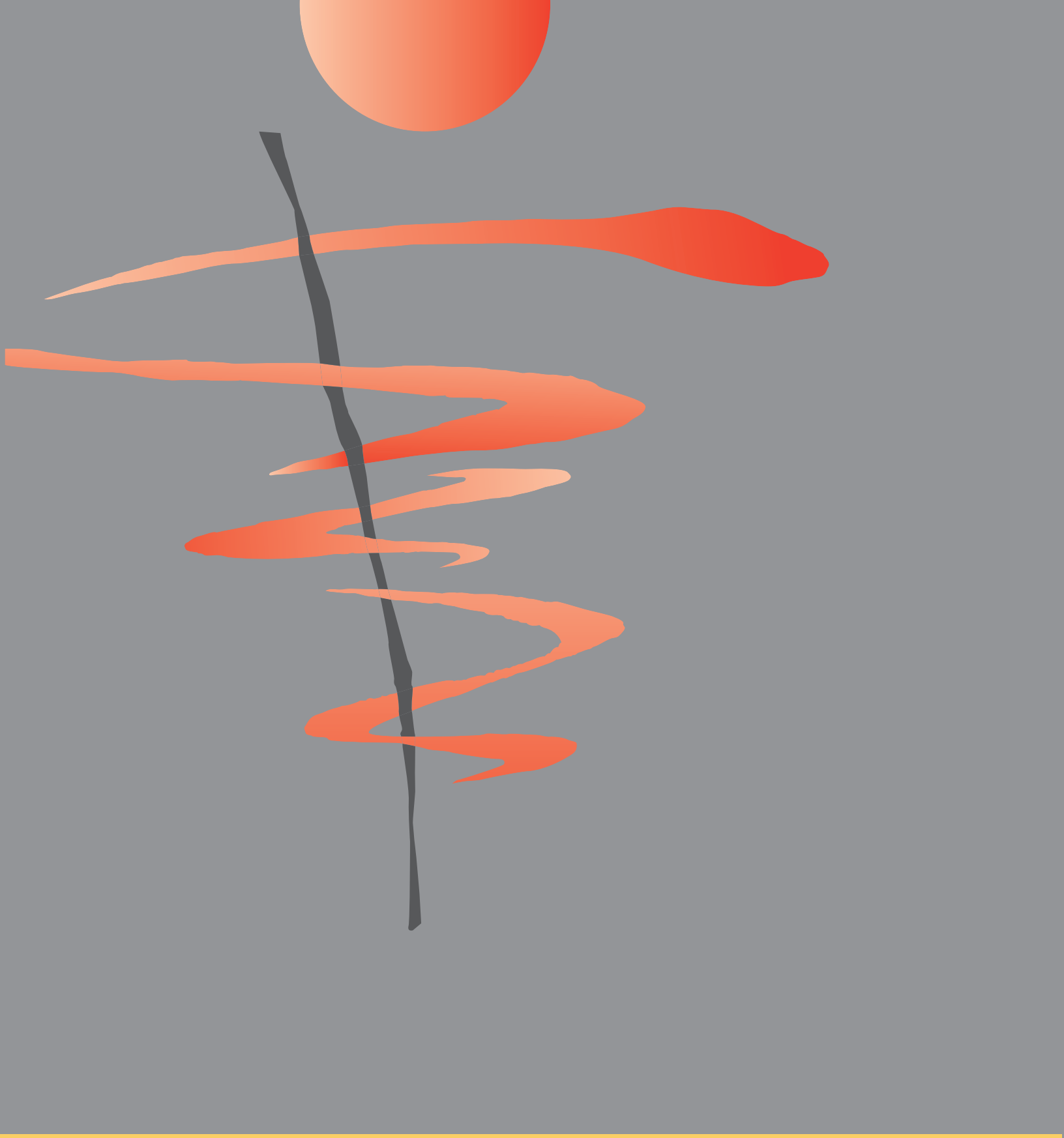

BSMMU Journal
Bangabandhu Sheikh Mujib Medical University
Volume 18 | Issue 1 (Jan - Mar) | 2025

BSMMU Journal
An official journal of Bangabandhu Sheikh Mujib Medical University
ISSN: 2224-7750 (Online), 2074-2908 (Print)

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Published by the BMU (www.bmu.ac.bd). The online publication service is provided by Bangladesh Journals Online (www.banglajol.info).

Journal office

Room 901-902, Basic Science BuildingBangladesh Medical University Shahbag, Dhaka 1000, Bangladesh.
Email: journal.executiveeditor@bsmmu.edu.bd
Website: www.banglajol.info/index.php/BSMMUJ

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BSMMU Journal
An official journal of Bangabandhu Sheikh Mujib Medical University
ISSN: 2224-7750 (Online), 2074-2908 (Print)

Volume 18 | Issue 1 (Jan – Mar) | Year 2025

Contents

Commentaries

Perspective

Bangabandhu Sheikh Mujib Medical University Journal 2025;18(1):e80740
ISSN 2074-2908 | eISSN 2224-7750 |

EDITORIAL

Desk-rejection of manuscripts: A necessary step for quality and efficiency

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Publication history
Received: 23 Mar 2025
Accepted: 23 Mar 2025
Published online: 24 Mar 2025

Responsible editor
None

Reviewer
None

Keywords
editorial triage, desk-rejection, editorial, Bangabandhu Sheikh Mujib Medical University Journal

Ethical approval
Not applicable

Funding
None

Trail registration number
Not applicable

Journal publication is essential to science and academia, relying on the collaboration of authors, reviewers, and editors. As gatekeepers, editors play a crucial task in ensuring the quality of publications while balancing with efficiency. This responsibility often requires editorial triage to determine which manuscripts should proceed to the peer review stage. Thus, some manuscripts are not subjected to peer review and are rejected without receiving peer review comments. These are referred to as desk rejections, [1] which occur in around half of the instances [2]. The common causes of such rejections are the mismatch between the manuscripts and the journal's scope, non-compliance with author guidelines, and poor readability (in our case, unclear storytelling and subpar English) [3].

We have examined the causes of desk rejections in the Bangabandhu Sheikh Mujib Medical University Journal. In 2024, we received 223 submissions; of which 85 (38%) were desk-rejected before reaching the peer review process. This rate is not unexpected, as high-standing journals, such as the New England Journal of Medicine and the British Medical Journal, experience desk rejections of 80%–90% [4]. Conducting an audit of the triage process is essential to inform potential authors and prevent unnecessary time and effort from being wasted on both sides.

The major reasons for desk rejections are shown in Figure 1. The rejections were largely due to formatting and preparation issues, such as non-compliance with the IMRD (Introduction, Methods, Results, and Discussion), as well as the failure to submit the necessary documents, including the EQUATOR (Enhancing the QUAlity and Transparency Of health Research) checklists [5]. It appears that a substantial proportion of the authors do not carefully review the submission guidelines [6]. Additionally, some submissions lacked institutional ethical approval. In a few cases, the scientific writing quality was exceptionally poor. Many manuscripts did not meet the fundamental criteria, including word count, the number of data visuals, and the ORCID of the corresponding authors. Although our threshold for initiating peer review was a text similarity index of 15%, we allowed authors with a higher similarity index to revise their manuscripts to an acceptable level before making a final decision. However, submissions having more than 30% similarity index were rejected.

Desk rejections can be frustrating and demotivating for authors, but they enhance journal efficiency and allow authors to submit their manuscripts to other journals more quickly [7]. It is equally important for editors to select appropriate articles that meet essential criteria [8]. There is a notion that journals should allow free-format submissions and handle the formatting later [9]. However, we abandoned this practice because many papers could not be properly formatted due to missing mandatory components, such as ethical clearance and ORCIDs. Additionally, obtaining suitable reviewers and receiving their timely responses has become challenging. Therefore, sending all submissions to peer review creates an unnecessary burden on our reviewers. Regulating the number of manuscripts sent to the peer review helps

Key messages

Desk rejections are frustrating for the authors but necessary for quality and efficiency publications. Major formatting problems and delays in author response to mechanical review comments are the most common causes of the rejections in Bangabandhu Sheikh Mujib Medical University Journal. Potential authors could avoid these rejections by paying attention to the submission guidelines and promptly responding to mechanical review comments.

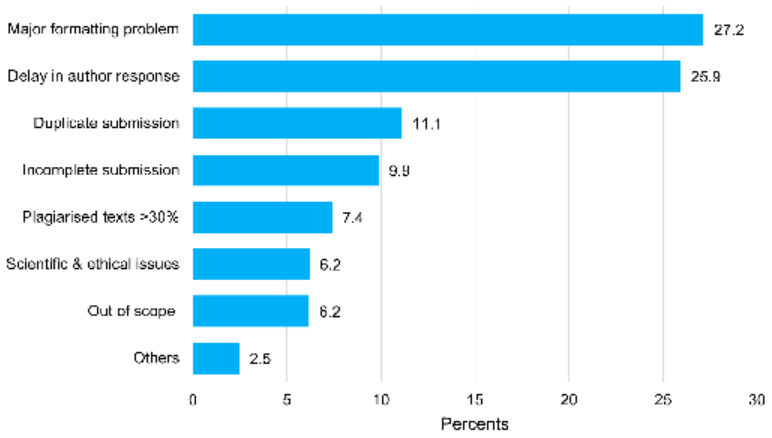

Figure 1 Causes of desk rejections in Bangabandhu Sheikh Mujib Medical Journal in 2024 (n=85)

maintain an efficient and high-standard peer review process [10]. For Bangabandhu Sheikh Mujib Medical University Journal, we have incorporated a mechanical review stage, through which authors can resubmit updated versions of their manuscripts within a reasonable timeframe to address formatting, word count, text similarity, or readability issues. But, an appropriate and timely response from the authors is the cornerstone of this stage as well as the entire review process. In conclusion, we hope this analysis will help potential authors to reduce the likelihood of desk rejections.

Acknowledgments

Special thanks to Dr Tanvir Turin Chowdhury of the University of Calgary, Canada (ORCID: https://orcid.org/0000-0002-7499-5050) for his comments on a previous draft of this editorial.

Conflict of interest

I do not have any conflict of interest

Data availability statement

I confirm that the data supporting the findings of the study will be shared upon reasonable request.

Supplementary file

None

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Bangabandhu Sheikh Mujib Medical University Journal 2025;18(1):e76227
ISSN 2074-2908 | eISSN 2224-7750 |

REVEIEW ARTICLE

Astaxanthin as a potential therapeutic agent for knee osteoarthritis: A review of mechanisms and clinical evidence

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Abstract

Bakground: Knee osteoarthritis (KOA) poses an important challenge in musculoskeletal healthcare, prompting the need for innovative therapeutic strategies. Astaxanthin, a potent antioxidant carotenoid, has gained interest due to its multifaceted mechanisms of action and potential role in KOA management. This review aims to examine the therapeutic mechanisms of astaxanthin in KOA, alongside clinical evidence supporting its effectiveness through a narrative synthesis of preclinical and clinical studies.

Methods: A comprehensive review of the literature was conducted across Web of Science, Pubmed, Scopus and Google Scholar, focusing on studies that explored astaxanthin's antioxidative, anti-inflammatory, and cartilage-protective properties in the context of KOA. Articles published in English between 2014 and 2024 were included (n=44).

Results: The review identified several key mechanisms by which astaxanthin exerts its therapeutic effects, including reducing oxidative stress, attenuating inflammation, and preserving cartilage integrity. Clinical studies also provided promising evidence of its efficacy in alleviating symptoms and improving joint function in patients with KOA.

Conclusion: Astaxanthin demonstrates considerable potential as a therapeutic agent for KOA, though further research is needed to fully understand its long-term efficacy and optimal dosing. Future studies should focus on refining methodological approaches to better elucidate astaxanthin's role in KOA management.

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Publication history
Received: 20 Sep 2024
Accepted: 21 Dec 2024
Published online: 4 Feb 2025

Responsible editor
M Mostafa Zaman
0000-0002-1736-1342

Reviewer
A: Iftekhar Hussain Bandhan
0000-0002-3800-6155

Keywords
astaxanthin, knee osteoarthritis, therapeutic agent, antioxidant

Ethical approval
No ethical approval was needed.

Funding
We did not received any fund for this work.

Trail registration no.
None

Key messages

Astaxanthin, a powerful antioxidant, shows promise in managing knee osteoarthritis by reducing pain, inflammation, and cartilage degradation. It modulates key inflammatory pathways and strengthens antioxidant defenses, offering symptom relief and potential disease modification. Future research should focus on optimizing dosages, exploring long-term effects, and testing combination therapies.

Introduction

Knee osteoarthritis (KOA) stands as a prevalent and burdensome musculoskeletal ailment characterized by the gradual degradation of cartilage, accompanied by inflammation and debilitating pain.[1] The global prevalence of KOA underscores its significant influence on healthcare systems, necessitating effective treatment strategies. Nevertheless, existing therapeutic approaches for KOA often prioritize symptom management over disease modification, leaving a critical gap in addressing the underlying pathophysiology.[2] Subsequently, there is a growing impetus to explore alternative treatments, particularly natural compounds, with the potential to mitigate the progression of KOA and improve patient outcomes.[3] Among these compounds, astaxanthin, a xanthophyll carotenoid abundant in algae, seafood, and also select plants, has garnered considerable attention for its multifaceted therapeutic properties, including potent antioxidative, anti-inflammatory, and also cartilage-protective effects.[4]

Mechanical factors, such as obesity, excessive joint use, and poor muscle strength, along with anatomic factors like joint shape and alignment abnormalities, contribute significantly to the development of KOA. Genetic predispositions and inflammatory processes further exacerbate cartilage degradation and joint dysfunction.[5] As researchers increasingly recognize the potential of astaxanthin in KOA management, there arises a need for a comprehensive review elucidating its mechanisms of action, efficacy in preclinical and clinical studies, safety profile, and avenues for future research. [5]Thus, this review endeavors to provide an extensive exploration of astaxanthin as a promising therapeutic agent for KOA, targeting to inform and guide further advancements in the field of osteoarthritis management.

Methods

Study selection criteria

A comprehensive search was conducted across databases such as Web of Science, PubMed, Scopus, and Google Scholar, focusing on peer-reviewed articles published between 2014 and 2024 regarding the therapeutic potential of astaxanthin in knee osteoarthritis (KOA). The search utilized specific terms related to astaxanthin and KOA, encompassing both preclinical and clinical studies. Predefined inclusion criteria ensured relevance, including studies on astaxanthin supplementation in KOA, full-text availability, and publication in English. Out of 68 initially identified studies, 44 were selected based on these criteria for further analysis.

Data extraction

Data extraction was performed systematically from the 44 selected studies to gather essential information on astaxanthin's effects on KOA. Key details included study design, sample size, dosage and duration of supplementation, and primary outcomes measured. Focus was placed on astaxanthin's mechanisms of action, efficacy, and safety concerns. Findings were meticulously recorded to facilitate a thorough understanding of astaxanthin's therapeutic implications.

Synthesis of results

The synthesis of results involved a detailed analysis of the extracted data from the selected studies. This aimed to clarify astaxanthin's mechanisms of action in KOA, its overall efficacy, and its safety profile. The synthesis also identified future research directions, highlighting gaps in the literature and suggesting areas for further investigation. This comprehensive approach provided valuable insights into astaxanthin's role in managing knee osteoarthritis and potential clinical applications.

Results

Antioxidant activity of astaxanthin

KOA, a condition that affects the joints, oxidative stress is a major problem. An excess of harmful molecules causes this stress called reactive oxygen species (ROS).[6] These ROS damage the tendon in the joints and increase inflammation, making the condition worse over time. Astaxanthin is a powerful antioxidant that can help protect the joints from this damage. Antioxidants are substances that neutralize reactive oxygen species, preventing them from harming cells. When ROS levels get too high, they disrupt the balance between harmful molecules and the body's natural defenses.[6] This is where astaxanthin comes in: it efficiently neutralizes these harmful molecules, stopping them from damaging the cartilage. Astaxanthin does more than just neutralize ROS. It also prevents lipid peroxidation, a process where ROS damage the fats in cell membranes.[7] This damage can lead to further inflammation and instability in the cells. By stopping lipid peroxidation, astaxanthin helps continue the integrity of cell membranes, reducing inflammation and protecting the joints.[7] Moreover, astaxanthin enhances the activity of crucial enzymes like superoxide dismutase (SOD) and catalase.[8] These enzymes play a key role in defending against oxidative stress. SOD converts superoxide radicals, a type of ROS, into less harmful molecules, while catalase breaks down hydrogen peroxide, another harmful molecule, into water and oxygen. By boosting the activity of these enzymes, astaxanthin strengthens the body's natural defenses against oxidative stress, further protecting the cartilage in the joints from injury.[8]

Anti-inflammatory properties of astaxanthin

In the painful world of arthritis, where inflammation causes significant damage to the joints, astaxanthin acts like a calming force, reducing this inflammation effectively.[9] Inflammation in the joints is controlled by complex signaling pathways, much like a complicated web. Astaxanthin phases in and skillfully manages these pathways, especially the important ones like nuclear factor kappa B (NF-κB) and mitogen-activated protein kinase (MAPK).[9] These pathways are accountable for producing substances that cause inflammation. When NF-κB is activated, it triggers a chain reaction that leads to increased inflammation. Astaxanthin helps by stopping NF-κB from being activated, which in turn reduces the production of inflammatory substances.[10] Similarly, it affects the MAPK pathways, preventing the chain of events that would normally lead to more inflammation. By

controlling these pathways, astaxanthin reduces the levels of pro-inflammatory cytokines like interleukin-1 beta (IL-1β) and also tumor necrosis factor-alpha (TNF-α), which are main contributors to pain and stiffness in arthritis.[11] As the levels of these cytokines decrease, so does the pain and also stiffness in the joints. This makes astaxanthin a valuable aid in providing relief from the symptoms of arthritis and also in managing the disease.[12]

Cartilage protection mechanism by astaxanthin

In the delicate balance of joint health, preserving the integrity of cartilage is crucial for slowing the progression KOA.[13] Picture astaxanthin as a vigilant guardian of this precious cartilage, armed with the ability to protect it from the forces that seek to degrade it.[13] This powerful antioxidant does more than just defend; it actively supports the regeneration of cartilage by stimulating the production of essential components like collagen and proteoglycans.[14] These components are vital, as they provide the cartilage with the strength and resilience it needs to endure the constant pressure and movement of the joints.[14] Astaxanthin's protective reach extends to combating matrix metalloproteinases (MMPs), enzymes that play a significant role in the breakdown of cartilage. MMPs can be thought of as destructive architects, chiseling away at the cartilage and weakening its structure. By inhibiting the activity of these enzymes, astaxanthin prevents this relentless destruction, helping to maintain the cartilage's integrity and function.[15]The multifaceted benefits of astaxanthin in KOA management are remarkable. It acts as an antioxidant, neutralizing harmful molecules that contribute to oxidative stress. It also has anti-inflammatory properties, reducing the inflammation that causes pain and swelling in the joints.[15] Furthermore, by protecting and regenerating cartilage, astaxanthin addresses one of the root causes of KOA, offering more than just symptomatic relief. Astaxanthin stands out as a beacon of hope for those suffering from KOA. Its ability to reduce pain and inflammation while also preserving joint function makes it a powerful ally in the fight against this debilitating condition.[15] However, the full extent of astaxanthin's capabilities is still being uncovered. Researchers are continually exploring its mechanisms to better understand how it can be used to its fullest potential.[16] As science delves deeper into the benefits of astaxanthin, there is hope that it will lead to even more effective treatments for those afflicted by knee osteoarthritis, offering not just relief but a chance at better joint health and improved quality of life.[16] These detailed mechanisms underscore the multifaceted therapeutic potential of astaxanthin in KOA management. By targeting oxidative stress, inflammation, and cartilage degradation, astaxanthin offers a promising approach for alleviating symptoms and slowing disease progression in KOA (See Table 1 for summary of the mechanism of action of astaxanthin).

Table 1 Summary of astaxanthin's mechanisms of action in knee osteoarthritis

Mechanism description	References
Antioxidant activity	
Astaxanthin scavenges ROS, inhibits lipid peroxidation, and enhances the activity of endogenous antioxidant enzymes like SOD and catalase.	7, 8, 9
Anti-inflammatory	
Astaxanthin modulates NF-κB and MAPK signaling pathways, leading to downregulation of pro-inflammatory cytokines such as IL-1β and TNF-α.	10, 11, 12
Cartilage protection	
Astaxanthin promotes cartilage matrix synthesis, inhibits MMP activity, and preserves cartilage integrity, thereby mitigating disease progression in knee osteoarthritis.	13, 14

ROS, reactive oxygen species; SOD, superoxide dismutase

Therapeutic effect of astaxanthin

Preclinical evidence of astaxanthin

Preclinical studies have played a key role in revealing the potential benefits of astaxanthin for treating KOA.[17] By using a variety of animal models that closely mimic the complex characteristics of KOA in humans, researchers have been able to investigate how astaxanthin affects various aspects of the disease.[17] These studies have shown that astaxanthin can reduce pain and inflammation, protect against cartilage degradation, and improve overall joint health. Through these detailed investigations, researchers have gained valuable insights into the mechanisms by which astaxanthin works, providing strong evidence of its therapeutic potential in managing KOA.[18] In the realm of preclinical exploration, a rich tapestry of animal models serves as the canvas upon which the effects of astaxanthin unfold. From surgically induced models, such as the destabilization of the medial meniscus (DMM) in rodents, to chemically induced models like the monosodium iodoacetate (MIA) injection model, each animal model offers unique insights into astaxanthin's therapeutic potential.[19] Additionally, non-traditional models, including genetically modified mice with cartilage-specific alterations, further enrich the narrative, providing a nuanced understanding of astaxanthin's effects across diverse disease phenotypes.[20]

The narrative of preclinical studies resonates with a symphony of findings, each chord a testament to astaxanthin's transformative potential in KOA management.[21] Histological examinations unveil a landscape adorned with signs of healing, as astaxanthin supplementation attenuates cartilage degradation, suppresses synovial inflammation, and mitigates osteophyte formation.[21] Beyond the realm of histology, functional assessments illuminate the path to restoration, with astaxanthin offering respite from the shackles of pain and dysfunction.[21] Moreover, mechanistic insights gleaned from these studies unveil a tapestry of molecular interactions, as astaxanthin's antioxidative and anti-inflammatory virtues emerge as guiding beacons in the realm of joint homeostasis[22] (See Table 2 for summary).

Clinical evidence of astaxanthin

As the curtain rises on the realm of clinical inquiry, the narrative of astaxanthin's therapeutic potential unfolds, offering a beacon of hope amidst the shadows of disease. Within the realm of clinical inquiry, a diverse array of study designs serves as a crucible for testing the waters of astaxanthin's efficacy in KOA

Table 2 Preclinical evidence of astaxanthin's therapeutic effects on knee osteoarthritis

Animal Model	Characteristics	Astaxanthin effects	References
Surgically induced models	Destabilization of the medial meniscus)	Attenuation of cartilage degradation suppression of synovial inflammation Mitigation of osteophyte formation	19, 20, 21, 22
Chemically induced models	Monosodium iodoacetate injection model	Reduction in pain and inflammation Protection against cartilage degradation Improvement in overall joint health	17, 18, 19, 20, 21, 22
Genetically modified mice	Cartilage-specific alterations	Insights into astaxanthin's effects across diverse disease phenotypes	20

management.[23] From randomized controlled trials meticulously crafted to elucidate causality to observational studies offering glimpses into real-world effectiveness, each study design contributes to the evolving narrative of astaxanthin's therapeutic potential. Moreover, meta-analyses serve as compasses, guiding the trajectory of evidence synthesis and informing clinical decision-making amidst the sea of uncertainty.[24] At the heart of clinical inquiry lie outcome measures, each offering a window into the realm of patient experience and disease progression.[25] From the subjective realms of pain assessment, as measured by visual analog scales and numeric rating scales, to the objective domains of joint function, as quantified by the Western Ontario and McMaster Universities Osteoarthritis Index, each measure serves as a touchstone for evaluating astaxanthin's impact on KOA-related symptoms and functional outcomes.[26] Within the annals of clinical inquiry, astaxanthin emerges as a harbinger of hope, offering respite from the burdens of disease and the promise of a brighter tomorrow.[26] Across diverse study populations and intervention regimens, astaxanthin supplementation consistently demonstrates significant improvements in pain relief, joint function, and quality of life among KOA patients.[26] Furthermore, biomarker analyses unveil a landscape adorned with signs of healing, as astaxanthin supplementation mitigates inflammatory markers and preserves cartilage integrity, offering a glimmer of hope amidst the shadows of disease progression.[27] As the saga of astaxanthin's therapeutic potential continues to unfold, each chapter offers a glimpse into the transformative power of this natural compound in the realm of KOA management. Yet, amidst the triumphs lie untrodden paths of exploration, beckoning researchers to delve deeper into the intricacies of astaxanthin's mechanisms and optimize its therapeutic potential for the betterment of those afflicted by knee osteoarthritis.[27] See Table 3 as a summary of clinical trials on astaxanthin for KOA.

Comparative analysis with existing treatments

Astaxanthin presents an auspicious alternative in the management of KOA when compared to conventional treatments like nonsteroidal anti-inflammatory drugs (NSAIDs) and corticosteroids.[23] While NSAIDs are widely used for their rapid relief from pain and inflammation, they often come with noteworthy long-term side effects, such as gastrointestinal issues, cardiovascular risks, and kidney damage. Corticosteroids, on the other hand, provide effective short-term relief but can lead to joint degradation and systemic complications when used frequently. In contrast, astaxanthin, a natural antioxidant, offers a safer profile with its potent anti-inflammatory and cartilage-protective effects, without the adverse effects typically associated with synthetic drugs.[19] As a therapeutic agent that addresses the root cause of inflammation, rather than just masking the symptoms, astaxanthin's ability to neutralize RO and inhibit key inflammatory pathways like NF-κB positions it. Unlike corticosteroids, which can accelerate cartilage breakdown over time, astaxanthin promotes cartilage regeneration by stimulating collagen production and inhibiting matrix metalloproteinases. This dual action of reducing inflammation and protecting cartilage makes astaxanthin not just a symptom-reliever, but a potential disease-modifying agent in KOA management.[28] Furthermore, while NSAIDs provide temporary relief, they do not halt the progression of osteoarthritis. Astaxanthin's antioxidative properties help in slowing the degradation process, potentially leading to better long-term joint health. Its natural origin also makes it a more appealing option for patients seeking alternatives to synthetic drugs with fewer side effects.[29] Thus, in the landscape of KOA treatment, astaxanthin stands out for its holistic approach to managing both the symptoms and underlying pathology of the disease, offering a safer and potentially more effective long-term solution compared to traditional treatments.

Safety profile and adverse effects of astaxanthin

In harnessing astaxanthin's therapeutic potential for KOA management, ensuring its safety profile is paramount.[30] Both preclinical and clinical investigations have shed light on the safety considerations surrounding astaxanthin supplementation, offering valuable insights into its tolerability and potential adverse effects. Preclinical studies serve as foundational pillars in the assessment of astaxanthin's safety profile, providing a preliminary glimpse into its tolerability and toxicity in animal models.[31] These studies have yielded reassuring findings, indicating that astaxanthin is usually well-tolerated at therapeutic dosages, with no significant toxic effects reported.[32] Animal models have exhibited minimal adverse effects following astaxanthin supplementation, further bolstering confidence in its safety for potential clinical use. Furthermore, long-term toxicity studies have failed to unveil any discernible adverse outcomes, reaffirming the benign nature of astaxanthin supplementation in animal subjects.[32]

Transitioning from the controlled confines of preclinical investigations to the dynamic landscape of clinical trials, the safety profile of astaxanthin

Table 3 Summary of clinical trials on astaxanthin for knee osteoarthritis

Study design	Sample size	Dosage and duration	Outcome measures	Key findings	References
Randomized controlled trial	100 patients	12 mg/day for 6 months	Pain scores, joint function, quality of life	Significant reduction in pain, improved joint function, and quality of life	23, 24
Double-blind, placebo-controlled trial	80 patients	8 mg/day for 3 months	Pain scores, inflammatory markers	Decreased pain and inflammatory markers compared to placebo	24
Open-label study	50 patients	16 mg/day for 12 weeks	Pain scores, cartilage thickness	Reduction in pain, preservation of cartilage thickness	25,26

continues to shine brightly. Clinical trials exploring the safety of astaxanthin supplementation in KOA patients have reported a paucity of adverse effects, underscoring its favorable tolerability profile.[33] Among the few adverse effects reported, mild gastrointestinal symptoms such as nausea and diarrhea feature prominently, albeit transient in nature and typically resolving with continued supplementation.[33] Furthermore, anecdotal reports of temporary changes in skin pigmentation have surfaced, although these effects are considered benign and reversible upon discontinuation of astaxanthin supplementation.[33] Overall, clinical studies have painted a reassuring picture of astaxanthin's safety, suggesting that it is well-tolerated by most individuals, even at relatively high doses.[34]

While astaxanthin's safety profile appears commendable, prudent consideration of potential interactions and contraindications is warranted. Astaxanthin's purported antiplatelet effects raise concerns regarding potential interactions with certain medications, particularly anticoagulants and antiplatelet agents.[35] As such, individuals concurrently using these medications should exercise caution and seek guidance from healthcare professionals before embarking on astaxanthin supplementation. Moreover, individuals with known allergies to astaxanthin or related compounds should approach supplementation with caution to mitigate the risk of allergic reactions. While astaxanthin holds promise as a safe and efficacious therapeutic adjunct for KOA management, judicious evaluation of individual medical histories and medication regimens is imperative to ensure optimal safety and efficacy outcomes. Preclinical and clinical studies have shown that astaxanthin is generally well-tolerated, with minimal adverse effects such as mild gastrointestinal symptoms and temporary skin pigmentation changes.[36] However, individuals on anticoagulant medications or those with specific allergies should consult healthcare professionals before using astaxanthin to avoid potential interactions and ensure safety (see Table 4 for a summary).

Table 4 Safety profile of astaxanthin supplementation in knee osteoarthritis

Adverse Effects	Frequency	Severity	Management	References
Gastrointestinal symptoms (e.g., nausea, diarrhea)	Common	Mild	Usually transient; resolves with continued supplementation	28,29
Skin pigmentation changes	Rare	Gentle	Reversible upon discontinuation of supplementation	32,33
Allergic reactions	Rare	Variable	Avoid supplementation in individuals with known allergies	30,36

Future research directions and research gaps

As the horizon of astaxanthin research expands, navigating the uncharted territories of future investigations holds the promise of unlocking new frontiers in KOA management.[36] Within this landscape, several critical avenues beckon researchers to delve deeper, bridging existing knowledge gaps and charting a course toward enhanced clinical efficacy and patient outcomes. The journey to perfecting astaxanthin therapy for KOA hinges on discovering the optimal dosing regimens. This quest is akin to solving a complex puzzle, where each piece represents a different aspect of treatment. Researchers are on a mission to understand how various doses of astaxanthin interact with different patient characteristics, such as age, the severity of the disease, and the length of treatment.[37] Imagine this process as a detailed exploration. Scientists need to map out the relationships between dose and response, meticulously examining how astaxanthin works in diverse scenarios. They aim to uncover the ideal amounts and frequencies of administration that offer the best therapeutic results while minimizing any potential side effects. Consider a patient with KOA—perhaps an elderly person with advanced disease or a younger individual in the early stages. Each of these patients might require a different approach to astaxanthin therapy. By conducting thorough research and trials, scientists can determine the specific dosing thresholds that are most effective for each type of patient. This way, they can craft personalized treatment plans that cater to individual needs, much like a tailor customizes a suit to fit perfectly.[38] The ultimate goal of this research is to create a roadmap for astaxanthin dosing that doctors can follow, ensuring that each patient receives a treatment plan that is both safe and highly effective. This personalized approach promises not only to alleviate symptoms more efficiently but also to enhance the overall quality of life for that battling knee osteoarthritis. Through dedicated research and careful consideration of various patient factors, the future of astaxanthin therapy looks bright, offering hope for a more precise and effective management of KOA.[38]

While we've seen some promising glimpses of astaxanthin's potential benefits in short-term clinical trials, there's a vast horizon of inquiry awaiting exploration, particularly concerning its long-term effects and potential for modifying the progression of KOA. To truly understand the impact of astaxanthin over time, researchers are calling for prospective longitudinal studies that track patients for extended durations. These studies would help ascertain whether astaxanthin supplementation can sustainably halt the progression of KOA and maintain the integrity of the joints.[38] Researchers carefully observe how astaxanthin affects patients' health over time. By scrutinizing structural outcomes such as changes in cartilage thickness and narrowing of the joint space, scientists aim to uncover whether astaxanthin has the potential to change the natural course of KOA. This isn't just about relieving symptoms; it's about finding

Table 5 Future research directions for astaxanthin in knee osteoarthritis (KOA)

Research direction	Description
Optimization of dosing regimens	Explore dose-response relationships and optimal treatment durations to establish effective and sustainable dosing strategies for long-term KOA management.
Exploration of long-term effects and disease modification	Conduct longitudinal studies to assess the sustained efficacy of astaxanthin in modifying disease progression, joint integrity, and structural outcomes in KOA patients over extended treatment periods.
Investigation of combination therapies	Investigate synergistic effects of astaxanthin with conventional therapies and natural compounds in combination therapy approaches to enhance treatment outcomes and address multiple pathophysiological pathways in KOA.
Exploration of mechanistic insights	Utilize advanced molecular techniques to elucidate the molecular pathways modulated by astaxanthin in KOA, providing deeper mechanistic insights and identifying potential therapeutic targets.
Assessment of patient stratification and personalized medicine	Investigate patient stratification strategies based on clinical characteristics, biomarkers, and genetic profiles to personalize astaxanthin supplementation in KOA management and optimize treatment outcomes through personalized medicine approaches.

treatments that could fundamentally alter the trajectory of the disease itself. Instead of just managing symptoms, they could have access to therapies that slow down or even stop the progression of the disease, preserving joint function and quality of life for years to come. It's a vision of hope—an aspiration for disease-modifying interventions that could revolutionize the way we approach osteoarthritic degeneration. But to reach this goal, we need dedicated research—studies that delve deep into the long-term effects of astaxanthin and its potential to transform the lives of KOA patients. These studies hold the promise of unlocking new avenues of treatment, offering a glimmer of hope in the ongoing battle against osteoarthritis.[38]

The potential synergy between astaxanthin and conventional therapies in managing KOA opens up a rich landscape for further investigation. Researchers are eager to delve into the realm of combination therapies, where astaxanthin could be paired with established treatments like NSAIDs, pain relievers, and physical therapy. By studying how these treatments work together, scientists hope to uncover new ways to improve outcomes for KOA patients. But the exploration doesn't stop there.[39] Researchers also want to explore multimodal approaches, which involve combining astaxanthin with other natural compounds that have complementary effects. These compounds might have different ways of targeting the symptoms and causes of KOA, and when combined with astaxanthin, they could enhance treatment efficacy while reducing side effects. By combining the strengths of traditional treatments with the potential of astaxanthin and other natural compounds, they aim to create a more holistic approach to care. This integrative approach could offer patients a wider range of treatment options and ultimately lead to better outcomes and improved quality of life for those living with KOA. Beyond its promising therapeutic potential, astaxanthin holds secrets within its molecular structure that scientists are eager to uncover. Imagine diving into a mysterious labyrinth beneath the surface, where each pathway leads to a deeper understanding of how astaxanthin works. In the future, researchers plan to embark on a journey of discovery, using advanced molecular techniques like transcriptomics, proteomics, and metabolomics to decode the intricate mechanisms behind astaxanthin's effects in KOA. This exploration as a scientific endeavor, where researchers employ sophisticated tools to elucidate the intricate molecular pathways traversed by astaxanthin within the body. As they unravel these molecular mysteries, they hope to find new targets for treatment—like unlocking secret doors in a maze, revealing pathways to better care for KOA patients. This journey into the molecular world of astaxanthin isn't just about understanding how it works; it's about opening doors to precision medicine, where treatments are tailored to each individual's unique needs.[40]

In the era of precision medicine, the quest for tailored therapeutic strategies represents a beacon of hope in optimizing treatment outcomes for KOA.[26] Looking ahead, future research endeavors are poised to embark on a multifaceted journey of patient stratification. This intricate process involves the integration of diverse parameters, including clinical phenotypes, biomarkers, and genetic profiles, to categorize individuals into distinct subgroups. By adopting such a multidimensional approach, researchers aim to gain deeper insights into the heterogeneous nature of KOA and its varied treatment responses across different patient cohorts. This endeavor holds promise for unraveling the underlying mechanisms driving divergent disease trajectories and treatment outcomes. Moreover, it presents an opportunity to identify prognostic biomarkers that serve as reliable indicators of both treatment efficacy and disease progression.[41] Through meticulous patient stratification, researchers envision a paradigm

shift towards personalized medicine in KOA management. By tailoring astaxanthin supplementation to the unique profiles of individual patients, clinicians can optimize treatment efficacy while minimizing the risk of adverse effects.[42] This personalized approach not only enhances therapeutic precision but also fosters a more patient-centric model of care, wherein interventions are finely tuned to address the specific needs and characteristics of each individual. In essence, the pursuit of tailored therapeutic approaches in KOA heralds a new era of precision medicine, wherein the convergence of clinical insights, molecular biomarkers, and genetic profiling empowers clinicians to deliver customized care that is both effective and personalized.[43] Future research in astaxanthin therapy for KOA should focus on optimizing dosing regimens, exploring long-term effects, investigating combination therapies, delving into mechanistic insights, and assessing patient stratification for personalized medicine.[44] By addressing these research gaps, it can be paved the way for more effective, personalized treatments that improve outcomes and quality of life for KOA patients, marking a significant stride towards precision medicine in KOA management (see Table 5 for summary). These future research directions aim to address key knowledge gaps and advance our understanding of astaxanthin's role in knee osteoarthritis management, paving the way for improved treatment strategies and better outcomes for affected individuals.

