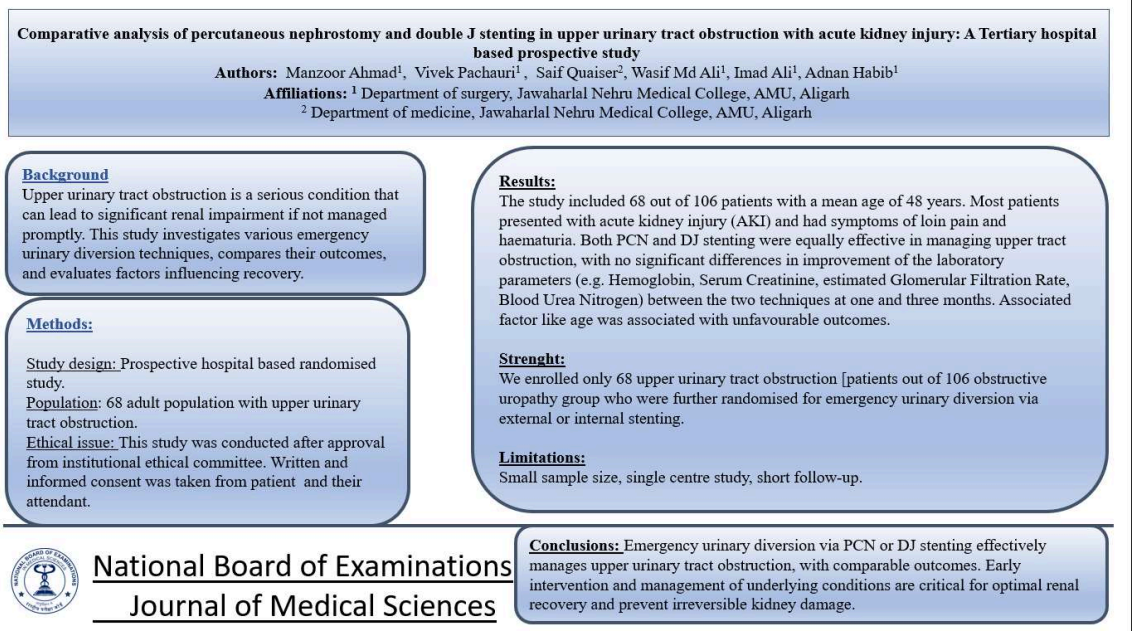
Graphical Abstract



Introduction

Obstructive uropathy is a urological emergency characterized by impediments to normal urinary outflow, which can lead to renal dysfunction and ultimately renal failure. Obstructive uropathy incorporates approximately 10% of all acute and chronic kidney diseases, including 5% of the chronic dialysis population [1]. The etiopathogenesis varies from benign to malignant conditions largely determined by age of the patient. In young adults urolithiasis is the commonest cause while in elders benign prostatic hyperplasia, urolithiasis and malignancies are the leading etiologies.In young adults urolithiasis is primary cause of upper urinary tract infection [2,3].

Obstruction can be acute or chronic, complete or incomplete, unilateral or bilateral. Both the renal parenchyma and the ureter proximal to the obstruction may undergo long-term alterations as a result of obstructive uropathy. To avoid such morbidity and mortality related to obstruction, it must be promptly diagnosed and treated in time.

It is well recognized that obstructive uropathy frequently contributes to chronic kidney disease/end stage kidney disease (CKD/ESKD) in children and it is also linked to acute kidney injury (AKI) in adults [4]. The diagnosis of obstruction of the urinary system and associated anomalies is done using imaging modalities such as ultrasonography, computed tomography, intravenous urography along with urine analysis and blood investigations. In the emergency setting urinary diversion is the method of choice for pelvic or ureteral obstruction, when the underlying pathophysiology of the obstruction cannot be resolved definitely. Urinary diversion techniques include percutaneous nephrostomy (PCN) and retrograde double J (DJ) ureteral stenting [5]. We conducted this study to compare the outcomes of PCN and DJ stenting in the emergency management of upper urinary tract obstruction.

Materials and Methods

Study Design and Setting

A prospective, hospital-based simple randomised study was conducted from August 2022 to July 2024 at the Urology and Nephrology units of Jawaharlal Nehru Medical College, Aligarh Muslim University, Uttar Pradesh, India.

Sample Size

68 patients with upper urinaryobstructive uropathy.

Inclusion Criteria

- Adults ≥18 years old.
- Diagnosed with AKI, Acute Kidney Disease (AKD), or <G4A3 Chronic Kidney Disease (CKD) due to upper urinary tract obstruction.
- Patients undergoing either PCN or DJ stenting.
- Patients giving informed consent for the participation.

Exclusion Criteria

- Pregnant or lactating women.
- Severe comorbidities (e.g., myocardial infarction, heart failure).
- Known G5A3 CKD.
- Previous PCN or DJ stenting before hospital presentation.
- Severe Chronic Obstructive Pulmonary Disease (COPD).
- PCN as well as DJ stenting in a single patient.

Procedures

Patients were initially assessed through hemogram, serum creatinine, blood urea nitrogen (BUN), and imaging (X-ray KUB, USG KUB, NCCT scan, cystoscopy). Out of 106 obstructive uropathy patients 36 patients with lower urinary obstruction were excluded. 70 out of 106 obstructive uropathy patients were diagnosed with upper urinary tract obstruction and they were randomised for either PCN or DJ stenting. 2 patients who underwent both PCN and DJ stenting on either side were also excluded. In 68 patients, follow-up included clinical assessments and laboratory tests at 1 and 3 months to evaluate renal recovery and identification of factors associated with non-recovery.

Techniques

1. **Percutaneous Nephrostomy (PCN):** A SAMSUNG HS50 ultrasonography machine with 2.2 MHz curvilinear and 4.7 MHz linear transducers was used for the ultrasound examination. We assessed the kidneys' cortical thickness, echogenicity, and dimensions after ultrasonography (USG). The damaged kidney had a longitudinal USG scan, with the help of which the puncture site's location was confirmed. The surface area with the best sonographic visibility of the dilated pelvis and calyx was chosen as the puncture site. The renal calyx was punctured at the location with the shortest skin to pelvic distance following local anaesthetic infiltration of 2% lignocaine. A 15 cm, 18 gauge, two-part trocar needle with a diamond tip is inserted into the renal pelvis through calyx under USG guidance. Free flow of urine was used to verify correct position. Under ultrasound guidance, a 150 cm long, 0.035 inch diameter Terumo guide wire was introduced into the needle. Fascial dilators were used to achieve serial tract dilatation over the guide wire. Thereafter, 8 Fr x 30 cm (blueneem) PCN tube was passed into the renal pelvis. After USG confirmed the PCN

catheter's position, silk 1-0 and adhesive strapping were used to fix the catheter to the skin.

2. **Double-J (DJ) Ureteral Stenting:** The Karl Storz 19 Fr rigid cystoscope was inserted after lubrication with 2% lignocaine jelly. The bladder trigone was identified following the ureteral ridge with both vesico-ureteric junctions at opposite ends. After locating the Ureteric Orifice (UO) with a cystoscope, a Terumo 0.035 x 150 cm guidewire was placed into the scope and routed through the UO to enter the ureter. 6 Fr x 26 cm Uromed Double 'J' stent with both ends open was pushed above it. C- arm was used to confirm the correct placement of DJ stent. It was then removed 3- 4 weeks after discharge, if serum creatinine returned to baseline.

Statistical Analysis

Descriptive statistics, Pearson Chi-Square test, independent and paired t-tests were used for data analysis. P-value of <0.05 was considered significant. SPSS version 25.0 was employed for statistical computations.

Results

Patient Demographics

- Mean age: 48 years.
- Majority were males with common symptoms including loin pain and haematuria.
- Most common aetiology in upper urinary tract obstruction in our study was b/l nephrolithiasis.

Table 1. Comparison of laboratory parameters in patients undergoing PCN vs DJ stenting

Changes in Laboratory Parameters from baseline		**PCN (n=32)**	**DJ Stenting (n=36)**	**P-Value**
		Mean	**Mean**	
Hb (g/dL)	At 1 Month	0.06	-0.45	0.294
	At 3 Months	-0.21	0.12	0.062
BUN (mg/dL)	At 1 Month	-21.71	-19.50	0.715
	At 3 Months	-1.07	-4.00	0.106
eGFR (ml/min)	At 1 Month	42.36	41.29	0.889
	At 3 Months	13.43	9.53	0.537
Serum Creatinine (mg/dL)	At 1 Month	-2.93	-2.48	0.255
	At 3 Months	-0.36	-0.22	0.247

*Anova-t test (minus sign (-) indicates decrease in value)

(Abbreviations: Hb= Hemoglobin, BUN= Blood Urea Nitrogen, eGFR= estimated Glomerular Filtration Rate)

Table 1 represented the changes in various laboratory parameters between PCN and DJ ureteral stenting at one month and three months. The mean change and p-value were provided for each parameter.

There was no significant difference in the changes in haemoglobin levels

between PCN and DJ stenting at one month (p=0.294) or three months (p=0.062). The changes in BUN levels were not significantly different between PCN and DJ stenting at one month (p=0.715) or three months (p=0.106).The changes in eGFR were not significantly different between PCN and DJ stenting at one month (p=0.889) or three months (p=0.537). Similarly, changes in serum creatinine levels were not significantly different between PCN and DJ stenting at one month (p=0.255) or three months (p=0.247). This suggested that both procedures had similar effects on these laboratory parameters and were equally effective in patients with obstructive uropathy.

Table 2. Outcome of patients undergoing Per Cutaneous Nephrostomy (PCN) or Double J stenting in upper urinary tract obstruction.

Outcome	PCN (n=32)	DJ Stenting (n=36)	P-Value
Recovered	22	31	0.084

*chi-square test (recovered: return of serum creatinine to baseline)

This data (Table 2) presented recovery outcomes between two renal drainage techniques: Double J (DJ) Stenting and Bilateral PCN. The analysis focuses on the number of patients who recovered and those who did not, with a total of 32 patients undergoing bilateral PCN and 36 patients receiving bilateral DJ stenting. In the PCN group, 22 out of 32 patients (68.75%) recovered, while in the DJ stenting group, 31 out of 36 patients (86.11%) recovered. Additionally, 10 patients (31.25%) in the PCN group did not recover, compared to just 5 patients (13.89%) in the DJ stenting group The P-value associated with this comparison is 0.084. This p-value indicates that there is no statistically significant difference in recovery rates between the two groups.

Table 3. Factors responsible for non-recovery of study subjects

S.No.	Non Recovery Patients		Cases (n=15)	P-Value
1	Age	Older Age (>60)	1	<0.01
		Younger Age (<60)	14	
2	Sex	Male	7	0.796
		Female	8	
3	Co-morbidities	Nil	13	0.004
		Present	2	
4	Urine Culture at Presentation	Negative	8	0.796
		Positive	7	

*Chi-square test

Above mentioned table (Table 3) represents association of various factors like age, sex, co-morbidities, urine culture profile with non-recovery in patients undergoing urinary diversion in upper urinary tract obstruction. On analysis for age with non-recovery, we found that 14 out of 15 cases were young adults whereas 1 out of 15 was in older group with p-value of <0.01. 7 out of 15 were male patients whereas 8 patients were female. This data had a p-value of 0.796 which suggest it to be an insignificant data. Only 2 out of 15 non-recovery patients had co-morbidities and 13 patients were without any associated disease.This suggest that most of the patients in non-recovery group were without any co-morbidity with a p-value of 0.004. On analysis of urine culture profile at presentation among non-recovery patients, we found 8 patients with sterile culture profile and vice-versa with p-value of 0.796.

Discussion

This study aimed to compare the efficacy and outcomes of PCN and DJ ureteral stenting in the emergency management of upper urinary tract obstruction with AKI. Our results show that both PCN and DJ stenting were effective in managing upper urinary tract obstruction. The changes in laboratory parameters, including haemoglobin levels, BUN, estimated glomerular filtration rate (eGFR), and serum creatinine, did not differ significantly between the two techniques. These finding aligns with study conducted by Azwadi et al. and Mertens et al., as they have also demonstrated comparable outcomes between these two methods in terms of renal function recovery and symptom relief [6,7]. PCN is often preferred in cases of severe obstruction or when DJ stenting is not feasible. It provides immediate relief from obstruction and can be quickly performed under local anesthesia. On the other hand, DJ stenting offers the advantage of preserving renal anatomy and function over a longer period, which can be beneficial in cases where a temporary solution is needed while addressing the underlying cause of obstruction.

The study also explored factors associated with non-recovery, including age, sex, co-morbidities, and urine culture results. Furthermore, we identified age and co-morbidities as significant factors influencing recovery. As explained by Tang (2014), urolithiasis is leading cause of obstructive uropathy in younger population [2]. Most of the patients in our study belong to less than 60 age group and most common diagnosis in this group was stone disease. This helped us to correlate positive association of young adults with non-recovery in upper tract obstruction. Whereas, patients with no comorbidities were more common in non-recovery group with significant p-value of 0.004 as most of the patients were young. There is no other recent study with similar non-recovery outcomes. This could be attributed to small sample size and highlights the need of further research on upper urinary obstructive uropathy.

Limitations

Small sample size, single centre study, short follow-up.

Conclusion

PCN and DJ ureteral stenting are both equally effective for management of upper urinary tract obstruction in the context of acute kidney injury. The choice of technique should be individualized based on patient-specific factors and clinical circumstances. Early and effective management, including addressing underlying factors like age, co-morbidities and duration of symptoms is essential for optimizing recovery and preventing long-term renal damage. Future research should focus on validating these findings across different populations and exploring the long-term outcomes of these emergency interventions.

Statements and Declarations

Conflicts of interest

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

Funding

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Ethical approval

This study was conducted after approval from institutional ethical committee. Written and informed consent was taken from patient and their attendant.

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ORIGINAL ARTICLE

Evaluating Medical Students' Perspectives on the CBME Curriculum: A Qualitative Exploration of Curriculum Structure, Pedagogical Approaches, and Educational Integration

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Abstract

Introduction: The introduction of the Competency-Based Medical Education (CBME) curriculum by the National Medical Commission (NMC) in India in 2019 has reshaped medical education by integrating foundational courses, learning strategies, and assessment methods that emphasize competencies essential for modern healthcare. Unlike the traditional knowledge-centric model, CBME aims to produce well-rounded physicians equipped with clinical skills, ethical grounding, and communication abilities. This study aims to examine medical students' perspectives on the CBME curriculum, focusing on its foundational components, learning strategies, integration practices, and assessments. **Materials and Methods:** This cross-sectional qualitative study was conducted over April and May 2023 at the Andaman and Nicobar Islands Institute of Medical Sciences (ANIIMS), Port Blair, among MBBS students from the 2019-2022 batches. Students were surveyed using a semi-structured questionnaire addressing key CBME components. Open-ended questions were utilized to capture students' insights on CBME's perceived benefits, challenges, and improvement suggestions. Thematic analysis was applied to identify recurrent themes, offering a comprehensive understanding of student experiences within the CBME framework. **Results:** Feedback revealed high student appreciation for foundational components, notably Basic Life Support and ethics. Recommendations for new curriculum elements included mental health support, interactive learning formats, and direct patient exposure. Common challenges cited were the extensive logbook requirements and lengthy assessments. Notably, students suggested restructuring self-directed learning (SDL) to include more guidance and advocated for case-based, scenario-driven assessments over traditional formats. Integration practices were valued, though students expressed a need for alignment between subject teachings and integrated sessions to maximize holistic learning. **Conclusion:** This study highlights a generally positive reception of the CBME curriculum, with specific areas identified for enhancement, including reducing administrative burdens, incorporating more practical learning activities, and adjusting assessment formats. Student feedback underscores the curriculum's strengths in fostering competency but also suggests the need for flexibility and responsive updates to meet evolving educational demands.

Keywords: Competency-Based Medical Education, qualitative study, curriculum assessment, medical students, integrated learning

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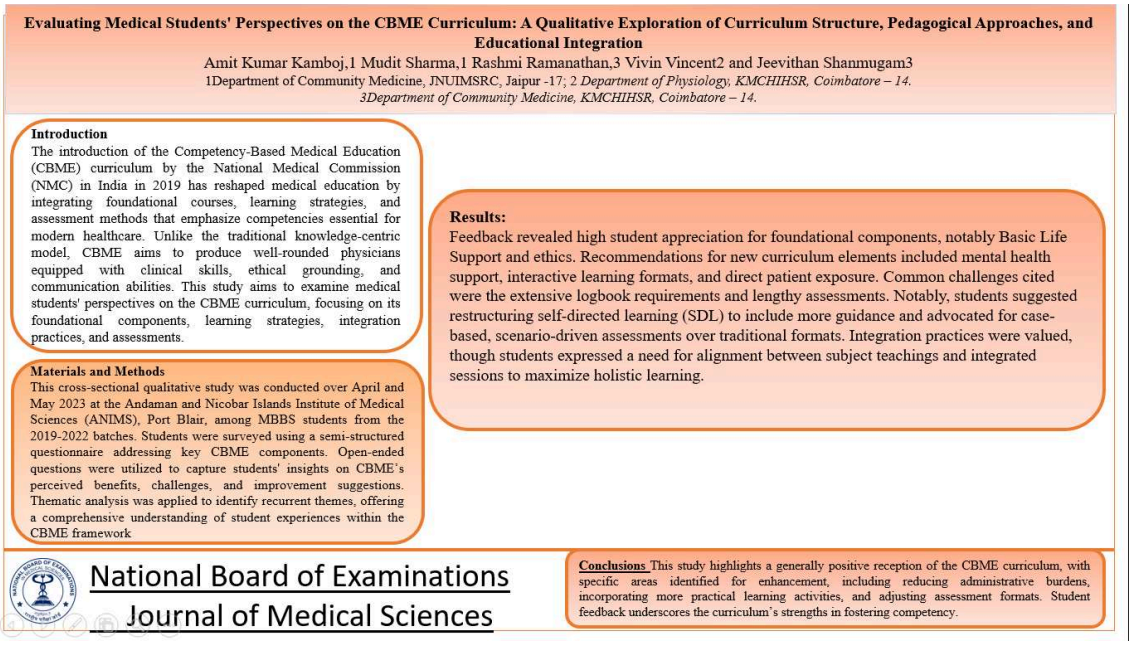
Graphical Abstract



Introduction

The introduction of the Competency-Based Medical Education (CBME) curriculum in India has marked a significant shift in medical training, aiming to equip future physicians with the essential competencies required for modern healthcare delivery. Launched by the National Medical Commission (NMC) in 2019, the CBME curriculum emphasizes a holistic approach to medical education, incorporating foundational courses in professionalism, ethics, and communication skills in the early phases of training. Unlike the traditional curriculum, which predominantly focused on knowledge acquisition, CBME is designed to integrate knowledge, skills, and attitudes through contextualized learning experiences and assessments [1-4].

Foundation courses, a core component of the CBME framework, have been structured to address critical skills such as basic life support, stress management, and biomedical waste handling [1,2]. These courses aim to develop essential competencies at the outset of training, thus setting a strong foundation for clinical education. Early Clinical Exposure (ECE), Self-Directed Learning (SDL), and integrated teaching sessions are other hallmark features introduced within the CBME model, fostering self-sufficiency and interdisciplinary learning among students. However, the effectiveness of these components has been the subject of ongoing debate, with variations observed in their acceptance across different student cohorts [3-9].

Integration of medical sciences, both horizontally across subjects within a single phase and vertically across different phases, has also been a focal point within CBME [10]. Research suggests that integrated curricula may facilitate a more comprehensive understanding of complex medical topics, though the implementation of such integrated sessions presents logistical challenges, including time constraints and content overlap [11,12].

Furthermore, assessment methods under CBME have shifted to include a blend of formative and summative evaluations, prioritizing problem-solving, case-based learning, and objective assessments [13]. While this shift intends to enhance clinical readiness, students have reported concerns about increased academic stress and the practical difficulties associated with assessment methods, such as extensive logbook maintenance and rigorous 100-mark theory papers [3-5].

As medical schools continue to refine and adapt the CBME curriculum, qualitative feedback from students can offer valuable insights into its efficacy and areas for improvement. Gathering perceptions directly from students enrolled in the program allows educators and policymakers to better align the curriculum with the evolving needs of the medical profession and healthcare delivery. This study aims to explore students' views on the strengths and limitations of the CBME curriculum, particularly focusing on foundational courses, learning strategies, integration practices, and assessment methods, to inform ongoing curricular development.

Materials and Methods

This qualitative cross-sectional study was conducted over two months, from April to May 2023, among MBBS students at the Andaman and Nicobar Islands Institute of Medical Sciences (ANIIMS), Port Blair. The primary objective was to explore medical students' perspectives on the implementation of the Competency-Based Medical Education (CBME) curriculum, introduced by the National Medical Commission (NMC) of India, with an emphasis on understanding their lived experiences, perceived benefits, and challenges within the curriculum. Ethical clearance was secured from the institutional ethics committee at ANIIMS, ensuring adherence to ethical standards and protecting participant rights.

Participants included students from the 2019, 2020, 2021, and 2022 MBBS batches who had completed their first year. The 2023 batch was excluded from participation, as these students had not yet completed the first MBBS and would be unable to address all aspects of the CBME curriculum. Students were informed about the study's objectives, its significance, their rights, and relevant ethical considerations through an information sheet. After consenting to participate, each student provided written informed consent, affirming their voluntary involvement and confidentiality of responses.

Data were collected using a semi-structured questionnaire designed to elicit in-depth responses on key CBME curriculum components, including foundational courses, learning strategies, integration, ethics, and assessment methods. Open-ended questions allowed students to express their thoughts on the perceived benefits, challenges, and suggestions for curriculum enhancement, providing nuanced insights into their experiences.

Thematic analysis was conducted on the collected responses to identify recurrent themes and patterns across students' feedback. Coding was performed, followed by categorization of themes related to student perceptions on the curriculum components. Key themes were extracted to highlight common perspectives and unique insights, with quotes used to illustrate these findings. This qualitative approach allowed for an in-depth exploration of student experiences,

revealing areas of strength in the curriculum as well as potential opportunities for improvement.

Results

This qualitative analysis explored student perspectives on the CBME curriculum, highlighting both the appreciated aspects and areas for enhancement. Feedback was gathered on potential additions to the curriculum, aspects students felt could be omitted, sessions they found beneficial, and recommendations for improving specific course elements. The verbatims of the students are quoted in Table 1 below.

Table 1. Perceptions of Students towards CBME curriculum

Category	**Verbatim Excerpts**
Interactive Learning	"Interactive learning such as skit, role play, debate etc."
Extracurricular Focus	"Sports and skill development," "Stress management games," "Outdoor games," "Fitness-related programs."
Mental Health Sessions	"Mental health of medical students," "Stress Management," "Mental health importance, self-defense."
Field Exposure	"Visit to rural and vulnerable areas for experience and to break language barrier."
Direct Patient Interaction	"Direct patient interaction," "Introduction to every department," "Field visits and medico-legal importance."
Technology Integration	"More digital and technological use than just mere writing notes."
Skill-based Modules	"Case-based learning," "First aid care," "Basic skills, like bandaging and wound care."
Logbooks	"Maintaining separate logbooks is very hectic," "Should be one logbook per phase."
SDL (Self-Directed Learning)	"I feel SDL is a waste, no one studies to be honest."
Lengthy Theory Assessments	"80 marks in 2.5 hours is hard to write," "100 mark, 3-hour papers are too long."
Non-Clinical Topics	"Unnecessary history and topics with no clinical relevance."

Sports and Group Activities	"Group activities to know our colleagues better," "Sports was useful for bonding."
Ethics and Professionalism	"Ethics and communication skills exposure is essential," "Career guidance sessions in first year will improve our focus"
Stress and Mental Health	"Stress management sessions are frequently needed," "Mental health sessions are critical for understanding ourselves"
Career Guidance	"Orientation to what life as a doctor in India is really needed."
Assessment Preparation	"Explain the marking scheme, paper structure and Preparation for university exams is a must"
Hands-On Skills	"Hands-on practice of basic skills," "Sessions on self-defense, dealing with patients."
Interactive and Case-Based	"Should be case-based," "Religiosity and spirituality should be considered alongside ethical discussions."
Encouraging Open Dialogue	"Encourage healthy, open discussions on ethical scenarios," "Integrate real-world cases that consider cultural factors."
Integrated and Personal Reflection	"Students should integrate ethics with personal values," "Sessions should reflect on both patient and provider perspectives."
Application-Oriented Approach	"Make it application-oriented within the manageable limits of time and information load."
Gradual Integration	"Introduce horizontal integration first, then vertical," "Ensure integration reflects in assessments and learning goals."
Continuous Revision and Assessment	"Conduct assessments of prior year subjects in later years to refresh memory," "Weekly short tests could aid integration."
Case-Based and Problem-Solving	"Case-based questions in exams," "Problem-based learning assessments," "Scenarios and viva voce."
MCQs and Frequent Testing	"More MCQs, reducing weight of theory papers," "Frequent university-style exams," "Weekly tests to reduce stress."

Students provided multiple suggestions for "*newer components*" that could enhance the MBBS curriculum. Many expressed interest in interactive learning formats such as skits, debates, and role plays to enhance engagement. Extracurricular activities, particularly sports and stress-relief games, were frequently mentioned as effective tools for managing academic pressures. Students also highlighted the need for mental health support and field exposure, including visits to rural or underserved areas, to foster practical skills and real-world empathy. Additionally, students advocated for more skill-based modules, including basic patient care, first-aid skills, and exposure to direct patient interactions. These suggestions reflect a strong desire for practical, hands-on learning and interactive teaching methods that foster both clinical competence and emotional resilience.

In terms of "*elements students felt could be omitted*", the most common theme was the burden of maintaining extensive logbooks for each department. Students consistently suggested a consolidated logbook system, arguing that the current structure is too time-consuming and detracts from learning. Another area of concern was the emphasis on lengthy theory assessments, with students suggesting that the current 100-mark, three-hour format may not adequately capture clinical understanding and application. Additionally, self-directed learning (SDL) was viewed skeptically by some students who felt it lacked effectiveness without structured guidance, further emphasizing a preference for teacher-led or hands-on learning approaches.

"*Sessions found useful*" by students spanned a range of topics. They highly valued sessions promoting student-teacher interaction and appreciated guidance from senior students on adjusting to the demands of medical training. Extracurricular sessions, such as sports activities and team-building events, were also positively received for their role in helping students build relationships and manage stress. Notably, sessions focusing on ethics, professionalism, and communication skills were viewed as essential, underscoring the importance of these topics in medical training. Students frequently suggested extending these sessions throughout the MBBS course to reinforce these foundational skills.

In addition to the current curriculum, students proposed "*enhancements to existing sessions*". Many advocated for more specific career guidance and early orientation to the realities of the medical profession, including how to handle patient interactions and workplace challenges. Practical skill-building was another area of focus, with students recommending hands-on practice in areas like wound care, self-defense, and basic medical procedures. They also highlighted the need for assessment preparation sessions to better understand university marking schemes and examination formats. These suggestions indicate a desire for the curriculum to include direct, practical preparation for real-world medical scenarios and assessments.

To improve the effectiveness of "*ethics-related sessions*", students suggested integrating case-based learning to foster critical thinking and real-world application. They emphasized the importance of an open and interactive format, encouraging dialogue around ethical dilemmas and cultural considerations. Additionally, they proposed

that sessions on ethics should include personal reflection, guiding students to align professional values with personal beliefs to develop a more holistic understanding of ethical practice.

For "*integrated classes*", students suggested a gradual approach to integration, beginning with horizontal integration of subjects within the same academic year, followed by vertical integration across years. They expressed a preference for assessments that reflect integrated learning goals and advocated for weekly short tests or case-based quizzes to reinforce integrated concepts in a manageable format. These recommendations reflect an understanding that integrated learning is most effective when supported by frequent assessments that reinforce and revisit prior material.

Finally, students provided input on "*alternative assessment methods*". Many recommended case-based or problem-solving questions to better gauge clinical reasoning, while others suggested frequent, university-style mock exams and weekly quizzes to reduce stress during major exams. This feedback underscores the need for assessment formats that balance theoretical knowledge with practical application, helping students to develop and demonstrate clinical competency effectively.

