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REVIEW ARTICLE

The Intersection of Islam and Nursing: A New Perspective on Cleanliness and Care.

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Abstract

Introduction: Cleanliness is a key pillar of health, vital for infection prevention, patient safety, and overall well-being. In both nursing and Islamic teachings, cleanliness is essential to health and ethical responsibility. Nursing focuses on clinical hygiene and sanitation, while Islamic jurisprudence (Fiqh) provides a broader framework encompassing physical, spiritual, and moral dimensions. This study explores cleanliness from both perspectives, identifying similarities and potential integration into nursing practice. **Objective:** This article examines cleanliness in nursing and Islamic teachings, highlighting similarities and differences. It also discusses integrating Islamic principles of cleanliness into nursing to enhance culturally and religiously competent care. **Methodology:** A qualitative content analysis approach was used, drawing from nursing literature and Islamic sources, including the Qur'an, Hadith, and scholarly interpretations. Hygiene frameworks and infection control guidelines were analysed alongside Islamic purification concepts to develop an integrated understanding. **Results:** Both nursing and Islamic teachings emphasise cleanliness for disease prevention and patient care. Nursing focuses on hygiene protocols and infection control, while Islamic jurisprudence extends cleanliness to ritual purity, spiritual well-being, and ethical conduct. Integrating Islamic principles can enhance patient-centred care, address Muslim patients' religious needs, and foster ethical cleanliness in healthcare settings. **Conclusion:** Integrating Islamic cleanliness principles into nursing bridges clinical hygiene with spiritual and ethical care. This integration can improve cultural sensitivity, patient satisfaction, and holistic well-being. Future research should assess its impact on nursing education, healthcare policy, and patient outcomes to promote inclusive healthcare practices.

Keywords: *Cleanliness, clinical practice, hygiene, Islamic jurisprudence, nursing, spiritual well-being.*

Introduction

Cleanliness is fundamental to healthcare, ensuring patient safety, infection prevention, and overall well-being. Nursing, a profession rooted in care and hygiene, emphasises strict adherence to cleanliness protocols to minimise healthcare-associated infections (HAIs) and enhance patient recovery outcomes. Florence Nightingale revolutionised nursing practice by advocating for sanitation, hygiene, and infection control measures, which remain core components of modern nursing education and practice [1]. Similarly, Islam places significant emphasis on cleanliness, viewing it as both a physical necessity and a spiritual obligation. Islamic jurisprudence (Fiqh) categorises cleanliness into physical purification (ṭahārah) and ritual purification, integrating hygiene with religious obligations [2]. While nursing primarily focuses on clinical hygiene, disinfection, and sterilisation, Islamic teachings expand the concept of cleanliness to include ethical, spiritual, and environmental dimensions. However, despite these shared values, integrating Islamic cleanliness principles into modern nursing remains underexplored.

A major challenge in contemporary nursing practice is addressing the religious and cultural needs of diverse patient populations. This is particularly relevant in Muslim-majority settings, where cleanliness holds both medical and spiritual significance. Studies indicate that inadequate cultural competence in nursing can lead to patient dissatisfaction and barriers to effective healthcare delivery [3,4]. While nursing institutions implement infection control measures based on scientific evidence, there is a gap in integrating Islamic perspectives on cleanliness, which could enhance culturally competent care. Islamic guidelines provide detailed rulings on bodily hygiene, environmental cleanliness, and purification methods, influencing Muslim patients' expectations regarding healthcare practices [5,6]. Despite the alignment between Islamic and nursing perspectives on hygiene, healthcare settings often lack structured policies to accommodate religious cleanliness practices, potentially affecting Muslim patients' comfort and adherence to medical advice.

This article explores cleanliness from both nursing and Islamic perspectives, identifying areas of convergence and potential integration within clinical practice. This study aims to bridge the gap between medical and religious cleanliness principles to foster culturally sensitive and ethically sound nursing care by comparing nursing hygiene standards with Islamic jurisprudence. The discussion highlights the implications of incorporating Islamic cleanliness concepts in patient care, nursing education, and hospital policies to support holistic and patient-centered healthcare. Future research should focus on evaluating the impact of such integration on patient satisfaction, nurse-patient communication, and overall healthcare outcomes in Muslim-majority and multicultural settings.

Materials and Methods

This study employs a qualitative content analysis approach to examine the concept of cleanliness from both nursing and Islamic perspectives. The analysis involves an extensive review of contemporary nursing literature on hygiene, infection control, and environmental cleanliness, alongside Islamic jurisprudential sources, including the Qur'an, Hadith, and scholarly interpretations related to purification (*ṭahārah*). A comparative framework was applied to identify thematic intersections between the two perspectives, allowing a deeper understanding of how Islamic cleanliness principles align with modern nursing standards. This method ensures a comprehensive cleanliness analysis as both a clinical requirement and a spiritual obligation in healthcare settings.

Data collection was conducted through a systematic search of academic literature on nursing-related studies from databases such as PubMed, Scopus, and Google Scholar. Islamic

perspectives were sourced from classical and contemporary Islamic texts, fatwa compilations, and scholarly articles on Islamic jurisprudence. Search terms included "nursing hygiene," "infection control in healthcare," "Islamic cleanliness principles," "Islamic jurisprudence on hygiene," and "spiritual aspects of cleanliness in healthcare." Boolean operators (AND, OR) were applied to refine search results. The inclusion criteria comprised peer-reviewed articles, authoritative Islamic sources, and studies published in English focusing on cleanliness in both nursing and Islam. Articles unrelated to healthcare or Islamic jurisprudence, non-peer-reviewed sources, and those without full-text accessibility were excluded from the review.

Following the identification of relevant sources, a manual thematic analysis was conducted to categorise the findings into key domains such as nursing hygiene standards, infection prevention measures, Islamic purification practices, and their application in clinical settings. The data were systematically coded by hand, with researchers independently identifying and labelling recurring concepts and patterns across the selected texts. To ensure trustworthiness and credibility, each researcher first performed individual coding, followed by a consensus-building process in which interpretations were compared, discussed, and refined collectively. Discrepancies in coding or theme categorisation were resolved through deliberation until a shared understanding was reached. This iterative approach helped to reduce researcher bias, enhance analytical rigor, and ensure that the resulting themes accurately reflected both the nursing literature and Islamic jurisprudential perspectives. This approach strengthened the validity of the findings and minimised researcher bias in analysing scientific and religious perspectives [7].

However, as with any qualitative content analysis, this study acknowledges certain limitations. Despite efforts to enhance rigour, the risk of researcher interpretation bias remains due to the subjective nature of thematic categorisation. Additionally, while multiple reviewers were involved in the analysis process, the scope of source selection may have been constrained by language, availability, and relevance filters. These limitations necessitate cautious interpretation of the findings and encourage further empirical validation and cross-disciplinary exploration in future research.

Results

The analysis revealed significant overlaps between nursing hygiene principles and Islamic cleanliness (ṭahārah) guidelines, demonstrating that both emphasise the importance of cleanliness for infection control, patient safety, and overall well-being. In nursing, hygiene protocols are guided by evidence-based infection control measures, including hand hygiene, environmental sanitation, and sterilisation of medical instruments. Similarly, Islam mandates ritual purification practices, such as ablution (wudhu'), full-body purification (ghusl), and the removal of impurities (najasah), all of which contribute to personal and environmental hygiene. Integrating these principles in clinical practice can enhance culturally sensitive patient care, particularly in Muslim-majority healthcare settings.

The findings also highlight that nursing education and clinical training focus primarily on physical cleanliness and infection prevention, whereas Islamic teachings extend the concept to encompass spiritual and ethical dimensions. Islam not only emphasises bodily cleanliness but also promotes an ethical approach to hygiene, such as avoiding contamination, maintaining personal modesty, and ensuring cleanliness in food preparation and consumption. This suggests that incorporating Islamic cleanliness principles into nursing curricula could provide a more holistic understanding of hygiene that aligns with medical and religious imperatives.

From a clinical application perspective, the study identified key areas where Islamic cleanliness guidelines can complement nursing hygiene protocols. For instance, Muslim patients may require access to ablution facilities in hospitals, prefer ritual purification before prayer, and seek medical care that respects Islamic rulings on impurity and cleanliness. Nurses with knowledge of Islamic purification practices can facilitate better patient experiences by ensuring culturally appropriate hygiene accommodations, such as providing clean water for ablution, understanding patient preferences regarding contact with impure substances (e.g., blood, urine), and guiding them on maintaining ritual purity during hospitalisation.

Lastly, the findings suggest that a structured integration of Islamic cleanliness principles into nursing policies can enhance culturally competent care and patient satisfaction. Hospitals and healthcare institutions that accommodate religious cleanliness needs may improve patient trust and compliance with treatment. Additionally, healthcare providers who understand Islamic cleanliness laws can help address common patient misconceptions, reinforcing medical and religious well-being. Future studies should assess the practical outcomes of such integration, including its impact on patient care quality, nurse-patient relationships, and institutional policies on hygiene standards in diverse healthcare settings.

The figure 1 presents the assumed relevance of various aspects of Islamic cleanliness principles in nursing practice, as derived from the authors' qualitative thematic analysis. The percentages are not based on quantitative measurements but reflect conceptual weighting and perceived alignment identified through interpretive analysis of the reviewed literature and Islamic jurisprudential sources. They are intended to visualise thematic prominence and integration potential within clinical nursing practice. The percentages reflect the conceptual alignment between nursing hygiene protocols, Islamic cleanliness guidelines, ethical dimensions, clinical applications, and healthcare integration, highlighting areas where religious and professional hygiene standards can complement each other.

Discussion

Alignment of nursing hygiene and Islamic cleanliness

Cleanliness is a fundamental component of modern nursing practice and Islamic teachings, emphasizing its role in preventing infections, maintaining health, and ensuring patient well-being. Florence Nightingale's advocacy for sanitation, hand hygiene, and environmental cleanliness has shaped contemporary nursing protocols, reinforcing the importance of maintaining high hygiene standards in healthcare settings [1,8]. Similarly, Islamic teachings mandate ritual purification (ṭahārah) as an essential aspect of daily life, integrating bodily cleanliness with spiritual well-being. The Qur'an and Hadith explicitly outline guidelines on personal hygiene, environmental sanitation, and removing impurities (najasah), ensuring that cleanliness is maintained at all times [2,9]. This demonstrates that nursing and Islamic principles share common objectives in promoting health, safety, and disease prevention, although the latter extends beyond physical cleanliness to incorporate ethical and spiritual dimensions.

Despite these similarities, nursing hygiene primarily focuses on scientific evidence-based infection control measures, while Islamic cleanliness guidelines incorporate religious obligations into daily hygiene routines. For instance, the five daily prayers in Islam require ablution (wudhu'), ensuring that a person maintains cleanliness multiple times daily as Allah mentioned in chapter 5 verse 6 of the Qur'an, *"O you who believe! When you stand up for the prayer, then wash your face and your hands till the elbows, wipe your head and your feet till the ankles. But if you are (in) a state of ceremonial impurity then purify yourselves."*

Islam also mandates specific purification methods for different impurities, such as washing with mutlaq (pure) water when removing blood or excrement [2]. In nursing practice, hand hygiene, sterilisation, and surface disinfection are strictly regulated to prevent the spread of infections in clinical settings. However, Islamic teachings reinforce not just the act of cleaning itself but also the intention (niyyah) behind it, reflecting an ethical obligation that aligns with the principles of holistic and patient-centered nursing care [6,11]. Understanding these shared values can help nurses provide culturally appropriate care, particularly for Muslim patients who seek medical treatment in compliance with their religious beliefs.

Integrating Islamic cleanliness principles into nursing practice can enhance culturally competent and patient-centered care, particularly in Muslim-majority settings. Hospitals can accommodate religious hygiene practices by providing access to ablution facilities, ensuring the availability of clean water, and respecting patients' need for purification rituals. Additionally, nurses who understand Islamic purification laws can offer better guidance to Muslim patients, particularly when handling situations such as urinary incontinence, menstruation, and post-surgical cleanliness [12,13]. By acknowledging the religious significance of hygiene alongside scientific infection control measures, healthcare professionals can bridge the gap between clinical protocols and patients' spiritual needs, fostering trust, compliance, and improved healthcare outcomes.

Education and ethical aspects of cleanliness

Education plays a critical role in shaping nurses' understanding of hygiene, and integrating ethical considerations enhances their ability to provide holistic and culturally competent care. In nursing curricula, infection prevention, hygiene protocols, and patient safety are fundamental competencies, ensuring that nurses uphold professional standards in clinical practice [14]. However, ethical dimensions of cleanliness are often overlooked, despite their significance in nursing professionalism and patient-centered care. Islam extends the concept of cleanliness beyond physical hygiene, linking it to moral conduct, spiritual purification, and ethical responsibility [10,13]. Islamic teachings emphasise that cleanliness is not merely an act but a moral obligation (farḍ) and a sign of faith (īmān), as reflected in the hadith: *"Cleanliness is part of faith" (Muslim, 223)* [15]. By incorporating Islamic cleanliness ethics into nursing education, healthcare professionals can develop a broader perspective on hygiene, recognising its spiritual and ethical implications and medical necessity.

Nursing ethics emphasise duty of care, respect for patient autonomy, and cultural sensitivity, yet there remains a gap in interactions and overall patient satisfaction [16]. For instance, some Muslim patients may decline medical interventions due to concerns about impurity (najasah), requiring nurses to navigate these situations with both clinical expertise and religious awareness. Highly purified insulin is commonly used to treat diabetic patients, but it can raise concerns among some Muslim patients due to its potential origin from impurities (mughallāzah). Nurses may feel guilty or uncertain about administering it. However, since some patients depend on insulin to stay healthy, avoiding it could harm their health. The Fatwa Committee of the National Council for Islamic Religious Affairs Malaysia ruled on 10 October 1983 that using such insulin is permissible in medical emergencies. If synthetic insulin, made from human DNA and E. coli bacteria without pork, is available, nurses should consult the doctor to prescribe it instead [17].

Islamic teachings guide ethical cleanliness practices, such as covering the body appropriately, ensuring purity in food and drink, and maintaining a hygienic environment. These principles align with nursing professionalism,

infection control, and holistic patient care, reinforcing the need for cultural competence training in nursing education. Nurses can enhance their ethical reasoning, improve patient rapport, and provide more inclusive care by integrating religious perspectives on cleanliness into nursing curricula.

The inclusion of Islamic cleanliness principles in nursing education can bridge the gap between professional ethics and religious obligations, promoting a more comprehensive understanding of hygiene in healthcare. Training programs with religious sensitivity modules can prepare nurses to handle situations where Islamic cleanliness laws influence patient preferences, such as menstruation, postpartum care, and ablution requirements before prayer [18,19]. Additionally, structured education on cross-cultural hygiene ethics can equip nurses with the skills to accommodate diverse patient needs while adhering to clinical safety standards. Future research should examine how enhancing nursing curricula with religious and ethical hygiene education impacts nurse-patient relationships, healthcare accessibility, and adherence to treatment plans among Muslim patients. Strengthening ethical literacy in nursing hygiene will ensure that cleanliness is upheld as a medical practice and a moral and culturally respectful commitment to patient well-being.

Clinical applications in nursing care

Cleanliness is a crucial component of nursing care, directly influencing infection prevention, patient safety, and overall healthcare quality. In clinical settings, nurses are responsible for maintaining hygiene standards, including hand hygiene, environmental sanitation, sterilisation of medical instruments, and personal protective measures to prevent hospital-acquired infections (HAIs) [20]. These practices align with Islamic cleanliness principles, emphasising bodily purity, environmental hygiene, and the ethical responsibility of ensuring cleanliness in all aspects of life. For instance, Islamic teachings prescribe specific purification methods (ṭahārah) for removing impurities, including mutlaq water for cleansing body fluids such as blood and excrement [21]. By understanding these religious hygiene principles, nurses can offer more culturally appropriate care, ensuring that Muslim patients' needs are respected while maintaining clinical safety protocols.

One significant clinical application of Islamic cleanliness principles in nursing is assisting Muslim patients with ritual purification (wudhu' and ghusl). Many hospitalised patients may face challenges maintaining their religious hygiene due to mobility restrictions, medical devices (e.g., IV lines, catheters), or post-surgical conditions [22]. Nurses aware of Islamic guidelines on ablution and dry purification (tayammum) can provide practical support by facilitating partial ablution when full wudhu' is impossible or guiding patients in performing tayammum when water use is restricted. Additionally, nurses can ensure that patients have access to clean water, maintain privacy for purification rituals, and accommodate religious concerns regarding bodily cleanliness. These small but significant adjustments can enhance patient comfort, dignity, and spiritual well-being, leading to greater compliance with medical treatments and improved patient satisfaction.

Another critical aspect of clinical application is handling patient hygiene needs in a way that aligns with Islamic jurisprudence. In certain situations, nurses may need to cleanse patients who cannot do so themselves, such as assisting with perineal care, postpartum hygiene, or managing incontinence. Islamic teachings emphasise the removal of najasah (impurity) using proper cleansing methods, which require flowing water rather than just wipes or dry cleaning methods [23]. By adhering to these principles, nurses can ensure patients feel reassured about their ritual purity while maintaining high infection control standards. Furthermore, nurses can educate patients on

balancing Islamic cleanliness obligations with medical care, such as advising on religious exemptions in cases of medical necessity (e.g., when delaying purification due to severe illness is permitted in Islam). Integrating Islamic cleanliness principles into nursing practice guidelines can help create an inclusive healthcare environment where religious sensitivities are acknowledged without compromising medical standards.

Impact on healthcare practice

Integrating Islamic cleanliness principles into nursing practice and healthcare policies can enhance patient-centered care, improve cultural competence, and strengthen infection control measures. In healthcare settings, hygiene protocols are designed to prevent infections and ensure patient safety, but they often overlook religious considerations, particularly for Muslim patients who adhere to specific cleanliness rituals [24]. Accommodating Islamic cleanliness practices, such as providing access to ablution facilities, ensuring privacy for purification rituals, and respecting religious views on bodily purity, can significantly enhance patient comfort and satisfaction. Research has shown that culturally competent care leads to better health outcomes, increased patient trust, and improved adherence to medical recommendations [25,26]. By incorporating Islamic cleanliness guidelines into hospital policies and nursing protocols, healthcare institutions can create a more inclusive and respectful environment for Muslim patients, reducing anxiety and improving the overall care experience.

Beyond individual patient care, integrating Islamic cleanliness principles can also benefit healthcare workers and institutions by enhancing infection control measures and reinforcing ethical hygiene standards. Islamic teachings emphasise that cleanliness is a personal and social responsibility, encouraging healthcare workers to maintain high hygiene standards in their professional and personal lives [27]. For example, the Islamic practice of regular handwashing before prayer (wudhu') aligns with evidence-based hand hygiene protocols recommended for infection prevention in hospitals. Additionally, the emphasis on environmental cleanliness in Islam, such as keeping hospital wards free from contamination and ensuring proper waste disposal, complements modern hospital sanitation guidelines. Healthcare facilities that recognise and support these religious hygiene principles may see improvements in workplace cleanliness culture, leading to lower infection rates and higher compliance with hygiene protocols among healthcare staff.

Implementing structured policies that incorporate religious cleanliness considerations requires collaboration between healthcare administrators, Islamic scholars, and medical professionals to ensure that these accommodations align with both medical best practices and religious guidelines. Hospitals can develop standardized training programs for nurses and other healthcare providers, equipping them with knowledge on Islamic hygiene laws and culturally competent care strategies [27]. Such initiatives not only benefit Muslim patients but also contribute to a broader movement toward patient-centered and culturally responsive healthcare delivery.

Despite the promising benefits of integrating Islamic cleanliness principles into nursing care, several practical challenges and potential resistance may arise in real-world implementation. One major barrier is the lack of awareness or understanding among non-Muslim healthcare providers regarding Islamic hygiene requirements, which could lead to unintentional disregard or misinterpretation of religious needs. Additionally, institutional constraints, such as rigid hygiene protocols, time limitations, or resource availability (e.g., access to clean water or private spaces for ablution), may impede efforts to accommodate religious practices. Furthermore, some healthcare professionals may perceive the integration of religious principles as conflicting

with secular or evidence-based clinical environments, raising concerns about the balance between religious accommodations and standardised medical care.

To address these challenges, interdisciplinary collaboration is essential—bringing together healthcare administrators, Islamic scholars, and nursing educators to create context-specific guidelines that align religious principles with medical protocols. Incorporating cultural competence training into nursing curricula and continuous professional development can build empathy, awareness, and practical skills among healthcare workers. Institutions can also develop flexible policies that support reasonable accommodations without compromising safety or care quality. By fostering open dialogue, providing targeted education, and embedding inclusive practices within healthcare systems, potential resistance can be reduced, and the integration of Islamic cleanliness principles can become both feasible and sustainable in diverse clinical settings.

Conclusion

Integrating Islamic cleanliness principles into nursing practice provides a comprehensive approach to hygiene that aligns scientific infection control measures with religious and ethical obligations. This study has demonstrated that nursing and Islamic teachings emphasise cleanliness as essential for disease prevention, patient care, and ethical healthcare practice. By incorporating Islamic cleanliness guidelines into nursing education, clinical applications, and hospital policies, healthcare professionals can enhance culturally competent care, improve patient satisfaction, and reinforce ethical hygiene standards. The findings suggest that nurses' understanding of Islamic purification laws can better accommodate Muslim patients' needs, leading to greater trust, improved compliance with medical treatments, and better healthcare outcomes. Future research should explore the long-term effects of integrating religious hygiene principles into nursing curricula and hospital policies, ensuring that healthcare environments remain inclusive, ethical, and patient-centered while upholding the highest medical hygiene standards.

Conflict of interest

The authors have no conflict of interest in this study.

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Authors' contributions

MFMI conceptualised the study, conducted the Islamic jurisprudential analysis, and led the manuscript writing. SZS performed the nursing literature review, contributed to the thematic analysis, and assisted in drafting and revising the manuscript. Both the authors reviewed and approved the final version of the manuscript.

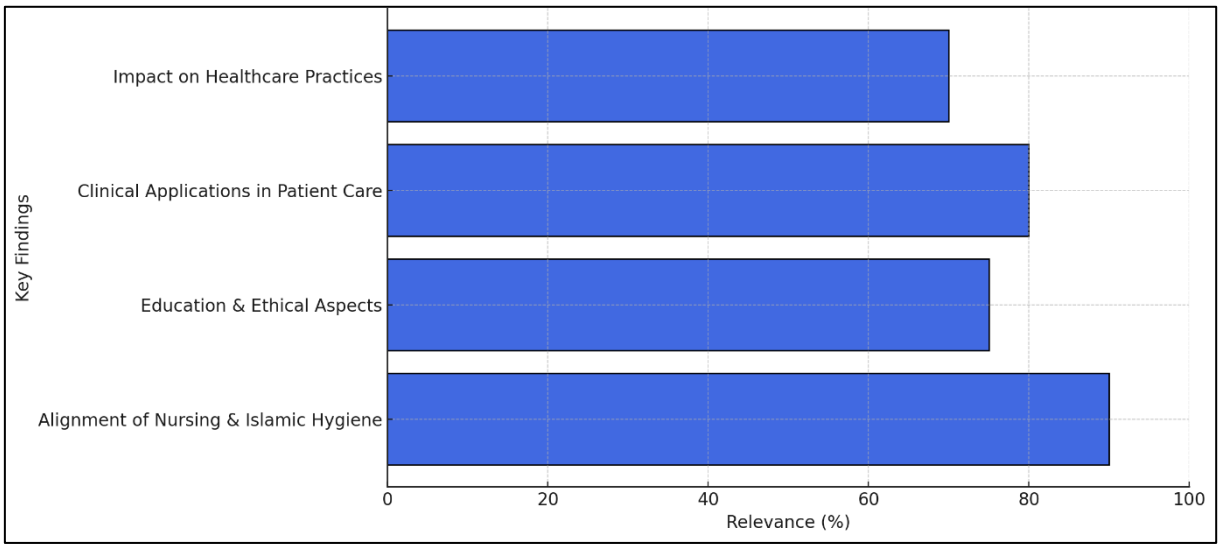

Figure 1. Conceptual Alignment of Islamic Cleanliness Principles with Nursing Practice

References

[1]. Broodkoorn M. Nursing the world to health. Kai Tiaki: Nursing New Zealand. 2020;26(3):2.

[2]. Office of the Regional Mufti. Irsyad al-Fatwa Series 416: How to clean urine on a thick and heavy mattress. Mufti WP [Internet]. 2020 [cited 2025 Mar 13]. Available from: https://muftiwp.gov.my/artikel/irsyad-fatwa/irsyad-fatwa-umum/4167-irsyad-al-fatwa-siri-ke-416-cara-membersihkan-air-kencing-di-atas-tilam-tebal-dan-berat

[3]. Harkess L, Kaddoura M. Culture and cultural competence in nursing education and practice: The state of the art. Nursing Forum. 2015;50(4):255-67.

[4]. Ghasemi S, Shariatpanahi S, Dabaghi S, Sarbakhsh P. The effects of an educational intervention based on the Campinha-Bacote model on cultural competence of undergraduate nursing students. BMC Nurs. 2025;24(1):228. https://doi.org/10.1186/s12912-025-02876-6.

[5]. National Health Service (NHS). National Standards of Healthcare Cleanliness 2021 [Internet]. 2021 [cited 2025 Mar 13]. Available from: https://www.england.nhs.uk/publication/national-standards-of-healthcare-cleanliness-2021/

[6]. Mahmood MA, Mohd Yusof N, Saidi S, Che Ahmad A. The Integration of Islamic Values in Daily Clinical Practice among Healthcare Professionals: A Scoping Review. IIUM Medical Journal Malaysia. 2023;22(3). https://doi.org/10.31436/imjm.v22i3.2273.

[7]. Baldwin JR, Pingault JB, Schoeler T, Sallis HM, Munafò MR. Protecting against researcher bias in secondary data analysis: challenges and potential solutions. Eur J Epidemiol. 2022;37(1):1-10.

[8]. Smith T, Brown J. Florence Nightingale's Environmental Theory and its application in contemporary 21st century nursing practice. Aust J Nurs Midwifery. 2020;23(2):10-15.