Discussion

Astaxanthin has gathered significant attention as a therapeutic candidate for KOA, given its unique ability to address multiple aspects of the disease's pathophysiology. This review emphasizes the compound's antioxidative, anti-inflammatory, and also cartilage-protective mechanisms, which composed offer a comprehensive approach to managing KOA. By neutralizing oxidative stress, a known driver of cartilage degradation, and inhibiting pathways responsible for inflammation, astaxanthin not only alleviates symptoms but also shows potential for varying disease progression. Moreover, its role in promoting cartilage synthesis positions it as more than a symptomatic treatment, setting it apart from conventional opportunities. When compared to usually used therapies such as NSAIDs and corticosteroids, astaxanthin presents distinct advantages. These conventional treatments often target immediate symptom relief, yet their long-term use is flawed by side effects including gastrointestinal issues and also accelerated cartilage breakdown. Astaxanthin's natural origin and also minimal side effect profile make it a practical alternative or adjunct, especially for patients looking for sustainable and holistic options. While the findings are promising, several research gaps must be talked to fully harness astaxanthin's potential. Current studies are limited in duration, leaving questions about its long-term efficacy and also safety unanswered. Additionally, inconsistencies in dosing protocols across studies complicate the growth of standardized treatment guidelines. The potential for synergistic effects when shared with other therapies remains largely unexplored, representing a missed opportunity to improve treatment outcomes. Lastly, the lack of stratified studies considering patient-specific factors, such as age or genetic predisposition, underscores the need for personalized approaches to maximize efficacy. The combination of astaxanthin into clinical practice could mark a paradigm shift in KOA management. Future research must aim to fill these gaps by conducting long-term, well-designed studies that explore optimal dosing, combination therapies, and also personalized treatment strategies. This would not only solidify astaxanthin's position as a therapeutic option but also improve outcomes for patients living with this incapacitating condition.

Limitations

This review is limited by its reliance on published data, which may introduce bias due to the selective reporting of positive outcomes. Additionally, including studies with diverse methodologies and varying quality poses challenges to drawing definitive conclusions. Future reviews should incorporate more standardized and comprehensive criteria to address these limitations.

Conclusion

Astaxanthin presents a compelling prospect as a therapeutic intervention for KOA, due to its potent antioxidative and anti-inflammatory properties. Future research endeavors should prioritize refining dosing strategies, elucidating long-term effects, and also uncovering the underlying mechanisms of astaxanthin's action in KOA management. Such investigations hold the potential to inform the development of personalized treatment modalities personalized to the individual needs of KOA patients, thereby enhancing clinical outcomes and quality of life. Astaxanthin's auspicious safety profile, coupled with its demonstrated efficacy in preclinical and clinical studies, underscores its role as a promising adjunctive therapy in the comprehensive management of KOA.

Acknowledgments

None

Author contributions

Conception or design of the work; or the acquisition, analysis, or interpretation of data for the work: AHMMR. *Drafting the work or reviewing it critically for important intellectual content:* AHMMR, SS, AHB. *Final approval of the version to be published:* AHMMR, SS. *Accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved:* AHMMR, SS, AHB.

Conflict of interest

We do not have any conflict of interest.

Data availability statement

We confirm that the data supporting the findings of the study will be shared upon reasonable request.

Supplementary file

None

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Bangabandhu Sheikh Mujib Medical University Journal 2025;18(1):e76604
ISSN 2074-2908 | eISSN 2224-7750 |

RESEARCH ARTICLE

Effectiveness of lateral femoral cutaneous and femoral nerve block in managing postoperative pain for hemiarthroplasty patients

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Abstract

Background: The fascia iliaca compartment block is commonly used for postoperative analgesia after hemiarthroplasty. However, the method often fails to adequately manage pain due to frequent sparing of the lateral femoral cutaneous nerve. This randomised controlled study was conducted to compare the efficacy of lateral femoral cutaneous and femoral nerve blocks compared to fascia iliaca compartment block for postoperative pain management following hemiarthroplasty.

Methods: Sixty patients were randomly assigned to either the fascia iliaca compartment (FIC) block group or the lateral femoral cutaneous nerve and femoral nerve (LFCN plus FN) block group. All patients received a subarachnoid block for surgery. Pain was assessed using a visual analogue scale (VAS) in the recovery room. When patients reported VAS score 3 or 4, the FIC and LFCN plus FN blocks were performed according to group allocation. VAS scores were reassessed 20 minutes after the blocks and recorded. Subsequently, the pain was assessed using VAS at two-hour intervals until the patients required rescue analgesia.

Results: The VAS scores differed significantly between the two groups. In the LFCN plus FN block group, 13.3% reported VAS 0, 30% reported VAS 1, and the rest reported VAS 2. In the FIC block group, 53.3% reported VAS 2, and 46.7% reported VAS 3. None reported VAS 0 in the FIC group. The average time to demand rescue analgesia was 4.9 (0.8) hours in the FIC group and 9.4 (1.5) hours in the LFCN plus FN group. Adjusted time based on age, sex, body mass index, and Anesthesiologists class for the FIC block group was 6.8 (0.9) hours, while the LFCN plus FN block group recorded 7.5 (0.8) hours (P=0.003).

Conclusion: Administering the LFCN and FN block separately but simultaneously provides better postoperative analgesia than the conventional FIC block following hemiarthroplasty.

Key message

Elderly patients undergoing hemiarthroplasty are particularly vulnerable to opioid side effects. Nerve blocks targeting the lateral femoral cutaneous and femoral nerves provide extended pain relief, reducing the need for rescue analgesics. Continuous nerve block techniques can eliminate opioids, resulting in faster recovery, fewer side effects, and lower healthcare costs.

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Publication history
Received: 2 Oct 2024
Accepted: 7 Jan 2025
Published online: 10 Feb 2025

Responsible editor
M Mostafa Zaman
0000-0002-1736-1342

Reviewers
C: Anonymous
E: Krishna Priya Das
0000-0002-4963-4018

Keywords
fascia iliaca compartment block, lateral femoral cutaneous nerve block, femoral nerve block, hemiarthroplasty, postoperative analgesia

Funding
Funded by Bangabandhu Sheikh Mujib Medical University, Memo number BSMMU/2023/13314(63)

Ethical approval
IRB of Bangabandhu Sheikh Mujib Medical University (No. BSMMU/2023/6687, dated 6 May 2023)

Trial registration number
None

Introduction

Optimal postoperative pain management is imperative for facilitating a prompt recovery after surgery. Hemiarthroplasty is a surgical procedure commonly practised in orthopaedics, involving the replacement of one-half of the hip joint with a prosthesis. The significance of effective pain management following this surgery cannot be overstated. Inadequate pain control has been correlated with prolonged immobilisation, which in turn can lead to disruptions in the rehabilitation process and delays in regaining the ability to walk unaided. These setbacks may heighten the risk of thromboembolic complications, compromise functional recovery, and ultimately extend the patient's hospital stay [1]. Therefore, ensuring optimal pain management is crucial in promoting successful outcomes and minimising postoperative complications in hemiarthroplasty patients.

Hip fracture is a condition that predominantly affects older adults. Managing pain in these patients presents significant challenges due to the high prevalence of polypharmacy and consequential drug interactions within this population [2]. In addition, insufficient pain control can exacerbate comorbidities such as airway disease and cognitive impairment [3]. Hemiarthroplasty is performed under spinal anaesthesia. Surgical approaches may be anterior, lateral, or posterior. Most surgeons prefer the lateral approach due to its convenience and fewer complications. Following hemiarthroplasty, it is common practice to manage postoperative pain using opioid analgesics and adjuvants. However, it is essential to note that opioids have a range of adverse effects. These include nausea, vomiting, constipation, sedation, dizziness, life-threatening respiratory depression, withdrawal symptoms, hypotension, an increased risk of seizures, sweating, dysphoria, and euphoric mood. Additionally, opioids may lead to cardiovascular events, such as tachycardia, bradycardia, and palpitations. Cutaneous reactions may manifest as pruritus, urticaria, and rash [4]. Opioids also affect long-term outcomes and influence the entire lives of patients, like potentially developing opioid dependence or opioid-induced hyperalgesia [5].For these reasons, the use of opioids is reduced by peripheral nerve blocks, and opioids are reserved for rescue analgesia. Fascia iliaca compartment (FIC) block or femoral nerve block is commonly performed for postoperative pain management in hemiarthroplasty patients. However, the study shows that none of these can adequately manage postoperative pain after hemiarthroplasty.

As the name suggests, the FIC block is a fascial plane block. Following local anaesthetic administration, drugs must diffuse to reach the femoral nerve (FN) and lateral femoral cutaneous nerve (LFCN). These two nerves run behind the fascia iliaca and are located together in the fascia iliacus space [6]. FIC block often results in inadequate blockade of the LFCN [7]. Dolan J *et al.* showed the success rate of ultrasound-guided fascia FIC block is 87% [8]. For lateral approach hemiarthroplasty, a surgical incision is made in the lateral thigh. The LFCN of the thigh supplies this area. So, a significant amount of postoperative pain originates from this site. There is a substantial variation in sensory coverage among individuals because of the highly variable course of the LFCN and branches [9]. That's why the FIC block couldn't consistently block the lateral LFCN of the thigh. Blocking the LFCN and FN separately with real-time ultrasound guidance may offer better pain management after hemiarthroplasty. So, this randomised control trial was designed to compare the efficacy and time to demand rescue analgesia between FIC block versus individual femoral cutaneous nerve block and FN block following hemiarthroplasty surgery.

Methods

This was a randomised control trial approved by the Institutional Review Board (IRB) of Bangabandhu Sheikh Mujib Medical University (BSMMU) under protocol memo no. BSMMU/2023/6687, dated 6 May 2023. The study was conducted at the orthopaedic surgery operation theatre and postoperative ward of BSMMU. Sixty patients scheduled for hemiarthroplasty at BSMMU from May 2023 to May 2024 were recruited. The eligibility criteria included patients' age >50 years, body mass index <30 kg/m^2 and American Society of Anesthesiologists (ASA) physical status I to II. Exclusion criteria were bilateral surgery, revision hemiarthroplasty, uncooperative patient, inability to communicate, neurological deficits involving the lower extremities, significant psychiatric or mental disorders, history of drug allergies, clinically significant coagulopathy, infection at the injection site, allergy to local anaesthetics, diabetic or other neuropathies and inability to comprehend visual analogue score (VAS). Patients were randomly allocated into two groups using a computer-generated random number table method. Group information was sealed in an envelope, numbered, and used sequentially. Randomisation was conducted by one of the research team members in the pre-anaesthetic assessment room who was not involved in the block procedure and evaluation. Each group comprises thirty participants - one group received the ultrasound-guided FIC block (FIC block group), and another group received the ultrasound-guided individual LFCN and FN block (LFCN plus FN block group). Demographic and clinical data, including age, weight, height, BMI, and ASA physical status, were recorded for all patients.

Ethical consideration

The study's objectives, procedure, risks, and benefits were explained to the patients in an easily understandable local language. All participating subjects were assured that they had the full right to withdraw from the study at any time for any reason, and their refusal to participate or withdraw from the project would not hamper their treatment. They were also assured that all data would be kept confidential and not disclosed except for the study.

Intraoperative anaesthesia and analgesia management

A subarachnoid block was administered to all patients for surgical anaesthesia. The surgeon did hemiarthroplasty in the lateral approach. After the surgery, 1 gm of intravenous paracetamol and 5 mg of

intravenous dexamethasone were administered as part of multimodal analgesia, and the patient was transferred to the recovery room.

Visual analogue scale assessment

In the recovery room patients were asked to mark a point on a 10 cm line to record their VAS score. This line shows a range from "no pain" on the left (0 cm) to the "worst pain" on the right (10 cm). Measurements from the starting point (left end) of the scale to the patients' marks are recorded in centimetres and are interpreted as their pain [10]. The patient's pain was assessed at an interval of 15 minutes using a visual VAS. When the VAS score reached 3 or 4, according to group allocation, FIC block was administered in the control group; on the other hand, LFCN and FN block were administered in the study group using ultrasound guidance. Both procedures were done by the same anesthesiologist who has three years of experience in doing ultrasound-guided nerve blocks. Data was recorded by the three resident doctors trained before the study to assess the VAS. Data collectors were blinded regarding the group allocation.

Fascia iliaca compartment block

The patient was placed supine, and the skin was disinfected. Then, the transducer was positioned to identify the femoral artery, the iliopsoas muscle, and the fascia iliaca. The transducer was moved laterally until the sartorius muscle was identified. Local skin infiltration was done with 1% lignocaine. Then the needle was inserted in-plane. As the needle pierces the fascia, a "pop" was felt. After negative aspiration, 1–2 mL of local anaesthetic was injected to confirm the proper injection plane between the fascia and the iliopsoas muscle 30 mL of 0.5% bupivacaine was injected [6].

Lateral femoral cutaneous nerve block

Block of the LFCN was performed with the patient in the supine position. At first, the anterior superior iliac spine (ASIS) was palpated, and the transducer was positioned at two cm inferior and medial to the ASIS parallel to the inguinal ligament. The tensor fasciae latae muscle (TFLM) and sartorius muscle (SaM) were then identified. The nerve appeared as a small hypoechoic oval structure with a hyperechoic rim between the TFLM and SaM in a short-axis view. After local skin infiltration with 1% lignocaine, a 10 cm block needle was inserted in-plane in a lateral-to-medial orientation through the subcutaneous tissue, and 5 mL of 0.5% bupivacaine was injected [6].

Femoral nerve block

With the patient supine, the skin over the femoral crease was disinfected, and the transducer was positioned to identify the femoral artery and nerve. Once the femoral nerve is identified, the skin weal of local anaesthetic is made 1 cm away from the lateral edge of the transducer. The needle is inserted in-plane in a lateral-to-medial orientation and advanced toward the femoral nerve. Once the needle tip was adjacent, after careful aspiration 1–2 mL of local anaesthetic was injected to confirm the proper needle placement. After confirmation, 15 mL of 0.5% bupivacaine was injected [6].

Outcome variables

After twenty minutes of performing the block, the VAS score was assessed and recorded in both groups. This was the primary outcome variable. In addition, patients' motor function was evaluated using the Bromage scale for any weakness. Subsequently, the VAS was assessed at a two-hour interval until patients demanded rescue analgesia. The VAS score at the time of requesting rescue analgesia and the total duration from 20 minutes after the block placement to rescue analgesia were recorded. These were the secondary outcomes. Twenty-five micrograms of fentanyl were then promptly administered as rescue analgesia.

Statistical analysis

Data analysis was performed using the Statistical Package for Social Sciences version 26.0 for Windows. The categorical variables (age group, sex, ASA class and time to demand rescue analgesia) are presented as number percentages, while numerical variables (e.g. BMI) are expressed as mean and standard deviation. The comparison was performed using the Chi-square test for categorical variables and the unpaired *t* test mean for continuous variables. Time to rescue analgesia was subjected to a linear regression procedure to obtain the adjusted values for variation in age, sex, BMI and ASA class. A *P* value of less than 0.05 was considered statistically significant.

Results

A total of sixty patients were analysed in the study. Thirty patients were in the control group (FIC block group) and thirty patients in the study group (LFCN plus FN block group). Most patients in both groups were female and elderly (over 60 years) [11]. The (standard deviation) BMI was 26.1 (2.5) for patients receiving the fascia iliaca block and 25.1 (3.6) for those receiving the LFCN plus FN block (Table 1). In the FIC block group, 40% of patients were ASA class 1, whereas 60% were ASA class 2. Whether in the LFCN plus FN block group, 70% were in ASA class 1, and 30% were in ASA class 2 .

After the block was given in the recovery room, 13.3% of patients in the LFCN plus FN block group reported a VAS score of 0, 30% reported a VAS score of 1, and the rest reported a VAS score of 2. On the other hand, in the FIC block group, 53.3% reported a VAS

Table 1 Distribution of the participants according to demographic and clinical variables

Variables	Study group (n=30)	Control group (n=30)	*P*
Age years, mean (SD[a])	64.3 (11.4)	65.6 (16.4)	0.13
<60	7 (23.3)	9 (30.0)	0.56
≥60	23 (76.7)	21 (70.0)	
Sex			
Male	11(37.0)	8 (27.0)	0.21
Female	19 (63.0)	22 (77.0)	
Body mass index, mean (SD[a])	25.1(3.6)	26.1(2.5)	0.24
ASA[b] class			
ASA class 1	21 (70.0)	12 (40.0)	0.02
ASA class 2	9 (30.0)	18 (60.0)	

[a]SD indicates standard deviation; [b]American Society of Anesthesiologists; Values are number (%) unless indicated otherwise

Table 2 Distribution of the participants according to the visual analogue scale (VAS) score after 20 minutes of block in the study and control group

Variables	Study group (n=30)	Control group (n=30)	*P*
VAS, number (%)			
0	4 (13.3)	0 (-)	0.001
1	9 (30.0)	0 (-)	
2	17 (56.7)	16 (53.3)	
3	0 (-)	14 (46.7)	
Time to rescue analgesia			
Crude mean (SD)[a]	9.4 (1.5)	4.9 (0.8)	0.001
Adjusted[b] mean (SD)[a]	7.5 (0.8)	6.8 (0.9)	0.003

[a]SD indicates standard deviation; [b]Time to rescue analgesia was adjusted according to age, sex, body mass index, and American Society of Anesthesiologist class

score of 2, and 46.7% of patients reported a VAS score of 3. The *P* for these comparisons was 0.001, indicating a significant difference in VAS scores between the two groups following blocks . The average time to demand rescue analgesia in the FIC block group was 4.9 (0.8) hours, and in the LFCN plus FN block group was 9.4 (1.5) hours (*P*=0.001) (Table 2). The adjusted time to demand rescue analgesia for the FIC block group was 6.8 (0.9) hours, and in the LFCN plus FN block group was 7.5 (0.8) hours (*P*=0.003). There was no motor weakness after the block in any group.

Discussion

Our study found that the time to patients' demand for rescue analgesia is longer in the case of individual lateral femoral cutaneous nerve and femoral nerve block. A study done by Wojciech Gola *et al.* showed that patients in the FIC block group needed the first rescue opioid dose an average of 4.5 (1.0) hour after the surgery. Our study results match this finding [12].

Due to anatomical variations of the LFCN, the FIC block often remains inadequate for postoperative analgesia. A study done by Shariat *et al.* reported no significant difference in postoperative pain score and 24-hour opioid consumption between FIC versus placebo in total hip arthroplasty [13]. In their study, only two patients out of sixteen had successful blocks for both femoral and lateral femoral cutaneous nerve following FIC, and the overall success rates of femoral nerve and LFCN block were 38% and 31%, respectively.

Helayel PE *et al.* reported that the adequate volumes of local anaesthetics in the FIC block capable of producing a block in 99% of cases were 37.3 mL [14]. A human cadaver pilot study done by Vermeylen K *et al.* in 2018 suggests that the volume of 40 mL is the effective volume to reach the femoral and lateral femoral cutaneous nerve [15]. Using 40 ml of local anaesthetic Bang S. *et al.* showed with and showed a significant opioid-sparing effect in the first 24 hours of hemiarthroplasty [16]. Though their study didn't report any case of local anaesthetic systemic toxicity (LAST), this large volume may cause systemic toxicity. LAST is a rare but life-threatening complication of fascia iliaca compartment blocks. Most instances of toxicity are related to inadvertent intravascular administration of local anaesthetics. Following systemic absorption, bupivacaine binds avidly to voltage-gated sodium channels of cardiac muscle, leading to conduction abnormalities, contractile dysfunction, and ventricular arrhythmias [17]. Therefore, by increasing the volume of local anaesthetics, adequate analgesia can be ensured at the risk of local anaesthetic systemic toxicity.

On the contrary, we showed that only 20 ml volume is sufficient for applying separate LFCN and FN blocks with the benefit of prolonged analgesia following hemiarthroplasty.

Most of the patients who came for hemiarthroplasty were elderly people. These groups of patients remain at risk for postoperative cognitive dysfunction [18]. Opioids are associated with increased cognitive dysfunction. As the FIC block group demanded rescue analgesia early in comparison to the study group, they may require more opioids for subsequent pain control in comparison to our study group.

Our study had some limitations. We could not show the actual number of patients screened for eligibility criteria. Another limitation is resource constraints, and we could not use a continuous catheter technique for FN and LFCN blocks. However, we believe that implementing the continuous catheter technique could potentially result in opioid sparing for postoperative pain management, leading to early recovery, decreased hospital stays, and overall cost following hemiarthroplasty.

Conclusion

Separate blocks for the LFCN and FN have been found to offer more effective postoperative pain relief than the FIC block in patients undergoing hemiarthroplasty.

Acknowledgments

We sincerely thank all study participants and the MD (Doctor of Medicine) residents of Anaesthesiology for their invaluable contributions to collecting the data.

Author contributions

Conception or design of the work; or the acquisition, analysis, or interpretation of data for the work: KMA, SS. *Drafting the work or reviewing it critically for important intellectual content:* KMA, SS, MAH, AS, CSK, AKM . *Final approval of the version to be published:* KMA, SS, MAH, AS, CSK, AKM. *Accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved:* AKMA.

Conflict of interest

We do not have any conflict of interest.

Data availability statement

We confirm that the data supporting the findings of the study will be shared upon reasonable request.

Supplementary file

None

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Bangabandhu Sheikh Mujib Medical University Journal 2025;18(1):e78898
ISSN 2074-2908 | eISSN 2224-7750 |

RESEARCH ARTICLE

Depression, anxiety and stress assessment in women with polycystic ovary syndrome attending a tertiary care hospital in Bangladesh

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Publication history
Received: 31 Dec 2024
Accepted: 16 Feb 2025
Published online: 25 Feb 2025
Handling editor
Tahniyah Haq
0000-0002-0863-0619
Reviewer
A: Masuda Mohsena
0000-0002-4963-8799
B: Hurjahan Banu
0000-0002-8115-1761

Keywords
depression, anxiety, stress, PCOS
Funding
The Ministry of Science and Technology provided financial support for the study (Memo no: 39.00.0000.009.94.019.29-745; grant number: 539 MS, dated 15 Dec 2021)
Ethical approval
Approved by IRB of Bangabandhu Sheikh Mujib Medical University (Reference number BSMMU/2022/742, dated 24 Jan 2022)
Trail registration number
Not applicable

Abstract

Background: This study evaluated depression, anxiety, and stress in women with polycystic ovary syndrome (PCOS) using the depression, anxiety, and stress scale-21 (DASS-21) and examined their live experiences with this endocrine disorder.

Methods: A mixed-methods study, combining an analytical cross-sectional study and qualitative grounded theory, was conducted from February to June 2022 at Bangabandhu Sheikh Mujib Medical University. The study involved 266 pre-diagnosed women with PCOS. Psychological symptoms were assessed using the DASS-21. Additionally, 10 in-depth patient interviews and 6 key-informant interviews with mothers explored the personal and societal dynamics of PCOS.

Results: The survey revealed significant psychological distress among participants, with 32% as "moderate" for depression, 68% as "extremely severe" for anxiety, and 45% as "severe" for stress. Participants had a mean age of 24.2 years (standard deviation 5.4) and were pre-diagnosed cases of PCOS. Married women had higher odds of anxiety (OR 2.0; 95% CI 1.1–3.2), while menstrual problems predicted both anxiety (OR 2.0; 95% CI 1.0–3.4) and stress (OR 2.0; 95% CI 1.0–3.4). Insomnia significantly predicted anxiety (OR 3.0; 95% CI 1.4–6.2) and stress (OR 2.3; 95% CI 1.1–5.1). Societal stigma compounded these challenges, with unmarried girls concerned about acne and hirsutism, and their mothers focusing on menstrual irregularities and fertility. Married women delayed care-seeking by 2–3 years, driven by infertility concerns, highlighting societal pressures around marriage and childbearing as more significant stressors than PCOS itself.

Conclusion: Women with PCOS face significant mental health challenges which are exacerbated by marital status, insomnia, menstrual issues, and societal stigma. Family support plays a role in coping with the condition.

Key messages

Women with polycystic ovary experience significant psychological distress, with high anxiety, stress, and moderate depression levels. Insomnia, marital status, and menstrual issues are key predictors. The societal stigma surrounding acne, hirsutism, and infertility intensifies the emotional burden and delays healthcare-seeking. Enhancing awareness, reducing stigma, and strengthening mental health support are crucial for improving well-being and timely intervention.

Introduction

Polycystic ovarian syndrome (PCOS) is a multifaceted endocrine condition [1]. While traditionally recognized for its reproductive and metabolic aspects. Recent research highlights its connection with psychological well-being, notably depression and anxiety [2]. With an estimated 8-13% prevalence among reproductive-aged women and a high rate of underdiagnosis, PCOS poses a substantial public health concern [3, 4]. Recent research indicates that women with PCOS are up to six times more [5] likely to experience moderate to severe anxiety and up to four times more [6] likely to exhibit symptoms of depression [7, 8]. In a narrative review conducted in Bangladesh, the prevalence of PCOS ranged from 6.11% (among the subjects visiting the gynecology OPDs) to 92.16% (in subjects consulted for hirsutism) [9], yet research on its psychological effects in this context is limited, especially in tertiary care settings [10]. Understanding these effects is crucial for effective disease management, quality of life improvement, and treatment adherence [11]. This study aimed to highlight the psychosocial aspects of PCOS, helping healthcare providers create interventions for both the physical and emotional needs of affected women.

Methods

Study design, sampling methodology

A mixed-methods study was conducted from February to June 2022 at the Endocrinology and Obstetrics and Gynaecology outpatient departments (OPDs) of Bangabandhu Sheikh Mujib Medical University (BSMMU). The sample size, calculated using the formula $Z^2p(1-p)/d^2$, was based on a 52% prevalence of depression among women with PCOS (Sulaiman et al., 2017). With a 95% confidence level (Z=1.96) and a 5% margin of error, the required sample size was 384. Due to practical constraints, 266 participants were purposively enrolled, achieving 40% statistical power. Grounded theory served as the basis of the qualitative component. Purposive sampling selected participants with diverse perspectives on PCOS. 16 in-depth interviews (IDI) were conducted in Bangla using IDI guidelines, with informed written consent from adolescent girls, their mothers, and women. The sample size was determined by data saturation.

Data collection tool

The severity of depression, anxiety, and stress was measured using a Bangla-validated version of the depression anxiety and stress scale (DASS)-21[12]. Each subscale has 7 items, with participants rating items on a 4-point scale (0–3). Participants rated each item on a 4-point scale reflecting their experiences during the previous week. Scores are normal, mild, moderate, severe, and extremely severe. Depression ranges from 0–9 (normal) to 28+ (extremely severe), anxiety from 0–7 (normal) to 20+ (extremely severe), and stress from 0–14 (normal) to 34+ (extremely severe) [12]. Other questions were translated into Bangla and pre-tested with 10 PCOS patients to ensure clarity and cultural relevance.

Data collection procedure

Participants were recruited from the PCOS clinic at BSMMU. Women aged 18–40 years with PCOS were selected. Those with severe psychiatric conditions, unrelated chronic illnesses, or unwilling to participate were excluded. Two female research officers underwent five-day training. Survey tools were designed in English and translated into Bangla. Respondents were briefed on research objectives and ice-breaking questions. Qualitative interviews, lasting 45–60 minutes, were conducted face-to-face in Bangla and audio recorded. Surveys ensured privacy and confidentiality.

Quantitative statistical analysis

Quantitative statistical analysis involves both descriptive and inferential statistics. Descriptive statistics were used for age and other demographic variables. Depression, anxiety, and stress were quantified using the DAS scale, with mean scores. Logistic regression explored relationships between predictor and dependent variables. The statistical analysis was performed using the SPSS version 25.

Qualitative thematic analysis

For qualitative data analysis, recordings were downloaded and transcribed, with field notes cross-referenced with transcripts. A-priori codes were developed with additional inductive codes generated through repeated transcript review. These codes were further broken down into subcodes, resulting in 15 a-priori codes and 5 themes. Transcripts were organised according to predefined codebooks for data clustering, comparison, and theme identification. Thematic analysis was manually conducted to explore emerging patterns and insights.

Ethical consideration

This study received ethical approval from the Institutional Review Board (IRB) of Bangabandhu Sheikh Mujib Medical University and was conducted following the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants, outlining the study objectives, participation rights, and the option to withdraw at any stage. For participants under 18 years of age, written assent was required, accompanied by informed consent from a parent or legal guardian.

Results

Among the 266 participants, the majority of them were in their mid-twenties. The participants had a nearly equal distribution of married and unmarried individuals. Most resided in urban areas, and most participants attained at least higher secondary education (Table 1).

Psychological impact of PCOS

Quantitative findings

The DASS-21 showed that anxiety was the most prevalent distress among participants, with 68.0% classified as "extremely severe." Stress followed at 44.7% "Severe." Depression was lower, with 23.3% "extremely severe." Table 2.