Discussion

The implementation of the Competency-Based Medical Education (CBME) curriculum represents a transformative shift in medical education, designed to cultivate key competencies in students through an integrated and student-centered approach [1-5]. This qualitative study highlights both the strengths and challenges perceived by MBBS students at the Andaman and Nicobar Islands Institute of Medical Sciences (ANIIMS), offering insights that are valuable for understanding and improving the CBME curriculum.

Thematic analysis of student responses underscored the foundational course components as essential but with varied levels of perceived benefit. Many students emphasized the practical relevance of skills such as Basic Life Support and Biomedical Waste Management, aligning with the CBME's focus on building core competencies essential for early medical training. However, some students indicated the need for a more contextual approach, suggesting that foundational components could be made more interactive and directly related to clinical scenarios. Interactive learning methods, such as role plays and case discussions, have been shown to enhance engagement and retention, supporting the student feedback advocating for these approaches [14].

In the area of CBME learning strategies, students responded positively to the integration of self-directed learning (SDL), but raised concerns regarding its implementation. While SDL is a core component of CBME, encouraging autonomous and reflective learning, students noted difficulties in adapting to this method without sufficient guidance. The need for balanced instructor-led support has been noted in other studies on SDL in medical education, suggesting that its effectiveness depends significantly on students' preparedness and the provision of resources that scaffold their learning journey. Another notable aspect was the endorsement of small group teaching and early clinical exposure, which students found to be beneficial for reinforcing theoretical knowledge through real-world application. This observation aligns with

existing literature, which posits that small group settings and early clinical interactions can enhance critical thinking and facilitate deeper understanding [15,16].

Integration, a hallmark of the CBME approach, was well received, particularly in its horizontal and vertical forms, where students recognized the value of interconnected learning across disciplines. Students suggested, however, that the integration sessions could be better synchronized with the timing of other subject teachings, indicating that misalignment might hinder holistic learning. The suggestion for concurrent, subject-aligned integration has been proposed in other CBME studies, which emphasize timing as a critical factor for maximizing the integration of medical knowledge. Students also expressed interest in more frequent interactive sessions within the integration component, supporting studies that found interactive, interdisciplinary sessions improve engagement and comprehensive learning [11-14].

Ethics and professionalism were recognized as integral to the CBME curriculum, with students endorsing the relevance of ethics education at the undergraduate level. They suggested enhanced approaches, including discussions that incorporate cultural and spiritual perspectives, reflecting an awareness of patient diversity and individual values in clinical practice. Students' suggestions align with the evolving perspective that ethics teaching should address personal and cultural contexts, providing a foundation for compassionate, patient-centered care [17].

In the area of assessment, students offered insights into the perceived challenges with the CBME's formative assessments, particularly logbook maintenance and the emphasis on multiple-choice questions (MCQs). While students agreed on the necessity of structured assessment, they highlighted the excessive time demands of logbook maintenance, suggesting that it detracts from study time and could benefit from simplification or digital solutions. Previous studies have similarly noted the administrative burden of logbooks, proposing more efficient alternatives such as electronic portfolios [3,15]. Additionally, students proposed viva voce as an effective supplement to MCQs, aligning with findings that suggest verbal assessments enhance clinical reasoning and verbal communication skills [18].

Conclusion

This qualitative study provides valuable insights into student perspectives on the CBME curriculum, revealing areas where the curriculum succeeds in fostering competency as well as opportunities for refinement. Foundational and integration components were generally well-received, but there is room for enhancing interactivity and aligning integration sessions more closely with other subjects. The feedback on SDL indicates the need for a balanced approach that supports student autonomy while providing adequate guidance. Furthermore, the perspectives on ethics suggest that broader cultural contexts could enrich ethics education. In terms of assessment, students' suggestions for reducing the time burden of logbook maintenance and incorporating more verbal assessments could help improve efficiency and practical relevance. These findings underscore the importance of a responsive approach to CBME implementation, one that considers student feedback to enhance the curriculum's efficacy in preparing

competent, patient-centered healthcare providers.

Statements and Declarations

Ethical Approval

Ethical clearance was secured from the institutional ethics committee at ANIIMS

Conflicts of interest

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

Funding

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ORIGINAL ARTICLE

A Study on Histomorphological Spectrum in Abnormal Uterine Bleeding at a Tertiary Care Center

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Abstract

Introduction: A common gynecological problem that affects women, especially throughout their reproductive and perimenopausal years, is abnormal uterine bleeding (AUB). It includes any alteration in frequency, length, or volume that deviates from typical menstrual rhythms. The PALM-COEIN approach, which incorporates both non-structural factors like coagulopathy and ovulatory dysfunction as well as structural causes including polyps, adenomyosis, leiomyoma, and cancer, is used by the International Federation of Gynecology and Obstetrics (FIGO) to categorize AUB. For chronic AUB that does not respond to conservative management, hysterectomy is still the only effective option. For a precise diagnosis, histopathological examination (HPE) of hysterectomy tissues is essential, particularly in cases where imaging alone cannot provide a definitive answer. **Materials and Methods:** This retrospective cross-sectional study was conducted in the Department of Pathology at KMCH Institute of Health Sciences and Research from July 2023 to June 2024. A total of 150 reproductive-age, peri-menopausal, and post-menopausal women with complaints of abnormal uterine bleeding (AUB) who underwent hysterectomy were included in the study. **Results:** The most common histopathological finding was uterine fibroids, observed in 45.3% of cases, followed by adenomyosis in 19.3%. Among the endometrial abnormalities, non-secretory endometrium and disordered proliferative endometrium were identified in 31.3% and 27.35% respectively. Ultrasonography was effective in detecting fibroids but showed limited sensitivity in diagnosing adenomyosis, which was better confirmed through histopathology. **Conclusion:** Histopathological evaluation plays a vital role in diagnosing the causes of AUB, particularly in cases where imaging does not provide clear results.

Keywords: Abnormal uterine bleeding, Histopathological, Hypertension, Anemia, Proliferative endometrium

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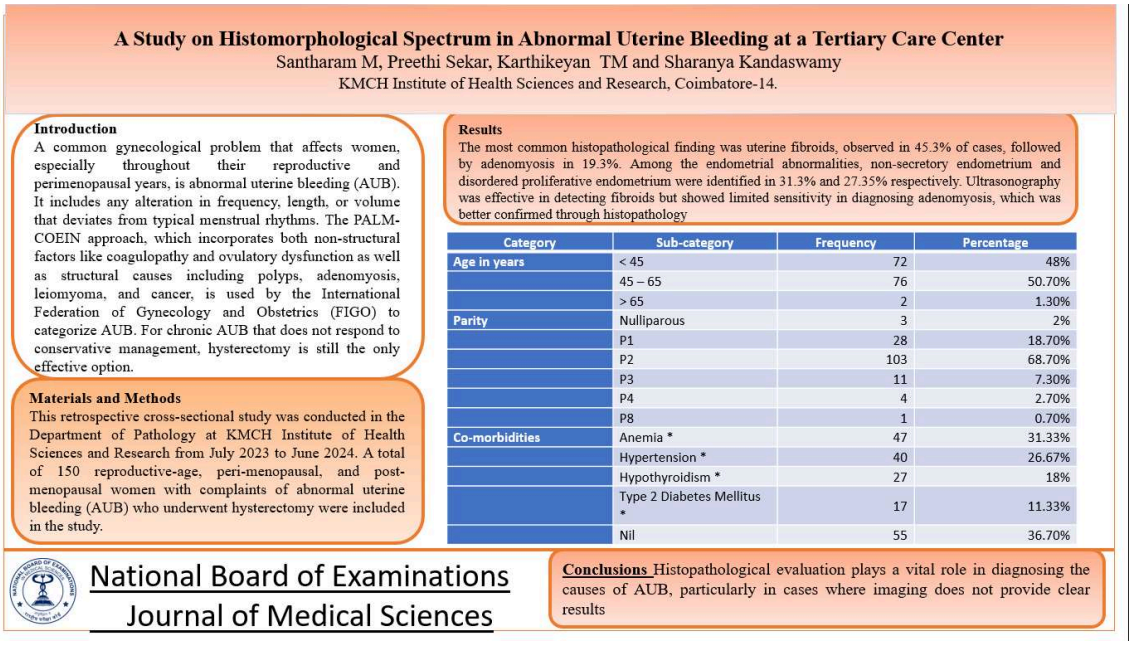
Graphical Abstract



Introduction

One of the most prevalent gynecological disorders, abnormal uterine bleeding (AUB) has an adverse effect on women's health, especially throughout the reproductive and perimenopausal years [1,2]. It includes any alteration to the regular menstrual cycle, such as shifts in the volume, frequency, or length of bleeding [1–3]. Polyps, adenomyosis, leiomyoma, and cancer are among the structural causes of AUB, while coagulopathy, ovulatory dysfunction, endometrial, iatrogenic, and not classified are among the non-structural causes, according to the International Federation of Gynecology and Obstetrics (FIGO), which classifies the causes of AUB under the PALM-COEIN system [3,4]. For women with persistent AUB who do not improve with medical care, hysterectomy is still the only effective option [5]. Because of its accessibility and non-invasiveness, ultrasound (USG) is frequently the first diagnostic technique employed [6]. However, the gold standard for verifying the cause of AUB is histopathological examination (HPE) of hysterectomy tissues, particularly in cases where cancer is suspected [7]. The analysis of clinical, radiographic, and pathological data in this study is crucial for creating evidence-based recommendations for the best hysterectomy treatment plans in AUB. In a tertiary care context, the purpose of this study is to assess the histopathological results from hysterectomy tissues and their relationship to preoperative ultrasonographic results.

Materials and Methods

The Department of Pathology at KMCH Medical College Hospital in Coimbatore conducted this retrospective cross-sectional study between July 2023 and June 2024. IHEC approval and Waiver of consent was acquired. Assessing histopathology results from hysterectomy specimens taken from patients who presented with abnormal uterine bleeding (AUB) and contrasting them with preoperative ultrasound (USG) results were the main objectives of the study. Retrospective data, including clinical

information, USG results, and histopathological examination (HPE) reports, were gathered from hospital records.

150 patients who had hysterectomy for AUB were included in the study; these patients included women of reproductive, perimenopausal, and postmenopausal ages. To guarantee the study's exclusive emphasis on AUB brought on by gynecological diseases, patients with a history of bleeding disorders, pregnancy-related issues, or trauma-induced bleeding were excluded when the case records were scrutinized. Data on patient demographics, age, parity, menstrual history, concomitant conditions, and USG results were analyzed from the clinical records.

In the pathology section, every hysterectomy specimen underwent a thorough gross and microscopic histological examination. Endometrial, myometrial, cervical, and adnexal diseases were assessed in the specimens, which comprised the uterus, cervix, fallopian tubes, and ovaries. Histopathological findings, such as fibroids, adenomyosis, endometrial hyperplasia, chronic cervicitis, and adnexal cysts, were grouped according to the kind and character of abnormalities seen. The results of the ultrasound were also examined, with particular attention paid to the size of the uterus, the thickness of the endometrium, and the existence of fibroids or other anomalies. To evaluate the diagnostic accuracy and uncover any differences, the HPE and USG data were compared.

By anonymizing data during analysis, the study protocol complied with ethical guidelines and guaranteed patient confidentiality. With histopathology acting as the gold standard, the results of HPE and their association with USG results were statistically examined to assess the usefulness of USG in identifying structural and non-structural causes of AUB. Histopathological findings, clinical profiles, and patient demographics were compiled using descriptive statistics. To evaluate the correlation between ultrasonographic and histological findings for endometrial and myometrial abnormalities, chisquare was computed. Statistical significance was defined as a p-value of less than 0.05.

Results

According to the age distribution of women who had hysterectomy for AUB, the majority (50.7%) were between the ages of 45 and 65, with those under 45 coming in second (48%). Merely 1.3% of the population was over 65. The majority of patients were P2 (68.7%), according to parity analysis, which showed that most patients were multiparous. Just 2% of women were nulliparous. The most prevalent comorbidity was anemia (31.33%), which was followed by type 2 diabetes mellitus (11.33%), hypertension (26.67%), and hypothyroidism (18%). Interestingly, Table 1 shows that 36.7% of patients did not have any concomitant diseases.

Table 1. Age wise distribution, parity, and co-morbidities of women undergone hysterectomy for AUB

Category	Sub-category	Frequency	Percentage
Age in years	< 45	72	48%
	45 – 65	76	50.70%
	> 65	2	1.30%
Parity	Nulliparous	3	2%
	P1	28	18.70%
	P2	103	68.70%
	P3	11	7.30%
	P4	4	2.70%
	P8	1	0.70%
Co-morbidities	Anemia *	47	31.33%
	Hypertension *	40	26.67%
	Hypothyroidism *	27	18%
	Type 2 Diabetes Mellitus *	17	11.33%
	Nil	55	36.70%

* Multiple response

According to uterine histopathological analysis, the most prevalent endometrial pathology was non-secretory endometrium (31.3%), which was followed by disorganized proliferative endometrium (27.3%) and secretory endometrium (14.7%). Only 0.7% of cases had endometrial cancer, compared to 8.7% with benign endometrial polyps. The most common finding in the myometrium was leiomyoma (45.3%), and a considerable percentage of cases had both leiomyoma and adenomyosis coexisting (29.3%). 14% of individuals showed just adenomyosis, whilst 11.3% of cases had no noteworthy myometrial abnormalities (Table 2).

Table 2. Histopathological findings of uterus among the women undergone hysterectomy for AUB

Category	Histopathology findings	Frequency	Percentage
Endometrium	Benign Endometrial Polyp	13	8.70%
	Disordered Proliferative Endometrium	41	27.30%
	Endometrial Hyperplasia Without Atypia	3	2%
	Endometrial Carcinoma	1	0.70%
	No Specific Pathology	1	0.70%
	Non-Secretory Endometrium	47	31.30%
	Proliferative Endometrium	15	10%

	Secretory Endometrium	22	14.70%
	Senile Cystic Atrophy	7	4.70%
Myometrium	Adenomyosis	21	14%
	Leiomyoma	68	45.30%
	Leiomyoma and Adenomyosis	44	29.30%
	Unremarkable	17	11.30%

The majority of endometrial diseases were more accurately diagnosed with HPE when endometrial histopathology findings were compared to USG results. In both normal (30.4%) and thickened (36%), non-secretory endometrium was the most often observed feature on USG. However, HPE offered more diagnostic detail; for example, it detected rare diseases including endometrial cancer (0.7%) and disorganized proliferative endometrium in 27.3% of cases, which USG missed. USG and endometrial histopathology results did not significantly correlate, according to the statistical analysis (Rho = -0.014, P = 0.869, Table 3).

Table 3. Comparison of Histopathological findings of the endometrium and Ultrasonographic Results

Histopathology findings	**USG Findings Endometrium**				**Total**		**Chisquare Value (P - Value)**
	Normal		**Thickened**				
	N	**%**	**N**	**%**	**N**	**%**	
Benign Endometrial Polyp	9	7.20%	4	16.00%	13	8.70%	-0.014
Disordered Proliferative Endometrium	37	29.60%	4	16.00%	41	27.30%	(0.869) NS
Endometrial Hyperplasia Without Atypia	2	1.60%	1	4.00%	3	2.00%	
Endometrium Carcinoma	1	0.80%	0	0.00%	1	0.70%	

No Specific Pathology	1	0.80%	0	0.00%	1	0.70%	
Non-Secretory Endometrium	38	30.40%	9	36.00%	47	31.30%	
Proliferative Endometrium	14	11.20%	1	4.00%	15	10.00%	
Secretory Endometrium	19	15.20%	3	12.00%	22	14.70%	
Senile Cystic Atrophy	4	3.20%	3	12.00%	7	4.70%	

The most common disorder seen on both USG and HPE, according to a comparison of myometrial findings, was leiomyoma. But in 14% of patients, HPE found adenomyosis, which USG found less consistently. Histopathology revealed that adenomyosis and leiomyoma coexisted in 29.3% of cases, highlighting the limits of USG in identifying overlapping diseases. USG and myometrial histopathology results did not significantly correlate, according to the statistical analysis (Rho = 0.12, P = 0.143, Table 4).

Table 4. Comparison of Histopathological findings of the myometrium and Ultrasonographic Results

Histopathology findings	**USG Findings**						**Total**		**Chi square Value (P - Value)**
	Adenomyosis		**Leiomyoma**		**Nil**				
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	
Benign Endometrial Polyp	3	10.30%	9	9.80%	1	3.40%	13	8.70%	0.12

Disordered Proliferative Endometrium	12	41.40%	23	25.00%	6	20.70%	41	27.30%	(0.143) NS
Endometrial Hyperplasia Without Atypia	0	0.00%	1	1.10%	2	6.90%	3	2.00%	
Endometrium Carcinoma	0	0.00%	0	0.00%	1	3.40%	1	0.70%	
No Specific Pathology	1	3.40%	0	0.00%	0	0.00%	1	0.70%	
Non-Secretory Endometrium	6	20.70%	31	33.70%	10	34.50%	47	31.30%	
Proliferative Endometrium	2	6.90%	10	10.90%	3	10.30%	15	10.00%	
Secretory Endometrium	3	10.30%	15	16.30%	4	13.80%	22	14.70%	
Senile Cystic Atrophy	2	6.90%	3	3.30%	2	6.90%	7	4.70%	

Discussion

The results of the study show that uterine fibroids were the most common cause of AUB, with histology confirming leiomyomas in 45.3% of patients and ultrasonography identifying 61.3% of cases. Although fibroids were successfully identified by ultrasonography, histology offered conclusive proof, highlighting their higher diagnostic accuracy. This finding is in line with that of Talukdar et al. [3], who determined that fibroids were the main

structural anomaly causing AUB in the perimenopausal age range. As also mentioned by Gupta et al. [8], fibroids are known to damage the uterine surface, increasing menstrual blood flow and prolonging bleeding.

Histopathological analysis revealed that 19.3% of patients had adenomyosis, another important cause of AUB. However, as noted by Mahajan et al. [7], ultrasonography demonstrated low sensitivity in diagnosing adenomyosis, mainly because of its widespread infiltration into the myometrium. Additionally, Elkholi and Nagy highlighted that imaging methods cannot accurately detect diffuse adenomyotic alterations [9]. These results highlight how important histology is as the gold standard for identifying adenomyosis and associated disorders.

According to histopathological investigation, the most common results were non-secretory and disorganized proliferative endometrium, which were found in 31.3% and 27.3% of patients, respectively. According to Pillai et al. [4], these endometrial alterations point to hormonal abnormalities, especially in women who have anovulatory periods. These perimenopausal alterations, which are frequently invisible on ultrasonography, emphasize the need of histopathology in obtaining a precise diagnosis [10].

Larger lesions such fibroids and a big uterus were successfully detected by ultrasonography, but more subtle endometrial and myometrial abnormalities were not adequately described. According to Bindroo et al., histological analysis is still crucial in cases when ultrasonographic results are not conclusive, confirming its function in improving the diagnostic strategy [11]. The accuracy and management of AUB are greatly enhanced by the combination of imaging and histology.

Significant endometrial disease, including polyps and hyperplasia, was more common in patients with irregular menstrual periods. According to Jetley et al., irregular bleeding patterns are important clinical markers of structural problems that need careful histological analysis to inform the best course of treatment [12]. This demonstrates how ultrasonography is limited in its ability to identify structural abnormalities in these situations.

In the study population, comorbidities such as anemia and hypertension were common; 17.3% of patients had anemia. Anemia is frequently made worse by chronic blood loss brought on by AUB, making clinical management more difficult. In addition to managing the underlying causes of AUB, Dias et al. emphasized the significance of addressing these comorbidities [13]. When histopathology is successfully included into the diagnostic framework, it aids in both determining the underlying cause of AUB and customizing treatment to enhance patient outcomes [6,13].

In 96% of cervical specimens, histopathological analysis also showed chronic cervicitis. This conclusion is in line with Verma and Verma's identification of chronic inflammation as a possible cause of AUB [10]. Additionally, 18.7% of cases had benign ovarian cysts, especially follicular cysts, highlighting the necessity of a thorough adnexal examination, which is frequently more effectively accomplished by histology than by imaging alone [10].

Ultrasonography's limits in identifying specific uterine and adnexal diseases make a multimodal diagnostic approach that includes histopathology

essential. Combining imaging with histological examination improves diagnosis accuracy, especially when there are non-specific imaging abnormalities or suspected malignancies, according to Emanuel et al. [14]. By ensuring a more conclusive diagnosis, this integrated approach improves patient care and makes focused treatment solutions possible [15].

Conclusion

The results of this investigation highlight how important histological evaluation is for making a conclusive diagnosis of AUB, especially when imaging is not enough. The most frequent cause of AUB was found to be uterine fibroids, although adenomyosis and other endometrial abnormalities also played important roles. Although ultrasonography proved successful in detecting leiomyomas, tissue testing is essential for a precise diagnosis because of its low sensitivity in detecting disorders like adenomyosis. In order to increase diagnostic precision and support individualized, patient-centered treatment plans, this study promotes an integrated diagnostic strategy that blends imaging methods with histopathological investigation. A thorough strategy like this can greatly improve patient outcomes, particularly for women with unclear or persistent instances of AUB.

Statements and Declarations

Conflicts of interest

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

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REVIEW ARTICLE

Adaptive Genetic Traits in Human Populations: Evolutionary Responses to Malaria

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Abstract
Malaria continues to be a significant health concern in tropical and subtropical areas. The disease is caused by *Plasmodium* parasites and spread through mosquito bites. This review investigates the genetic adaptations that humans have developed over time as a response to malaria. Notable adaptations include hemoglobinopathies (sickle cell trait, thalassemias, hemoglobin C), enzyme disorders (G6PD deficiency, pyruvate kinase deficiency), and membrane protein variations (Duffy antigen negativity, hereditary ovalocytosis). These traits disrupt the malaria parasite's life cycle or enhance immune responses, thereby protecting against severe disease. However, they also introduce health risks, such as chronic anemia and complications with certain medications. Future research focuses on gene-editing technologies and new treatments to improve malaria management while addressing these associated health challenges.

Keywords: Malaria, Genetic adaptations, Population genetics

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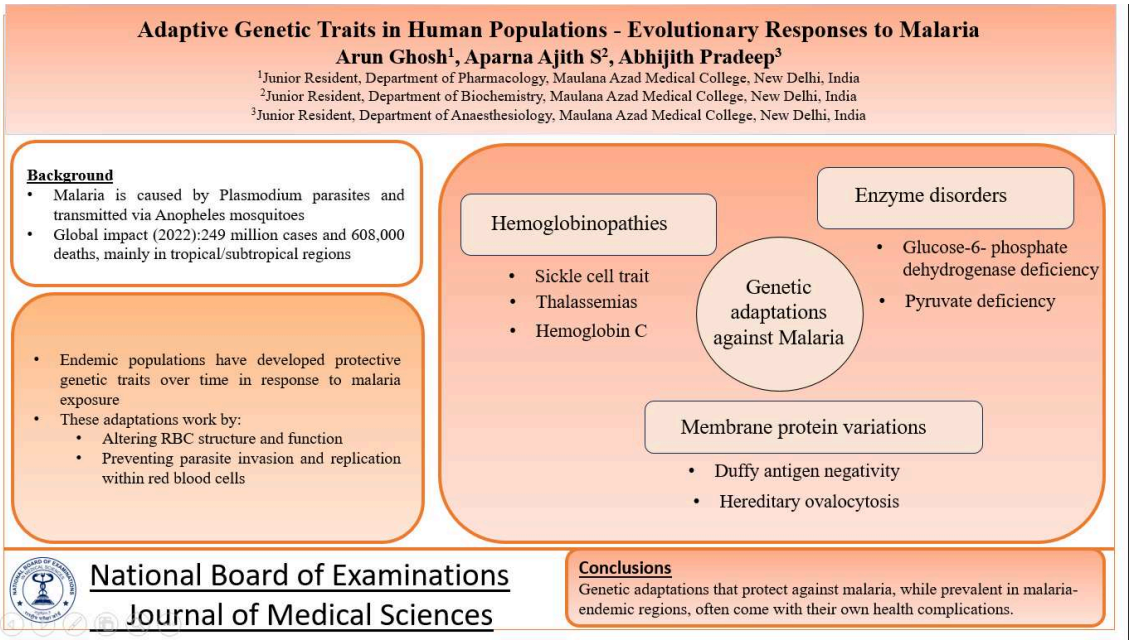
Graphical Abstract



Introduction

Malaria, a parasitic disease caused by *Plasmodium* and transmitted by *Anopheles* mosquitoes, has posed a persistent public health problem. The disease still impacts millions of people globally, especially in tropical and subtropical regions including Africa and Southeast Asia. Globally in 2022, there were an estimated 249 million malaria cases and 608 000 malaria deaths in 85 countries [1].

The malarial parasites first invade the liver cells before targeting red blood cells (RBCs), which causes symptoms like fever, chills, and anemia. In severe cases, it can be potentially fatal. A targeted Plasmodium infection begins when Anopheles mosquitoes inoculate sporozoites during blood feeding, followed by hepatic invasion and subsequent erythrocytic cycles of merozoite proliferation and host cell lysis. The parasitic cycle reaches completion through gametocyte formation in human blood, followed by sexual reproduction and sporozoite development within the mosquito vector [2].

Over time, populations where malaria is endemic have developed various genetic traits as protective adaptations. These adaptations primarily affect the structure and function of RBCs, and hinder the invasion by the parasites or their replication within RBCs [3].

This review article examines the adaptations humans have developed, including their underlying mechanisms and the geographical distribution. It also discusses how these adaptations provide protection while potentially impacting health in other ways.

Genetic adaptations against malaria

These genetic traits can be classified into (1) hemoglobinopathies, (2) enzyme disorders, and (3) membrane protein variations.

I. Hemoglobinopathies

Certain blood disorders, including sickle cell trait and thalassemias, provide

protection against malaria by making red blood cells less suitable for the survival and reproduction of the Plasmodium parasite. These genetic variations typically lead to altered red blood cell structure or reduced hemoglobin production, which can impair the parasite's ability to invade, grow, or reproduce effectively, thereby conferring a degree of protection against severe malaria.

1. *Sickle cell trait*

Sickle cell anemia is an autosomal recessive disorder characterized by the production of abnormal hemoglobin S (HbS), with the genotype SS. Sickle cell trait results when an individual inherits a gene for normal hemoglobin (A) and a gene for sickle hemoglobin Hb (S) that results in the genotype AS [4].

When malarial parasites enter the red blood cells of individuals with sickle cell trait, the infected cells tend to undergo sickling, likely due to deoxygenation and the reduction in pH caused by the parasite. This selective sickling of parasitized red blood cells in individuals with AS genotype facilitates their recognition and removal by phagocytosis, thereby disrupting the parasite's life cycle and mitigating the severity of the infection [5].

Sickle cell trait is more prevalent among individuals of African descent. In the United States, the prevalence of sickle cell trait is approximately 9% among African Americans and 0.2% among Caucasians. Globally, an estimated 300 million people carry the sickle cell trait, with one-third of this population residing in sub-Saharan Africa, a region where malaria is highly endemic [6].

2. *Thalassemias*

Thalassemias are inherited blood disorders that result from mutations in either α-globin or β-globin genes. The protective effect of thalassemia against malaria is attributed to several mechanisms.

These include reduced parasite growth in altered red blood cells, enhanced phagocytosis of infected cells, increased oxidative stress unfavorable to the parasite, and the presence of malaria-resistant fetal hemoglobin in some thalassemia variants [7].

This evolutionary advantage explains the high prevalence of thalassemia in malaria-endemic regions, such as in the Mediterranean region, as it confers a survival benefit against severe malaria, particularly *Plasmodium falciparum* infections [8].

3. *Hemoglobin C*

Hemoglobin C is a variant of normal adult hemoglobin resulting from a mutation in the beta-globin gene, where glutamic acid is replaced by lysine at position 6.

This variant confers protection against malaria, particularly *Plasmodium falciparum* infections, through several mechanisms. These include altering red blood cell structure to inhibit parasite growth, enhancing immune recognition of infected cells, reducing cytoadherence of infected cells to blood vessel walls, and potentially damaging the parasite through crystal-like structures formed under low oxygen condition [9].

Several studies have observed a protective effect in both heterozygotes (HbAC) and homozygotes (HbCC) against malaria infection [9,10]. It has also been observed that the hemoglobin variant occurs at a high frequency in Western Africa, a region known for being endemic to malaria [11].