[9]. Al-Zoubi M, El-Amad W, Sultan N, Shihadeh K, Ameen Ghalia M, Rbeihat R, Abu Arqoub H, Btoush A, Rababeh F, Zoubi A, Ababneh H. Sanitation for Millions - WASH in Islam: Guide on Water, Sanitation and Hygiene (WASH) from an Islamic Perspective. Deutsche Gesellschaft für Internationale Zusammenarbeit (GIZ) GmbH and Sanitation for Millions Jordan. 2020

[10]. Al-Hassan A, Al-Shahri M, Al-Harbi A. The Integration of Islamic Values in Daily Clinical Practice. IMJM. 2023;22(3):36.
[11]. Ardian I, Nursalam N, Ahsan A, Haiya NN, Azizah IR. The development of an islamic nursing care model to improve patient satisfaction. Jurnal Ners. 2024;19(1):3-12.
[12]. Sange C, Thomas L, Lyons C, Hill S. Urinary incontinence in Muslim women. Nursing Times. 2008;104(25):49-52
[13]. Rassool GH. The crescent and Islam: healing, nursing and the spiritual dimension. J Adv Nurs. 2000;32(6):1476-84
[14]. Carrico R, Garrett A. Infection Prevention and Control Core Practices: A Roadmap for Nursing Practice. Am J Infect Control. 2018;46(8):883-888
[15]. Sahih Muslim. Hadith 223: Cleanliness is part of faith. [Internet]. Available from: https://sunnah.com/search?q=+Hadith+223
[16]. Alpers LM, Hanssen I. Hospital food: When nurses' and ethnic minority patients' understanding of Islamic dietary needs differ. Nurs Open. 2019;6(4):1455-1463.
[17]. Wan Ismail WNES, Mahamad Maifiah MH. Porcine and bovine-derived ingredients: Islamic rules in halal pharmaceutical products. J Fatwa Manag Res. 2023;28(3):42-57. DOI: 10.33102/jfatwa.vol.28no3.549.
[18]. Farokhzadian J, Tirgari B. Empowerment of nurses for integrating clients' religion/spirituality into clinical practice: an online training program. BMC Nurs. 2021;20:210
[19]. Rassool GH. Cultural competence in nursing Muslim patients. Nurs Times. 2015;111(14):12-15
[20]. Garvey M. Medical Device-Associated Healthcare Infections: Sterilization and the Potential of Novel Biological Approaches to Ensure Patient Safety [Internet]. Int J Mol Sci. 2024;25(1):201.
[21]. Al-Shadiq A. Water Treatment and Purification in Fiqh [Internet]. USIM Repository; 2024 May 29. Available from: https://oarep.usim.edu.my/bitstreams/4d647fa4-af40-4beb-b7a1-9b867227a303/download
[22]. Mason M, Wakefield J, Sparke V, Basseal JM, Zimmerman P-A. Religious influences on infection prevention and control practices in healthcare settings: A scoping review. Infect Dis Health. 2025 Mar 12; [In Press, Corrected Proof]. Available from: https://doi.org/10.1016/j.idh.2025.02.004.
[23]. Noordin MF. The ruling of using baby wipes. Mufti of Federal Territory's Office [Internet]. 2019 Sep 6 [cited 2025 Mar 14]; Available from: https://muftiwp.gov.my/en/artikel/al-kafi-li-al-fatawi/3677-al-kafi-1364-hukum-menggunakan-wipe-baby-ketika-membersihkan-najis-bayi.
[24]. Blenkharn JI. Rigid infection prevention and control rules and religious discrimination: An uncomfortable juxtaposition? J Infect Prev. 2020;21(1):35-39. doi: 10.1177/1757177419884690.
[25]. Handtke O, Schilgen B, Mößko M. Culturally competent healthcare – A scoping review of strategies implemented in healthcare organizations and a model of culturally competent healthcare provision. PLoS One. 2019;14(7):e0219971. doi: 10.1371/journal.pone.0219971.
[26]. Lauwers EDL, Vandecasteele R, McMahon M, De Maesschalck S, Willems S. The patient perspective on diversity-sensitive care: a systematic review. Int J Equity Health. 2024;23(117). doi: 10.1186/s12939-024-02189-1.
[27]. Irfan B, Khleif A, Badarneh J, Abutaqa J, Allam A, Kweis S, et al. Considering Islamic frameworks to infectious disease prevention. Open Forum Infect Dis. 2025;12(1):ofaf011.

REVIEW ARTICLE

A Bibliometric Review of Holy Basil (*Ocimum tenuiflorum*) and its Therapeutic Potential in Dermatological Applications.

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Abstract

Ocimum tenuiflorum (*O. tenuiflorum*), commonly recognised as Holy Basil or Tulsi, has garnered growing interest within the scientific and industrial communities due to its extensive phytochemical profile and diverse therapeutic properties. This bibliometric review examines global research trends concerning *O. tenuiflorum* from 2000 to 2024, utilising data from Web of Science (WoS) alongside bibliometric tools including VOSviewer and Biblioshiny. The analysis indicates a consistent increase in publication output, with India leading research contributions and notable inputs from the USA, Thailand, and other nations. Research clusters identify five principal thematic areas: traditional medicine, phytochemistry, pharmacology, nanotechnology applications, and dermatology. The plant's bioactive compounds, such as eugenol, ursolic acid, rosmarinic acid, and luteolin, exhibit significant antioxidant, anti-inflammatory, adaptogenic, anti-diabetic, and dermatological effects. Particularly in dermatology, *O. tenuiflorum* demonstrates promising roles in anti-ageing, skin barrier protection, acne management, and wound healing via mechanisms involving collagen synthesis, cytokine inhibition, and UV protection. This comprehensive bibliometric and phytochemical review underscores the versatile therapeutic potential of *O. tenuiflorum*, thereby supporting its development within cosmeceutical and pharmaceutical sectors, while also highlighting opportunities for further multidisciplinary research.
Keywords: *Bibliometric analysis, dermatology, Ocimum tenuiflorum, skin health, tulsi.*

Introduction

The trend of using natural products for skin health has gained significant momentum in recent years, reflecting a broader shift among consumers towards cleaner, safer, and more environmentally sustainable options. Currently, the natural skin care market revenue has skyrocketed to 28.71 billion USD, with a projected compound annual growth rate (CAGR) of 2.66% [1]. This movement includes a wide range of ingredients sourced from natural compounds, mainly plants, that are valued for their health benefits and therapeutic qualities. Due to their perceived effectiveness and milder characteristics, natural products are becoming increasingly popular compared to synthetic options, especially among health-focused consumers and younger generations who prioritise ethical sourcing and sustainability in their buying choices. Plant-based products such as cannabidiol oil, bakuchiol, marine algae, ginseng, and ashwagandha continue to be highly popular due to their anti-inflammatory, anti-oxidant, anti-microbial, and sebum-regulating properties, which assist in managing conditions such as eczema, psoriasis, and acne [2]. Other examples, like aloe vera, are also making a strong comeback due to their soothing, hydrating, and healing properties, making them ideal for calming irritation and redness without clogging pores [3].

Among the many natural botanicals gaining attention, *Ocimum tenuiflorum* (synonym of *Ocimum sanctum*), commonly known as holy basil or Tulsi, stands out due to its extensive medicinal properties and cultural significance, particularly in Indian traditions [4]. Studies have demonstrated its potential to address various health conditions, including diabetes, cardiovascular diseases, and stress-related disorders, reinforcing its reputation as an essential element of both traditional and modern medicine [4,5].

Traditionally, various parts of the plant have been used to treat skin problems as well as wounds, inflammation, and other ailments. In recent years, dermatological interest has grown in *O. tenuiflorum* adaptogenic, anti-inflammatory, and antioxidant properties, suggesting potential benefits for acne, atopic dermatitis, psoriasis, wound healing, and skin ageing. For example, recent clinical researchers now incorporate *O. tenuiflorum* into botanical nutraceuticals for acne and in cosmeceutical anti-ageing applications. A 2020 study found that an *O. tenuiflorum* extract (rich in rosmarinic acid) delivered by nanocarriers significantly enhanced skin retention by 27.1 ± 1.8%, with sustained release of rosmarinic acid over 24 hours while inducing no irritation and not permeating deeply through the skin [6]. A recent review by Bhattacharjee and colleagues highlighted that the nanotherapeutic delivery of ursolic acid from *O. tenuiflorum* represents a paradigm shift in skincare, bringing forth a promising molecular strategy to combat skin ageing [7]. Similarly, pre-clinical models show that the plant extracts accelerate wound closure and increase collagen and antioxidant enzymes in healing tissue [8]. Furthermore, studies also highlighted its effectiveness in treating common skin problems like acne, irritation, and early ageing, making it a popular ingredient in cosmetic products [2,9,10]. The plant's ability to fight skin pathogens, especially *C. acnes*, along with its potential to improve wound healing, highlights its importance in dermatological uses [9].

Studies concerning *O. tenuiflorum* have been growing over the years, demonstrating the rising interest in this plant in multiple industries. Some review articles have been recently published regarding this plant, focusing on the phytochemicals and their numerous pharmacological activities, including its therapeutic potential against COVID-19 [5,11]. However, a document that collates the most important and relevant studies, as well as demonstrates the main trends and developments concerning *O. tenuiflorum,* is necessary. Bibliometric analysis has now become widely popular for researchers as a statistical method to quantify, analyse and evaluate scientific publications [12]. This methodology facilitates the identification of various principles, including

the research trends within a specific domain [12,13]. Researchers are able to discern notable research gaps, emerging topics, and influential studies through the analysis of publication patterns and citation networks. This review will focus on the research trends of *O. tenuiflorum* and its potential application in the skin care industry.

Materials and methods

Research design and data collection procedure

A bibliometric analysis was performed using the Web of Science© (WoS) databases (www.webofknowledge.com) to investigate the worldwide literature concerning *O. tenuiflorum*. Web of Science (WoS) was selected for its selective coverage and is considered a scholarly source for measuring scientific output, identifying scope, coverage, and data volume [13]. The terms 'holy basil', OR 'ocimum sanctum', OR '*ocimum tenuiflorum'*, OR Tulasi, OR Tulsi, were used in the "topic item", which includes the title, abstract, keywords, and keywords plus of articles indexed in the databases. As shown in Figure 1, a search was performed to include the last 24 years (2000–2024), with a total of 4,210 scientific articles being retrieved (WoS = 1,491). From the data, we extracted the number of publications, categories, the top ten most cited papers, the top ten most productive authors, countries, and the 50 most frequent keywords. Additionally, the data of the most productive countries were processed using the VOSViewer software (Java version build 1.8.0_461-b11) in order to gather information concerning international collaborations among nations, and the 50 most frequent keywords were processed to evaluate the research focus on *O. tenuiflorum*.

Additionally, Biblioshiny was used to identify the topic trends over the 24 years. Specifically, the visualisation of keyword trends and thematic evolution plots reveals the trajectory and importance of certain topics within the dataset. Then the users can interpret thematic maps that categorise topics by their maturity and significance in the domain, gaining insights into the dynamic development of the field.

Bibliometric review of *O. tenuiflorum* from the past 24 years

Global paper publication trend and categories

The annual number of publications serves as an intuitive indicator of the pace of development and change within specific fields [14]. The statistics pertaining to *O. tenuiflorum*-related articles demonstrate that the annual volume has remained comparatively modest, with all years reporting fewer than 200 articles. The trend exhibited a gradual increase from 2000 to 2005. Subsequently, the annual number of publications experienced steady growth, rising from 17 articles in 2006 to 69 in 2019. Following this period, there was a marked increase in publication numbers from 2020 to 2024, with a publication count exceeding 125 articles annually after 2020. As of December 2024, a total of 154 articles have been published (see Figure 2). The observed upward trend clearly indicates a growing scholarly interest in *O. tenuiflorum*.

The analysis of research areas serves as a valuable instrument for identifying gaps within the scholarly domain [12,13]. An examination of the WoS database reveals that, at present, the articles are associated with a total of 139 entries within the WoS Categories. Figure 3 illustrates the leading categories, namely Pharmacology & Pharmacy (198), Plant Sciences (197), Food Science & Technology (135), Medicinal Chemistry (113), and Multidisciplinary Chemistry (98). This distribution indicates that research concerning *O. tenuiflorum* encompasses multiple disciplines, underscoring its multidisciplinary and interdisciplinary characteristics. According to these research areas and grouped publications, it was concluded that the predominant topics are linked to extensive investigations in medicinal chemistry and molecular biology, thereby reflecting a robust multidisciplinary engagement in both traditional uses and contemporary biomedical applications.

Authors and affiliations publication

Within the domain of *O. tenuiflorum*, the WoS has documented a total of 5,285 authors and 1,731 affiliated institutions. Among these top three authors, Shanmugam Rajeshkumar emerges as a leading figure with 11 publications and 73 citations, indicative of sustained scholarly output, although with a moderate citation rate (**Table 1**). The consistent contributions imply ongoing engagement in investigating various biological or pharmacological aspects of *O. tenuiflorum* [15–17]. Similarly, Balaji Raju also exhibits significant academic productivity, with 9 publications and 49 citations, reflecting a focused yet potentially less widely cited body of research. In contrast, Kusindarta Dwi Liliek, despite matching Balaji in publication count (9 records), stands out because of a significantly higher citation count (255 citations), indicating a strong impact in research. This high citation-to-publication ratio suggests that Kusindarta's work may have tackled a notably novel or clinically relevant aspect of *O. tenuiflorum*, possibly in immunological or therapeutic fields [17,18]. Such a pattern highlights the importance of both publication volume and research significance in progressing scientific discussion.

On an institutional level, the Council of Scientific and Industrial Research (CSIR) India stands out as the most active and influential organisation, with 89 publications and a total of 2,868 citations (Table 1). This showcases CSIR's key contribution to India's phytopharmaceutical and ethnobotanical fields, supported by its extensive network of research centres across the country [19,20]. The Indian Council of Agricultural Research (ICAR) follows closely with 57 publications and 1,232 citations, underlining its vital role in agricultural research and plant-based therapies, including the cultivation, genetic improvement, and analysis of bioactive compounds in *O. tenuiflorum* [21–23]. The third leading institution, CSIR–Central Institute of Medicinal and Aromatic Plants (CIMAP), has contributed 48 publications with 1,128 citations, highlighting the importance of India's national research agencies in producing high-impact work. As a dedicated branch of CSIR, CIMAP has likely made significant strides in standardising, profiling bioactivity, and supporting industrial applications of *O. tenuiflorum*. The impressive citation counts from both CSIR and CIMAP emphasise their crucial role in not only basic research but also in translating traditional knowledge into modern pharmacology.

These findings collectively emphasise the geographical and institutional clustering of *O. tenuiflorum* research within India, driven by a combination of prolific individual researchers and government-supported institutions. The strong output and impact from these authors and affiliations reflect both national interest and the global significance of *O. tenuiflorum* as a medicinal plant with considerable therapeutic potential.

National publication and collaboration analysis

According to Table 2, the global research landscape on *O. tenuiflorum* is prominently shaped by contributions from three leading countries, India, the United States, and Thailand, each demonstrating distinct strengths in publication volume and citation impact. Unsurprisingly, India leads the field with an impressive 1,074 publications and 23,896 citations, firmly establishing itself as the centre of *O. tenuiflorum* research. This dominance reflects India's deep-rooted cultural, medicinal, and scientific engagement with the herb, widely known in the region as Tulsi. Indian research covers a broad range, from pharmacological and agronomic studies to clinical and therapeutic applications, largely driven by major national research organisations such as the Council of Scientific and Industrial Research (CSIR) and the Indian Council of Agricultural Research (ICAR). The high citation count indicates that Indian research is both fundamental and widely referenced internationally, making a significant contribution to the global knowledge base.

The United States, despite producing a comparatively smaller number of publications (89 records), has amassed 1,899 citations, reflecting a high citation-per-publication ratio. This suggests that American research, although more selective, tends to exert greater influence and frequently focuses on specific therapeutic mechanisms, clinical applications, and the incorporation of *O. tenuiflorum* into nutraceuticals, stress management strategies, and functional foods [24–26]. The United States presumably plays a crucial role in translating traditional knowledge into evidence-based health solutions compatible with Western healthcare systems. Thailand occupies the third position with 81 publications and 1,547 citations, highlighting Southeast Asia's active contribution to the advancement of research on *O. tenuiflorum*. Thai research often seeks to bridge traditional herbal practices with contemporary scientific validation, with particular emphasis on anti-microbial, anti-oxidant, and dermatological applications [27–29]. The country's research initiatives are further supported by national policies aimed at herbal medicine development and biodiversity conservation, with *O. tenuiflorum* frequently featured in integrated healthcare and cosmeceutical studies.

Apart from the country's publication and citation count, the collaboration network between countries is also analysed (Figure 4). The VOSviewer co-authorship network visualisation illustrates the international collaboration landscape in *O. tenuiflorum* research. The size of each node reflects a country's total publication output, while the thickness of connecting lines (edges) indicates the strength of collaborative links [30]. The colour groupings represent clusters of countries that frequently co-publish together [30].

Consistent with its predominant role in *O. tenuiflorum* research, India occupies the central and most prominent position within the network. Its extensive and numerous co-authorship connections, particularly with the United States of America (USA), Thailand, Saudi Arabia, and South Korea, underscore its significance as a collaborative hub. The substantial linkages among India, Saudi Arabia, the USA, and South Korea indicate a notably robust bilateral research relationship. Thailand also exhibits strong collaborative ties, notably with India and the USA, demonstrating active engagement in international research networks, often centred on anti-microbial and cosmetic applications. Although the United States has a smaller volume of publications, it sustains strong co-authorship relations with principal nations such as India, Thailand, and South Korea. Additionally, Saudi Arabia, Pakistan, Bangladesh, and Malaysia form a dense cluster with moderate link strengths among other countries, reflecting regional collaboration patterns potentially driven by shared ethnobotanical interests and institutional partnerships. Overall, the network highlights India's central coordinating role, with Saudi Arabia, the USA, and South Korea serving as key nodes in promoting international collaboration. This structure indicates a collaborative environment that integrates traditional knowledge, regional biodiversity, and modern scientific methods to enhance the global understanding of *O. tenuiflorum's* health benefits.

Publication citation and research field

Table 3 shows the citation profile of the ten most frequently cited papers in *O. tenuiflorum* research, underscoring significant themes and the evolving scientific interest in this medicinal plant. A noteworthy observation from this selection is the predominance of studies related to nanotechnology, which constitute six of the top ten publications, thereby indicating a robust connection between green synthesis methodologies and the biomedical applications of *O. tenuiflorum* [31–33]. The most frequently cited investigation, titled "Biosynthesis of silver nanoparticles using *Ocimum sanctum* (Tulsi) leaf extract and screening its anti-microbial activity" (with 483 citations, published in 2011), along with the second most cited publication (with 476 citations, published in 2010), both underscore the green synthesis of silver nanoparticles (AgNPs)

[33,34]. These research works highlight the attractiveness of *O. tenuiflorum* as a sustainable, plant-derived reducing and capping agent possessing robust anti-microbial properties. The consistent publication of such scholarly articles in esteemed journals such as the Journal of Nanoparticle Research and Colloids and Surfaces B-Biointerfaces exemplifies this interdisciplinary focus, bridging botany, materials science, and microbiology.

Further articles like the 2015 Journal of Saudi Chemical Society and 2017 Scientific Reports continue to affirm that green nanotechnology remains central in *O. tenuiflorum's* high-impact research [35,36]. Beyond nanoscience, traditional pharmacology is well represented. The 2003 Journal of Ethnopharmacology study (327 citations) compares the hypoglycaemic activity of *O. tenuiflorum* with other Indian medicinal plants in diabetic rats, showing ongoing interest in its metabolic role [37]. The 2000 Phytomedicine study (261 citations) identifies cyclooxygenase-inhibitory and anti-oxidant compounds, unveiling anti-inflammatory mechanisms [26]. Another significant study (260 citations, Plant Science, 2004) investigates the effect of heavy metal stress (chromium) on the physiological and biochemical parameters of *O. tenuiflorum*, including eugenol biosynthesis [20]. This reflects interests in ecological and agricultural research concerning how environmental conditions impact the plant's phytochemical profile and therapeutic potential. Further broadening the metabolic application theme, the 2011 BMC Complementary and Alternative Medicine paper (235 citations) assesses α-amylase inhibition, positioning *O. tenuiflorum* as a promising anti-diabetic agent through enzyme inhibition pathways [38]. A 2017 article concerning carbon dots synthesised from Tulsi for the purposes of detecting Pb^{2+} ions and live-cell imaging (Sensors and Actuators B: Chemical, cited 324 times) highlights *O. tenuiflorum's* increasing significance in bioimaging and environmental sensing, further extending its applications beyond conventional phytotherapy [35].

Notably, while all highly cited studies encompass diverse fields, they consistently emphasise *O. tenuiflorum's* biochemical richness, ecological resilience, and compatibility with contemporary scientific methodologies. These attributes have positioned it not merely as a medicinal plant but also as a valuable bioresource platform for nanoscience, pharmacology, and environmental biotechnology.

Keywords and trends analysis

To better understand researchers' current interests, a keyword analysis was also employed as a strategy to gain an overview of the trends related to *O. tenuiflorum*. The WoS database categorises keywords into two fields, author keywords (AKs) and keywords plus (KP), both of which are significant in bibliometrics [12]. Here, we focus only on the most cited AKs to identify the key trends highlighted by authors (Figure 5).

The co-occurrence network of author keywords in *O. tenuiflorum* research, visualised through VOSviewer, reveals a rich and interconnected thematic landscape shaped by both traditional and modern scientific approaches [30]. The most prominent terms, *Ocimum sanctum*, *Ocimum tenuiflorum*, antioxidant, Tulsi, holy basil, eugenol, and essential oil, highlight the centrality of the plant's identity, phytochemical composition, and its widely studied anti-oxidant properties.

The network reveals five major thematic clusters with strong interconnections. Red Cluster (traditional medicine & bioactivity) connects keywords such as medicinal plants, Ayurveda, molecular docking, phytochemicals, diabetes, and COVID-19. It highlights research linking *O. tenuiflorum* to traditional medicine and modern applications like computational pharmacology, anti-diabetic effects, and COVID-19. The combination of conventional uses with molecular studies shows active exploration of *O. tenuiflorum* for therapeutic leads through in silico modelling and ethnomedicine-based drug development. Green Cluster (phytochemistry & essential oils), centred around holy basil, eugenol, essential oil, *Lamiaceae*, methyl eugenol, and

rosmarinic acid, this cluster highlights the chemical profiling and bioactivity screening of specific phytoconstituents. The strong link between phytochemicals and bioactivity highlights ongoing efforts to isolate compounds responsible for anti-oxidant, anti-inflammatory, and anti-microbial effects.

With keywords like silver nanoparticles, green synthesis, anti-bacterial activity, anti-microbial activity, plant extract, and nanoparticles, Blue Cluster (Nanotechnology & Antimicrobial Research) is aligned with the green nanotechnology trend. The prominence of green synthesis shows ongoing interest in *O. tenuiflorum* as a biogenic source for metal nanoparticle production, used in anti-microbial therapies and biosensing. Meanwhile, Purple Cluster (oxidative stress & cellular mechanisms) represents studies probing the cellular and biochemical mechanisms underlying the plant's therapeutic effects, with terms like oxidative stress, apoptosis, cytotoxicity, and anti-oxidant. Lastly, the Yellow Cluster (anti-microbial phytotherapy) suggest a focus on comparative anti-microbial studies across species in the Ocimum genus and their nanoparticle-enhanced bioactivity, with keywords like anti-bacterial, anti-fungal, *Ocimum gratissimum*, and AGNPs (silver nanoparticles).

Figure 6 shows the Biblioshiny topic visualisation, which shows research evolution on *O. tenuiflorum*, reflecting shifts in focus over time. Early trends (2007–2015) centred on diabetes, antioxidants, oxidative stress, immunomodulation, and traditional medicine terms like *Curcuma longa* and *Tinospora cordifolia*, highlighting its role in metabolic and immune health, in combination with or without other natural products. Later, research shifted toward mechanistic and molecular studies, with terms like apoptosis, GC-MS, and eugenol, demonstrating increased interest in bioactive compounds and biochemical mechanisms.

By the mid to late 2010s, research focus shifted to phytochemicals and pharmacology, with keywords like rosmarinic acid, essential oils, anti-bacterial, and anti-oxidant activity gaining prominence. Attention increased on *Ocimum sanctum* L*., Ocimum basilicum,* and *Withania somnifera*, showing broader interspecies studies. After 2020, research expanded into green synthesis, silver nanoparticles, cytotoxicity, molecular docking, and COVID-19 applications. These themes reflect *O. tenuiflorum's* role in nanotech, drug discovery, and public health crises. The latest trending terms like phytochemicals, Tulsi, plant extract, green synthesis, and molecular docking indicate a merging of traditional knowledge with modern science, focusing on natural therapeutics, sustainable methods, and in silico validation. Research on *O. tenuiflorum* has shifted from ethnopharmacology to molecular pharmacology and nanotechnology, maintaining its core while embracing new scientific approaches. In summary, the bibliometric insights show that *Ocimum tenuiflorum* research has expanded significantly in scope and complexity. It has evolved from ethnobotanical validation into an interdisciplinary field involving molecular pharmacology, nanotechnology, and computational modelling, while retaining its foundation in traditional health applications.

Phytochemical constituents of *O. tenuiflorum*

O. tenuiflorum originates from the Indian subcontinent and adjacent tropical regions of Asia, including India, Nepal, Sri Lanka, and Malaysia, with a range extending to tropical areas of Australia and the western Pacific. This short-lived and small perennial herb is extensively cultivated and has also become naturalised in other tropical regions, including the Caribbean and parts of Africa, owing to its medicinal, culinary, and religious importance. Nowadays, the plant is recognised for its rich phytochemical profile, which contributes to its therapeutic properties. The plant contains a variety of bioactive compounds, including phenolic compounds (flavonoids & phenolic acids), terpenoids, steroids, monoterpenes and sesquiterpenes, esters,

aldehydes and ketones, which play significant roles in its health benefits (Table 4).

Flavonoids & phenolic acids

Flavonoids and phenolic acids are the most common secondary metabolites with low molecular weight polyphenol structures, recognised for their diverse biological activities, including anti-oxidant properties [39,40]. *O. tenuiflorum* contains various flavonoids and phenolic acids, which are responsible for the plant's therapeutic effects. Some flavonoids commonly found in *O. tenuiflorum* include apigenin, luteolin, kaempferol, quercetin, vicenin, eupalitin, esculetin, isoorientin, orientin, galuteolin, genkwanin, vitexin, isovitexin, cirsimaritin, chrysoeriol, cirsilineol, isothymusin, molludistin, demethylnobiletin, salvigenin, luteolin-7-O-glucuronide, apigenin-7-O-glucuronide, kaempferide, chrysoeriol, isosakuranetin, luteolin-5-glucoside, esculin, robinetintrimethyl ether, and xanthomicrol [5]. *O. tenuiflorum* is also well-known for its anti-oxidant properties owing to the presence of several phenolic acids. Some of these include rosmarinic acid, (E)-p-coumaroyl 4-O-β-D-glucoside, chlorogenic acid, caffeic acid, vanillin, methylisoeugenol, vanillic acid, sinapic acid, p-coumaric acid, 3-(3,4-dihydroxyphenyl) lactic acid, protocatechuic acid, 3,4-dimethoxycinnamic acid, p-hydroxybenzoic acid, ferulic acid, and bieugenol [4,5,41].

Esters, aldehydes, and ketones

O. tenuiflorum contains various esters, aldehydes, and ketones that exhibit significant biological activities. Some of them are methyl isovalerate, ethyl isovalerate, pentanal, hexane-3-one, 4-methyl-4-hepten-3-one, and octyl ester [4,5].

Sesquiterpenes and monoterpenes

Sesquiterpenes and monoterpenes are important secondary metabolites with significant pharmaceutical values. Both metabolites are mostly found in the essential oils of the plant, contributing to the plant's flavour and aroma, and play a significant role in various biological applications. The plant *O. tenuiflorum* contains a variety of sesquiterpenes, including copaene, zingiberene, bourbonene, guaiene, bergamotene, sesquiphellandrene, farnesene, sesquisabinene, humulene, bicyclogermacrene, germacrene, bisabolene (Z), δ-cadinene, α-bisabolene, amorphene, caryophyllene oxide, c-muurolene, α-muurolene, α-cadinol, c-cadinene, α-caryophyllene, β-caryophyllene, germacrene D, β-guaiene, α-longipinene, α-panasinsen, selina-6-en-4-ol, nerolidol, spathulenol, aromadendrene oxide, α-calacorene, 1,4-cadinadiene, β-bisabolene, alloaromadendrene, β-gurjunene, β-cubebene, β-elemene, and c-eleneme [5]. Some important monoterpenes reported in *O. tenuiflorum* are α-pinene, camphene, sabinene, β-pinene, 1,8-cineole, β-trans-ocimene, camphor, borneol, tricyclene, myrcene, phellandrene, terpinene, limonene, ocimene, terpinolene, sabinene hydrate, carene, fenchone, linalool, camphenehydrate, terpinen-4-ol, terpineol, estragole, and eugenol [5].