Table 1 Background characteristics of the respondents (n=266)

Variables	n (%)
Marital status	
Married	134 (50.4)
Unmarried	132 (49.6)
Residence	
Urban	187 (70.3)
Rural	79 (29.7)
Education	
Upto secondary	81 (30.5)
Higher secondary and above	185 (69.5)
Occupation	
Students	128 (48.0)
govt. employee and non-govt. employee	21 (8.0)
Homemakers	117 (44.0)
Number of children of the married respondent (n=134)	
Yes	61 (45.5)
No	73 (54.5)
Menstrual problems (menorrhagia, amenorrhea, and dysmenorrhea)	
Yes	151 (56.8)
No	115 (43.2)
Hirsutism	
Yes	241 (90.6)
No	25 (9.4)
Acne	
Yes	154 (57.9)
No	112 (42.1)
Insomnia	
Yes	200 (75.2)
No	66 (24.8)
Hormonal problems (hyperthyroidism, and hypothyroidism)	
Yes	41 (15.4)
No	225 (84.6)
Increased appetite	
Yes	130 (48.9)
No	136 (51.1)
Infertility	
Yes	50 (18.8)
No	216 (81.2)

Qualitative insights into psychological stress

In-depth interviews revealed the emotional burden of PCOS, with participants expressing sadness, frustration, and hopelessness over their condition's unpredictability. "Why am I not recovering from this disease? I wonder if this disease will ever get better! Or will it get worse? There have been other problems as well. I am always stressed. I find it difficult to stay relaxed" (Unmarried woman, 24 years)

Table 2 Scores of depression, anxiety and stress among participants with polycystic ovarian syndrome (n=266)

Psychological condition	Depression, anxiety and stress 21 scale				
	Normal	Mild	Moderate	Severe	Extremely severe
Depression range	0-9	10–12	13–20	1–27	28–42
Depression n (%)	39 (14.7)	0 (0.0)	86 (32.2)	79 (29.7)	62 (23.3)
Anxiety range	0–7	8–9	10–14	15-19	20–42
Anxiety n (%)	3 (1.1)	5 (1.9)	37 (13.9)	40 (15.0)	181 (68.0)
Stress range	0–14	15–18	19–25	26–33	34–42
Stress n (%)	2 (0.8)	25 (9.4)	107 (40.2)	119 (44.7)	13 (4.9)

Stigma and social support

Experience of stigma

Participants reported stigma related to PCOS. Unmarried girls were especially concerned about appearance, with acne and hirsutism often overshadowing the PCOS diagnosis. Mothers of these unmarried girls, however, were more focused on menstrual irregularities and the potential impact on fertility after marriage. "I came here today because my daughter's periods have been irregular since she started menstruating. She bleeds once every 2 to 3 months. This can be problematic in the future for having children" (Mother of unmarried female, 52 years)

Role of social support

Despite facing stigma, participants also highlighted the importance of social support networks in navigating the challenges of PCOS. Participants expressed gratitude for supportive family members and friends who offered empathy and encouragement throughout their PCOS journey. "My family supports me immensely. They say no matter how long it takes they will bear my treatment cost. Though we have financial issues, my brother and mother have always been very helpful towards me" (Unmarried female, 21 years old)

Psychological burden and societal pressures associated with PCOS

Concerns over body image and marriage

Qualitative interviews further illuminate the emotional and social consequences of PCOS, with participants expressing significant concerns regarding body image and societal expectations. Physical symptoms of PCOS, such as weight gain, acne, and hirsutism, often result in dissatisfaction with appearance, reduced social confidence, and feelings of inadequacy, exacerbated by societal comparisons and stigmatization. "My daughter always feels upset. She doesn't like to go outside because of her physical appearance. She is always irritable and sometimes feels too tired from dealing with all of this" (mother, 48 years old).

PCOS symptoms like facial hair and acne, significantly impact self-esteem, causing internalized stigma and negative self-perceptions. Unmarried participants reported distress over societal beauty standards, fear of marital rejection, and narratives linking PCOS to infertility. "People behave oddly when they see this facial hair, perhaps it is just me who feels odd coming in front of people. People pass remarks on facial hair, and some people may forget these hurtful words, but for me, it is quite difficult to get these words out of my head" (Unmarried female, 19 years)

Fertility related anxiety and marital pressure

In qualitative interviews, participants expressed distress over potential infertility, with irregular menstrual cycles and anovulation contributing to feelings of uncertainty and frustration. Societal pressures to conceive amplify this anxiety, leading to feelings of inadequacy. "Everyone thinks that women with PCOS have difficulty conceiving. One of my

cousins had PCOS, and after marriage, she couldn't conceive. She eventually got divorced because of it" (unmarried female, 18 years old).

"I am trying for a baby, and the doctor said it might take 7 to 8 months. But my in-laws think it's all my fault" (married female, 28 years old).

Quantitative association with psychological distress

Multivariate Logistic regression (Table 3) revealed marriage as a significant predictor of anxiety, with married women showing a twofold increase in anxiety (95% CI 1.1–3.2). Menstrual problems were associated with elevated stress, with affected participants being twice as likely to experience higher stress levels (95% CI 1.0–3.4). Women with insomnia had three times the odds of anxiety (95% CI 1.4–6.3) and over twice the odds of stress (95% CI 1.1–5.1) compared to those without insomnia.

Table 3 Multivariate logistic regression model for the dependent variables' depression, anxiety, and stress (n=266)

Predictor value	Dependent variables		
	Depression Odds ratio (95% CI)[c]	Anxiety Odds ratio (95% CI)[c]	Stress Odds ratio (95% CI)[c]
Marriage	2.2 (1.0–5.3)	2.0 (1.1–3.2) [a]	2.0 (1.0–3.0)
Menstrual problem	1.0 (0.2–1.3)	2.0 (1.0–3.2) [a]	2.0 (1.0–3.4) [a]
Hirsutism	0.4 (0.1–1.5)	2.2 (1.0–7.0)	1.0 (0.2–2.0)
Acne	1.1 (1.0–3.0)	1.0 (0.4–1.3)	1.0 (0.4–2.0)
Insomnia	1.0 (0.3–2.0)	3.0 (1.4–6.2) [b]	2.3 (1.1–5.1) [a]
Hormonal problem	1.1 (0.1–11.0)	1.0 (0.2–3.4)	1.0 (0.2–3.0)
Increased appetite	1.0 (0.3–2.0)	1.3 (1.0–2.3)	1.2 (1.0–2.2)
Infertility	0.3 (0.3–2.0)	0.2 (0.0–1.0) [a]	1.0 (0.2–2.0)

[a]$P<0.05$, [b]$P<0.01$, [c]CI indicates confidence interval

Healthcare experiences and access to treatment

Unmarried participants sought medical help 3 to 5 years after experiencing symptoms. Married individuals sought help when facing conception challenges. Access to healthcare varied due to socioeconomic status, location, and healthcare infrastructure, affecting the availability of PCOS-specific resources and expertise. "I stopped taking tablets between because we have financial problems. I am just a student and my brother is the only earning member. I am now thinking of starting again because my symptoms have reappeared". (Unmarried female, 18 years old).

Most patients were satisfied with the care for depression and anxiety among women with PCOS at a tertiary hospital in Bangladesh. Participants praised the competence, compassion, and attentiveness of healthcare providers.

Family and societal roles in PCOS management

Participants highlighted the importance of understanding and support from loved ones and society, advocating for a stigma-free environment. They emphasised the need for awareness, positive attitudes, and support systems that foster empowerment and well-being, underscoring the transformative impact of acceptance in promoting resilience and holistic management of PCOS. 'I just want to say that every family has to create a positive mind about PCOS. For that they should be informed about the disease and support the woman to overcome the disease' (Married female, 28 years old).

Discussion

This study sheds light on the psychological impact, stigma, and healthcare experiences of women with PCOS at a tertiary hospital in Bangladesh. High levels of anxiety (68% "extremely severe") and stress (45% "severe") were found, with insomnia as a significant predictor. The stigma around acne, hirsutism, and infertility was a dominant stressor, exacerbated by societal expectations. Delays in healthcare-seeking due to financial and social barriers were noted, despite overall satisfaction with care. Family support, while protective, did not fully mitigate psychological distress.

The psychological burden observed, characterized by elevated anxiety and moderate depression, aligns with findings from global research. Talbott *et al.* similarly note higher anxiety levels in PCOS patients compared to depression. Compared to western studies, the higher anxiety levels found in this study suggested that the culture of Bangladesh may amplify anxiety [13, 14].

Stigma was a pervasive issue, with participants expressing shame over symptoms like acne and hirsutism, as seen in studies from the US and India. Stigma worsened psychological distress, highlighting the need for targeted interventions. Family support, crucial for coping, aligns with global studies showing its benefits [15-17].

The association between insomnia and psychological distress aligns with global research linking sleep disturbances to anxiety and stress. The relationship is likely bidirectional, with insomnia predicting anxiety and stress, and psychological distress contributing to sleep disturbances. Participants' concerns about body image and fertility reflect broader issues also found in UK and Australian studies [18, 19].

Regarding healthcare experiences, our findings reveal delays in seeking treatment, mirroring barriers of timely diagnosis in resource-limited settings. Socioeconomic challenges, such as financial constraints, significantly impact healthcare access. Despite these barriers, participants reported satisfaction with care, contrasting with findings in some western studies where dissatisfaction is more prevalent [19, 20].

The study provides valuable insights but has limitations. The small sample size resulted in a statistical power of only 40% for detecting true associations. Therefore, the findings may have limited generalisability and sensitivity to subtle associations.

Conclusion

This study highlights the psychological burden of PCOS, worsened by the stigma around symptoms like acne and hirsutism. Familial support aids coping, emphasizing the need for context-specific interventions in Bangladesh to reduce stigma, enhance mental health support, and improve healthcare access.

Acknowledgments

The authors would like to thank all the participants for participating in this study. We are grateful to the Department of Obstetrics and Gynecology, Department of Public Health and Informatics, Department of Psychiatry, and Department of Endocrinology, Bangabandhu Sheikh Mujib Medical University.

Author contributions

Conception or design of the work; or the acquisition, analysis, or interpretation of data for the work: FH, NA, UH, H. *Drafting the work or reviewing it critically for important intellectual content:* FH, SS, RKK, MSA, NA, UH, H, BN, SSI. *Final approval of the version to be published:* FH, SS, RKK, MSA, NA, UH, H, BN, SSI. *Accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved:* FH.

Conflict of interest

We do not have any conflict of interest.

Data availability statement

We confirm that the data supporting the findings of the study will be shared upon reasonable request.

Supplementary file

None

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Bangabandhu Sheikh Mujib Medical University Journal 2025;18(1):e77827
ISSN 2074-2908 | eISSN 2224-7750 |

RESEARCH ARTICLE

Knowledge, attitude and practice on cervical cancer screening and human papillomavirus vaccination among adolescent girls residing in a slum of Kolkata

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Abstract

Background: Cervical cancer has emerged as an important public health concern among Indian women as it contributes to significant mortality. Early diagnosis and its prevention are thus of vital importance in the current scenario. This study assessed the knowledge, attitude and practice regarding screening and human papillomavirus vaccination among adolescent girls in a slum area of Kolkata.

Methods: This cross-sectional study was conducted among 227 adolescent girls (aged 14–19 years) at Arpuli Lane, Kolkata. A pre-designed questionnaire was used for data collection. Chi-square test and binary logistic regression analysis were done to findout the factors associated with knowledge, attitude and practice.

Results: Approximately 91% had inadequate knowledge regarding the prevention of cervical cancer, 47% had an unfavourable attitude towards the prevention of cervical cancer, and 22% had undergone a Pap smear examination/HPV test, while only 13% had received HPV vaccination. The educational status of the participants and their mothers was significantly associated with knowledge, attitude and practice regarding cervical cancer screening and HPV vaccination.

Conclusion: Appropriate behaviour change communications should be initiated considering the propensity for high-risk behaviour and poor knowledge and attitude. Future studies should reveal the causes of their poor behaviour to ensure timely screening and adequate vaccine coverage.

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Publication history
Received: 18 Nov 2024
Accepted: 17 Feb 2025
Published online: 15 Mar 2025

Responsible editor
M Mostafa Zaman
0000-0002-1736-1342

Reviewers
B: Md Foyjul Islam
0000-0001-6601-5772

Keywords
attitude, cervical cancer, knowledge, HPV vaccination, adolescents

Funding
None

Ethical approval
Approved by Institutional Ethics Committee of Medical College, Kolkata (No. MC/KOL/IEC/NON-SPON/2238/02/2024, dated 19 Feb 2024).

Trial registration number
Not applicable

Key messages

Knowledge, attitude and practice regarding cervical screening and human papillomavirus vaccination among adolescent slum dwellers in Kolkata are poor. Participants' education was found to be associated with such poor knowledge, attitude and behaviour. Appropriate behaviour change communications should be initiated considering the propensity for poor knowledge, unfavourable attitude and high-risk behaviour.

Introduction

Cervical carcinoma, a malignant neoplasm arising from the epithelial cells of the cervix uteri caused by an infectious disease, having a well-known causal relationship with human papillomavirus (HPV) [1]. It is the second most common of all genital malignancies among women, with developing countries contributing to a massive 80% of all cases [2, 3].

The World Health Organization's Cervical Carcinoma Crisis Card, 2013 paints a grim picture: 500,000 women develop cervical carcinoma every year, a further 275,000 succumbing to the disease and a predicted 500,000 more losing their lives to this condition by 2030, with more than 98% of them being from low- to mid-income countries [4]. Such enormous numbers for what is essentially a vaccine-preventable disease clearly show the need for improved vaccine coverage and the proper address of social and logistic barriers to immunisation.

Risk factors for contracting HPV infection and progression of such an infection to malignancy include sexual promiscuity, early coitarche, multiparity, prolonged usage of combined oral contraceptive pills and/or oestrogen-based hormone replacement therapy and tobacco consumption [5, 6]. It remains asymptomatic or presents with non-specific symptoms initially, eventually progressing to features such as unexplained weight loss, intermenstrual bleeding, post-coital bleeding, post-menopausal bleeding and persistent pelvic pain [7].

Owing, perhaps, to various psychosocial pressures, adolescent girls of slum communities tend to fall victim to multiple of the aforementioned risk factors, thus potentially forming a significant pool of future cervical carcinoma patients in the city. With the ever-increasing emphasis given on early immunisation against HPV, and considering the limited resources of a country like India, vaccination of high-risk populations, such as slum-dwelling adolescent females, is of tantamount importance.

For maximising the efficacy and acceptability of HPV immunisation, it is important to have prior knowledge about the understanding of carcinoma cervix among the recipients, their attitude towards the disease and their stance about vaccination and screening for the same. Thus, a knowledge-attitude-practice study regarding cervical carcinoma among slum-dwelling adolescent girls is essential, and coincidentally, no similar studies were found to have been conducted in a Kolkata-based slum.

This study was done to assess the knowledge, attitude and practice of participants regarding the prevention, screening and treatment of cervical cancer and assess any association between sociodemographic characteristics and the knowledge, attitude and practice of the participants

Methods

A cross-sectional study was done among 227 adolescent girls (14–19 years) residing for more than 6 months in the slum area of Arpuli Lane, Kolkata from March to April 2024. Arpuli Lane comes under the purview of the urban field practice area of the Medical College, Kolkata, where essential health services are provided. Adolescent girls who could not be contacted even after three attempts on three separate days during non-school hours were excluded from the study.

Sampling

A list of adolescent girls aged 14–19 years residing in the study area was collected from the updated family folder registers of the urban health training centre of Medical College, Kolkata. It was found that 389 adolescent girls satisfied the inclusion criteria. The minimum sample size was estimated as 227, by considering the prior prevalence of adequate knowledge regarding cervical screening among women in Mangalore city, Karnataka, India, as 18% from a study by Kumar *et al.* [8]. Epi Info™, version 4.0 was used for sample size calculation.

Data collection

A pretested semi-structured questionnaire comprised four sections, i.e., (1) sociodemographic details of the participants; (2) 16 questions focussing on the subjects' assessment of the knowledge component. Responses could be either 'Yes' or 'No', in which the maximum total scores ranged between 0 to 16. A cut-off score of 8 (50% of the maximum attainable score) was taken for adequate knowledge; (3) 10 questions focussing on the assessment of the attitude component of subjects. Responses ranged between 'strongly agree', 'agree', 'neutral', disagree', and 'strongly disagree' in a 4-point Likert scale. The total scores in this section ranged from 10 to 50, and 30 (50% of the score range) was taken as the cut-off for a favourable attitude; and (4) 2 questions focussing on assessing the practice component of subjects whose responses were dichotomous: either 'Yes' or 'No'.

One-on-one 10-interviews were done. Variables were selected from an extensive literature review, and correct responses were coded from the existing national-level guidelines. The demographic variables were age in completed years, level of education indicated by school enrolment, and last class passed, which was then classified as illiterate, primary (Class 4 passed), middle school (class 8 passed) and secondary level of education. Other variables included religion (Hinduism, Islam, Christianity and others) and educational level and occupation of both their parents.

The tool was pretested on 20 adolescent girls who were excluded from the study. The Cronbach's alpha for internal consistency was 0.73. Test-retest reliability was around 70%. Semantic equivalence was assessed by a team consisting of an epidemiologist, a communication and linguistic expert and a psychologist. The tool was translated from its original English version to Bangla and Hindi and back-translated to English to check for semantic and statistical invariance.

Statistical analysis

Data were analysed using Microsoft Excel 2019 and SPSS software, version 23. Data were described using number and percent. Univariate and multivariable binary logistic regression analysis was done to estimate the unadjusted and adjusted odds ratios

Table 1 Knowledge level on cervical cancer screening and human papillomavirus among adolescent girls (n=227)

Knowledge questions	No, n (%)
Is human papillomavirus infection a risk factor for cervical carcinoma?	178 (78.5)
Is having multiple sexual partners a risk factor for cervical carcinoma?	178 (78.5)
Is having sex at an early age a risk factor for cervical carcinoma?	167 (73.8)
Do genital infections increase the risk of cervical cancer?	169 (74.6)
Is smoking a risk factor for cervical carcinoma?	119 (52.3)
Does having children at an early age increase the risk of cervical carcinoma?	190 (83.8)
Does the HPV virus cause cancers in other body parts?	169 (74.6)
Is foul-smelling vaginal discharge a symptom of cervical carcinoma?	162 (71.5)
Is postcoital bleeding a symptom of cervical carcinoma?	169 (74.6)
Is postmenopausal bleeding (PMB)/intermenstrual/ irregular bleeding a symptom of cervical carcinoma?	199 (87.7)
Can cervical cancer be symptomless in its early stages?	185 (81.5)
Are you aware of the screening methods for cervical cancer? Can you name one?	169 (74.6)
Is it possible to detect cervical cancer in the pre-cancer stage with routine screening?	194 (85.4)
Are you aware cervical carcinoma, if detected early, is treatable?	143 (63.1)
Do you know that it is preventable with a vaccine against HPV?	197 (86.9)
Do you know the government is going to promote vaccination against HPV?	140 (61.5)

(95% confidence intervals) for determining the factors associated with the knowledge and attitude of the study participants. A chi-square test was done to find the associates of practice regarding cervical cancer screening and HPV vaccination.

Results

Among 227 participants, the mean (standard deviation) age was 16.7 years, and 80.8% of participants were Hindus. Twelve (5.3%) participants were illiterate, and 75 (54.6%) participants had education up to the primary level. While considering the education level of the mothers, 48 (34.6%) were illiterate, and 95 (28.5%) had an education level up to the primary level. The median (interquartile range) number of siblings was 3 (2–4). Sixty percent of the mothers were homemakers, and 72.3% of the fathers of the study participants were unskilled workers.

Table 2 Attitude regarding prevention of cervical cancer among the study participants (n=227)

Attitudes	Strongly disagree n (%)	Disagree n (%)	Neutral n (%)	Agree n (%)	Strongly agree n (%)
Cervical cancer is a common cancer in women in India	28 (12.3)	59 (26.2)	38 (16.2)	52 (23.1)	50 (22.3)
Any adult woman could develop cervical cancer during her lifetime	24 (10.8)	67 (29.2)	50 (22.3)	63 (27.7)	23 (10.0)
All women aged 30–65 years should undergo cervical screening	33 (14.6)	43 (19.2)	70 (30.8)	65 (28.5)	16 (6.9)
Screening can help in early detection of cancer cervix	30 (13.1)	56 (24.6)	47 (20.8)	78 (34.6)	16 (6.9)
Would you go for cervical cancer screening if available free of cost?	24 (10.8)	72 (31.5)	42 (18.5)	63 (27.7)	26 (11.5)
Would you like to go for a cervical cancer screening if it would cause no harm?	38 (16.9)	66 (29.2)	43 (18.5)	59 (26.2)	21 (9.2)
Would you like to go for HPV vaccination after knowing its role in the prevention of cervical carcinoma?	26 (11.5)	56 (24.6)	45 (20.0)	70 (30.8)	30 (13.1)
Would you go for an HPV vaccination if it is available free of cost?	26 (11.5)	63 (27.7)	63 (27.7)	51 (22.3)	24 (10.8)
Would you like to go for an HPV vaccination if it causes no harm?	33 (14.6)	77 (33.8)	54 (23.8)	44 (19.2)	19 (8.5)
All women need an HPV vaccine	30 (13.1)	47 (20.8)	56 (24.6)	61 (26.9)	33 (14.6)

Knowledge, attitude and practice on cervical cancer screening and HPV vaccination

Approximately 90.8% had inadequate knowledge regarding the prevention of cervical cancer (Table 1). Nearly half (47.0%) had unfavourable attitudes towards preventing cervical cancer (Table 2). Out of 227 study participants, only 51 (22.3%) have undergone a Pap smear examination/HPV test, while only 29 (12.8%) have received HPV vaccination

Factors associated with knowledge, attitude and practice regarding cervical cancer screening and HPV vaccination

Multivariable binary logistic regression analysis showed that the primary and below educational status had higher odds (aOR 2.2; 95% CI 1.8–2.7) of having inadequate knowledge compared to those with higher levels of education (Table 3). While considering attitude, again, the educational status of primary and below showed higher chances of having an unfavourable attitude towards cervical cancer screening (aOR 2.0; 95% CI 1.8–4.3) (Table 4). Both the multivariable models fit well (Hosmer-lemeshow test $P>0.05$). While analysing factors regarding practice for prevention and early diagnosis of cervical cancer, it was found that the educational status of both the participant as well as their mothers had a significant association with undergoing screening for cervical cancer through Pap smear examination (Table 5). None of the sociodemographic variables were associated with HPV vaccination (Table 6).

Discussion

The key takeaways from this study may be summarised as follows: i) a vast majority of the subjects had inadequate knowledge regarding the causes, symptoms and preventive measures for carcinoma cervix; ii) nearly half of them have unfavourable attitudes towards prevention of the disease, and iii) Level of education of the subjects and their mothers have essential bearings on the knowledge and attitude regarding cervical cancer, as well as the likelihood of the subject undergoing a Pap smear examination.

Table 3 Factors associated with inadequate knowledge among the study participants: Univariate and multivariable binary logistic regression analysis (n=227)

Variables	Unadjusted odds ratio (95% CI)[a]	Adjusted odds ratio (95% CI)[a]
Decreasing age	1.1 (1.0–1.2)	1.1 (1.0–1.2)
Religion		
Hindu	1.2 (0.9–2.4)	
Others	Ref	
Educational status		
Primary and below	2.4 (2.0–3.5)	2.2 (1.8–2.7)
Above primary	Ref	Ref
Educational status of mother		
Primary and above	1.5 (0.8–2.4)	
Below primary	Ref	
Occupation of mother		
Homemakers	1.3 (0.9–2.0)	
Others	Ref	
Occupation of father		
Unskilled	1.2 (1.1–2.2)	1.0 (0.9–1.6)
Semi-skilled/ unskilled	Ref	Ref

[a]CI indicates confidence interval

These findings are consistent with those of a study done on reproductive age-group females in an urban slum of Karnataka by Bathija *et al.* [9]. The current adolescent female age group will form a major portion of the reproductive age group for approximately the next 3 decades, contributing significantly to the cervical carcinoma incidence rate of 22 per 100,000 woman years [10]. This, coupled with the fact that nearly one-third of Kolkata's population resides in slums, could lead to a significant burden on the healthcare system, as well as psychosocial and economic turmoil for the families of those affected [11, 12]. Therefore, targeting the preventive measures towards the main future beneficiaries, adolescent females, is essential in controlling the disease.

Table 4 Factors associated with unfavourable attitude among the study participants: Binary logistic regression analysis (n=227)

Variables	Unadjusted odds ratio (95% CI)[a]	Adjusted odds ratio (95% CI)[a]
Decreasing age	0.9 (0.7–1.2)	
Religion		
Hindu	1.3 (1.0–1.8)	
Others	Ref	
Educational status		
Primary and below	2.7 (2.2–5.3)	1.98 (1.8–4.3)
Above primary	Ref	Ref
Educational status of mother		
Primary and above	1.4 (1.0–2.4)	
Below primary	Ref	
Occupation of mother		
Homemakers	1.0 (0.7–1.4)	
Others	Ref	
Occupation of father		
Unskilled	1.6 (1.1–2.4)	1.2 (0.9–1.8)
Semi-skilled/ unskilled	Ref	Ref

[a]CI indicates confidence interval

The target population's baseline knowledge and pre-conceived notions are key considerations for optimal acceptance of any preventive intervention. Cervical carcinomais a stigmatised issue in various conservative sections of society, thereby compounding the, perhaps expected, lack of knowledge among young slum-dwellers by an unfavourable attitude towards various aspects of the disease [13].

This study demonstrates the association between the level of schooling and knowledge and favourable attitudes among the subjects, highlighting the necessity of secondary and higher education among girls in improving the overall health outlook of the nation. This is especially important here because 60% of the subjects are illiterate or have completed primary schooling. A holistic approach to reproductive health education, along with basic instructions for self -detection of reproductive tract infections (including HPV infections) may be adopted in schools [14]. Paying attention to maternal educational level might contribute to better screening.

A closer look into the answers to the questionnaire revealed a profound ignorance about the spread, symptoms, treatment options and preventive strategies. Religion and the father's occupation were not found to be as strongly associated as the education of the subjects.

Table 5 Association of practice regarding Pap smear examination with selected socio-demographic variables (n=227)

Variables	Undergone Pap smear examination		*P*
	Yes, n (%)	No, n (%)	
Education level of adolescent			
Primary and below (n=136)	20 (14.7)	116 (85.3)	<0.01
Above primary (n=91)	31 (34.1)	60 (65.9)	
Education of mother of adolescent			
Illiterate (n=78)	7 (8.9)	71 (91.1)	<0.01
Primary school (n=66)	6 (8.1)	60 (91.9)	
Middle school (n=73)	31 (42.9)	42 (57.1)	
High School (n=10)	7 (66.7)	3 (33.3)	
Occupation of mother			
Homemakers (n=136)	25 (17.9)	111 (82.1)	0.21
Unskilled (n=51)	16 (31.0)	35 (69.0)	
Semi-skilled (n=38)	9 (22.7)	29 (77.3)	
Skilled (n=2)	1 (50.0)	1 (50.0)	
Occupation of father			
Unskilled (n=164)	37 (22.3)	127 (77.7)	0.63
Semi-skilled (n=61)	13 (21.3)	48 (80.0)	
Skilled (n=2)	1 (50.0)	1 (50.0)	
Religion			
Hinduism (n=183)	42 (22.9)	141 (77.1)	0.80
Islam (n=37)	7 (19.0)	30 (81.0)	
Christian (n=7)	2 (25.0)	5 (75.0)	

Among the subjects in middle and high school, only 15.4% had received HPV vaccination, which falls way short of the coverage rates recommended by the WHO for low to middle-income countries [15]. Along with lack of knowledge and unfavourable attitude, hesitancy among physicians in routine recommendation, coupled with logistic barriers, acts as possible deterrents from achieving a desirable rate of HPV prophylaxis [16].

Table 6 Association of practice regarding human papillomavirus vaccination with selected socio-demographic variables (n=227)

Variables	Received HPV vaccination		*P*
	Yes, n(%)	No, n (%)	
Education level of adolescent			
Illiterate (n=12)	1 (8.3)	11 (91.6)	0.80
Primary School (n=124)	14 (11.6)	110 (88.4)	
Middle school (n=58)	9 (15.2)	49 (84.8)	
High School (n=33)	5 (15.8)	28 (84.2)	
Education of mother of adolescent			
Illiterate (n=78)	9 (11.5)	69 (88.5)	0.15
Primary school (n=66)	5 (7.6)	61 (92.4)	
Middle school (n=73)	12 (16.4)	61 (83.6)	
High school (n=10)	3 (30.0)	7 (70.0)	
Occupation of mother			
Homemakers (n=136)	12 (8.8)	124 (91.2)	0.06
Unskilled (n=51)	8 (15.7)	43 (84.3)	
Semi-skilled (n=38)	8 (21.0)	30 (79.0)	
Skilled (n=2)	1 (50.0)	1 (50.0)	
Occupation of father			
Unskilled (n=164)	18 (10.9)	146 (89.1)	0.16
Semi-skilled (n=61)	10 (16.4)	51 (85.6)	
Skilled (n=2)	1 (50.0)	1 (50.0)	
Religion			
Hinduism (n=183)	23 (12.6)	160 (87.4)	0.42
Islam (n=37)	4 (10.8)	33 (89.2)	
Christian (n=7)	2 (28.6)	5 (71.4)	

Inculcating basic knowledge about the mode of transmission, risk factors and symptoms of HPV infection at an early level, as well as behaviour change communication, targeted both at the adolescent females and their mothers, is essential in improving both the knowledge and the attitude of the slum-dwelling population [17]. In particular, discussions about the safety and efficacy of HPV vaccines may help mitigate pre-conceived prejudices and misplaced concerns about prophylaxis, especially seeing that 78.2% of the respondents either outright refused or were unsure about getting vaccinated even if the vaccination causes no harm. Outreach programmes to the slums may also prove to be beneficial. Additional studies should be conducted regarding the logistic barriers, and steps should be taken accordingly to address them.

Taking into account the annual expenditure for HPV vaccination and cervical carcinoma treatment, prophylaxis among adolescents has been demonstrated to be a very cost-effective strategy [18]. Slum-dwelling adolescents are more likely to indulge in unsafe sexual practices and tobacco addiction, both of which are well-known risk factors for carcinoma cervix [19]. Coupled with poor health-seeking behaviour, the burden of HPV infection is, therefore, relatively high, with a large number of cases probably lying undetected. Early detection of cervical neoplasms is a key aspect of their management, hence the importance of detecting and protecting the undiagnosed cases. A study among adolescent slum-dwellers by Jain and Mohan shows that they are eager to know about safe sexual practices, perhaps earmarking the subjects as potential subjects of successful educational campaigns [20].

Conclusion

Education of the slum-dwelling girls could be instrumental to the cervical cancer prevention. Considering the economic implications, propensity for high-risk behaviour, slum-dwelling adolescents are ideal candidates for behaviour change communication. A knowledge, attitude, and practices study is essential to determine the knowledge and perceptions of HPV infections, cervical carcinoma and preventive measures at periodic intervals. Addressing the subjects' concerns and dispelling any misgivings and prejudices is essential for ensuring adequate vaccine coverage which will ultimately contribute to a healthy female population in the years to come.

Acknowledgments

We are grateful to the study participants and the field heath workers for their support to the study.

Author contributions

Conception or design of the work; or the acquisition, analysis, or interpretation of data for the work: AD, SS, AB, HN. *Drafting the work or reviewing it critically for important intellectual content:* AD, SS, AB, HN, DS, SM. *Final approval of the version to be published:* AD, SS, HN, DS, SM, AB. *Accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved:* AD, SS, AB.

Conflict of interest

We do not have any conflict of interest.

Data availability statement

We confirm that the data supporting the findings of the study will be shared upon reasonable request.

Supplementary file

None

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Bangabandhu Sheikh Mujib Medical University Journal 2025;18(1):e77103
ISSN 2074-2908 | eISSN 2224-7750 |

RESEARCH ARTICLE

Social media and depression among young adults in Bangladesh: Patterns, predictors, and implications

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Abstract

Background: Consequences have arisen about the impact of growing social media use on users' psychological adverse well-being. Especially in young adults, it can increase feelings of loneliness, inadequacy, and social comparison. This study examines the role of social media in contributing to depression among young adults in Rajshahi city, Bangladesh.

Methods: A cross-sectional study was conducted among 450 young adults in Rajshahi city, Bangladesh, using a structured questionnaire administered through face-to-face interviews and a purposive sampling technique. The Patient Health Questionnaire-9 (PHQ-9) was used to assess respondents' depression status. Univariate and multivariate logistic regression were used to identify the factors of depression.

Results: Over half of the respondents (57.8%) experienced depression, predominantly at moderate to severe levels, with higher rates observed among younger individuals (21–24 years) and females. Depression status was found to be significantly associated with respondents' age, social media usage, time spent on social media, and following specific types of accounts such as celebrities or models, gaming, and animals or birds. Ultimately, Facebook usage (odds ratio (OR) 2.1; 95% confidence interval (CI) 0.9–5.0), WhatsApp usage (OR 0.5; 95% CI 0.3–0.7), and following accounts related to celebrities or models (OR 1.5; 95% CI 0.9–2.6), gaming (OR 1.9; 95% CI 1.0–3.6) were identified as significant factors of depression among young adults.

Conclusion: More than half of young adults had depression. Social media usage, online time, and following accounts such as celebrities, models, and gaming are key contributors, emphasising the need for targeted mental health interventions, awareness campaigns, and digital literacy programs.

Key messages

Social media usage is positively associated with depression, particularly among young adults in Rajshahi city, Bangladesh. Age and time spent on social media significantly increase the likelihood of depression. Depression levels vary based on the platforms used, the accounts followed, and the content consumed. Platforms like Facebook, X, and Pinterest are linked to higher depression rates.

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Publication history
Received: 21 Oct 2024
Accepted: 8 Mar 2025
Published online: 16 Mar 2025

Responsible editor
M Mostafa Zaman
0000-0002-1736-1342

Reviewers
C: Sandeep
0000-0002-5249-5397
E: Muhammad Kamal Uddin
0000-0003-2033-8933

Keywords
social media, depression, young adults, patient health questionnaire-9

Funding
None

Ethical approval
Approved by Institutional Animal, Medical Ethics, Biosafety, and Biosecurity Committee of the Institute of Biological Sciences at the University of Rajshahi, Bangladesh (No. 249(35)/320/IAMEBBC/IBSc, dated 16 Jan 2024).

Trial registration number
Not applicable

Introduction

With social media's smooth integration into our daily lives, a large segment of the world's population now relies heavily on it for information, communication, and enjoyment. Social media once addressed as a revolutionary tool for global connectivity and communication, is now increasingly being questioned for its potential negative impact on mental health [1]. Recently, there has been growing concern about the widespread influence of platforms designed to facilitate interaction and information sharing [2]. Social media engagement's quick pleasure contributes to addictive use. This addictive use of social media, which is characterised by an overwhelming concern for social media, an insatiable urge to use or log in to social media, and a commitment to social media, takes up so much time and energy that it interferes with other significant aspects of life. Numerous researches on addiction and the effects of social media have been done. The results suggest that extended usage of social media may be linked to problems like stress, anxiety, depression, loneliness, low self-esteem, and poor sleep quality [3–14].

Social media provides an idealized picture of people's lives, encouraging ongoing social comparison. Young people may compare themselves to others, resulting in low self-esteem and inadequacy [15]. According to many researchers, people are becoming the victims of lower self-esteem (which ultimately results in self-loathing) because of the steep increase in social media usage [16]. Moreover, constant pressure to uphold an idealized online identity leads to fear of missing out (FOMO) and an overpowering need to present a flawless life [17]. The genuine difficulties that young adults encounter are frequently hidden by this facade, making it challenging to ask for help. Additionally, spending too much time on social media might lead to a sedentary lifestyle associated with less restful sleep [18].