II. Enzyme disorders

Glucose-6-phosphate dehydrogenase deficiency and pyruvate kinase deficiency are two genetic disorders affecting red blood cell metabolism that, despite their potential health drawbacks, protect against severe malaria caused by *Plasmodium falciparum*.

Glucose-6-phosphate dehydrogenase deficiency

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most common enzymatic disorder of red blood cells, affecting over 400 million people worldwide. This X-linked genetic condition results in reduced activity of G6PD, a crucial enzyme in the pentose phosphate pathway that protects cells from oxidative stress [12].

Paradoxically, this deficiency confers protection against severe malaria, particularly caused by *Plasmodium falciparum*. The protective mechanism is multifaceted: G6PD-deficient erythrocytes are more susceptible to oxidative damage, leading to their premature hemolysis when infected by malaria parasites. This accelerated destruction of infected cells limits parasite proliferation and disease severity [13].

The prevalence of G6PD deficiency closely mirrors the historical distribution of *Plasmodium falciparum* malaria. In areas with high malaria transmission, G6PD deficiency can reach frequencies of 5-25%, as in Sub-Saharan Africa and Southeast Asia, compared to a global prevalence of 4.9% [12].

1. *Pyruvate Kinase deficiency*

Pyruvate kinase deficiency is an inherited disorder of red blood cell metabolism caused by mutations in the PKLR gene. This enzyme deficiency leads to impaired glycolysis in erythrocytes, resulting in decreased ATP production, shortened red blood cell lifespan, and chronic hemolytic anemia of varying severity, with symptoms ranging from mild to severe depending on the specific genetic mutations involved [14].

Pyruvate kinase deficiency confers protection against *Plasmodium falciparum* malaria through a dual mechanism. First, in homozygous individuals, there is an invasion defect where erythrocytes are more resistant to parasite entry. Second, both homozygotes and heterozygotes exhibit enhanced macrophage clearance of ring-stage infected erythrocytes. These combined effects result in a reduced overall parasite burden and limit the progression of infected cells to more mature stages [15].

III. Membrane protein variations

1. *Duffy antigen negativity*

The Duffy antigen, also known as the Duffy Antigen Receptor for Chemokines (DARC), serves as the primary receptor for P. vivax merozoites to invade human RBCs.

Without the Duffy antigen receptor on RBCs, P. vivax merozoites cannot attach to and invade the cells, effectively blocking the parasite's ability to establish infection and reproduce within the host.

The genetic basis of Duffy antigen negativity is a point mutation (-33T>C) in the GATA box of the FY gene promoter, which disrupts the binding site for the GATA-1 transcription factor, specifically abolishing Duffy antigen expression in erythroid cells. This erythroid-specific mutation is found in African Americans (70%) and West Africans (approaching 100%) [16].

Plasmodium vivax is considered to be absent from Western Africa, where the

prevalence of Duffy-negative red blood cell phenotype proves to be very high [17].

2. *Hereditary Ovalocytosis*

Ovalocytosis, particularly Southeast Asian Ovalocytosis (SAO), protects against malaria by altering the structure and function of red blood cells. The red blood cells in individuals with ovalocytosis are more rigid and less deformable due to a mutation in the SLC4A1 gene, which affects the membrane protein Band 3. This rigidity makes it difficult for malaria parasites, especially *Plasmodium falciparum*, to invade and thrive within the ovalocytic cells. The parasite relies on flexible red blood cells to enter, replicate, and spread. With the stiffened ovalocytes, invasion and intracellular growth are hindered, providing a degree of natural protection against malaria [18].

Several studies have observed reduced severity and incidence of malaria in regions where ovalocytosis is more prevalent, such as Southeast Asia and the Pacific Islands, including Papua New Guinea and Malaysia [19].

A summary of adaptive genetic traits that offer protection against malaria is given in Table 1.

Table 1. Adaptive genetic traits that offer protection against malaria

Genetic Trait/Disease	**Mechanism of Protection**	**Active Against**	**Regions with Most Prevalence**
Sickle Cell Trait (HbAS)	Infected red blood cells undergo sickling, leading to their early removal by the immune system, disrupting parasite growth.	*Plasmodium falciparum*	Sub-Saharan Africa, parts of the Americas
Thalassemias (α and β)	Reduced parasite growth in altered RBCs, enhanced phagocytosis of infected cells, increased oxidative stress.	*Plasmodium falciparum*	Mediterranean, Southeast Asia, Middle East
Hemoglobin C (HbAC, HbCC)	Alters RBC structure to inhibit parasite growth, enhances immune recognition, reduces cytoadherence, damages parasite in low oxygen conditions.	*Plasmodium falciparum*	Western Africa
G6PD Deficiency	Infected RBCs are more prone to oxidative damage and hemolysis, limiting parasite proliferation and reducing disease severity.	*Plasmodium falciparum*	Sub-Saharan Africa, Southeast Asia, Mediterranean
Pyruvate Kinase Deficiency	Erythrocytes are more resistant to invasion, enhanced macrophage clearance of infected cells, leading to reduced parasite burden.	*Plasmodium falciparum*	Scattered worldwide, rare, with cases in the Middle East and Europe
Duffy Antigen Negativity	Prevents *Plasmodium vivax* merozoites from invading RBCs, as they rely on the Duffy antigen for entry.	*Plasmodium vivax*	West Africa, African Americans
Hereditary Ovalocytosis	Rigid RBCs make it difficult for parasites to invade and thrive, reducing replication and spread of malaria.	*Plasmodium falciparum*	Southeast Asia, Pacific Islands (e.g., Papua New Guinea, Malaysia)

Health consequences of protective mechanisms

The protective mechanisms against malaria, such as hemoglobinopathies, enzyme disorders, and membrane protein variations, come with significant health consequences also. For example, individuals with the sickle cell trait are protected from *Plasmodium falciparum*, but homozygotes (HbSS) suffer from sickle cell disease, a debilitating condition characterized by chronic pain, anemia, and organ damage. Thalassemias also offer defense against malaria but come with their own health challenges, mainly the ongoing anemia due to red blood cell destruction. In severe cases, patients need regular blood transfusions throughout their lives.

Balancing selection maintains these traits in populations where the survival advantage against malaria outweighs the health burdens. This evolutionary pressure is particularly strong in areas where malaria is common. In these areas, individuals with heterozygous genes experience a survival benefit, which contributes to the persistence of these genetic traits within the population.

Conclusion

Various genetic adaptations, including hemoglobinopathies, enzyme deficiencies, and membrane protein variations, have been observed to be protective against malaria, especially Plasmodium falciparum malaria. These variations are also found to be prevalent in regions that are highly endemic for malaria. Despite their protective role against malaria, these genetic variations also introduce certain health challenges that demand careful management.

Statements and Declarations

Conflicts of interest

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

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REVIEW ARTICLE

Deciphering the Role of Artificial Intelligence in Medical Sciences: An Update

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Abstract

Background: The utilization of Artificial intelligence (AI) computer systems is widespread globally, and the growing body of data in diverse scientific fields highlights the significance and requirement of computer-aided, advanced AI systems in contemporary educational systems. AI is becoming more and more of a versatile actor in the medical sciences, spanning all specializations and including diagnostics. Pharmaceutical companies, payers, and healthcare providers are already using various forms of AI. It's related techniques (machine to deep learning) are frequently employed in disease diagnosis, treatment procedure, and in the evaluation of its side effect. AI techniques utilizes various types of medical diagnostics test data in order to disease diagnosis such as MRI, CT scan, MRI and biochemistry lab reports etc. Better patient-physician communication, remote patient treatment, transcribing prescriptions and other medical documents, and ethical dilemmas are all aided by AI. While humans are still faster at some jobs than computers, the accuracy of modern computer algorithms has lately surpassed that of human experts in the medical sciences. There exist speculations suggesting that medical science roles will eventually be supplanted by people. The current article focused on how AI is transforming medical science along with allied health sector and helping to distinguish between hype and truth, as well as how it might be used to resolve ethical dilemmas and intellectual property rights issues.

Keywords: Machine learning, Health care, IPR, Ethical issues, dental care, medical diagnostics

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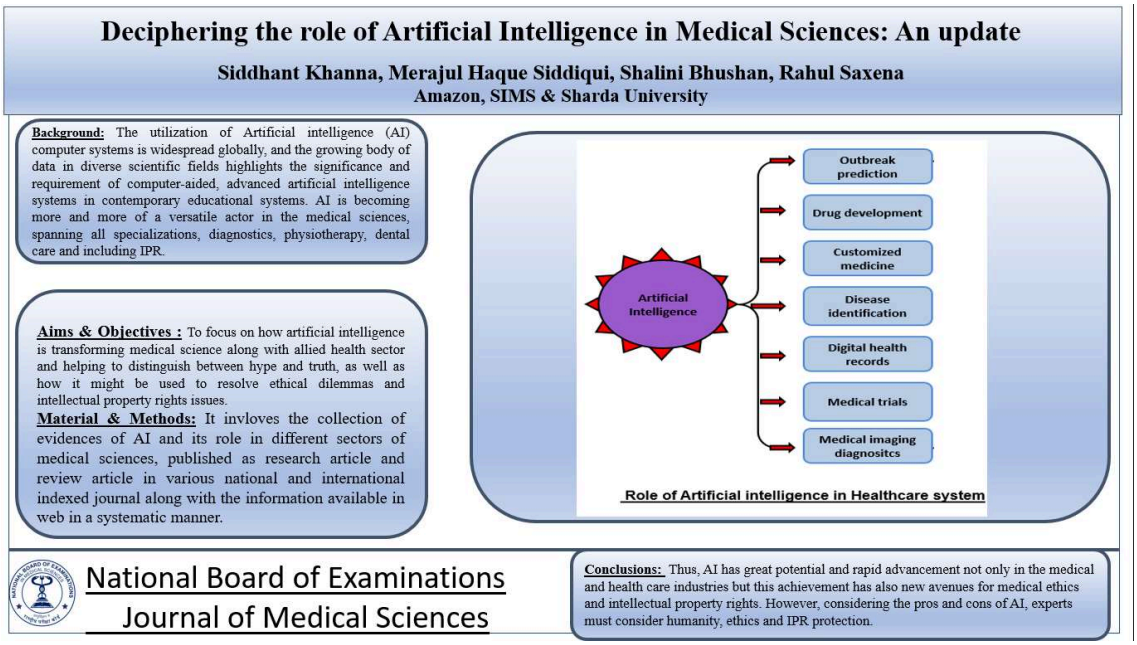
Graphical Abstract



Introduction

Various functions of humans which are done by computer based novel machines on the basis of data available in digital form is known as Artificial Intelligence (AI). When American computer scientist John McCarthy and colleagues hosted the Dartmouth Conference in 1956, the phrase AI was initially used. Prior to that time, chess program created by Dietrich Prinz and intelligence of machine measured by Alan Turing's test were some of the advancements in the field of AI [1,2]. Automated interfaces for speech recognition, vision, decision-making, and language translation are just a few of the well-known applications of AI. It has transformed many sectors of the economy and aspects of daily life, offering both exciting new prospects and challenging circumstances. Previously, AI appears as a science fiction but now a days, AI has applicable globally and involved in most of the branch of science. AI can perform similar function as that of human intelligence and covers a broad range of cognitive abilities, from simple to complicated cases in an automated decision-making mode. Interestingly, AI is universal and various sorts of industries such as banking, entertainment, health and education industry etc. utilizes this technology in an effective manner. Apart from its role in enhancing productivity and efficiency, AI has encouraged the culture of innovation in various streams such as information evaluation, predictive modelling, and tailored services. It has been observed that AI has achieved an amazing success and enhanced pace by virtue of neural network, advanced information analytics and computer-based system research. This success rate has been attributed to the availability of smart processing ability in corporation with availability of huge electronic data. These days, AI is an interdisciplinary science that has spread throughout many scientific fields, including medicine [3].

The digital age's use of AI, 3D printing, robotics, nanotechnology, and other technologies in the medical science has drawn much attention lately. The following general trend is observed in artificially intelligent systems in the medical sciences and healthcare sector. A significant amount of data is the starting point for an AI system. Machine learning methods are then used to extract knowledge from this data, which is subsequently utilized to produce an output that is helpful in resolving a specific problem in the medical system. AI has many advantages, such as lowering human mistake rates, enhancing clinical results, tracking data over time, etc. AI is being used in the medical sciences to connect patients with the right doctor based on their symptoms, diagnose and prognostic patients, find new drugs, and create bot assistants that can translate across languages, transcribe notes, and organize data and photographs.

Furthermore, from machine learning to deep learning, AI utilizes healthcare related several domains which includes novel biochemical assay system, the administration of patient data and records, and the treatment of various ailments [4]. Additionally, AI approaches are the most effective in diagnosing various disorders. However, there are several IPR, legal, and ethical difficulties in this scientific realm. The present review article focuses on various important aspect of AI in the diverse field of medical sciences including healthcare system, medical diagnostics, physiotherapy, dental care and issues related to ethics and intellectual property rights involved in health care sector.

Role in Healthcare system

Today, from creating new health assessment methods to handling patient information and finances, AI, including its subcategories of machine learning and deep learning, is moving towards becoming a fundamental part of the healthcare system. Managing and carrying out organizational duties is a major challenge for physician practices today. By automating them, healthcare companies may help solve the issue and free up physicians' time to do what they do best so that they can spend more time with patients [5,6]. Various healthcare applications in which AI has a role, are listed below, as seen in Figure 1 [7].

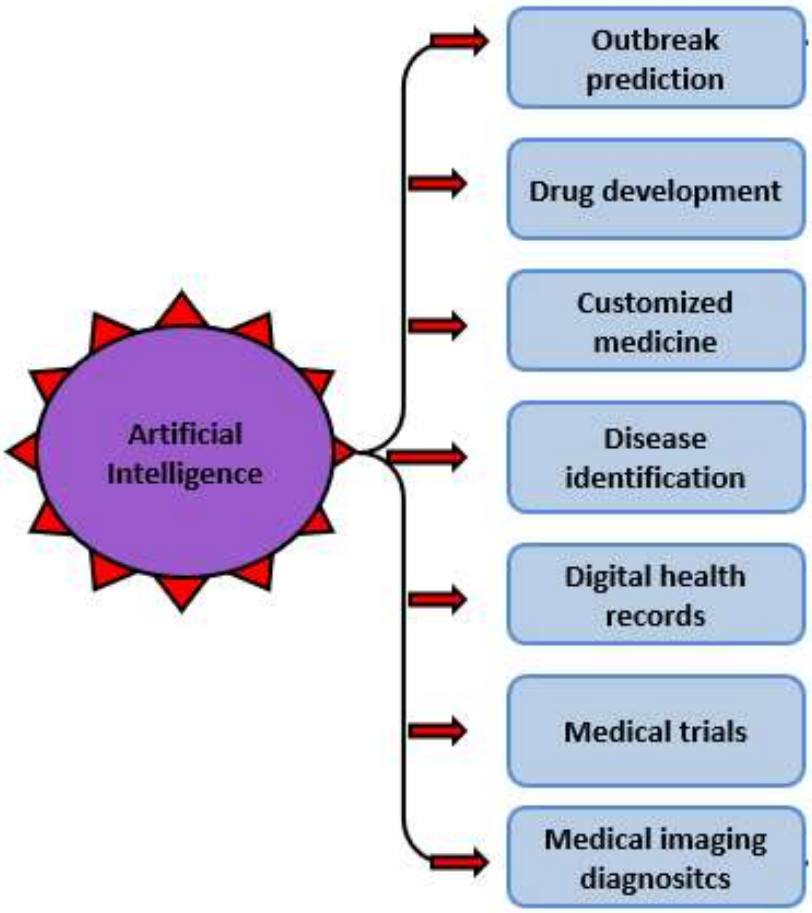


Figure 1. Role of AI in health system.

In addition, several AI techniques have been used to detect illnesses needing early detection, like skin, liver, heart, and Alzheimer's disease. AI techniques can have an impact on the creation of new medications, intensive care, their clinical validation, and many other aspects of cancer therapy [7,8]. Pradhan et al. (2020) assessed several adaptable algorithms of machine learning for lung cancer diagnosis in relation to the internet of things. To use a machine learning system to forecast various diseases, they analysed several publications. Based on the current approaches, they also defined and illustrated some future directions [9]. In general, AI has a cutting-edge strategy in the field of precision medicine also referred to as "personalized medicine," and now a days, it is receiving considerable attention. It entails customizing illness prevention and therapy to account for variations in people's genetic makeup, habits, and environments [10]. Furthermore, numerous methods employed for disease diagnosis with more accuracy includes decision tree, fuzzy logic, SVM (support vector machine), Boltzmann machine, support vector machine (SVM), logistic regression and artificial neural network etc., are employed to identify diseases with greater accuracy. Using a backpropagation neural network, Dabowsa et al. (2017) were able to diagnose skin diseases with the best degree of accuracy [11].

Role in medical diagnostics

Medical diagnostics, the process of evaluating illnesses or disorders by analysing test results, medical backgrounds, and symptoms, are used to identify the cause of a medical problem and correctly diagnose the disease so that the right treatment can be given. This might involve different diagnostic procedures such as blood tests, biopsy surgeries, and imaging tests such as MRIs, CT scans, and X-rays. Healthcare professionals can choose the optimal treatment for their patients based on the results of these tests. In general, all the diagnostic test related to health care system provide information not only limited to disease diagnosis but also about progression of effect of treatment in order to prevent the mishappening in future. By virtue of AI, the diagnostic process and access of information is getting quiet fast and accurate with more efficient manner. Thus, incorporation of AI programs in medical diagnostics assist medical practitioner in examining various digital images or reports such as DXAs, S-rays, MRIs, CT scans, pathological reports and ultrasound etc., in more efficient and accurate manner in less time [12,13].

AI has the ability to examine extensive patient information, such as medical 2D/3D pictures, biosignals (ECG, EEG, EMG, and HER), vital signs (like body temperature, pulse rate, breathing rate, and blood pressure), demographic details, medical background, and laboratory test outcomes. This could help with making decisions and give precise prediction outcomes. This can assist medical professionals in making better decisions about patient treatment. The variety of information from patients, including different types of data like images, signals, and text, is a good way to make better decisions when diagnosing. Healthcare providers can improve their understanding of a patient's health and the reasons for their symptoms by using different sources of data. Pooling information from various sources can result in a more precise assessment and a more comprehensive understanding of a patient's well-being, reducing the likelihood of an incorrect diagnosis. Healthcare workers can improve the treatment and control of long-term diseases by using multiple forms of data to monitor a patient's condition over time. Currently, healthcare providers that use Explainable XAI can detect potential health problems early on, before they get worse and become life-threatening, due to the use of multiple types of medical data. Furthermore, it has been conceived that by automating repetitive tasks with XAI technology, doctors or healthcare professionals can focus on more patient care related to complex clinical conditions [14].

Role in Dental Care

AI technology could have a big impact on many different parts of dental treatment. Accurate diagnosis is one of the main areas where AI can have an impact. AI can help dentists find patterns and provide precise diagnoses by analyzing massive datasets. This capacity allows for early intervention and treatment planning along with accurate diagnostic feature, all this eventually enhance patient outcomes. Both bettering treatment planning and dental processes can be greatly aided by AI. Customized intervention recommendations can be made by AI-driven systems through a thorough examination of patient clinical information and past results. This facilitates the workflow for dental care practitioners while simultaneously increasing treatment precision. Oral surgeons and practitioners

are getting benefits from AI based interventions instead of spending time in administration task. Thus, AI making them free for more important task related to patient treatment by automating regular tasks and offering evidence-based recommendations Patient education and their engagement are also supported by AI so that patient can easily understand their oral health, available treatment and recommendation options as an individualized and case specific manner. This in turn facilitates the patient overall to get satisfaction in their oral health treatment with more perfection [15].

Virtual consultation platform assisted by AI system has been found to be more patient friendly as patient from distant area can get proper information, advice and treatment option about their dental health from specialized dental expert without meeting them physically. Furthermore, availability of teledentistry, AI chatbots and virtual support system can resolve the personalized queries of patients, providing them suitable and appropriate treatment recommendations, boosts the dental services and thereby enhances the easily approachable and convenient services to the patient related to oral health disorder [16]. Thus, the patient ultimately benefits from better dental health outcomes that result from this active participation.

Role in Physiotherapy

Promising uses of AI can be found in the physiotherapy industry. Physiotherapists can improve patient outcomes, customize therapy programs, and improve their diagnostic skills by utilizing AI technologies. AI-maneuverer structures can examine movement patterns, medical histories, and results in order to assist physiotherapists in creating customized rehabilitation plans for their patients. In addition to increasing therapy efficacy, this individualized approach promotes patient participation and adherence to rehabilitation guidelines. By evaluating movement data and finding tiny patterns and irregularities that the human eye can find difficult to notice, AI technologies have the potential to revolutionize the diagnostic process in physical therapy. By recognizing these patterns, AI can help physiotherapists diagnose musculoskeletal disorders with accuracy and develop individualized therapy programs that address the specific requirements of each patient. In addition, AI-powered systems can analyse massive amounts of data, combining past rehabilitation results with intervention reactions, to suggest tailored therapy regimens. Physiotherapists are supported by AI in optimize prognostic tactics and customize exercise schedule as per needed for individual patient according to their specific profile and treatment responses. Thus, specific required treatment strategy can be framed for each patient individually [17].

In addition to diagnostic and treatment planning skills, AI has the potential to improve patient engagement, adherence to strategy associated with rehabilitation. Physiotherapists can provide their patients with individualized instructional content, exercise regimens, and progress tracking with the aid of AI-powered solutions. This personalized development encourages patients to actively participate in their recovery, which in turn promotes motivation and a sense of accountability, leading to improved rehabilitation outcomes [18].

Healthcare associated Ethical Concerns in AI

It has been encountered that the role of AI in the field of medical science is vast and its application involve the use and assess of compiled electronic data related to MRI, biochemical findings of diagnostic lab reports, preventive medicine and all the healthcare service-related data. The use of patient and health service-oriented data is always associated with various legal and ethical concerns. In communities, AI has extended their wings in an impressive manner to improve the patient treatment and its related outcomes, however, in general, it is not affordable to all. Many under developed and developing countries have not access to latest and emerging technologies as well. In addition, challenges occur while using AI cannot be ignored e.g. data protection, data privacy, ethical concerns, patient information sheet along with their consent form, advice (both social and medical) and empathy-sympathy. Therefore, while integrating AI involved in healthcare system, practitioners and surgeons will have to remember the inclusion of major medical principles related to ethical issues such as freedom, beneficence, nonmaleficence and fairness in all dimensions related to medical professionalism [19].

Healthcare practitioners must handle ethical issues, data secrecy problems, and biases involved in the utilization of various AI technologies into the area of physiotherapy. Physiotherapists can use these technologies to provide patient-centred, individualized, and efficient rehabilitation care by adhering to ethical principles and using AI ethically. This will ultimately improve the provision of physiotherapy services. By virtue of transformed patient involvement, improved treatment procedures and diagnostic patterns, AI plays a dynamic role in the field of physiotherapy. Moreover, involvement of AI technology, can provide deeper insights into patient data, movement patterns, and treatment outcomes, to the physiotherapists. This can lead to the development of more specific, better and individualized rehabilitation strategies for their patients [20].

The reliance on AI for medical decision-making is another problem. Healthcare professionals must have both a personal touch and critical thinking skills in order to provide high-quality care. The function of physiotherapists in developing individualized treatment programs based on each patient's needs and preferences may be diminished if AI tools are used excessively. Achieving a balance between using AI to gain insights and maintaining vital human components in healthcare delivery is crucial. Concerns of data privacy and security are also raised by the integration of AI into physical therapy, since AI is dependent on a large quantity of patient data, including genetic information and sensitive medical descriptions. To effectively protect patient information, physiotherapists need to navigate a complicated web of laws and regulations pertaining to data privacy. The potential bias present in AI algorithms is another thing to think about [21].

Healthcare disparities and inequities may inadvertently be perpetuated by AI trained on biased or small datasets. Physiotherapists are need to assess AI training data sources attentively and take proactive measures to reduce biases that can compromise their ability to provide all patients with just and equitable therapy. Even though AI has a lot of potential for physiotherapy, medical professionals must

integrate AI with caution and critical thinking. Physiotherapists can guarantee that AI-enhanced care stays ethical, patient-centered, and compliant with customized rehabilitation principles by recognizing and resolving these challenges [22].

Role in Intellectual property rights

Intellectual property (IP) rights and the medical sciences, both have a significant and transformative link in the modern era. IPR can be applicable in all the innovative developments of surgical instruments, therapeutic techniques, and chemicals with medical qualities. As the advancement in medical sciences occur due to involvement of AI system, the health care industry has more opportunity to develop enhanced creative and inventive approach at faster rate. The legal landscape around the intersection of AI and intellectual property rights is intricate, dynamic, and fraught with important philosophical and legal questions. In order to protect creative and inventive approach of human, IPR laws were designed but these laws are facing difficulty now due to involvement of AI in developing new AI created tasks and inventions. This calls into question the notion of authorship and inventorship in the era of AI [23].

The subject of copyrights concerns whether AI-generated creations, such as novel shapes, arts, and patterns, as well as literary works, may be protected, and if so, who is entitled to do so. Regarding patents, the discussion focuses on whether AI is capable of being considered an inventor and how AI-generated innovations in the healthcare industry fit within the traditional definitions of novelty and non-obviousness. AI can generate and use their own new brand names and logos. In addition, healthcare industry also face difficulties in another section of IPR i.e. trademarks. Previously, the rights of artistic and literary work has been granted to human authors but now paradigm shift in copyright law occurs due to the unique ability of AI in such type of works. AI-generated works question the basic idea of "authorship," such as the creation of novel surgical instruments, medication component formulations, and literary texts. Authorship and Ownership: Which party holds the copyright for works generated by AI? This is one of the main concerns. The usual interpretation of originality and creativity in the healthcare industry—two concepts that are essential to copyright law—is called into doubt by this query. Evaluating whether AI-produced works adhere to the originality and inventiveness requirements outlined in copyright laws. This entails reassessing these terms' legal definitions in the light of AI in the healthcare system. Economic Rights and Moral Rights examine whether AI should have moral rights including the right to integrity and credit, as well as how rights like replication, adaptation, and distribution pertain to works created by AI [24-26].

Conclusion

Rapid technology breakthroughs and related healthcare concerns have created a dynamic environment at the nexus of AI and the healthcare sector. AI will surely push the boundaries of present medical science frameworks as it develops, requiring constant technological reform and adaptation. Medical professionals may provide advanced, cutting edge, customized care that enhances patient outcomes and revolutionizes the medical sciences by ethically and professionally utilizing AI. Future healthcare, however, will have to strike a balance that is both commercially

and morally feasible between the results of various diseases and the recommended course of treatment. To address the global character of AI technology and medical sciences, there will be a growing demand for international collaboration in the development of harmonized standards and regulations. Furthermore, there are several chances for improving diagnostic precision, expediting treatment planning, streamlining workflow, and encouraging patient involvement and education through AI integration in allied healthcare. It is essential that providers of allied health consider the ethical implications, potential biases, and data privacy concerns associated with AI in the fields of diagnostics, rehabilitation, and dental care in order to ensure the equitable and responsible provision of allied healthcare services. Nevertheless, despite AI's great potential and rapid advancement in the medical and health care industries, this achievement has set new guidelines for medical ethics and intellectual property rights. Because of this, we should be aware that its disadvantages can outweigh its benefits. To overcome this problem, experts must consider humanity, ethics and IPR protection.

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Conflict of interest

There is no conflict of interests. All authors are equally contributed.

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Authors Contributions

Conceptualization and designed the review, M.H.S. and R.S.; resources, abstract screening and data extraction, S.B.; writing—original draft preparation, G.K and R.S.; writing—review and editing, R.S.; edited and added major contents to the manuscript, S.B.; supervision and project administration, R.S.

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REVIEW ARTICLE

Understanding Tobacco Control: Global and National Strategies

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Abstract

Tobacco use is a significant global health crisis, impacting over 1.1 billion individuals and leading to approximately 8 million deaths annually. This narrative review evaluates the tobacco control policies worldwide, focusing on India, where both smoked and smokeless tobacco prevalence remains high. Historical interventions highlight ongoing efforts to combat tobacco use; however, challenges in public awareness and access to cessation resources persist. There is an urgent need for effective policies and comprehensive public health strategies to reduce tobacco consumption, underscoring the critical role of health professionals in promoting cessation efforts.