Triterpenoids

Triterpenoids are a large group of natural products, mostly derived from squalene, that have significant pharmaceutical importance. *O. tenuiflorum* contains multiple triterpenoids, which hold important therapeutic value. Studies have identified various triterpenoids such as β-sitosterol, stigmasterol, campesterol, ocimic acid, ursolic acid, trihydroxyursolic acid, β-sitosterol-3-Oβ-D-glucopyranoside, oleanolic acid (OA), urs-12-en-3β,6β,20β-triol-28-oic acid, and 16-hydroxy-4,4,10,13-tetramethyl-17-(4-methyl-pentyl)-hexadecahydrocyclopenta [α] phenanthrene -3-one [4,5,41].

Therapeutic properties of *O. tenuiflorum* and its potential in dermatological applications

Established health benefits of *O. tenuiflorum*

One of the most prominent effects of *O. tenuiflorum* is its adaptogenic capacity, particularly in reducing stress and improving

mental well-being [42,43]. Clinical trials have shown that standardised extracts of *O. tenuiflorum* can significantly lower perceived stress levels, decrease cortisol production, and enhance sleep quality in healthy adults [44,45]. These benefits are linked to the plant's ability to modulate the hypothalamic-pituitary-adrenal (HPA) axis and its influence on neurotransmitter regulation, especially through bioactive compounds such as eugenol and ursolic acid. In addition to its psychological advantages, *O. tenuiflorum* has demonstrated promising potential in managing blood sugar levels [46,47]. Both clinical and animal studies report that holy basil supplementation can reduce fasting and postprandial blood glucose levels and improve overall glycaemic control. The mechanisms behind this include increased insulin secretion, better pancreatic β-cell function, and the modulation of key metabolic enzymes. These effects make it a valuable complementary option for individuals with type 2 diabetes or metabolic syndrome.

A further well-established therapeutic property of *O. tenuiflorum* is its anti-oxidant and anti-inflammatory activity. Rich in phenolic compounds such as rosmarinic acid, apigenin, and eugenol, the plant strongly inhibits pro-inflammatory cytokines and oxidative stress markers. Laboratory and *in vivo* research confirm its ability to suppress pathways such as NF-κb and COX-2, while boosting the activity of natural anti-oxidant enzymes like superoxide dismutase and catalase [48–50]. Studies demonstrate that bioactive compounds from *O. tenuiflorum*, such as eugenol and ursolic acid, inhibit NF-κb signalling by modifying residues of IKKβ (inhibitor of κB kinase β), preventing the phosphorylation and degradation of IκB proteins that normally sequester NF-κB in the cytoplasm [51]. These actions block NF-κB nuclear translocation and subsequent inflammatory gene transcription, and help protect cells and are relevant in preventing or managing inflammatory and oxidative stress-related conditions.

Cardiovascular advantages also constitute a significant part of *O. tenuiflorum's* therapeutic profile. Supplementation with the plant has been linked to improved lipid profiles, including reductions in total cholesterol, LDL, and triglycerides, alongside increases in HDL levels. Clinical trials indicate it can modestly lower blood pressure, likely through vasodilatory and anti-oxidant mechanisms [52–54]. These findings support its use in promoting heart health and reducing risk factors associated with cardiovascular disease. Moreover, *O. tenuiflorum* has shown immunomodulatory and anti-microbial properties. Human studies have revealed that supplementation can boost immune function by increasing natural killer (NK) cell activity and the production of key cytokines that help regulate T-helper cell differentiation, such as interferon-gamma (IFN-γ), that promotes the development of Th1 cells (involved in cell-mediated immunity), and interleukin-4 (IL-4) which promotes Th2 cells (involved in allergic responses and parasitic infections) [55]. Additionally, its essential oils exhibit broad-spectrum anti-microbial effects against various bacterial and fungal pathogens, including resistant strains like *S. aureus* (MRSA) and *E. coli* [56,57]. These combined immunological and anti-microbial mechanisms highlight *O. tenuiflorum's* significance in supporting host defences and combating infections.

O. tenuiflorum **emerging potential in skin health applications**

Antimicrobial activity for skin infections

As previously noted, *O. tenuiflorum* exhibits significant potential in the treatment of skin infections through its broad-spectrum anti-microbial properties. The essential oil constituents, notably eugenol, have been shown to be effective against skin pathogens such as *S. aureus, E. coli,* and *P. aeruginosa*, major causative agents of skin and soft tissue infections [16,57]. This anti-microbial efficacy, coupled with the herb's anti-inflammatory attributes, renders it especially beneficial for the

management of infected wounds and the prevention of secondary infections.

Prevention and treatment of acne

The anti-bacterial and anti-inflammatory properties of *O. tenuiflorum* make it highly effective in treating acne. Eugenol and other bioactive compounds neutralise bacteria that cause acne while reducing inflammation and redness linked to breakouts [58,59]. Besides, traditional formulations combining *O. tenuiflorum* with honey show promising effectiveness in reducing acne lesions and preventing scars, however, limited studies have been conducted to support this claim. *O. tenuiflorum* essential oil-regulating properties may help to keep sebum production balanced, addressing one of the main causes of acne [60,61].

Anti-ageing and collagen enhancement

O. tenuiflorum exhibits considerable anti-ageing properties via various mechanisms. Ursolic acid, an important triterpenoid, fosters collagen synthesis and improves skin elasticity [62,63]. Studies suggested that ursolic acid could be a promising candidate for treating skin fibrosis due to its dual effects on collagen homeostasis, inhibiting collagen production and promoting collagen degradation [62]. Apart from that, the anti-oxidant substances help guard against free radical damage, thereby preventing premature ageing and supporting skin firmness [64].

Wound healing and tissue repair

The wound healing properties of *O. tenuiflorum* are well-documented in preclinical studies. The herb accelerates epithelialization, increases wound breaking strength, and enhances the formation of granulation tissue [65–67]. These effects are attributed to the combined action of eugenol, ursolic acid, and other bioactive compounds that stimulate cellular repair mechanisms [64]. Studies demonstrate that *O. tenuiflorum*-treated wounds show faster healing rates and improved cosmetic outcomes compared to controls [67,68]. The anti-microbial properties provide additional protection against wound infections, making *O. tenuiflorum* valuable for both acute and chronic wound management.

Photoprotection and skin brightening

Research reveals that *O. tenuiflorum* possesses natural sun protection properties [69,70]. The phenolic compounds and flavonoids in *O. tenuiflorum* extracts demonstrate UV absorption capabilities, with studies showing Sun Protecting Factor (SPF) values ranging from 2.87 to 13.29 depending on concentration and extraction method [71,72]. While these values are moderate compared to commercial sunscreens, they provide valuable supplementary protection when combined with other photoprotective agents. The photoprotective effects extend beyond UV absorption to include anti-oxidant protection against UV-induced free radical damage. This dual mechanism helps prevent both immediate sun damage and long-term photoaging effects. Apart from that, vitamin C and rosmarinic acid from *O. tenuiflorum can* contribute to its skin-brightening properties, helping to reduce melanin production and fade dark spots, promoting a more even skin tone [73–75].

Key bioactive compound and the potential mechanism

Studies suggest natural phytochemicals help protect skin cells from oxidative stress, inflammation, and UV damage, supporting wound healing, anti-ageing, and skin barrier health [76,77]. This profile highlights five main compounds from *O. tenuiflorum*, such as eugenol, ursolic acid, rosmarinic acid, apigenin, and luteolin. Focusing on their chemical compound, anti-oxidant actions, and skin benefits like anti-ageing, anti-inflammatory effects, and UV protection.

Eugenol

Eugenol, or 4-allyl-2-methoxyphenol ($C_{10}H_{12}O_2$), is a key phenolic in *O. tenuiflorum* essential oil [20,78]. It exhibits potent anti-oxidant activity via its hydroxyl group, donating hydrogen to

neutralise free radicals and inhibiting oxidative enzymes like lipoxygenase, reducing oxidative stress [79]. In skin applications, eugenol offers anti-inflammatory, anti-microbial, and local anaesthetic benefits, aiding wound healing and skin barrier repair [80]. It reduces inflammation by downregulating pro-inflammatory mediators like TNF-α and IL-6 and supports tissue regeneration by boosting collagen. Studies show eugenol lessens UVB-induced inflammation and accelerates tissue recovery [58,81]. Formulations with eugenol from *O. tenuiflorum* effectively prevent chemically-induced skin cancer, mainly through anti-oxidant and anti-inflammatory pathways like NF-κb [82]. Overall, eugenol enhances *O. tenuiflorum* skin protection, healing, and anti-ageing properties in context.

Ursolic acid

Ursolic acid ($C_{30}H_{48}O_3$), found in *O. tenuiflorum* leaves, is a pentacyclic triterpenoid with strong anti-oxidant and anti-inflammatory properties, valuable in dermatology [83,84]. It scavenges reactive oxygen species (ROS) and activates the Nrf2 pathway, boosting enzymes like superoxide dismutase (SOD) and catalase (CAT) [85,86]. It also inhibits NF-κB and TLR4 pathways, reducing cytokine production and skin inflammation [87,88]. Studies show ursolic acid alleviates atopic dermatitis symptoms by lowering oxidative stress and inflammation, decreasing redness, swelling, and itching. It promotes collagen synthesis, inhibits Matrix Metalloproteinases (MMPs), and maintains skin elasticity, supporting anti-ageing and skin rejuvenation [86,89,90]. Overall, ursolic acid enhances *O. tenuiflorum* skin benefits by protecting against oxidative damage, inflammation, and ageing.

Rosmarinic acid

Rosmarinic acid ($C_{18}H_{16}O_8$) is a polyphenolic compound found in *O. tenuiflorum* leaves, recognised for its anti-oxidant and skin-protective properties [5,91]. It has hydroxyl groups on aromatic rings, enabling it to neutralise free radicals through hydrogen donation and metal ion chelation [92,93]. This process inhibits lipid peroxidation, reduces DNA damage, and maintains redox balance [93]. It activates the Nrf2 pathway, boosting protective enzymes such as HO-1 [94,95]. In dermatology, it inhibits skin-ageing enzymes like collagenase, elastase, and hyaluronidase, thereby preserving skin elasticity [96–98]. It also suppresses NF-κB signalling, leading to a reduction in pro-inflammatory cytokines such as IL-1β [99]. Studies demonstrate that it protects skin cells from UV damage, decreasing UVB-induced apoptosis and inflammation by downregulating NLRP3 inflammasome and enhancing Nrf2/HO-1 activity [100]. These effects improve *O. tenuiflorum's* anti-ageing, photoprotective, and anti-inflammatory potential.

Apigenin

Apigenin ($C_{15}H_{10}O_5$) is a natural flavonoid in *O. tenuiflorum*, known for its anti-oxidant and anti-inflammatory benefits in skin health [101]. As a flavone, it scavenges reactive oxygen species (ROS) via hydroxyl groups, maintaining oxidative balance in skin cells [102,103]. It inhibits inflammatory pathways like NF-κB, MAPK, and COX-2, which are often upregulated in chronic skin conditions [104,105]. Studies suggest apigenin can treat inflammatory skin issues like dermatitis and psoriasis by reducing cytokines such as IL-1β, IL-6, IL-31, TNF-α, and IL-33, easing inflammation [106,107]. It also promotes barrier repair by increasing proteins like filaggrin and involucrin, which are essential for hydration and integrity, supports skin homeostasis by enhancing epidermal differentiation, and reduces pruritus signals [108]. Combining anti-oxidant, anti-inflammatory, and barrier-enhancing effects, apigenin from *O. tenuiflorum* is a promising ingredient for soothing sensitive skin, eczema, psoriasis, and overall skin health.

Luteolin

Luteolin ($C_{15}H_{10}O_6$), a flavonoid in *O. tenuiflorum*, exhibits strong anti-oxidant and anti-inflammatory properties, relevant for dermatology [5]. Its hydroxyl groups enable it to scavenge reactive oxygen species (ROS) and inhibit lipid peroxidation, protecting skin cells from oxidative stress [109]. Luteolin also modulates inflammatory pathways like NF-κB, AP-1, and JAK/STAT, reducing cytokines IL-1β, IL-6, and TNF-α [110,111]. It has notable anti-photoaging effects, diminishing UVB-induced erythema, wrinkles, and collagen breakdown by inhibiting MMPS, stimulating collagen, and activating the SIRT3/ROS/MAPK axis [112–114]. It supports dermal cell survival under oxidative stress, preventing premature ageing and UV damage. This broad activity makes luteolin valuable in skincare for photoprotection, wrinkle prevention, and calming inflammation.

Conclusion

O. tenuiflorum illustrates that the traditional botanical knowledge aligns with modern scientific validation. Its well-documented properties of adaptogenic, anti-microbial, anti-inflammatory, and antioxidant, thanks to its various bioactive compounds including eugenol, ursolic acid and rosmarinic acid, support a wide range of therapeutic uses, from overall health to emerging dermatological treatments. These activities support traditional uses for acne, eczema, wounds, and ageing skin, with recent studies confirming their potential, such as improved wound healing and photoprotection. However, the literature regarding the application of *O. tenuiflorum* in clinical trials is limited, and standardised formulations are still under development. Future research should focus on rigorous clinical trials for acne, dermatitis, and skin repair, as well as mechanistic studies on *O. tenuiflorum* effects. Overall, *O. tenuiflorum* is a bioactive herb with potential benefits for skin health, deserving more research in dermatologic treatments.

Conflict of Interest

The authors have no conflicts of interest to declare.

Author's Contribution

M.F.Z.: Formal analysis, Writing, Review & Editing, M.H.Z: Writing, Review, & Editing, N.S.I.M: Writing, Review, & Editing, S.H: Writing, Review, & Editing, P.M.R.: Project Administration, Writing, Review, & Editing,

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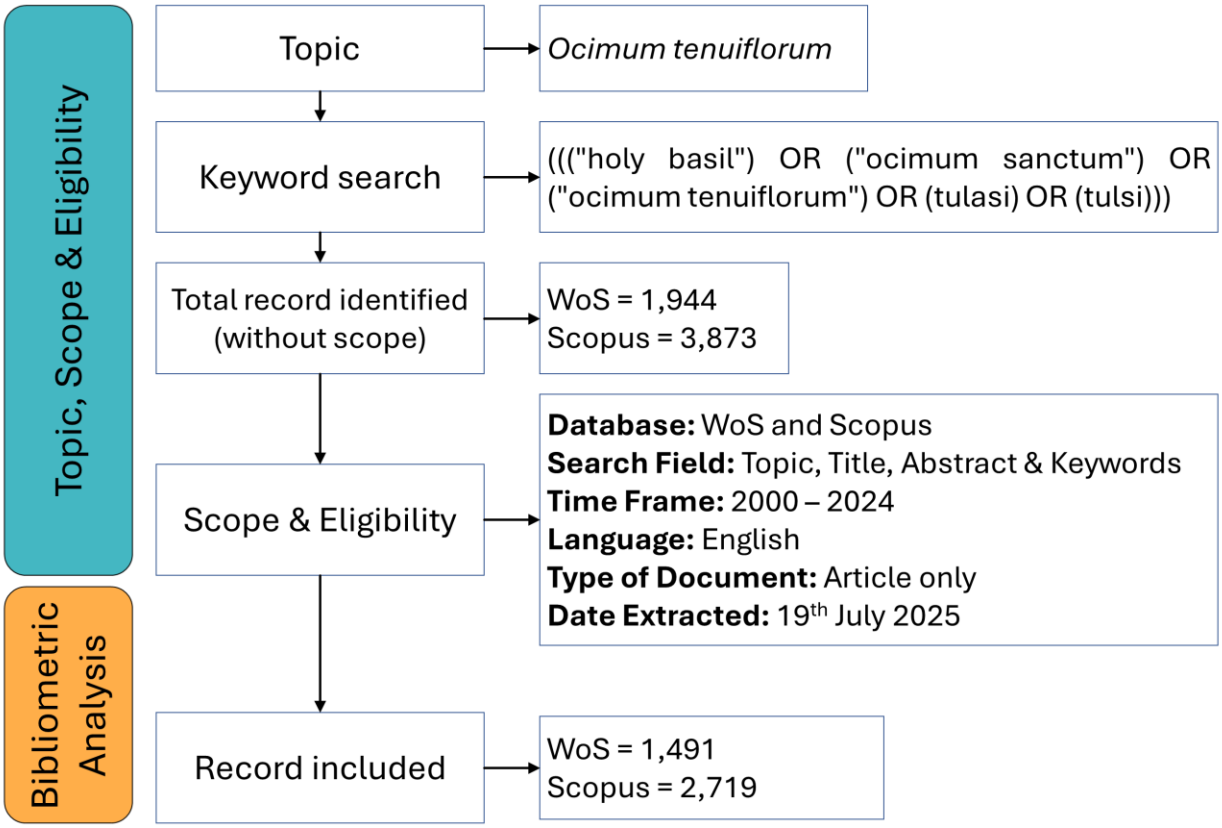

Figure 1. PRISMA flow diagram of the search strategy. (WoS = Web of Science)

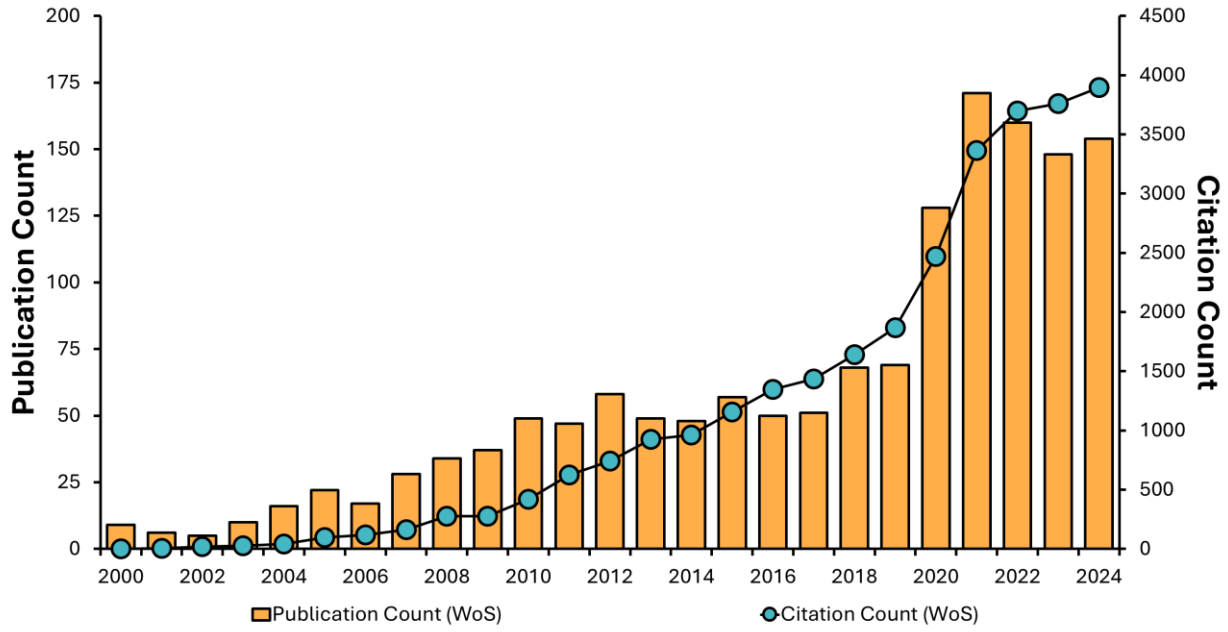

Figure 2. The evolution of publication and citation count of *O. tenuiflorum* during the period 2000 – 2024. (WoS = Web of Science)

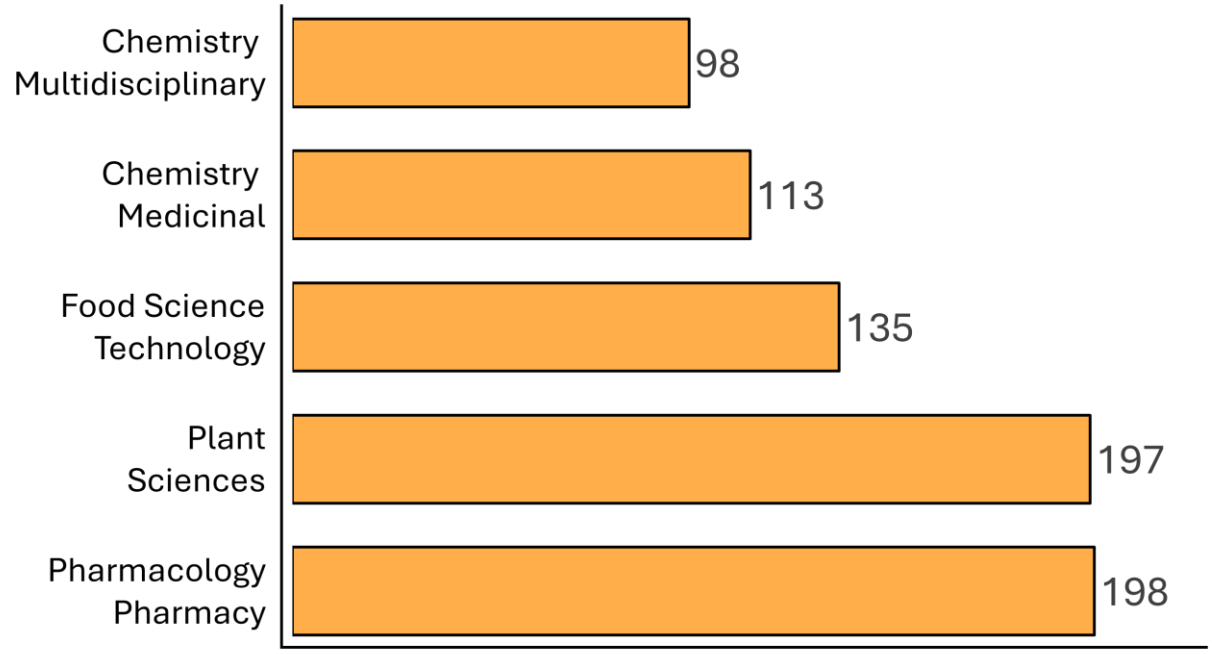

Figure 3. Top WoS categories based on the publication count over the last 24 years.

Table 1. Ranking of the 10 top authors and affiliations based on the number of publications and citations over the last 24 years of bibliometric analysis.

Author's Name	Record Count	Citation Count
Shanmugam, Rajeshkumar	11	73
Balaji, Raju	9	49
Kusindarta, Dwi Liliek	9	255
Wihadmadyatami, Hevi	9	168
Varghese, Remmiya Mary	8	204
Kumar, S. Aravind	6	116
Kustiati, Ulayatul	6	77
Ledwani, Lalita	5	252
Singh, Mumal	5	338
Vajpayee, Mona	5	372
Affiliations	**Record Count**	**Citation Count**
Council of Scientific Industrial Research (CSIR) India	89	2,868
Indian Council of Agricultural Research (ICAR)	57	1,232
CSIR Central Institute of Medicinal Aromatic Plants (CIMAP)	48	1,128
Indian Institute of Technology System (IIT) System	38	1,684
Saveetha Institute of Medical Technical Science	36	179
All India Institute of Medical Sciences (AIIMS), New Delhi	31	1,233
National Institute of Technology (NIT) System	30	579
Saveetha Dental College Hospital	30	161
Banaras Hindu University Bhu	29	727
King Saud University	23	258

Table 2. Top 10 countries with the highest record count in the *O. tenuiflorum* research over the last 24 years.

Countries	Record Count	Citation Count
India	1074	23,896
United States of America (USA)	89	1,899
Thailand	81	1,547
Saudi Arabia	65	899
Pakistan	48	548
Bangladesh	33	529
South Korea	31	1,322
Malaysia	27	383
People's Republic of China	27	523
Indonesia	21	172

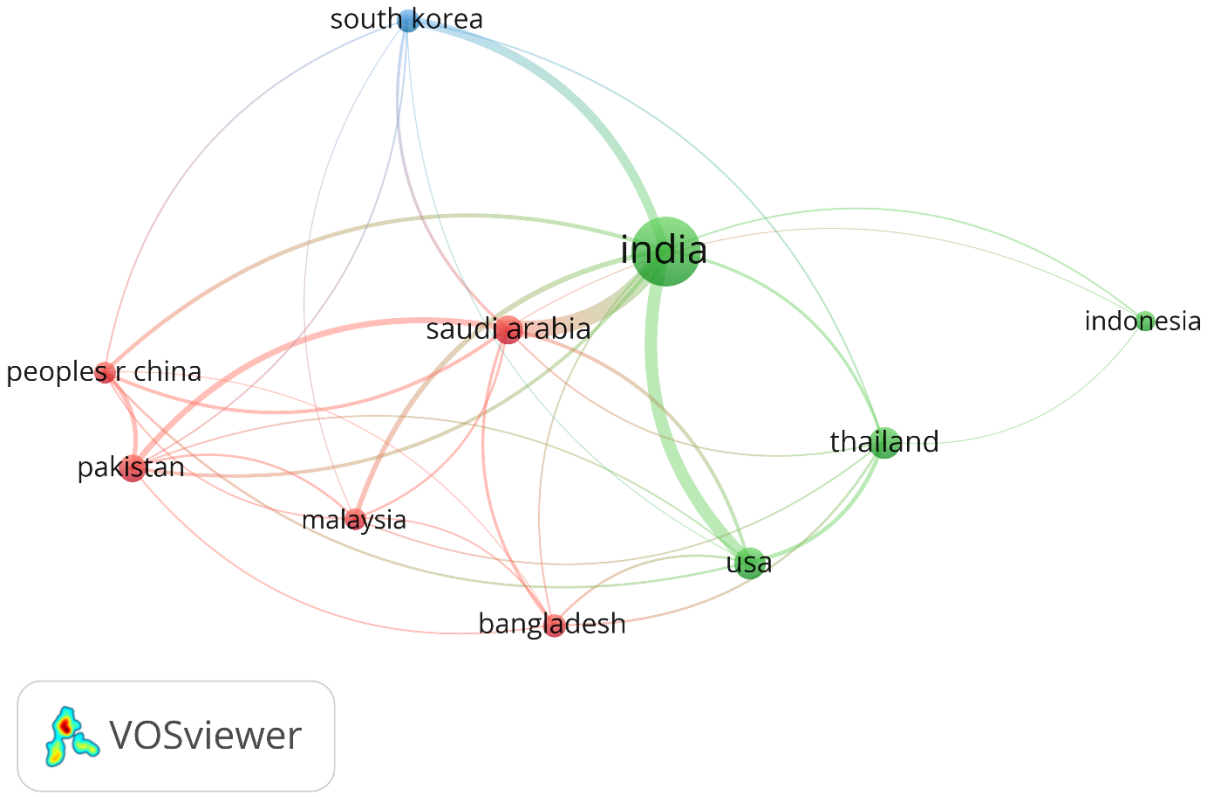

Figure 4. Collaborations among the 10 most prolific *O. tenuiflorum* research countries, as shown by co-authorship analysis (Network visualisation map).