The nighttime social media usage can impact users' sleep hygiene by lengthening their sleep onset latency and shortening their sleep amount [19, 20]. Individuals on social media might be exposed to a steady stream of information, including unpleasant news, comparisons to others, and cyber bullying, which causes stress and anxiety levels to rise and makes it more difficult to relax and go to sleep [21]. A survey revealed that extensive social media use, with most students spending over four hours daily across multiple platforms, significantly impacts their mental health [22]. Another study found a significant positive relationship between social media use and depression among college students [23]. In this line Mamun *et al.* [24]. conducted a pilot study in Bangladesh to explore the connection between 'Facebook addiction' and its supporting factors, using data from a sample of 300 students from the University of Dhaka, Bangladesh. Their findings showed that depression is a major comorbid factor among the students, and the risk of Facebook addiction emerged as a significant concern. Again, the National Mental Health Survey (NMHS) of Bangladesh 2019 found that the overall prevalence of mental disorders among individuals aged 18 and above was 18.7%, with higher rates observed among urban youth [25].

There is a lack of comprehensive studies on how specific patterns of social media usage affect mental health outcomes. These patterns include platform preferences, content types, and interaction behaviors. Most existing research focuses on individual platforms or general usage. Limited studies explore cultural and regional differences, such as in Bangladesh. The psychological effects of social media on young adults, including FOMO, social comparison, and addiction, are not fully addressed. Therefore, this study aims to investigate the impact of social media on depression among adults in Rajshahi city, Bangladesh.

This study investigated the impact of social media use on depression among young adults in Rajshahi city, Bangladesh, considering multiple social media platforms. It found a strong link between using multiple platforms and experiencing depressive symptoms, with high social media activity correlating with increased mental health issues. Increased social media use, especially across multiple platforms, was shown to negatively affect students' mental health, contributing to depression. These findings can inform the development of preventive strategies for depression. Therefore, the primary research question of this study was: 'Does social media use contribute to depression among young adults in Bangladesh?' The study hypothesises that higher social media engagement is associated with increased depressive symptoms.

Methods

Study participants, area, and sampling technique

A cross-sectional study among young adults (both students and non-students) aged 18–30 years in Rajshahi city, Bangladesh, who have access to the internet, were selected as respondents. Data were collected from 500 respondents through purposively face-to-face interviews using a structured questionnaire between October 2023 and February 2024. Depression status was assessed using the Patient Health Questionnaire 9 items (PHQ–9) [26], and the sampling method was chosen due to time and financial constraints. The survey excluded individuals who were physically disabled, or provided incomplete or inconsistent responses.

Sample size

A total of 500 participants were surveyed, and 450 valid responses were included in the final analysis. However, this size far exceeded the minimum required number 237 which was calculated using the formula: $n=z^2pq/d^2$ [27] considering prevalence as 18.7% [25] with 95% confidence level and 5% margin of error.

Procedure for gathering data

The questionnaire assessed social media use by focusing on several aspects: the average daily time spent on social media, preferred platforms (*e.g.,* Facebook, Instagram), types of content engaged with (*e.g.,* text, images, videos), and whether participants primarily created or consumed content. It also explored the purpose of use (*e.g.,* social connection, entertainment, news) and frequency of access (*e.g.,*

multiple times a day, daily, or weekly). The self-administered questionnaires were distrusted to participants. The purpose of the study was explained, and consent was obtained. The ethical approval was granted by the ethics committee of the University of Rajshahi, Bangladesh. Demographic characteristics (age and sex), the names of the social media sites the respondents used, time spent, the type of accounts/contents they follow on social media, etc., and a standard scale (PHQ-9) to assess depression were included in the questionnaire.

Patient health questionnaire-9 items

The PHQ-9 is a widely used, validated, self-reported instrument to screen and assess the severity of depression. It consists of nine items based on the Diagnostic and statistical manual of mental disorders, 4th Edition (DSM-IV) [28] criteria for major depressive order, with each question graded on a 4-point Likert scale to measure how often depressive symptoms were felt in the past two weeks [28]. Responses range from 0 (not at all) to 3 (nearly every day), with a total score ranging from 0 to 27. The cut-off scores for diagnosing depression are as follows: 0–4 for minimal or no depression, 5–9 for mild depression, 10–14 for moderate depression, 15–19 for moderately severe depression, and 20–27 for severe depression [29]. Higher scores indicate greater severity of depression. This investigation used a score of ≥10 to identify depression, utilising the Bengali version of the questionnaire [29, 30]. The format was confirmed to be suitable, with language levels that participants could understand. The survey was conducted in English and Bengali using Triandis's [31] back-to-back translation method.

The PHQ-9 not only helps assess the presence and severity of depressive symptoms but also includes a final question on the impact of symptoms on daily functioning, enhancing its clinical utility. It is commonly used in both clinical and research settings to monitor treatment progress or identify at-risk populations. Numerous studies have validated the PHQ-9 across diverse populations and cultural contexts, confirming its reliability and sensitivity in detecting depression symptoms [29].

Statistical analysis

Gender, age, social media platforms, time spent on social media, *etc.*, were the explanatory variables, and respondents' depression status was the outcome variable. Variable were described using frequency and percentage. Chi-square test was used to examine the association between depression, and demographic and social media related variables. The Cronbach's [32] was used to assess the internal consistency or reliability of the test items of PHQ-9. A commonly accepted threshold, , indicates acceptable reliability, though this can vary depending on the context and the measured construct. Based on a study [33], some psychometric indicators (mean, standard deviation, Cronbach's and inter-item correlation matrix for each of the PHQ-9 items) were calculated for testing validity and reliability of PHQ-9. Significantly associated variables determined by Chi-square test were considered as factors for the binary logistic regression model to explore the effects of demographic and social media related factors on depression status. Later on, all factors were entered into the model for adjustment. Adjusted odds ratio (aOR) with 95% confidence interval (CI) were calculated to explain the determinants of depression. The data were analysed using SPSS software (version 26.0). $P<0.05$ was considered as statistically significant.

Table 1 Background characteristics of the respondents (n=450)

Variables	Number (%)
Age (in years)	
≤20	181 (40.2)
21–24	219 (48.7)
≥25	50 (11.1)
Gender	
Male	281 (62.4)
Female	169 (37.6)
Usage of social media	
Facebook	420 (93.3)
YouTube	364 (80.9)
X	57 (12.7)
Instagram	161 (35.8)
Pinterest	50 (11.1)
WhatsApp	131 (29.1)
Time spent on social media (in hours)	
1–5	264 (58.7)
6–10	159 (35.3)
≥11	27 (6.0)
Is it (the amount of time spent on social media) good for health?	
Yes	57 (12.7)
No	393 (87.3)
Follows on social media	
Family/friends	325 (72.2)
News	324 (72.0)
Celebrity	138 (30.7)
Gaming accounts	80 (17.8)
Funny accounts	143 (31.8)
Animals/birds	114 (25.3)
WhatsApp	96 (21.3)
Severity of depression	
Minimal depression (0–4)	89 (19.8)
Mild depression (5–9)	101 (22.4)
Moderate depression (10–14)	92 (20.4)
Moderately severe depression (15–19)	90 (20.0)
Severe depression (≥20)	78 (17.3)
Depression status	
Absent (≤9)	190 (42.2)
Present (≥10)	260 (57.8)

Results

Background characteristics of the respondents are presented in Table 1. The sample is primarily young adults, with the largest age group (48.7%) between 21 and 24 years, followed by those aged 20 or younger (40.2%), and a smaller proportion aged 25 or older (11.1%). Males constitute 62.4% of the respondents, while females make up 37.6%, indicating a gender disparity. Social media usage is widespread, with nearly all respondents using Facebook (93.3%) and a high proportion on YouTube (80.9%). Other platforms like Instagram (35.8%) and WhatsApp (29.1%) are also popular, while Twitter (12.7%) and Pinterest (11.1%) are less commonly used. Most respondents spend 1–5 hours daily on social media (58.7%), though fewer spend 6–10 hours (35.3%) or 11 or more hours (6.0%). A significant majority (87.3%) believe their social media use negatively affects their health, with only 12.7% considering it beneficial. Family/friends

Table 2 Mean, standard deviation, item-total correlation, Cronbach's alpha if item deleted, Skewness and Kurtosis of the patient health questionnaire-9 (PHQ-9)

Items	Mean	SD[a]	Corrected item-total correlation	Cronbach's α if the item deleted	Skewness	Kurtosis
I_1	1.2	1.2	0.7	0.8	0.5	-1.4
I_2	1.2	1.2	0.6	0.8	0.5	-1.3
I_3	1.4	1.2	0.5	0.8	0.3	-1.3
I_4	1.3	1.2	0.5	0.8	0.4	-1.5
I_5	1.5	1.3	0.5	0.8	0.1	-1.7
I_6	1.1	1.3	0.6	0.8	0.6	-1.4
I_7	1.3	1.3	0.7	0.8	0.3	-1.6
I_8	1.3	1.3	0.7	0.8	0.3	-1.6
I_9	1.2	1.2	0.6	0.8	0.4	-1.4

[a]SD indicates Standard deviation; I_1: Little interest or pleasure in doing things, feeling down, depressed, or hopeless; I_2: Trouble falling or staying asleep, or sleeping too much; I_3: Feeling tired or having little energy; I_4: Poor appetite or overeating; I_5: Feeling bad about yourself- or that you are a failure or have let yourself or your family down; I_6: Trouble concentrating on things, such as reading the newspaper or watching television; I_7: Moving or speaking so slowly that other people could have noticed; I_8: Or the opposite- being so fidgety or restless that you have been moving around a lot more than usual; I_9: Thoughts that you would be better off dead, or of hurting yourself in some way.

(72.2%) and news/entertainment sources (72.0%) are the most common follows, while celebrity/model (30.7%), funny accounts (31.8%), and animals/birds (25.3%) are also popular, though less so. Depression is notably prevalent, with more than half of the sample (57.8%) reporting some level of depressive symptoms, ranging from mild (22.4%) to severe (17.3%).

Mean scores for each item are moderate (1.1 to 1.5), and corrected item-total correlations indicate good internal consistency. Cronbach's for most items is high, between 0.82 and 0.84, confirming the questionnaire's reliability. Skewness and kurtosis values are within acceptable ranges, supporting the items' suitability for psychometric analysis (Table 2).

Inter-item correlations for the PHQ-9, revealing moderate correlations (0.2 to 0.5) between items. The strongest correlation is found between items such as 'Moving or speaking slowly' and 'Being restless or fidgety' (1.0), suggesting that these items may capture similar depressive symptoms. Overall, these correlations indicate that while some items are related, each item assesses distinct aspects of depression (Table 3).

The results of Chi-square test reveal significant associations between depression status and several factors. Younger adults, especially those aged 21–24, show higher depression rates, while females report slightly more depression than males, though this is not statistically significant. Social media usage patterns indicate that Facebook, Twitter, and Pinterest users are more likely to report depression, with prolonged use (6–10 hours or more) linked to higher depressive symptoms. Additionally, following celebrity/model, gaming, funny, and animal/bird accounts is associated with increased depression, highlighting how both social media habits and content type may affect mental health (Table 4).

The results of the logistic regression analysis, identifying factors associated with increased odds of depression. Facebook users are over twice as likely to report depressive symptoms (aOR 2.1; 95% CI 0.9–5.0), while WhatsApp use appears protective, reducing the likelihood of depression (aOR 0.5; 95% CI 0.3–0.7). Following celebrities or gaming accounts also increases the odds of experiencing depression (aOR 1.6; 95% CI 0.9–2.6 and aOR 1.9; 95% CI 1.0–3.6, respectively). These findings underscore the impact of both platform choice and content type on mental health, particularly regarding depressive symptoms. Finally, the binary logistic model explains 15.6% (Nagelkerke R^2=0.2) of the variability in depression status based on the explanatory variables (Table 5).

Table 3 Inter-item correlation matrix for the patient health questionnaire-9 (PHQ-9)

Items	I_1	I_2	I_1	I_3	I_4	I_5	I_6	I_7	I_8
I_1	1.0								
I_2	0.4	1.0							
I_3	0.3	0.4	1.0						
I_4	0.3	0.3	0.4	1.0					
I_5	0.3	0.3	0.4	0.4	1.0				
I_6	0.3	0.5	0.4	0.3	0.3	1.0			
I_7	0.3	0.4	0.3	0.3	0.3	0.5	1.0		
I_8	0.3	0.4	0.3	0.3	0.3	0.5	1.0	1.0	
I_9	1.0	0.4	0.3	0.3	0.2	0.3	0.3	0.3	1.0

I_1: Little interest or pleasure in doing things, feeling down, depressed, or hopeless; I_2: Trouble falling or staying asleep, or sleeping too much; I_3: Feeling tired or having little energy; I_4: Poor appetite or overeating; I_5: Feeling bad about yourself- or that you are a failure or have let yourself or your family down; I_6: Trouble concentrating on things, such as reading the newspaper or watching television; I_7: Moving or speaking so slowly that other people could have noticed; I_8: Or the opposite- being so fidgety or restless that you have been moving around a lot more than usual; I_9: Thoughts that you would be better off dead, or of hurting yourself in some way.

Discussion

The usage of social media into individuals' daily lives has had a significant impact on mental health. Identifying how social media affects, especially young adults, is essential. This study has attempted to find out some factors that might be associated with depression among young adults. This study identified that 57.8% of the study population suffers from depression, a substantially higher prevalence compared to the 18.7% prevalence of mental disorders among adults reported in the 2019 NMHS of Bangladesh [25]. The National Mental Health Survey (NMHS) data reflects the overall adult population; whereas our study sample may have specific characteristics or risk factors that increase the likelihood of depression. Moreover, variations in the tools and diagnostic criteria used to measure depression may contribute to the difference. The NMHS reported overall mental disorders, while this study focused specifically on depression using the PHQ-9, which is highly sensitive to depressive symptoms. According to the World Health Organization (WHO), depression is more prevalent in women than in men [25]. Similarly, our findings align with those of the previous study conducted by the WHO. As we check the severity of depression, we find that 19.8% had minimal depression, 22.4% had mild depression, 20.4% had moderate depression, 20.0% had moderately severe depression, and 17.3% had severe depression.

One of the previous studies on the issue of time spent on social media shows a positive association between time spent on social media and depression, with a higher prevalence of depression among individuals who spend a significant amount of time on social media [34]. This study strongly supports this finding, as the results also validate the patterns observed in the previous research. The consistency of these outcomes further reinforces the link between increased social media usage and a higher prevalence

Table 4 Association between depression and selected factors, (n=450)

Characteristics	Depression status		*P*
	Absent, n (%)	Present, n (%)	
Age (in years)			
≤20	81 (44.8)	100 (55.2)	<0.01
21-24	79 (36.1)	140 (63.9)	
≥25	30 (60.0)	20 (40.0)	
Gender			
Male	126 (44.8)	155 (55.2)	0.15
Female	64 (37.9)	105 (62.1)	
Uses Facebook			
Yes	170 (40.5)	250 (59.5)	<0.01
No	20 (66.7)	10 (33.3)	
Uses YouTube			
Yes	148 (40.7)	216 (59.3)	0.17
No	42 (48.8)	44 (51.2)	
Uses X			
Yes	16 (28.1)	41 (71.9)	0.02
No	174 (44.3)	219 (55.7)	
Uses Instagram			
Yes	60 (37.3)	101 (62.7)	0.11
No	130 (45.0)	159 (55.0)	
Uses Pinterest			
Yes	13 (26.0)	37 (74.0)	0.01
No	177 (44.2)	223 (55.8)	
WhatsApp			
Yes	67 (51.1)	64 (48.9)	0.01
No	123 (38.6)	196 (61.4)	
Time spent on social media (in hours)			
1–5	119 (45.1)	145 (54.9)	0.01
6–10	55 (34.6)	104 (65.4)	
≥11	16 (59.3)	11 (40.7)	
Follows family/friend			
Yes	133 (40.9)	192 (59.1)	0.37
No	57 (45.6)	68 (54.4)	
Follows news/ Entertainment			
Yes	132 (40.7)	192 (59.3)	0.31
No	58 (46.0)	68 (54.0)	
Follows celebrity/model			
Yes	41 (29.7)	97 (70.3)	<0.01
No	149 (47.8)	163 (52.2)	
Follows gaming accounts			
Yes	19 (23.8)	61 (76.2)	<0.01
No	171 (46.2)	199 (53.8)	
Follows funny accounts			
Yes	44 (30.8)	99 (69.2)	<0.01
No	146 (47.6)	161 (52.4)	
Follows animals/birds			
Yes	34 (29.8)	80 (70.2)	<0.01
No	156 (46.4)	180 (53.6)	
Follows others			
Yes	32 (33.3)	64 (66.7)	0.47
No	158 (44.6)	196 (55.4)	
Total	190 (42.2)	260 (57.8)	

of depression. This study also examined the association between different social media platforms and depression, identified that Facebook, X (formerly Twitter), and Pinterest are positively linked to depression, which is in line with previous researches [2, 24]. For example, a study [2] analysed multiple platforms among young adults and found that increased usage was significantly associated with higher levels of depression. When considering the types of accounts followed by respondents, those following accounts related to celebrities, games, humorous content, animals, and other entertainment sources showed higher levels of depression. This aligns with previous studies, which suggest that visual social media platforms like Instagram and Pinterest, as well as following accounts related to lifestyle, celebrities, and funny content, can heighten feelings of inadequacy and social comparison, thereby increasing depression levels [10, 35]. Although demographic variables such as gender, age, and social media-related factors are significantly associated with depression.

To make the discussion more actionable, several recommendations are proposed: First, digital literacy programs should be introduced to educate youth on responsible social media use, focusing on privacy, critical thinking, and avoiding misinformation. Second, mental health awareness campaigns targeting youth are essential to raise awareness about the mental health impacts of social media, reduce stigma, and encourage open discussions. Lastly, interventions for high-risk users, such as excessive social media consumers, should be implemented, offering tailored support like counseling, digital detox programs, and self-regulation tools. These measures aim to promote responsible social media usage and support mental well-being.

Limitations

The current investigation used a purposive sampling technique. While conducting the study, the time was insufficient, and no funds were provided. Many respondents did not give their exact age and showed an inappropriate age on which this study had to depend. As a result, the respondent's age may be subjected to error. In many cases, respondents did not want to give information, which needed some time to get desirable information. The socio-demographic factors (e.g., income, area of residence, education, mother's education, father's education, mother's occupation, father's occupation, religion, marital

Table 5 Binary logistic regression analysis of variables associated with depression

Explanatory Variables	Adjusted odds ratio (95% CI[a])
Respondent's age (in years)	
≤20	Ref
21–24	1.2 (0.8–1.8)
≥25	0.7 (0.3–1.3)
Uses Facebook	
No	Ref
Yes	2.1 (0.9–5.0)
Uses X (Twitter)	
No	Ref
Yes	1.5 (0.8–3.0)
Uses Pinterest	
No	Ref
Yes	1.3 (0.6–2.6)
WhatsApp	
No	Ref
Yes	0.5 (0.3–0.7)
Time spent on social media (in hours)	
1–5	Ref
6–10	1.4 (0.9–2.1)
≥11	0.5 (0.2–1.3)
Follows celebrity/ model	
No	Ref
Yes	1.5 (0.9–2.5)
Follows gaming accounts	
No	Ref
Yes	1.9 (1.0–3.6)
Follows funny accounts	
No	Ref
Yes	1.4 (0.8–2.3)
Follows animals/ birds	
No	Ref
Yes	1.3 (0.8–2.2)

[a]CI indicates Confidence interval

status, *etc.*) were not taken into account, which can influence the results of the present study.

Conclusion

This study was aimed to examine how social media-related factors are associated with depression and identified its adverse impacts on mental health. Age and the amount of time spent on social media are found positively associated with depression and females being more affected compared to males. The study showed that a person's depression status can vary based on the social media platforms they use, the types of accounts they follow, and the content they consume. People who use Facebook, X, Pinterest, and WhatsApp platforms are more likely to experience depression. Based on the study's findings, increasing awareness about the negative impacts of excessive social media use, especially among youth, is recommended through educational programs. Providing mental health resources and parental guidance is essential. Social media platforms should implement mental well-being features, and further research into social media's impact on mental health should be supported. Future longitudinal research is vital to confirm findings and identify trends. Evidence-based policies, such as digital literacy programme and mental health campaigns, are recommended to help policymakers and professionals develop targeted interventions for mental well-being.

Acknowledgments

We would like thank to the Department of Population Science and Human Resource Development at the University of Rajshahi, Bangladesh, where the study was conducted. We also gratefully acknowledge the study participants, reviewers, and academic editors.

Author contributions

Conception or design of the work; or the acquisition, analysis, or interpretation of data for the work: MNIM, MRH, MH. *Drafting the work or reviewing it critically for important intellectual content:* MRH, MNIM. *Final approval of the version to be published: MMI, MHKS, SP, MNP. Accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved:* MNM.

Conflict of interest

We do not have any conflict of interest.

Data availability statement

We confirm that the data supporting the findings of the study will be shared upon reasonable request.

Supplementary file

None

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Bangabandhu Sheikh Mujib Medical University Journal 2025;18(1):e76754
ISSN 2074-2908 | eISSN 2224-7750 |

RESEARCH ARTICLE

Expression of BRCA1 mRNA in cancerous and non-cancerous breast tissue of Bangladeshi females attending a tertiary care hospital

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Publication history
Received: 9 Oct 2024
Accepted: 5 Feb 2025
Published online: 13 Feb 2025

Responsible editor
M Mostafa Zaman
0000-0002-1736-1342

Reviewers
F: Md. Fazlul Karim
0009-0008-5065-1887
G: Md. Jahirul Islam
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Keywords
BRCA1 mRNA expression, breast cancer, fibroadenoma, FFPE cancerous and non-cancerous breast tissue

Funding
Funded by Bangabandhu Sheikh Mujib Medical University, Memo No. BSMMU/2022/833, dated 26 Jan 2022.

Ethical approval
IRB of Bangabandhu Sheikh Mujib Medical University (No. BSMMU/2021/9244, dated 9 Oct 2021)
Ethics Committee of National Institute of Cancer Research and Hospital (No. NICRH/Ethics/2021/345 dated 29 Nov 2021).

Trial registration number
Not applicable

Abstract

Background: Dysfunctions of the BRCA1 (BReast CAncer gene1) gene are reported in cancerous and non-cancerous breast lesions. BRCA1 mRNA expression is variable in breast cancer, while this information is still inadequate in non-cancerous breast disorders. This study aimed to measure BRCA1 mRNA expression in cancerous and non-cancerous breast tissue of Bangladeshi females.

Methods: The cross-sectional study was conducted on 50 breast cancer and 19 non-cancerous females. RNA was extracted from formalin-fixed paraffin-embedded breast tissue. Real-time RT-PCR was done for measuring BRCA1 mRNA. BRCA1 mRNA expressions in cancerous and non-cancerous breast tissue were compared and analysed.

Results: BRCA1 mRNA expression was reduced or absent in most of the cancerous and non-cancerous (consisting of fibroadenoma, fibrocystic disease, ductal hyperplasia and normal breast tissue) breast tissue. Expression of BRCA1 in breast cancer and fibroadenoma was almost similar statistically. All cancers were invasive ductal carcinoma and of grade II, and most of them were sporadic (86%). BRCA1 expression was not associated with reproductive or cancer-related characteristics except consanguinity of marriage. The non-cancerous females were younger than the cancer patients (33.5 versus 43 years, respectively).

Conclusion: The study suggests the necessity of bringing fibroadenoma patients, in addition to breast cancer patients, into the screening programme and analysing the molecular profile because their BRCA1 expression is similar.

Key messages

BRCA1 mRNA expression was reduced or absent in most cancerous and non-cancerous breast tissue. Its expression was similar in both breast cancer and fibroadenoma of the breast. BRCA1 expression may be used for screening of fibroadenoma, fibrocystic disease and ductal hyperplasia of breast to prevent their progression to cancer.

Introduction

Breast cancer is one of the leading causes of cancer-related death worldwide; new cases and breast cancer -induced deaths are more rapidly increasing in the low-and-middle-income countries than in developed countries, and about 6.9% of cancer deaths are reported worldwide due to this cancer [1]. Genetic mutations, environmental factors, obesity and lifestyle changes are associated with the occurrence and prognosis of breast cancer. The incidence of this cancer in Asia is rising substantially due to increased life expectancy along with population growth and acceptance of the Western lifestyle [2, 3].

Mutations in the BRCA1 gene are found to be associated with breast cancer, and the frequency of these genetic mutations varies among ethnic groups and countries [2]. Methylation in BRCA1 promoter region, low expression, and copy number deletions also cause deficiency in BRCA1 and produce similar phenotypic features of tumours due to BRCA1 mutations [4, 5]. Dysfunction of this gene is associated with ovarian, prostatic, gastric and pancreatic cancers in addition to breast cancer [6, 7].

BRCA1 is a DNA repair gene. Its mRNA is expressed at the late G1/early S phase of the cell cycle before DNA synthesis. Expression of the BRCA1 protein closely follows its mRNA. Deficiency in this gene produces low expression of BRCA1 mRNA. Recent studies have shown that BRCA1-related breast cancers have clinico-pathological features that are usually associated with a poor prognosis, such as high -grade oestrogen receptor (ER) and progesterone receptor (PR) negative status, and over expression of the Her-2-Neu [8]. Studies also found that the expression of BRCA1 mRNA influences the effectiveness of chemotherapy and helps in the prediction of survival of the patients [9].

Other than breast cancer, BRCA1 gene mutations are found to be present in some benign non-cancerous breast lesions. Among the breast pathologies, most of the breast lesions are benign. A survey of literature from 1985 to 2019 found around 50% of clinical breast lesions were mastalgia and fibrocystic disease, and 25% were fibroadenomas [10].

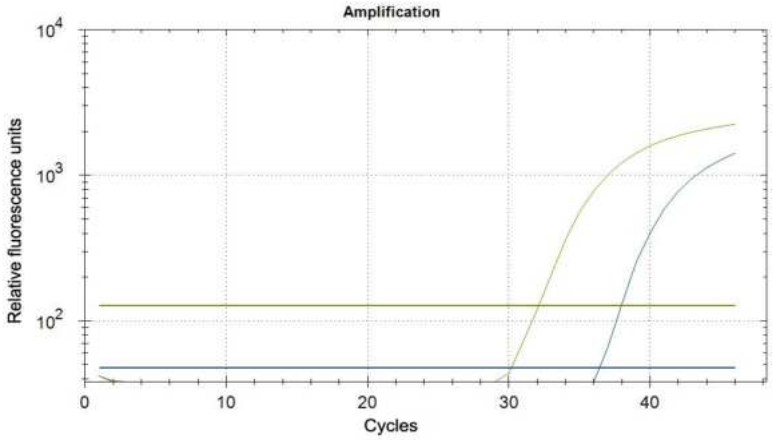

Figure 1 **Amplification curve of BRCA1 (blue) and glyceraldehyde-3-phosphate dehydrogenase (GAPDH) (green) in log scale of a formalin-fixed paraffin-embedded breast cancer tissue sample**

Benign breast diseases are evidenced as a risk factor for breast cancer, and the risk is higher with BRCA1 mutations [11].

Although high-income countries have achieved significant progress toward curing women with breast cancer, Bangladesh, like other low-and-middle-income countries, is now starting to recognise the extent and severity of the disease [3]. Breast cancer is the second most common cancer irrespective of gender in Bangladesh, and it is the leading cancer (29.3%) in females, according to a hospital-based cancer registry report [12]. Among the non-cancerous breast lesions, fibroadenomas are also more frequently reported in females of Bangladesh [13]. In this prevailing condition, there is still a paucity of information regarding the molecular characteristics of these breast disorders, including the expression of BRCA1 mRNA in Bangladeshi females.

The aim of this study was to measure the expression of BRCA1 mRNA in cancerous and non-cancerous breast tissue of Bangladeshi females. Thus, this research can provide the opportunity to improve the understanding of the molecular behaviour of breast cancer as well as non-cancerous breast lesions in this population for adopting appropriate therapeutic measures and predicting the prognosis of these diseases.

Methods

This was a cross-sectional study carried out in the Department of Anatomy, Bangabandhu Sheikh Mujib Medical University (BSMMU) from January to December 2022. Molecular tests were done in the Department of Immunology and Molecular Biology laboratory of the National Institute of Cancer Research and Hospital (NICRH), Mohakhali, Dhaka. A memorandum of understanding between the authorities of the concerned departments of BSMMU and NICRH was signed for this research.

Bangladeshi females with breast cancer and benign breast disorders attending NICRH participated in this research. The names and mobile numbers of the histologically diagnosed breast cancer patients and non-cancerous females with benign breast lesions from January 2021 to September 2022 were collected from the register of the Department of Histopathology of NICRH. Inclusion criteria were Bangladeshi female, aged 18 years or above, (i) for breast cancer patient: histologically diagnosed as breast cancer patients; (ii) for females with benign breast disorders: histologically diagnosed as non-cancerous patients with benign breast lesions. Exclusion criteria were having a history of other cancers and chemo or radiotherapy before FFPE block preparation.

Formalin-fixed paraffin-embedded (FFPE) cancerous and non-cancerous breast tissue blocks were collected from the Department of Histopathology of NICRH. A list of 915 breast cancer patients and 126 females with non-cancerous breast lesions was obtained during this period. Among them, 62 breast cancer patients (based on recently prepared tissue blocks) and 27 non-cancerous females (out of 68 available FFPE tissue blocks which had sufficient breast tissue) with benign breast lesions were invited to participate in this study. Fifty (50) breast cancer

patients and 19 non-cancerous females were finally selected from them based on quality and quantity of cancerous and non-cancerous breast tissue in the paraffin blocks (assessed by the histopathologist). Reproductive and cancer-related characteristics were collected from the participants through interviews and from hospital and medical records. BRCA1 mRNA expression in cancerous and non-cancerous breast tissue was measured and compared.

Isolation of RNA

The RNA extraction was done from four (10 µm thick) sequential sections of FFPE breast tissue using a commercial RNA extraction kit (PureLinkTM FFPE total RNA isolation kit, invitrogen by Thermo Fisher Scientific, USA) according to the manufacturer's instruction. The quality and quantity of the extracted RNA was checked by Eppendorf BioPhotometerTM D30 (Eppendorf AG, Germany).

Synthesis of cDNA

The first-strand cDNA synthesis was done by reverse transcription of RNA using Viva cDNA synthesis kit (Vivantis Technologies, Malaysia) according to the manufacturer's protocol. Random hexamer primers were used for cDNA synthesis.

Amplification of cDNA by real-time PCR

Template cDNA was amplified using the CFX96 Bio-Rad Touch Real-Time PCR (Bio-Rad Inc., USA). At first, 18 µl of the reaction mixture was prepared by adding 10 µl of Hot Star Taq Plus Master Mix (Qiagen, USA), 1µl of forward and 1 µl of reverse primers of each of the BRCA1 and GAPDH genes, 1 µl of probes of BRCA1 and 1 µl of probes of GAPDH gene and 2 µl of nuclease -free water. GAPDH was used as a reference gene. Then PCR mixture was prepared by adding 2µl of cDNA and 18 µl of reaction mixture. After that, amplification was performed in a 96-well optical plate at 95°C for 5 minutes, followed by 45 cycles at 94°C for 30 sec, 60°C for 30 sec and 72°C for 1 minute. Real-time PCR was done to measure the expression of these genes. In this study primers and probes for the wild BRCA1 and GAPDH genes were adopted from Egawa *et al.* [14]. The primers and probes were as follows: BRCA1 forward primer 5′-ACAGCTGTGTGGTGCTTCTGTG-3′, reverse primer 5′-CATTGTCCTCTGTCCAGGCATC-3′ and probe FAM-CATCATTCACCCTTGGCACAGGTGT-3′. GAPDH forward primer 5′-TCATTGACCTCAACTACATGGTTT-3′ and reverse primer 5′- GAAGATGGTGATGGGATTTC -3′ and probe JOE-CAAGCTTCCCGTTCTCAGCC-TAMRA.

Table 1 BRCA1 mRNA expression status in cancerous and non-cancerous breast tissue

Types of breast tissue	BRCA1 expression status, number (%)	
	Expressed (n=16)	Not expressed (n=34)
Cancerous tissue (n=50)	16 (32.0)	34 (68.0)
Non-cancerous tissue (n=19)	7 (36.8)	12 (63.2)
Fibroadenoma	3 (16.0)	7 (37.0)
Fibrocystic disease	1 (5.0)	1 (5.0)
Ductal hyperplasia	-	1 (5.0)
Fibrocystic disease with ductal hyperplasia	1 (5.0)	3 (16.0)
Normal breast tissue	2 (10.5)	-

Real-time PCR analysis for the expression of BRCA1mRNA

The expression of the BRCA1 gene was calculated from the quantified cycle threshold (Ct) value. For each sample, the Ct values of BRCA1 and GAPDH were determined (Figure 1). The ∆Ct of BRCA1 was obtained by the formula ∆Ct = Ct of BRCA1 - Ct of GAPDH to calculate the difference. Gene expression level in a given sample was represented as $2^{-\Delta\Delta Ct}$.

Data analysis

Statistical analysis was done using SPSS, version 25, 2017. Expression levels of BRCA1 mRNA in cancerous and non-cancerous breast tissue were compared using the *t* test and, Mann-Whitney U test, as appropriate. The association between BRCA1 mRNA expression status and reproductive and cancer-related characteristics was determined using Chi-square or Fisher's Exact test, as appropriate. All statistical tests were two-sided, and a $P<0.05$ was considered statistically significant.

Ethical concerns

The study was conducted after ethical approval was obtained from the Institutional Review Board of BSMMU and NICRH. Informed written consent was taken from the participant before data collection. Participation in this study was entirely voluntary, and the participants were assured that they would maintain the confidentiality and anonymity of data and that they would have the right to withdraw their participation at any time. The sample was taken from the previously prepared FFPE tissue blocks; thus, there was no chance of injury during sample collection. Permission was obtained from the participants to publish the findings anonymously in seminars, workshops, or journals.