Keywords: Tobacco Control, Health Policy, Smoking

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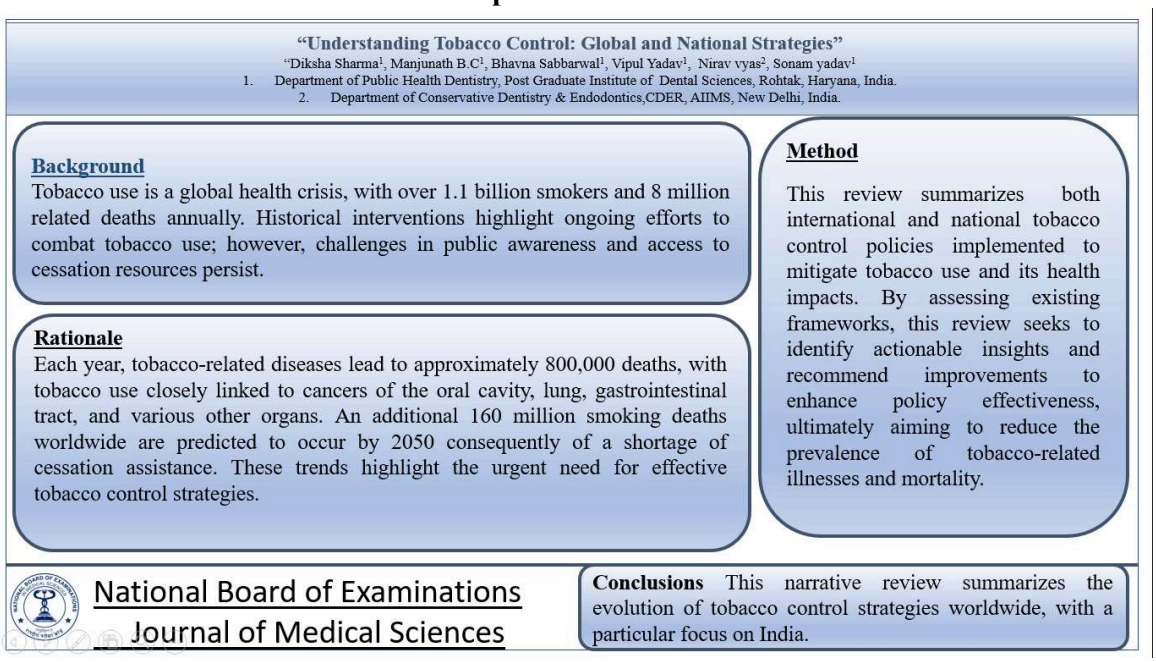
Graphical Abstract



Introduction

As stated by WHO (World Health Organization), 1.1 billion individuals smoke worldwide, representing one-third of the global population aged 15 and over, resulting in 8 million deaths each year [1,2]. 10% of global mortality is due to tobacco smoking, with developing countries expected to experience the impact of disease by 2030, accounting for 80% of cases [3]. During the Mughal Empire, 400 years back tobacco had been bought to India by Portuguese. In India tobacco is mostly used in 2 forms: smokeless tobacco and smoke tobacco. The most common way to smoke tobacco is with a beedi, then with cigarettes. An estimated 2% of women and 19% of males in India smoke tobacco. According to age-specific information from the National Family Health Survey-2, the estimated smoking prevalence among men in the thirty-plus age group is 41.2% [2]. Compared to the rest of the planet, in India, smokeless tobacco is more common (21.4percent) than smoked tobacco (10.7percent) [4]. As a result of smokeless tobacco becoming more common in India compared to the other countries, the incidence of oral cancer is high among users (50%) [5,6]. It is widely known that tobacco usage is one of the primary reasons for illness and mortality in India, accounting for about eight lakh deaths annually [2].

The IARC (International Agency for Research on Cancer) monograph declares that there is enough data to conclude that tobacco use raises chance of developing cancers of the gastrointestinal tract, throat, urogenital tract, mouth, and larynx [7]. Smoking is the primary reason for lung cancer fatalities in men (about 90%) and women (about 80%) [8]. Tuberculosis (TB) is another disease that is linked to even small amounts of tobacco smoking [9]. So, it can be wise to say that not a single part of the body is spared by harmful effects of tobacco [2].

Historical Intervention to prevent tobacco habits

- The Prevention of Food Adulteration Act (1954) mandated that cigarette packages display legislative warnings with a minimum diameter of 3 mm in both English and the local language. The act also restricted smoking in public areas in Karnataka and Maharashtra [10].
- With the passage of the Cigarettes Act in 1975, tobacco control began in India [11].
- The Motor Vehicles Act of 1988 barred smoking and spitting on public transportation. The Cinematograph Act was amended by the Central Government in 1991 to outlaw the facilitation of smoking in motion pictures [10].
- In addition to these national initiatives, certain Indian states had attempted to address tobacco usage through state laws. Kerala followed Delhi in 1999 as the 1st state to outlaw smoking in public places, having done so since 1996 [10].
- In 1999, Goa passed the anti-tobacco legislation. Ultimately it became the diluted version of the original bill due to intense lobby from pro-tobacco groups. Within the next 12 months, Andhra Pradesh, Madhya Pradesh, Bihar, Maharashtra, and Tamil Nadu banned marketing and sales of gutkha [10].

Global and Indian initiative for tobacco control

Global Tobacco Surveillance System (GTSS)

The GTSS has been launched in 1998 by WHO, the CPHA (Canadian Public Health Association), and the Centre for Disease Control and Prevention (CDC) in U.S.A. The principal objective was to augment the nation's capacity to formulate, execute, and assess tobacco control measures while overseeing essential provisions of the WHO FCTC (Framework Convention on Tobacco Control). GTSS encompasses several surveys.

1. **Global Youth Tobacco Survey (GYTS)**
   The GYTS survey, which was self-administered and conducted in schools, measures juvenile tobacco use, cessation, exposure to secondhand smoke, as well as an understanding of anti-tobacco messages. The target demographic is youth aged 13 to 15. GYTS-4 India 2019 report stated that there had been 42percent decline in tobacco consumption among 13 to 15-year-old kids who are still going to school. For boys, the prevalence of tobacco use was 9.6 percent, while for girls it was 7.4 percent. Tobacco usage among school-going children was highest among Arunachal Pradesh as well as Mizoram (58percent) while the lower rates were found in Karnataka (1.2percent) along with Himachal Pradesh (1.1percent) [12,13].
2. **Global Adult Tobacco Survey (GATS)**
   Working with WHO, the Centers for Disease Control and Prevention, & participating national governments, the GATS was launched in 2007 and was finished in 32 countries between 2008 and 2021. The initiative gathers information on tobacco use prevalence and related health policy,

with an emphasis on adults aged 15 and above.

3. **Tobacco questions for surveys (TQS)** Provides standardized questions for integration into other surveys to promote comparability over time [13].

Global School-Based Student Health Survey (GSHS)

It had been a cooperative initiative established by the WHO in partnership with several UN agencies, including UNICEF, UNESCO, and UNAIDS. This survey was designed to gather information on various health behaviours as well as protective factors among youth worldwide, with students in the 13–17 age range serving as the main target demographic. The GSHS addresses ten major areas. The following are considered risk factors: 1) alcohol consumption; 2) food habits; 3) using drugs; 4) personal hygiene; 5) psychological wellness; 6) Exercises; 7) protective aspects; 8) Sexual practices that raise the possibility of contracting HIV, other STDs, and unplanned pregnancy; 9) tobacco use; along with 10) violence & accidental damage. The survey employs a self-administered questionnaire, allowing students to report their health behaviors anonymously. It uses a stage sampling process. Till now GSHS has been conducted in 104 countries, providing valuable insights into adolescent health behaviors [14].

Tobacco cessation clinic

In 2002, GOI (Government of India), the WHO, and the Ministry of Health and Family Welfare (MoHFW) collaborated to develop the nation's first official tobacco cessation clinics to help individuals stop smoking. The first stage entailed establishing and developing Indian tobacco cessation centers and creating models for cessation [2]. These facilities are located throughout India in different settings, involving psychiatric clinics, medical colleges, cancer treatment centers, and non-governmental organizations. The steps in the WHO algorithm for quitting smoking include evaluating the tobacco habit, followed by basic advice, behavioral therapy, and, if necessary, medical treatment [15].

A 5-10% quit rate for tobacco has been observed with just thirty seconds of counsel from a health care professional. Every patient who smokes ought to be provided with a quick intervention technique called 5 A′s, or ASK (about tobacco usage)- Advice (to stop) - Assess (commitment and change-related obstacles) ASSIST (individuals dedicated to effecting change) – ARRANGE (monitoring progress through follow-up).

According to Indian TCCs, six weeks after the intervention, the overall cessation rate was about 16%. A TCC's clinic approach's main drawbacks were its limited population reach and loss of follow-up. The effectiveness of quitting and the avoidance of relapses depend on frequent contact counselling. Therefore, it is imperative to go beyond clinics to serve the millions of Indians who currently use tobacco. Community outreach clinics, workplace initiatives, youth groups, women's groups, and other settings can all be examples of this [16].

COTPA ACT

- In India, the Cigarettes (Regulation of Production, Supply, & Distribution) Act, which had been passed by the GOI in 1975, mandates the inclusion of a statutory health warning on every cigarette packet as well as

advertisements. The Indian Parliament enacted the Cigarettes and Other Tobacco Products (Prohibition of Advertisement and Regulation of Trade and Commerce, Production, Supply and Distribution) Bill, in April 2003. In 2003, on 18 May, this Bill became an Act – COTPA. Rules had been developed and put into effect on May 1, 2004. The Act covers the whole nation and applies to each item which involve tobacco in any one form. The key provisions of the COTPA acts were as follows:

A nationwide initiative to reduce tobacco use included outlawing smoking in public areas starting on October 2, 2008; a ban on tobacco product promotion and advertising; limits on sales to children and near educational institutions; mandatory health warnings in English and an Indian language on packaging; and regulations for disclosing tar and nicotine content [17].

Amendment in COTPA 2023

The COTPA Act No. 2, which prohibits the sponsorship, promotion, and direct & indirect advertisement of tobacco products, has been amended. The amended rules were as follows:

Health spots and disclaimers must be included in online curated content that features tobacco products. A warning in audio-visual format about the risks of tobacco use must be played at the beginning and middle of the program, lasting at least 20 seconds, and a clear health warning must be visible at the screen's bottom. Anti-tobacco health spots must be displayed for at least 30 seconds. The warning must be in the same language as the content, using black font on a white background with a warning as “Tobacco causes cancer” or “Tobacco kills.” Additionally, tobacco products or their use should not be shown in promotional materials or through brand placement [18].

WHO framework convention on tobacco control

In reaction to the tobacco pandemic's globalization, the WHO FCTC was established as a global public health treaty to declines the load of tobacco-related disease as well as death. The World Health Assembly endorsed it in May 2003, and on February 5, 2004, India became the eighth nation to do so. The FCTC supports methods that depend on scientific data which have been proven to be successful in lowering tobacco use. Though not a part of the legislation, it provided guidance for several national and international initiatives aimed at discouraging smoking and discouraging others from adopting the habit. The worldwide political determination to achieve considerably more extensive and effective tobacco control was evidenced by the WHO FCTC, which by July 2009 had > 160 parties representing 86percent of the population of the world [19]. Global Progress Report on WHO Implementation for 2023 According to FCTC estimates, 29% of individuals aged 15 or older worldwide (45% of men as well as 13% of women) had been current tobacco users in 2005. Tobacco consumption rates fell to an average of 20% by 2022 (33% of men and 7% of women) [20].

Bloomberg initiative to reduce tobacco use

It has been launched in 2005 by Bloomberg Philanthropies. It was a significant global effort aimed at combating

tobacco use and its health impacts, particularly in low- as well as middle-income countries. The initiative has committed nearly $1.58 billion to support tobacco control efforts worldwide. The program focused on countries where tobacco use is a more common reason for death, especially in China and India, which together account for around 40% of global smokers. This initiative operated on principles of MPOWER. Bloomberg Philanthropies announced an extra $420 million in February 2023, with the goal of lowering teen e-cigarette usage in the US and assisting international programs in low- as well as middle-income nations. Since the launch of the program, the percentage of people who smoke worldwide has reduced from 22.7 to 17.5percent. There has been a significant decrease in cigarette sales as well; in 2021, 750 billion fewer cigarettes were sold than in 2012 [21].

Global Health Professions Student Survey (GHPSS)

It has been cross-sectional research designed conducted in 2005-2007 to evaluate tobacco use & related behaviours between health professions students. As a section of the GTSS, the GHPSS gathers information via the GYTS, GSPS, GATS, and GHPSS surveys, among others. Students in their third year of graduate degrees in medicine, dentistry, pharmacy, and nursing participated in a poll conducted at their school. The study employed a standard questionnaire that inquires about the participants' demographics, smoking habits, exposure to second-hand smoke, intention to quit, and training in cessation approaches received for patient counselling. Sreerama Reddy et al. (2018) used GHPSS survey in their study and found a higher prevalence of smoking (40percent) in nations surveyed in Europe along with the Americas. Notably, dental and medical students from eastern and central Europe had greater smoking rates [22-23].

MPOWER

As part of the FCTC agenda, the WHO introduced MPOWER in 2008, which consisted of six highly effective but reasonably priced methods to fight tobacco consumption. Currently, the majority of countries and 40percent of the population of the world have implemented at least one of MPOWER's recommendations. The following were the actions that Mpower recommended: **M**onitoring the use of tobacco, **P**rotection of people from tobacco smoke, **O**ffering help to people to quit tobacco use, **W**arning everyone about the dangers of tobacco, **E**nforcing the ban on tobacco advertising, promotion and sponsorship and **R**aising taxes on tobacco [24].

WHO report on the global tobacco epidemic, 2023 for MPOWER

Over the past 15 years, Mpower has implemented regulations requiring 100% smoke-free areas, protecting nearly 2 billion additional individuals. Since 2007, the number of countries implementing MPOWER measures has increased from 44-151, while the number of nations implementing two or more MPOWER measures has increased by nearly ten times, from 11 to 101. At least three plans covering 1.5 billion people are in existence in 48 nations. As per the report, 71% of the global population over 5.6 billion covered by at least one measure in 2022. A completely smoke-free environment now covers 2.1 billion people living in 74 countries. The second most popular

MPOWER initiative, smoke-free settings have been implemented in seven times as many nations since 2007 [25].

National tobacco control programme (NTCP)

In the XI Five Year Plan, the MoHFW, GOI, launched the NTCP to expedite the enforcement of Tobacco Control Laws, raise public awareness of the detrimental impacts of tobacco use, and fulfill its commitments under the WHO-FCTC. It was a national initiative that had the first-ever state and federal funding for tobacco control and was implemented in 21 states covering 42 districts [17]. In India, 26.7percent of smokeless tobacco users and 46.3percent of smokers who saw a healthcare provider in 2009–10 were counselled to give up, based on the GATS [26]. To improve on the momentum it generated at the time of the 11th 5-Year Plan and baseline data produced by the GATS India 2009 to 2010, which indicated a greater level of prevalence of tobacco use, the NTCP was upgraded in the 12th 5-Yrs. By the end of the plan, aim to lower the prevalence of tobacco usage by 5percent. The GATS's second round (2016–17) stated that there were 8.1 million fewer tobacco users overall.

The goal was to create tobacco cessation centres (TCCs) around the nation and train the workforce—which included teachers and healthcare professionals—in tobacco cessation counselling. This program also included training and research for growing crops other than tobacco, laboratories for testing tobacco products, efforts to raise public awareness to encourage behaviour changes, and GATS-based tobacco usage surveillance [10,27]. The NTCP's activities involve organizing seminars, exhibitions, & banners at the level of district; putting the anti-tobacco legislation into practice in letter & spirit; and providing the state with monthly reports on the district-level anti-tobacco initiatives. The program was intended to be implemented at 3 levels: the state, centre, and district levels. However, because of a lack of resources, including personnel and infrastructure, the program's execution and the consequences of infractions could not be carried out effectively. Currently, 36 States and Union Territories—or around 612 districts across the country—are implementing the Program.

National Tobacco Control Cell (NTCC)

The MoHFW's NTCC is in charge of developing overall policy as well as organizing, carrying out, overseeing, and assessing the various initiatives included in the NTCP. The National Cell operates directly under the direction and control of the MoHFW Joint Secretary, who is in control of the program. The designated officers in the Directorate General of Health Services are in charge of providing technical support. This program was implemented at the national, state, & district level [28].

M-CESSATION PROGRAM

The program was initiated in 2016 as a part of the government's digital India initiative based on the aim that utilization of mobile technology can help address the limited coverage of developed TCCs, particularly in the rural and suburban regions [29]. Working with the WHO as well as the International Telecommunication Union, the Indian government adopted a cessation program depending on the "Be Healthy Be Mobile" campaign of WHO for use with mobile phones. Those who wanted to quit smoking

were the target audience for this M-Cessation program. The user can register for the quit program and get a customized Short Text Message (SMS) from 5616115 by sending a missed call to 01122901701. After that, the user receives 150 SMS tailored to their needs, which will help them in their efforts to quit smoking. On the GOI website, out of millions who had signed up, a 16% quit rate has been seen after 30 days of enrolment [30]. The M-Cessation tool is available in both Hindi and English, and as it is free to use and doesn't require an internet connection, it is proven as a cost-effective measure. The national tobacco quit line was offered in the languages of South India started in September 2018. It has been controlled by NIMHANS, and individuals who were unable to stop using the quit line alone were directed to the closest TCC [31].

NIMHANS & IDA INITIATIVE

The Tobacco Cessation Centre at NIMHANS, Bangalore, offered a 1month course for health professionals on treatment for substance abuse, including tobacco issues. Also, the Indian Dental Association (IDA) trained dental professionals to establish tobacco cessation clinics, resulting in 115 TII (Tobacco Intervention Initiative) centres throughout 16 states within a year, primarily run by private individuals who are on their practice were trained in a 24-hour program [32,33].

The Prohibition of Electronic Cigarettes Act, 2019

The objective of the act was that it is illegal for e-cigarettes or electronic nicotine delivery systems (ENDs) to be produced, manufactured, imported, exported, transported, sold, distributed, stored, and advertised in India. The fine for first time offenders is up to ₹1 lakh, or imprisonment up to a year. For subsequent offenders, the maximum sentence for imprisonment is three years, and the maximum punishment is ₹5 lakh. After an ordinance was issued in September 2019, this legislation was presented, and in late 2019, both houses of Parliament passed it. Individuals were prohibited from continuing to keep e-cigarettes and ENDs in storage. If discovered storing them, offenders risk a fine of ₹50,000 or up to six months of jail. Owners of existing stock were required to report and deposit it at specified offices [34].

Nasha Mukt Bharat Abhiyan (Drug-Free India Campaign)

The program was introduced on 26 June 2020, by the Ministry of Social Justice and Empowerment in India. The initiative aimed to combat substance abuse across the country, particularly focusing on vulnerable districts. The main objectives of the program were to generate awareness programs, capacity building programs, and community engagement, and its main focus was on university campuses, schools, hospitals and rehabilitation centres. The Ministry of Social Justice and Empowerment conducted the National Comprehensive Survey, which found that there were over 60 million drug users between the age of 10 and 17 in the country. The campaign focused on 272 districts identified as high-burden areas for drug use, based on data from the Narcotics Control Bureau and comprehensive national surveys. More than 8000 young volunteers were actively engaged in educating people about the harmful effect of drug abuse and assisted in the rehabilitation of victims of substance abuse. More than 500 voluntary organizations

were involved in implementing the campaign, supported financially under the NAPDDR (National Action Plan for Drug Demand Reduction) [35].

In India, a large number of voluntary groups have been actively engaged in tobacco control initiatives, including Voluntary Health Association of India, HealthBridge, Salaam Mumbai Foundation, CPAA-Cancer Patients Aids Association, The Indian cancer society, SEEDS- socio-economic and educational development society, HRIDAY-SHAN, and others. Healis is actively involved in an excellent tobacco control study. Furthermore, it engages in public education, workshops for various stakeholders, scientific conferences as well as meetings at the national and international levels, and media mobilization for tobacco control [36].

Conclusion

The Indian government and MoHFW have implemented many laws and taken several steps to limit the usage of tobacco. However, the efficacy of these measures is largely based on public perception and accessibility. The monetary burden of medical expenses as well as lost productivity related to smoking highlighted how urgent it is to solve this public health emergency. An additional 160 million smoking deaths worldwide are predicted to occur by 2050 consequently of a shortage of cessation assistance. To combat smoking effectively, key strategies include enhancing tobacco control legislation, increasing funding for cessation programs, expanding digital public awareness campaigns, investing in research to monitor trends, and fostering global collaboration to share successful strategies. As public health professionals, particularly in the dental field, it is an ethical obligation of the clinician and public health dentist to promote awareness regarding tobacco cessation as well as to support individuals who are motivated to quit this habit.

Statements and Declarations

Conflicts of interest

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REVIEW ARTICLE

Uncertainty in a Medico's Mind: The Way Out

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Abstract

The transition from medical education to clinical practice is often marked by significant uncertainty for new medical graduates. This uncertainty stems from a variety of factors, including the complexity of real-world patient care, the application of theoretical knowledge to practical scenarios, and the emotional and psychological weight of clinical decision-making. New medicos are thrust into environments where they must navigate intricate medical conditions, make decisions under time pressure, and manage expectations from patients, families, and healthcare teams. Despite rigorous training, the gap between theoretical knowledge and clinical application can foster self-doubt and feelings of inadequacy.

Keywords: Medical education, Self-criticism, The three-day monk, Fresh medico

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"*The core predicament of medicine — the thing that makes being a patient so wrenching, being a doctor so difficult, and being a part of society that pays the bills they run up so vexing — is uncertainty ... Medicine's ground state is uncertainty. And wisdom — for both the patients and doctors — is defined by how one copes with it*"…….

Atul Gawande

While undergoing training in medical colleges, sometimes in our student or resident ship days, we feel that we are not progressing and that a sense of uncertainty surrounds us - usually, it is a sense of self-exhaustion. This feeling is further compounded when we come to know that our classmates from school are entering lucrative jobs, have started earning handsome salaries, and even enjoying overseas holidays, while we are toiling with our studies on one hand and back-breaking hospital duties on the other. Some of us will choose to blame those around us for our predicament, some blame the system, while others will criticize themselves in such a way that will paralyze them, while some will actually overcome these obstacles and move forward. But what is certain is that there is no lack of reasons that inhibit us in our path to self-realization and success in life [1].

Uncertainty in medicos mind is reaped during their initial days of formative education at the school level when a student decides to choose their profession. It is not the desire to serve humanity which is the prime essence for which a student pursues to choose medicine as their career. Rather during their pursuit of becoming a medic, this is highlighted as a safe green pasture molded with financial gain rather than service to humanity. It is from this desire coupled with family instinct (especially first-generation doctors) and coaching centers that they start their profession. They look up to the materialistic objects of successful doctors, undermining the effort (education and training) put in by them in their formative years. Later, as they ascend through the ladder the intense pressure of studying lures them to avenues that distract them from their goal. Additionally, school peers early life settlement further derails their futuristic goals. The desire for early success (which cannot be out of the blue) drives all the negative instincts as described by the author. It requires a change in the mindset of the student most of whom choose the profession by default and pressure, rather than by desire. Choosing the right mentor as delved in detail in the mentorship program of the National Medical Commission is of paramount importance.

So, when do these dark thoughts creep into our minds and disturb our steady progress toward our noble goal of becoming a good doctor? What are the reasons of these rude interruptions in a budding medical student's or a resident's mind?

1. The pursuit of impossible dreams

We all like to dream and say that we have dreams, but some of us tend to make them a way of life, unable to break away from the illusion and be grounded in reality. In addition, this makes us live in our imaginary world as if we are waiting for a miracle to happen, and so we take no action to achieve and fulfill our dreams. When we don't take a step and are only sucked into

our dreams, the likelihood of them coming true is significantly lower. To improve our chances, we must break free of the big dreams we are immersed in. Instead, we must try to break them down into small dreams or, alternatively, into steps that we need to take in order to achieve the bigger dream. No dream can materialize without sacrifices, so we have to stop and ask ourselves, what are we prepared to sacrifice in order to achieve our dream – our social media time, our procrastination, our daydreaming?

Most of us have big dreams that we strive to achieve, but we sometimes aim too high or expect quick success that is almost impossible. It is very important to understand that your dreams can become goals for life, but you need to learn to set them in implementable ways - analyze the resources you have, how long you will need to achieve them and how realistic they are. When you learn to set goals for success that are achievable, you will also feel satisfaction and you can track your progress. Moreover, even if the goals that you set yourself becoming illogical, there is a way out, try to rewrite them or break them down into smaller goals, to ensure your goals are met.

2. The inability to concentrate on one task at a time

Many people are led by the principle of "a few more minutes on Facebook and then I'll start..." The problem is that our world is rich in various technological platforms that suck us in and it is very difficult to ignore them. Thanks to these diverse technologies and our addiction to them, we can't concentrate on just one task. As a result, we lag behind at work, have a pile of case sheets to be completed, dressings to be done and post-operative patients to be reviewed. Only after that we can start to study for the upcoming seminar or journal club. So, if we remain drawn and addicted to screens when will we study? In order to be more efficient, we need to set task deadlines and track them in order to be able to accomplish them successfully.

3. The inability to maintain consistency

We often start doing several tasks at once and are not able to finish any of them. We are sure that it's happened to most of us at least once in our lives. This includes exercising, dieting, learning something new (like a language), having a hobby and so on, and things we started to do with great excitement and stop after a week or a month. There is only one reason for this concession - lack of perseverance and failure to set measures of success or desired results. In Japan, there is a special term for this syndrome – The Three-Day Monk, the number three symbolizes the average amount of days it takes for the excitement to fade and we give up what we started. To overcome this syndrome, you can use the kaizen approach that teaches how to succeed in tasks by working slowly and continuously over time. Success in the medical field cannot be a flash in the pan, our training teaches us to make success a way of life, because we simply can't afford failures. Maintaining consistency is extremely important in academics, clinical work, and research.

4. The inability to feel responsible

Not every bad thing that happens in our life is necessarily our fault, but most of

it is our responsibility. We can blame other people or obstacles along the way but that will not change the situation and certainly will not solve it. However, by taking full responsibility for the events, we can improve, learn and build a better future. If in a limb salvage surgery the patient goes into renal failure, there is no harm in realizing the mistake, amputate the limb and save the patient. The ability to admit and correct our mistakes is the first and most important step on our path to success. We must learn to take responsibility for our decisions and our life in order to be able to turn our ideas and dreams into reality. 'I am responsible, the buck stops here' should be our motto in life.

5. Not being supported by the environment

One of the secrets to personal success is the support we receive from our institution, our teachers and our loved ones. But sometimes instead of getting support from them, we get a lack of understanding and negativity, things that make it very difficult for us to continue on our path. In such a situation, it is very important to relax and not to fight or argue with the people who are close to us. Instead, we have to tell them how much we love them, explain to them that the things we are doing are very important to us, clarify to them what we are trying to achieve, and how important their support is to us. Issues like permission to attend conference and present a paper, getting first authorship in our research publication, permission to graduate from simulator to patient for performing laparoscopic surgery can be freely discussed with teachers and seniors and we can always put our point of view most politely [1].

6. Plagued with self-criticism

Self-criticism can be of great benefit but at high doses, it can actually cause us to become attracted to negative thoughts and settle in our problems. As a result, critical thoughts feed our brains and make us feel sad; this can lead to depression. Not only does self-criticism not lead us to success, but it also keeps us away from it. We aren't saying that self-criticism isn't good, we just have to approach it consciously, so that we control it and it does not start controlling us. This is what will help us to snap out of our negative thoughts and intelligently reevaluate the various possibilities that we face for future success.

7. Pointing fingers

There are two kinds of people in the world - those who blame everyone around them and those who take responsibility for their mistakes and actions. The former will point an accusing finger at the government, the country they live in or even their parents – who according to them, are the factors that did not give them the chance to succeed in life. 'I am here because my parents wanted me to become a doctor' is a dangerous line of thought. It means the individual has failed to develop an interest in Medicine and now is blaming his/her parents. 'My thesis does not have clinical photographs because my colleague who shot them, misplaced them' – again instead of accepting the responsibility, blaming a colleague. There is however the second type of people, those who take responsibility for their actions achieved the

goals they set in life. People of the second type know that success depends on the effort they invest, the persistence, the goals they set, and the knowledge that blaming the other will lead them nowhere. Surprisingly, failures can even motivate them to achieve success [2].