Table 3. Top 10 most cited articles in the *O. tenuiflorum* research over the last 24 years.

Rank	Title	Citation Count	Year	Journal (IF)	Ref
1	Biosynthesis of silver nanoparticles using *Ocimum sanctum* (Tulsi) leaf extract and screening its antimicrobial activity	483	2011	Journal of Nanoparticle Research (2.6)	[33]
2	Rapid synthesis of silver nanoparticles using dried medicinal plant of basil	476	2010	Colloids and Surfaces B-Biointerfaces (5.6)	[34]
3	Synthesis of silver nanoparticles using plant extract and analysis of their antimicrobial property	373	2015	Journal of Saudi Chemical Society (5.8)	[36]
4	Comparative evaluation of hypoglycaemic activity of some Indian medicinal plants in alloxan diabetic rats	327	2003	Journal of Ethnopharmacology (5.4)	[37]
5	Green synthesis of carbon dots from *Ocimum sanctum* for effective fluorescent sensing of Pb2+ ions and live cell imaging	324	2017	Sensors and Actuators B-Chemical (7.7)	[35]
6	Antioxidant and cyclooxygenase inhibitory phenolic compounds from *Ocimum sanctum Linn.*	261	2000	Phytomedicine (8.2)	[26]
7	Effect of chromium accumulation on photosynthetic pigments, oxidative stress defence system, nitrate reduction, proline level and eugenol content of *Ocimum tenuiflorum L.*	260	2004	Plant Science (4.1)	[20]
8	Potent α-amylase inhibitory activity of Indian Ayurvedic medicinal plants	235	2011	BMC Complementary and Alternative Medicine (3.4)	[38]
9	Green Synthesis of Silver Nanoparticles Using Ocimum Leaf Extract and Their Characterisation	233	2011	Digest Journal of Nanomaterials and Biostructures (1.3)	[115]
10	Medicinal Plant Leaf Extract and Pure Flavonoid Mediated Green Synthesis of Silver Nanoparticles and their Enhanced Antibacterial Property	226	2017	Scientific Reports (3.9)	[31]

*IF = Impact Factor

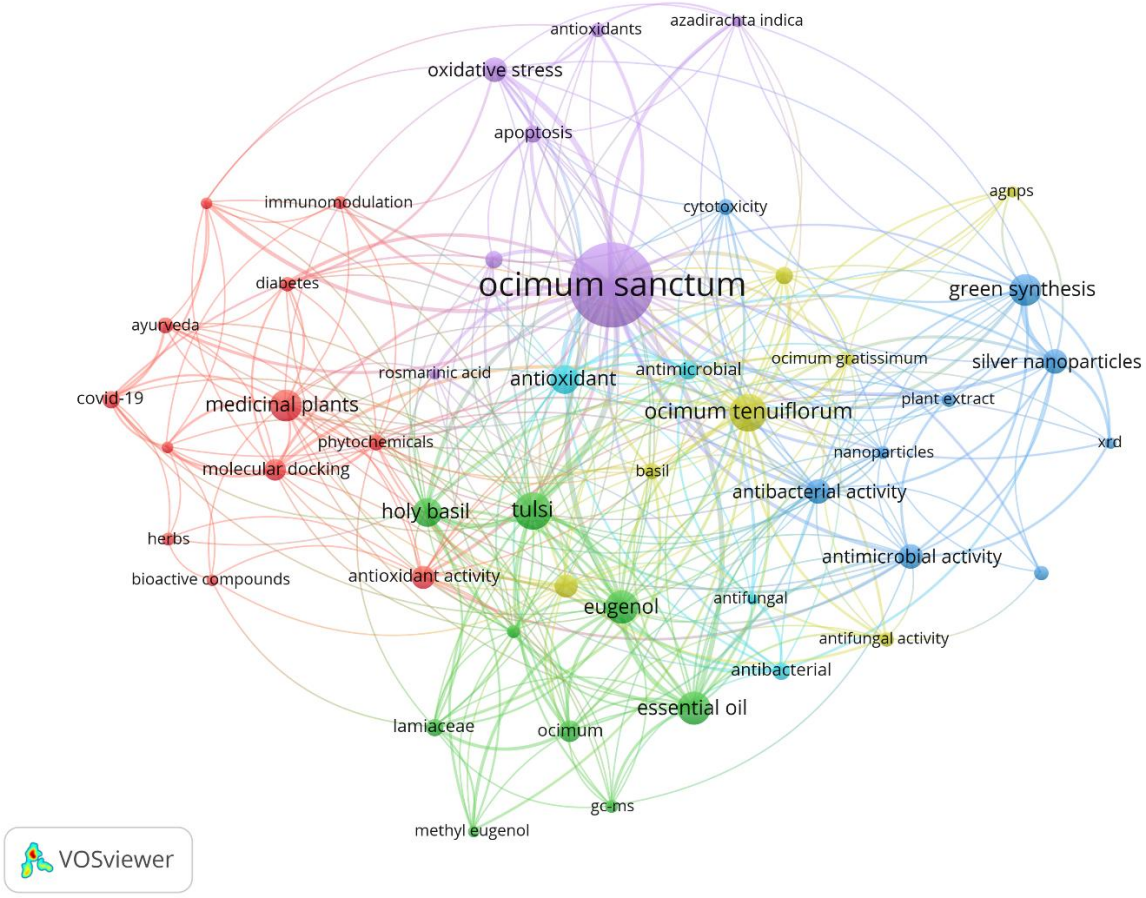

Figure 5. Co-occurrences of author keywords map with 50 of the most occurring words (Network visualisation map).

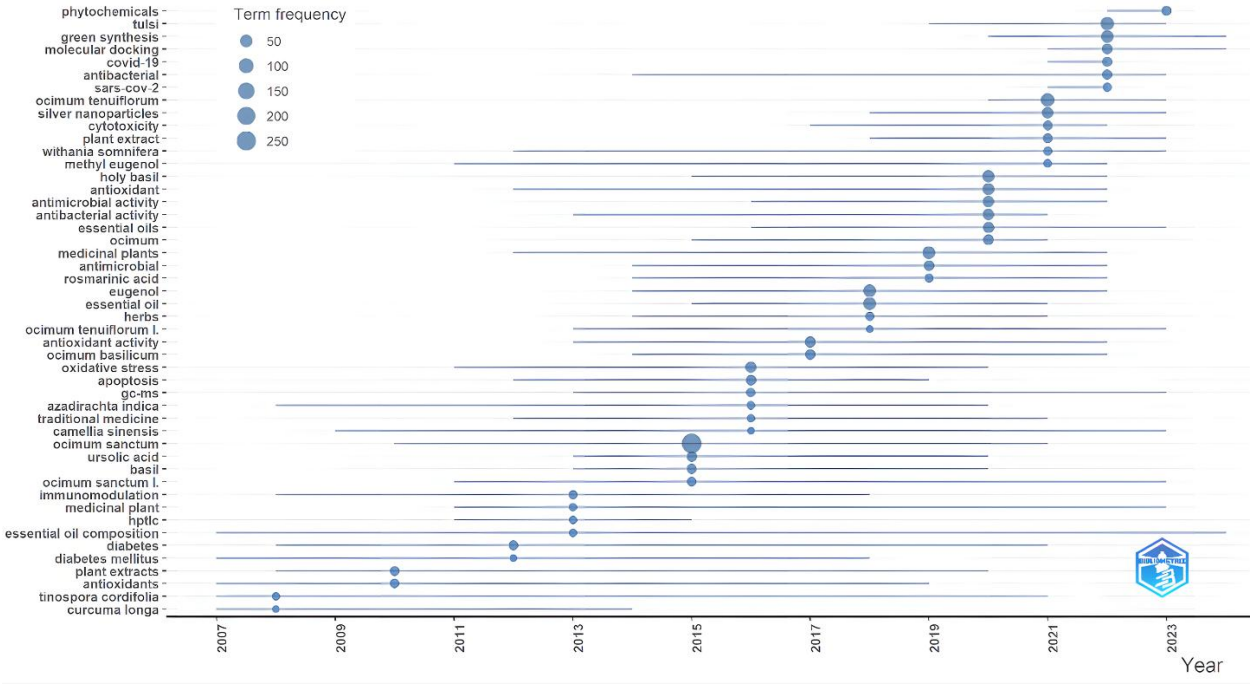

Figure 6. The trend topic visualisation from Biblioshiny highlights the evolving research focus on *O. tenuiflorum* over time (24 years).

Table 4. The biological activities of each compound group that is present in *O. tenuiflorum*

Compound Group	Biological Activities
Flavonoids	Anti-oxidant activity, anti-bacterial activity, anti-inflammatory activity, anti-proliferative, anti-cancer activity, anti-diabetic activity, anti-asthmatic activity, anti-convulsant effects, anti-depressant effects, anti-hypoxia / ischemia injury activity, enhances lipid metabolism, vasodilatation effects, antinociceptive effects, immunomodulatory activity, anti-atherosclerosis activity, and anti-thrombotic activity.
Phenolic Acids	Anti-oxidant activity, anti-microbial activity, anti-cancer activity, anti-proliferative on colon cancer cells, restores cognitive functions, anti-hepatitis B virus, regulation of carbohydrate and lipid metabolism, protects liver and kidney, protects the nervous system, protective effects against Huntington's disease, anti-sickling agent, anti-necrotic and anti-cholestatic effects against liver injury, anti-amoebic activity, hypo-pigmenting agent, anti-osteoporotic, analgesia, anti-wrinkle properties, hepatoprotective, anti-ageing properties, and angiogenic agent.
Triterpenoids	Anti-oxidant, anxiolytic effects and sedative effects, anti-bacterial activity, anti-inflammatory, anti-diabetic, wound-healing effect, neuroprotective activity, herbicidal activity, anti-hypertensive activity, and hepatoprotective effect.
Sesquiterpenes and Monoterpenes	Anti-oxidant effect, anti-bacterial activity, anti-fungal activity, anti-leishmanial activity, anti-inflammatory activity, neuroprotective activity, anti-apoptotic activity, anti-tumour activity, insecticidal activity, anti-diabetic activity, gastroprotective effect, anti-stress effect, anti-convulsant activity, insecticidal activity, and anti-ulcer activity.

References

[1] Statista Market Forecast [Internet]. 2025 [cited 2025 Jul 8]. https://www.statista.com/outlook/cmo/beauty-personal-care/skin-care/natural-skin-care/worldwide. Accessed 8 Jul 2025

[2] Fernandes A, Rodrigues PM, Pintado M, Tavaria FK. A systematic review of natural products for skin applications: Targeting inflammation, wound healing, and photo-aging. Phytomedicine [Internet]. Urban & Fischer; 2023 [cited 2025 Aug 3];115:154824. https://doi.org/10.1016/J.PHYMED.2023.154824

[3] Selwyn A, Govindaraj S. Study of plant-based cosmeceuticals and skin care. South African

Journal of Botany [Internet]. Elsevier; 2023 [cited 2025 Aug 3];158:429–42. https://doi.org/10.1016/J.SAJB.2023.05.039

[4] Yadav R, Fatima SK, Dhawan SS. Unlocking the medicinal potential of Ocimum africanum: A review of its phytoconstituents and pharmacological activities. South African Journal of Botany [Internet]. Elsevier; 2025 [cited 2025 Jul 23];184:617–30. https://doi.org/10.1016/J.SAJB.2025.06.020

[5] Bhattarai K, Bhattarai R, Pandey RD, Paudel B, Bhattarai HD. A Comprehensive Review of the Phytochemical Constituents and Bioactivities of Ocimum tenuiflorum. Scientific World Journal. John Wiley and Sons Ltd; 2024;2024. https://doi.org/10.1155/2024/8895039

[6] Chaiyana W, Anuchapreeda S, Somwongin S, Marsup P, Lee KH, Lin WC, et al. Dermal Delivery Enhancement of Natural Anti-Ageing Compounds from Ocimum sanctum Linn. Extract by Nanostructured Lipid Carriers. Pharmaceutics [Internet]. Pharmaceutics; 2020 [cited 2025 Oct 13];12. https://doi.org/10.3390/PHARMACEUTICS12040309

[7] Bhattacharjee S, Rastogi V, Durgapal S, Verma A, Singh B, Chandra A. Nanotherapy targeting anti-aging skin cells: harnessing ursolic acid from Ocimum sanctum Linn for precision skin rejuvenation - a molecular perspective. Nat Prod Res [Internet]. Taylor and Francis Ltd.; 2025 [cited 2025 Oct 13];1–16. https://doi.org/10.1080/14786419.2025.2474157

[8] Shetty S, Udupa S, Udupa L. Evaluation of Antioxidant and Wound Healing Effects of Alcoholic and Aqueous Extract of Ocimum sanctum Linn in Rats. Evid Based Complement Alternat Med [Internet]. Evid Based Complement Alternat Med; 2008 [cited 2025 Oct 13];5:95–101. https://doi.org/10.1093/ECAM/NEM004

[9] Ahidin D, Rohadi D, Indawati I, Yani Zamzam M, Susilo R. Phytochemical screening and antibacterial activity of ethanol extract of basil leaves (Ocimum sanctum L.) against Propionibacterium acne bacteria. Medical Sains: Jurnal Ilmiah Kefarmasian [Internet]. 2024 [cited 2025 Jul 31];9. https://www.creativecommons.org/licenses/by-sa/4.0/. Accessed 31 Jul 2025

[10] Wijaya N, Agung G, Sriyani A. Effectiveness of Azadirachta indica and Ocimum gratissimum for Acne Vulgaris: A Literature Review. International Journal of Research and Review (ijrrjournal.com). 2024;11. https://doi.org/10.52403/ijrr.20241001

[11] Bhattacharya R, Bose D, Maqsood Q, Gulia K, Khan A. Recent advances on the therapeutic

potential with Ocimum species against COVID-19: A review. South African Journal of Botany [Internet]. Elsevier; 2024 [cited 2025 Jul 23];164:188–99. https://doi.org/10.1016/J.SAJB.2023.11.034

[12] van Eck NJ, Waltman L. Visualizing Bibliometric Networks. Measuring Scholarly Impact. Springer International Publishing; 2014. p. 285–320. https://doi.org/10.1007/978-3-319-10377-8_13

[13] Romanelli JP, Gonçalves MCP, de Abreu Pestana LF, Soares JAH, Boschi RS, Andrade DF. Four challenges when conducting bibliometric reviews and how to deal with them. Environmental Science and Pollution Research. Environmental Science and Pollution Research; 2021;28:60448–58. https://doi.org/10.1007/s11356-021-16420-x

[14] Donthu N, Kumar S, Mukherjee D, Pandey N, Lim WM. How to conduct a bibliometric analysis: An overview and guidelines. J Bus Res. Elsevier Inc.; 2021;133:285–96. https://doi.org/10.1016/j.jbusres.2021.04.070

[15] Raina AP, Kumar A, Dutta M. Chemical characterization of aroma compounds in essential oil isolated from “Holy Basil” (Ocimum tenuiflorum L.) grown in India. Genet Resour Crop Evol. 2013;60:1727–35. https://doi.org/10.1007/S10722-013-9981-4

[16] Kumar A, Shukla R, Singh P, Dubey NK. Chemical composition, antifungal and antiaflatoxigenic activities of Ocimum sanctum L. essential oil and its safety assessment as plant based antimicrobial. Food and Chemical Toxicology. 2010;48:539–43. https://doi.org/10.1016/J.FCT.2009.11.028

[17] Bawankule D, Kumar A, Agarwal K, Maurya A, Shanker K, Bushra U, et al. Pharmacological and phytochemical evaluation of Ocimum sanctum root extracts for its antiinflammatory, analgesic and antipyretic activities. Pharmacogn Mag. SAGE Publications; 2015;11:217. https://doi.org/10.4103/0973-1296.157743

[18] Mataram MBA, Hening P, Harjanti FN, Karnati S, Wasityastuti W, Nugrahaningsih DAA, et al. The neuroprotective effect of ethanolic extract Ocimum sanctum Linn. in the regulation of neuronal density in hippocampus areas as a central autobiography memory on the rat model of Alzheimer’s disease. J Chem Neuroanat. Elsevier B.V.; 2021;111. https://doi.org/10.1016/J.JCHEMNEU.2020.101885

[19] Bhatt S, Bhatt M, Kumar A, Vyas G, Gajaria T, Paul P. Green route for synthesis of multifunctional fluorescent carbon dots from Tulsi leaves and its application as Cr(VI) sensors, bio-imaging and patterning agents. Colloids Surf B Biointerfaces. Elsevier B.V.;

2018;167:126–33. https://doi.org/10.1016/J.COLSURFB.2018.04.008

[20] Rai V, Vajpayee P, Singh SN, Mehrotra S. Effect of chromium accumulation on photosynthetic pigments, oxidative stress defense system, nitrate reduction, proline level and eugenol content of Ocimum tenuiflorum L. Plant Science. 2004;167:1159–69. https://doi.org/10.1016/J.PLANTSCI.2004.06.016

[21] Sharma H, Mendiratta SK, Agrawal RK, Gurunathan K, Kumar S, Singh TP. Use of various essential oils as bio preservatives and their effect on the quality of vacuum packaged fresh chicken sausages under frozen conditions. LWT. Academic Press; 2017;81:118–27. https://doi.org/10.1016/J.LWT.2017.03.048

[22] Srivalli B, Sharma G, Khanna-Chopra R. Antioxidative defense system in an upland rice cultivar subjected to increasing intensity of water stress followed by recovery. Physiol Plant. 2003;119:503–12. https://doi.org/10.1046/J.1399-3054.2003.00125.X

[23] Reddy KRN, Reddy CS, Muralidharan K. Potential of botanicals and biocontrol agents on growth and aflatoxin production by Aspergillus flavus infecting rice grains. Food Control. 2009;20:173–8. https://doi.org/10.1016/J.FOODCONT.2008.03.009

[24] Walters KJ, Currey CJ. Hydroponic greenhouse basil production: Comparing systems and cultivars. Horttechnology. American Society for Horticultural Science; 2015;25:645–50. https://doi.org/10.21273/HORTTECH.25.5.645

[25] Zheljazkov VD, Cantrell CL, Tekwani B, Khan SI. Content, composition, and bioactivity of the essential oils of three basil genotypes as a function of harvesting. J Agric Food Chem. 2008;56:380–5. https://doi.org/10.1021/JF0725629

[26] Kelm MA, Nair MG, Strasburg GM, DeWitt DL. Antioxidant and cyclooxygenase inhibitory phenolic compounds from Ocimum sanctum Linn. Phytomedicine. Urban und Fischer Verlag Jena; 2000;7:7–13. https://doi.org/10.1016/S0944-7113(00)80015-X

[27] Tangpao T, Chung HH, Sommano SR. Aromatic profiles of essential oils from five commonly used Thai basils. Foods. MDPI Multidisciplinary Digital Publishing Institute; 2018;7. https://doi.org/10.3390/FOODS7110175

[28] Juntachote T, Berghofer E, Siebenhandl S, Bauer F. The antioxidative properties of Holy basil and Galangal in cooked ground pork. Meat Sci. 2006;72:446–56. https://doi.org/10.1016/J.MEATSCI.2005.08.009

[29] Sutaphanit P, Chitprasert P. Optimisation of microencapsulation of holy basil essential oil in gelatin by response surface methodology. Food Chem. Elsevier Ltd; 2014;150:313–20.

https://doi.org/10.1016/J.FOODCHEM.2013.10.159

[30] van Eck NJ, Waltman L. Software survey: VOSviewer, a computer program for bibliometric mapping. Scientometrics. Springer Netherlands; 2010;84:523–38. https://doi.org/10.1007/s11192-009-0146-3

[31] Jain S, Mehata MS. Medicinal Plant Leaf Extract and Pure Flavonoid Mediated Green Synthesis of Silver Nanoparticles and their Enhanced Antibacterial Property. Sci Rep. Nature Publishing Group; 2017;7. https://doi.org/10.1038/S41598-017-15724-8

[32] Patil RS, Kokate MR, Kolekar SS. Bioinspired synthesis of highly stabilized silver nanoparticles using Ocimum tenuiflorum leaf extract and their antibacterial activity. Spectrochim Acta A Mol Biomol Spectrosc. 2012;91:234–8. https://doi.org/10.1016/J.SAA.2012.02.009

[33] Singhal G, Bhavesh R, Kasariya K, Sharma AR, Singh RP. Biosynthesis of silver nanoparticles using Ocimum sanctum (Tulsi) leaf extract and screening its antimicrobial activity. Journal of Nanoparticle Research. 2011;13:2981–8. https://doi.org/10.1007/S11051-010-0193-Y

[34] Ahmad N, Sharma S, Alam MK, Singh VN, Shamsi SF, Mehta BR, et al. Rapid synthesis of silver nanoparticles using dried medicinal plant of basil. Colloids Surf B Biointerfaces. 2010;81:81–6. https://doi.org/10.1016/J.COLSURFB.2010.06.029

[35] Kumar A, Chowdhuri AR, Laha D, Mahto TK, Karmakar P, Sahu SK. Green synthesis of carbon dots from Ocimum sanctum for effective fluorescent sensing of Pb2+ ions and live cell imaging. Sens Actuators B Chem. Elsevier B.V.; 2017;242:679–86. https://doi.org/10.1016/J.SNB.2016.11.109

[36] Logeswari P, Silambarasan S, Abraham J. Synthesis of silver nanoparticles using plants extract and analysis of their antimicrobial property. Journal of Saudi Chemical Society. Elsevier B.V.; 2015;19:311–7. https://doi.org/10.1016/J.JSCS.2012.04.007

[37] Kar A, Choudhary BK, Bandyopadhyay NG. Comparative evaluation of hypoglycaemic activity of some Indian medicinal plants in alloxan diabetic rats. J Ethnopharmacol. 2003;84:105–8. https://doi.org/10.1016/S0378-8741(02)00144-7

[38] Sudha P, Zinjarde SS, Bhargava SY, Kumar AR. Potent α-amylase inhibitory activity of Indian Ayurvedic medicinal plants. BMC Complement Altern Med. 2011;11. https://doi.org/10.1186/1472-6882-11-5

[39] Mutha RE, Tatiya AU, Surana SJ. Flavonoids as natural phenolic compounds and their role

in therapeutics: an overview. Futur J Pharm Sci [Internet]. Springer Science and Business Media LLC; 2021 [cited 2025 Aug 3];7:25. https://doi.org/10.1186/S43094-020-00161-8

[40] Kuljarusnont S, Iwakami S, Iwashina T, Tungmunnithum D. Flavonoids and Other Phenolic Compounds for Physiological Roles, Plant Species Delimitation, and Medical Benefits: A Promising View. Molecules 2024, Vol 29, Page 5351 [Internet]. Multidisciplinary Digital Publishing Institute; 2024 [cited 2025 Aug 3];29:5351. https://doi.org/10.3390/MOLECULES29225351

[41] Kasmara DP, Singarimbun NB, Amenta S, Perangin-Angin B. Ocimum Tenuiflorum Linne: A Narrative Review. International Journal of Nursing Information [Internet]. Qualitative and Quantitative Research Center; 2024 [cited 2025 Jul 30];3:25–41. https://doi.org/10.58418/IJNI.V3I1.62

[42] Srivastava AK, Singh VK. Tulsi (Ocimum sanctum): A Potent Adaptogen. Clinical Research Notes. Auctores Publishing LLC; 2021;2:01–5. https://doi.org/10.31579/2690-8816/037

[43] Tóth-Mészáros A, Garmaa G, Hegyi P, Bánvölgyi A, Fenyves B, Fehérvári P, et al. The effect of adaptogenic plants on stress: A systematic review and meta-analysis. J Funct Foods [Internet]. Elsevier; 2023 [cited 2025 Aug 3];108:105695. https://doi.org/10.1016/J.JFF.2023.105695

[44] Mohan Gowda CM, Murugan SK, Bethapudi B, Purusothaman D, Mundkinajeddu D, D'Souza P. Ocimum tenuiflorum extract (HOLIXERTM): Possible effects on hypothalamic–pituitary–adrenal (HPA) axis in modulating stress. PLoS One [Internet]. Public Library of Science; 2023 [cited 2025 Aug 3];18:e0285012. https://doi.org/10.1371/JOURNAL.PONE.0285012

[45] Lopresti AL, Smith SJ, Metse AP, Drummond PD. A randomized, double-blind, placebo-controlled trial investigating the effects of an Ocimum tenuiflorum (Holy Basil) extract (HolixerTM) on stress, mood, and sleep in adults experiencing stress. Front Nutr [Internet]. Frontiers Media S.A.; 2022 [cited 2025 Aug 3];9:965130. https://doi.org/10.3389/FNUT.2022.965130

[46] Arya R, Faruquee HM, Shakya H, Rahman SA, Begum MM, Biswas SK, et al. Harnessing the Antibacterial, Anti-Diabetic and Anti-Carcinogenic Properties of Ocimum sanctum Linn (Tulsi). Plants [Internet]. Multidisciplinary Digital Publishing Institute (MDPI); 2024 [cited 2025 Aug 3];13:3516. https://doi.org/10.3390/PLANTS13243516

[47] Hannan JMA, Marenah L, Ali L, Rokeya B, Flatt PR, Abdel-Wahab YHA. Ocimum sanctum leaf extracts stimulate insulin secretion from perfused pancreas, isolated islets and clonal pancreatic β-cells. Journal of Endocrinology [Internet]. BioScientifica; 2006 [cited 2025 Aug 3];189:127–36. https://doi.org/10.1677/JOE.1.06615

[48] Ayu P, Kasih Permatananda N, Sumardika W, Putu W, Yasa S, Gde I, et al. Antioxidant Effects of Ocimum tenuiflorum on Catalase and Glutathione Peroxidase In Vivo. Integrative Biomedical Research (Journal of Angiotherapy) [Internet]. Eman Research Publishing LLC, USA; 2024 [cited 2025 Aug 3];8:1–6. https://doi.org/10.25163/ANGIOTHERAPY.81110040

[49] Muralikrishnan G, Pillai SK, Shakeel F. Protective effects of Ocimum sanctum on lipid peroxidation and antioxidant status in streptozocin-induced diabetic rats. Nat Prod Res [Internet]. Nat Prod Res; 2012 [cited 2025 Aug 3];26:474–8. https://doi.org/10.1080/14786419.2010.531016,

[50] Patel J, Arora S. A Systematic Analysis of Compounds Present in Ocimum Tenuiflorum (Tulsi) Regarding its Anti-Inflammatory Properties Using In-Silico Techniques. Aresty Rutgers Undergraduate Research Journal [Internet]. Rutgers University Libraries; 2021 [cited 2025 Aug 3];1. https://doi.org/10.14713/ARESTYRURJ.V1I3.173

[51] Guo Q, Jin Y, Chen X, Ye X, Shen X, Lin M, et al. NF-κB in biology and targeted therapy: new insights and translational implications. Signal Transduct Target Ther [Internet]. Springer Nature; 2024 [cited 2025 Oct 14];9:1–37. https://doi.org/10.1038/S41392-024-01757-9;SUBJMETA