Results

BRCA1 mRNA was expressed in 16 (32%) breast cancer patients in reduced amounts and seven (37%) non-cancerous females. The non-cancerous breast tissue consists of fibroadenoma, fibrocystic disease, ductal hyperplasia and fibrocystic disease with ductal hyperplasia and normal breast tissue. Among the non-cancerous females, BRCA1 expression was observed in three patients (out of 10) with fibroadenoma in reduced amounts, two with normal breast tissue and the others with fibrocystic disease of the breast (Table 1). BRCA1 mRNA expression level ($2^{-\Delta\Delta Ct}$ value) was not significantly different in the cancerous and non-cancerous breast tissue (Figure 2).

Association between the expressions of BRCA1 mRNA in breast cancer tissue and selected reproductive and cancer-related characteristics were analysed (Table 2). BRCA1 mRNA expression was not associated with reproductive and cancer-related characteristics except for consanguinity of marriage ($P=0.03$). Association between the expression of BRCA1 and the histological type and grade of breast cancer was not done, as all breast cancers were in invasive ductal carcinoma and of grade II.

In this study, the majority of the breast cancers were diagnosed at or below the age of 45 years. Most of the cancers were sporadic or non-familial (86%), family history of cancers was reported in seven

patients. Lymph node metastasis was present in almost all patients (96%), whereas distant metastasis was reported in 4 (8%) patients. Hormone receptor negativity was reported in most of the patients (Table 2).

Reproductive characteristics of the breast cancer patients and females with non-cancerous benign breast disorders were not statistically different except the age; the non-cancerous females were relatively younger (mean age 33.5 years) than the cancer patients (mean age 43 years). A comparison of the reproductive characteristics of the participants is shown in Table 3.

Discussion

In this research, the BRCA1 mRNA expression status of breast cancer patients and females with non-cancerous breast lesions was not statistically different. The probable reason might be the presence of 10 fibroadenoma patients out of 19 non-cancerous females. Malignant transformation of fibroadenoma is very rare; only about 100 cases of breast cancer have been reported to arise from this benign lesion worldwide [15]. Burnetti *et al.* found a BRCA1 mutation in a patient with fibroadenoma, which progresses to triple-negative breast cancer [16]. Another case was reported in the USA where carcinoma in situ progressed from multiple bilateral fibroadenomas with BRCA1 mutation [17]. Mutation in the BRCA1 gene is responsible for reduced or absent expression of BRCA1 mRNA [18]. This finding of our research signifies the importance of analysing the mutation profiles of the BRCA1 gene in fibroadenoma patients in addition to breast cancer.

BRCA1 protein is required for the prevention of breast transformation. BRCA1 expression status in non-cancerous benign breast lesions indicates the malignant potential of the breast. Non-expression or reduced expression of this gene in non-cancerous benign lesions requires close monitoring and follow-up, as inactivation of BRCA1 causes blunted ductal development, breast hyperplasia and tumour formation [19]. We have few non-cancerous patients other than fibroadenoma. They were histologically diagnosed as fibrocystic disease, ductal hyperplasia and the concomitant presence of fibrocystic disease with ductal hyperplasia. Non-expression of BRCA1 mRNA was observed more in patients with concomitant presence of fibrocystic disease with ductal hyperplasia in our study. This finding also warns us to keep close monitoring of the patients with non-cancerous benign breast disorders.

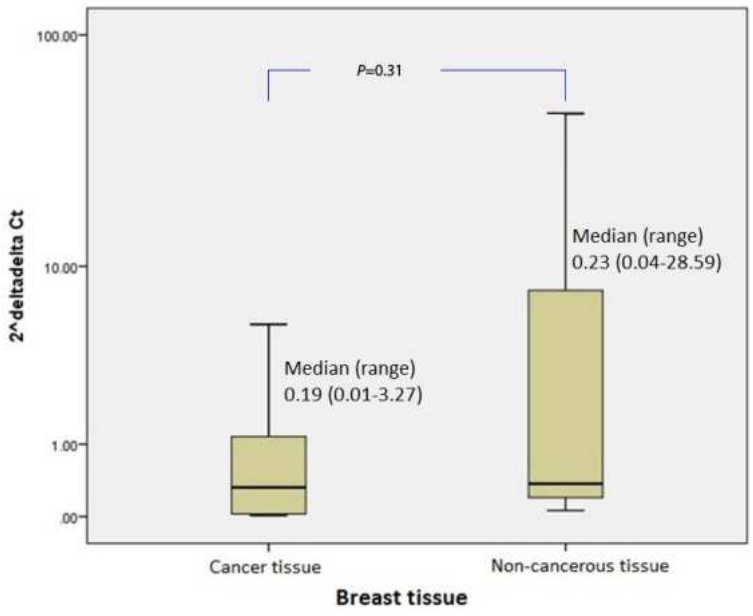

Figure 2 BRCA1 mRNA ($2^{-\Delta\Delta Ct}$ value) expression level in cancerous and non-cancerous breast tissue

Table 2 Association between the expression of BRCA1 mRNA and reproductive and cancer-related characteristics of the breast cancer patients (n=50)

Reproductive and cancer-related characteristic	BRCA1 expression status, number (%)		*P*
	Expressed (n=16)	Not expressed (n=34)	
Age at diagnosis (years)			
28–45	8 (50.0)	26 (76.5)	0.06
46–69	8 (50.0)	8 (23.5)	
Body mass index (kg/m²)			
18.5–24.9	11 (68.8)	19 (55.9)	0.39
≥25	5 (31.2)	15 (44.1)	
Age at menarche (years)			
12–13	15 (93.8)	26 (76.5)	0.24
14–15	1 (6.2)	8 (23.5)	
Age at menopause (years) (n=19)			
37–44	2 (25.0)	5 (45.5)	0.63
45–58	6 (75.0)	6 (54.5)	
History of consanguinity of marriage			
Yes	4 (25.0)	1 (2.9)	0.03
No	12 (75.0)	33 (97.1)	
Number of children			
1–2	11 (68.8)	26 (76.5)	0.73
3–5	5 (31.2)	8 (23.5)	
Duration of breastfeeding (years)			
1–2	4 (25.0)	7 (20.6)	0.73
>2	12 (75.0)	27 (79.4)	
Duration of contraceptive use (years)			
Never used	1 (6.2)	6 (17.6)	0.21
1–5	7 (43.8)	19 (55.9)	
≥6	8 (50.0)	9 (26.5)	
Family history of cancer			
Positive	1 (6.2)	7 (20.6)	0.41
Negative	15 (93.8)	27 (79.4)	
Lymph node metastasis			
Present	15 (93.8)	33 (97.1)	0.54
Absent	1 (6.2)	1 (2.9)	
Other organ metastasis			
Present	1 (6.2)	3 (8.2)	0.99
Absent	15 (93.8)	31 (91.8)	
Her-2/Neu (n=49)			
Positive	5 (33.3)	9 (26.5)	0.62
Negative	10 (66.7)	25 (73.5)	
Oestrogen receptor (n=49)			
Positive	4 (26.7)	5 (14.7)	0.43
Negative	11 (73.3)	29 (85.3)	
Progesterone receptor (n=49)			
Positive	3 (20.0)	5 (14.7)	0.69
Negative	12 (80.0)	29 (85.3)	

Table 3 Reproductive characteristics of the participants

Reproductive characteristic	Breast cancer patient (n=50)	Non-cancerous female (n=19)	*P*
Age (years)[a]	43.0 (9.5)	33.5 (10.0)	0.001
Body mass index (kg/m^2)[a]	24.4 (3.5)	24.2 (3.0)	0.98
Age at menarche (years)[a]	12.8 (0.8)	13.0 (0.7)	0.80
Menstrual status, n (%)			
Menstruating	31.0 (62.0)	16.0 (84.2)	0.13
Postmenopausal	19.0 (38.0)	3.0 (15.8)	
Age of menopause (years)[a]	45.2 (4.6)	43.3 (5.7)	0.63
Consanguinity of marriage, n (%)			
Yes	5.0 (10.0)	1.0 (5.3)	0.99
No	45.0 (90.0)	18.0 (94.7)	
Number of children[b]	2.0 (1.0–5.0)	2.0 (1.0–3.0)	0.56
Total duration of breast feeding (years)[b]	3.0 (1.5–8.0)	3.0 (2.0–6.5)	0.79
Use of contraceptives, n (%)			
No	7.0 (14.0)	4.0 (21.0)	0.48
Yes	43.0 (86.0)	15.0 (79.0)	
Duration of contraceptive use (years)[b]	5.0 (1.0–20.0)	6.0 (1.0–14.0)	0.28

[a]Mean and standard deviation; [b]Median and range

In our study, BRCA1 was expressed in 32% of breast cancer patients. Al Mullah *et al.* observed BRCA1 mRNA expression in 21% of EEPE tissue block. They also observed that the reduced or no expression of BRCA1 mRNA was more in the high histological grade of the tumour [20]. Taylor *et al.* found reduced expression of BRCA1 in non-familiar breast cancer and non-expression in 20% of non-familiar and 20% of familial breast cancer patients. They conducted the research on 142 non-familiar, 25 familial breast cancer patients and 28 non-cancerous females with fibrocystic disease, fibroadenoma and normal breast tissue [21]. In their study, mutation was reported in breast cancer patients with a family history of cancers and loss of heterozygosity (LOH) was reported in non-familial patients. If the normal functional allele of BRCA1gene is lost in LOH, this gene will exhibit non-expression. Silvia *et al.* reported 47% of LOH in the BRCA1 region (17q21) in patients with breast cancer [22]. In addition to LOH, hypermethylation is another cause of non-expression of the BRCA1 gene in breast cancer. The CpG islands of the promoter regions of tumour suppressor genes are usually unmethylated, and hypermethylation or abnormal methylation of these sites causes non-expression of those genes [23]. Hypermethylation at these sites of BRCA1 causes the inactivation of this gene, known as LOH. Esteller *et al.* found hypermethylation in the promoter region of the BRCA1 gene in 13% of primary breast cancer. That study also noticed abnormal methylation was more common in patients with breast cancer at or below the age of 45 years, and it was present in grade II or III invasive ductal carcinoma [24]. Therefore, considering the cancer-related characteristics of our participants, we can assume abnormal methylation or LOH might be a cause of reduced or non-expression of BRCA1 mRNA in our patients.

Taylor *et al.* did not find any correlation of BRCA1 expression with age, menopausal status, hormonal status, histological type and tumor size [21]. Li *et al.* also did not find any association between BRCA1 mRNA expression and clinicopathological characteristics of the breast cancer patients [5]. Our finding is consistent with the findings of these literature.

In our study association was found betweenBRCA1 mRNA expression and breast cancer patients with family history of consanguinity. The progeny of the consanguineous couples has more chance to get homozygous alleles. Thus, the frequency of genetically determined diseases in offspring of consanguineous parents is influenced by the homozygosity of the genes responsible for that conditions [25]. The frequency of breast cancer among the daughters of consanguineous parents varies in different populations. Studies on Pakistani, Croatian and North American population found that the younger women of parents with first-cousin marriages have increased risk of developing breast cancer, whereas, several studies conducted on Arab, North African and non-Jew Israeli population found low incidence of breast cancer in daughters of consanguineous parents [26–28]. Medimegh *et al.* conducted a study on Tunisian breast cancer patients and did not find homozygosity in BRCA1 haplotypes in consanguineous patients with familial breast cancer. They reported more BRCA1 haplotypes homozygotes in healthy consanguineous controls and more heterozygotes in non-consanguineous group. They explained their findings by the facts that there were three possible genotypes in consanguineous families: the first- without mutations gave healthy progeny, the second- with deleterious mutations at heterozygote state and caused breast cancer and the third- the deleterious mutations at homozygote state which was lethal [25]. Mice model studies proved the lethal effects of BRCA1 knockout homozygotes [29], [30]. Moreover, a computer simulated study on the consequences of long term practice of consanguineous marriage on the prevalence of lethal cancer genes found that mutation carrier rate of BRCA1/2 genes decreased six times faster in a highly consanguineous population than non-consanguineous population if spontaneous abortion and gene flow were considered to be absent [31]. From the above-mentioned findings we can assume that the patients from consanguineous parents have factors other than BRCA1 gene responsible for tumourogenesis.

Estimation of BRCA1 expression in breast cancer is important for selection of effective chemo and targeted therapy. Studies found that the cancer cells deficient of BRCA1 or BRCA2 genes are more sensitive to PARP1 inhibitors whereas the cells with normal BRCA expression are unaffected by these drugs [32]. Estimation of BRCA1 expression is required for BRCA replacement therapy.

Limitations

Relatively small number and heterogeneity of non-cancerous females with benign breast disorders may reduce the strength of interpretation of BRCA1 expression status in non-cancerous breast tissue.We found 126 females with non-cancerous benign breast lesions and 915 breast cancer patients in the register of the Department of Histopathology, NICRH during this period. Usually surgery is not done in patient with non-cancerous breast lesions unless it is highly susceptible to malignancy. FNAC (fine needle aspiration cytology) or core biopsy is done for

diagnosis. Redundancy operation of breast is also very low in Bangladesh. Therefore, getting normal breast tissue block is less likely. Inspite of this limitation, we used FFPE tissue blocks, because gene expression status due to somatic and germ line mutations is yielded from the tissue. We included available all (68) FFPE blocks of non-cancerous breast lesions, 27 of which had sufficient amount of breast tissue and ultimately genetic analysis was possible from 19 samples. Among the breast cancer patients, all cancers were invasive ductal carcinoma and of grade II, thus comparison of BRCA1 expression in different types and histological grades was not possible.

Conclusion

This study revealed similar type of BRCA1 expression in breast cancer and fibroadenoma patients. This finding indicates the importance to bring the fibroadenoma patients under screening to prevent progression of cancer by appropriate and timely intervention. This study also suggests more research for analyzing the molecular profile to find out the LOH and methylation pattern of promoter region of BRCA1 gene other than mutations of breast cancer patients as well as fibroadenoma even though it is marked as a benign breast disease.

Acknowledgments

We thank the colleagues of the Department of Anatomy, Bangabandhu Sheikh Mujib Medical University and the National Institute of Cancer Research and Hospital, Bangladesh for providing the infrastructure, and other research facilities. We also express our gratitude to the patients participated in our research.

Author contributions

Conception or design of the work; or the acquisition, analysis, or interpretation of data for the work: LN, SHZR, FA, ZAY, LN, UHL, SSA, FA. *Drafting the work or reviewing it critically for important intellectual content:* LN, SHZR, FA, ZAY, LN, UHL, SSA, FA. *Final approval of the version to be published:* LN, SHZR, FA, ZAY, LN, UHL, SSA, FA. *Accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved:* LN, SHZR, FA.

Conflict of interest

We do not have any conflict of interest.

Data availability statement

We confirm that the data supporting the findings of the study will be shared upon reasonable request.

Supplementary file

None

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Bangabandhu Sheikh Mujib Medical University Journal 2025;18(1):e75339
ISSN 2074-2908 | eISSN 2224-7750 |

RESEARCH ARTICLE

Effect of hypnotherapy on paediatric cancer pain management in Indonesia: A quasi-experimental study

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Abstract

Background: Paediatric cancer patients often experience pain related to their condition and treatment. Hypnotherapy, a non-pharmacological intervention, has shown promise in pain management. This study aimed to investigate the effects of hospital-based hypnotherapy on pain reduction in paediatric cancer patients.

Methods: A pretest-posttest experimental design without a control group was done with 60 paediatric cancer patients (ages 6–12) at Central General Hospital, Dr. Kariadi Semarang, Indonesia, from February to May 2024. Pain levels were assessed using the visual analogue scale (scores from 0 to 10) at the baseline, after two follow-up sessions at a week interval. Pain scores were recorded starting from 0 to 10. These were categorised as no score 0, mild (1–3), moderate (4–6) and severe (7–10) pain. Pain scores were compared using ANCOVA, but pain categories were compared using the chi-square test.

Results: The mean age of the subjects was 8.8 (standard deviation, 4.2) years; 60% were boys. Hypnotherapy significantly reduced pain scores from a baseline mean score of 4.7 to 0.7 at the second assessment (P<0.001). Severe pain (13.3%) declined to 0%, and conversely, no pain category (0%) increased to 51.7% (P<0.001).

Conclusion: Hypnotherapy at hospital significantly reduces pain in paediatric cancer patients. Therefore, hypnotherapy could be a valuable adjunct to conventional pain management strategies in paediatric oncology.

Key messages

Paediatric cancer patients often face treatment-related pain, ranging from mild to severe grades. Hypnotherapy is known to have some role in pain mitigation. In a hospital-based sample of patients, we observed that hypnotherapy substantially decreases pain intensity. Therefore, hypnotherapy should be considered to complement conventional non-pharmacological pain management strategies in paediatric oncology.

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Publication history
Received: 5 Aug 2024
Accepted: 25 Nov 2024
Published online: 2 Feb 2025

Responsible editor
M Mostafa Zaman
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Reviewer
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Keywords
hospital-based hypnotherapy, pain, children, cancer, oncology

Funding
This study was funded by STIKES Telogorejo Semarang.

Ethical approval
Approved by the research ethics committee of RSUP Dr Kariadi Semarang (No: 1647/EC/KEPK-RSDK/2023) on 15 Dec 2023.

Trail registration no.
None

Introduction

The incidence of paediatric cancer is gradually increasing.[1] Cancers occur in every location irrespective of their economic conditions: developed, developing or underdeveloped. In Indonesia, cancer is the seventh leading cause of death, with paediatric cases presenting unique challenges to the healthcare system.[2] In Indonesia, cancer and tumours account for 5.7% of all causes of mortality, making them the seventh most common cause of death. One of the most distressing symptoms experienced by children with cancer is pain, which can stem from the disease itself, treatment side effects, or associated procedures.[3]

Effective pain management in paediatric cancer patients is crucial for improving quality of life and potentially influencing treatment outcomes.[4] While pharmacological interventions are the mainstay of pain management, they often come with side effects and may not address the multidimensional nature of cancer-related pain.[5] As a result, there is growing interest in complementary approaches to pain management, including non-pharmacological interventions.[6] Nurses can assist patients by employing complementary medicine practices. Relaxation techniques are the most critical non-pharmacological intervention for pain management.[6]

Hypnotherapy, a technique involving focused attention and increased suggestibility, has shown promise in managing various types of pain in both adult and paediatric populations.[7] By potentially modulating pain perception and reducing anxiety, hypnotherapy could offer a valuable tool in the comprehensive management of cancer-related pain in children.[8] The function of the hypothalamus is to reduce the activity of the sympathetic nervous system and release catecholamines; relaxation can reduce muscle tension and the dangerous physiological effects of stress, such as high blood pressure, tachycardia, and muscle spasms. Since the seventh century, hypnotherapy has been used as a standard approach to psychotherapy. However, the efficacy of hypnotherapy for pain management in paediatric cancer patients, particularly in the Indonesian context, remains underexplored. Therefore, this study aimed to investigate the association between hospital-based hypnotherapy and pain reduction in paediatric cancer patients at a tertiary care hospital in Indonesia.

Methods

Study design, setting and participants

A quasi-experimental (pretest-posttest) study without a control group was conducted at the Paediatric Oncology Unit of Central General Hospital, Dr. Kariadi Semarang, Indonesia, from February to May 2024. Sixty paediatric cancer patients aged 6-12 were recruited using convenience sampling. Inclusion criteria were a cancer diagnosis, cancer-related pain, and the ability to communicate and follow the therapists' instructions. The consent of the parents and the children was obtained before enrolling in the study.

Data collection techniques

Data on age, gender, cancer types, and duration of treatment were collected. Before each hypnotherapy session, participants underwent a pain assessment using the facial expression images from the Baker-Wong Faces[9] but recorded using the visual analogue scale (VAS) scores (0–10). The advantages of using this measuring instrument are that it is the most sensitive method for measuring pain intensity, is easy to make, has a good correlation with other measurement scales, can measure all types of pain, and is applied to all patients. Pain is measured by observation and asking patients about their pain. The scores obtained are categorised as follows: no pain, 0; mild pain (can still be tolerated, activities are not disturbed), 1-3; moderate pain (interferes with activities), 4-6; severe pain (unable to carry out activities independently), 7-10. The VAS pain scale was valid with r = 0.62 and reliable with Cronbach's alpha 0.95.

Trained and certified hypnotherapists experienced in paediatric care conducted all pain assessments to minimise bias. The sessions were conducted in a quiet, comfortable room within the Paediatric Oncology Unit to ensure privacy and reduce external distractions. Each session lasted for 30 minutes. Assistants were trained to adequately to administer the scale, including explaining it to children to record responses accurately. The same therapist conducted pre- and post-session assessments for each participant using the same tool to ensure consistency. Two sessions of hypnotherapy were done one week apart for each participant. The hypnotherapy protocol had four main components. The induction phase utilised a progressive relaxation technique, guiding participants to relax different body parts gradually. This was followed by a deepening phase, where participants were led on an imaginary journey to a safe, comfortable place of their choice. The therapeutic suggestion phase included positive affirmations for pain reduction, comfort, and healing imagery tailored to the paediatric context. Finally, the emergence phase involved a gradual return to full awareness, with suggestions for continued comfort and well-being. The hypnotherapist used age-appropriate language and imagery throughout the session to ensure the intervention was engaging and understandable for this age group.

Ethical concerns

Upon being provided with detailed information regarding the study, all volunteers proceeded to affix their signatures on a written consent form. They were assured that rejecting participation in the study would not affect their professional status, and their data would be kept confidential and anonymous.

Statistical analysis

Data were analysed using SPSS version 26.0. Descriptive statistics (numbers and percents) were used to summarise participant characteristics (sex, education, cancer types, and pain categories). Pain categories were compared using chisquare test. ANCOVA was done to get the adjusted VAS scores for three sessions (pre-, post-1, and post-2). Adjustment was made for age and sex. $P<0.05$ was considered statistically significant.

Results

The mean age was 8.8 years (standard deviation 2.4). The most common cancer diagnosis was acute lymphoblastic leukaemia (55%), followed by retinoblastoma (8.3%), acute myeloid leukaemia (6.7%), and non-Hodgkins lymphoma (6.7%) (Table 1). Hypnotherapy significantly reduced adjusted pain scores from a baseline mean score of 4.7 to 0.7 at the second assessment (P<0.001). Severe pain (13.3%) declined to 0%, and conversely, no pain (0%) increased to 51.7% (P<0.001) (Table 2).

Table 1 Characteristics of cancer child at the paediatric oncology unit of Central General Hospital, Dr. Kariadi Semarang, Indonesia (n=60)

Categories	Number (%)
Sex	
Male	36 (60.0)
Female	24 (40.0)
Age in years[a]	8.8 (4.2)
Education	
Pre-school	20 (33.3)
Elementary school	24 (40.0)
Junior high school	16 (26.7)
Cancer diagnoses	
Acute lymphoblastic leukemia	33 (55)
Retinoblastoma	5 (8.3)
Acute myeloid leukemia	4 (6.7)
Non-Hodgkins lymphoma	4 (6.7)
Osteosarcoma	3 (5)
Hepatoblastoma	2 (3.3)
Lymphoma	2 (3.3)
Neuroblastoma	2 (3.3)
Medulloblastoma	1 (1.7)
Neurofibroma	1 (1.7)
Ovarian tumour	1 (1.7)
Pancreatic cancer	1 (1.7)
Rhabdomyosarcoma	1 (1.7)

[a]Mean (standard deviation)

Discussion

This study demonstrates a significant reduction of pain in paediatric cancer patients (aged 6–12) with hospital-based hypnotherapy in an Indonesian tertiary care setting. This suggests that hypnotherapy could be a valuable adjunct to conventional pain management strategies in paediatric oncology. Previous research indicates that hypnotherapy substantially diminishes sensory and emotional pain perceptions, facilitating effective pain management for patients and thereby significantly alleviating discomfort in cancer patients.[10] Our findings align with previous research on the efficacy of hypnotherapy for pain management in various clinical contexts.[11] The significant pain reduction observed in our study may be attributed to several factors.[12] First, hypnotherapy can modulate pain perception through multiple mechanisms, including altering sensory processing and reducing anxiety.[13] Second, the age group of our participants (6-12 years) may be particularly receptive to hypnotic suggestions due to their vivid imaginations.[14]

Our study's strong association between hypnotherapy and pain reduction has important clinical implications. By providing an effective non-pharmacological option for pain management, hypnotherapy could help reduce reliance on analgesic medications, potentially minimising side effects and improving the overall quality of life for paediatric cancer patients.[15] Moreover, as a non-invasive intervention, hypnotherapy could be easily integrated into existing care protocols without significant additional resources.

Hypnotherapy affects the anterior cingulate cortex, affecting the pain experience. Affection modulation will influence the brain's perception of the pain experience to lead to positive coping. Pain cannot be eliminated, but positive coping will enable a person to accept and realise pain more comfortably as the brain's perception changes during the hypnotherapy and post -hypnotherapy process.[16,17,18]Hypnotherapy is a mind-body therapy that has been clinically proven to be effective for pain, chronic pain, and mood disorders. Although hypnotherapy has been suggested to work through a placebo effect, recent research has found that it is a different phenomenon. Like cognitive behavioural therapy, it works on the individual's response to pain; however, unlike cognitive behavioural therapy, new ways of thinking and responding are implanted in the mind through suggestion so that new responses occur automatically rather than being learned or done with difficulty. Although the mechanism of action is not yet fully understood, brain imaging techniques show marked changes in neural activity while under hypnosis. Changes in neural activity are responsible for increased focus, somatic and emotional regulation, decreased self-awareness, and increased capacity to respond to suggestions are characteristic of hypnosis.[19,20]

Limitation

The experimental design without a control group limits our ability to definitively attribute the observed pain reduction solely to the hypnotherapy intervention. Future research using randomised controlled trials would provide stronger evidence of causality. Additionally, while our study demonstrated short-term effects, longer-term follow-up would be valuable to assess the durability of pain reduction and the potential cumulative effects of repeated hypnotherapy sessions. Future studies should also explore the impact of hypnotherapy on other cancer-related symptoms and quality-of-life measures.

Conclusion

This study provides evidence for a significant association between hospital-based hypnotherapy and pain reduction in paediatric cancer patients in Indonesia. While further research is needed to establish causality, these findings suggest that hypnotherapy can be an effective pain management strategy in paediatric oncology care. Future studies should employ more robust designs to confirm these results and explore the long-term effects of hypnotherapy on pain and other symptoms in this vulnerable population.

Table 2 Pain levels before and after (post 1 and post 2) hypnotherapy to cancer children at the paediatric oncology unit of Central General Hospital, Dr. Kariadi Semarang, Indonesia (n=60)

Pain level	Number (%)			*P*
	Pre	Post 1	Post 2	
Mean (SD)[a] pain score	4.7 (1.9)	2.7 (1.6)	0.8 (1.1)	<0.001
Pain categories				
No pain (0)	-	1 (1.7)	31 (51.7)	<0.001
Mild pain (1-3)	15 (25.0)	43 (70.0)	27 (45. 0)	
Moderete pain (4-6)	37 (61.7)	15 (25.0)	2 (3.3)	
Severe pain (7-10)	8 (13.3)	2 (3.3)	-	

[a]Pain scores according to the visual analogue scale raging from 0 to 10; SD indicates standard deviation

Acknowledgments

We thank all participants of this study.

Author contributions

Conception or design of the work; or the acquisition, analysis, or interpretation of data for the work: SHMA, NN, SP, MO. *Drafting the work or reviewing it critically for important intellectual content:* SHMA, SPK. *Final approval of the version to be published:* SHMA, NN, SP. *Accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved:* SHMA.

Conflict of interest

We do not have any conflict of interest.

Data availability statement

We confirm that the data supporting the findings of the study will be shared upon reasonable request.

Supplementary file

None

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Bangabandhu Sheikh Mujib Medical University Journal 2025;18(1):e76559
ISSN 2074-2908 | eISSN 2224-7750 |

RESEARCH ARTICLE

Association of Syndecan-1 immunoexpression with epithelial dysplasia in oral verrucous carcinoma

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Abstract

Background: Oral verrucous carcinoma (OVC) is an uncommon variant of well-differentiated squamous cell carcinoma with an excellent prognosis. Epithelial dysplasia in OVC is a sign of a poorer prognosis. Syndecan-1 immunoexpression is absent in squamous epithelial dysplasia and squamous cell carcinoma. This study aimed to investigate the association between Syndecan-1 immunoexpression and epithelial dysplasia in oral verrucous carcinoma.

Methods: A cross-sectional study was done at the Department of Pathology, Bangabandhu Sheikh Mujib Medical University, from 2021 to 2023 and included 45 cases of histologically diagnosed OVC. Histopathological variables were assessed and Syndecan-1 immunoexpression was determined. Fisher's exact test was done to examine the relationship between the loss of Syndecan-1 and OVC dysplasia.

Results: Out of 45, histologically diagnosed OVC subjects, 66.7% showed no features of epithelial dysplasia, and 33.3% of cases revealed the presence of epithelial dysplasia in routine hematoxylin and eosin stains. The cases which revealed no epithelial dysplasia showed positive expression of Syndecan-1. Among the cases that revealed epithelial dysplasia, 26.7% showed loss of Syndecan-1 expression in the dysplastic area, and 6.7% showed positive expression of Syndecan-1. The loss of Syndecan-1 expression was significantly ($P<0.01$) associated with epithelial dysplasia in OVC.

Conclusion: Syndecan-1 immunostain and routine hematoxylin and eosin stain can help detect epithelial dysplasia in oral verrucous carcinoma. Therefore, early detection of epithelial dysplasia in OVC will help the clinician properly manage the patient.

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Publication history
Received: 30 Sep 2024
Accepted: 24 Feb 2025
Published online: 5 Mar 2025

Responsible editor
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0009-0009-4037-3833

Keywords
oral verrucous carcinoma, epithelial dysplasia, Syndecan-1

Funding
Funded by thesis grant of Bangabandhu Sheikh Mujib Medical University, memo number 1505, dated 14 May 2023.

Ethical approval
Approved by IRB of Bangabandhu Sheikh Mujib Medical University (Memo no. BSMMU/2021/10975, dated 23 Nov 2021).

Trail registration number
Not applicable

Declaration
This article encompasses MD thesis of Dr. Md. Akhtaruzzaman

Key messages

Epithelial dysplasia in oral verrucous carcinoma indicates the increased possibility of transformation into a conventional squamous cell carcinoma. Syndecan-1, also known as CD138, expression of which is absent in epithelial dysplasia of oral verrucous carcinoma and squamous cell carcinoma. Syndecan-1 immunostain, in conjunction with routine hematoxylin and eosin stain, can help to detect epithelial dysplasia in oral verrucous carcinoma.

Introduction

Oral cancer is the sixth most frequent malignancy worldwide [1]. Oral invasive squamous cell carcinomas account for about 90% of reported oral cavity cancers, with a five-year survival rate of around 45% [2]. Oral verrucous carcinoma (OVC) is an uncommon, well-differentiated squamous cell carcinoma variant [3]. It commonly appears in the mucous membrane of the head and neck region, most frequently in the oral cavity and larynx [4]. Risk factors for OVC include alcohol, tobacco, betel nuts, human papillomavirus, and poor oral hygiene [5]. It more commonly affects males over the fifth to sixth decade [4]. Among all primary oral cavity cancers, the reported rate of OVC is 3% worldwide [6]. The prevalence of OVC in Bangladesh is 2.5% [1].

OVC shows grey-white, painless growth that spreads outward and fungates on the oral mucosa. OVC typically lacks the characteristics of epithelial dysplasia. It has a long survival period and better prognosis than conventional squamous cell carcinomas or hybrid verrucous carcinoma. OVC can eventually show epithelial dysplasia, a sign that it is turning into a conventional squamous cell carcinomas . If left untreated, this type of cancer can invade the basement membrane and metastasize [7]. Surgical resection of the primary tumour with adequate margin alone treats OVC, while surgical resection of the tumour with neck dissection and adjuvant radiation therapy if indicated by overall pathologic stage, treats conventional squamous cell carcinomas or OVC with a component of invasive squamous cell carcinomas [8]. Given the differences in treatment protocol and prognosis, it is crucial to diagnose these lesions appropriately [9].

Syndecan–1 is a heparan sulfate proteoglycans, which is also known as CD 138 [10]. It is found in the squamous epithelial cells of various organs, goblet and columnar epithelial cells of the gastrointestinal tract, plasma cells and hepatocytes. It is involved in a number of biological processes such as cellular proliferation, differentiation, adhesion and migration. The downregulation of Syndecan-1 may allow the cells to separate and invade. Keratinocyte differentiation induces the expression of Syndecan-1, which is absent in epithelial dysplasia, squamous cell carcinoma, and OVC, having the features of epithelial dysplasia [11]. Malignant transformation, invasion and metastasis are associated with loss of Syndecan-1 expression [12].

In previous studies, some authors found the presence of epithelial dysplasia in OVC. Significant downregulation of Syndecan-1 expression in epithelial dysplasia was also observed in some studies. However, the expression of Syndecan-1 in OVC in relation to the presence or absence of epithelial dysplasia was not evaluated in previous studies, which we evaluated in our study. The presence of epithelial dysplasia in OVC indicates a worse prognosis and an increased possibility of developing a conventional squamous cell carcinomas if not treated. Detection of epithelial dysplasia in OVC is sometimes difficult when using conventional hematoxylin and eosin stain only. Therefore, Syndecan-1 immunostain in conjunction with traditional hematoxylin and eosin stain can help early detection of epithelial dysplasia in OVC and assist the clinician in properly managing the patient. The objective of this study was to examine the association between the immunohistochemical expression of Syndecan-1 and epithelial dysplasia in OVC.

Methods

We examined 45 paraffin blocks and hematoxylin and eosin stained slides of histologically diagnosed cases of OVC from the Department of Pathology, Bangabandhu Sheikh Mujib Medical University during 2021-2023. We evaluated hematoxylin and eosin stained sections of each case to see the presence of epithelial dysplasia. The following characteristics were considered indicative of epithelial dysplasia: expansion of the basal layer by enlarged or hyperchromatic cells, decreased maturation with enlarged or hyperchromatic nuclei above the basal layers, cytologic atypia or pleomorphism, cells with high nuclear to cytoplasmic ratio above the suprabasal layer and multiple or atypical mitoses above the basal or suprabasal layers [8].

We stained representative sections from the paraffin block with Syndecan-1 antibody using a standard protocol compatible with the DAKO Envision TMFLEX + detection system for immunohistochemistry.