8. Previous Failures

Each of us experiences failures, sometimes we can try and do everything in our power, but we simply will not get the desired result. In this case, we have two options: to sink into depression and continue to feel sorry for ourselves or we can analyze the situation, understand that we have done things wrong and try starting again from zero. If after watching the teacher perform a flap surgery we try to emulate him in an emergency situation and the flap fails then should we give up on that flap or go back to our books and atlases, our YouTube videos and then discuss again with our teacher, perhaps help him next time when he performs the same flap, and try to master the technique! We can achieve success from experiencing failure. J.K. Rowling, Bill Gates, Steve Jobs, Stephen King, Walt Disney, Oprah Winfrey, Thomas Edition, Abraham Lincoln all made big in life eventually, despite failing and being rejected by the world in the start of their career. Failures are stepping stones towards success and nothing more serious [3].

Conclusion

When we enter the medical profession it is not just a job choice; it's a deep calling. Those who choose this path are driven by a strong commitment to reduce suffering, improve well-being, and make a lasting impact on people's health and society. Medicine is where science meets compassion and so being a doctor cannot be just another profession, It is about giving, healing, and serving, going beyond personal gain. Once we have chosen this life, there is no room for uncertainties in our mind. So, we must have a clear clutter free mind, an appetite for hard work with scanty appreciation and we must be prepared to make sacrifices in terms of social time and social media time. Techniques like meditation, yoga, or breathing exercises are useful to cope with stress.

Conflicts of interest

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

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REVIEW ARTICLE

Effectiveness of School Dental Health Programs: A Review with Insights from India

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Abstract

Schools provide a vital platform for dental health promotion since children spend a large amount of time there, which shapes their habits and overall health. Oral health initiatives in schools are designed to reduce the burden of dental problems including dental caries and gingival disease, which have an impact on their oral health and general well- being. These worldwide initiatives encompass dental hygiene instructions, fluoride application, and preventative measures. With an emphasis on India's experience, this review addresses the school dental health programmes worldwide influence.

Keywords: School dental health programs, Oral health, India

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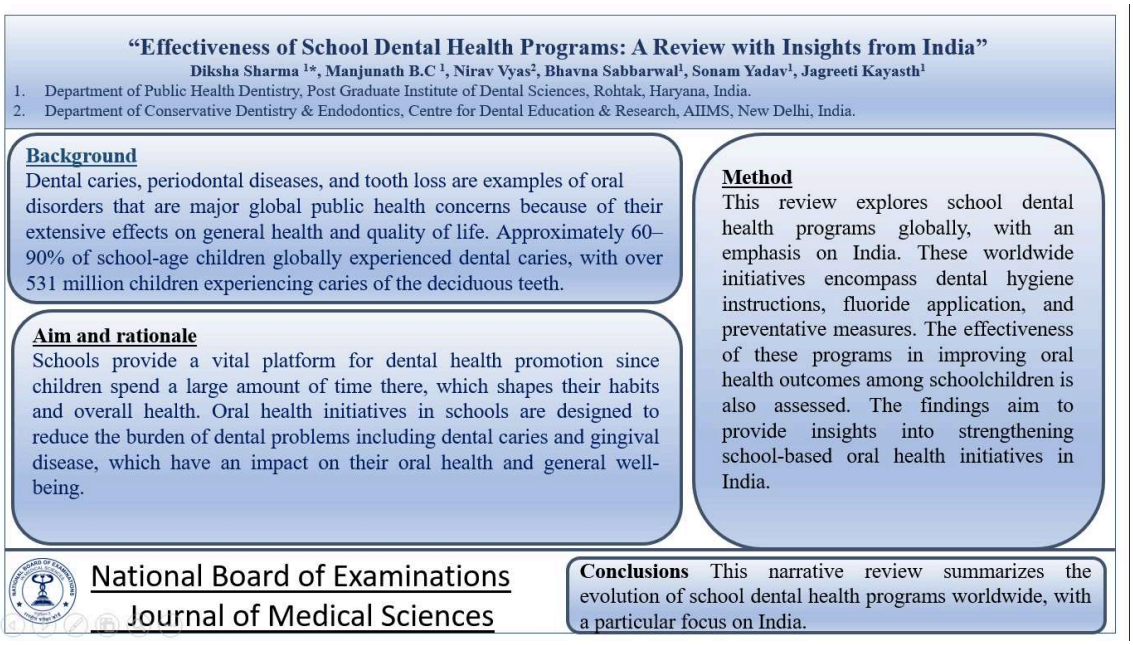
Graphical Abstract



Introduction

Dental caries, periodontal diseases, and tooth loss are examples of oral disorders that are major global public health concerns because of their extensive effects on general health and quality of life [1]. Approximately 60–90% of school-age children globally experienced dental caries, with over 531 million children experiencing caries of the deciduous teeth [2-3]. Dental caries is the most common multifactorial preventable disease [4]. Gingivitis symptoms were present in the majority of children and adolescents and adverse periodontitis, which can result in early tooth loss, affected about 2% of children [2]. In addition to causing pain and limiting oral functions, oral illnesses can also impede nutrition, induce emotional stress, lower self-esteem, poor attendance, and substandard academic achievement [5-8]. Schools are the best places to promote health because they can reach the majority of school-age children and act as vital support systems for their families and communities [9-10]. While there are significant differences between nations and genders, 60% of children worldwide finish at least four years of schooling, and 80% of children attend primary schools [11]. Overall, school-based initiatives can improve children's access to dental care, particularly for those from low-income families [12].

Historical background of school dental health program in India

- In 1909 the beginning of school dental health in India was started when for the first time medical examination of school children was carried out in Baroda city of Gujarat.
- In 1946 Bhore committee stated that school health services were practically non-existent in India, and if existed they were in underdeveloped state.
- In 1957, WHO and Nutrition Education Committee assisted set up of school health education project.

- In 1960 the, government of India constituted a school health committee, and submitted its report in 1961.
- In 1977 centrally sponsored National School Health Scheme was started. In January 1982, the task force constituted by the government of India to accomplish the School Health Survey Project, submitted its report. Only 14 states had shown some progress with their own health department budgets.
- The Tokyo declaration was made on July 19th, 2001 at the 1st Asian conference of oral health promotion for school children, held in Tokyo.
- Ayutthaya Declaration (2003) and Bangalore Declaration (2005) also stressed on oral health promotion among school children [13].

School Dental Health Programs

1. **Fit for school programmes**
   The **"Fit for School"** program is a school-based initiative focused on improving water, sanitation, and hygiene (WASH) to enhance child health in Southeast Asia, particularly in countries like Cambodia, Indonesia, and Lao PDR. The program was launched in 2009. As part of its oral health component, this program promotes regular teeth brushing with fluoride toothpaste (0.3 ml, 1450 ppm). The results of this program was promising in terms of decrease in dental caries prevalence compare to the children of control school [14].
2. **Fluoride 'mouth rinse' programme**
   In 1974, FDA had given official recognition of safety for fluoride mouth rinsing program followed by ADA in 1975. Fluoride mouth rinse was most widely used in-school fluoride program in the US. Apart from the United States, 7 other nations- Denmark, Finland, New Zealand, Netherlands, Norway, Thailand and Sweden also supported the mouth rinse programmes. It is usually supervised by classroom teachers or other adult volunteers. Several research conducted in schools have shown that administering fluoride tablets daily or rinsing the mouth with fluoride solution once a week resulted in reduction of dental caries incidence by 30 to 40 percent in areas lacking fluoride [15]. In fluoride deficient places, it is advised to rinse once a week with 0.2% neutral NaF solution [16].
3. **Fluoride tablet programme**
   The fluoride tablet program was first initiated in 1960. This program was developed as part of efforts to provide fluoride supplementation to children, particularly in areas where the drinking water supply lacked adequate fluoride levels. This self-applied fluoride regimen has been utilized for more than 40 years in the US and other countries. In places with low fluoride levels, swallowing a neutral 2.2 mg NaF tablet (1.0 mg F) every day was advised. The main drawback of this program was it has to be done daily in low fluoride areas [15,17].
4. **Fluoridated milk (milk fluoridation)**
   The use of fluoridated milk for dental caries prevention was first proposed by Zeigler in 1953 [18]. In the late 1950's, this approach was tested in several nations, including Australia, Germany, Japan, Switzerland, and the United States. Through this preventive program, children were guaranteed daily access to milk and the extra benefit of fluoride exposure, which guards against tooth cavities [19]. In 1984 Stephen et al. reported on a 5-year school based double blind randomized controlled trial, which resulted in a statistically significant 31% reduction in dmft and a

43% reduction in dmfs in the test group [20].

5. **School water fluoridation**
   In 1954, a school water fluoridation pilot study was initiated at St.Thomas V.S. Virgin Islands, by the U.S Public Health Service division of dental health. Fluoridating the school's water was comparable to fluoridating public water systems as it required no personal effort from the public other than drinking the water or eating food made with it [17]. For school water supply, a fluoride content of 4.5 parts per million was recommended. The school water fluoridation was developed and tested in 1950s and 1960s and after 12 years, researchers found a 40% decrease in dental caries levels [21]. The major limitations of this program was that only few schools were able to bear the cost of installation, supply and maintenance. Also, the children do not receive benefits until they begin school [13].
6. **School oral health program Kuwait**
   The School Oral Health Program (SOHP), Kuwait, is probably the only comprehensive oral health program for school children in the Middle East. The program was started in 1983 and now it's present in all the 6 governorates of Kuwait. In Kuwait, the SOHP provides treatment, prevention, and oral health education to about 280,000 school-age children. Improvements in positive consents, a decrease in composite fillings, and an increase in pit and fissure sealants had all been found as an outcome of this program [22].
7. **Sealants placement**
   Sealants of various types were used to prevent pit and fissure dental caries. Pit and fissure sealant placement was best suited for a school programs [23]. It would be ideal to selectively intervene in the first, second, sixth, and seventh grades to prevent pit and fissure lesions (1st and 2nd graders, because- First permanent molars are sufficiently erupted to place the sealant. 6th and 7th graders for 2nd molars) [13]. One of the studies had found 78% effectiveness of pit and fissure sealant placement as a caries preventive program. The study formed the basis for a policy decision to introduce fissure sealants for selected children in the school dental service [24].
8. **Trinity Care Foundation – Bengaluru**
   Trinity care foundation is a charitable trust registered under the Indian trust act which carries out school health programs in Bengaluru and nearby areas of it. It focuses on teacher training and increasing the awareness about health issues, ill effects of tobacco and tooth brushing techniques to students in government schools [25].
9. **Incremental dental care**
   One method of delivering priority dental care to a group of school children was the incremental care. George Cunningham in England proposed this system in 1907.

   When dental illness developed, they were addressed as soon as possible with accurate diagnosis and efficient treatment. This approach prevented dental problems from building up unnecessarily [26]. The basic process was to provide the lowest priority age group with the essential dental treatment in a single year, then each year add a new age group to the group getting care. Specific attention to only deciduous teeth, financial burden and drop out of children were major drawbacks of this program [13].
10. **Tattle Tooth Program**
    The Tattle Tooth Program was developed in 1974-76 as a co-operative effort between health professional organizations, the Texas department of health and Texas education agency. In 1989 the bureau of dental health

developed a new programme - "Tattle Tooth II, a new generation" for kindergarten to 6th grade. Three videotapes were produced as a part of 'Teacher - Training Package'. The videotape familiarizes the teacher with the lesson format and content. Brushing and flossing - for dual purpose of teacher training and as educational unit and a third video tape provided teachers with additional background. Program evaluation was as follows: 1) 80% of teacher judge the program to be helpful. 2) 88% of teachers spent 4.5 - 6.5 hrs teaching the "Tattle Tooth Program". 3) Students were brushing 4-5 times and the teachers were teaching at least 8 out of 10 "Tattle Tooth Program". 4) 1989 Tattle Tooth II- curriculum showed positive effect and 94% of the teachers felt that teaching oral health can have a positive effect [13].

11. **Askov dental demonstration**

The Minnesota department of health's dental health branch supervised a demonstration school dental health program in Askov from 1949 to 1957. The program included dental care, dental health education, and caries prevention and control. Findings from a 10-year period showed: 28% reduction in dental caries in deciduous teeth of children aged 3 to 5 years. 34% reduction in caries in permanent teeth of children 6 to 12 years and 14% reduction in children 13 to 17 years old. The major limitation was that the cost of program was greater and the caries reductions smaller when compared to water fluoridation [13].

12. **North Carolina statewide dental public health programme development**

In 1970, resolutions were passed by the North Carolina dental society in support of a comprehensive program to prevent dental diseases. This program included fluoridation of schools and communities, fluoride treatments for school-age children, continuing education for dental professionals on prevention, and plaque control education in schools and communities. According to 1986 - 1987 North Carolina school oral health survey, 53% of children 5-17 years of age have never had a cavity in their permanent teeth [13].

13. **Healthy Teeth, Happy Smiles**

In an effort to promote better oral health from infancy, Leicester launched the Healthy Teeth, Happy Smiles program in 2014 as part of the city's first Oral Health Promotion Strategy for preschoolers. The initiative included supervised tooth brushing and the distribution of oral health packs with toothbrushes and fluoride toothpaste in order to address the high rates of dental decay among youngsters in Leicester. As of April 2017, approximately 780 members of staff have been trained to deliver supervised tooth brushing with 6,300 children benefiting from daily supervised brushing [1]. Between 2011/2012 and 2014/2015, there was a statistically significant 8% decrease in the percentage of 5-year-old children in Leicester who had dental decay [27].

14. **MaliMali program**

The MaliMali program, named after the Tongan word for "smile," was a school-based program designed and managed by south pacific medical team (SPMT) to improve children's oral health in 1998. The MaliMali program consisted of the following three main programs in addition to extracurricular activities: a program that teaches students in kindergarten and primary school how to prevent cavities (by giving out leaflets, giving lectures, and suggesting foods to eat in between meals), a project that encourages the use of fluoride toothpaste and provides toothbrushing tips,

and a fluoride mouthwash delivery program. At the time of evaluation, the mean DMFT score and the DMF person rate among both boys and girls showed significant reduction in 2011 compared with 2001. The MaliMali Program's primary limitation was the need to go to the schools in order to provide fluoride for the school-based program [28].

15. **Love Teeth Day**
The minister of health in China initiated the signing of a joint declaration on July 14, 1989, and nine government and non-government organizations declared September 20 to be "love teeth day" (LTD). The objectives were to encourage individual awareness of and engagement in dental self-care as well as community participation in oral health education programs. Newspapers, radio, and television were among the mass media that provided information to the public regarding oral health issues. After 3 surveys 12-year-old children demonstrated near to 62% reduction in caries incidence in year 2005 [29].
16. **Childsmile**
The Childsmile program was sparked by the Scottish executive's 2005 policy statement. A strategy for advancing oral health and improving dentistry services in Scotland. The Childsmile nursery and school programmes had provided 28,000 fluoride varnish treatments to nursery and primary school children. Daily supervised toothbrushing and distribution of oral health packs covered almost 100% of nursery schools and P1 and P2 classes in primary schools in the most deprived areas of Scotland. By the end of the 2008-2009 school year more than 95% of school children have participated in supervised school brushing program [30]. Over two third of children aged five years have not reported significant tooth decay, indicating a significant improvement in oral health (dmf = 0, 2016). The mean DMFT among 11-year-olds dropped from 1.29 in 2005 to 0.49 in 2017. Since it does not target the fundamental causes of disease, there will always be a new emergence of fresh cases [31-32].
17. **Colgate's "Young India" Bright Smiles, Bright Futures**
Colgate-Palmolive and IDA collaborated in 1976 to impart dental health education to students, and launched a campaign to promote oral health in schools in 2001. Children between the ages of 6 and 14 of elementary school were taught proper dental hygiene techniques, the importance of night brushing, and the proper brushing techniques using a toothbrush and tooth model. More than 162 million schoolchildren between the ages of 6 and 14 have benefited from the program in India [33].
18. **Neev school dental health program**
The government of the NCT of Delhi is currently operating the school dental program "Neev" from September 2014 in government schools throughout Delhi state as a pilot project. The program covered all public schools in Delhi state (at least 50 schools), involving parents, teachers, and school administrators as team members and providing instruction for all students in classes 6 to 10. The program was expected to cover around 80,000 school children in one district of the state and cost a total of Rs. 2,00,00,000 each year [34]. The Neev program has demonstrated a significant long-term reduction in dental caries among children. Statistical data indicates a decrease in caries prevalence by approximately 22.2% to 46.2% among children aged 7 to 11 years who participated in the program [35].

19. **Chacha Nehru Sehat Yojna School Health Scheme**
    The government of Delhi Directorate of Health Services established SHS in 1979 with the goal of providing comprehensive health services to school-age children through the establishment of six school health clinics**.** It was announced by Hon'ble Chief Minister of Delhi, in her budget speech on 22nd march 2011 and launched on 14th November, 2011**.** The dental component of the school health program was managed by two government organizations, the Maulana Azad Institute of Dental Sciences and DDU hospital, both conducted regular screening programs and served as the referral centers. Program expansion and the opening of 64 school clinics were carried out under the seventh five-year plan [36].
20. **Pit and Fissure Sealant Pilot Project – National Oral Health Program (NOHP), AIIMS, New Delhi**
    It was started on May 1st 2017 and representatives from 12 dental colleges received training for the pit and fissure sealant project, which was a major component of NOHP. By sealing 53,750 permanent molars, it aimed to prevent dental cavities in kids between 6 to 14 age group [37].
21. **Save our smiles – Fluoride mouth rinse program for new jersey schools**
    New Jersey's voluntary fluoride mouth rinse program, "SAVE OUR SMILES" which began in 1981 has historically served more than 30,000 children each year. The fluoride mouth rinse program was for students in grades one to six only, also conducted in grades 7-8 under special circumstances. Students rinse with 10 milliliters, or around two teaspoonfuls, of a 0.2% neutral sodium fluoride solution once a week. The kids are supposed to swish the solution between their teeth for a minute. Therefore, during the course of the school year, it required less than five minutes of classroom time per week. Every week, mouth rinsing performed on the same day and at the same time [38].
22. **Learning about Your Oral Health**
    This program was a prevention-based school programme. This program was developed by American dental association (ADA) and their consultants in coordination with the 1971 ADA House of delegates and is presently available to school systems throughout the United States of America. The main objective of this program was to create the attitudes, skills, and knowledge necessary for oral disease prevention. The program's primary goal was to give school children the necessary knowledge and abilities for plaque control [13].
23. **Preschool dental health programme (Head Start and Smiling for life)**
    Under the economic opportunity act of 1964, **Head Start**, a nationwide preschool program, was launched in the United States in 1965 to give poor and underprivileged kids access to early learning experiences.

    Smiling for life - In 1995, a nutritional assessment of preschool British children revealed that the consumption of non-milk extrinsic sugars (NMES) was substantially higher than the recommended threshold of 10% of total energy. The program successfully promoted the sustained behaviour changes in oral hygiene practices, emphasizing regular tooth brushing and healthy eating habits [13].
24. **School health additional referral programme**
    The SHARP program was instituted in Philadelphia in year 1967. This program aimed to enhance the effectiveness of

school health services by providing intensive health counselling and referral services to students with identified health defects, particularly in low-income areas. During the day, the nurses visited the households. Improved communication between the home and school is achieved through one-to-one basis of health advising between a health provider and the parent [13]. The program significantly increased the rate of improvement in health status among children. Prior to SHARP, only about 30% of children with identified health issues received necessary corrections. This percentage rose up to 54% in the first year of SHARP and further increased to 63% in the second year, demonstrating a substantial improvement in addressing health needs through intensive counselling and follow-up by school nurses [39].

25. **Intensive Dental Health Care Program – Punjab**

Punjab introduced its Intensive Dental Health Care Program in 1989–1990. Schools are covered under the present program according to subdivision. Apart from providing tooth Health Education to schoolchildren and conducting comprehensive oral health examinations, every kid receives a fluoride mouthwash to halt the onset and advancement of tooth caries. This procedure was repeated every six months. The current status of this program is not known [40].

26. **St. David's Dental Program - A Mobile School- Based Dental Program for Children**

The program's inception was in 2000. The primary goal of the program was to remove barriers to dental care, such as cost and transportation. By providing services directly at schools, the program ensured that children receive necessary dental care without requiring parents to take time off work or arrange transportation. St. David's Mobile Dental Program offered free dental care to children at Title 1 elementary schools in Central Texas, as well as adults referred by area clinics. From August to May, the mobile dental program treated elementary school children who attended title I and charter schools in Austin, Del Valle, Hays, Manor, Pflugerville, and Round Rock ISDs. Beyond addressing urgent needs, this program also educated students about dental hygiene habits that will last a lifetime. In 2005, the program provided $2.1 million worth of services at a cost of $1.2 million. The program provided a range of services including exams, X-rays, fillings, cleanings, sealants, and oral health education. It had placed over 93,000 sealants, which help prevent tooth decay [41].

27. **THETA program**

In the spring of 1974, 181 students from Nokomis Elementary School and high school students took part in a THETA program. In the THETA program, high school students have to learn the proper oral hygiene procedures for themselves and teach the elementary school children. First, the THETA students and elementary school teachers are trained in preventive care. Then the THETA students developed a classroom plan of instruction and work with the children [42].

Impact on Current School Dental Health in India

Historical developments have led to several key outcomes in India's current state of school dental health:

Increased awareness - School dental health programs incorporate targeted educational interventions that enhance children's understanding of oral hygiene.

These initiatives promote effective brushing and flossing techniques, emphasize the importance of regular dental visits, and address dietary choices that affect dental health, fostering positive habits from an early age [43].

Reduction in dental issues - The introduction of fluoride application programs and sealants in some regions had aimed to reduce dental caries among children. This has been particularly important in areas with high levels of dental caries [34].

Holistic Health Approach- School health programs are increasingly incorporating oral health as a fundamental component of overall health education. This integration helps to address the interconnection between oral health and general health issues, such as nutrition and chronic diseases [44].

By learning from past programs and integrating modern approaches like technology and community involvement, India aims to improve the effectiveness of its school oral health initiatives.

Discussion

Educational interventions through games and shows have proven more effective in enhancing oral hygiene knowledge and skills among children compared to traditional verbal instructions [45]. Specifically children engaged in role-playing or drama-based health education demonstrated superior oral hygiene outcomes compared to those receiving conventional education from a dentist or trained teacher, or those without any intervention [46-47]. Furthermore, incorporating educational programs for parents, teachers, and children alongside preventive measures, such as sodium fluoride application and supervised tooth brushing with fluoride, has led to notable improvements in oral health indicators. This approach significantly reduced gingival and plaque index scores, while there were no changes observed in decayed, missing, and filled teeth (dmft) and decayed, missing, and filled surfaces (dmfs) scores. Conversely, in the absence of such educational support, there were significant increases in both gingival and plaque index scores, as well as dmft and dmfs scores [48].

In studies evaluating school-based dental health programs, various interventions have demonstrated significant benefits over control groups. One comprehensive program that included oral health education (OHE) for children, teachers, and parents, along with supervised tooth brushing and the provision of fluoridated toothpaste and toothbrushes, resulted in a 30.6% reduction in the increment of decayed, missing, and filled surfaces (dmfs) and a higher percentage of children brushing their teeth twice daily [49]. Another program, which featured OHE for children and teachers, supervised tooth brushing, and the use of 1100 ppm fluoride toothpaste, also achieved a significant reduction in dmfs increment compared to the control group [50]. Additionally, among boys, a school-based supervised tooth brushing initiative that included professional cross-brushing of the first permanent molar surfaces led to a 50% lower caries incidence density compared to a conventional tooth brushing program [51].

Incorporating oral health education (OHE) into the school curriculum has been shown to reduce the risk of new carious lesions by 35% [52]. This effect varies with parental socioeconomic status (SES), as children from high SES backgrounds in the

intervention group experienced a 94% reduction in incidence rate ratios (IRR) [53]. Programs that included OHE, teacher support, and competitive elements significantly enhanced oral health knowledge (OHK) and improved oral health-related quality of life (OHRQoL) [54].

Significant improvements in oral hygiene, gingival health, and oral health knowledge were observed when OHE was implemented over a six-month period, regardless of the educator [55]. Individual tooth-brushing training also markedly enhanced children's brushing skills compared to a control group [56]. However, a quasi-experimental study conducted in Burma indicated that a school-based tooth-brushing program did not significantly affect plaque or bleeding scores [57]. Additionally, children who participated in a two-month sense of coherence (SOC) intervention led by trained teachers reported significantly better OHRQoL and improvements in their sense of coherence compared to the control group [58]. Another study confirmed that the soc intervention group exhibited better OHRQoL, SOC, oral health beliefs, and gingival health compared to those who did not receive the intervention [59].

A two-week display of educational posters on dental trauma notably increased children's understanding of how to manage such injuries [60]. Additionally, children who received a loss-framed pamphlet intervention demonstrated improved oral health behaviours, attitudes, and intentions to brush their teeth after two weeks. At a 24-week follow-up, this group also had lower dental plaque levels, better oral health-related quality of life (OHRQoL), and enhanced gingival health compared to other participants [61]. Furthermore, frequent teacher-led oral health education (OHE) sessions, combined with the provision of oral hygiene aids, resulted in significant decreases in simplified oral hygiene index (OHI-S), plaque index (PI), and gingival index (GI) scores. In contrast, children who received infrequent dentist-led OHE or no intervention at all experienced increases in these scores [62]. Dental hygienists delivering OHE and preventive measures, such as fluoride varnish, in schools effectively reduced the incidence of enamel caries, though there was no significant effect on dentin caries. This intervention also improved children's oral health knowledge and hygiene practices, but it did not influence their attitudes toward tobacco use [63]. The children who participated in motivational interviewing sessions had fewer new carious teeth, reduced their snacking habits, and increased their tooth-brushing frequency compared to those who received conventional OHE [64].

Conclusion

In conclusion, this narrative review summarizes the evolution of school dental health programs worldwide, with a particular focus on India. Historically, the majority of these programs focused on school dental health education, but recently focus have been shifted toward preventive strategies, including use of pit and fissure sealants, fluoride mouth rinses, fluoride toothpaste, school water fluoridation, and improved brushing techniques. The findings reveal that these educational efforts have led to significant reductions in dental caries among children. However, it is concerning that less attention has been given to critical areas such as gingivitis, periodontitis, dental trauma prevention, and tooth loss management. Many schools' dental health education programs in India

have shown promising results in reducing caries incidence and improving oral health knowledge among children, while several others are still underway, with their results awaited. This underscores the need for long-term studies to comprehensively assess their effectiveness. Additionally, the potential integration of artificial intelligence in school dental health education presents an exciting opportunity for enhancing awareness and improving outcomes.

Future Recommendation

Policymakers and public health officials should prioritize integrating oral health education into schools by encouraging collaboration among healthcare professionals, teachers, parents, and students. It is crucial to incorporate oral health within broader health initiatives and allocate funding for comprehensive training programs including oral health education and preventive strategies. These measures will promote overall well-being and lifelong healthy habits among students.

Statements and Declarations

Conflicts of interest

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

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REVIEW ARTICLE

Enhancing Biomedical Research Through Strategic Funding: A Comprehensive Review

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Abstract

Background and Aims: Biomedical research play a vital role in driving health innovations, but the intricate funding landscape presents significant hurdles for researchers. This review seeks to explore the significance of funding in biomedical research, the obstacles encountered in obtaining such funding, and the economic ramifications of these investments. **Methods:** A narrative review was performed through an extensive literature search in databases such as PubMed, Scopus, and Web of Science from December 1 to 10, 2024. The search targeted peer-reviewed articles, government reports, and publications related to biomedical research funding, using keywords like "biomedical research funding," "grant application processes," and "diversity in research funding." **Results:** The findings underscore the essential role of funding in promoting research productivity and innovation. Major challenges identified include a complicated grant application process, insufficient financial support for underrepresented groups, and a lack of transparency in funding mechanisms. Additionally, while there are signs of positive returns from investing in biomedical research, thorough analyses of the economic impacts are still lacking. **Conclusions:** The review highlights the necessity for strategic reforms to improve collaboration and transparency in funding mechanisms. Tackling the identified challenges is crucial to strengthen biomedical research efforts and ensure a variety of perspectives in addressing the urgent health issues facing society. Improved funding strategies can lead to better research outcomes and advancements in public health.