[52] Yang J, Zhang C, Yu M, Yuan J, Mao Y, Liu M, et al. Comprehensive lipid profiling and metabolic pathway analysis of Ocimum: Unveiling key variations and regulatory mechanisms for breeding and metabolic exploration. Food Biosci [Internet]. Elsevier; 2025 [cited 2025 Aug 3];66:106275. https://doi.org/10.1016/J.FBIO.2025.106275

[53] Parasuraman S, Balamurugan S, Christapher PV, Petchi RR, Yeng WY, Sujithra J, et al. Evaluation of Antidiabetic and Antihyperlipidemic Effects of Hydroalcoholic Extract of Leaves of Ocimum tenuiflorum (Lamiaceae) and Prediction of Biological Activity of its Phytoconstituents. Pharmacognosy Res [Internet]. Medknow Publications; 2015 [cited 2025 Aug 3];7:156. https://doi.org/10.4103/0974-8490.151457

[54] Suanarunsawat T, Devakul Na Ayutthaya W, Songsak T, Thirawarapan S, Poungshompoo S. Lipid-Lowering and Antioxidative Activities of Aqueous Extracts of Ocimum sanctum

L. Leaves in Rats Fed with a High-Cholesterol Diet. Oxid Med Cell Longev [Internet]. 2011 [cited 2025 Aug 3];2011:962025. https://doi.org/10.1155/2011/962025

[55] Mondal S, Varma S, Bamola VD, Naik SN, Mirdha BR, Padhi MM, et al. Double-blinded randomized controlled trial for immunomodulatory effects of Tulsi (Ocimum sanctum Linn.) leaf extract on healthy volunteers. J Ethnopharmacol [Internet]. J Ethnopharmacol; 2011 [cited 2025 Aug 3];136:452–6. https://doi.org/10.1016/j.jep.2011.05.012

[56] Khaliq T, Waseem MA, Lone AM, Hassan QP. Oscimum sanctum extract inhibits growth of Gram positive and Gram negative bacterial strains. Microb Pathog [Internet]. Academic Press; 2018 [cited 2025 Aug 3];118:211–3. https://doi.org/10.1016/J.MICPATH.2018.03.040

[57] Yamani HA, Pang EC, Mantri N, Deighton MA. Antimicrobial activity of Tulsi (Ocimum tenuiflorum) essential oil and their major constituents against three species of bacteria. Front Microbiol [Internet]. Frontiers Media S.A.; 2016 [cited 2025 Jul 31];7:195885. https://doi.org/10.3389/FMICB.2016.00681/BIBTEX

[58] Pandey TP, Mishra JN, Vishwakarma DK. Therapeutic effectiveness and development of eugenol topical gel to reduce irritant effect on skin. World Journal of Pharmaceutical Sciences [Internet]. World Journal of Pharmaceutical Sciences; 2022 [cited 2025 Aug 3];10:273–84. https://doi.org/10.54037/WJPS.2022.100305

[59] Fajdek-Bieda A, Pawlińska J, Wróblewska A, Żwierełło W, Łuś A, Klimowicz A. Antibacterial and Preservative Potential of Eugenol and Isoeugenol in Cosmetics: A Natural Solution for Product Stability. Applied Sciences 2025, Vol 15, Page 2129 [Internet]. Multidisciplinary Digital Publishing Institute; 2025 [cited 2025 Aug 3];15:2129. https://doi.org/10.3390/APP15042129

[60] Kothari SK, Bhattacharya AK, Ramesh S. Essential oil yield and quality of methyl eugenol rich Ocimum tenuiflorum L.f. (syn. O. sanctum L.) grown in south India as influenced by method of harvest. J Chromatogr A [Internet]. Elsevier; 2004 [cited 2025 Aug 3];1054:67–72. https://doi.org/10.1016/J.CHROMA.2004.03.019

[61] Pandey VK, Tripathi A, Srivastava S, Dar AH, Singh R, Farooqui A, et al. Exploiting the bioactive properties of essential oils and their potential applications in food industry. Food Sci Biotechnol [Internet]. The Korean Society of Food Science and Technology; 2023 [cited 2025 Aug 3];32:885–902. https://doi.org/10.1007/S10068-023-01287-0

[62] He T, Xiang Y, Quan H, Liu Y, Guo C, Quan T. Ursolic Acid Inhibits Collagen Production

and Promotes Collagen Degradation in Skin Dermal Fibroblasts: Potential Antifibrotic Effects. Biomolecules [Internet]. Multidisciplinary Digital Publishing Institute (MDPI); 2025 [cited 2025 Jul 31];15:365. https://doi.org/10.3390/BIOM15030365/S1

[63] Bhattacharjee S, Rastogi V, Durgapal S, Verma A, Singh B, Chandra A. Nanotherapy targeting anti-aging skin cells: harnessing ursolic acid from Ocimum sanctum Linn for precision skin rejuvenation – a molecular perspective. Nat Prod Res [Internet]. Taylor and Francis Ltd.; 2025 [cited 2025 Jul 31]; https://doi.org/10.1080/14786419.2025.2474157

[64] Chandimali N, Bak SG, Park EH, Lim HJ, Won YS, Kim EK, et al. Free radicals and their impact on health and antioxidant defenses: a review. Cell Death Discovery 2025 11:1 [Internet]. Nature Publishing Group; 2025 [cited 2025 Aug 3];11:1–17. https://doi.org/10.1038/s41420-024-02278-8

[65] Jayaraman R, Yusoff N, Salleh RM. Comparative Wound Healing Study of Ocimum tenuiflorum Leaves Extract and its Formulation on Sprague Dawley Rats. ASM Science Journal. Akademi Sains Malaysia; 2021;15:1–6. https://doi.org/10.32802/ASMSCJ.2021.695

[66] Saleih F, Malik Shah A. Preliminary screening on wound healing potential of Ocimum tenuiflorum l. using in vitro assays. Journal homepage. 2019;3:258–64. https://doi.org/10.26656/fr.2017.3(3).010

[67] Gupta VK, Pathak SS, Jain MK. Evaluation of burn wound healing property of ocimum sanctum by monitoring of period of re-epithelization in rabbits. Int J Basic Clin Pharmacol [Internet]. Medip Academy; 2016 [cited 2025 Aug 3];5:146–8. https://doi.org/10.18203/2319-2003.IJBCP20160117

[68] Shetty S, Udupa S, Udupa L. Evaluation of Antioxidant and Wound Healing Effects of Alcoholic and Aqueous Extract of Ocimum sanctum Linn in Rats. Evid Based Complement Alternat Med [Internet]. 2007 [cited 2025 Aug 3];5:95. https://doi.org/10.1093/ECAM/NEM004

[69] Mahajan UN, Wasule DD. Sunscreen and Anti-Oxidant Activities of Herbal Gel Formulations. Pharmacogn Mag. 2008;4.

[70] Dwivedi AK. Spectrophotometric determination of sunscreen potential of Ocimum sanctum. World Journal Of Advance Healthcare Research. 2024;8:114–7.

[71] Ghazi S. Do the polyphenolic compounds from natural products can protect the skin from ultraviolet rays? Results Chem [Internet]. Elsevier; 2022 [cited 2025 Aug 3];4:100428.

https://doi.org/10.1016/J.RECHEM.2022.100428

[72] García Forero A, Villamizar Mantilla DA, Núñez LA, Ocazionez RE, Stashenko EE, Fuentes JL. Photoprotective and Antigenotoxic Effects of the Flavonoids Apigenin, Naringenin and Pinocembrin. Photochem Photobiol [Internet]. Blackwell Publishing Inc.; 2019 [cited 2025 Aug 3];95:1010–8. https://doi.org/10.1111/PHP.13085

[73] Sanadi RM, Deshmukh RS. The effect of Vitamin C on melanin pigmentation – A systematic review. J Oral Maxillofac Pathol [Internet]. Medknow; 2020 [cited 2025 Aug 3];24:374. https://doi.org/10.4103/JOMFP.JOMFP_207_20

[74] Maniarasu N, Hasham R, Jemon K, Latif NA, Bahari H. A review on rosmarinic acid rich extract for skin regeneration through rapamycin signaling pathway. Chemical and Natural Resources Engineering Journal (Formally known as Biological and Natural Resources Engineering Journal) [Internet]. IIUM Press; 2023 [cited 2025 Aug 3];7:1–9. https://doi.org/10.31436/CNREJ.V7I1.85

[75] Sánchez-Campillo M, Gabaldon JA, Castillo J, Benavente-García O, Del Baño MJ, Alcaraz M, et al. Rosmarinic acid, a photo-protective agent against UV and other ionizing radiations. Food and Chemical Toxicology [Internet]. Pergamon; 2009 [cited 2025 Aug 3];47:386–92. https://doi.org/10.1016/J.FCT.2008.11.026

[76] Dammak M, Ben Hlima H, Fendri I, Smaoui S, Abdelkafi S. Phytochemicals in skin health: enhancing beauty and protecting against aging. Phytoceuticals in Food for Health and Wellness [Internet]. Academic Press; 2026 [cited 2025 Oct 14];261–74. https://doi.org/10.1016/B978-0-443-26494-8.00016-1

[77] Tomas M, Günal-Köroğlu D, Kamiloglu S, Ozdal T, Capanoglu E. The state of the art in anti-aging: plant-based phytochemicals for skin care. Immunity and Ageing [Internet]. BioMed Central Ltd; 2025 [cited 2025 Oct 14];22:1–23. https://doi.org/10.1186/S12979-025-00498-9/TABLES/5

[78] Paidi RK, Jana M, Raha S, McKay M, Sheinin M, Mishra RK, et al. Eugenol, a Component of Holy Basil (Tulsi) and Common Spice Clove, Inhibits the Interaction Between SARS-CoV-2 Spike S1 and ACE2 to Induce Therapeutic Responses. Journal of Neuroimmune Pharmacology [Internet]. Springer; 2021 [cited 2025 Aug 3];16:743. https://doi.org/10.1007/S11481-021-10028-1

[79] da Silva FFM, Monte FJQ, de Lemos TLG, do Nascimento PGG, de Medeiros Costa AK, de Paiva LMM. Eugenol derivatives: synthesis, characterization, and evaluation of

antibacterial and antioxidant activities. Chem Cent J [Internet]. Springer; 2018 [cited 2025 Aug 3];12:1–9. https://doi.org/10.1186/S13065-018-0407-4/TABLES/3

[80] Ulanowska M, Olas B. Biological Properties and Prospects for the Application of Eugenol—A Review. International Journal of Molecular Sciences 2021, Vol 22, Page 3671 [Internet]. Multidisciplinary Digital Publishing Institute; 2021 [cited 2025 Aug 3];22:3671. https://doi.org/10.3390/IJMS22073671

[81] Barboza JN, da Silva Maia Bezerra Filho C, Silva RO, Medeiros JVR, de Sousa DP. An Overview on the Anti-inflammatory Potential and Antioxidant Profile of Eugenol. Oxid Med Cell Longev [Internet]. Hindawi Limited; 2018 [cited 2025 Aug 3];2018:3957262. https://doi.org/10.1155/2018/3957262

[82] Kaur G, Athar M, Sarwar Alam M. Eugenol precludes cutaneous chemical carcinogenesis in mouse by preventing oxidative stress and inflammation and by inducing apoptosis. Mol Carcinog [Internet]. Mol Carcinog; 2010 [cited 2025 Aug 3];49:290–301. https://doi.org/10.1002/MC.20601,

[83] Woźniak Ł, Skąpska S, Marszałek K. Ursolic Acid—A Pentacyclic Triterpenoid with a Wide Spectrum of Pharmacological Activities. Molecules 2015, Vol 20, Pages 20614-20641 [Internet]. Multidisciplinary Digital Publishing Institute; 2015 [cited 2025 Aug 3];20:20614–41. https://doi.org/10.3390/MOLECULES201119721

[84] Vetal MD, Lade VG, Rathod VK. Extraction of ursolic acid from Ocimum sanctum leaves: Kinetics and modeling. Food and Bioproducts Processing [Internet]. Elsevier; 2012 [cited 2025 Aug 3];90:793–8. https://doi.org/10.1016/J.FBP.2012.07.003

[85] Pei J, Wu M, Cai S, Peng J, Zhan X, Wang D, et al. The Protective Effect of Ursolic Acid on Unilateral Ureteral Obstruction in Rats by Activating the Nrf2/HO-1 Antioxidant Signaling Pathway. Comput Intell Neurosci [Internet]. John Wiley & Sons, Ltd; 2022 [cited 2025 Aug 3];2022:3690524. https://doi.org/10.1155/2022/3690524

[86] Fu Y, Liu T, He S, Zhang Y, Tan Y, Bai Y, et al. Ursolic acid reduces oxidative stress injury to ameliorate experimental autoimmune myocarditis by activating Nrf2/HO-1 signaling pathway. Front Pharmacol. Frontiers Media SA; 2023;14:1189372. https://doi.org/10.3389/FPHAR.2023.1189372/BIBTEX

[87] Feng W, Yang K, Zou Y, Xiao Z, Qian R, Qian R. Progress of ursolic acid on the regulation of macrophage: summary and prospect. Front Immunol [Internet]. Frontiers Media SA; 2025 [cited 2025 Aug 3];16:1576771. https://doi.org/10.3389/FIMMU.2025.1576771

[88] Wang Y, Li L, Deng S, Liu F, He Z. Ursolic acid ameliorates inflammation in cerebral ischemia and reperfusion injury possibly via high mobility group box 1/toll-like receptor 4/NFκB pathway. Front Neurol [Internet]. Frontiers Media S.A.; 2018 [cited 2025 Aug 3];9. https://doi.org/10.3389/FNEUR.2018.00253,

[89] Zhao M, Wu F, Tang Z, Yang X, Liu Y, Wang F, et al. Anti-inflammatory and antioxidant activity of ursolic acid: a systematic review and meta-analysis. Front Pharmacol [Internet]. Frontiers Media SA; 2023 [cited 2025 Aug 3];14:1256946. https://doi.org/10.3389/FPHAR.2023.1256946/FULL

[90] He T, Xiang Y, Quan H, Liu Y, Guo C, Quan T. Ursolic Acid Inhibits Collagen Production and Promotes Collagen Degradation in Skin Dermal Fibroblasts: Potential Antifibrotic Effects. Biomolecules [Internet]. Multidisciplinary Digital Publishing Institute (MDPI); 2025 [cited 2025 Aug 3];15:365. https://doi.org/10.3390/BIOM15030365/S1

[91] Shanmuga Sundaram R, Ramanathan M, Rajesh R, Satheesh B, Saravanan D. LC-MS quantification of rosmarinic acid and ursolic acid in the Ocimum sanctum Linn. leaf extract (Holy Basil, Tulsi). J Liq Chromatogr Relat Technol [Internet]. 2012 [cited 2025 Aug 3];35:634–50. https://doi.org/10.1080/10826076.2011.606583

[92] Guan H, Luo W, Bao B, Cao Y, Cheng F, Yu S, et al. A Comprehensive Review of Rosmarinic Acid: From Phytochemistry to Pharmacology and Its New Insight. Molecules [Internet]. MDPI; 2022 [cited 2025 Aug 3];27:3292. https://doi.org/10.3390/MOLECULES27103292/S1

[93] Harindranath H, Susil A, S R, Sekar M, Kumar BRP. Unlocking the potential of Rosmarinic acid: A review on extraction, isolation, quantification, pharmacokinetics and pharmacology. Phytomedicine Plus [Internet]. Elsevier; 2025 [cited 2025 Aug 3];5:100726. https://doi.org/10.1016/J.PHYPLU.2024.100726

[94] Wu L, Lv L, Xiang Y, Yi D, Liang Q, Ji M, et al. Rosmarinic Acid Protects Against Acetaminophen-Induced Hepatotoxicity by Suppressing Ferroptosis and Oxidative Stress Through Nrf2/HO-1 Activation in Mice. Mar Drugs [Internet]. Multidisciplinary Digital Publishing Institute (MDPI); 2025 [cited 2025 Aug 3];23:287. https://doi.org/10.3390/MD23070287

[95] Lu YH, Hong Y, Zhang TY, Chen YX, Wei ZJ, Gao CY. Rosmarinic acid exerts anti-inflammatory effect and relieves oxidative stress via Nrf2 activation in carbon tetrachloride-induced liver damage. Food Nutr Res [Internet]. Swedish Nutrition

Foundation; 2022 [cited 2025 Aug 3];66:10.29219/fnr.v66.8359. https://doi.org/10.29219/FNR.V66.8359

[96] Shim KS, Kim HJ, Ji KY, Jung DH, Park SH, Song HK, et al. Rosmarinic Acid Ameliorates Dermatophagoides farinae Extract-Induced Atopic Dermatitis-like Skin Inflammation by Activating the Nrf2/HO-1 Signaling Pathway. International Journal of Molecular Sciences 2024, Vol 25, Page 12737 [Internet]. Multidisciplinary Digital Publishing Institute; 2024 [cited 2025 Aug 3];25:12737. https://doi.org/10.3390/IJMS252312737

[97] Gupta D, Sharma RR, Rashid H, Bhat AM, Tanveer MA, Abdullah ST. Rosmarinic acid alleviates ultraviolet-mediated skin aging via attenuation of mitochondrial and ER stress responses. Exp Dermatol [Internet]. John Wiley & Sons, Ltd; 2023 [cited 2025 Aug 3];32:799–807. https://doi.org/10.1111/EXD.14773

[98] Ding Y, Ma T, Zhang Y, Zhao C, Wang C, Wang Z. Rosmarinic acid ameliorates skin inflammation and pruritus in allergic contact dermatitis by inhibiting mast cell-mediated MRGPRX2/PLCγ1 signaling pathway. Int Immunopharmacol [Internet]. Elsevier; 2023 [cited 2025 Aug 3];117:110003. https://doi.org/10.1016/J.INTIMP.2023.110003

[99] Hussain MS, Rana AJ, Ashique S, Jakhmola V, Gupta G. Rosmarinic acid as a targeted modulator of NF-κB signaling in colorectal cancer: A promising adjunct to chemotherapy. World J Clin Oncol [Internet]. World J Clin Oncol; 2025 [cited 2025 Aug 3];16. https://doi.org/10.5306/WJCO.V16.I7.108086

[100] Kowalczyk A, Tuberoso CIG, Jerković I. The Role of Rosmarinic Acid in Cancer Prevention and Therapy: Mechanisms of Antioxidant and Anticancer Activity. Antioxidants 2024, Vol 13, Page 1313 [Internet]. Multidisciplinary Digital Publishing Institute; 2024 [cited 2025 Aug 3];13:1313. https://doi.org/10.3390/ANTIOX13111313

[101] Baliga MS, Jimmy R, Thilakchand KR, Sunitha V, Bhat NR, Saldanha E, et al. Ocimum Sanctum L (Holy Basil or Tulsi) and its phytochemicals in the prevention and treatment of cancer. Nutr Cancer [Internet]. Nutr Cancer; 2013 [cited 2025 Aug 3];65:26–35. https://doi.org/10.1080/01635581.2013.785010,

[102] Martínez-Gutiérrez A, Sendros J, Noya T, González MC. Apigenin and Phloretin Combination for Skin Aging and Hyperpigmentation Regulation. Cosmetics [Internet]. Multidisciplinary Digital Publishing Institute (MDPI); 2024 [cited 2025 Aug 3];11:128. https://doi.org/10.3390/COSMETICS11040128/S1

[103] Majma Sanaye P, Mojaveri MR, Ahmadian R, Sabet Jahromi M, Bahramsoltani R.

Apigenin and its dermatological applications: A comprehensive review. Phytochemistry [Internet]. Pergamon; 2022 [cited 2025 Aug 3];203:113390. https://doi.org/10.1016/J.PHYTOCHEM.2022.113390

[104] Peanlikhit T, Aryal U, Welsh JS, Shroyer KR, Rithidech KN. Evaluation of the Inhibitory Potential of Apigenin and Related Flavonoids on Various Proteins Associated with Human Diseases Using AutoDock. Int J Mol Sci [Internet]. Multidisciplinary Digital Publishing Institute (MDPI); 2025 [cited 2025 Aug 3];26:2548. https://doi.org/10.3390/IJMS26062548/S1

[105] Allemailem KS, Almatroudi A, Alharbi HOA, AlSuhaymi N, Alsugoor MH, Aldakheel FM, et al. Apigenin: A Bioflavonoid with a Promising Role in Disease Prevention and Treatment. Biomedicines [Internet]. Multidisciplinary Digital Publishing Institute (MDPI); 2024 [cited 2025 Aug 3];12:1353. https://doi.org/10.3390/BIOMEDICINES12061353

[106] Che DN, Cho BO, Kim JS, Shin JY, Kang HJ, Jang S Il. Effect of Luteolin and Apigenin on the Production of Il-31 and Il-33 in Lipopolysaccharides-Activated Microglia Cells and Their Mechanism of Action. Nutrients [Internet]. MDPI AG; 2020 [cited 2025 Aug 3];12:811. https://doi.org/10.3390/NU12030811

[107] Che DN, Cho BO, Shin JY, Kang HJ, Kim JS, Oh H, et al. Apigenin Inhibits IL-31 Cytokine in Human Mast Cell and Mouse Skin Tissues. Molecules [Internet]. MDPI AG; 2019 [cited 2025 Aug 3];24:1290. https://doi.org/10.3390/MOLECULES24071290

[108] Yoon JH, Kim MY, Cho JY. Apigenin: A Therapeutic Agent for Treatment of Skin Inflammatory Diseases and Cancer. Int J Mol Sci [Internet]. MDPI; 2023 [cited 2025 Aug 3];24:1498. https://doi.org/10.3390/IJMS24021498

[109] Xu H, Linn BS, Zhang Y, Ren J. A Review on the Antioxidative and Prooxidative Properties of Luteolin. Reactive Oxygen Species [Internet]. 2019 [cited 2025 Aug 3];7:136-147–136–147. https://rosj.org/index.php/ros/article/view/198. Accessed 3 Aug 2025

[110] Eddy AC, Rajakumar A, Spradley FT, Granger JP, Rana S. Luteolin prevents TNF-α-induced NF-κB activation and ROS production in cultured human placental explants and endothelial cells. Placenta [Internet]. W.B. Saunders Ltd; 2024 [cited 2025 Aug 3];145:65–71. https://doi.org/10.1016/J.PLACENTA.2023.12.004,

[111] Gour A, Manhas D, Bag S, Gorain B, Nandi U. Flavonoids as potential phytotherapeutics to combat cytokine storm in SARS-CoV-2. Phytotherapy Research [Internet]. John Wiley

and Sons Ltd; 2021 [cited 2025 Aug 3];35:4258. https://doi.org/10.1002/PTR.7092

[112] Mu J, Ma H, Chen H, Zhang X, Ye M. Luteolin Prevents UVB-Induced Skin Photoaging Damage by Modulating SIRT3/ROS/MAPK Signaling: An in vitro and in vivo Studies. Front Pharmacol. Frontiers Media S.A.; 2021;12. https://doi.org/10.3389/FPHAR.2021.728261/

[113] Żynda W, Ruczaj A, Galicka A. Natural Compounds with Beneficial Effects on Skin Collagen Type I and Mechanisms of Their Action. Antioxidants 2025, Vol 14, Page 389 [Internet]. Multidisciplinary Digital Publishing Institute; 2025 [cited 2025 Aug 3];14:389. https://doi.org/10.3390/ANTIOX14040389

[114] Mu J, Ma H, Chen H, Zhang X, Ye M. Luteolin Prevents UVB-Induced Skin Photoaging Damage by Modulating SIRT3/ROS/MAPK Signaling: An in vitro and in vivo Studies. Front Pharmacol [Internet]. Frontiers Media S.A.; 2021 [cited 2025 Aug 3];12:728261. https://doi.org/10.3389/FPHAR.2021.728261/FULL

[115] Mallikarjuna K, Narasimha G, Dillip G, Praveen B, Shreedhar B, Lakshmi C, et al. Green synthesis of silver nanoparticles using ocimum leaf extract and their characterization. Digest journal of nanomaterials and biostructures. 2011;6:181–6.

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REVIEW ARTICLE

A Scoping Review on Back Care Education Strategies for Farmers with Low Back Pain.

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Abstract

Background: Farmers frequently experience low back pain (LBP), which arises from the physically demanding nature of their work combined with multiple contributing factors. Hence, it is important to provide tailored back care education (BCE) to manage pain and enhance functionality effectively. **Objective:** This scoping review aims to identify, map, and synthesize the evidence on back care education (BCE) strategies designed to reduce pain and improve function for farmers with LBP. **Materials and methods:** The literature search was conducted in PUBMED, Scopus, and Web of Science to identify articles published between 2012 and 2024. The eligibility criteria included studies focusing on BCE in farming populations with LBP regardless of study design. **Result:** From 1,395 articles initially screened, only nine studies met the inclusion criteria. Thematic analysis identified three main BCE components: (1) ergonomic training for agricultural tasks, (2) prescribed therapeutic exercise, and (3) pain science and self-management education. Multi-component BCE programs were generally effective in reducing pain and improving function, although intervention protocols and outcome measures varied substantially. **Conclusion:** This review demonstrates that BCE is a promising strategy for the management of low back pain in farmers, particularly when adapted to the specific demands of agricultural work. Nevertheless, the heterogeneity of the interventions identified indicates the need for further research to formulate standardized and context-specific protocols, as well as to apply consistent outcome measures to build a more robust evidence base.

Keywords: *Back care education, ergonomic, farmers, low back pain, patient education.*

Introduction

Among musculoskeletal disorders, low back pain (LBP) occurs with the highest frequency worldwide, affecting a large number of individuals, regardless of the nature of their activities. Agricultural farmers are among the most affected populations, with a prevalence of LBP ranging from 23.7 to 71.2%. [1-3] LBP among farmers can result in recurring pain, decreased functions, frequent hospital visits, work absenteeism or loss of employment, and reduced quality of life. [4-6] Farmers, in particular, have a likelihood of experiencing LBP, perhaps due to the physical demands of their work or biomechanical factors that require repetitive activities such as bending, twisting, and heavy lifting. [1,7,8] Furthermore, several studies have shown that LBP among farmers is a complex multifactorial condition that is influenced by a combination of occupational and non-occupational factors such as stress (psychological factors) and social factors (e.g., work environment). [9,10] Addressing these issues through musculoskeletal disorder-focused interventions can raise awareness among agricultural farmers, empowering them to effectively mitigate this disorder within the agricultural sector. Hence, intervention for LBP among farmers must be tailored to address the unique occupational context within the biopsychosocial (BPS) aspects of LBP framework. [11]

This multidisciplinary approach is supported by high-quality evidence; for example, a systematic and meta-analysis concluded that multidisciplinary BPS rehabilitation interventions are more effective than usual care (moderate-quality evidence) and physical treatments (low-quality evidence) in reducing pain and disability in people with LBP. [12,13] Another recent systematic review found that BPS interventions that prioritize psychosocial components, including pain cognition, modification of maladaptive beliefs, adaptive coping mechanisms, and the establishment of personalized goals, are more effective than education or advice alone and as effective as physical activity interventions for managing LBP. [14] Presently educational efforts often take a backseat to drug treatments, manual therapy, and surgery; hence, healthcare services should prioritize implementing strategies to educate individuals with pain, as well as employers, insurance systems, policymakers, and society as a whole. [15]An education-based paradigm should begin by offering information on functional recovery, tailored to patients' needs, while being backed by evidence-based practices. [8] Furthermore, comprehensive education should be integrated into treatment plans that emphasize restoration through measures and rehabilitation programs. [16] Therefore, a new definition of back care education (BCE) should encompass not only advice or cognitive behavioral change, but it should include physical activity or exercise training with empowerment and goal setting for patients to perform as a life-long lifestyle.