Syndecan-1 immunoreactivity appears as cell membrane staining of squamous epithelial cells. We observed Syndecan-1 immunoreactivity and classified it into two categories: negative/loss of expression and positive expression. Positive expression of Syndecan-1 immunostain in the cell membrane of the squamous epithelial cells of normal oral mucosa was used as positive control and loss of expression of Syndecan-1 immunostain in a diagnosed case of invasive squamous cell carcinoma of oral mucosa was used as negative control.

We coded the participants' paraffin blocks with unidentifiable numbers, such as cases 1 and 2, to prevent bias. Coding was done in every step of data collection. In our study, potential confounding variables were staining processes of hematoxylin and eosin stain and Syndecan-1 immunostain. We were aware of these confounders and addressed them in our research.

Statistical analysis

The statistical analysis was done using SPSS. Descriptive statistics (frequencies and percentages) were used to summarise the patients' data and presented in tables and figures. Fisher's exact test was used to examine the relationship between loos of Syndecan-1 and OVC dysplasia. $P<0.05$ was considered statistically significant.

Results

In this study, 45 histologically diagnosed OVC cases were included. The mean (standard deviation) age of the patients was 60.2 (9.7) years. Females (51.1%) were affected slightly more than males (48.9%).

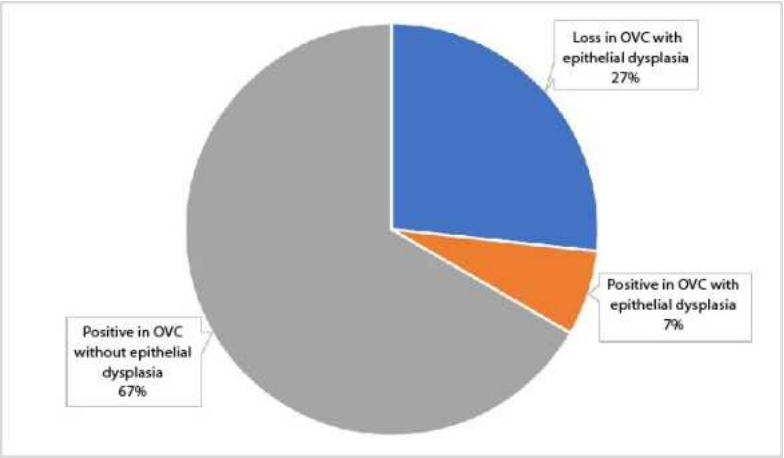

Figure 1 Distribution of the study subjects according to Syndecan-1 expression (n=45). OVC indicates oral verrucous carcinoma.

Right and left buccal mucosa (75.5%) was the most commonly involved site for OVC. Other sites of involvement were the lower lip (11.1%), right and left gingivobuccal sulcus (9.6%) and tongue (4.4%). Most patients presented with an exophytic lesion (51.1%). Other clinical presentations were ulcerative lesions (35.6%), ulcer-proliferative lesions (6.7%) and whitish patches (6.7%). Among the study cases, 44.4% had a history of chewing betel nut, 40% had a history of tobacco smoking, 8.9% had a history of both tobacco smoking and betel nut chewing, and 6.6% cases had poor oral hygiene.

Thirty cases (67%) revealed no epithelial dysplasia in hematoxylin and eosin stain, which showed intact expression of Syndecan-1. Twelve cases (26.7%) revealed loss of Syndecan-1 expression and 3 cases (6.7%) showed intact expression of Syndecan-1 (Figure 1) Hematoxylin and eosin stain in OVC is shown in Figure 2. In this study, all the cases histologically showed hyperkeratosis, parakeratosis, acanthosis, and occasional papillomatosis and extended downwards with broad pushing strands. In most cases, the keratinocytes appeared well differentiated and showed no features of epithelial dysplasia. Statistical analysis showed that loss of Syndecan-1 immunoexpression was associated with the presence of epithelial dysplasia in OVC (Table 1).

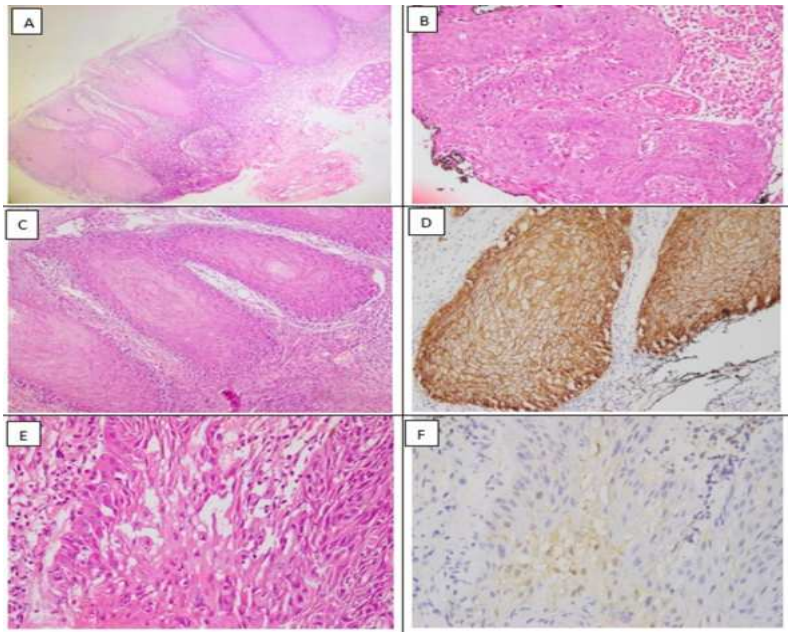

Figure 2 Hematoxylin and eosin stain and Syndecan-1 immunostain in oral verrucous carcinoma: (A) OVC without epithelial dysplasia (4x), (B) OVC with epithelial dysplasia (40x), (C) OVC without epithelial dysplasia (20x), (D) positive Syndecan-1 expression in OVC without epithelial dysplasia (40x), (E) OVC with epithelial dysplasia (40x), and (F) loss of Syndecan-1 expression in OVC with epithelial dysplasia (40x). OVC indicates oral verrucous carcinoma.

Table 1 Number (%) of subjects with or without epithelial dysplasia (n=45)

Loss of Syndecan-1	OVC[b] with dysplasia (n=15)	OVC[b] without dysplasia (n=30)	*P*
Yes	12 (80.0)	0	<0.01[a]
No	3 (20.0)	30 (100.0)	

[a]Fisher's exact test; [b]OVC indicates oral verrucous carcinoma

Discussion

OVC is a rare variant of well-differentiated squamous cell carcinoma. It has an excellent prognosis, indolent clinical behaviour, and a prolonged survival without distant metastases. It typically lacks the characteristics of epithelial dysplasia. However, Some OVCs show epithelial dysplasia without conventional invasive squamous cell carcinomas, and some OVCs have just a minor component of invasive squamous cell carcinomas. Tumours with these limited changes are difficult to diagnose. OVC exhibiting epithelial dysplasia signifies the emergence of a conventional squamous cell carcinomas. If left untreated, this cancerous growth may breach the basement membrane and metastasize [7]. Therefore, evaluation and early detection of epithelial dysplasia in verrucous carcinoma is very important.

In routine hematoxylin and eosin stain, we found 33.3% of cases revealing one or more features of epithelial dysplasia. Sonalika and Anand histopathologically found a proliferation of well-differentiated squamous epithelium without or with minimal atypia in most of the OVC cases in their study. However, they found that 20% of cases showed distinct epithelial dysplasia [13]. In another study, Patel *et al.* found that 44% of cases of OVC had epithelial dysplasia. They found local recurrence in these cases 2–3 times higher than for OVC without having epithelial dysplasia [8]. Syndecan –1 is a heparan sulfate proteoglycan involved in cellular proliferation, differentiation, adhesion, and migration. Loss of Syndecan-1 expression is associated with malignant transformation, invasion and metastasis [12]. We evaluated Syndecan-1 expression immunohistochemically and found a significant number of cases showing loss of Syndecan-1 expression in dysplastic areas. This study found a statistically significant association between a loss of Syndecan-1 immunoexpression and the presence of epithelial dysplasia in OVC. In their study, Daskalopoulos *et al.* found significant downregulation of Syndecan-1 expression in OVC and invasive

squamous cell carcinomas [14]. Soukka *et al.* also found an association between loss of Syndecan-1 immunoexpression and dysplastic changes in oral epithelium in their study [11].

Limitations

The present study has some limitations. We selected the study population from Bangabandhu Sheikh Mujib Medical University only, which may not accurately represent the country. Moreover, the small sample size was a limitation of the present study. As OVC is a rare tumour and our study period was only for two years, we were able to include 45 cases. A larger sample size could be achieved through multicenter study.

Conclusion

In conclusion, a statistically significant loss of Syndecan-1 immunoexpression was found in epithelial dysplasia of OVC. Therefore, the combination of Syndecan-1 immunostain and routine hematoxylin and eosin stain can aid in the detection of epithelial dysplasia in OVC. Epithelial dysplasia in OVC is a significant predictor of the emergence of a conventional squamous cell carcinoma, which, if left untreated, can infiltrate the basement membrane and metastasize subsequently. Therefore, early detection of epithelial dysplasia in OVC can assist the clinician in appropriately managing the patient.

Long-term follow-up of the patients to correlate the expression of this immunomarker with the progression and recurrence of the disease and survival of the patients would be beneficial to establish the role of this biomarker.

Acknowledgments

We gratefully acknowledge all the members of the Department of Pathology, Bangabandhu Sheikh Mujib Medical University, for their help and cooperation. We extend special gratitude to Drs Kassim Hagi Hussain and Nafisa Abedin for their extensive support.

Author contributions

Conception or design of the work; or the acquisition, analysis, or interpretation of data and drafting the work: MA, BPD, IJ, MMA, SGB. *Drafting the work or reviewing it critically for important intellectual content:* MA, BPD, IJ, MMA, SGB. *Final approval of the version to be published:* MA, BPD, IJ, MMA, SGB. *Accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved:* MA.

Conflict of interest

We do not have any conflict of interest.

Data availability statement

We confirm that the data supporting the findings of the study will be shared upon reasonable request.

Supplementary file

None

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Bangabandhu Sheikh Mujib Medical University Journal 2025;18(1):e76027
ISSN 2074-2908 | eISSN 2224-7750 |

RESEARCH ARTICLE

Patterns of maternal healthcare use among the urban poor of Bangladesh: A cross-sectional survey

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Abstract

Background: Despite some progress, in Bangladesh access to high quality essential maternal healthcare remains inadequate. Women living in urban slums may face additional obstacles to maternal healthcare, but evidence remains limited. The study aims to explore the patterns of maternal healthcare utilisation in urban slums.

Methods: This cross-sectional survey was conducted in April 2022 using an established health and demographic surveillance system operating in Dhaka North, Dhaka South and Gazipur city corporations. Six hundred thirty five married women of reproductive age with a baby aged ≤12 months were interviewed. Univariate and multivariate analysis were done to determined the factors affecting utilisation of maternal healthcare services.

Results: Overall, 36% of respondents had at least four antenatal care checkups, 56% had facility-based delivery, 58% had delivery with a skilled attendant and received postnatal care within two days of delivery. Use of essential services was low among uneducated women. Geographical differentials were found, raising questions about the low antenatal care and high private facility delivery in Gazipur. Many women opt for private delivery care, and 35% reported having a C-section.

Conclusion: Attention is needed across the whole pregnancy journey to improve access to high quality affordable antenatal care, delivery care and postnatal care for urban slum women. A complex of factors appears to be at play, with women's awareness, household decision-making, and provision of accessible, affordable, high-quality services all requiring action by policy makers.

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Publication history
Received: 4 Sep 2024
Accepted: 21 Feb 2025
Published online: 10 Mar 2025

Responsible editor
M Mostafa Zaman
0000-0002-1736-1342

Reviewers
F: Pramita Shrestha
00000-0003-4039-5118
G: Mst. Khaleda Akter
0000-0001-8857-1649

Keywords
maternal healthcare, ANC, PNC, facility birth, slum

Funding
Funded by Ministry of Local Government, Rural Development and Cooperatives, the Government of the People's Republic of Bangladesh through Urban Primary Health Care Services Delivery Project (UPHCSDP) (GR-01927).

Ethical approval
Approved by IRB of International Centre for Diarrhoeal Disease Research, Bangladesh (Protocol # PR-15045, dated 26 July 2015)

Trail registration number
Not applicable

Key messages

Among women living in urban slums (two in Dhaka city and one in Gazipur), a little more than one-third received four antenatal care, half had facility-based delivery, three half had delivery by skilled birth attendants, and half accessed timely postnatal care. Service uptake of essential services was particularly low among uneducated women; and access to affordable services was found inadequate in Gazipur. Many women opt for private delivery care, and one-third reported having a C-section.

Introduction

Despite remarkable progress in reducing maternal mortality, Bangladesh is yet to achieve the Sustainable Development Goal (SDGs) of maternal mortality ratio (MMR) of 70 or lower per 100,000 live births [1].

Utilisation of high quality maternal health services, including antenatal care (ANC), postnatal care (PNC) and institutional delivery, has been shown to reduce maternal mortality and improve neonatal outcomes [2-6]. However, 40% (35% of rural and 57% of urban) of women had received the recommended four or more ANC check-ups [7], while 70% of deliveries were attended by a medically trained provider (65% of rural women and 82% of urban women), and just 56% of infants and 55% of mothers received PNC within 2 days of delivery [7]. However, overall figures mask important differentials between those living in slum and non-slum areas [8]. The urban poor population is growing rapidly and the lack of affordable health services for this population is a persistent concern [9,10]. Compared to rural areas, provision of government health services in urban areas is patchy and diversified. The Ministry of Local Government, Rural Development and Cooperatives (MoLGRDC) is responsible for primary health care provision in urban areas [9,11], while secondary and tertiary level health services are largely supplied by the private health sector, and some Ministry of Health and Family Welfare run hospitals [12,13]. This pluralistic healthcare system is highly unregulated and results in large out-of-pocket expenditures for urban residents [14].

Little up-to-date data are available on the patterns urban slum women's maternal healthcare utilisation. This study aimed to explore the patterns of maternal healthcare utilisation, and to assess the factors associated with use of these services, to generate evidence to inform policy and programmes.

Methods

Study area and data collection

This cross-sectional study was conducted in slums of Dhaka North, Dhaka South and Gazipur City Corporations (CC) in April, 2022 where International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b) was operating a health and demographic surveillance system among around 34,000 population.

Based on past evidence of 51% prevalence of institutional delivery, with 95% confidence interval, 5% margin of error, 10% non-response and 1.5 design effect, the estimated sample size was 641. After distributing this sample across the three city corporations using probability proportional to size, the sample was drawn from the sampling frame of this larger population at random. Eligible respondents were women with reproductive age and had a baby aged 12 months or less.

Data were collected using Android tablets. To ensure high quality of data, the data collector and supervisor together sorted out any inconsistencies found. For the inconstancies the respective data collector revisited the respondent and corrected the inconsistencies.

The survey questionnaire was developed based on existing literature and national surveys conducted in the country [15]. Before data collection the questionnaire had been pre-tested in similar setting.

We asked women about the number of ANC visits and information on the content of ANC visits like the provider of ANC and the services received during ANC (*e.g.* blood pressure measurement, provision of iron supplement, counselling *etc.*). Respondents were also asked about place of delivery, attendant at delivery; timing and the number of PNC check-ups received. The questionnaire included questions on women's involvement in maternal healthcare decision-making and whether any difficulty was faced in accessing money during pregnancy.

Ethical concerns

The study was conducted following the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants, outlining the study objectives, participation rights, and the option to withdraw at any stage.

Data analysis

For reliability and validity of the data we did basic exploration, data cleaning, plausibility and consistency checking. Descriptive analysis was done for key outcomes. Unibivariate and multivariate logistic regression analysis was then performed to explore the association between outcome indicators of healthcare use and putative independent variables. The multivariate model included sociodemographic characteristics, indicators of healthcare decision-making as covariates. There was no missing data in this analysis. Data analysis was completed using Stata, version 15.

Results

Sociodemographic characteristics

Six hundred thirty five women aged 15 to 45 years participated in the survey. The mean (standard deviation) age of the participants was 25.8 (6.1) years. About half of the respondents had been schooled for 1 to 5 years, while less than 5% had more than 10 years of schooling, and 18% had no education at all. The vast majority (94%) of the women were homemakers.

ANC during last pregnancy

Eighty three percent of respondents stated that they received some form of ANC during their last pregnancy (Table 1). However, only around 36% of the mothers had the recommended four or more ANC check-ups (Table 2). Around 36% mentioned receiving ANC from a private hospital or clinic, 33% from NGO clinics and 16% from government hospitals. In terms of providers of ANC, the most commonly reported was MBBS doctor (68%), followed by nurses/ paramedics (46%).

Place and mode of delivery

Around 44% of respondents delivered at home, while 26% delivered at a private hospital, 30% delivered at a government hospital or NGO clinic. Overall, 58% of respondents reported having a skilled birth attendant, of them 48% reported being attended by an MBBS doctor and 16% a nurse/family welfare volunteer/ family welfare assistant/midwife/skilled birth attendant. Overall, 35% had delivered by C-section.

PNC during last pregnancy

A little over half (57%) of mothers received PNC within 48 hours of delivery, while 64% mothers had PNC within 42 days. The majority (73%) mothers received PNC from an MBBS doctor and 37% from nurses/ paramedics.

Table 1 Sociodemographic characteristics and status of healthcare decision-making among women residing in urban slums (n=635)

Characteristics	Had any antenatal care		*P*
	Yes (n=530)	No (n=105)	
Slum location			
Dhaka north CC[a]	252 (86.3)	40 (13.7)	0.02
Dhaka south CC[a]	192 (84.2)	36 (15.8)	
Gazipur CC[a]	86 (74.8)	29 (25.2)	
Years of schooling			
No education	85 (75.2)	28 (24.8)	<0.01
1–5	258 (82.7)	54 (17.3)	
6–10	158 (87.3)	23 (12.7)	
10+	29 (100)	0 (0)	
Difficulty accessing money during pregnancy			
Easy	198 (85.7)	33 (14.3)	0.25
Hard	332 (82.2)	72 (17.8)	
Difficulty in taking decision about care during pregnancy			
Easy	423 (87.2)	62 (12.8)	<0.01
Hard	107 (71.3)	43 (28.7)	
Mother was primary decision maker			
Yes	168 (86.2)	27 (13.8)	0.23
No	362 (82.3)	78 (17.7)	
All women	530 (83.5)	105 (16.5)	

[a] CC indicates city corporation

Factors influencing access to maternal healthcare

Geographical differentials were found, in Gazipur there was low uptake of ANC and high private facility delivery.

Recommended four ANC check-ups likely to be higher among educated women compared to uneducated. Women who reported that it was easy to take decisions during pregnancy were more likely to have had ANC, and to have had four check-ups than those who reported it was hard (Table 2).

Women with 10 or more years of education also stood out as using a different profile of delivery services compared to less educated women, with far more using private facilities and far fewer having their delivery at home or in a government or NGO setting. There was a positive correlation between use of ANC and facility-based birth. Among women who had not had any ANC, 78% reported having their delivery at home, compared to less than a quarter of those who had had four or more ANC check-ups (Table 3).

Table 2 Sociodemographic characteristics, indicators of healthcare decision-making and antenatal care uptake among women residing in urban slums (n=530)

Characteristics	Number of antenatal care visit[a]		*P*
	1–3	≥4	
Slum location			
Dhaka north CC[a]	132 (52.4)	120 (47.6)	<0.01
Dhaka south CC[a]	139 (72.4)	53 (27.6)	
Gazipur CC[a]	66 (76.7)	20 (23.3)	
Years of schooling			
No education	64 (75.3)	21 (24.7)	0.04
1–5	160 (62.1)	98 (37.9)	
6–10	99 (62.7)	59 (37.3)	
10+	14 (48.3)	15 (51.7)	
Difficulty accessing money during pregnancy			
Easy	126 (63.6)	72 (36.4)	0.99
Hard	211 (63.5)	121 (36.5)	
Difficulty in taking decision about care during pregnancy			
Easy	253 (59.8)	170 (40.2)	<0.01
Hard	84 (78.5)	23 (21.5)	
Mother was primary decision maker			
Yes	91 (54.2)	77 (45.8)	<0.01
No	246 (68.0)	116 (32.0)	
All respondents	337 (63.6)	193 (36.4)	

[a]Among those who had any antenatal care; CC, city corporation

PNC uptake was found to be higher in slums in Dhaka South CC compared to Dhaka North CC (aOR 2.7; 95% CI 1.3–5.6). However, education was positively associated, women with 10 or more years of schooling standing out as being most likely to received PNC (90% compared to 60% of women without education). Women who reported that it was easy to take decision about the care during pregnancy were more likely to have received PNC (68%) compared to those who reported that it was hard to take decisions (53%), (P<0.01). Women who had received four or more ANC check-ups were most likely to report PNC (Table 4).

Discussion

Our study findings showed comparable levels to national estimates of recommended four ANC check-ups (36% of all respondents versus a national overall percentage of 40%) but less than the 57% among all urban women estimated nationally [7]. In common with national data, we found far more women having some ANC than receiving the full Government of Bangladesh mandated four check-ups (a recommendation which is fewer than the current WHO recommended eight check-ups) [16]. Also reiterating earlier national findings [17], we found incomplete coverage of key elements of ANC check-ups.

In terms of intra-partum care, our slum women appear to be disadvantaged with just 58% reporting a skilled attendant, compared to national estimates of 65% of rural women and 82% of urban women [7]. Nevertheless, and in common with a growing body of evidence for Bangladesh, the rate of C-section was worryingly high at 35%, and reflects the high percentage of women opting for delivery in private facilities where normal delivery is rarely on offer [18].

Table 3 Place of delivery by sociodemographic characteristics, indicators of healthcare decision-making and antenatal care uptake among women residing in urban slums (n=635)

Characteristics	Place of delivery			*P*
	Home	Private	Govt. or NGO[a]	
Slum location				
Dhaka north CC[a]	130 (44.5)	62 (21.2)	100 (34.3)	<0.01
Dhaka south CC[a]	106 (46.5)	45 (19.7)	77 (33.8)	
Gazipur CC[a]	47 (40.9)	56 (48.7)	12 (10.4)	
Year of schooling				
No education	57 (50.4)	29 (25.7)	27 (23.9)	<0.01
1–5	147 (47.1)	67 (21.5)	98 (31.4)	
6–10	74 (40.9)	47 (26.0)	60 (33.2)	
10+	5 (17.2)	20 (69.0)	4 (13.8)	
Difficulty accessing money during pregnancy				
Easy	101 (43.7)	67 (29.0)	63 (27.3)	0.30
Hard	182 (45.1)	96 (23.8)	126 (31.2)	
Difficulty in taking decision about care during pregnancy				
Easy	206 (42.5)	134 (27.6)	145 (29.9)	0.08
Hard	77 (51.3)	29 (19.3)	44 (29.3)	
Mother was primary decision maker				
No	193 (43.9)	112 (25.5)	135 (30.7)	0.74
Yes	90 (46.2)	51 (26.2)	54 (27.7)	
Had any ANC				
No	82 (78.1)	5 (4.8)	18 (17.1)	<0.01
Yes	201 (37.9)	158 (29.8)	171 (32.3)	
Had >=4 ANC				
1–3	155 (46.0)	84 (24.9)	98 (29.2)	<0.01
≥4	46 (23.8)	74 (38.3)	73 (37.8)	
All women	283 (44.6)	163 (25.7)	198 (29.8)	

[a]NGO indicates non-governmental organization; CC, city corporation

Our findings also tallied with national data, indicating that PNC is received by only around half of all mothers and infants in the two days after birth [7]. Compared to urban slums in Bangladesh, the uptake of 4 or more ANC uptake (51%), as well as institutional delivery (91%) found to be higher in urban slums in Western India [19]. The related picture in urban slums in Nepal was, 79% had 4 or more ANC, 71% had facility delivery and 29% had made visit for PNC [20].

Our analyses sought to characterise the differentials between groups of women, and to begin to throw light on factors that may shape access. Women with more education were more likely to have received skilled maternal care than those who were uneducated. Well educated women were also more likely to use private facilities for delivery. Also, women who reported that it as easy to take decisions, and those who reported that they were the main decision-maker during pregnancy, were more likely to have had had four ANC check-ups than their counterparts with less control over decisions.

Our findings suggest that geographic accessibility of affordable government or NGO services may be an issue in Gazipur, and it may be that these women experience high out of pocket expenses as they are forced to use private delivery options. This deserves more investigation.

Women who reported receiving four or more ANC visits were more likely to deliver in a facility and to receive PNC than those who did not. This may reflect continuity of care, with healthcare providers encouraging women to maintain contact with services. It may also, however, reflect women and family-side characteristics that predispose towards use of services throughout the pregnancy journey.

The strengths of the study include being nested within an established health and demographic surveillance system which meant high levels of familiarity and trust among respondents leading to a high response rate and skilled data collectors, giving

Table 4 Percentage of women receiving any postnatal care (PNC) within 42 days of delivery by sociodemographic characteristics, indicators of healthcare decision-making and service use (n=635)

Characteristics	Had any PNC in 42 days		Odds ratio (95% CI[a])	Adjusted odds ratio (95% CI[a])
	Yes, n (%)	No, n (%)		
Slum location				
Dhaka North CC[a]	177 (60.6)	115 (39.4)	1	1
Dhaka South CC[a]	159 (69.7)	69 (30.3)	1.5 (1–2.2)	3.3 (1.7–6.7)
Gazipur CC[a]	72 (62.6)	43 (37.4)	1.1 (0.7 - 1.7)	1 (0.4–2.5)
Year of schooling				
No education	67 (59.3)[b]	46 (40.7)	1	1
1–5	192 (61.5)	120 (38.5)	1.1 (0.7–1.7)	0.8 (0.3–1.7)
6–10	123 (68.0)	58 (32)	1.5 (0.9–2.4)	0.7 (0.3–1.6)
10+	26 (89.7)	3 (10.3)	6.0 (1.7–20.8)	1.2 (0.2–7.9)
Difficulty accessing money during pregnancy				
Easy	156 (67.5)	75 (32.5)	1	1
Hard	252 (62.4)	152 (37.6)	0.8 (0.6–1.1)	1.2 (0.6–2.2)
Difficulty in taking decision about care during pregnancy				
Easy	328 (67.6)[c]	157 (32.4)	1	1
Hard	80 (53.3)	70 (46.7)	0.5 (0.4–0.8)	0.8 (0.4–1.6)
Mother was primary decision maker				
Yes	118 (60.5)	77 (39.5)	1	1
No	290 (65.9)	150 (34.1)	1.3 (0.9–1.8)	1.4 (0.7–2.8)
Had any ANC[a]				
No	31 (29.5)[c]	74 (70.5)	-	-
Yes	377 (71.1)	153 (28.9)		
Had ≥4 ANC[a]				
1–3	211 (62.6)[c]	126 (37.4)	1	1
≥4	166 (86)	27 (14)	3.7 (2.3–5.8)	3.6 (1.9–7)
Place of delivery				
Home	75 (26.5)[c]	208 (73.5)	1	1
Private	160 (98.2)	3 (1.8)	147.9 (45.8–477.6)	131.9 (37.9–458.6)
Govt or NGO[a]	173 (91.5)	16 (8.5)	30.0 (16.9–53.4)	28.1 (14.1–56.0)
All women	408 (64.3)	227 (35.8)		

[a]CI, indicates confidence interval; CC, city corporation; ANC, antenatal care; NGO, non-governmental organization; [b]*P*<0.05; [c]*P*<0.01

confidence in the quality of the data. Due to the cross-sectional nature of the study inevitably there would be some recall error. Furthermore, we could not claim evidence of causal relationships.

Conclusion

Urban slum women continue to have inadequate uptake of essential maternal healthcare and many rely on private, fee-taking services. Attention is needed across the whole pregnancy journey to improve access to high quality affordable ANC, delivery care and PNC. A complex of factors appears to be at play, with women's awareness, household decision-making, and provision of accessible, affordable, high-quality services all requiring more attention. Area-based as well as lower-educated women-targeted intervention should be taken to increase maternal healthcare utilization uptake.

Acknowledgments

We acknowledge Drs Sabrina Rashid and A M Rumayan Hasan for their support in the study. We also gratefully acknowledge the generosity of our respondents in consenting to participate in the research, and the hard work of the field team in completing the study data collection.

Author contributions

Conception or design of the work; or the acquisition, analysis, or interpretation of data for the work: SIS, HR. *Drafting the work or reviewing it critically for important intellectual content:* SIS, HR. *Final approval of the version to be published:* SIS, HR. *Accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved:* SIS, HR.

Conflict of interest

We do not have any conflict of interest.

Data availability statement

We confirm that the data supporting the findings of the study will be shared upon reasonable request.

Supplementary file

None

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Bangabandhu Sheikh Mujib Medical University Journal 2025;18(1):e75888
ISSN 2074-2908 | eISSN 2224-7750 |

RESEARCH ARTICLE

Patterns and predictors of intimate partner violence among married women living in urban informal settlements of Bangladesh: A cross-sectional survey

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Abstract

Background: Despite legal and policy proscriptions, intimate partner violence remains a pervasive issue worldwide, with particularly severe implications for marginalised and vulnerable women. In Bangladesh, women living in urban slums may face increased risks, but evidence remains limited. This study aimed to address this knowledge gap.

Methods: Cross-sectional survey was done among ever-married women resident (aged 18 years or older) in slums-dwelling in Dhaka North, Dhaka South and Gazipur. Data was collected using face-to-face interview on four types of intimate partner violence: physical, sexual, emotional and economic. Univariate and multivariate logistic regression analyses were done to explore the association between the violence outcome variables and sociodemographic characteristics.

Results: Six hundred seven women participated in the survey. The overall level of any form of life-time violence was 82%. Physical violence was most reported (66%), followed by economic (47%), sexual (44%), and emotional (38%). Uneducated women, and those whose husbands were uneducated, faced particularly high risks of violence. Gazipur stood out as an area with higher intimate partner violence than other slum areas. Working women also experienced more life-time violence than non-working women.

Conclusion: Urban slum women face high levels of violence in Dhaka and Gazipur. Policy level interventions, workplace-based actions and community-level measures should be taken to curb this epidemic. Specific steps should be taken to increase awareness related to intimate partner violence, and improve attitudes towards gender roles among women residing in urban slums.

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Publication history
Received: 1 Sep 2024
Accepted: 11 Feb 2025
Published online: 17 Feb 2025

Responsible editor
M Mostafa Zaman
0000-0002-1736-1342

Reviewer
C: Fariha Haseen
0009-0004-9040-1664

Keywords
IPV, GBV, VAW, urban slums, violence

Funding
Funded by Ministry of Local Government, Rural Development and Cooperatives, the Government of the People's Republic of Bangladesh through Urban Primary Health Care Services Delivery Project (GR-01927).

Ethical approval
Approved by IRB of International Centre for Diarrhoeal Disease Research, Bangladesh (No. PR-15045, dated: 26 July 2015).

Trail registration number
Not applicable

Key messages

Women living in urban slums face increased risks of intimate partner violence in Bangladesh. In our survey nested within existing health and demographic surveillance system, eighty-two percent women reported of any form of life-time violence and among four types of violence physical violence was most reported. High risk of violence is more common among uneducated women, and those whose husbands were uneducated. Working women experienced more life-time violence than non-working women. Urgent action is required to curb this epidemic.

Introduction

Gender-based violence (GBV) is a pervasive issue affecting millions of women worldwide, with particularly severe implications for those living in marginalised and vulnerable communities [1]. Among different forms of GBV intimate partner violence (IPV) is prevalent in all countries at alarming rates, [2] and violence against women (VAW) is a worldwide concern [3]. Approximately one in three women and girls worldwide experience physical or sexual violence in her lifetime by their intimate partner [4]. Many women not only suffer from physical or sexual violence, but may also be deprived of their rights to access financial and other resources [5]. Husbands or other relatives are often the perpetrators of VAW, and the effects extend beyond the women themselves, to children, families and society as a whole [6]. Despite international commitments including the convention on the elimination of all forms of discrimination against women [7] and national-level legal protections against GAW in many countries, [8] in practice significant barriers inhibit women's access to justice. Poor implementation of legal rights and policies, and inadequate knowledge among women of their rights are common [9, 10]. Moreover, relevant data and evidence related to GBV including IPV remains inadequate in low-and middle-income countries (LMICs), inhibiting evidence-based policies and interventions [11].

In LMICs, including Bangladesh, IPV is a matter of great concern which impacts public health and is a major burden on the society and economy [12]. Domestic violence against women is criminalised under the 2010 domestic violence act in Bangladesh. Despite this, implementation of measures to curb violence and prosecute offenders continues to face significant challenges, including the widespread perception that domestic violence is a private matter. The national VAW Survey 2015 revealed that 73% of ever-married women had ever experienced any type of violence by their current husband and 55% experienced violence during the past 12 months [13]. Available evidence suggests that the prevalence of IPV is higher in urban slums than non-slum and rural populations,[14] and may be particularly high among women with no or little education [15]. Despite the high prevalence and severe consequences of IPV in these settings, there is a significant gap in evidence. Research is needed to understand the levels and correlates of various forms of violence.

This study aims to provide a comprehensive picture of levels and types of intimate partner violence experienced and identify factors associated with the risk of experiencing intimate partner violence for generating evidence for policymakers to formulate strategies and interventions to improve the lives of the urban poor.

Methods

Study area and data collection

The study was conducted in slums of Dhaka North, Dhaka South and Gazipur City Corporations during May to June, 2022. The study was carried out within the areas where International Centre for Diarrhoeal Disease Research, Bangladesh (icddr'b) was operating a high quality Health and Demographic Surveillance System, visiting around 34,000 households on a quarterly basis.

Sample size

Earlier work had provided an estimate that 54.3% women had suffered from violence,[16] and we used this together with 95% confidence interval, 5% margin of error, 10% non-response and 1.5 design effect, to determine the required sample size of 637. We then distributed the sample across the three city corporation areas within the HDSS using probability proportional to size of each area to ensure representativeness. Eligible respondents were ever married women aged 18 years or over. For omitting biasness samples were drawn at random.