Keywords: Biomedical research, funding, grant application, economic impact, diversity, transparency

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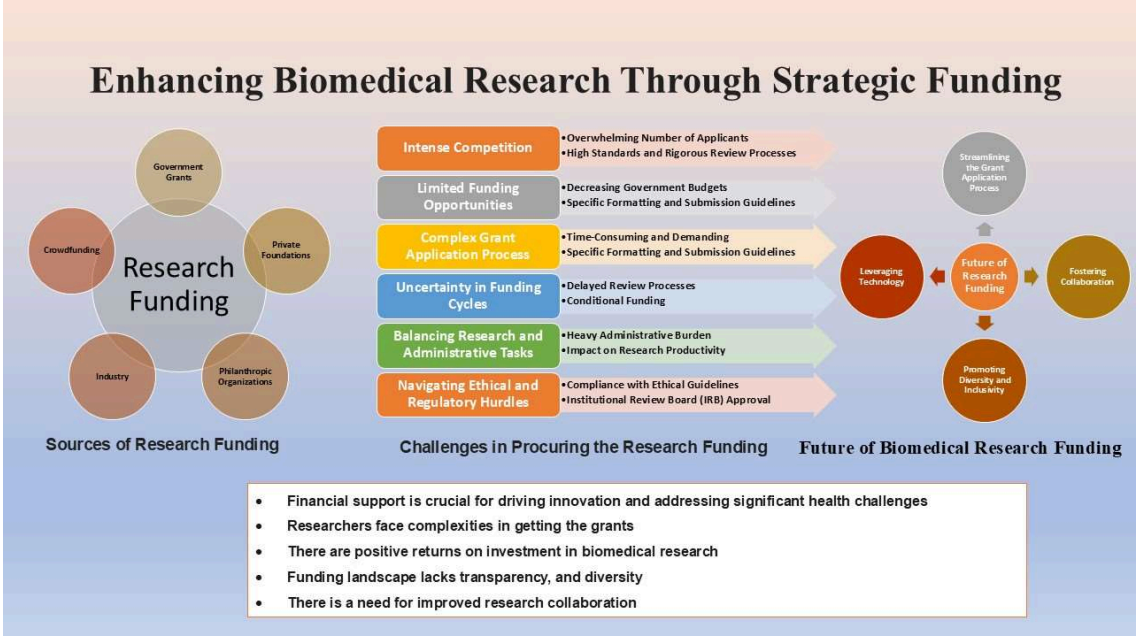
Graphical Abstract



Key Highlights

- Financial support is crucial for driving innovation and addressing significant health challenges
- Researchers face complexities in getting the grants
- There are positive returns on investment in biomedical research
- Funding landscape lacks transparency, and diversity
- There is a need for improved research collaboration

Introduction

In the field of health and medicine, biomedical research is fundamental for driving innovation and progress, essential for enhancing our understanding of human health and creating effective treatments. Research funding refers to the financial backing typically obtained through a competitive application process to support scientific studies [1]. This funding is vital for tackling some of the most pressing health challenges we face today, including chronic diseases like diabetes and cancer, as well as emerging global health threats such as epidemics and pandemics [2]. The influence of biomedical research is clear in the creation of groundbreaking therapies, life-saving drugs, and the swift development of vaccines, particularly highlighted during the COVID-19 pandemic, where scientific responsiveness and funding support enabled an unprecedented and timely vaccine rollout [3]. Additionally, funding programs significantly boost research productivity, leading to about one more published article each year. Funded researchers also enjoy greater visibility and impact, as shown by increased citation counts and altmetric scores [4]. The ever-evolving nature of biomedical research requires substantial financial resources, and the success of these efforts largely depends on access to consistent and robust funding [5,6].

However, despite its vital importance, the funding landscape for

biomedical research is becoming more intricate and competitive [7]. Researchers frequently encounter challenges in securing the necessary funding, including a complicated grant application process and limited resources allocated for innovative projects [8]. There is also a rising concern about the insufficient financial support for underrepresented groups and early-career researchers, which ultimately restricts the diversity of viewpoints crucial for tackling complex health issues. Furthermore, while the significance of funding is widely recognized, there is often a lack of transparency and clarity in the funding mechanisms [9].

There are still significant gaps in our understanding of the economic impact of investing in biomedical research. While previous studies suggest that these investments yield positive returns [10], a thorough examination of how funding affects innovation outcomes and public health metrics is still necessary. Additionally, there is a lack of empirical evidence demonstrating how diversity within research teams influences scientific progress and the success of research proposals.

This review intends to highlight the critical role of funding in biomedical research by delving into the complexities and challenges that the researchers encounter when seeking financial support, the economic ramifications of these investments, and the pressing need for improved collaboration and transparency in funding processes. By reviewing existing literature, this analysis aims to offer a well-rounded perspective on the funding landscape, pinpoint essential areas for enhancement, and ultimately encourage strategic reforms that will strengthen biomedical research initiatives to address the changing health challenges faced by society.

Methodology

This narrative review aims to explore different aspects of funding mechanisms, the challenges researchers encounter, and the economic effects of investments in this area. A thorough literature search was performed using databases like PubMed, Scopus, and Web of Science from December 1st to 10th, 2024. The search encompassed peer-reviewed articles, government reports, and publications from leading research organizations that concentrate on funding for biomedical research. Specific keywords such as "biomedical research funding," "grant application processes," "funding challenges," "economic impact of research," and "diversity in research funding" were employed to find relevant materials.

The inclusion criteria targeted studies published in the last twenty years that examine funding sources (government, private sector, philanthropic) and their effects on biomedical research. Additionally, studies addressing funding challenges and diversity issues in grant applications were included. Articles that did not primarily focus on biomedical research and opinion pieces lacking substantial data were excluded.

The extracted data encompassed findings related to various funding sources, challenges in securing funding, and the economic impact of funding on biomedical research. Key themes and trends were identified across the literature to facilitate a comprehensive understanding of the funding landscape. Thematic analysis was employed to categorize the identified

challenges and implications of funding into coherent sections.

Results and Discussion

Complexities of Biomedical Research

Biomedical research is an intricate and demanding field characterized by the time-consuming nature of scientific discovery [11,12]. Transformative breakthroughs take time to happen; they require years, if not decades, of rigorous investigation and testing. This multi-stage process often encompasses basic research, clinical trials, and the transition to market-ready solutions [13]. Funding for biomedical research is drawn from a diverse array of sources. Government agencies, such as the National Institutes of Health (NIH) and the National Science Foundation (NSF), allocate substantial budgets to support innovative research initiatives. The NIH primarily invests its nearly $48 billion budget in medical research benefiting the American population. A significant portion of this funding, around 83%, is distributed through competitive grants to over 300,000 researchers across the United States (U.S.). Approximately 11% of the budget supports research conducted by NIH scientists in their laboratories, while the remaining 6% is allocated to administrative and operational expenses [14]. The NSF supports approximately 25% of all federally funded basic research conducted by U.S. colleges and universities. With an annual budget of roughly $9.9 billion (fiscal year 2023), the NSF plays a crucial role in advancing scientific discovery [15]. Private-sector investments, including pharmaceutical companies and biotechnology firms, play a crucial role, particularly in the later stages of research, where significant capital is needed to bring products to market. Non-profit organizations and philanthropic contributions also represent key funding avenues, often targeting specific diseases or health conditions. Despite the presence of these various funding sources, the landscape of biomedical research needs to be revised. Researchers often need help to secure the funding necessary for their projects, which can stifle creativity and slow the pace of progress (Figure 1).

Figure 1: Sources of Research Funding

Challenges in Securing Funding

One of the primary challenges in the biomedical research funding landscape is the highly competitive grant application process [16]. Researchers are frequently faced with numerous applicants vying for a limited pool of resources [17]. For example, there has been fierce competition for research funding in China, which is especially difficult for early-career scientists. In 2024, there was a massive jump in applications, more than 380,000 overall, up 26% compared with last year. Only 13% of those were successful, compared with 16% in 2023 [18].

The review process can be quite challenging, demanding a lot of time and effort to satisfy strict requirements while showcasing the potential impact and feasibility of the proposed research (Figure 2). Additionally, funding levels often need to be increased to fully support innovative projects. Many grants only provide partial funding for research proposals, forcing researchers to look for extra resources to fill the financial gaps. This situation puts significant pressure on research teams and may deter young scientists and underrepresented groups from taking on ambitious projects. The issue of diversity in research funding is particularly urgent. Underrepresented groups and early-career researchers may struggle to navigate the complicated landscape of funding opportunities, which often results in a lack of diverse perspectives in biomedical research. Committing to diversity in funding is not just a moral obligation but also a crucial factor in promoting new ideas and comprehensive solutions [19]. Diverse teams contribute unique experiences and viewpoints that foster innovation and a deeper understanding of health challenges.

Figure 2. Challenges in procuring the research funding

Economic Impact of Research Funding

The economic implications of funding biomedical research extend far beyond improved health outcomes. The return on investment in this field is significant, with research yielding substantial economic benefits. According to the NIH, every dollar invested in biomedical research generates approximately $2.70 in economic returns [20]. This statistic underscores the rationale for continued public investment in research, as government appropriations directly impact the capacity of researchers to explore novel ideas and translate them into practical applications. Funding for biomedical research also contributes to job creation and economic growth. As research institutions expand and new projects emerge, they generate employment opportunities for scientists, technicians, and support staff, thereby stimulating local economies.

Additionally, successful research initiatives can lead to the establishment of new companies and industries, particularly in biotechnology and pharmaceuticals, further driving economic development. As we navigate an era characterized by unprecedented health threats and scientific advancements, it is crucial to prioritize funding in biomedical research not only for immediate health benefits but also for long-term economic sustainability [21]. Investments in research are essential to position nations as leaders in scientific innovation and to ensure global competitiveness.

Funding Organizations

In the realm of biomedical research, securing adequate funding is essential for driving innovation and advancing scientific inquiry. Various organizations play a pivotal role in providing this support, and they can be broadly categorized into government agencies, private foundations, and other organizations (Table 1). Starting with government agencies, the National Institutes of Health (NIH) in the USA stands out as the world's largest public funder of biomedical research, steering substantial resources towards understanding health and disease. Complementing the NIH, the National Science Foundation (NSF) also provides critical funding across a wide range of scientific research areas, including biomedical and health-related fields. Over in the UK, the Wellcome Trust operates as a global charitable foundation dedicated to supporting biomedical research both within the UK and internationally (Table 1). The Medical Research Council (MRC), another UK agency, is explicitly focused on funding medical and health research initiatives.

In Europe, the European Research Council (ERC) offers competitive funding for excellent frontier research across various scientific disciplines. Additionally, the Canadian Institutes of Health Research (CIHR) is the federal agency responsible for funding health research in Canada, ensuring a commitment to advancing knowledge in the field.

China has been spearheading research and publications in the past couple of decades and has achieved the 2nd rank globally after the U.S. [22,23]. Increased research funding by the Chinese government significantly influences this substantial improvement in its ranking. There has been a consistent increase in funding for science and technology, with a 10% increase in 2024 compared to the previous year. This includes GBP 10.7 billion for basic research in 2024 [24]. The National Natural Science Foundation of

China (NSFC), based in Beijing, oversees several programmes that provide funding through competitive grants, which received US$5 billion in funds in 2024. China also has international cooperation agreements with other countries, such as the EU, to support collaborative research projects [25].

In India, the Indian Council of Medical Research (ICMR) serves as the apex body for formulating, coordinating, and promoting biomedical research. The Department of Biotechnology (DBT) in India also plays a significant role in promoting biotechnology research and development, complemented by the Department of Science and Technology (DST), which funds a wide range of scientific research, including in biomedical and health-related spheres. The Council of Scientific and Industrial Research (CSIR) is another key player, providing support for research across various fields, including biomedical sciences (Table 1).

Recognizing the breadth of funding sources, we must also consider private foundations. The Bill & Melinda Gates Foundation is a major global philanthropic entity, funding an array of health and development programs aimed at improving lives across the globe. In the USA, the Howard Hughes Medical Institute (HHMI) is a non-profit medical research organization that supports biomedical research and science education, contributing significantly to advancements in these fields. The Kavli Foundation is another noteworthy private entity that invests in scientific research across disciplines like astrophysics, neuroscience, and nanoscience.

Table 1. Major Global Research Funding Organizations

Organization	Country	Focus Areas	Website
National Institutes of Health (NIH)	USA	Biomedical and health research	https://www.nih.gov/
National Science Foundation (NSF)	USA	Biomedical and health research	https://www.nsf.gov/
Bill & Melinda Gates Foundation	USA	Global health and development	https://www.gatesfoundation.org/
Howard Hughes Medical Institute (HHMI)	USA	Biomedical research and science education	https://www.hhmi.org/
European Research Council (ERC)	EU	Frontier research across all scientific disciplines	https://erc.europa.eu/homepage
Medical Research Council (MRC)	UK	Biomedical and health research	https://www.ukri.org/councils/mrc/
Wellcome Trust	UK	Biomedical and health research	https://wellcome.org/

Canadian Institutes of Health Research (CIHR)	Canada	Health Research	https://cihr-irsc.gc.ca/e/193.html
World Health Organization (WHO)	Switzerland	Health Research and Programs	https://www.who.int/
National Natural Science Foundation of China (NSFC)	China	Science and Technology	https://www.nsfc.gov.cn/
Department of Biotechnology (DBT)	India	Biotechnology research and development	https://dbtindia.gov.in/
Indian Council of Medical Research (ICMR)	India	Biomedical research	https://www.icmr.gov.in/
Department of Science and Technology (DST)	India	Science and technology research, including health sciences	https://dst.gov.in/
Council of Scientific and Industrial Research (CSIR)	India	Scientific and industrial research, including medical research	https://www.csir.res.in/
Tata Trusts	India	Philanthropic funding for various fields, including health and medical research	https://www.tatatrusts.org/

Additional organizations that fund global health initiatives include the World Health Organization (WHO), which allocates resources toward health research and programs aimed at improving health outcomes worldwide. The American Cancer Society and the Alzheimer's Association are prominent organizations that provide funding for specific disease research and patient support programs, focusing efforts on advancing treatments and improving the quality of life for affected individuals.

Many public and private organizations are dedicated to offering financial support for biomedical and healthcare research. The specific funding opportunities can differ significantly based on the research area, the researcher's location, and other contextual factors. Thelwall et al. discussed various aspects of research funding and emphasized the need to take these aspects into account when quantitatively assessing the value of research funding. They recommended that organizations gathering funding data should incorporate these aspects into their data collection methods. When comparing funding sources or assessing the impact of funding, it is essential to consider as many

relevant aspects as possible to ensure fair evaluations [12].

Publication and dissemination plan for research funded by government or philanthropic agencies are crucial to ensure the public benefits from the investment. These plans outline how research findings will be shared with the scientific community and the broader public. The plans typically include details on the types of publications (e.g., journal articles, conference presentations, reports), target audiences, and dissemination channels (e.g., websites, social media, public outreach events). Clear and explicit policies regarding these plans help to ensure transparency and accountability in research funding. In the USA, the recommendation for open access to federally funded research has gained significant traction [26]. This means that research findings would be freely available to the public, potentially accelerating scientific progress and benefiting society. Similarly, making research data publicly accessible can facilitate secondary research and meta-analyses, leading to new insights and discoveries. While open access policies have numerous benefits, there are also challenges to consider. For example, ensuring the quality and integrity of research data while making it publicly accessible requires careful planning and implementation. Additionally, concerns about intellectual property rights and potential misuse of data need to be addressed.

Scientific and professional associations like the Indian Orthopaedics Association (IOA) and Indian Medical Association (IMA) can play a vital role in fostering research by offering grants to researchers working in specific specialties or on relevant topics [27]. These associations possess a deep understanding of the field's challenges and priorities, enabling them to strategically allocate funds to projects that address critical needs. By supporting research, these associations not only advance scientific knowledge but also contribute to improving patient care, developing innovative treatments, and enhancing the overall quality of healthcare.

Agile Funding Mechanisms

The COVID-19 pandemic has clearly shown the need for flexible and responsive funding mechanisms in biomedical research. The quick development and rollout of vaccines against the virus demonstrated the effectiveness of targeted investments. Organizations, governments, and private entities collaborated to allocate resources rapidly, leading to record-breaking timelines for vaccine development. This experience underscores the necessity of establishing adaptable funding frameworks that can quickly respond to emerging health threats. Policymakers and funding agencies should focus on maintaining ongoing investment in biomedical research that supports both new and experienced scientists, ensuring that essential resources are available when crises occur. Additionally, creating resilient funding strategies will enable a proactive stance toward future health emergencies [28,29]. By cultivating an environment where researchers can quickly mobilize their efforts, we can enhance our preparedness for unforeseen challenges, minimizing potential harm to public health and promoting swift recovery.

Collaboration Between Public and Private Sectors

A key element in securing funding for biomedical research is the collaboration

between the public and private sectors [30,31]. Public funding lays the groundwork for exploratory studies that investigate new ideas and concepts. However, advancing these ideas to market readiness often necessitates private-sector involvement, where substantial capital is required for later-stage development. These partnerships can create a synergistic effect, accelerating the research and development process while ensuring that the most promising scientific ideas receive the resources they need to thrive. Collaborative models, like public-private partnerships, have proven effective in various therapeutic areas and can be adapted to stimulate innovation in other medical fields [32]. A prominent example is the collaboration that led to the development of COVID-19 vaccines. Governments worldwide teamed up with pharmaceutical companies, providing funding and support that enabled swift progress from research to distribution. Such collaborations not only yield successful results but also demonstrate how combining the strengths of both sectors can enhance the overall impact of biomedical research efforts.

Transparency and Accountability

In addition to collaboration, there is a crucial need for transparency and accountability in how research funds are allocated. Stakeholders must ensure that financial resources are distributed fairly, based on scientific merit rather than personal connections or biases. Transparency in funding processes not only enhances the integrity of research but also fosters public trust, which is vital for securing further support for biomedical initiatives. Clear criteria and guidelines for fund allocation will ensure that researchers from diverse backgrounds have equal opportunities to compete for support. Establishing and upholding ethical standards within the funding process will build confidence in the system, encouraging more individuals and organizations to invest in biomedical research. Furthermore, regular reporting and assessment of the outcomes and impacts of funded research projects can help illustrate the effectiveness of these investments [33]. This practice will provide stakeholders with valuable insights into the progress made and will serve as an important feedback loop for refining funding processes and structures over time.

Tips for Grant Application Success

Perils, pitfalls, and recommendations for young researchers, for making their grant applications a success is summarized in Table 2.

Table 2. Perils, Pitfalls, and Recommendations for Young Researchers

Perils and Pitfalls	Recommendations
Lack of clarity and focus	Develop a strong research question and hypothesis by **c**learly articulating the project's significance and innovation.
Inadequate budget justification	Provide detailed and realistic cost estimates by **j**ustifying each expense and demonstrate value for money.
Weak writing and communication	Seek feedback from mentors and colleagues. Proofread carefully and ensure the proposal is well-written and easy to understand.
Insufficient preliminary data	Conduct pilot studies or gather preliminary data to support the proposed research by demonstrating feasibility and preliminary success.
Inadequate mentorship and support	Seek guidance from experienced mentors and **b**uild a strong support network within the institution and field.
Not understanding the funding agency's priorities	Thoroughly review the funding agency's guidelines and priorities; and **t**ailor the proposal to their specific interests.
Underestimating the time commitment	Allocate sufficient time for proposal development and submission by **s**tarting early and allowing ample time for revisions and feedback.
Not addressing potential risks and challenges	Identify potential obstacles and develop mitigation strategies by demonstrating a realistic understanding of the project's challenges.
Overlooking the importance of dissemination	Develop a plan for disseminating research findings. Outline how the results will be shared with the scientific community and the public.

Research Gaps and Future Directions

Despite the acknowledged role of funding in advancing biomedical research, significant research gaps persist. A primary gap is the need for comprehensive studies quantifying the direct economic impact of funding on research outcomes. This includes examining how financial investments translate into innovative solutions and improved health metrics. Additionally, there needs to be more empirical evidence addressing the challenges faced by under-represented groups and early-career researchers in securing funding **[**34]. This hinders efforts to promote diversity within the field. Furthermore, research on the relationship between team diversity and research productivity or innovation still needs to be completed. While transparency in funding mechanisms is crucial, systematic evaluations of existing practices and their effectiveness in fostering collaboration and ensuring equitable access to resources still need to be improved [35,36].

To address these gaps and enhance the future of biomedical research funding, several directions can be pursued (Figure 3).

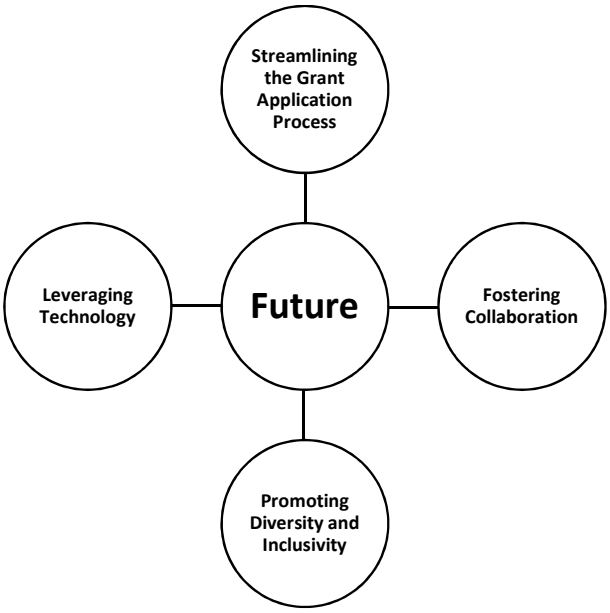


Figure 3. Future of Biomedical Research Funding

a) **Streamlining the Grant Application Process:** Funding agencies should streamline grant application processes to reduce administrative burdens and promote efficiency, ensuring that innovative projects receive the necessary resources.
b) **Fostering Collaboration:** Increased collaboration between government, private sector, and philanthropic organizations can create a more integrated funding ecosystem, enabling shared risk and investment in high-potential research areas.
c) **Promoting Diversity and Inclusivity:** Emphasizing diversity and inclusivity in grant awarding processes will foster a broad range of perspectives and solutions, driving innovation.
d) **Leveraging Technology:** Utilizing data analytics can facilitate informed decision-making in funding allocations and identify emerging trends and research needs.

Conclusion

This review highlights the pivotal role of strategic funding in driving biomedical research and innovation, particularly in addressing significant health challenges. The complexities of the funding landscape, marked by a convoluted grant application process and limited support for underrepresented groups, impede researchers' ability to secure necessary financial resources. While investments in biomedical research yield positive economic returns, comprehensive analyses linking funding to concrete health outcomes remain scarce. The need for enhanced transparency in funding mechanisms is critical to fostering creativity and efficiency in research efforts. Addressing these challenges will strengthen biomedical research and ensure a diverse array of perspectives is represented in the pursuit of effective health solutions.

Disclosure Statements

Conflicts of interest

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

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Authors' Contribution

RV- Conceptualization, data collection and analysis, literature search, manuscript writing, editing and final approval; AV- Literature search, manuscript writing, editing and final approval; MMS - Conceptualization, manuscript writing, editing and final approval.

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Use of AI tool: We have used Bard/Gemini Google and Grammarly to improve the English and readability of the article, but have rechecked the final manuscript and take full responsibility for its contents.

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PERSPECTIVE ARTICLE

Changing Trends in Agrochemical Poisoning in India: A Cautionary Note for Primary Care Physicians

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Suicidal poisoning by agrochemical substances is almost a unique problem in the eastern countries of the world. With a significant proportion of the population being engaged in agriculture, the accessibility of agrochemicals becomes more pronounced. In times of distress, individuals often turn to these readily available substances, as they attempt to end lives. The increased unintentional use of agrochemicals in India can also be partly attributed to an ill-regulated pesticide manufacture, storage, distribution and retailing systems in place.

In recent times, there has been a shift in the trend of suicidal poisoning cases in our country, particularly when it comes to the unintended use of agrochemical substances. A noticeable shift has emerged in the patterns of self-harm, marked by a distinct decrease in the prevalence of traditional agrochemical substances. For instance, in the past, Endrin was infamous as a suicide weapon, but its use declined following its ban in the 1990s, during which the abuse of Endosulfan became more prevalent. Similarly, while the use of organophosphates and rodenticides has not declined significantly, people are increasingly turning to other agrochemicals for suicide. Contemporary individuals prone to suicide increasingly favour novel agrochemicals, with paraquat emerging as a popular choice due to its lethal properties. Reported cases also encompass neonicotinoids, pyrethroids, and chloroacetanilides like pretilachlor [1].

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There is a concerning trend where individuals from various backgrounds, not limited to agriculture, are resorting to suicide by acquiring agrochemicals like paraquat through e-marketplaces. This disturbing pattern, emerging even among school students and office executives in major cities, demands urgent regulatory attention. A deeply concerning trend has emerged where individuals attempting suicide by abusing agrochemical substances intentionally consume only lesser amounts. This results in symptoms that mimic natural diseases, allowing them to disguise their suicide attempt as a death from natural causes, thereby avoiding the stigma associated with suicide. They frequently withhold this poisoning plot from healthcare providers until the situation becomes critical, leading to life-threatening consequences. It is imperative for clinicians to consider agrochemical substance poisoning as a potential differential diagnosis, particularly in common presentations such as gastrointestinal illnesses, vomiting, diarrhoea, or generalized malaise and stupor [2]. Early recognition and intervention play a pivotal role in preventing severe outcomes associated with deceptive poisoning cases. The significance of forensic nursing in such scenarios cannot be underestimated.

It is important to exercise caution when providing primary care for individuals exposed to agrochemical substances. The *agrochemical cholinergic toxidrome*, once associated exclusively with organophosphates in clinical practice, now extends to include carbamates and chloroacetanilides quite commonly. Therefore, accurate differentiation in treatment approaches becomes imperative, emphasizing the importance of utilizing point-of-care tests. An approach to identifying the aetiology of an unknown agrochemical poisoning is summarized in Figure 1.

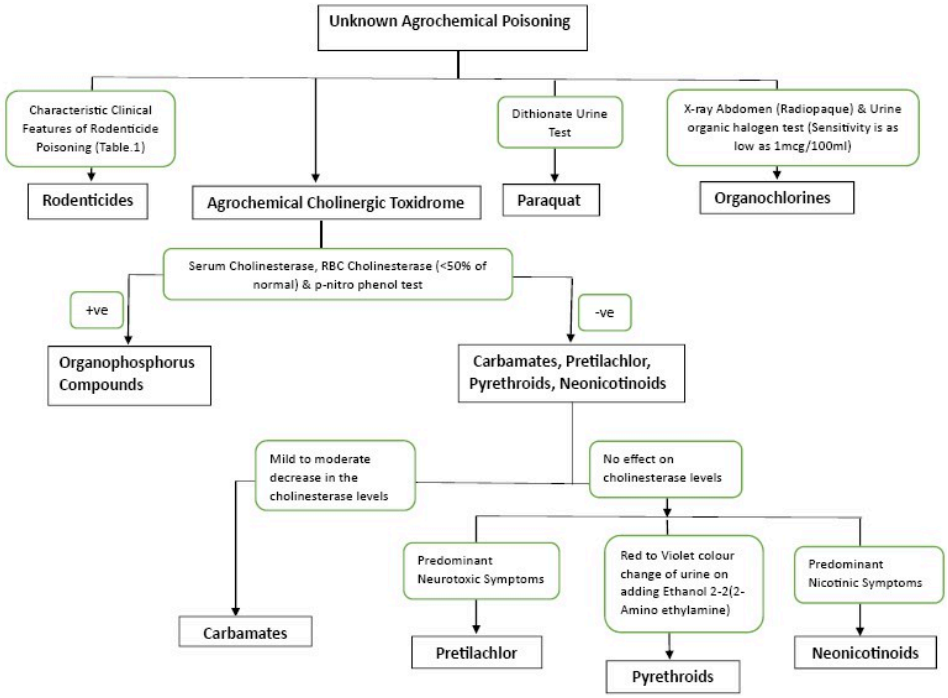

Figure 1. Approach to a Case of Unknown Agrochemical Poisoning for Identifying Aetiology

While agrochemical poisoning cases present with similar clinical manifestations, physicians must discern subtle differences among organophosphorus (OP) compounds, carbamates, pyrethroids, organochlorines, neonicotinoids and chloroacetanilides, specifically pretilachlor, for effective case management. Traditionally, carbamates were considered less fatal than organophosphate (OP) compounds; however, recent studies have shown contrasting results, indicating that fatal outcomes associated with carbamates. Both OP compounds and carbamates, including chloroacetanilides like pretilachlor, exhibit similar cholinergic symptoms, but the initial presentation of carbamate poisoning often may involve direct cardiotoxic effects like arrhythmias [3].