Developing BCE for agricultural farmers may be more complex due to their physically demanding nature of their activities. Several factors need to be considered that may tailor management guidelines specific to the nature of farming. For instance, some may need to use ergonomically designed tools that minimize strain on the lower back. [17] Generalized recommendations may not fully address the specific challenges for those who perform labor-intensive tasks such as bending, twisting, and repetitive movements, especially among farmers involved in planting and harvesting. Current LBP guidelines may not fully address biopsychosocial aspects of LBP, especially for agricultural farmers. While guidelines like NICE recommend self-management and pacing techniques, these are challenging to implement for farmers whose work is dictated by seasonal demands and unpredictable weather, often precluding the ability to pace activities or avoid strenuous tasks like harvesting. [18] Strategies also include maintaining activity levels, employing pacing techniques, and utilizing methods to protect the back from further injury. [19]

Based on this gap, we propose that BCE for agricultural farmers with LBP should include several key components, such as educating clients on the importance of physical activity and specific exercises, goal-setting, cognitive behavioral therapy, and ergonomic practices. The existing literature highlights the necessity for guidelines to extend beyond general recommendations and incorporate strategies that address the unique physical demands and ergonomic challenges encountered by farmers, encompassing the biopsychosocial factors. Therefore, this scoping review aims to map the current efficacy and strategies of BCE for farmers (Population) in managing LBP. We will analyse interventions compared to general or no intervention (Comparison), with the primary focus on outcomes related to pain reduction and functional improvement or quality of life. Studies published within the last decade were included to capture recent developments in BCE (Time). Consolidating evidence-based practices may provide physiotherapists and other healthcare professionals with tools to plan prevention and rehabilitation programs tailored to farmers with LBP. Moreover, the insights gained from this review are crucial for guiding research scholars toward areas that require in-depth investigation. From a policy-making standpoint, these findings establish a foundation for formulating and refining the biopsychosocial strategies that can be delivered via a series of BCE programs specifically designed for agricultural farmers.

Materials and methods

The scoping review was performed as the optimal methodological choice to comprehensively map the extent, nature, and characteristics of evidence regarding Back Care Education (BCE) for farmers with low back pain (LBP), identify knowledge gaps, and clarify conceptual frameworks within this field. This approach was selected due to the expected heterogeneity in interventions, outcomes, and study designs across the existing literature. [20] The review followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) guidelines, ensuring transparency, reproducibility, and methodological rigor. The methodological framework was informed by the recommendations of Peters et al. (2015) and incorporated into the following subsections. [21] The protocol consists of four stages; (1) Formulating the research question for the scoping review using PICOT (Table 1) as recommended. [22]; (2) Developing inclusion criteria; (3) Defining the search strategy; and (4) Summarizing the findings.

ELEMENT PICOT	Description
Population	Farmers with low back pain, back pain, particularly engaged with agricultural task (e.g., planting, harvesting, heavy lifting, grass, etc)
Intervention	Back education, back care education, self-care management, education, exercise component (e.g., stretching exercise, strengthening), patient education.
Comparison	Not applicable for scoping reviews; studies with or without a comparator were considered.
Outcome	Pain intensity, functional disability, quality of life, mental health, psychological health.
Time	Studies published between 2012 to 2024.

We focused our study on farmers who experience LBP, examining the strategies employed by patients and healthcare teams in their respective settings. To guide our research, we formulated the following review questions;

1. How effective is BCE in managing pain and enhancing functions among farmers?
2. What are the delivery methods used to provide BCE for farmers?
3. What specific topics are covered in BCE for farmers?

To identify studies, we established criteria for inclusion as the following;

1. The methodologies discussed should aim to promote BCE.
2. Studies were eligible if they specifically addressed BCE as an intervention for farmers with LBP, included comparative outcomes with other interventions or no intervention,

and reported pain, functionality, or quality of life measures as outcomes.
3. The target audience of these methodologies should be farmers with LBP (For this review, 'farmer',refers to individuals engaged in labour-intensive agricultural tasks such as planting, harvesting, and handling heavy materials regularly).
4. Studies must be written in English.
5. The effects of the BCE interventions should be reported.

We excluded studies that were:

1. Not specifically addresses BCE or interventions for managing LBP among farmers.
2. Non-farmer populations.
3. Case reports, case series, narrative reviews, opinion pieces, and editorials.
4. Non-English language studies, due to language constraints in the review process.
5. Absent of clear outcomes related to pain management, function, or quality of life.

To search for the relevant studies, we utilized PubMed, Scopus, and Google Scholar as databases from 2012 to 2024. We utilized the Medical Subject Headings (MeSH) and relevant keywords to ensure we obtained the targeted search. We combined terms using Boolean operators such, as "AND" and "OR". Our search string was structured as follows; ("Low Back Pain". "Farmers". "Health Education". Back Care Education") AND ("Program Development" OR "Intervention"). Our approach aimed to cover a range of literature while staying focused on the main topics of interest. Studies were included if they addressed BCE as part of a broader intervention, allowing a comprehensive review of education's role within diverse approaches to LBP management. While BCE was the main intervention of interest, studies incorporating complementary interventions were included if they provided distinct outcomes relevant to back care and functional improvement.

We initially identified a total of 1,395 records. Mendeley software was used to manage these records effectively and eliminate duplicates. The data from the final studies included in the review were then extracted and charted to discern themes and issues from each study. We developed a data extraction table following the recommendations of Peters et al (2015).(21) The table consisted of details of the following; the author(s), year of publication, country of origin, study objectives, population, research design, the BCE intervention regimes (such as frequency, intervals between sessions, and responsible parties), as well as the study outcomes.

To guarantee that our data extraction and analysis processes were consistent and dependable, and to limit potential biases in the review, we implemented a two-phase screening. Firstly, we involved two independent reviewers to perform a thorough examination of the information and address any inconsistencies through dialogue. A third researcher was engaged for further consultation, if additional clarification was required.

Results

Our initial search found a total of 1395 papers; however, after evaluating their titles and abstracts, only 18 papers were included for a full review (Fig.1). We independently read through the texts of these 18 papers, but eventually, we found 9 studies met the inclusion criteria. Among the excluded studies, one was not published in English and therefore did not meet the language inclusion criteria. Five studies did not specifically focus on farmers with low back pain (LBP) and thus did not align with the target population. The remaining three studies were excluded due to their non-experimental nature; these were narrative reviews that did not involve any form of intervention, which was a core inclusion criterion for this review. The included studies varied considerably in terms of design (randomized controlled trials, quasi-experimental studies), intervention type (e.g., BCE only vs. BCE combined with exercise or ergonomic adjustments), and target populations (e.g., rice farmers, clam farmers, general rural farmers).

Table 1 shows the 9 studies included in this scoping review; three were randomized controlled trials, [23-25] one was semi-experimental, [26] one was a quasi-experimental, [27] one was experimental, [28] one was a survey and educational intervention, [29] and two were pilot studies.[30,31]

The majority of the included studies have examined the use of BCE or patient education as an intervention for farmers. [23-25,27-29,31] These studies compared BCE with a control approach. In contrast, one study focused exclusively on evaluating the outcomes of self-management strategies as the intervention.[30] The considerable heterogeneity among the included studies—in terms of study design, intervention modalities, target populations, and geographical settings—substantially affects the interpretability and generalizability of the findings. This variability limits the ability to make direct comparisons across studies or to draw firm conclusions regarding the effectiveness of Back Care Education (BCE) among farmers with LBP. Nevertheless, such diversity underscores a critical research gap and emphasizes the necessity for more standardized, rigorously controlled, and contextually tailored research. Accordingly, this heterogeneity should not only be viewed as a limitation but also as a strong research justification for conducting further research, including the implementation of structured BCE programs tailored to specific populations, such as Indonesian rice farmers, to generate more consistent and applicable evidence.

How effective are BCE in managing pain and enhancing functions among farmers?

The included studies in the review consistently demonstrated the effectiveness of BCE in improving clinicals outcomes (Table 2). Pain reduction was a significant finding across multiple studies, with one reporting a 24% decrease in pain scores,[26] and another noting a significant reduction in pain intensity following a linguistically-adapted BCE program.[23] Functional improvement was also widely reported, with interventions leading to decreased functional disability,[23] and enhanced LBP prevention behaviors.[27] Furthermore, participatory ergonomic approaches were found to be feasible and effective in simultaneously reducing pain and improving productivity. [30]

What are the delivery methods used to provide BCE for farmers?

The delivery methods for BCE varied among the studies (Table 3). BCE delivery methods were diverse and could be categorized into three main approaches. 1) Face-to-Face Education: The most common method involved direct interaction, often delivered in the farmers' local language and enhanced with practical demonstrations, lectures, and visual aids.[23,25,31] 2) Technology-Assisted Delivery: Some studies utilized modern technology, including mobile applications for self-exercise programs.[24] and video-based feedback for developing self-management strategies.[30] 3) Multi-Modal Approaches: Several interventions combined methods, integrating face-to-face discussions with educational materials like booklets and audio-visual content.[27,31] This diversity highlights the adaptability of BCE to varying contexts, resources, and literacy levels.

What specific topics are covered in BCE for farmers?

The specific topics covered in BCE varied among the studies (Table 3), reflecting the diverse needs and settings of the farming populations. The content of BCE programs was comprehensive, generally encompassing three thematic domains. 1) Biomechanical and Ergonomic Principles – This domain emphasized job-specific ergonomics, including proper lifting techniques, postural correction during farming tasks, and working behave modification tailored to agricultural work demands.[23,27,30] 2) Therapeutic Exercise – Programs frequently incorporated active components, such as stretching routines, core stabilization exercises, and motor control training aimed at improving functional capacity and reducing injury risk.[25-27] 3) Psychosocial and

Self-Management Education – Education in this domain addressed fundamental spinal anatomy, the neuroscience of pain, postural hygiene, and self-management strategies to foster autonomy and long-term adherence.[25,31]

Discussion

This scoping review shows that while ergonomic and physical interventions are crucial, back pain management in farmers may benefit from a holistic approach that incorporates psychological and social support, as stress coping mechanisms and access to resources also influence pain and disability outcomes.[9,10,15] BCE interventions appear generally effective in reducing pain and improving functionality, particularly when delivered through participatory, hands-on approaches and tailored to the farming context.[30] Rostami et al demonstrated improvements in productivity and pain reduction through active learning and ergonomic strategies—findings consistent with broader occupational health literature, which emphasizes participatory and context-specific approaches for optimal health outcomes.[33]

Significant reductions in back pain and functional disability, as reported in culturally adapted programs for Thai rice farmers,[23,26] highlight the role of behavioral and physical conditioning components in enhancing back health.[33] However, the absence of a formal quality assessment in this review limits the strength of conclusions, and the diversity of interventions and populations underscores the need for methodological rigor in future research.

Compared with other occupational groups, farmers seem to benefit more consistently from BCE, possibly because agricultural work allows for immediate application of ergonomic and exercise-based strategies. Nevertheless, the variation in program delivery—from active learning and face-to-face lectures to mobile applications—reflects a growing recognition of the need for flexibility and accessibility in rural communities.[24] Technology-based approaches offer potential to extend program reach, but their effectiveness relative to traditional methods remains uncertain. Evidence from e-health and m-health interventions suggests promise for promoting healthy behaviors and self-management, yet their applicability to farming populations warrants further evaluation.[33] Face-to-face interventions may have advantages for complex lifestyle changes, offering real-time feedback, tailored messaging, and trust-building between educator and participant. A meta-analysis comparing face-to-face and remote interventions found higher adherence and greater behavioral change in face-to-face formats for interventions requiring significant lifestyle adjustments.[34] These insights suggest that BCE delivery should balance accessibility with the level of engagement needed to achieve meaningful outcomes.

The range of topics in BCE programs—ergonomic strategies, self-management, anatomy, postural hygiene—reflects the multifaceted nature of LBP prevention in farming,[27,30,35] Yet, notable content gaps remain. For example, Ayanniyi and Ige (2015) focused on back anatomy and biomechanics but omitted definitions and causes of LBP, farming ergonomics, self-care strategies, and specific exercises. Including these elements alongside physical training could create a more comprehensive approach. The variation in content points to a lack of standardization, which limits comparability and generalizability across studies. Demographic and regional differences further complicate implementation, as farming practices, environmental conditions, and cultural norms can shape both LBP risk and intervention effectiveness. Tailoring BCE to regional agricultural contexts, while identifying core universal components, may improve both relevance and impact.

LBP poses significant disability and economic challenges for farmers.[32] Understanding regional variations in farming practices is critical to identifying activity-specific causes and consequences of LBP and developing

multifaceted prevention and treatment strategies. Although specific guidelines for LBP management in farming are scarce, the findings of this review offer a preliminary evidence base for integrating BCE into occupational health programs. Such initiatives could be supported through agricultural cooperatives, community health networks, and local extension services to enhance adoption and sustainability.

This review did not include a formal quality appraisal of included studies, limiting the strength of evidence. Heterogeneity in study designs, intervention content, and outcome measures also restrict comparability. Many studies were conducted in homogeneous populations within single regions, and follow-up periods were generally short. Future research should: Develop standardized BCE frameworks with core components adaptable to local contexts. Incorporate psychological and social support strategies into BCE content. Compare the long-term effectiveness of technology-based, and face-to-face delivery modes among farming populations. Conduct high-quality trials with diverse farming groups and longer follow-up periods. By addressing these gaps, BCE interventions can be made more targeted, impactful, and scalable, ultimately reducing the burden of LBP among farmers.

Conclusion

The findings of this review suggest that BCE, particularly when tailored to the physical demands of farming, holds promise for reducing pain intensity and enhancing functionality among agricultural farmers. However, due to the heterogeneity and methodological limitations of the included studies make it difficult to draw definitive conclusions about efficacy. Furthermore, the under-representation of key aspects such as home-based exercises, ergonomic training, self-care strategies, and occupationally relevant advice indicates an area deserving of future research.

While the review indicates that BCE can reduce pain and improve function among farmers, the heterogeneity in study designs and populations and interventions suggests a need for more targeted, context-specific research. Future studies should aim to standardize intervention components to better compare BCE efficacy across different agricultural settings while addressing the biopsychosocial aspects of the development of BCE. Healthcare providers and policymakers should consider integrating BCE into routine health education for farmers to reduce the burden of LBP and improve functional outcomes. Especially within the policy sector, government-driven actions are essential, and it is important for agricultural workers to recognize that safety and ergonomic considerations hold equal significance to productivity concerns. This review has several limitations, including the restriction to English-language studies and the potential variability in the methodological quality of the included studies.

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Authors' contributions

All authors contributed to the conception, design, data collection, analysis, and writing of the manuscript. All authors reviewed and approved the final version.

Conflict of interest

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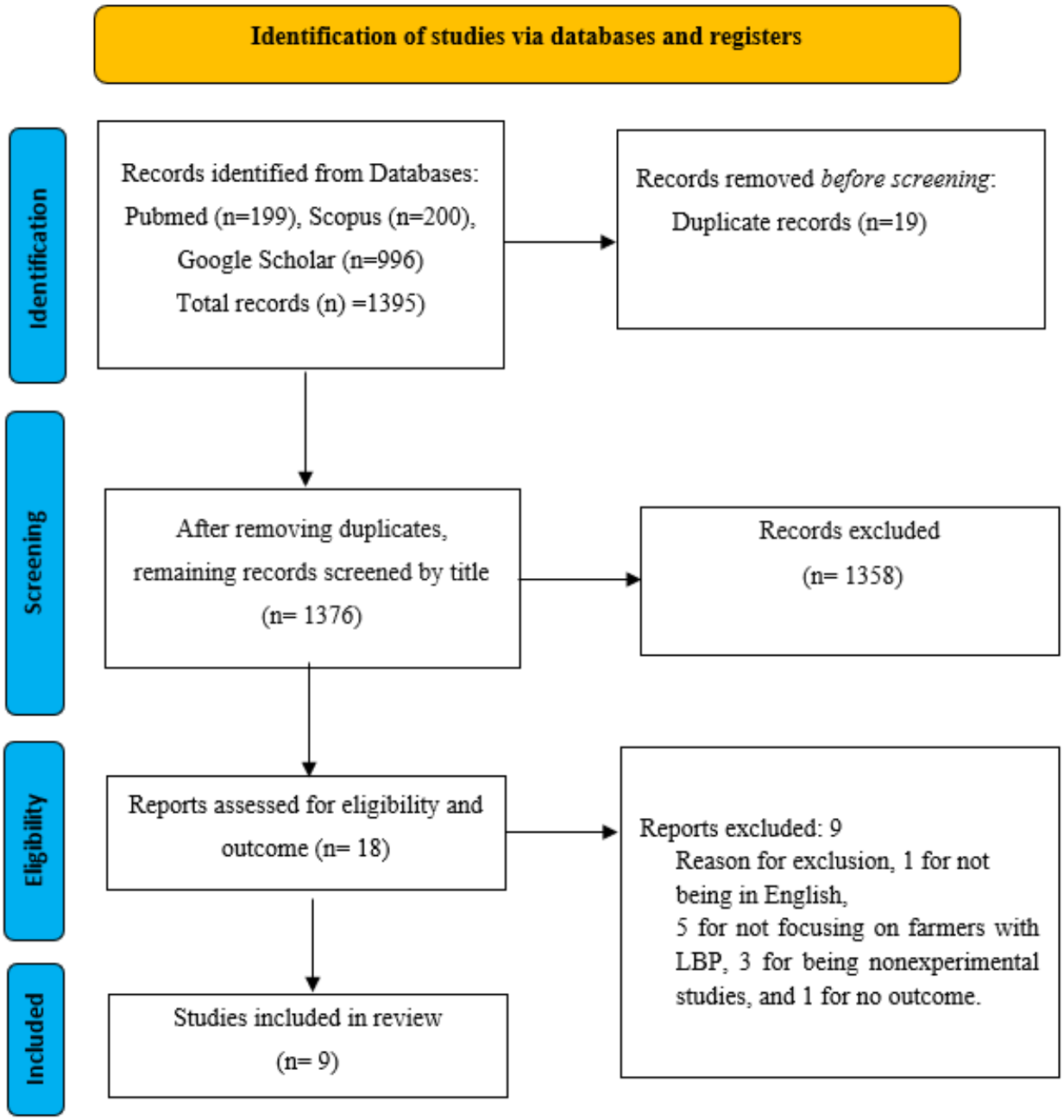

Figure 1. PRISMA flow diagram showing the literature search and selection of studies.

Table 1. Characteristics of study included in the scoping review (Target population, Delivery design sample size, results)

Authors	Study Design	Location/Setting	Target Population	Delivery Design	Sample Size	Results	Research Gaps
Dunleavy et al., (2021)	Pilot Study	Florida, America	Agriculture and Aquaculture clam farmers Age 34 years with 9.5 years of experience Male Farmers	Active learning using video examples and feedback. A rapid prototype participatory ergonomic approach was utilized to design self-management strategies tailored to the specific work context. Methods for adapting lifting techniques and mitigating repetitive stress were conveyed through video presentations, live demonstrations, and interactive discussions within the workplace	N=19	Team strategies were preferred, yet individual methods were used more frequently. They were easy to use, accepted, and consistently applied, improving productivity and reducing pain. Challenges included changing habits, culture, and team dynamics.	Potential gaps need stronger methodological approach, such as randomized control trial to expanding the sample size or designing the study with a more precise control group according to strict inclusion and exclusion criteria
Baek et al., (2020)	Two-phase randomized control trials (MODE-I and MODE-II).	Rural areas in Gangwon-do, South Korea	Female farmers, aged 41-70 years, using smartphones.	Delivered through a mobile application (app) and booklets, providing a tailored self-exercise program for musculoskeletal health.	200 participants planned, divided into experimental and control groups in both phases.	No publications containing the results of this study have been published or submitted to any journal. The study aims to assess the effectiveness of the app-delivered self-exercise program compared to traditional booklets, and the additional benefit of real-time feedback via the app	Potential gaps include the need for individual randomization of participants and controlling treatment received by the control group.

Ibrahim et al., (2023)	RCT	Tsakuwa Primary Health Care Center, Kano State, Northwestern Nigeria	Adults with chronic low back pain, both male and female, aged 18-70.	Lecturer/Class Visual aids such as slides or prepared diagrams were be used where necessary to aid descriptions. Intervention delivered through	120 participants, randomized into MCE + PE, MCE, or PE groups. MCE plus PE=40 MCE =40 PE groups=40	Primary outcome, NPRS, ODI, Secondary outcome Quality of Life PCS, MCS, GRCS, FABQ-FABQ-W, PCS, BBQ	This study was conducted in a rural Nigerian setting, so its applicability to populations in other countries with different socioeconomic structures and healthcare delivery systems is limited, differences in demographic factors with other countries can be a consideration for future research in different countries
Izadirad et al., (2018)	Semi-experimental study	Aq-Qala, Golestan Province, Iran	Farmers Age 30-60 years General rural farmer Male & Female farmers.	Lecturer Physical education instructor/trainer about corrective exercise training/ Intervention group participated in an 8-session sports training program.	N=100 BG=50 CG=50	The intervention group showed a significant reduction in back pain by 24% after the exercise program	The study highlights the effectiveness of exercise training in reducing low back pain among farmers, suggesting the need for broader application and evaluation of similar programs in different settings.
Ibrahim et al., (2018)	pilot study randomized clinical trial	Tsakuwa village of Dawakin-Kudu Local Government Area, Kano state,	Male & female between 18-65yold,	Physiotherapist instructed for MCE 20-30 min, stretching 20 min per session, aerobic (walk) 30 min PE 60 minutes.	N=30 PE=10 MCE=10 MCE+PE=10	MCE+PE was more effective than PE for pain group, and MCE for disability group.	Need larger samples and different trial considering the demographics in different countries such as Asia.

		northwestern Nigeria					
Ayanniyi & Ige, (2015)	Randomized Controlled Trial.	Rural farming communities located in the Ibarapa East Local Government Area of Oyo State, Nigeria.	Male peasant farmers with chronic mechanical low back pain. /Peasant farmers in rural communities Age 25-60 years General agriculture Male peasant farmers	BCE was delivered face-to-face in the local language (Yoruba), with practical demonstrations using human models and posters.	A total of 247 participants were initially enrolled, with 126 assigned to the back care education group and 121 to the control group; the final analysis comprised 200 participants, evenly split with 100 in each group	Reduce in pain intensity and functional disability in the BCE group compared with the control group.	Potential gaps include the need for individual randomization of participants and controlling treatment received by the control group.
Nochit et al., (2014)	A quasi-experimental, two group pre-test & post-test group design	Province central Thailand and involved in rice cultivation.	Rice farmers Age Mean Experiment (mean age = 47.13; SD = 7.14 and control 46.75; SD = 6.77) Male & Female farmers	The intervention included an educational program and a back stabilization exercise regimen. The experimental group participated in the program grounded in Protection Motivation Theory, while the control group received standard information	N=80 BG=40 CG=40	The results show that this program can improve behaviors for preventing low back pain and increase back muscle endurance among Thai farmers	Potential gaps include the need for individual randomization of participants and controlling treatment receive.
Parekh & Phatak (2014)	Experimental design (study comparative)	District Vadodara, Gujarat, India	Farmers Age 30-50 years General Agricultural farmers	Lecturer before active learning about Ergonomic Intervention And Physiotherapy plus ergonomic	N=30 BG=15 CG=15	This study concludes that combining physiotherapy with ergonomic	Potential gaps include the need for individual randomization of

			Male Farmers			interventions leads to greater improvements in pain relief and functional performance for farmers suffering from chronic low back pain.	participants and controlling treatment receive.
Vyas, (2012)	Survey and educational intervention study.	Agricultural fields in India.	Male and female agricultural workers. Aged 35-40 years	Educational intervention using audio-visual aids and printed literature in Hindi.	N= 120 Male=60 Female= 60	The study aimed to assess musculoskeletal problems and body discomfort and the effectiveness of an educational intervention.	Further research could focus on long-term effects of such interventions and inclusion of more diverse agricultural settings.

N: Sample; BG: Treatment Group; CG: Control Group; MCE: Motor Control Exercise; PE: Patient Education

Table 2. Characteristics and main results of the educational activities from the reports included in this study

Authors	Contents of activities	Frequency/ Number of activities/Meetings	Duration of each meeting	Educator	Observed Outcomes (Outcome measures)	Remarks (Drop-outs/ Adverse events/etc)
Dunleavy et al., (2021)	Rapid prototype list of tasks and strategies to develop self-management and ergonomic strategies. 1. Review of existing video 2. Observation and video of task 3. Interview key stakeholders 4. Selection of outcome measure The most common work activities regarded as difficult due to back pain were: lifting bags onto/off the boat, moving baskets or boxes, standing while working	An accelerated participatory ergonomic method to create tailored self-management strategies over 8 weeks.	Adjust the time of day and working hours per week	Research Assistant qualified, not mention	PSFS Functional PSFS Pain ODI VAS PSS PSEQ-2 CSQ	19 Subjects Totals. 9 dropped out, about 32% from 28 people with 7 teams, 3 people were excluded for not meeting the scores in phase 1, 3 people resigned due to unrelated medical issues, and 3 people quit their jobs leaving
Baek et al., (2020)	Individualized exercise programs for shoulder, knee, and low back, with exercises varying in type, frequency, and intensity. 3-level Exercise for low back ½ Bird-dog easy Abdominal exercise easy Side-bridging exercise easy 3 Supine bridging 4 Plank	Mode I 3-month self-exercise using a smartphone app or physical education data (booklets). Mode II 9-months app-delivered + feedback/non-feedback	Total 6 exercises per day); frequency: 3 times per week; duration: 20 min/day; and intensity.	Not mentioned, as it's a self-exercise program guided by an app or booklet.	Completion rate of the exercise program, musculoskeletal pain and disability, and health behavior changes. Reduce pain, improve disability, and Depression. Low Back Outcome 1. SPADI 2. WOMAC 3. TUG 4. NRS 5. Muscle & Fat Mass 6. ODI	Includes assessments of musculoskeletal pain, disability, and health behaviors at multiple time points; also, mention of the potential of remote health management.