Data collection

After 3-day training on data collection tool, data collectors collected data for this survey using Android tablets. Prevalence estimates of lifetime violence by an intimate partner were obtained by asking direct, clearly worded questions about the respondent's experience of specific acts [17]. For different type of violence, women were asked whether a current or former partner had ever done any of the acts listed in Table 1, and recorded as 'yes' if any one of these was reported. Women who reported experiencing life-time physical or sexual violence were asked to give the reasons for the violence as they understood it. Respondents could report multiple reasons.

Table 1 Measuring different types intimate-partner violence among women in urban slums

Types of violence	Question
Physical violence	• hit or hurt her with anything • slapped her, or thrown something at her that could hurt her; • hit her with a fist or something else that could hurt; • kicked, dragged or beaten her up;
Sexual violence	• being physically forced to have sexual intercourse against her will; • being forced to do something sexual she found degrading or humiliating.
Emotional violence	• insulted you or made you feel bad about yourself; • intimidated you
Economic violence	• ever taken earnings or savings against her will; • refuse to give you money for household expenses, even when he has money for other things; • left job because of husbands' disapproval

Ethical consideration

Ethical approval and favourable scientific review of the study was approved by IRB of International Centre for icddr'b. Furthermore, before enrolling in study,

written informed consent from each of the participant preceding data collection were taken from each participant and maintained privacy during data collection.

Data analysis

Wealth index was calculated using principal component analysis based on the wealth profile for the whole HDSS population (i.e. household's ownership of selected assets, including televisions and bicycles; housing construction materials for roofs, wall and floor; and types of water access and facilities for sanitation) [18].

Univariate statistical analysis was performed to explore different types of violence and its association with sociodemographic characteristics. Subsequently, four multivariate logistic regression models were fitted to further examine the adjusted associations in order to explore the correlates of different types of violence. In the final multivariate logistic regression models, 78 cases with missing data in socio-demographic variables (husband education, household asset information) were excluded. The model included age, years of schooling, working status, marital status, parity, wealth index and husbands' schooling as covariates. Data analyses were performed using Stata v15.

Table 2 Sociodemographic characteristics of ever married women aged 18 years old or above and their husbands/ partners by slum locations, number (%)

Socio-demographic characteristics	Dhaka North (n=230)	Dhaka South (n=197)	Gazipur (n=180)	Total (n=607)
Age (years)				
18–29	101 (43.9)	74 (37.6)	64 (35.6)	239 (39.4)
30–34	54 (23.5)	42 (21.3)	28 (15.6)	124 (20.4)
35–39	33 (14.3)	38 (19.3)	33 (18.3)	104 (17.1)
≥40	42 (18.3)	43 (21.8)	55 (30.6)	140 (23.1)
Mean (SD)*	31.1 (8.2)	32.7 (8.5)	35.0 (10.2)	32.8 (9.0)
Schooling (years)				
No education	28 (12.2)	61 (31.0)	68 (37.8)	157 (25.9)
1–5	136 (59.1)	65 (33.0)	60 (33.3)	261 (43.0)
≥6	66 (28.7)	71 (36.0)	52 (28.9)	189 (31.1)
Working status				
Not working	157 (68.3)	113 (57.4)	91 (50.6)	361 (59.5)
Working	73 (31.7)	84 (42.6)	89 (49.4)	246 (40.5)
Marital status				
Currently married	217 (94.3)	180 (91.4)	152 (84.4)	549 (90.4)
Widowed	7 (3.0)	15 (7.6)	15 (8.3)	37 (6.1)
Divorced/ separated	6 (2.6)	2 (1.0)	13 (7.2)	21 (3.5)
Parity				
0–1	87 (37.8)	84 (42.6)	69 (38.3)	240 (39.5)
2	73 (31.7)	70 (35.5)	61 (33.9)	204 (33.6)
≥3	70 (30.4)	43 (21.8)	50 (27.8)	163 (26.9)
Wealth index	n=213	n=173	n=167	n=553
Lowest	77 (36.2)	24 (13.9)	38 (22.8)	139 (25.1)
Second	43 (20.2)	31 (17.9)	46 (27.5)	120 (21.7)
Third	45 (21.1)	52 (30.1)	64 (38.3)	161 (29.1)
Highest	48 (22.5)	66 (38.2)	19 (11.4)	133 (24.1)
Husbands' schooling (years)	n=229	n=175	n=179	n=583
No education	46 (20.1)	60 (34.3)	71 (39.7)	177 (30.4)
1–5	107 (46.7)	63 (36.0)	52 (29.1)	222 (38.1)
≥6	76 (33.2)	52 (29.7)	56 (31.3)	184 (31.6)

*SD indicates standard deviation.

Results

Sociodemographic characteristics

Our final study sample consisted of 607 ever-married women aged 18 years and over: 230 were from Dhaka North, 197 were from Dhaka South and 180 were from Gazipur city corporations.

The majority of the respondents were aged 30 years and above (61%), currently married (90%) and had had at least one child (95%). Approximately one quarter of the respondents had no education at all, 43% had been schooled for 1 to 5 years, while only 6% had more than 10 years of education. Almost 60% of the women were housewives. Among others, 18% were domestic workers, followed by 10% were garments worker. Among the participants' who were garment workers, 58% of them are from Gazipur City Corporation.

In terms of husband's characteristics, 30% had no formal education and 38% had 1-5 years of schooling. There were clear differentials in many of these indicators between respondents in the three city corporation areas with Gazipur residents standing out as disadvantaged compared to those living in Dhaka North and Dhaka South (Table 2).

Experiences of violence

The proportion of women who reported that they had experienced any type of violence perpetrated by an intimate partner at any time during their lifetime was 83%. Physical violence was most commonly reported (66%), followed by economic violence (47%), sexual violence (44%), and emotional violence (38%).

Among those reported experiencing lifetime physical and/or sexual violence by an intimate partner, 60% could not identify a specific reason. Financial reasons were stated by 44% of respondents, followed by problems with partner's family members (27%), partner's unemployment (16%), disruption in work (15%), wife's disobedience (11%).

Patterns and predictors of violence

Across all four types of violence, currently working women were more likely to report experiencing lifetime violence than women who were not currently working. Considering all forms of violence combined, over 90% of respondents without education reported experiencing some form in their lifetime compared to 69% of those with 6 or more years of education. The husband's education level also showed the same pattern, and an even more pronounced difference in prevalence of any lifetime violence. Women who were divorced, separated, and widowed at the time of the survey were more likely to report violence than those who were currently married. Bivariate results suggested that economic violence varied significantly between the wealth quintiles, with the prevalence

being the highest among the lowest quintile (50%) and the lowest among the highest wealth quintile (23%). Bivariate results also showed differences across the three city corporation areas in the levels of all types of violence, except physical violence, with Gazipur residents being most likely to report violence. Parity and age groups showed no differences across any of the forms of violence (Table 3).

Table 3 Lifetime experience of various types of violence by socio-demographic characteristics

Characteristics	Physical violence (n=485)	Sexual violence (n=268)	Emotional violence (n=233)	Economic violence (n=284)	Any violence (n=501)
Age (years)					
18–29	59.4	43.9	37.2	40.2	82.4
30–34	59.7	41.1	42.7	52.4	81.5
35–39	68.3	43.3	35.6	51.9	79.8
≥40	70.0	47.9	38.6	49.3	85.7
Schooling (years)					
No education	73.3[b]	60.0[b]	47.8[b]	65.0[b]	92.4[b]
1–5	66.7	45.6	39.1	46.4	86.6
≥6	50.8	30.7	29.6	32.3	68.8
Working status					
Not working	59.8[a]	40.0[b]	29.4[b]	42.4[b]	79.8[a]
Working	68.7	53.3	51.6	53.3	86.6
Marital Status					
Married	62.7[b]	44.3	36.6[b]	45.9[b]	82.3
Widowed	56.8	37.8	32.4	37.8	75.7
Divorced/separated	95.2	52.4	95.2	85.7	100
Parity					
0–1	60.8[a]	43.3	39.2	42.5	81.3
2	61.8	44.6	40.7	50.0	81.4
≥3	69.3	44.8	34.4	49.1	85.9
Wealth Index					
Lowest	64.8	48.9[b]	46.8	49.6	84.2
Second	60.0	46.7	34.2	44.2	79.2
Third	65.8	49.1	36.0	49.1	85.7
Highest	60.2	28.6	33.8	42.1	77.4
Husband's schooling (years)					
No education	77.4[b]	54.2[b]	46.3[b]	61.6[b]	95.5[b]
1–5	64.0	46.9	40.1	46.0	83.3
≥6	51.6	35.3	27.2	37.0	72.3
City corporation					
Dhaka North	64.4	39.6[b]	30.4[b]	33.9[b]	79.6[b]
Dhaka South	60.4	23.9	37.1	52.3	79.2
Gazipur	65.6	72.2	50.0	57.2	90.0

[a]<0.05, [b]<0,01

Women married to husbands with no education had higher odds of experiencing physical violence than women in all other categories, even those whose husbands had just 1-5 years of schooling. Women who were currently working had odds of ever experiencing lifetime sexual and emotional violence twice those of non-working women and women resident in Gazipur had higher odds than that of those in Dhaka North.

Economic violence was negatively associated with women's education and husband's education. The odds of reporting economic violence were again higher among women in Gazipur and Dhaka South than those in Dhaka North (Table 4).

Discussion

This study sought to contribute to the body of evidence on IPV by describing the levels of different types of violence among a relatively under-researched group - women living in urban slums in Bangladesh - and to explore some of the predictors.

The strengths of the study include being nested within an established HDSS which meant high levels of familiarity and trust among respondents leading to a high response rate and skilled data collectors, giving confidence in the quality of the data. The cross-sectional nature of the study inevitably means there will be some recall error and causal relationships cannot be confidently determined (for instance between working status and experience of violence). Furthermore, this study did not consider other factors like cultural norms and access to social services in the models which could have an influence on the risk of violence and the predictors examined.

Levels of lifetime violence were extremely high, with 82% of respondents reporting experiencing at least one form of violence by their husband in their marital life, higher than the national estimates for urban and rural areas, of a little over 70% [13].

More working women in the sample reported lifetime experiences of all four types of violence than those who were not working at the time of the survey. Also, women with lower education, and those whose husbands had lower education, were more likely to report violence than those with higher education. We also found important differences across the three city corporations, with Gazipur standing out as a place where women experienced higher levels of all forms of lifetime violence, except physical.

Findings across the different types of violence were complex, but this in part may reflect low power to detect some differences. In common with previous research, [15] our study provided evidence that education, of both women and their husbands, may be a protective factor. Husband's education was found to be independently negatively associated with physical violence and with economic violence, while women's own education was negatively associated with economic violence.

Women's working status was also a relevant factor, showing independent associations with both sexual violence and emotional violence. Since we asked about lifetime violence and used a cross-sectional survey, it is not possible to determine the direction of causality, though it seems plausible, and other research has suggested, that working women are exposed to greater risk of violence from their husbands because their employment threatens the gendered hierarchy within the household [19-21].

Even having controlled for measures of education, marital status, working status and wealth, models indicated independent associations between being resident in Gazipur and emotional violence, economic violence, sexual violence, and any type of violence, compared to Dhaka North. These findings suggest that there may be differences in local area sub-cultures relating to the legitimacy and tolerance of violence against women.

Table 4 Factors associated with lifetime different types of violence experience among married women in urban slums: adjusted odds ratios (95% confidence intervals) from logistic regression* (n=607)

Characteristics	Physical	Sexual	Emotional	Economic
Age (years)				
18–29	1	1	1	1
30–34	0.8 (0.5–1.5)	0.9 (0.5–1.6)	1.0 (0.6–1.8)	1.7 (1.0–3.0)
35–39	1.3 (0.7–2.5)	0.7 (0.4–1.3)	0.7 (0.4–1.4)	1.2 (0.7–2.2)
≥40	1.3 (0.7–2.4)	0.9 (0.5–1.7)	0.9 (0.5–1.7)	0.9 (0.5–1.7)
Schooling (years)				
No education	1	1	1	1
1–5	1.2 (0.7–2.2)	0.7 (0.4–1.2)	1.0 (0.6–1.7)	0.6 (0.3–1.0)
≥6	0.8 (0.4–1.6)	0.4 (0.2–0.8)	0.6 (0.3–1.2)	0.4 (0.2–0.8)
Working status				
Not working	1	1	1	1
Working	1.5 (1.0–2.2)	2.1 (1.4–3.2)	2.4 (1.6–3.6)	1.3 (0.9–1.9)
Marital status				
Currently married	1	1	1	1
Widowed	0.4 (0.1–0.8)	0.3 (0.1–0.8)	0.6 (0.2 –1.3)	0.3 (0.1–0.8)
Divorced/ separated	5.4 (0.7–43.2)	0.3 (0.1–0.9)	14.4 (1.8–114.6)	5.6 (1.2–26.5)
Parity				
0–1	1	1	1	1
2	1.1 (0.7–1.7)	1.0 (0.6–1.6)	1.2 (0.7–2.0)	1.2 (0.7–1.9)
≥3	1.3 (0.8–2.4)	0.8 (0.5–1.5)	1.0 (0.6–1.7)	1.0 (0.6–1.8)
Wealth index				
Lowest	1	1	1	1
Second	1.0 (0.6–1.7)	0.8 (0.5–1.5)	0.5 (0.3–0.9)	0.8 (0.5–1.4)
Third	1.1 (0.6–2.0)	0.7 (0.4–1.2)	0.6 (0.4–1.1)	0.8 (0.5–1.4)
Highest	1.0 (0.6–1.7)	0.8 (0.5–1.5)	0.5 (0.3–0.9)	0.8 (0.5–1.4)
Husbands' schooling (years)				
No education	1	1		
1–5	0.5 (0.3–0.9)	0.9 (0.5–1.6)	1.3 (0.8–2.3)	0.8 (0.5–1.4)
≥6	0.4 (0.2–0.6)	0.7 (0.4–1.2)	0.7 (0.4–1.4)	0.5 (0.3–0.9)
City corporation				
Dhaka North	1	1		
Dhaka South	0.9 (0.6–1.5)	0.5 (0.3–0.9)	1.3 (0.8–2.2)	2.8 (1.8–4.6)
Gazipur	0.8 (0.5–1.3)	4.0 (2.5–6.6)	2.1 (1.3–3.5)	2.3 (1.4–3.7)

*Multivariate model included age, years of schooling, working status, marital status, parity, wealth index and husbands' schooling as covariates.

Women's direct reports of the reasons for violence suggested that financial hardship, and related reasons (unemployment, lack of food, disruption in work) are often a factor at play. However, surprisingly, our logistic regression models did not provide evidence to support this, except in relation to sexual violence, where the highest wealth quintile had lower odds compared to the lowest wealth quintile.

Conclusion

The study findings highlight worryingly high levels of all types of violence among women living in Bangladesh urban slums. Urgent action is clearly needed to curb this epidemic. Specifically, women who are themselves uneducated or are married to men who are uneducated require particular attention. Specific measures like educational interventions or support services for working women should be taken. Some community-level measures also need to be taken to increase awareness related to IPV, and improve attitudes towards gender roles, among women residing in urban slum areas. So too does the existence of geographic areas where IPV is particularly prevalent so that area-based interventions can be designed.

Acknowledgments

We acknowledge the contribution of Dr. Sabrina Rashid and Rumayan Ahmed for reviewing the manuscript and helping in designing the study. We are thankful to our respondents in consenting to participate in the research. We also acknowledge the hard work of the field team in completing the study data collection. We are thankful to the Government of Bangladesh and Canada for their core/ unrestricted support to icddr,b research.

Author contributions

Conception or design of the work; or the acquisition, analysis, or interpretation of data for the work: SIS, HR. *Drafting the work or reviewing it critically for important intellectual content:* SIS, HR. *Final approval of the version to be published:* SIS, HR. *Accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved:* SIS, HR.

Conflict of interest

We do not have any conflict of interest.

Data availability statement

We confirm that the data supporting the findings of the study will be shared upon reasonable request.

Supplementary file

None

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Bangabandhu Sheikh Mujib Medical University Journal 2025;18(1):e75386
ISSN 2074-2908 | eISSN 2224-7750 |

RESEARCH ARTICLE

Experience of nurses in identifying delirium among cancer patients: A qualitative study

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Abstract

Background: Information about how nurses screen for delirium in cancer patients can provide insights into improving recognition. This study aimed to investigate the experiences of nurses while identifying delirium in cancer patients.

Methods: The study's design was qualitative, using thematic analysis. Data were gathered via a focus group discussion with ten nurses from two oncological wards of Nursing and Health Research Universitas Riau, Pekan Baru Riau, Indonesia. The focus group discussion lasted roughly 90 minutes. Participants provided feedback on their experiences with assessment in delirium through semi-structured and open-ended questions. Data collection occurred in September 2023 at two oncology wards. Data analysis in this phenomenological research used the Collaizzi method to describe the meaning of an experience identified through the important themes of a phenomenon consisting of seven stages.

Results: Categories, subcategories and themes were constructed. Experiences of nurses in identifying delirium among cancer patients were identified i) delirium, agitation and confusion are almost similar (the term delirium is not well known, and the type of delirium is not familiar); ii) tools for assessing delirium are needed (the tool does not exist and is unknown, used clinical experiences supported by laboratory testing); and iii) nurses can play an important role in identifying delirium (important role in assessing delirium, advising to prevent delirium among healthcare professionals).

Conclusion: Nurses who work in oncology wards need to know more about delirium screening since they play an important role in early detection and treatment. Therefore, appropriate knowledge and measurement tools are required to identify delirium earlier among cancer patients.

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Publication history
Received: 10 Aug 2024
Accepted: 14 Feb 2025
Published online: 13 Mar 2025

Responsible editor
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Keywords
delirium, assessment, nursing, cancer

Funding
Funded by Universitas Riau, Memo No. 241789URI.FKP, dated 7 Apr 2023.

Ethical approval
Approved by Ethics Committee of Nursing and Health Research Universitas Riau (No. 150/UN.19.5.1.8/KEPK.FKP/2023, dated 25 Oct 2023).

Trial registration number
Not applicable

Key messages

Nurses play an important role in identifying delirium. However, they need more knowledge and skills to identify and differentiate delirium from other levels of consciousness. This lack is mainly due to an absence of appropriate measurement tools. The training of nurses should focus on delirium identification using an appropriate tool.

Introduction

Delirium could be the most common neurological symptom in cancer patients [1]. Delirium occurs when a person has extreme confusion due to a physical or mental ailment. This condition may impair their ability to focus, direct, maintain, and transfer attention [2, 3]. Patients who received therapy in a hospital setting typically have this syndrome. According to a comprehensive review study, the incidence of delirium varies from 3% to 29% per hospitalisation, with a prevalence of approximately 20% among newly admitted patients [4]. According to various studies, delirium affects 22–44% of cancer patients, which may rise up to 87% in their final days of life [5].

The management and treatment of patients with delirium in cancer care settings provide complex challenges. Despite being treatable with skilled nursing care, delirium is frequently misdiagnosed and, as a result, either ignored or improperly managed in cancer patients [4, 6, 7]. It can be difficult to determine if a given delirium episode is reversible, and doctors may find it difficult to make decisions about delirium care. Nearly 50% of cancer patients receiving palliative care had permanent delirium episodes, according to a prior study, which raised the death rate [8–10]. As a result, the symptoms are not recognised as indicators of a severe acute illness for which appropriate actions and treatment have not been started [1, 11, 12].

Nurses have an important role in providing nursing care to cancer patients [7, 8]. The nursing care to prevent delirium can begin by evaluating cognitive function. Observations are carried out on patients who experience changes in mental status and behaviour, such as observing orientation towards people, time and place, which must be carried out every 6 hours [13]. Nonetheless, there appears to be a deficiency in clinical practice regarding delirium, including inadequate knowledge regarding the treatment of delirium in patients, insufficient abilities to give patient care and a conflict in making judgments regarding patient care [7, 8]. Few studies have investigated nurses' experiences with delirium and its detection in cancer patients. Therefore, the purpose of this study was to investigate the experiences of nurses identifying delirium in cancer patients.

Methods

Study design

A qualitative study was done using thematic analysis through focus group discussion (FGD). The FGD method was chosen to explore in-depth information and understand participants' experiences identifying delirium among cancer patients. Through FGD, each respondent can express his opinion or add additional information if he recognises that other respondents still lack the information the researcher needs. The FGD took about 90 minutes to explore nurses' experiences to assess delirium in cancer patients. The guideline from the FGD has been piloted before being applied to the respondents. The pilot was conducted to ensure that the FGD steps had gone well and that everything was ready before the FGD sessions.

Samples, time and locations

FGDs were conducted with ten nurses who worked in two oncology wards at the Nursing and Health Research referral hospital Universitas Riau, Pekan Baru Riau, Indonesia. The number of nurses in the two wards reached 30, but only 10 met the criteria to participate. Nurses who have worked for at least 1 year in the oncology ward and treated patients with delirium were included. Written informed content was obtained from the respondents. The participants were also explained that they would be protected confidentially and could withdraw from the study at any time without consequences. Data collection took place in September 2023. The nurses who were selected as respondents in this study, on average, had the similar length of service and did not have more positions than others to avoid not being open with each other in giving opinions during the FGD.

Data collection

The FGD was digitally recorded. The researchers took brief notes on each participant's responses to semi-structured, open-ended questions about nurses' experiences doing delirium assessments in cancer patients. If everything has reached the same understanding, then data saturation was considered to be reached. Questions during FGD were: 1) How do you identify patient delirium?; 2) is there training about delirium provided by the hospital?; 3) are there special tools provided by the hospital to identify delirium?; and 4) the role taken by nurses in the care of delirium patients so far is limited to what actions?

Data analysis

Data analysis in this phenomenological research uses the Collaizzi method to describe the meaning of an experience identified through the important themes of a phenomenon consisting of seven stages [14]. Data analysis in this study was manual. Information was obtained using open coding. The discussion was verbatim transcribed, and the Indonesian transcripts underwent content analysis before translation. All transcripts were meticulously read several times, as were the participants' experiences. Categories, subcategories, and themes were then constructed. Data were verified by member checking, peer questioning, and cross-examination to ensure trustworthiness, reliability, and authenticity. We gave respondents the opportunity to see if there is still data they feel do not represent all the answers they provided.

Results

A total of 10 nurses (1 men and nine women) had participated (Table 1). The emergent themes, however, clearly reflected similar experiences and were titled as follows: 1) more knowledge about delirium is essential; 2) lack of appropriate measurement tools; and 3) nurses play an important role in identifying delirium.

More knowledge about delirium is essential

The participants stated that they believe nurses in oncological wards should be more knowledgeable about delirium since they play an important role in therapy, particularly early screening.

Table 1 Participant characteristics

Participant Code	Gender	Age (years)	Education	Position	Clinical experience (in years)	Clinical experience in an oncology ward
P1	Female	46	Bachelor of Nursing	Head of nurse	23	14
P2	Female	44	Master in Nursing	Head of the ethical committee	15	12
P3	Female	49	Bachelor of Nursing	Nurse	23	15
P4	Male	35	Bachelor of Nursing	Nurse	13	12
P5	Female	45	Bachelor of Nursing	Nurse	23	15
P6	Female	45	Bachelor of Nursing	Nurse	23	14
P7	Female	45	Bachelor of Nursing	Nurse	22	14
P8	Female	36	Bachelor of Nursing	Nurse	12	12
P9	Female	43	Bachelor of Nursing	Nurse	20	14
P10	Female	48	Bachelor of Nursing	Head of nurse	25	14

The term delirium is not well known

Interviews revealed that the term "delirium" is rarely used. Instead, most nurses utilised perplexity when the patient's mental state changed without first conducting an assessment.

".....nurses need to know about delirium; so far, delirium has only been identified based on suspicion and experience that nurses have gained while caring for patients in hospital ...." (P7)

The type of delirium is not familiar

It is pretty difficult for them to differentiate between delirium and confusion. Therefore, it makes nurses misdiagnosed.

".....cancer patients with delirium are difficult to study because they are calm....." (P2)

".....another patient is different, they calmer instead of agitation and confusion....."(P3)

Lack of appropriate measurement tools

The participants stated that techniques for diagnosing delirium do not exist and are unknown. Nurses will judge the patient's condition based on their clinical experience and support the results by sending blood specimens for laboratory examination.

The tool does not exist and is unknown

Data obtained from participants found that they never used the assessment tool which focused on delirium. Instead, they used the Glasgow Coma Scale (GCS) to measure patients' condition if they showed mental status changes.

"... in the room used by GCS, then converted to apathetic, poor awareness status....." (P2)

".... from the beginning, we used GCS and then we assessed qualitative awareness..." (P4)

"..... if you assess consciousness using GCS, if consciousness decreases using EWS...." (P3)

".....not studied, we only GCS is studied....." (P5)

Used clinical experiences supported by laboratory testing

When they are still not sure what happened to the patients, they will refer them to the doctor and ask for a laboratory examination, particularly for electrolyte imbalance.

".....we used our clinical judgment when we found any changes in patients....." (P10)

".....just check their blood electrolytes, then see whether there are imbalances....." (P5)

Nurses play an important role in identifying delirium

Since the nurse is the closest person in the ward, the nurse should know more about delirium and how to identify those cases.

An important role in assessing delirium

Nurses are always by the patient's side for almost 24 hours. Therefore, they have an important role in the early screening of delirium symptoms and in preventing the worsening of delirium.

".....I believe that we have a significant role, so we need to master delirium assessment because delirium in cancer patients is different from other patients....." (P5)

Advising to prevent delirium among healthcare professionals

Nurses make many observations that other healthcare professionals do not. Based on their assessment, the nurse plays a vital role in giving advice and suggestions to other healthcare professionals regarding the patient's condition. So the appropriate treatment will run smoothly.

".....we then give some advice and suggestions to our colleagues based on our assessment....."(P9)

Discussion

From FGDs, nurses admitted that 1) more knowledge about delirium is essential, 2) a lack of appropriate measurement tools to assess delirium, and 3) nurses can play an important role in identifying delirium.

Knowledge about delirium is essential because delirium is a common occurrence when caring for cancer patients from the first diagnosis to the latter stages of the disease. Nevertheless, this condition is commonly disregarded. Because delirium can exacerbate a patient's condition and raise their risk of death, health professionals must be aware of the disorder's many features and be able to recognise common underlying causes [15]. It was the same with a study which mentioned that a neurological disorder called delirium makes people abruptly disoriented. Delirium patients may have difficulty in articulating their circumstances or suffer from hallucinations or delusions [16]. Other studies mention that every patient receiving cancer therapy who is admitted to the hospital should have their delirium levels evaluated [17]. The physician or nurse must determine and address reversible triggering factors after diagnosing delirium [18]. The research results from other studies support the theme found in this research, which is how important it is for a nurse to understand how to identify delirium. It will ensure patient safety because it can prevent patients from experiencing dangerous situations if they are misdiagnosed and mistreated [15].

Delirium goes undetected if structured detection measures are not used. When hypoactive delirium occurs in cancer patients, it is frequently misinterpreted as dementia, Wernicke's aphasia, anxiety disorders, or depression [19]. Several validated delirium detection or screening instruments have been created for various patient populations admitted to hospital wards, intensive care units, and emergency rooms [20]. A comprehensive evaluation of the patient's state of awareness should be carried out using a Sedation-Agitation Scale (SAS), such as the Richmond Agitation–Sedation Scale (RASS), before delirium screening. The level of consciousness is used to categorise patient assessments. Patients must be able to speak to be screened for delirium at the preferred level of consciousness. RASS-3 screening should start after the level of consciousness has been determined [21]. The ICU patients, in particular, require greater attention because they are frequently sedated, intubated, and physically weak, making them more likely to be diagnosed with delirium [17]. The results of existing studies show that instruments that detect delirium do not exist. Detection using existing instruments still allows for multiple interpretations, potentially leading to interpretation errors.

Nurses can play an important role in identifying delirium since they spend more time at the patient's bedside than physicians. Nurses interact with patients frequently and continuously; they are more able to notice changes in their attention, consciousness, and cognitive function. As a result, nurses' observations are crucial for the early identification of delirium symptoms and ongoing monitoring, which is necessary to track the patient's clinical progression. Nurses can effectively monitor delirium signs with supervision and training. A study mentions that monitoring and early detection of delirium in cancer patients is the nurse's responsibility to expedite treatment [17]. As a result, nurses' observations are crucial for the early identification of delirium symptoms and ongoing monitoring, which is necessary to track the patient's clinical progression [19]. The data supported the idea that nurses can effectively monitor delirium signs with supervision and training [16]. The overall experience of nurses in detecting delirium in cancer patients cannot be represented broadly. Perhaps this study only represents nurses in hospitals in the Riau region, Indonesia, so research with a stronger methodology, especially grounded theory, might be needed. Moreover, one FGD, with male and all female participants and different roles and designations of the participants, is a limitation of the study. The number of female nurses is greater in the ward than male nurses. This condition meant that only a few male nurses were included in the criteria for research respondents. Respondents have the similar work experience, so we don't think gender and position differences are problematic in this study.

Conclusion

The study shows nurses who work in oncology wards need to know more about delirium screening since they play an important role in early detection and treatment. Therefore, appropriate knowledge and measurement tools are required to identify delirium earlier among cancer patients.

Acknowledgments

We would like to thank all participants who participated in this study.

Author contributions

Conception or design of the work; or the acquisition, analysis, or interpretation of data for the work: NH, SP, HD, SW, E, SW. *Drafting the work or reviewing it critically for important intellectual content:* NH, SP, HD, SW, E, SW. *Final approval of the version to be published:* NH, SP, HD, SW, E, SW. *Accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved:* NH.

Conflict of interest

We do not have any conflict of interest.

Data availability statement

We confirm that the data supporting the findings of the study will be shared upon reasonable request.

Supplementary file

None

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Bangabandhu Sheikh Mujib Medical University Journal 2025;18(1):e77865
ISSN 2074-2908 | eISSN 2224-7750 |

RESEARCH LETTER

Relation of smoking behaviour with severity of COVID-19 infections in a sample of Iraqi patients

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Publication history
Received: 20 Nov 2024
Accepted: 10 Jan 2025
Published online: 5 Feb 2025

Responsible editor
M Mostafa Zaman
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Reviewer
C: S M Rashed Ul Islam
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Keywords
COVID-19, smoking, cigarette, hookah

Ethical approval
From the MREB of Mustansiriyah University (decision no: 782, date: 17 Dec 2020).

Funding
None

Trail registration number
Not applicable

The World Health Organization (WHO) reported that smokers have a higher risk of developing severe disease with COVID-19 compared to non-smokers.[1] However, a few reports refuted this relationship[2] despite established knowledge that smoking raises the risk of bacterial and viral illness infections, especially respiratory infections.[3] We have examined the differences in COVID-19 symptom severity between smokers and non-smokers, its frequency and type with COVID-19 symptom severity in a sample of Iraqi COVID-19 recovered individuals.

We have recruited 658 (411 women and 247 men) COVID-19 Iraqi patients (aged 20-39) who recovered from a recent attack (before two weeks) of COVID-19 at Al-Yarmok Teaching Hospital and Al-Shifa Medical Centre between January and August 2021. Their participation was voluntary, and informed consent was obtained. The data collection questionnaire included age, sex, severity of symptoms (severe: symptoms that required hospitalisation and oxygenation therapy; moderate: those bedridden; and mild: flue-like symptoms), and smoking, its frequency (daily, non-daily) and types (cigarette, hookah, both). We excluded those with asthma, chronic respiratory, and other chronic systemic diseases.

The key results of the chi-square analysis are presented in Table 1. The smoking proportions, frequencies, and types are similar across the COVID-19 severity categories (P>0.1 for all). Nicotine has been demonstrated to impede the growth of SARS-CoV-2, possibly by reducing the lungs' cytokine storm and lessening the severity of COVID-19 infection.[4] However, smoking is arguably the biggest risk factor that can be avoided.[5] Giving up smoking can reduce SARS-CoV-2 infection risk in addition to illnesses associated with tobacco use.[6] Nicotine increases the amount of viral entry, and SARS infection downregulates the expression of angiotensin-converting enzyme-2 as a regulatory mechanism after infection.[7] Well-designed clinical trials are necessary to examine the effect of nicotine on this.

According to the German news website N-TV, a medical team at Pitié Salpêtrière Hospital in the French capital, Paris, conducted a study that

Table 1 Smoking behaviour of patients with severity of COVID 19 patients, results are number (per cent)[a]

Characteristic	Mild (n=187)	Moderate (n=358)	Severe (n=113)
Age			
20s	65 (34.8)	105 (29.3)	44 (38.9)
30s	122 (65.2)	53 (70.7)	269 (61.1)
Sex			
Men	85 (45.5)	199 (55.6)	63 (55.8)
Women	102 (54.5)	159 (44.4)	50 (44.2)
Smoking			
No	139 (74.3)	282 (78.8)	94 (83.2)
Yes	48 (25.7)	76 (21.2)	19 (16.8)
Frequency of smoking			
Daily	40 (21.4)	56 (15.6)	12 (10.6)
Non-daily	8 (4.3)	20 (5.6)	7 (6.2)
Method of smoking			
Cigarette	18 (9.6)	35 (9.8)	10 (8.8)
Hookah	20 (10.7)	23 (6.4)	3 (2.7)
Both	10 (5.3)	18 (5.0)	6 (5.3)

[a]None of these variables were significantly different between pain categories

Key messages

This cross-sectional study done in 658 adult Iraqi patients (aged 20 to 39) did not find an association between smoking habit, its types and frequencies with the severity of COVID-19 symptoms.

suggested nicotine may have protective properties against the COVID-19 virus, meaning that smokers may be less likely to get the virus than non-smokers.[2] This finding has surprised the scientific community because the harms of smoking are beyond debate nowadays.[8] There are reports of higher mortality among smokers compared to non-smokers. Well-designed studies do not refute the smoking habits' putative effect on COVID-19.[1] Our results agree with a few previous studies that smoking's association with COVID-19 severity is not cognisable. While tobacco smoking may provide some protection against respiratory infections, it is a potentially dangerous chemical that may negatively affect the respiratory epithelium and health in general. In conclusion, we did not find any protective or putative relationship between smoking and COVID-19 severity in this Iraqi sample of post-COVID-19 patients.

Acknowledgments

We acknowledge the COVID-19 Centers in Al-Karkh and Al-Rusafa for their assistance in this work.