In organophosphate (OP) poisoning, while clinical diagnosis is often clear, measuring serum cholinesterase levels is essential for effective management of the poisoning. The treatment approach includes decontamination, atropinisation, administration of oximes (which is time-sensitive), benzodiazepines, and other supportive care. Pralidoxime is widely used in the treatment of organophosphate poisoning and remains a crucial part of the recommended management guidelines. The cause of death in these cases is respiratory failure, primarily due to bronchorrhea, bronchospasm, and muscle weakness leading to respiratory paralysis. Bradycardia and hypotension further contribute to the deterioration. Pneumonia is often a later complication, developing as a result of prolonged intubation, aspiration, or immobility leading to acute respiratory distress syndrome. (ARDS) [3,4].

It is important to note that oximes do not significantly aid in the treatment of carbamate poisoning. However, they are often given early on when the specific poison is not yet identified. In fact, oximes are contraindicated in carbamate poisoning because carbamylated oximes can become even stronger cholinesterase inhibitors than the carbamates themselves, potentially leading to fatal outcomes [5].

It is important to emphasize that the reliability of acetylcholinesterase (AChE) levels as a test for of acute cholinergic toxidrome can vary but their continuous monitoring is of importance in linking to the aetiology (agrochemical) and improving patient care. In carbamate poisoning, the transient nature of AChE inhibition may result in better-preserved enzyme activity unlike organophosphates.

In a case of chloroacetanilide poisoning (pretilachlor) [6], the clinical manifestations are exactly similar to OP poisoning. However, differentiation is possible by the absence of the characteristic garlicky odour and the presence of normal serum cholinesterase levels, which are not observed in OP poisoning [6]. The management primarily involves supportive care, and in cases of symptomatic bradycardia, correction is pursued through atropinisation. This emphasizes the importance of accurately distinguishing the type of agrochemical poison for effective management, as most of them closely resemble organophosphate (OP) poisoning.

Pyrethroids and neonicotinoids, popular groups of insecticides, are now increasingly being used as suicidal poisons. Pyrethroids affect the sodium and chloride channels of neurons and muscle cells, causing a spectrum of neurological manifestations. Neonicotinoids act at nicotinic acetylcholine receptors (nAChRs), and the spectrum of clinical features include gastrointestinal erosions,

haemorrhagic gastritis, leucocytosis, and convulsions. For both groups, the management is supportive, and knowledge of the definitive type of poison is fundamental, as they do not affect acetylcholinesterase enzymes. Administering atropine to these patients just because it mimics OP poisoning, can cause atropine toxicity including an unwarranted psychosis, worsening the condition [7]. However, it is worth mentioning that atropine is used across the spectrum of agrochemical cholinergic toxidrome to manage the muscarinic symptoms initially.

Next in the list are rodenticides that are highly potent and among the most dangerous compounds, with a high mortality rate. They consist of three groups: yellow phosphorus, aluminium, and zinc phosphide, and coumarins (Table 1). The compound should be identified before charting out treatment plan, as clinical manifestations and management also differ. It is important to note that gastric lavage should be done with caution in the case of metal phosphide poisoning, as the liberation of phosphine gas endangers the lives of medical professionals [8-10]. Instead, lavage with 1:10,000 potassium permanganate is recommended to oxidize phosphorus into less toxic compounds [11].

Table 1. Summary of Rodenticide Poisonings [8-10]

Type of compound	Clinical manifestation	Management
Yellow phosphorus Children often accidentally ingest this substance, mistaking it for toothpaste.	It is believed to affect ribosomal protein synthesis and affects major systems such as hepatic, gastrointestinal, neurological, and renal. Symptoms range from mild nausea and vomiting to acute liver failure, coagulopathy, acute kidney injury and cardiac arrythmias. The cause of death is due to direct cardiotoxicity or complications of acute liver injury.	Symptomatic care. Use of N-acetyl cysteine may help in acute liver injury. The efficacy of steroids is equivocal. Liver transplantation may be needed.
Aluminium and Zinc Phosphide These substances form phosphine gas by reacting with hydrochloric acid and water in the stomach.	They inhibit mitochondrial oxidative phosphorylation. Initial symptoms include nausea, vomiting and epigastric pain followed by circulatory collapse, hypotension, myocarditis, pericarditis etc. The cause of death is circulatory collapse.	Supportive intensive care. Correction of dyselectrolytemia and hypoglycaemia. N-acetyl cysteine is used for acute liver failure and the use of pralidoxime is being assessed.

Coumarins The second generation coumarins are about one hundred times more potent than warfarin.	They inhibit the synthesis of clotting factors and cause coagulopathy. Mild to severe bleeding can be seen across all systems. Paradoxical thrombosis can also be seen in some cases Diagnosis can be established by deranged Prothrombin time and by measuring 4-hydroxycoumarin levels.	Misdiagnosis is common in children, thinking of other haematological disorders. Vitamin K supplementation is the mainstay of treatment.

Furthermore, paraquat has emerged as the *new endrin* in the Indian agrochemical suicide landscape, often labelled as a deadly weapon, with claims that even a single sip can be fatal. It stands out as the ubiquitous choice in cases of suicidal agrochemical poisoning in India. Despite paraquat poisoning can be certainly identified through the point-of-care dithionate test, the absence of an antidote contributes to a high fatality rate.

The diagnosis of Paraquat poisoning can be relatively easily established, as it produces characteristic effects on the gastrointestinal (GI) tract, especially the tongue, commonly referred to as *"Paraquat tongue,"* which is almost universally observed. Even in small doses, GI toxicity such as mucosal lesions and perforations can be seen. Paraquat also exerts significant toxicity on the kidneys and lungs. While renal failure develops rapidly, death through this mechanism is rare. Initially, alveolitis/pulmonary oedema can develop in the lungs, later progressing to fibrosis, leading to hypoxia, multiple organ dysfunction syndrome (MODS), and ultimately death. Diagnosis can be confirmed through the urine dithionite test as mentioned earlier and measurement of plasma paraquat levels. Management involves supportive care, monitoring serum cystatin-C levels, and providing intensive respiratory care [12]. Immunosuppressive therapy and Ambroxol have been found to be efficacious in management of paraquat poisoning [13].

Organochlorine pesticides are a variety of chlorinated hydrocarbons available in forms such as dusting powders, wettable powders, emulsions, granules, and solutions. Contrary to a popular assumption among certain doctors, these pesticides do not depress cholinesterase enzymes. The mechanism of action of organochlorines involves disrupting nerve function by affecting sodium channels, inhibiting GABA-mediated chlorine channels, and interfering with calcium ATPase activity. Additionally, they induce liver drug-metabolizing enzymes, leading to liver damage. Clinical features include neurological and gastrointestinal symptoms such as seizures, tremors, confusion, headache, nausea, vomiting, abdominal pain, and diarrhoea [14].

The diagnosis of organochlorine pesticide poisoning can be aided by performing an abdominal radiograph, which may reveal the presence of certain radiopaque organochlorine compounds, particularly those with heavier chlorination. However, the diagnostic utility of this radiographic feature is limited. Additionally, measuring organic halogen compounds in urine serves as an indicator

of exposure, with a sensitivity as low as 1 mcg of organic halogen per 100 ml of urine. It is important to note that the urine halogen test is generally more useful in cases of chronic exposure rather than acute poisoning.

The importance of analytical toxicology in identifying the ingested substance is acknowledged; however, the focus of the current discussion is on improving the diagnosis of these poisonings in peripheral settings. The goal is to equip primary care practitioners with the knowledge and tools necessary to accurately diagnose cases before they reach tertiary care hospitals, thereby reducing the risk of misdiagnosis and mismanagement.

In conclusion, there is a critical need for caution and awareness regarding the diverse possibilities in agrochemical poisoning. The primary care physician should be aware of differential diagnosis (aetiology) of agrochemical cholinergic toxidrome and the importance of point of care tests. In instances of uncertainty, the first contact healthcare practitioners are advised to promptly consult the National Poison Information Centre operated by the All-India Institute of Medical Sciences, New Delhi. With the continuous introduction of new agrochemicals, it is essential for physicians to stay abreast with the several types and their distinct clinical presentations to prevent misdiagnosis, considering the variations in management approaches.

The urgent need for a National Poison Incident Database in India continues to be an unfulfilled goal to this day [15]. Additionally, there is a significant demand to ban certain herbicides, such as paraquat, which is classified among highly hazardous pesticides and has already been prohibited in many countries worldwide [16].

Nevertheless, the proper regulation of highly lethal agrochemical substances becomes imperative to mitigate risks and prevent untoward pesticide suicides. The easy accessibility of these compounds, both through e-commerce websites and over the counter, coupled with the lack of antidotes for many, poses a significant public health threat. Urgent national-level regulations are imperative for the distribution, storage, and sale of agrochemicals to address this growing concern and ensure public safety.

Statements and Declarations

Conflicts of interest

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

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CASE SERIES

Different Clinical Presentations of Pulmonary Embolism: A Case Series

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Abstract

Pulmonary embolism can present with a wide spectrum of clinical symptoms ranging from asymptomatic to life threatening phase to emergency department. It is one of the medical challenges with respect to its diagnosis and treatment. We present a case series of five such cases of presented to a tertiary care centre Subbaiah Institute of Medical Sciences and Research Centre, Shivamogga, Karnataka, India. Clinical, electrocardiographic and point of care ultrasound of heart, lungs and bilateral lower limb two point compression ultrasound done at the bedside along with all the initial stabilization steps done and their outcome are described in this case series. Early high degree of clinical suspicion and appropriate treatment is crucial. Failing which can lead to mortality. This case series highlights the different clinical presentations of pulmonary embolism including periarrest states that can present to emergency departments.

Keywords: Pulmonary embolism, Deep vein thrombosis, Hypercoagulability

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Introduction

Pulmonary embolism (PE) is the third most common cause of cardiovascular death after myocardial infarction (MI) and cerebrovascular accidents (CVA) [1]. Various conditions lead to the generation of PE. Virchow's triad of hypercoagulability, venous stasis, and vessel wall injury is the final mechanism for most of the risk factors for developing PE. Overall, major risk factors for thromboembolic events include recent immobilization, myocardial infarction, cerebrovascular accidents, recent surgery and trauma. Additional major risk factors include prior venous thromboembolism, advanced age, malignancy, known thrombophilia, and indwelling venous catheter [2]. Pulmonary embolism can present with varied clinical profile starting from asymptomatic to life threatening stages. Diagnosing and managing pulmonary embolism at their extreme conditions is very challenging in emergency departments (ED). Owing to their severity and time constrains, only our high degree of clinical suspicion and clinical scoring systems can guide in further stabilizing the patients. Here, we present five such cases of pulmonary embolism with different clinical profiles who presented to our tertiary care centre Subbaiah Institute of Medical Sciences and Research Centre, Shivamogga, Karnataka, India.

Case Presentation

Case 1

A 40 years old male patient was brought to ED with sudden onset dyspnoea, excessive sweating, severe pain in upper back and right joint for ten minutes. There was history of right lower limb swelling for three days. Patient was known case of tuberculosis of right hip with secondary arthritis of right hip for two years with total hip arthroplasty status for three weeks followed by bed rest since then. Patient had completed antitubercular therapy. He had no other comorbidities. On arrival to ED, Patient was conscious with tachypnea, tachycardia with normal blood pressure and hypoxia with cold extremities and sweating. Electrocardiogram (ECG) showed sinus tachycardia with S1Q3T3 (deep S wave in lead I, deep Q wave and inversion of T wave in lead III) pattern (Figure 1). Point of care ultrasound (POCUS) of heart showed dilated right atrium(RA) and right ventricle(RV) with strain with D-sign(bowing or flattening of the interventricular septum into the left ventricle) (Figure 2) with distended and non collapsible inferior venacava (IVC) and negative bilateral lower limb venous compression ultrasound. Blood samples for D-dimer and troponin i were sent and both of which found elevated. The initial clinical diagnosis of pulmonary embolism was made based on the presentation. Patient was initially started on supplemental oxygen, fluids resuscitation, unfractionated heparin and tramadol. Eventually patient’s sensorium got deteriorated and landed up in cardiac arrest. Cardiopulmonary resuscitation (CPR) was started along with injection adrenaline and airway was secured. Arterial blood gases showed high anion gap metabolic acidosis for which injection sodium bicarbonate was given. CPR was continued till next 2hours. Patient could not be revived inspite of achieving return of spontaneous circulation (ROSC) three times during resuscitation and was declared dead.

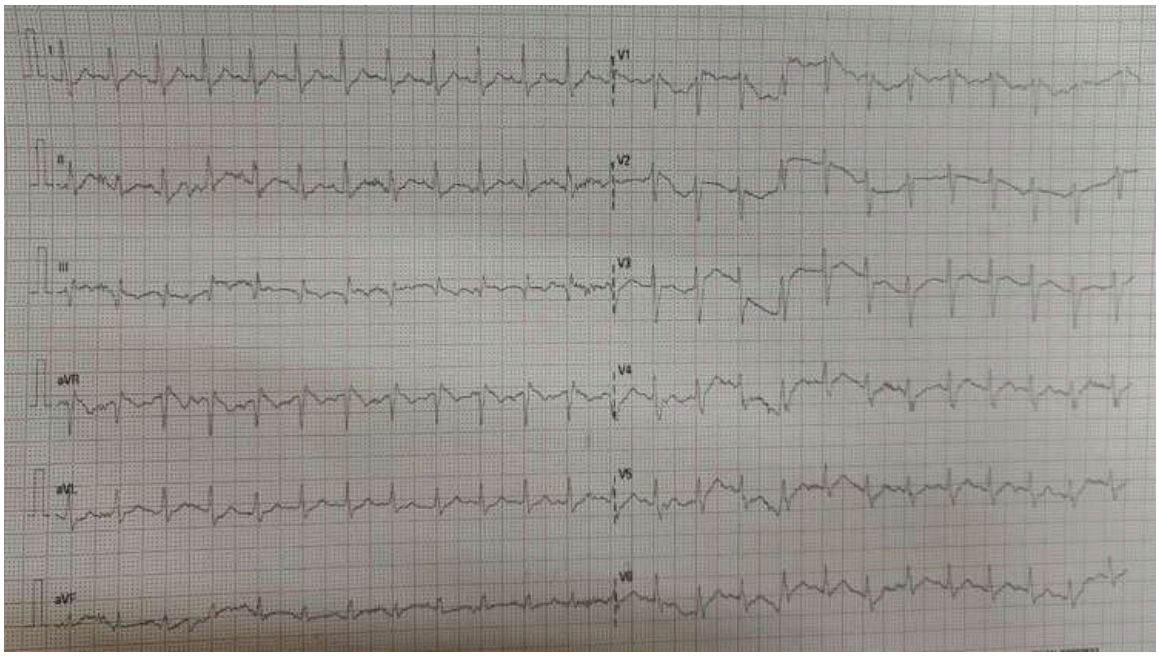

Figure 1. ECG showing sinus tachycardia and S1Q3T3 pattern

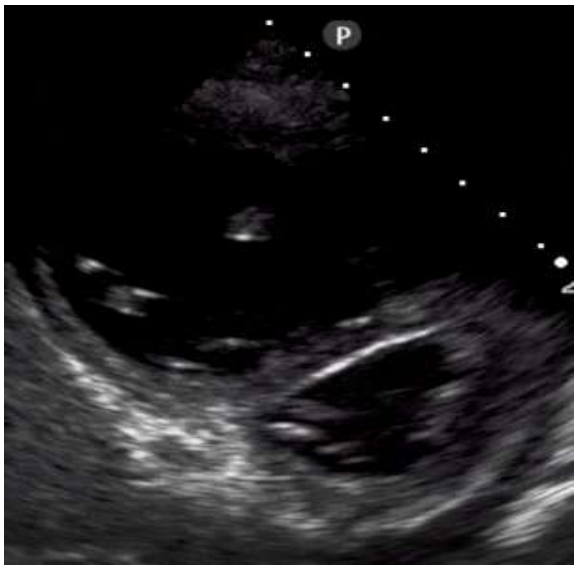

Figure 2. Cardiac POCUS showing D-sign (bowing of interventricular septum towards LV) in parasternal short axis view

Case 2

A 60 years old male presented to ED with vomiting and generalised weakness for 3 days. Patient was known case of metastatic carcinoma of tail of pancreas and had undergone exploratory laparotomy, palliative gastrojejunostomy and hepaticojejunostomy for duodenal obstruction 1 month before with stoma bag in situ containing bile stained fluid. Patient also had thrombosis of common femoral vein, superficial femoral vein, popliteal vein and proximal posterior tibial vein of right lower limb for which he was on tablet dabigatran 110 mg twice daily and tablet aspirin 150 mg once daily since 1

month. Patient was known smoker and alcoholic with no other comorbidities. At presentation to ED, he had tachycardia with normal oxygen saturation and blood pressure with mild pallor. Per abdomen was distended, mild tenderness in epigastrium and umbilical region with a sluggish bowel sounds. ECG showed sinus tachycardia (Figure 3). Ultrasound (US) of abdomen showed no new findings other than previous known pathology. Blood panel showed mild anemia with normal hematocrit with normal sodium, potassium and chloride levels. Patient was treated with fluids resuscitation, proton pump inhibitor, antiemetic, and intravenous anticoagulants. After two hours of arrival, patient developed sudden onset of breathlessness immediately followed by cardiac arrest. CPR was done according to advanced cardiac life support (ACLS) protocol for 30minutes along with securing the airway. POCUS while ongoing CPR showed dilated RV and IVC with a noncompressible right common femoral and popliteal veins (Figure 4 and 5). Unfractionated heparin was given while ongoing CPR. But the patient could not be revived and declared dead.

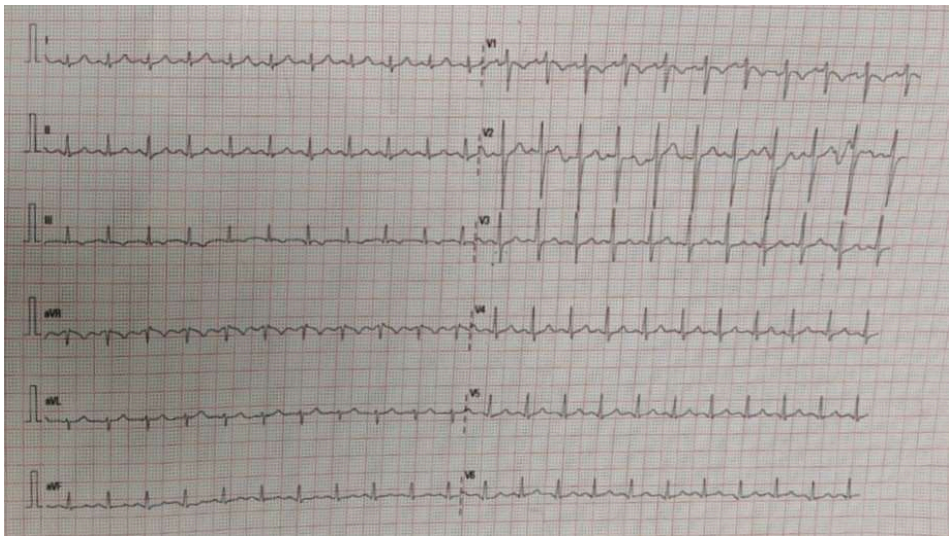

Figure 3. ECG showing sinus tachycardia

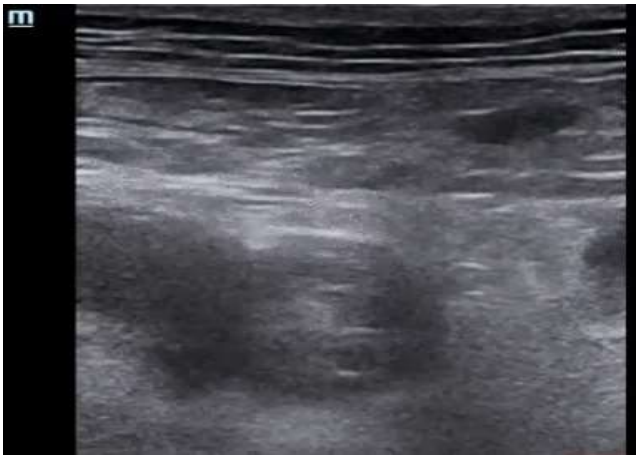

Figure 4. POCUS showing non compressible right common femoral vein with a thrombus inside

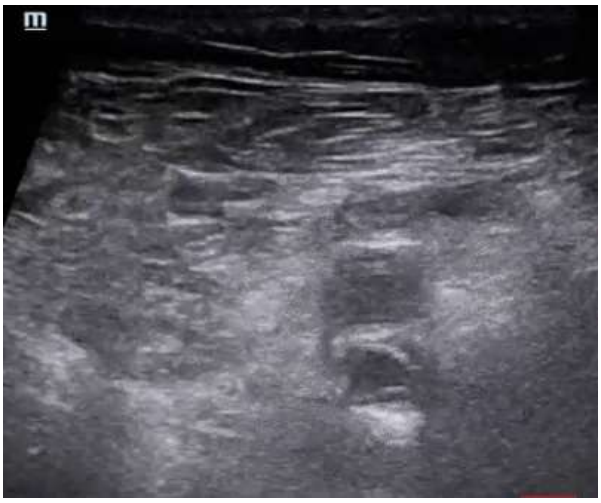

Figure 5. POCUS showing non compressible right popliteal vein

Case 3

A 44 years old female who was known case of systemic lupus erythematosus, antiphospholipid antibodies (APLA) positive status, hypothyroidism, type 2 diabetes mellitus, bilateral lower limbs deep vein thrombosis and pulmonary thromboembolism (PTE) for 6 years on home based oxygen therapy, tablet warfarin 5mg once daily, oral hypoglycemic agents and thyroxine supplements was brought to ED with complaints of exertional breathlessness and bilateral lower limb swelling for 1 month and fever for 3 days. At presentation, patient had tachycardia, tachypnoea and hypoxia of @ 80% @ room air which picked upto 95 % with 4 L/min of oxygen supplementation. Patient was put on noninvasive ventilation (NIV) support in view of increased work of breathing, but later got intubated. Electrocardiogram showed sinus tachycardia (Figure 6). POCUS of heart showed severe left ventricle (LV) dysfunction with ejection fraction (EF) of 35%, severe pulmonary arterial hypertension, dilated RA and RV with non collapsible IVC. POCUS of lungs showed showed bilateral A profile. Bilateral lower limbs US showed cellulitis with no evidence of current deep vein thrombosis (DVT). Bedside chest radiograph showed enlargement of right side of heart and large pulmonary arteries (Figure 7). Computed tomography of pulmonary angiogram (CTPA) was not done as the patient was unstable. On performing urinary catheterization, there was mild hematuria. International normalized ratio (INR) was 11.5, D-dimer was 400ng/mL and serum procalcitonin was 8.498 ng/ml. Antiplatelets and anticoagulants were withheld. Patient was started on injection vitamin K and 4 pints of fresh frozen plasma in view of high INR, broad spectrum antibiotics and other supportive therapies for the underlying conditions. After 4 hours, patient's consciousness was deteriorated and developed hypotension for which he was put on injection noradrenaline and vasopressin infusion. Eventually patient developed cardiac arrest. Code blue was announced and CPR was started according to ACLS protocol. Resuscitation was continued till next 20 minutes but couldn't revive. Later patient was declared dead.

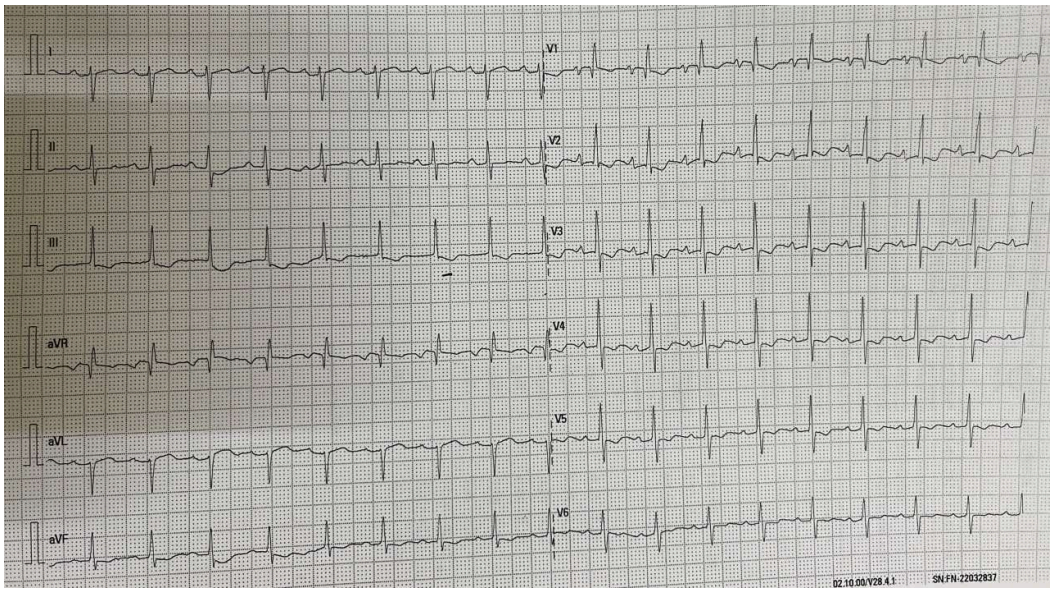

Figure 6. ECG showing sinus tachycardia

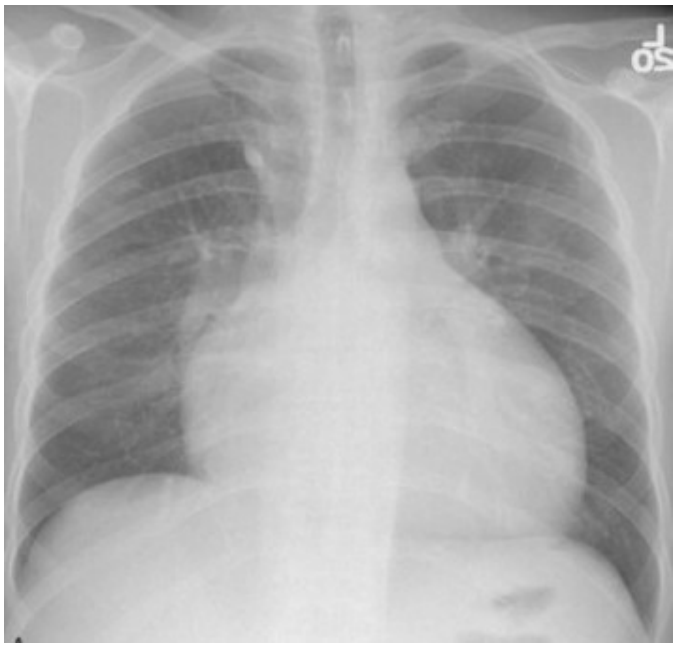

Figure 7. Bedside chest radiograph showing enlargement of right side of heart and large pulmonary arteries

Case 4

A 75 years old female with known case of hypertension and prior cardiac illness with no documents was presented to emergency department in drowsy state with a history of dyspnea from 1 day and progressive right leg swelling since 2 months. While examining the patient suddenly became unresponsive and went into cardiac arrest. Immediately code blue was announced and CPR started and resuscitation as per ACLS protocol after 5 minutes of CPR, ROSC achieved and endotracheal intubation was done and connected to ventilator. Post cardiac arrest care was initiated. ECG showed right axis

deviation, right bundle branch block with atrial fibrillation with fast ventricular rate (Figure 8). POCUS showed RA and RV dilated with global hypokinesia with normal left atrium (LA) (Figure 9). IVC was distended and non-collapsible. DVT scan of right leg showed no thrombus. Troponin I level was 25.9ng/L (>100ng/L to rule in). D-dimer level was 1500ng/mL. Since patient was unstable, CTPA was not done. Clinical examination, history, Well's score of 7.5 and cardiac POCUS were suggestive of pulmonary thromboembolism, hence injection streptokinase 2.5 lakh IU intravenous bolus was given. Again after 10 minutes, patient went into cardiac arrest. CPR was reinitiated and resuscitation was done for the next 15minutes. But the patient could not be revived and was declared dead.