					7. PHQ	
Ibrahim et al., (2023)	1. Interactive Session/discussion, question 2. Basic anatomy, pain causation 3. Basic pain education 4. Returning to work and maintaining activity levels 5. Self-care skills 6. Postural modification 7. Lifestyle modification 8. Review information and application	PE once a week for 8 weeks (8 sessions) Stretching and MCE were twice a week for 8 weeks (16 sessions) Aerobic Exercise 5 times per week (8 weeks)	PE 60 and 80 minutes per session Stretching for 20 minutes MCE 30 minutes per session Aerobic exercise for 30 minutes	Physical education supervised	Primary outcome, NPRS, ODI, Secondary outcome Quality of Life PCS, MCS, GRCS, FABQ-FABQ-W, PCS, BBQ	MCE plus PE=37 2 no longer interested, 1 time commitment. MCE =38 2 samples drop out due to time commitment. PE groups=38 1 no longer interested, 1 unknown.
Izadirad et al., (2018)	Corrective exercise training Strengthening the abdominal muscles and back extensors. The intervention included an exercise training program focusing on the waist region.	2 months with 8-week corrective exercise training program. Not specified, but the program consisted of 8 sessions.	Warming up and light stretching from 5 to 10 minutes, tensile training 20 to 25 minutes, and returning to the initial 5 to 10 minutes In total, 45 minutes. Not specified.	Physical education instructor.	Prevalence of low back pain measured using the Nordic questionnaire.	Significant difference in the reduction of back pain in the intervention group compared to the control group.
(Ibrahim et al., 2018)	1. Interactive session/discussions/question 2. Meaning of LBP 3. Common facts about LBP 4. Common beliefs about LBP 5. Basic anatomy 6. Pain causation 7. Basics of pain 8. Get back to activities and stay active. 9. Pain coping and pacing	PE once a week for 6 weeks (6 sessions) MCE was twice a week for 6 weeks (12 sessions) Aerobic Exercise and stretching were instructed to perform	MCE 20-30 min, stretching 20 min per session, aerobic (walk) 30 min PE 60 minutes	Physiotherapist experienced (Licensed)	NPRS, ODI	MCE n=9, 1 loss to follow up with unreachable PE n=10, MCE+PE n=9, 1 reason: health problem.

	10. Self-management 11. Postural hygiene 12. Increasing activity level 13. Lifestyle modification 14. Indicators of low back pain and recommended actions 15. Summary of discussions and practical applications.	home program, 5 times per weeks.				
Ayanniyi & Ige (2015)	Focused on anatomy of the back, biomechanical principles, proper lifting techniques, good postures for farming activities, and specific prophylactic instructions.	Weekly for the first three weeks, then once every two weeks for the next four weeks.	45 minutes to 1 hour.	Two principal investigators delivered the instruction.	Pain intensity and functional disability, assessed using the Chronic Pain Questionnaire.	Twelve participants withdrew from the back care education group, while no attrition occurred in the control group. The study was prematurely terminated due to participants' engagement in farming activities.
Nochit et al., (2014)	Working Behavior Modification Program. 1. Education and discussion about severity of LBP 2. Teaching and skill training of proper working postures 3. Stabilization Back Exercise 4. Self-practice and group exercise once a week. 5. Training of advanced SBE. 6. Follow up through home visits 2 times a week	The Working Behaviors Modification Program: 9 weeks to evaluation	Working Behaviors Modification 30-90 minutes	Research Assistant qualified, not mention	1. LBP-PBQ 2. PDSRT	To address the possible loss of participants, this study participants were added (20% of minimal sample size) 80 participants 40 per group
Parekh & Phatak (2014)	1. Take periodic short rest intervals, such as a 5-minute break after every hour of activity. 2. Workers/Laborers should transport seedlings or crops on their backs instead of	Ergonomic intervention for 4 weeks. Ergonomic Plus Physiotherapy 2 sessions/ week, up to 4 weeks.	Duration of each meeting Not mention	Research Assistant qualified, not mention	1. VAS 3. ODI	30 participants with 15 for ergonomic intervention and 15 for ergonomic plus physiotherapy

	their heads, considering the use of suitable backpacks. 3. Alternate between tasks with low repetition and those involving repetitive movements. 4. Sitting while working helps reduce strain on the lower back and legs. 5. Perform squats with heels flat on the ground. 6. Proper lifting technique involves holding the load at a level that falls between the hands and shoulders. 7. For efficient handling, bags, vegetable boxes, and frequently accessed chemicals can be moved using roller conveyors. 8. Bend the knees at a 90-degree angle. 9. To reduce discomfort, avoid sitting continuously in the same posture for over 30 minutes					
Vyas (2012)	Educational program and knowledge Safety and Hazards in Agriculture Work; land preparation, sowing, irrigation, plant protection, weeding, harvesting, Awareness of musculoskeletal disorders (MSDs), hazards, and safety during agricultural work.	Awareness of musculoskeletal disorders (MSDs), hazards, and safety during agricultural work.	Not specified.	Not specified.	Not specified. Analysis Musculoskeletal disorder and body discomfort 1. BPDS 2. VAD	Emphasized on the need for awareness and education about MSDs in agricultural work.

SPADI: Shoulder Pain and Disability Index; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index: TUG: Time UP and Go; NRS: Numerate Rating Score; ODI: Oswestry Disability Index; PHQ: Patent Health Questionnaire; BPDS: Body Part Discomfort Score; VAD: Visual Analogue Discomfort; NPSR: Numerical Pain Rating Scale; LBP-PBQ: Low Back Pain Prevention Behaviors; PDSRT: Prone Double Straight-leg Raise Test; PSFS: Patient-Specific Functional Scale; VAS: Visual Analogue Scale; PASS: Pain Anxiety Symptom Scale; PSEQ-2: Short-form pain self-efficacy questionnaire; CSQ: Coping strategies questionnaire PCS-12; Physical component summary-12, MCS-12; Mental health component summary-12, GRCS; Global rating of change scale, FABQ-PA; Fear-avoidance beliefs questionnaire – (physical activity), FABQ-W; Fear-avoidance beliefs questionnaire – (work), PCS; Pain catastrophizing scale, BBQ; Back beliefs questionnaire

Table 3. Contents of back care education

Authors	Contents of Back Care Education										
	A & P	Definition Causes Symtomps	Lifting Technique	Postural awareness	Ergonomics of farming	Self-Care Management	Pain & Disability	Exercise			Special Instructions (See Table below)
								Postural correction	Core Stability	Stretches	
Dunleavy et al., (2021)	none	NONE	lifting bags onto/ off the boat moving basket or boxes	Standing while working	none	none	none	none	none	none	Orally & Video
Baek et al., (2020)	none	none	none	none	none	none	none	none	Bird-dog easy Abdominal exercise easy Side-bridging exercise easy Supine bridging Plank	none	Video & written
Ibrahim et al., (2023)	Basic anatomy	none	none	Postural awareness control	NONE	Self-management	Basics of pain & causation	none	Drawing-in maneuver	Double knee to chest stretch Piriformis stretch Hamstring,erector spinae stretch Hip adductor stretch Triceps surae stretch, Prone on elbow Trunk Rotation Trunk Extension	Orally & written
Izadirad et al., (2018)	none	none	none	none	none	none	none	Corrective Exercise	Strengthening abdominal & back Extensor muscle	none	Orally

Ibrahim et al., (2018)	Basic anatomy	none	none	Postural hygiene	NONE	Self-management	Basics of pain & causation	none	Motor Control exercise with Abdominal drawing-in maneuver	Double knee to chest stretch Piriformis stretch Hamstring,erector spinae stretch Hip adductor stretch Triceps surae stretch, Prone on elbow Trunk Rotation Trunk Extension	Orally & written
Ayanniyi & Ige (2015)	Back anatomy and biomechanical principles of the spine, harmful postures and activities, and prevention methods. "	none	Proper and safe lifting techniques for carrying loads.	Proper postures that promote back health during various farming tasks and everyday activities like bathing, sitting, and getting in and out of bed.	none	none	none	none	none	none	Orally & Written
Nochit et al., (2014)	none	none	none	Proper working posture	none	none	none	none	Stability Back Exercise	none	Orally & Demonstration
Parekh & Phatak, (2014)	none	none	none	none	Ergonomic interventions	none	none	none	none	none	Orally

Vyas (2012)	Safety and Hazards in Agriculture Work including land preparation, sowing, weeding irrigation, plant protection, harvesting	none	none	none	none	none	none	none	none	none	Audio Visual & Written

References

[1]. Lee HJ, Oh JH, Yoo JR, Ko SY, Kang JH, Lee SK, et al. Prevalence of Low Back Pain and Associated Risk Factors among Farmers in Jeju. Saf Health Work. 2021 Dec;12(4):432–8.

[2]. Jegnie M, Afework M. Prevalence of Self-Reported Work-Related Lower Back Pain and Its Associated Factors in Ethiopia: A Systematic Review and Meta-Analysis. J Environ Public Health. 2021;2021.

[3]. Chokprasit P, Yimthiang S, Veerasakul S. Heliyon Development and efficacy evaluation of a personalised self-care programme for reducing work-related musculoskeletal disorders among rubber farmers in Thailand. Heliyon [Internet]. 2023;9(10):e20664. Available from: https://doi.org/10.1016/j.heliyon.2023.e20664

[4]. Allegri M, Montella S, Salici F, Valente A, Marchesini M, Compagnone C, et al. Mechanisms of low back pain: A guide for diagnosis and therapy [version 1; referees: 3 approved]. F1000Research. 2016;5:1–11.

[5]. Montazeri A, Mousavi SJ. 232 Quality of Life and Low Back Pain. 2010;2010.

[6]. Drazin D, Nuño M, Patil CG, Yan K, Liu JC, Acosta FL. Emergency room resource utilization by patients with low-back pain. J Neurosurg Spine. 2016;24(5):686–93.

[7]. Dianat I, Afshari D, Sarmasti N, Sangdeh MS, Azaddel R. Work posture, working conditions and musculoskeletal outcomes in agricultural workers. Int J Ind Ergon [Internet]. 2020;77(September 2019):102941. Available from: https://doi.org/10.1016/j.ergon.2020.102941

[8]. Du S, Hu L, Dong J, Xu G, Chen X, Jin S, et al. Self-management program for chronic low back pain: A systematic review and meta-analysis. Patient Educ Couns [Internet]. 2017;100(1):37–49. Available from: http://dx.doi.org/10.1016/j.pec.2016.07.029

[9]. Meucci RD, Fassa AG, Faria NMX, Fiori NS. Chronic low back pain among tobacco farmers in southern Brazil. Int J Occup Environ Health. 2015;21(1):66–73.

[10]. Keawduangdee P, Puntumetakul R, Swangnetr M, Laohasiriwong W, Settheetham D, Yamauchi J, et al. Prevalence of low back pain and associated factors among farmers during the rice transplanting process. J Phys Ther Sci. 2015;27(7):2239–45.

[11]. Mescouto K, Olson RE, Hodges PW, Setchell J. A critical review of the biopsychosocial model of low back pain care: time for a new approach? Disabil Rehabil [Internet]. 2022;44(13):3270–84. Available from: https://doi.org/10.1080/09638288.2020.1851783

[12]. Saragiotto BT, de Almeida MO, Yamato TP, Maher CG. Multidisciplinary biopsychosocial rehabilitation for nonspecific chronic low back pain. Phys Ther. 2016;96(6):759–63.

[13]. Gianola S, Andreano A, Castellini G, Moja L, Valsecchi MG. Multidisciplinary biopsychosocial rehabilitation for chronic low back pain: The need to present minimal important differences units in meta-analyses. Health Qual Life Outcomes. 2018;16(1):1–9.

[14]. van Erp RMA, Huijnen IPJ, Jakobs MLG, Kleijnen J, Smeets RJEM. Effectiveness of Primary Care Interventions Using a Biopsychosocial Approach in Chronic Low Back Pain: A Systematic Review. Pain Pract. 2019;19(2):224–41.

[15]. Traeger AC, Buchbinder R, Elshaug AG, Croftd PR, Mahera CG. Health-system challenges Access to suitable therapies. Bull etin World Heal Org [Internet]. 2019;97(March):423–433. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6560373/pdf/BLT.18.226050.pdf

[16]. George SZ, Lentz TA, Beneciuk JM, Bhavsar NA, Mundt JM, Boissoneault J. Framework for improving outcome prediction for acute to chronic low back pain transitions. Pain Reports. 2020;5(2).

[17]. Swangnetr M, Kaber DB, Puntumetakul R, Gross MT. Ergonomics-related risk identification and pain analysis for farmers involved in rice field preparation. Work. 2014;49(1):63–71.

[18]. Bernstein IA, Malik Q, Carville S, Ward S. Low back pain and sciatica: Summary of NICE guidance. BMJ. 2017;356:10–3.

[19]. George SZ, Fritz JM, Silfies SP, Hendren S. Interventions for the Management of Acute and Chronic Low Back Pain: Revision 2021. 2023;51(11):1–85.

[20]. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA extension for scoping reviews (PRISMA-ScR): Checklist and explanation. Ann Intern Med. 2018;169(7):467–73.

[21]. Peters MDJ, Godfrey CM, Khalil H, McInerney P, Parker D, Soares CB. Guidance for conducting systematic scoping reviews. Int J Evid Based Healthc. 2015;13(3):141–6.

[22]. Richardson WS, Wilson MC, Nishikawa J, Hayward RS. The well-built clinical question: a key to evidence-based decisions. Vol. 123, ACP journal club. United States; 1995. p. A12-3.

[23]. Ayanniyi O, Ige O. Back care education on peasant farmers suffering from chronic mechanical low back pain. J Exp Integr Med. 2015;5(4):215.

[24]. Baek S, Kim G, Park HWW. A mobile delivered self-exercise program for female farmers. Med (United States). 2020 Dec;99(52):e23624.

[25]. Ibrahim AA, Akindele MO, Ganiyu SO. Effectiveness of patient education plus motor control exercise versus patient education alone versus motor control exercise alone for rural community-dwelling adults with chronic low back pain: a randomised clinical trial. BMC Musculoskelet Disord. 2023 Dec 1;24(1).

[26]. Izadirad H, … FPIJ of, 2018 undefined. Effect of Exercise Training on Low Back Pain in Farmers; A Case Study of Aq-Qala, Golestan Province. EcopersiaModaresAcIr [Internet]. 2018;3(2):47–50. Available from: http://ecopersia.modares.ac.ir/article-32-20266-en.html

[27]. Nochit W, Kaewthummanukul T, Srisuphan W, Senaratana W. Effects of Working Behavior Modification Program on Low Back Pain Prevention Behaviors and Back Muscle Endurance among Thai Farmers. Pacific Rim Int J Nurs Res [Internet]. 2014;18(4):305–19. Available from: https://search.ebscohost.com/login.aspx?direct=true&db=cin20&AN=99988757&site=ehost-live

[28]. Parekh S, Phatak NR. A comparative study between ergonomic advices versus ergonomic plus physiotherapy intervention in low back pain among farmers. Int J Physiother Res. 2014;2(5):719–24.

[29]. Vyas R. Mitigation of musculoskeletal problems and body discomfort of agricultural workers through educational intervention. Work. 2012;41(SUPPL.1):2398–404.

[30]. Dunleavy K, Bishop M, Coffman A, Reidy J, Kane A, Dunleavy K, et al. Chronic lower back pain in aquaculture clam farmers: adoption and feasibility of self-management strategies introduced using a rapid prototype participatory ergonomic approach self-management strategies introduced using a rapid prototype participatory e. Int J Occup Saf Ergon [Internet]. 2021;0(0):1–11. Available from: https://doi.org/10803548.2021.1935543

[31]. Ibrahim AA, Akindele MO, Ganiyu SO. Motor control exercise and patient education program for low resource rural community dwelling adults with chronic low back pain: A pilot randomized clinical trial. J Exerc Rehabil. 2018;14(5):851–63.

[32]. Chokprasit P, Yimthiang S, Veerasakul S. Predictors of Low Back Pain Risk among Rubber Harvesters. Int J Environ Res Public Health. 2022;19(17).

[33]. Rostami M, Choobineh A, Shakerian M, Faraji M, Modarresifar H. Assessing the effectiveness of an ergonomics intervention program with a participatory approach: ergonomics settlement in an Iranian steel industry. Int Arch Occup Environ Health [Internet]. 2022;95(5):953–64. Available from: https://doi.org/10.1007/s00420-021-01811-x

[34]. Akhter K, Sutton S, Mirzaei V, Kassavou A. A Systematic Review and Meta-analysis of Face-to-face Medication Adherence Interventions for Patients with Long Term Health Conditions. Ann Behav Med [Internet]. 2022 Dec 1;56(12):1218–30. Available from: https://doi.org/10.1093/abm/kaac010

[35]. Brewer S, Eerd D Van, Amick BC, Irvin E, Daum KM, Gerr F, et al. Workplace interventions to prevent musculoskeletal and visual symptoms and disorders among computer users: A systematic review. J Occup Rehabil. 2006;16(3):325–58.

ORIGINAL ARTICLE

Understanding and Improving Workplace Violence Prevention Practices among Nursing Students: A Cross-Sectional Study in a Private College, Malaysia.

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Abstract

Background: Workplace violence (WPV) is a growing concern in healthcare settings, with nursing students at heightened risk due to their frontline roles during clinical placements. Although several studies have explored WPV among healthcare workers, research focusing on prevention practices among nursing students in Malaysia remains limited. This study aimed to assess nursing students' perception and practice of WPV prevention and identify associated factors. **Methods**: A cross-sectional survey was conducted among 245 nursing students enrolled at a private nursing college in Perak, Malaysia. Data were collected using a validated structured questionnaire assessing WPV perception and practice across multiple domains. Descriptive and inferential analyses were performed using chi-square tests and logistic regression to determine predictors of good perception and practice. **Results**: Most participants demonstrated moderate perception and high practice of WPV prevention. Binary logistic regression revealed that bachelor-level students (aOR = 114.5, p = 0.03) and those with ≥ 6 months of clinical experience (aOR = 1.89, p = 0.046) were more likely to exhibit good perception towards WPV prevention. Multinomial regression confirmed these associations, indicating that educational level and clinical experience independently predicted good perception. No significant predictors were found for practice outcomes. **Conclusion**: Academic preparation and clinical exposure play crucial roles in shaping nursing students' perception of WPV prevention. Integrating structured WPV prevention training into the nursing curriculum and strengthening institutional support mechanisms are essential to enhance awareness, preparedness, and safety culture among future nurses.

Keywords: *Clinical training, nursing education, perception and practice, violence prevention, workplace violence.*

Introduction

Workplace violence (WPV) in healthcare settings is increasingly recognised as a critical occupational hazard, posing significant threats to the safety, well-being, and professional development of healthcare workers, particularly nursing students. The World Health Organization and the International Labour Organization define WPV as physical, verbal, or emotional aggression occurring in the workplace, encompassing behaviours that may cause physical harm, psychological distress, or emotional trauma [1,2]. Such incidents disrupt clinical learning environments, compromise patient care, and adversely affect the mental health and job satisfaction of healthcare workers. Globally, the prevalence of WPV among healthcare workers, especially the nurses in clinical training, is alarmingly high, with nearly half reporting experiences of violence at some point in their careers [3,4]. The high incidence is attributed to the nature of healthcare work, which involves direct interaction with patients and their families in high-stress, emotionally charged situations, such as emergency care, mental health units, and long-term care facilities.

Nursing students represent a particularly vulnerable group due to their limited clinical exposure, ongoing skill acquisition, and lower hierarchical status within healthcare teams. While clinical placements are essential for translating theoretical knowledge into practical competence, they often expose students to various forms of WPV, including verbal abuse, physical intimidation, and psychological harassment from patients, visitors, or even colleagues [5,6]. Such encounters may result in immediate physical harm and longer-term psychological consequences, including heightened stress, anxiety, fear, diminished confidence, and erosion of professional identity [7,8]. Repeated exposure to WPV not only undermines nursing students' learning experiences but can also negatively influence career retention, potentially contributing to the ongoing global nursing shortage.

Previous research has established that WPV is a widespread problem across healthcare settings, and several systematic reviews have examined its prevalence, causes, and effects among nurses [3,4,9]. However, the majority of these studies have focused on registered nurses and hospital-based staff, with relatively few addressing WPV prevention among nursing students, particularly within the Southeast Asian context. Existing interventions and policies often prioritise permanent employees, neglecting the unique vulnerabilities of students who rotate through multiple clinical environments [10,11]. Moreover, studies from Malaysia have primarily explored WPV experiences among practising nurses [12,13], leaving a critical gap in understanding how nursing students perceive and practise prevention measures during their training.

This study is guided by Social Cognitive Theory, which posits that individuals learn behaviours through observation, imitation, and reinforcement within a social environment [14]. In the context of WPV prevention, students' perceptions and practices are shaped not only by their formal education but also by modelling from clinical supervisors and peers. Understanding these cognitive and environmental factors is therefore essential to strengthen preventive behaviour and self-efficacy.

Against this backdrop, the present study aims to examine the perception and practice of WPV prevention among nursing students in Malaysia, with a specific focus on identifying associated sociodemographic and educational factors. Conducted at a private nursing college in Perak, this study provides context-specific insights that contribute to the regional and global understanding of WPV prevention in nursing education. By exploring the determinants of perception and practice, the findings can inform the design of targeted training, institutional support mechanisms, and evidence-based policies that promote safer clinical learning environments.

Materials and methods

Study design

A quantitative, cross-sectional descriptive research design was employed to assess nursing students' perceptions and practices regarding workplace violence (WPV) prevention, as well as to identify associated sociodemographic factors. The cross-sectional design enabled the collection of data at a single point in time, providing a representative snapshot of students' attitudes, preparedness, and preventive behaviours. This design was chosen due to its efficiency in exploring prevalence patterns and associations within a defined population.

Study setting and population

The study was conducted at Universiti Kuala Lumpur Royal College of Medicine Perak (UniKL RCMP), a private higher education institution offering diploma and bachelor's degree programmes in nursing. The target population consisted of nursing students who had completed at least one clinical placement, ensuring participants had direct exposure to clinical environments where WPV might occur. Students from both diploma and bachelor's programmes were eligible to participate.

Sampling method and sample size

A convenience sampling technique was utilised to recruit participants. This approach was chosen due to accessibility and logistical feasibility within the study's timeframe. From an estimated 680 eligible nursing students, a sample size of 246 was calculated using OpenEpi software with a 95% confidence interval and a prevalence estimate of 51.6% from prior literature [9]. A total of 245 students completed the questionnaire, representing a high response rate that enhanced the reliability of the findings, although generalisability remains limited due to the non-probability sampling approach.

Research instrument

Data were collected using a structured, self-administered questionnaire adapted from the validated tool by Mohamad Yazid et al, [11], with modifications to suit the nursing student context (for example replacing "healthcare worker" with "student nurse") and removing items not applicable to students' roles (e.g., managerial responsibilities). To ensure the adapted instrument's reliability and validity, a pilot test was conducted with 30 nursing students from a comparable institution. Internal consistency was verified using Cronbach's alpha, yielding $\alpha = 0.91$ for the overall scale, indicating excellent reliability. Construct validity was confirmed through expert review by three nursing education and occupational safety specialists. The instrument comprised 53 items divided into two main domains:

1. Perception Domain (33 items): Covered subdomains such as forms of WPV, causes, impacts, benefits of prevention, barriers to prevention, high-strain job characteristics, reaction to WPV, protective measures, and encouragement for prevention.
2. Practice Domain (20 items): Addressed workplace safety measures, WPV prevention implementation, and incident reporting practices.

All items were rated on a five-point Likert scale ranging from strongly disagree (1) to strongly agree (5). Domain scores were calculated as percentages and categorised according to Bloom's cut-off: low (<60%), moderate (60–79%), and high (≥80%).

Data collection procedure

The questionnaire was distributed online between 1 December and 25 December 2024 via official class WhatsApp groups. Prior to participation, students received an explanation of the study purpose and were provided with the consent form embedded in the survey link. Only those who consented were able to proceed to the questionnaire.

Statistical analysis

Data were analysed using IBM SPSS Statistics version 25. Descriptive statistics (frequencies, percentages, means, and standard deviations) were used to summarise respondents' characteristics and domain scores. Inferential analyses included:

a.) Chi-square tests, to examine associations between sociodemographic variables (e.g., gender, age, education level, clinical experience) and perception or practice levels;
b.) Binary logistic regression, performed to identify independent predictors of good perception and good practice (dependent variables dichotomised as good = 1, poor/moderate = 0);
c.) Multinomial logistic regression, used as a supplementary analysis to confirm the robustness of results using all three perception categories (poor, moderate, good).

Statistical significance was set at $p < 0.05$, and all results were reported as adjusted odds ratios (aOR) or relative risk ratios (RRR) with 95% confidence intervals.

Ethical considerations

Ethical approval for this study was obtained from the Universiti Kuala Lumpur (UniKL) Research Ethics Committee (Approval No.: UNIKL REC/2024/PG/APV/01). All procedures adhered to the principles outlined in the Declaration of Helsinki. Participation was entirely voluntary, and informed consent was obtained from all respondents prior to data collection. The consent form clearly stated the study's objectives, the voluntary nature of participation, and the right to withdraw at any time without penalty. Data were anonymised and stored securely to ensure confidentiality.

Results

Demographic characteristics of respondents

The study included 245 nursing students from a private nursing college in Perak, Malaysia. The majority were female (n = 203; 82.9%), while males comprised 17.1% (n = 42), consistent with the global gender distribution in the nursing profession. Previous studies suggest that female nursing students may be more susceptible to verbal and psychological WPV compared to males [12]. The age distribution indicated that most students were between 18–20 years (n = 153; 62.4%), followed by 21–23 years (n = 81; 33.1%), and only 4.5% (n = 11) were above 24 years. This suggests that the majority were early in their clinical training, potentially affecting their WPV-related coping strategies.

Ethnically, the cohort was predominantly Malay (n = 240; 98.0%), with small proportions identifying as Indian (n = 3; 1.2%), Chinese (n = 1; 0.4%), and other ethnicities (n = 1; 0.4%). In terms of educational level, 58.4% (n = 143) were diploma students, and 41.6% (n = 102) were pursuing bachelor's degrees. Semester distribution showed the largest proportion in semester three (n = 96; 39.2%), followed by semester one (n = 69; 28.2%) and semester five (n = 35; 14.3%). Only 0.8% (n = 2) were in semester six, and 8.6% (n = 21) in semester seven. Regarding clinical placement, the vast majority (n = 233; 95.1%) had hospital-based postings, which are often high-risk environments for WPV [13, 14]. Only 4.9% (n = 12) had community-based placements. Most students (n = 179; 73.1%) had less than six months of clinical experience, while 26.9% (n = 66) had more than six months. A notable finding was that only 21.6% (n = 53) had received WPV prevention training, leaving 78.4% (n = 192) without formal preparation — indicating a major training gap in nursing education.

Perception towards WPV prevention

Perception was assessed using 33 Likert-scale items. The overall mean perception score was 68.4%, categorised as moderate based on Bloom's cut-off, suggesting general awareness of WPV but limited depth of understanding of prevention strategies. Within the perception subdomains, the highest score was for the Impacts

of WPV (mean = 89.1%), indicating strong awareness of the consequences, including physical harm, psychological trauma, and professional repercussions [15, 16]. The second-highest was the Benefits of WPV Prevention (mean = 83.1%), reflecting recognition of its role in creating safer workplaces and reducing organisational costs.

Workplace Violence Protection also scored relatively high (79.3%), while High-strain job characteristics (71.1%) and WPV Prevention Encouragement (69.7%) indicated moderate awareness. The lowest score was in Reactions to WPV (45.8%), highlighting limited knowledge on appropriate response mechanisms, reporting procedures, and post-incident support utilisation [9, 17].

Practice towards WPV prevention

The overall mean practice score was 81.5%, placing it in the high category. This suggests that students generally engage in WPV prevention behaviours, potentially influenced by observation and modelling from senior staff (Social Cognitive Theory) rather than formal training. The highest practice domain was Workplace Safety (82.5%), followed by WPV Prevention Implementation (82.2%), which included communication strategies, safety protocols, and environmental awareness [19, 20]. The lowest score was for Workplace Violence Reporting (75.0%), reflecting a common trend of underreporting in healthcare due to fear of repercussions, lack of clarity on procedures, or perceived ineffectiveness of reporting systems [18, 21].