Author contributions

Conception or design of the work; or the acquisition, analysis, or interpretation of data for the work: KIN, NHK, MES, RHG. *Drafting the work or reviewing it critically for important intellectual content:* KIN, NHK, MES, RHG*Final approval of the version to be published:* KIN, NHK, MES, RHG. *Accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved:* KIN.

Conflict of interest

We do not have any conflict of interest

Data availability statement

We confirm that the data supporting the findings of the study will be shared upon reasonable request.

Supplementary file

None

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Bangabandhu Sheikh Mujib Medical University Journal 2025;18(1):e75711
ISSN 2074-2908 | eISSN 2224-7750 |

RESEARCH LETTER

Factors influencing successful breastfeeding practices among post-cesarean section mothers in a selected hospital in Indonesia

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Publication history
Received: 27 Aug 2024
Accepted: 6 Dec 2024
Published online: 5 Feb 2025

Responsible editor
M Mostafa Zaman
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Reviewer
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Keywords
breastfeeding, post-cesarean section, Indonesia

Ethical approval
Approved by the Ethics Committee of Health Research, Faculty of Nursing Sultan Agung Islamic University Semarang, Indonesia (No. 085/A.1-KEPK/FIK-SA/I/2023).

Funding
This study was funded by Universitas Muhammadiyah Semarang.

Trail registration no.
None

Caesarean section is associated with postoperative pain ranging from moderate to severe.[1] As a result, the mothers may experience difficulty breastfeeding, leading to a low breastfeeding success rate.[2] Caesarean section makes mothers vulnerable to changes in their physical activity patterns, reducing their ability to breastfeed and care for their infants.[3] Consequently, there is a possibility of not achieving success in breastfeeding.[4] Mothers' breastfeeding experience at home is somewhat known. Understanding the mothers' breastfeeding experiences is necessary to identify factors influencing breastfeeding practices among post-caesarean section mothers. We have examined the factors related to successful breastfeeding in a selected Indonesian hospital. This would assist in developing interventions to eliminate any obstacle identified.[4,5]

This descriptive study interviewed 100 post-caesarean-section mothers with healthy infants in the Ayyub ward at Roemani Hospital Semarang from May to August 2023. The interview schedule of this study consisted of two components. The first component included the mother's age, education level, occupation, parity, and birth weight and appearance, pulse, grimace, activity and respiration (APGAR) scores of infants. The second component included the four variables related to the breastfeeding assessment score (BAS): previous breastfeeding experience, latching difficulty, breastfeeding interval,

Table 1 Comparison of variables between successful and unsuccessful breastfeeding attempts

Variables	Total (n=100)	Successful (n=81)	Failed (n=19)
Mother's age, years[a]	30.2 (4.4)	30.1 (4.5)	29.9 (4.4)
Education level			
Below college	60 (60.0)	45 (55.6)	15 (78.9)
College and above	40 (40.0)	36 (44.4)	4 (21.1)
Parity			
Primipara	30 (30.0)	31 (38.3)	11 (57.9)
Multipara	70 (70.0)	50 (61.7)	8 (42.1)
Infant's sex			
Boy	71 (71.0)	58 (71.6)	13 (68.4)
Girl	29 (29.0)	23 (28.4)	6 (31.6)
Infant's birth weight (gms)[a]	3370 (290.9)	3369 (290.8)	3371 (290.9)
Infant APGAR Score[b]			
Minute 1	9.6 (0.8)	9.4 (0.8)	9.2 (0.8)
Minute 5	9.8 (0.4)	9.7 (0.4)	9.9 (0.5)
Minute 10	10.0 (0.0)	10.1 (0.0)	9.8 (0.0)
Difficulty latching onto the nipple			
Every time, sometimes	69 (69.0)	50 (61.7)	19 (100.0)[c]
No difficulty	31 (31.0)	31 (38.3)	-
Frequency of baby feedings			
Every 3-6 hours	12 (12.0)	2 (2.5)	10 (52.6)[d]
Every <3 hours	88 (88.0)	79 (97.5)	9 (47.4)

[a]Results are mean (SD); SD indicates standard deviation; [b]AGAR, appearance, pulse, grimace, activity and respiration; [c]P = 0.07; [d]P = 0.001

Key messages

Mothers who have undergone a caesarea section deliveries encounter issues with the breastfeeding process. Latching difficulty, and shorter breastfeeding intervals influence successful breastfeeding practices among post-cesarean section mothers.

and formula milk quantity. Each of these variables was scored 2 for a favourable response. Therefore, a total score of 8 was considered a successful breastfeeding. Mothers' age, infant's birth weight and APGAR score were presented as mean (standard deviation), and compared using a t-test between successful and failed groups; all other variables were presented as numbers (per cent) and compared using a chi-square test.

The mean age of mothers was similar (30.1 vs 29.9) between groups. Infants' birth weight (3,369 vs 3,371) and APGAR scores (minute 1: 9.4 vs 9.2, minute 5: 9.7 vs 9.9, minute 10: 10.1 vs 9.8) were similar. Difficulty in latching onto the nipple and a shorter breastfeeding interval were significantly associated with successful breastfeeding (Table 1).

The role of knowledge in latching has a big impact on the success of breastfeeding. When someone has good knowledge and experience in providing breastfeeding, the baby's nutritional needs will be sufficient so that the baby will be healthier and grow better.[7] Breastfeeding at <3 hours frequency is known to be associated with better milk production.[8] This condition increases the mother's satisfaction in giving breast milk. Most mothers feel sad if the milk amount is insufficient, so they consider starting formula milk.[7] When babies consume formula milk, they will be more likely to consume formula milk because it is easier to suck. As a result, babies no longer want to consume breast milk anymore. Mothers should be counselled to breastfeed more frequently and demonstrate how to overcome the latching onto the nipple.

Acknowledgments

We would like to thank all participants.

Author contributions

Conception or design of the work; or the acquisition, analysis, or interpretation of data for the work: NK, M, E, PLR, SP. *Drafting the work or reviewing it critically for important intellectual content:* NK, M, E, PLR, SP. *Final approval of the version to be published:* NK, M, E, PLR, SP. *Accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved: NK.*

Conflict of interest

We do not have any conflict of interest.

Data availability statement

We confirm that the data supporting the findings of the study will be shared upon reasonable request.

Supplementary file

None

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Bangabandhu Sheikh Mujib Medical University Journal 2025;18(1):e78080
ISSN 2074-2908 | eISSN 2224-7750 |

COMMENTARY

Open Science: Knowledge for the people, by the people, and with the people

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Publication history
Received: 30 Nov 2024
Accepted: 8 Jan 2025
Published online: 5 Feb 2025

Responsible editor
M Mostafa Zaman
0000-0002-1736-1342

Keywords
Open Science, inclusive research, research paradigm

Funding
None

Ethical approval
Not applicable

Trial registration number
Not applicable

Shifting from siloed research to engaged research

Historically, research has been conducted in silos, with academics positioned as the primary proprietors of knowledge creation. Academics in universities and research institutions often operated in isolation. Under this practice, the dissemination of research findings primarily targeted knowledge-users such as policymakers and service providers. The academics (researchers and scholars/educators), service providers/practitioners (those who implement research findings in practice), and policymakers (who use research to inform decisions) constituted the traditional scientific community [1]. While this practice aimed to influence policy decisions and improve service delivery, it largely excluded the communities at the heart of the research. Such exclusion diminished the relevance and accessibility of findings for those most affected. Recognizing the limitations of siloed research, cross-sectoral collaboration gained prominence. This practice emphasizes partnerships between researchers, policymakers, and practitioners, aiming to bridge the gap between knowledge generation and practical implementation [1].

Over recent decades, community-engaged research has emerged as a paradigm prioritizing equity and inclusivity. Approaches like community-based participatory research or participatory action research focus on co-creation and shared decision-making, actively involving community members as collaborators rather than passive subjects [2]. This shift toward inclusive research [3] reflects a growing recognition of the value of lived experience and community expertise in shaping research questions and interventions. The conceptualization of communities as rights holders of the research conducted in the community represents a progressive shift. This perspective aligns with global movements to decolonize research, challenging traditional power dynamics and advocating for community ownership of data and research outcomes. Decolonizing research emphasizes dismantling extractive practices while promoting equitable and empowered partnerships, [4] fostering a more democratization of research ecosystem [5]. This evolution in research practices aligns with global frameworks such as the Sustainable Development Goals, which emphasize participatory decision-making (goal 16) and equitable access to resources [6]. UNESCO's Free and Open Science initiative [7]. further supports this shift by advocating for open access to research findings and inclusion of underrepresented groups in knowledge creation.

Open Science

Open Science is a movement aimed at making scientific research and its dissemination accessible to all levels of society [7]. The principles and practices of Open Science strive towards not only making scientific knowledge available for everyone but also that its creation is equitable, inclusive, and sustainable. It emphasises making the scientific process more transparent and democratic.

Open Science values

Based on the UNESCO recommendation on Open Science, [7] the core values of Open Science are given in Figure 1:

Key messages

Open Science treats scientific knowledge as a global public resource, ensuring equitable access for all, regardless of socioeconomic status. It promotes cross-boundary collaboration and includes marginalized communities, enhancing the relevance of research in addressing societal challenges. Open Science also shifts research from competition to collaboration, prioritizing transparency and democratizing knowledge sharing to build trust and drive innovation.

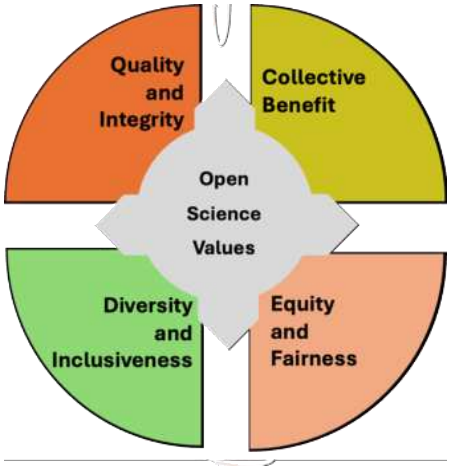

Figure 1 Open Science values

Quality and integrity

Open Science should ensure high-quality research that respects academic freedom and human rights. It emphasizes transparency in the evaluation processes and supports rigorous scrutiny of research methods and outputs by integrating multiple sources of knowledge.

Collective benefit

Recognizing science as a global public good, Open Science aims to benefit humanity as a whole. This value promotes the idea that scientific knowledge should be openly available and its benefits universally shared, ensuring that scientific practices are inclusive, sustainable, and equitable.

Equity and fairness

Open Science seeks to provide equitable access to scientific knowledge for all individuals, regardless of their location, nationality, race, age, gender, income, socio-economic status, career stage, discipline, language, religion, disability, ethnicity, or migratory status. This value emphasizes fair and reciprocal sharing of scientific inputs and outputs.

Diversity and inclusiveness

Open Science embraces a diversity of knowledge systems, practices, workflows, languages, research outputs, and topics. It champions the inclusion of various research communities and engages the wider public and knowledge holders beyond the traditional scientific community, including indigenous peoples and local communities.

Open Science principles

The UNESCO Recommendation on Open Science outlines several key principles that guide the implementation and practice of Open Science [7]. These principles, shown in Figure 2, aim to promote transparency, inclusivity, and collaboration in scientific research.

Transparency, scrutiny, critique, and reproducibility

This principle emphasizes the importance of open processes in scientific research to reinforce the rigor of scientific results. It encourages scrutiny and critique to enhance the positive impact of science on society and improve the ability to solve complex problems.

Equality of opportunities

Open Science aims to ensure that all individuals interested in science have equal access to participate in and benefit from scientific endeavors, regardless of their background or circumstances.

Responsibility, respect, and accountability

Researchers are encouraged to be aware of their public accountability and potential conflicts of interest. This principle highlights the importance of intellectual integrity and understanding the social or ecological consequences of research activities.

Collaboration, participation, and inclusion

This principle promotes scientific collaborations that transcend geographical, linguistic, and resource boundaries. It emphasizes the inclusion of knowledge from marginalized communities to address significant social issues.

Flexibility

Recognizing that there is no one-size-fits-all approach to Open Science, this principle encourages diverse methods and pathways for practicing Open Science while upholding its core values.

Sustainability

Open Science should be efficient and impactful by building on long-term practices, services, infrastructures, and funding models that ensure participation from scientists in less-privileged contexts.

Open Science pillars

According to UNESCO's recommendation on Open Science, [7] the four pillars of Open Science are essential for understanding how this movement seeks to enhance the quality and impact of research while addressing societal needs. The four pillars are given in Figure 3:

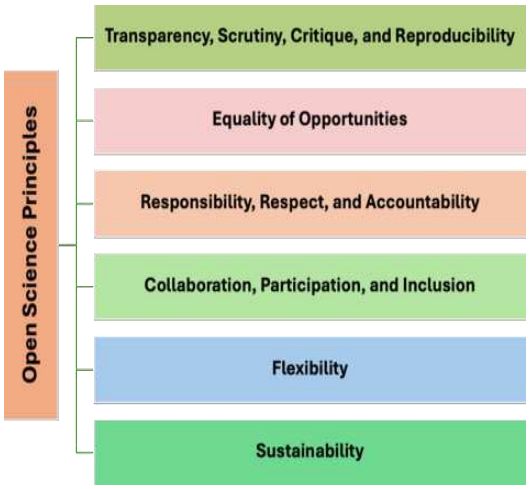

Figure 2 Open Science principles

Open scientific knowledge

This pillar includes the sharing of scientific publications, open research data, open educational resources, open-source software and source code, and open hardware. It emphasizes the importance of making scientific knowledge freely accessible to enhance collaboration and innovation.

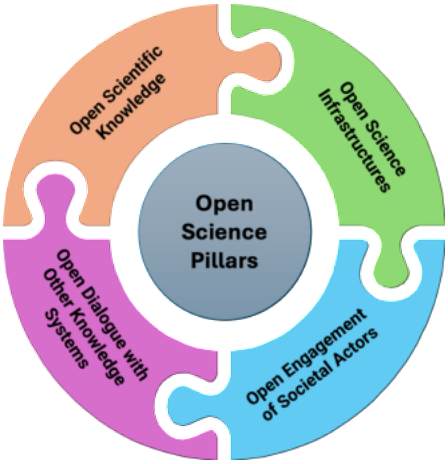

Figure 3 Open Science pillars

Open Science infrastructures

This refers to both virtual and physical infrastructures that support Open Science practices. These infrastructures facilitate access to research outputs, data repositories, and collaborative platforms that enable researchers to share their work effectively.

Open engagement of societal actors

This pillar highlights the importance of involving various societal stakeholders in the research process. It includes practices such as crowdfunding, crowdsourcing, scientific volunteering, citizen science, and participatory research, which enhance public engagement and ensure that research addresses societal needs.

Open dialogue with other knowledge systems

This pillar promotes the inclusion of diverse knowledge systems in scientific discourse. It encourages dialogue with local communities, marginalized community scholars, and vulnerable groups to enrich scientific understanding and ensure that multiple perspectives are considered in research.

Conclusion

Open Science is not merely a method; it represents a philosophical approach to conducting research that prioritizes transparency, collaboration, and inclusivity. We need to keep in mind that there is a difference between Open Science and Creative Common initiative [8.] Both these initiatives aim at promoting accessibility and collaboration, but they focus on different aspects of knowledge sharing. The aim of Creative Common initiative is to facilitate the distribution of content while protecting the rights of creators. On the other hand, the primary goal of Open Science is to enhance the rigor, accountability, and reproducibility of research while fostering inclusion and equity in scientific endeavors. For many researchers, however, the very commitment to Open Science reflects a paradigm shift concerning how they do their research activities. There is a culture where knowledge is freely shared, competition is replaced by collaboration, the public is engaged, and quality in the science is improved. Not only are the individual researchers affected, but the commitment also enriches the broader scientific community and society by encouraging openness, inclusiveness, and collective progress in acquiring knowledge.

Acknowledgments

We take full responsibility for the content of this paper. We acknowledge the use of AI (perplexity.ai) for assistance with English language editing. We used prompts to improve the structure of sentences that we deemed could be further improved. AI was prompted to improve clarity by improving grammar and choice of vocabularies used in the text. All suggestions were critically reviewed and revised to ensure the integrity of our own expressions.

Author contributions

Conception or design of the work; or the acquisition, analysis, or interpretation of data for the work: TCT. *Drafting the work or reviewing it critically for important intellectual content:* TCT, MMHR, NC. *Final approval of the version to be published:* TCT, MMHR, NC. *Accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved:* TCT, MMHR, NC.

Conflict of interest

We do not have any conflict of interest.

Data availability statement

Not applicable

Supplementary file

None

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Bangabandhu Sheikh Mujib Medical University Journal 2025;18(1):e76295
ISSN 2074-2908 | eISSN 2224-7750 |

COMMENTARY

Decoding the revolution of total arterial coronary artery bypass graft surgery

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Publication history
Received: 22 Sep 2024
Accepted: 15 Jan 2025
Published online: 5 Feb 2025

Responsible editor
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0000-0002-1736-1342

Reviewer
D: Montosh Kumar Mondal
0009-0009-8970-1674

Keywords
total arterial coronary artery bypass graft, TA-CABG, arterial grafts

Ethical approval
Not applicable

Funding
None

Trail registration no.
Not applicable

The revolutionary total arterial coronary artery bypass graft (TA-CABG) surgery approach represents a significant leap forward in managing coronary artery disease, promising groundbreaking advancements in long-term outcomes. In 1986, Loop and colleagues' landmark study first observed the long-term prognostic benefits of the left internal mammary artery to the anterior descending graft.[1] Nevertheless, TA-CABG surgery demonstrates a compelling alternative to conventional CABG by employing exclusively arterial conduits, such as the bilateral internal mammary artery (BIMA) and radial arteries, in anaortic in-situ "Y" grafts or free sequential grafts.[2] TA-CABG offers superior durability with sequential grafting and minimally invasive techniques in off-pump CABG, resulting in better long-term graft patency, fewer reoperations, and improved survival rates, especially for younger, high-risk patients.[2,3]

Downsides of saphenous vein grafts: What to know?

Albeit saphenous vein grafts can effectively relieve ischaemia, venous grafts are prone to early atherosclerosis and degenerative changes, resulting in graft failure or restenosis.[2] The harvested great saphenous vein often exhibits pre-existing vascular disease, which can compromise its long-term viability as a graft. Additionally, harvesting techniques, including graft preparation and conduit handling, can contribute to endothelial injury and vasospasm, impacting the effectiveness of venous grafts.[3] Unlike arterial conduits, post-CABG venous grafts exhibit diminished biological effects of endothelial nitric oxide, heightened prothrombotic properties, and increased smooth muscle cell proliferation, contributing to inferior patency rates.[4] However, advancements in graft preservation and minimally invasive techniques promise to mitigate these risks and enhance the longevity of venous grafts in CABG surgery.

TA-CABG: The rationale behind the revolution

The rationale behind the TA-CABG technique lies in the inherent characteristics of arterial conduits comprising robust muscular layers, which exhibit greater resistance to atherosclerosis and plaque formation compared to veins.[2] Arterial conduits, specifically the radial artery, demonstrate superior endothelium-dependent relaxation and remodelling under high-pressure circulation, crucial in maintaining vascular tone, regulating blood flow, and preventing graft thrombosis. Furthermore, the oxygen-rich, high-pressure environment of arteries fosters graft adaptation, reducing the risk of early failure. By performing multi-arterial CABG, surgeons can offer more resilient bypass grafts, potentially yielding superior long-term outcomes and enhancing patients' quality of life. Additionally, TA-CABG minimises the need for vein harvesting from the lower extremities, thereby reducing surgical morbidity and hastening

Key message

Total arterial coronary artery bypass graft utilising bilateral internal mammary artery and radial artery either in-situ, free, or "Y" graft techniques improves long-term survival rate and quality of life. Arterial grafts are less prone to atherosclerosis than veins, which is why arterial conduits in coronary artery bypass graft surgery reduce the likelihood of graft failure over time.

postoperative recovery. Patients undergoing TA-CABG experience less pain, reduced risk of wound complications except for uncontrolled diabetes mellitus, and shorter hospital stays.[3] Furthermore, preserving venous conduits for future interventions becomes increasingly crucial, particularly for patients necessitating multiple revascularisation procedures.

Strengths and overcoming challenges of TA-CABG

While TA-CABG surgery offers improved graft patency and clinical outcomes, it requires expert surgical skills for precise anastomoses.[2,3] Further, patients may require mixed arterial and venous grafts due to limited suitable arterial conduits due to prior coronary interventions and anatomical variations. While harvesting BIMA may be associated with a higher risk of sternal wound infection; studies have not found a direct causal link in the absence of specific comorbidities like diabetes mellitus.[1,3] Albeit rare, radial artery harvesting carries the risk of superficial radial nerve injury similar to the saphenous nerve during great saphenous vein harvesting; hence, the meticulous surgical technique is paramount to minimise harvest site complications.[5] Furthermore, TA-CABG might entail slightly higher procedural expenses due to the extra equipment and resource requirement, but the superior long-term graft patency offsets concern about cost-effectiveness.

Despite the compelling advantages of TA-CABG, widespread adoption was hindered by various factors, especially a lack of surgical expertise, technical challenges, and concerns regarding long-term graft patency. However, recent initiatives, including training programmes and international collaborations, have highlighted the benefits of arterial conduits due to physiology and structural resilience, preserved endothelial function, and resistance to graft disease in real-world scenarios. Moreover, the time has come to wholeheartedly embrace the innovative TA-CABG approach to advance arterial revascularisation and optimise patient clinical outcomes. Finally, preserving venous conduits for potential future interventions is highly recommended, especially in patients who may require multiple revascularisation procedures.

Acknowledgments

None

Author contributions

Conception or design of the work; or the acquisition, analysis, or interpretation of data for the work: RR, AM. *Drafting the work or reviewing it critically for important intellectual content:* RR, AM. *Final approval of the version to be published:* RR, AM. *Accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved:* RR, AM.

Conflict of interest

We do not have any conflict of interest.

Data availability statement

Not applicable

Supplementary file

None

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Bangabandhu Sheikh Mujib Medical University Journal 2025;18(1):e76190
ISSN 2074-2908 | eISSN 2224-7750 |

COMMENTARY

Artificial intelligence in unveiling herbal remedies for cancer: Advances and applications

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Publication history
Received: 17 Sep 2024
Accepted: 5 Jan 2025
Published online: 4 Feb 2025

Handling editor
Md Atiqul Haque
0000-0002-7598-2550

Reviewers
A: Anonymous
B: Anonymous

Keywords
artificial intelligence, natural remedies, cancer treatment

Funding
None declared

Ethical approval
Not applicable

Trial registration number
Not applicable

Cancer continues to pose a significant global health burden, with millions of new cases diagnosed each year. Despite advances in conventional treatments such as chemotherapy, radiation, and immunotherapy, these approaches often come with considerable challenges, including severe side effects, treatment resistance, and high costs. Artificial intelligence (AI) technologies such as Machine Learning and Deep Learning offer significant promise to overcome such challenges.[1] Machine learning techniques aid in discovering novel medications by analysing large datasets to predict the activity and efficacy of new compounds. It accelerates drug discovery by automating screening and modelling drug-target interactions, reducing time and costs compared to traditional methods. Deep learning, using artificial neural networks, analyses large datasets to identify complex patterns. In pharmaceuticals, deep learning predicts drug functionality, identifies treatment targets, and decodes biological structures, accelerating drug discovery and improving treatment outcomes. AI can be highly useful not only in the novel drug discovery but also in identification of promising anticancer compounds of natural origin. Herbal remedies are complex, containing multiple active constituents that often work synergistically. One requirement is the need for more stringent clinical validation.[2]

For the literature search in this commentary, specific inclusion and exclusion criteria were applied to ensure relevant studies were selected. Inclusion criteria included: (1) studies focused on the use of AI techniques (such as machine learning, deep learning, and natural language processing) in discovering herbal remedies for cancer. Exclusion criteria included: (1) studies not related to AI. AI plays a crucial role in personalized herbal treatments by integrating patient data (genetic, medical, lifestyle) to customize therapies, using predictive analytics to forecast responses and adjust treatments based on feedback for optimal outcomes and minimized side effects.[3]

Key messages

Artificial intelligence have revolutionised herbal anticancer medication discovery. AI has predicted bioactive molecules and optimised drug synergy. Improved clinical trial designs and customised therapy have boosted cancer herbal medicine research. Data quality, model transparency challenges and AI-driven strategies to expedite herbal cancer treatment development conclude the article. AI models could find new natural anticancer compounds, revolutionising cancer treatment.

Table 1 Summary of the applications of AI in drug discovery

Application	Description	AI techniques used	Benefits	Relevance to drug discovery
Identification of target	AI analyzes extensive datasets to detect proteins, genes, or pathways affecting disease mechanisms, aiding in identifying promising targets.	Machine learning, data mining	Focuses research on the most promising targets	Target identification is crucial for the success of drug discovery, helping streamline the search for effective treatments.
Substance testing	AI optimizes drug screening by predicting the most effective compounds, reducing the need for extensive experimental testing.	Predictive models, convolutional neural networks	Reduces experimental workload, accelerates discovery process	AI's predictive capabilities enhance efficiency by narrowing down the best candidates, saving time and resources.
Predictive modelling	AI-driven models predict ADMET[a] properties of drug candidates, helping assess potential effectiveness and safety before experimental validation.	Statistical techniques, machine learning	Expedites and reduces costs of drug development	Predictive modeling reduces failure rates in clinical trials by assessing the safety and efficacy of drugs early in the process.
Drug repurposing	AI finds new therapeutic uses for approved drugs by uncovering correlations between drugs and diseases.	Data analysis, natural language processing	Accelerates development using existing safety and efficacy data	Drug repurposing is a cost-effective strategy to quickly find new treatments, leveraging existing drugs for new indications.

[a]ADMET indicates absorption, distribution, metabolism, elimination and toxicity

AI implementation in herbal medicine faces several technical challenges. Data quality and accessibility issues include gaps in critical information, which limit prediction accuracy, and difficulties in integrating diverse data sources due to varying formats and standards. Algorithm limitations arise from models trained on specific datasets that may not generalize well to new or unseen data, particularly for diverse herbal compounds and patient populations. The complexity of herbal mixtures, with multiple active constituents, adds another challenge, as AI models may struggle to capture their synergistic effects. Additionally, high computational demands for advanced AI models can be a barrier for smaller research labs or organizations lacking access to powerful computing resources.[4]

AI techniques have significantly enhanced herbal drug discovery for cancer, with machine learning models identifying promising compounds like curcumin, paclitaxel, camptothecin, resveratrol and Epigallocatechin-3-gallate. Deep learning and natural language processing have accelerated drug-target interaction predictions, extracting key insights from databases with published studies. Advancements like transfer learning and Graph Neural Networks have optimized herbal compound synergy, increasing the accuracy of compound-target interaction models by 15%. Platforms like Atomwise have improved the success rate for compounds with anticancer potential by 30%, while DeepChem has significantly improved the discovery methodology (Table 1).[5]

Recognizing there are benefits to using AI to identify herbal anticancer agents, but there are challenges to overcome before implementation. The biggest challenge is data quality and accessibility. AI models need datasets to provide accurate predictions and insights. However, herbal medicine databases lack consistency, accessibility, and comprehensiveness. AI model creation is difficult due to the lack of formal documentation for many traditional knowledge systems and uneven dataset quality. AI struggles to acquire worldwide researchers' and clinicians' trust in innovative drug discovery, where clinical validation and regulatory approval are crucial.[6]

It can be concluded that AI has the capacity to enhance accuracy, expedite the discovery and optimise clinical studies in order to revolutionise the antineoplastic treatments with special reference to bioactive molecules.

Acknowledgments

None

Author contributions

Conception or design of the work; or the acquisition, analysis, or interpretation of data for the work: BSS, SHK, AHK, NG, AK. *Drafting the work or reviewing it critically for important intellectual content:* NG, AK. *Final approval of the version to be published:* BSS, HT. *Accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved:* HT.

Conflict of interest

We do not have any conflict of interest.

Data availability statement

Not applicable

Supplementary file

None

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Bangabandhu Sheikh Mujib Medical University Journal 2025;18(1):e77310
ISSN 2074-2908 | eISSN 2224-7750 |

PERSPECTIVE

Current issues with antibody-conjugated lipid nanoparticles

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Publication history
Received: 28 Oct 2025
Accepted: 2 Feb 2025
Published online: 10 Feb 2025

Responsible editor
M Mostafa Zaman
0000-0002-1736-1342

Reviewer
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0000-0001-9627-3617
F: Md. Fakhrul Islam Khaled
0000-0002-1003-6598

Keywords
antibody-conjugated lipid nanoparticles, nonviral gene delivery, immunogenicity

Ethical approval
Not applicable

Funding
None

Trail registration number
Not applicable

Lipid Nanoparticles (LNPs) have been utilised for many years to transfer nucleic acid cargos, such as therapeutic mRNAs and siRNAs [1]. The US FDA approved LNPs for use in humans after extensive development and optimisation. This includes the delivery of therapeutic siRNAs to hepatocytes via intravenous administration [2] and the delivery of mRNA vaccines via intramuscular administration. However, in the liver, the majority of intravenously injected nanoparticles are concentrated [1]. In particular, many LNPs obtain blood-borne ApoE lipoprotein coatings, encouraging hepatocytes to take up LNPs through interactions with the ApoE: LDL receptor [1].

It isn't easy to achieve nonliver gene editing mediated by LNPs since the majority of intravenously delivered LNPs naturally accumulate in the liver. [3] One way to counteract the inherent liver-targeting properties of LNPs is to inject them locally as opposed to intravenously. Several labs have shown successful nuclease and base editing in the mouse inner ear following local administration of lipid-encapsulated ribonucleoproteins (RNPs) [3]. However, the therapeutic utility of LNP administration would be expanded if it were possible to employ systemically given LNPs to transport gene-editing medicines to nonliver organs. LNPs can also be directed to nonliver tissues by conjugating targeting components, such as antibody fragments, to their surface [1] [2] [4]. One notable example of this approach is Epstein and colleagues' intravenously delivered anti-CD5 antibody-conjugated LNPs to attack T cells and temporarily develop chimeric antigen receptor T lymphocytes that may heal heart damage in rats [4].

The problem starts when we use antibody fragments to direct the LNPs to nonliver sites. Patients may become immunogenic due to antibody fragments. The absence of an Fc domain and in vivo mechanisms that prevent B cells from producing unstable antibody species are the causes of this. It can increase the risk of self-epitope formation through mechanisms such as structural exposure, high binding affinity, and lack of effector function modulation. These elements may increase the possibility of aggregation while producing or purifying antibody fragments [4]. Antibody fragments can also generate new epitopes that are potentially immunogenic. Multiple studies have shown antibodies to the top hinge region of Fab fragments and to the hinge portion of the F(ab')2 of IgG [4]. Without appreciable cell growth, allogeneic membrane fragments can activate cytotoxic T lymphocytes (CTLs) and elicit a secondary immunological response, indicating that specific antigens are sufficient to activate alloimmune T cells. [5].

Key messages

Lipid nanoparticles have only been used for liver-targeted gene editing due to their hepatocytic uptake. To target non-liver delivery systems, antibody-conjugated lipid nanoparticles are not the solution due to their ability to cause self-epitopes.

Integrating antibody fragments into LNPs presents several challenges that need to be addressed to optimise therapeutic efficacy. Compared with nontargeted LNPs, antibody fragment-conjugated lipid NPs may not always result in increased tumour localisation, as both can achieve similar tumour tissue accumulation [6]. acLNPs may not significantly improve tumour localisation compared to non-targeted LNPs due to systemic distribution challenges, such as rapid clearance by the immune system and the heterogeneous nature of tumour microenvironments. Additionally, off-target effects and variability in receptor expression can further limit the effectiveness of active targeting strategies, leading to unintended accumulation in healthy tissues. The physicochemical properties of antibody fragment-LNPs, such as size and charge, require careful optimisation to enhance tumour uptake, with smaller sizes resulting in improved uptake. For instance, the incorporation of PEGylation has been shown to produce smaller, more homogeneous LNPs with improved transfection efficiency and reduced cytotoxicity, while optimising formulations using design-of-experiment approaches has led to significant increases in encapsulation efficiency and targeted delivery capabilities, as demonstrated with biodegradable block copolymer-stabilized LNPs that achieved up to a 40-fold increase in transfection efficiency in certain cell lines6. While antibody fragments can improve the internalisation of lipid NPs into cancer cells, this does not necessarily translate to increased tumour localisation, indicating a need for further research into the mechanisms of NP distribution and uptake [7]. Developmental challenges such as low thermostability and weak binding to affinity purification resins can hinder the progress of antibody fragment-based LNPs from preclinical stages to clinical application.

In conclusion, while antibody fragments conjugated to lipid nanoparticles offer a targeted approach to cancer therapy, their use is not without disadvantages. The lack of increased tumour localisation, the necessity for optimisation of physicochemical properties, and developmental challenges such as stability and purification issues are key considerations that must be addressed to improve the efficacy of these therapeutic constructs. Despite these challenges, the potential for enhanced internalisation into cancer cells remains a promising aspect of antibody fragment-conjugated lipid NPs, suggesting that these systems could become more effective in clinical settings with further research and development. To enhance the targeting of LNPs to non-liver tissues, strategies such as using alternative targeting ligands, developing dual delivery systems, and employing novel conjugation techniques can be effective. These approaches aim to improve specificity, reduce immunogenicity, and enhance the overall therapeutic efficacy of LNPs in clinical applications.

Acknowledgments

I would like to thank Ms. Umaiya Muzaffar for her support, which made this perspective article possible after thorough research.

Author contributions

Not applicable

Conflict of interest

I do not have any conflict of interest.

Data availability statement

Not applicable

Supplementary file

None

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BSMMU Journal
An official journal of Bangabandhu Sheikh Mujib Medical University
ISSN: 2224-7750 (Online), 2074-2908 (Print)

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Letter to editor	-	400	50	6	-	-	-
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BSMMU Journal
Published by Bangabandhu Sheikh Mujib Medical University
Shahbag, Dhaka 1000, Bangladesh

https://www.banglajol.info/index.php/BSMMUJ

ISSN: 2224-7750 (Online), 2074-2908 (Print)