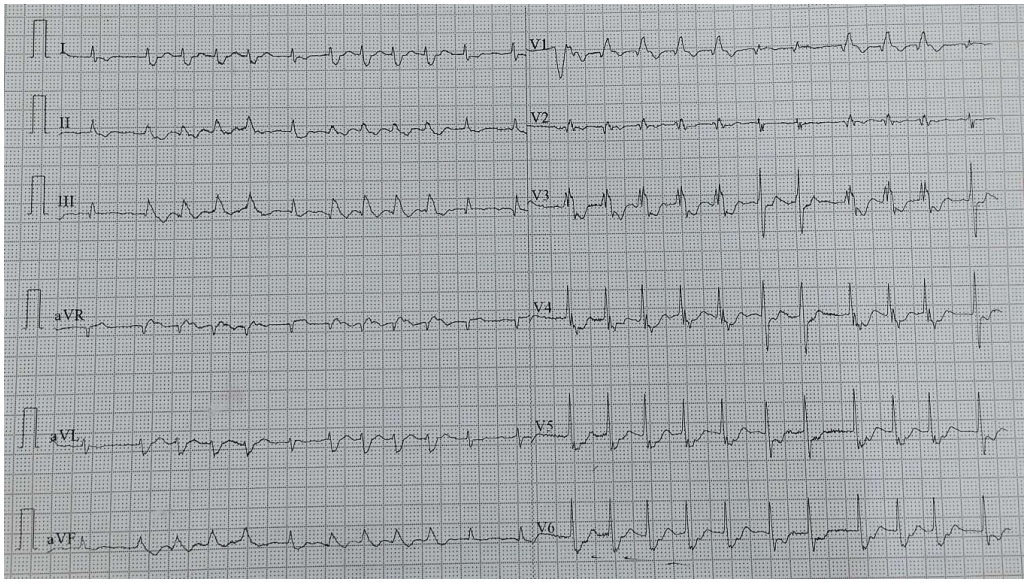

Figure 8. ECG showing right axis deviation, right bundle branch block and atrial fibrillation with fast ventricular rate

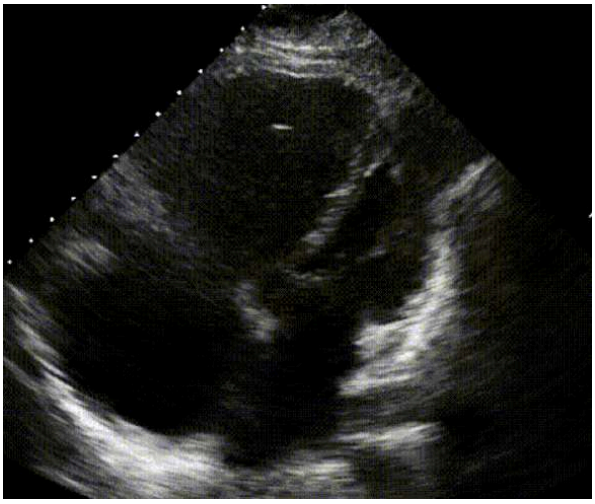

Figure 9. Cardiac POCUS showing dilated RA and RV in subcostal 4 chamber view

Case 5

A 61years old male with hypertension was brought to emergency department in gasping state with history of sudden onset of breathlessness since 4 hours and left leg swelling from 1 week. On examination, carotid pulse was absent. Immediately code blue was announced and CPR was started as per ACLS protocol and intubated after 2 cycles of CPR. POCUS during CPR showed dilated RV (Figure 10) and IVC. Left common femoral vein was non compressible (Figure 11). Unfractionated heparin 5000IU intravenous bolus was given. Effective resuscitation was continued till next 20 minutes. Despite adequate resuscitation and supportive care, the patient could not be revived and was declared dead.

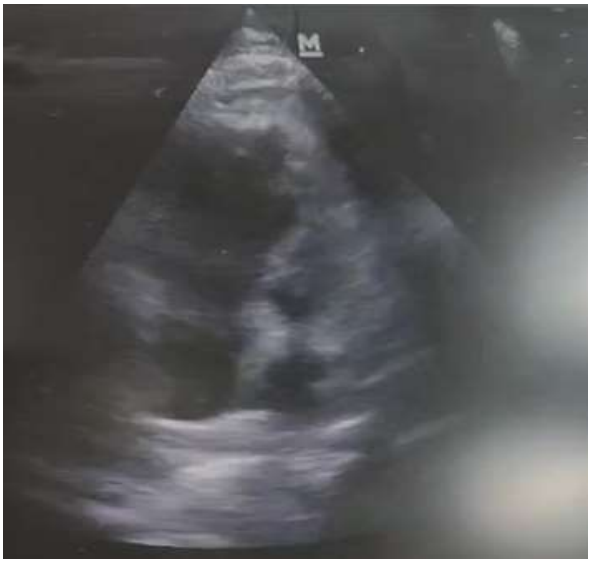

Figure 10. Cardiac POCUS showing dilated right ventricle with deviation of interventricular septum towards left ventricle in apical 4 chamber view

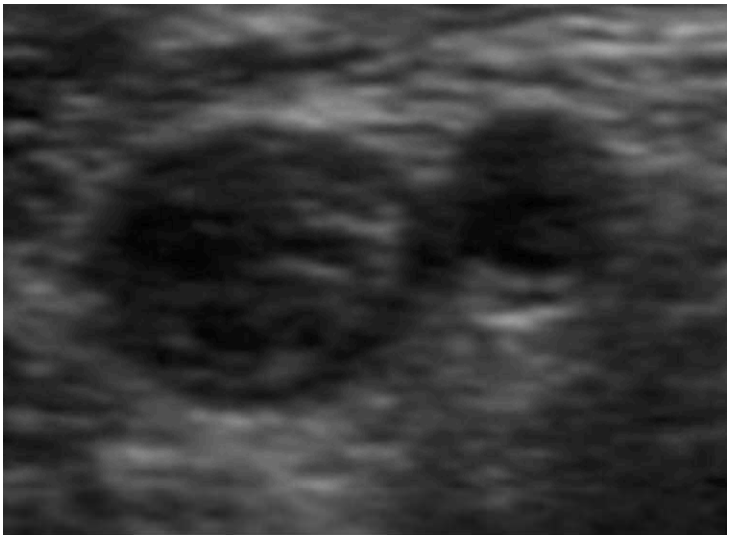

Figure 11. POCUS showing non compressible left common femoral vein

Discussion

Pulmonary embolism (PE) occurs when a thrombus originates elsewhere and enters the pulmonary circulation. In deep vein thrombosis, a thrombus develops within the deep veins, most commonly in the lower extremities. One or more risk factors were present in all 5 cases of the present study such as recent surgery, immobility, active malignancy, prior venous thromboembolism and deep vein thrombosis. Case 3 also had foci of sepsis which is a thrombogenic state, which could suggest it to be septic thromboembolism. Other risk factors for developing pulmonary embolism include advanced age, obesity, pregnancy, trauma, smoking, congestive heart failure, stroke, infections and associated inflammation and oral contraceptive pills. Pathophysiology typically involves the risk factors finally landed up in Virchow's triad i.e., stasis, vascular endothelial injury and hypercoagulable states and leading to pulmonary embolism.

Symptoms and signs were typical in all 5 patients. All patients had dyspnoea. Case 2 had only vomiting and generalized weakness with no respiratory involvement at initial presentation but later developed dyspnoea. Case 1, 2 and 3 had tachycardia and only case 1 and 3 had hypoxia. All cases except case 3 had unilateral lower limb swelling but only case 2 and 3 were previously known to be having deep vein thrombosis in lower limb. Case 3 had bilateral lower limb DVT as a consequence of APLA syndrome. Considering all risk factors, symptoms and signs, the modified Well's scores of all the cases in order were, 9, 11.5, 6, 7.5 and 6 respectively. All of them were >4 and are likely to have pulmonary embolism. Parameters of the modified Well's score system in pulmonary embolism have been depited in Table 1 [3].

Table 1: Modified Well's score for pulmonary embolism

Factor	Score*
Clinical symptoms of DVT	3
Other diagnoses less likely than pulmonary embolism	3
Heart rate >100 beats per min	1.5
Immobilization for 3 or more days or surgery in the previous four weeks	1.5
Previous history of DVT/PE	1.5
Hemoptysis	1
Malignancy	1

*Risk score interpretation (probability of pulmonary embolism): PE likely:>4.0, PE unlikely:≤4.0

Cases 1, 2 and 3 had sinus tachycardia, which is the most common ECG finding in PE. Case 1 had S1Q3T3 pattern as well which is pathognomonic of PE. Case 4 had right axis deviation, right bundle branch and atrial fibrillation with fast ventricular rate. For case 5, we couldn't get a 12 lead ECG as the patient was brought in cardiac arrest and CPR was started immediately.

POCUS was done for all 5 cases to assess the heart, lungs and both lower limbs for detecting deep vein thrombosis. Two point compression ultrasound, where

femoral vein and popliteal veins was used to assess for DVT. RV was dilated in all 5 cases. IVC was distended and non collapsible in all 5 cases. Case 1 had classical D-sign. Case 3 and 4 had LV hypokinesia also. Bilateral lower extremity compression ultrasound was positive in only case 2 and 5. In other cases it was negative. There could be a proximal DVT, distal DVT or DVT in a superficial vein which are not assessed in two point compression ultrasound [4]. At the same time, as in case 1, there were few cases reported as delayed fat embolism in patients who have undergone total hip replacement. So, this could create a dilemma whether its thromboembolism or delayed fat embolism. Other possible explanations for PE without DVT include complete embolization of lower extremity DVT, venous thromboembolism from uncommon sites (hepatic, renal, ovarian [5], neck, or upper extremity veins) [6,7], false-positive diagnosis of PE, false-negative venous leg ultrasound, isolated PE (I-PE) or de novo PE (DNPE) [8-10], and complete resolution of lower extremity DVT due to anticoagulation therapy in the short time interval between the diagnosis of PE and venous leg ultrasound [11].

D-dimer levels were elevated in cases 1, 2 and 4 and normal in case 3. It was not done in case 5 as the duration of resuscitation very short to send samples. Although CTPA having a gold standard value and highest diagnostic sensitivity and specificity for PE, it was not done in all 5 cases as all of them were hemodynamically unstable. One prospective study in the ED found that the triple POCUS exam (cardiac, lung, and leg veins ultrasound for DVT) in patients with a Well's score of 5 or more and positive D-dimer has a sensitivity of 90% and specificity of 86.2% for PE [12]. With the use of pretest probability, Well's score, ECG and POCUS of heart, lungs and bilateral lower extremity compression ultrasound, we can effectively suspect the hemodynamically unstable probable pulmonary embolism at the bedside.

Troponin I was elevated in case 1 and normal in case 4. However, troponin I being one of the cardiac biomarkers, can be elevated in pulmonary embolism also indicating the myocardial injury. INR was elevated in case 3. Based on the results of a study [13], and subsequent experience with other prospective clinical studies, the recommended therapeutic range is an INR of 2.0 to 3.0. An INR of 3.0 to 4.0 has been recommended for patients with antiphospholipid antibodies [14-16], although there is some disagreement on this issue [17]. Serum procalcitonin was done in case 3 which was found to be elevated. It indicates the presence of bacterial sepsis and guide the antibiotic approach.

Managing a case of massive pulmonary embolism is very challenging at ED. Early high degree of suspicion of the condition is crucial. While case 1 and 3 typically presented with symptoms of pulmonary embolism, for case 2 we did not have any clue that patient ends up in embolism. Case 4 and 5 presented to ED in periarrest condition. Although, there is only supportive therapy that can be given for fat embolism, we can still consider full anticoagulation until patient is not bleeding taking thromboembolism into account and this was considered in case 1. Case 1 was also treated with sodium bicarbonate in view of severe metabolic acidosis. Except case 3, all other patients received unfractionated heparin as full dose of anticoagulation. Case 3 was

initially treated with NIV support and early broad spectrum antibiotics as per sepsis guidelines. At the same time, while this patient was already on warfarin therapy and had high INR with mild hematuria at the presentation, the antiplatelets and anticoagulants were stopped and instead started on vitamin K and fresh frozen plasma to correct INR. Pulmonary embolism could still be the cause for the patient's breathlessness even with supratherapeatic INR values. The same had been reported as a case report in a study [18]. This is also supported by a study in which there was no clinically relevant difference in the INR values of patients who did or did not develop pulmonary embolism [19]. In case 4, with the background of history, examination and POCUS findings, fibrinolysis was done using streptokinase. Thrombolysis during ongoing CPR in presumed or confirmed PE has been supported in literature [20-22]. Periarrest patients like case 4 and 5 with suspected pulmonary embolism is not uncommon to receive in emergency departments. The effective use of bedside ultrasound (POCUS) of heart, lungs and DVT scan of limbs can be helpful. All 5 cases landed up in cardiac arrest and all of them received effective CPR according to ACLS guidelines and endotracheal intubation was also done in all patients. With the varied risk factors and comorbidities taken into account that led to pulmonary embolism, mortality will increase. Unfortunately, all 5 patients were died in spite of effective treatment done.

Conclusion

Pulmonary embolism has a wide range of clinical presentations ranging from asymptomatic to life threatening conditions. With the use of pretest probability, modified Well's score, electrocardiogram and point of care ultrasound, we can effectively diagnose the hemodynamically unstable probable pulmonary embolism at the bedside. Early high degree of suspicion and appropriate treatment is crucial. Failing which can lead to mortality. This case series highlights the different clinical presentations of pulmonary embolism including periarrest states that can present to emergency departments.

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.

Ethical Clearance

All ethical issues addressed by authors.

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CASE REPORT

Influenza B Pneumonia with Pneumomediastinum, Subcutaneous Emphysema and Encephalitis. A Rare Presentation

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Abstract

Children under the age of five are more vulnerable to influenza because they are an immunologically naïve population. When treating a child with viral pneumonia, severe consequences after an influenza infection must be considered. Here we are reporting a case series of 2 atypical severe influenza B pneumonia cases in children complicated with necrotising pneumonia, pneumothorax, and encephalitis.

Keywords: Viral pneumonia, Influenza, Pneumothorax, Viral encephalitis

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Introduction

Globally, influenza poses a serious risk to public health [1-3]. Children have a higher risk of infection. The influenza viruses are single-stranded RNA viruses that are part of the Orthomyxoviridae family [1,4,5]. The influenza B (IFB) virus changes its antigens through genetic reassortment and antigen drift caused by mutations that have built up over time [4,5].

Case 1

We are reporting a 2-year-old male child, developmentally normal for age, with uneventful antenatal, natal, and postnatal histories, immunised for age, who was admitted in November 2023 with complaints of fever for the initial 3 days, cough for 9 days, and tachypnea for 7 days, for which the child visited a local practitioner, where he was told about an air leak in the pleural cavity and an intercostal tube was placed. He later developed gastrointestinal subcutaneous emphysema. At presentation, the child had tachycardia, increased respiratory rate, and tense swelling around the eyes, neck, face, chest, abdomen, and scrotum, with crepitations felt on palpation. Routine investigations were suggested: Hb 9.78 g/dl, TLC 6800 cells/mm3, DLC N34L57, and platelet count of 62000/uL, s. creatinine 0.26, SGOT 89, SGPT 23, s. bilirubin 0.44, CRP negative, and left-sided pneumothorax were confirmed on ultrasonography. The child was managed on supportive measures, oxygen supplementation by mask, IV fluids, and IV antibiotics. The antibiotics were upgraded on subsequent days in view of fever and increased oxygen requirement to meropenem, clindamycin, and azithromycin. Blood cultures were drawn and a nasopharyngeal swab for respiratory viruses was sent. The child showed no improvement in subcutaneous emphysema, pneumomediastinum, and pneumoscrotum and continued to have fever and dependence on oxygen. The child's respiratory virus swab turned positive for influenza B virus, and oseltamivir was started for the same. In view of persistent fever episodes, pleural fluid cultures were drawn suspecting secondary bacterial infection, which showed pan-resistant Acinetobacter baumanii growth, and antibiotics were upgraded to colistin. Streptokinase was administered on day 20 of the hospital stay, and HRCT thorax was done, which showed left-sided hydropneumothorax with fibrocavitatory changes in the left lower lobe and diffuse fibrotic bands with areas of bronchiectasis in bilateral lungs. The patient's fever gradually responded; therefore, the ICD tube was clamped and subsequently removed. A diagnosis of **post-influenza necrotising pneumonia with pneumomediastinum** was made, and the patient was successfully discharged after 1 month of hospital stay.

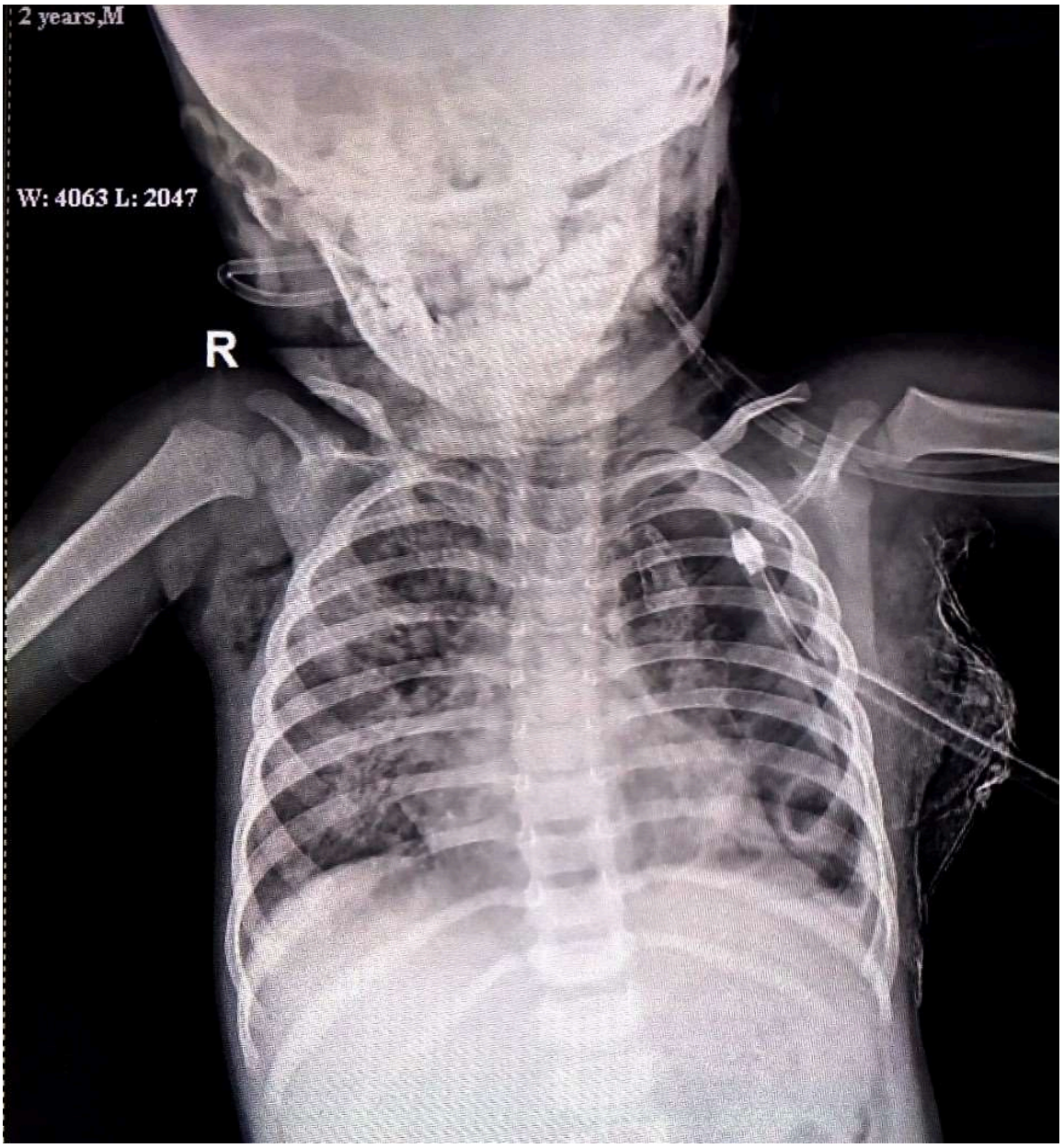

Figure 1. Chest X ray AP view at presentation to the hospital showing subcutaneous emphysema, bilateral nodular opacities and cystic changes in the lung field specially in the left lung with intercoastal drainage tube in the left pleural cavity

Case 2

A 6-year-old female child, developmentally normal for her age without any previous history of hospitalisation, immunised for age as per the national immunisation schedule developed fever and pain in the abdomen for 10 days, for which she consulted a local practitioner. Later, the symptoms worsened, and she developed difficulty breathing for 4 days and altered sensorium subsequently when she was referred to a tertiary care center. The child arrived with a gasping pattern of respiration and poor GCS and therefore was immediately

intubated and ventilated on SIMV mode of ventilation. On detailed examination, she had nasal flaring, intercostal and subcostal retractions, and decreased air entry in bilateral lung fields. Neurological examination revealed a GCS of E1VTM1, brisk DTR's, and planter reflex extensor with no signs of meningeal irritation. The child was managed as per acute encephalitis on IV antibiotics, IV fluids, IV antiepileptics, and other supportive measures. Chest radiography showed bilateral infiltrates and patchy areas of consolidation P:F ratio of 54, denoting hypoxaemia, thus falling into the classification of severe ARDS. Ventilator settings and pressures were upgraded in view of severe hypoxaemia, and the child subsequently developed pneumothorax and subcutaneous emphysema. Routine investigations and swabs for respiratory viruses and IgM mycoplasma were suspected and sent based on x-ray findings and rapid progress of symptoms. The child's shock worsened and progressed towards acute renal failure and developed pulmonary bleed, which was managed by upgrading vasopressors. By the 3rd day of hospital stay, she developed ventricular tachycardia; myocarditis was suspected, and DC cardioversion was tried, but the child could not be saved. She later turned positive for the influenza B virus.

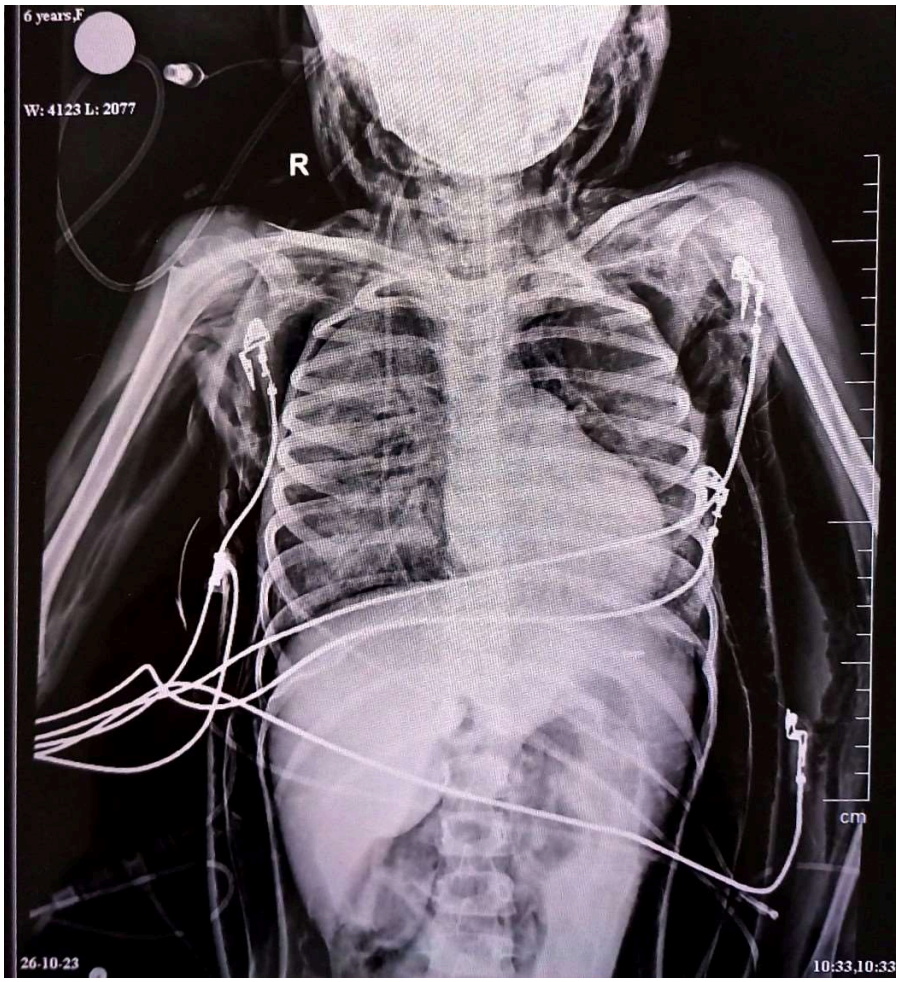

Figure 2. Chest X ray AP view at presentation to the hospital showing bilateral homogeneous opacities in the lung field.

Discussion

Influenza is among the most prevalent infectious respiratory conditions. Globally, the severity of the disease was higher in young children exposed to influenza B (IFB) than in adults [6–10].

According to an Indian study, 78.5% of children with IFB had upper respiratory tract infections, 19.6% had pneumonia, and 1.7% had severe pneumonia [9]. As highlighted in our first case, in which a 2-year-old boy developed severe influenza B pneumonia with spontaneous pneumothorax, an Indian study revealed that influenza-associated mortality was high in both the elderly population and children under the age of five [7]. Other studies have also reported the predominance of males in IFB illness [11-16]. Children under the age of five had a greater hospitalisation rate (82.9%), according to a similar case reported by Eski et al. [17]. Compared to other age groups (36.4%), children ≤ 2 years old had the greatest correlation between hospitalisation and age (63.6%). We here in our case series are emphasising the severity of influenza B infection to an extent of spontaneous pneumothorax, as was reported in a 17-day-old neonate admitted for neonatal sepsis since day 1 of life who developed worsening after acquiring influenza B pneumonia with spontaneous pneumothorax by van den Dungen et al. [18]. Antivirals help in decreasing the severity of illness and hospitalisation, as in our case, where the child improved clinically and was discharged.

Gastrointestinal complaints like abdominal pain, vomiting and diarrhea in IFB-positive children were observed by Lennon *et al.* [13], similar to our second case, who presented with fever and gastrointestinal symptoms initially. Later on, she experienced respiratory distress and encephalitis. McCullers et al. [19] reported a strikingly similar case of a 6-year-old child who had acute IFB viral encephalitis with neurological sequelae. Encephalitis is a rare manifestation of IFB. A 10-year-old child was reported to have IFB-associated encephalitis, severe weakness, and an oseltamivir response by Straumanis et al. [20]. Based on the x-ray picture, the child was evaluated and turned out to be influenza B positive but developed clinical worsening in a day and spontaneous pneumothorax with subcutaneous emphysema, as seen in our first case. This child also developed features of myocarditis and died of ventricular tachycardia. Research by Paddock C.D. et al. [21] found pathologic evidence of myocardial injury in 69% of case patients for whom cardiac tissue samples were available for analysis, primarily in fatal influenza B case patients under the age of 18 years.

Conclusion

When treating a child who has viral pneumonia with altered sensorium, especially in young children, it is important to consider the serious complications that may follow an influenza infection. Effective vaccinations are available for children beyond six months of age. Children respond well to the antiviral medication oseltamivir, especially when it comes to lowering the duration of symptoms, viral shedding, and secondary complications associated. Children are recommended to receive the quadrivalent flu vaccine, which contains the IFB strain.

Statements and Declarations

Conflicts of interest

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

Funding

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