The model in Figure 1, which presents conceptual framework of WPV illustrates the interrelationship between key determinants, the observed perception–practice gap, and the resulting consequences for nursing students' readiness to manage WPV. Educational level and clinical experience emerged as significant determinants of perception (p = 0.04 for both; Table 6), with Bachelor students and those having more than six months of clinical exposure achieving higher perception scores. Despite these positive influences, overall perception remained moderate (mean = 68.4%; Table 1), with the lowest subdomain score observed in reaction to WPV (mean = 45.8%), indicating limited confidence in managing incidents independently.

Conversely, preventive practice was high overall (mean = 81.5%; Table 2), with workplace safety (mean = 82.5%) and prevention implementation (mean = 82.2%) scoring highest. However, WPV reporting remained the weakest practice area (mean = 75.0%), reflecting possible cultural and institutional barriers to incident disclosure. Notably, no sociodemographic variable significantly influenced practice scores (Table 7), suggesting that once students are placed in clinical environments, standardised safety protocols promote uniform preventive behaviours across groups.

The framework underscores that the high practice–moderate perception disparity may stem from procedural adherence shaped by structured clinical environments rather than informed conviction. Without targeted interventions—such as WPV-specific training (currently received by only 21.6% of participants), mentorship, and robust reporting systems—students remain vulnerable to under preparedness, underreporting, and psychological distress. By addressing these determinants through curriculum integration, pre-placement orientation, and supportive institutional culture, both perception and practice can be enhanced, thereby reducing WPV-related harm and improving the resilience of the future nursing workforce.

Associations between sociodemographic variables and WPV perception and practice

Chi-square analysis revealed two statistically significant associations: (1) Education level was significantly associated with perception scores (p = 0.04), with bachelor's students demonstrating higher understanding than diploma students; (2) Clinical experience was significantly associated

with perception scores (p = 0.045), with those having more than six months of experience showing greater awareness and insight. No significant associations were found between sociodemographic variables and practice scores, suggesting that preventive behaviours may be influenced more by environmental and institutional factors than individual characteristics.

Furthermore, a binary logistic regression was performed to identify independent predictors of good perception and good practice towards WPV prevention (Table 6). Among the variables entered into the model, education level was the only statistically significant predictor of good perception. Bachelor-level students were significantly more likely to demonstrate good perception compared to diploma students (aOR = 114.5, p = 0.030). Although this high odds ratio may reflect small group differences or sparse data, the association direction remained consistent with prior evidence showing that higher academic training improves awareness and readiness towards WPV prevention. Other predictors, including gender, age, WPV training, semester, clinical experience, and clinical placement, were not statistically significant.

However, students with ≥6 months of clinical experience (aOR = 1.63, p = 0.48) and those with hospital placements (aOR = 9.93, p = 0.13) showed positive, though non-significant, trends toward better perception. For practice outcomes, none of the predictors were significant, suggesting that preventive actions may be more strongly influenced by institutional guidelines and standard operating procedures rather than individual characteristics. The overall model fit was acceptable, with Hosmer–Lemeshow $\chi^2(7) = 5.209$, p = 0.634, indicating good calibration. The model, however, did not achieve overall statistical significance (Omnibus $\chi^2(16) = 11.944$, p = 0.748) and explained approximately 9.4% of the variance (Nagelkerke $R^2 = 0.094$).

Additionally, to confirm the robustness of the binary model, a multinomial logistic regression was conducted using three perception categories (poor, moderate, good) (Table 7). Compared with poor perception, both bachelor-level education (RRR = 2.40, 95% CI: 1.20–4.82, p = 0.013) and ≥6 months of clinical experience (RRR = 1.95, 95% CI: 1.01–3.74, p = 0.046) were independently associated with good perception. No significant predictors were identified for moderate perception, suggesting that the strongest determinants of improvement occur between the lowest and highest perception groups. These findings corroborate the binary model, reinforcing that educational advancement and clinical exposure are central to developing students' understanding and awareness of WPV prevention.

Discussion and conclusion

This study contributes meaningfully to the workplace violence (WPV) literature by focusing on nursing students in a private institution in Perak, Malaysia (an under-represented yet highly vulnerable population in WPV research) [22,23]. We observed a clear disparity between domains: preventive practice was high (mean 81.5%), whereas perception was only moderate (mean 68.4%). Within perception, the highest means were recorded for the impacts of WPV (89.1%) and benefits of prevention (83.1%), while the lowest was reaction to WPV (45.8%). This pattern suggests students recognise the seriousness of WPV and the value of preventive measures but feel less confident about responding effectively during incidents. Similar gaps have been reported in Jordan and Turkey, where students frequently comply with safety procedures but feel underprepared in unstructured or high-pressure situations [22,24]. In our cohort, workplace safety (82.5%) and prevention implementation (82.2%) were the strongest practice subdomains, whereas reporting remained weakest (75.0%), mirroring international under-reporting linked to fear of retaliation, perceived

futility, and the normalisation of violence in clinical settings [17,25–28]. These findings align with Social Cognitive Theory, in which modelling and supervision can instil behaviours but deeper cognitive engagement and self-efficacy are required to translate observation into adaptive action [29–31].

Multivariate analyses were performed to identify independent determinants of perception. The binary logistic regression indicated that education level was the only statistically significant predictor of good perception (aOR = 114.5, p = 0.03). Although the overall model explained a modest proportion of variance (Nagelkerke R^2 = 0.094), the direction and magnitude reinforce the role of academic progression in shaping cognitive readiness for WPV prevention. Complementing this, the multinomial regression confirmed that both bachelor-level education (RRR = 2.40, 95% CI: 1.20–4.82, p = 0.013) and ≥6 months of clinical experience (RRR = 1.95, 95% CI: 1.01–3.74, p = 0.046) predicted good versus poor perception. Although the omnibus test for the binary model was not significant ($\chi^2(16) = 11.944$, p = 0.748), the convergence of binary and multinomial results strengthens confidence that educational exposure and prolonged clinical engagement driven the students' understanding of WPV (not demographic factors). The modest explanatory power points to unmeasured institutional and psychosocial influences (e.g., mentoring quality, safety culture, perceived organisational justice) that likely account for additional variance.

No sociodemographic predictors were associated with practice levels, consistent with reports from South Africa and Canada showing that clinical policies and supervision standardise preventive behaviours across student groups [34,35]. In other words, practice appears institutionally driven, whereas perception is education- and experience-sensitive. Notably, only 21.6% of respondents reported formal WPV prevention training. Given the documented risks (from verbal abuse to physical assault) during clinical placement this gap is concerning [10,36]. Prior studies show that structured, simulation-based WPV programmes improve both knowledge and confidence to de-escalate aggression [28,32,33,37,38]. Repeated or poorly managed exposure has been linked to stress, anxiety, and emotional exhaustion, with longer-term risks of burnout and attrition from the profession [39–42]. In Malaysia, where workforce shortages persist, failing to equip students with robust WPV competencies may exacerbate retention challenges and compromise patient care.

The persistently low reporting score underscores a "culture of silence." International evidence attributes under-reporting to retaliation fears, weak feedback loops, and scepticism that reports lead to change [25,27,43]. Ward culture strongly shapes students' safety behaviours; without explicit reinforcement from clinical instructors, students may absorb avoidance norms modelled by staff [43,44, 45]. Breaking this cycle requires confidential, easy-to-use reporting systems, zero-tolerance policies jointly upheld by nursing schools and hospitals, and mandated feedback to reporters. Jurisdictions that combined policy enforcement with routine training documented measurable reductions in WPV incidents, whereas settings without such structures continue to report persistent or rising rates [46,47, 48]. Although our study is local, its implications are global. For instance, the cross-cultural consistency of WPV from Europe to Asia and the Middle East which suggests that effective prevention rests on the same pillars of education, reporting, and institutional accountability [22,49,50].

In conclusion, nursing students demonstrate strong adherence to preventive procedures but only moderate cognitive readiness to anticipate and manage WPV. Education level and clinical experience which verified through binary and multinomial models have shape the perception, while practice remains largely a function of institutional protocols. The limited variance explained by sociodemographic and exposure variables indicates that organisational and psychosocial determinants deserve greater

attention. We recommend integrating comprehensive, simulation-based WPV modules early in the curriculum (particularly for diploma tracks), establishing transparent, non-punitive reporting systems, and embedding WPV prevention within hospital accreditation and supervision standards. Longitudinal and mixed-methods research should examine how perception evolves with repeated placements, how ward culture and mentoring influence reporting, and which educational designs best translate knowledge into confident, adaptive responses. By aligning education, policy, and culture, institutions can safeguard students and strengthen the resilience of the nursing workforce.

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Conflict of interest
None.

Authors' contributions
MNS was responsible for developing the concept and study design, conducting data collection, performing the analysis, and drafting the manuscript. DS contributed to data analysis and interpretation and participated in the critical review of the manuscript. HS contributed to drafting and reviewing the manuscript. All authors read and approved the final version of the manuscript.

Table 1. Demographic Characteristics of Participants (n = 245)

Variable	n	%
Gender		
Male	42	17.1
Female	203	82.9
Age Group (years)		
18–20	153	62.4
21–23	81	33.1
>24	11	4.5
Ethnicity		
Malay	240	98.0
Chinese	1	0.4
Indian	3	1.2
Others	1	0.4
Education Level		
Diploma	143	58.4
Bachelor	102	41.6
Semester of Study		
1	69	28.2
2	16	6.5
3	96	39.2
4	6	2.4
5	35	14.3
6	2	0.8
7	21	8.6
Clinical Placement Setting		
Hospital	233	95.1
Others	12	4.9
Clinical Experience		
<6 months	179	73.1
≥6 months	66	26.9
Previous WPV Prevention Training		
Yes	53	21.6
No	192	78.4

Note: WPV = Workplace Violence.

Table 2. Mean percentage scores for perception towards workplace violence (WPV) prevention domains in PPWVP (n = 245)

Domain	Min	Max	Mean	SD	Mean (%)
Impacts of workplace violence	2	10	8.9	1.5	89.1
Benefits of workplace violence prevention	5	25	20.8	4.0	83.1
Workplace violence protection	2	10	7.9	1.7	79.3
High-strain job characteristics	3	15	10.7	2.8	71.1
Workplace violence prevention encouragement	2	10	7.0	1.8	69.7
Barriers to workplace violence prevention	5	25	16.2	4.1	64.7
Form of workplace violence	8	40	25.3	7.6	63.2
Causes of workplace violence	3	15	9.4	2.5	62.3
Reaction to workplace violence	3	15	6.9	3.1	45.8
Overall score	33	165	112.9	17.7	68.4

Note: WPV = Workplace Violence; PPWVP = Perception and Practice of Workplace Violence Prevention questionnaire

Table 3. Mean percentage scores for practice towards workplace violence (WPV) prevention domains in PPWVP (n = 245)

Domain	Min	Max	Mean	SD	Mean (%)
Workplace safety	3	15	12.4	2.2	82.5
Workplace violence prevention implementation	15	75	61.6	10.3	82.2
Workplace violence reporting	2	10	7.5	1.6	75.0
Overall score	20	100	81.5	12.9	81.5

Note: WPV = Workplace Violence; PPWVP = Perception and Practice of Workplace Violence Prevention questionnaire.

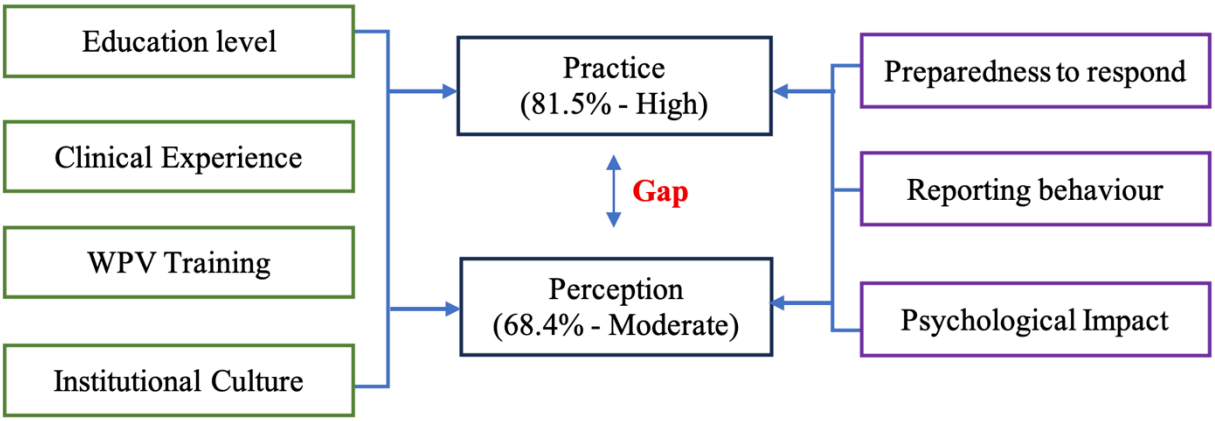

Figure 1. Conceptual framework illustrating the determinants, perception–practice gap, and consequences of workplace violence (WPV) prevention among nursing students in Malaysia.

Table 4. Perception Towards WPV Prevention by Sociodemographic Variables (n = 245)

Variable	n	Poor, n (%)	Moderate, n (%)	Good, n (%)	*p*-value
Gender					0.49
Male	42	6 (14.3)	29 (69.0)	7 (16.7)	
Female	203	34 (16.7)	148 (72.9)	21 (10.3)	
Age Group					0.84
18–20	153	26 (17.0)	112 (73.2)	15 (9.8)	
21–23	81	12 (14.8)	58 (71.6)	11 (13.6)	
>24	11	2 (18.2)	7 (63.6)	2 (18.2)	
Race					0.92
Malay	240	40 (16.7)	172 (71.7)	28 (11.7)	
Chinese	1	0 (0.0)	1 (100.0)	0 (0.0)	
Indian	3	0 (0.0)	3 (100.0)	0 (0.0)	
Others	1	0 (0.0)	1 (100.0)	0 (0.0)	
Education Level					**0.04**
Diploma	143	28 (19.6)	104 (72.7)	11 (7.7)	
Bachelor	102	12 (11.8)	73 (71.6)	17 (16.7)	
Semester					0.19
1	69	12 (17.4)	49 (71.0)	8 (11.6)	
2	16	6 (37.5)	9 (56.3)	1 (6.3)	
3	96	18 (18.8)	68 (70.8)	10 (10.4)	
4	6	1 (16.7)	4 (66.7)	1 (16.7)	
5	35	0 (0.0)	29 (82.9)	6 (17.1)	
6	2	1 (50.0)	1 (50.0)	0 (0.0)	
7	21	2 (9.5)	17 (81.0)	2 (9.5)	
Clinical Placement					0.05
Hospital	233	36 (15.5)	172 (73.8)	25 (10.7)	
Others	12	4 (33.3)	5 (41.7)	3 (25.0)	
Clinical Experience					**0.04**
<6 months	179	35 (19.6)	122 (68.2)	22 (12.3)	
>6 months	66	5 (7.6)	55 (83.3)	6 (9.1)	
WPV Prevention Training					0.73
Yes	53	10 (18.9)	36 (67.9)	7 (13.2)	
No	192	30 (15.6)	141 (73.4)	21 (10.9)	

Table 5. Practice Towards WPV Prevention by Sociodemographic Variables (n = 245)

Variable	n	Poor, n (%)	Moderate, n (%)	Good, n (%)	*p*-value
Gender					0.22
Male	42	1 (2.4)	22 (52.4)	19 (45.2)	
Female	203	2 (1.0)	81 (39.9)	120 (59.1)	
Age Group					0.29
18–20	153	3 (2.0)	70 (45.8)	80 (52.3)	
21–23	81	0 (0.0)	28 (34.6)	53 (65.4)	
>24	11	0 (0.0)	5 (45.5)	6 (54.5)	
Race					0.89
Malay	240	3 (1.3)	101 (42.1)	136 (56.7)	
Chinese	1	0 (0.0)	0 (0.0)	1 (100.0)	
Indian	3	0 (0.0)	2 (66.7)	1 (33.3)	
Others	1	0 (0.0)	0 (0.0)	1 (100.0)	
Education Level					0.95
Diploma	143	2 (1.4)	60 (42.0)	81 (56.6)	
Bachelor	102	1 (1.0)	43 (42.2)	58 (56.9)	
Semester					0.24
1	69	3 (4.3)	25 (36.2)	41 (59.4)	
2	16	0 (0.0)	3 (18.8)	13 (81.3)	
3	96	0 (0.0)	46 (47.9)	50 (52.1)	
4	6	0 (0.0)	4 (66.7)	2 (33.3)	
5	35	0 (0.0)	14 (40.0)	21 (60.0)	
6	2	0 (0.0)	1 (50.0)	1 (50.0)	
7	21	0 (0.0)	10 (47.6)	11 (52.4)	
Clinical Placement					0.92
Hospital	233	3 (1.3)	98 (42.1)	132 (56.7)	
Others	12	0 (0.0)	5 (41.7)	7 (58.3)	
Clinical Experience					0.89
<6 months	179	2 (1.1)	74 (41.3)	103 (57.5)	
>6 months	66	1 (1.5)	29 (43.9)	36 (54.5)	
WPV Prevention Training					0.14
Yes	53	2 (3.8)	20 (37.7)	31 (58.5)	
No	192	1 (0.5)	83 (43.2)	108 (56.3)	

Table 6. Multivariate binary logistic regression of factors associated with good perception towards WPV prevention (n = 245)

Predictor	B	Wald	*p*-value	Adjusted OR (Exp(B))
Gender (Male vs Female)	1.37	1.37	0.24	3.95
Age (≥ 21 vs < 21 years)	ns	–	> 0.45	–
WPV training (Yes vs No)	0.21	0.21	0.65	1.23
Education (Bachelor vs Diploma)	**4.74**	**4.74**	**0.030**	**114.5**
Semester (all levels)	ns	–	> 0.25	–
Clinical experience (≥ 6 months vs < 6 months)	0.49	0.49	0.48	1.63
Clinical placement (Hospital vs Other)	2.30	2.30	0.13	9.93

(Dependent variable: Perception (0 = Poor/Moderate, 1 = Good); ns = non-significant; model $\chi^2(16) = 11.944$, p = 0.748; Nagelkerke $R^2 = 0.094$; Hosmer–Lemeshow $\chi^2(7) = 5.209$, p = 0.634)

Table 7. Multinomial logistic regression for predictors of perception towards WPV prevention (n = 245)

Predictor	Moderate vs Poor (RRR = Exp(B))	95% CI	*p*-value	Good vs Poor (RRR = Exp(B))	95% CI	*p*-value
Gender (Male vs Female)	1.71	0.58–5.07	0.33	–	–	–
WPV training (Yes vs No)	0.74	0.31–1.78	0.50	–	–	–
Education (Bachelor vs Diploma)	ns	–	> 0.20	**2.40**	**1.20–4.82**	**0.013**
Clinical experience (≥ 6 months vs < 6 months)	0.37	0.13–1.05	0.06	**1.95**	**1.01–3.74**	**0.046**
Clinical placement (Hospital vs Other)	5.59	0.96–32.6	0.055	–	–	–

(ns = non-significant; RRR = Relative Risk Ratio)

References

[1]. World Health Organization. Framework guidelines for addressing workplace violence in the health sector. Geneva: WHO; 2022.

[2]. International Labour Organization. Framework guidelines for addressing workplace violence in the health sector. Geneva: ILO; 2020.

[3]. Aelameddin T, Arabi M, Saleh M, Salameh B. Workplace violence against nurses in

healthcare settings: A systematic review. J Nurs Manag. 2015. 23(6):764–74.
[4]. Halim M, et al. Workplace violence among nurses: Prevalence, consequences, and preventive strategies. J Clin Nurs. 2022. 31(9–10):1251–61.
[5]. Al-Omari H. Physical and verbal workplace violence against nurses in Jordan. Int Nurs Rev. 2015. 62(1):111–8.
[6]. Woodhead EL, Northrop L, Edelstein B. Stress, social support, and burnout among long-term care nursing staff. J Appl Gerontol. 2022. 41(3):769–79.
[7]. Cheung T, Yip PS. Workplace violence towards nurses in Hong Kong: Prevalence and correlates. BMC Public Health. 2017. 17:196.
[8]. Wang P, et al. Effects of workplace violence on Chinese nurses' mental health and sleep quality: The mediating role of perceived social support. J Nurs Manag. 2022. 30(4):892–902.
[9]. Papa A, Venella J. Workplace violence in healthcare: Strategies for prevention. J Emerg Nurs. 2013. 39(5):477–9.
[10]. Spector PE, Zhou ZE, Che XX. Nurse exposure to physical and nonphysical violence, bullying, and sexual harassment: A quantitative review. Int J Nurs Stud. 2014. 51(1):72–84.
[11]. Mohamad Yazid MN, Nik Husain NR, Daud A, Osman Y, Mustapa N, Abdul Hadi A. Development and Validation of a Questionnaire Assessing the Perception and Practice of Workplace Violence Prevention Among Employers at Healthcare Facilities in North-Eastern Malaysia. Cureus. 2023 Jan 21;15(1):e34046. doi: 10.7759/cureus.34046.
[12]. Bambi S, Foà C, De Felippis C, Lucchini A, Guazzini A, Rasero L. Workplace incivility, lateral violence and bullying among nurses. A review about their prevalence and related factors. Acta Biomed. 2019. 90(4):51–79.
[13]. Wolf LA, Delao AM, Perhats C, Clark PR, Moon MD, Zavotsky KE. Workplace violence and emergency nurses: A narrative review. Adv Emerg Nurs J. 2014. 36(4):315–26.
[14]. Bandura A. Social-cognitive theory. In: Pervin L, John O, editors. An introduction to theories of personality. New York: Psychology Press; 2014. p. 341–60.
[15]. Xiao Y, Wang J, Chen S, et al. Workplace violence against nurses in Chinese hospitals: A cross-sectional survey. BMJ Open. 2021. 11:e045872.
[16]. Cheung T, Yip PS. Workplace violence towards nurses in Hong Kong: Prevalence and correlates. BMC Public Health. 2017. 17(1):196.
[17]. Wang PX, Wang MZ, Hu GX, Wang ZM. Study on the relationship between workplace violence and psychological health in nurses. Zhonghua Lao Dong Wei Sheng Zhi Ye Bing Za Zhi. 2022. 40(6):427–32.
[18]. Halim NA, Mamat NH, Rahman HA, et al. Workplace violence among healthcare workers in Malaysia: A cross-sectional study. Med J Malaysia. 2022. 77(3):285–92.
[19]. Halim NA, Mamat NH, Rahman HA, et al. Barriers to reporting workplace violence in Malaysian healthcare settings. Malays J Med Sci. 2022. 29(4):69–78.
[20]. Venella J, Papa A. Addressing barriers to workplace violence prevention in healthcare. J Emerg Nurs. 2013. 39(2):153–7.
[21]. Mitchell R. Safety protocols and workplace violence prevention in nursing. J Nurs Manag.

2021. 29(5):1124–31.
[22]. Dafny M, Chammas G, Peterman T. Environmental safety and violence prevention in healthcare. Aust Health Rev. 2024. 48(1):35–42.
[23]. Al-Omari H. Physical and verbal workplace violence against nurses in Jordan. *Middle East Journal of Nursing*. 2015. 9(3):35–44.
[24]. Hamdan M, Abu Hamra A. Workplace violence towards workers in the emergency departments of Palestinian hospitals: a cross-sectional study. *Human Resources for Health*. 2017. 15(1):5.
[25]. Çelik SŞ, Çelik Y, Ağırbaş İ, Uğurluoğlu Ö. Verbal and physical abuse against nurses in Turkey. *International Nursing Review*. 2008. 54(4):359–66.
[26]. Campbell JC, Messing JT, Kub J, Agnew J, Fitzgerald S, Fowler B, et al. Workplace violence: prevalence and risk factors in the safe at work study. *Journal of Occupational and Environmental Medicine*. 2011. 53(1):82–9.
[27]. Ferri P, Silvestri M, Artoni C, Di Lorenzo R. Workplace violence in different settings and among various health professionals in an Italian general hospital: a cross-sectional study. *Psychology Research and Behavior Management*. 2016. 9:263–75.
[28]. Wang Y, Han P, Dai H, Fang L, Yang H, Yang X, et al. Workplace violence against healthcare workers in China: a national cross-sectional survey. *BMJ Open*. 2022. 12:e062465.
[29]. Shields M, Wilkins K. Factors related to on-the-job abuse of nurses by patients. *Statistics Canada Health Reports*. 2009. 20(2):7–19.
[30]. Bandura A. *Social Foundations of Thought and Action: A Social Cognitive Theory*. Englewood Cliffs, NJ: Prentice Hall; 1986.
[31]. Zimmerman BJ. Self-regulated learning and academic achievement: an overview. *Educational Psychologist*. 1990. 25(1):3–17.
[32]. Papa A, Venella J. Workplace violence in healthcare: strategies for advocacy. *Online Journal of Issues in Nursing*. 2013. 18(1):5.
[33]. Park M, Cho S-H, Hong H-J. Prevalence and perpetrators of workplace violence by nursing unit and the relationship between violence and the perceived work environment. *Journal of Nursing Scholarship*. 2015. 47(1):87–95.
[34]. Alshehry AS, Alquwez N, Almazan JU, Namis IM, Alfuqaha OA, Cruz JP. Workplace incivility and its influence on professional quality of life among nurses from multicultural backgrounds: a cross-sectional study. *Journal of Clinical Nursing*. 2021. 30(7–8):1074–84.
[35]. Shibiti R. Student nurses' perceptions of violence in a clinical setting: a qualitative study. *Curationis*. 2017. 40(1):1–8.
[36]. Edward K-L, Stephenson J, Ousey K, Lui S, Warelow P, Giandinoto J-A. A systematic review and meta-analysis of factors that relate to aggression perpetrated against nurses by patients/relatives or staff. *Journal of Clinical Nursing*. 2014. 23(7–8):1079–91.
[37]. Magnavita N, Heponiemi T. Workplace violence against nursing students and nurses: an Italian experience. *Journal of Nursing Scholarship*. 2011. 43(2):203–10.
[38]. Baby M, Glue P, Carlyle D. 'Violence is not part of our job': a thematic analysis of

psychiatric mental health nurses' experiences of patient assaults from a New Zealand perspective. *Issues in Mental Health Nursing*. 2018. 39(7):554–61.
[39]. Kling RN, Yassi A, Smailes E, Lovato CY, Koehoorn M. Evaluation of a violence risk assessment system (the alert system) for reducing violence in an acute hospital: a before and after study. *BMC Health Services Research*. 2011. 11:52.
[40]. Cheung T, Yip PSF. Depression, anxiety and symptoms of stress among Hong Kong nurses: a cross-sectional study. *International Journal of Environmental Research and Public Health*. 2017. 14(8):924.
[41]. Wei C-Y, Chiou S-T, Chien L-Y, Huang N. Workplace violence against nurses: prevalence and association with hospital characteristics. *International Journal of Nursing Studies*. 2024. 137:104436.
[42]. Estryn-Behar M, van der Heijden B, Camerino D, Fry C, Le Nezet O, Conway PM, et al. Violence risks in nursing—results from the European 'NEXT' study. *Occupational Medicine*. 2008. 58(2):107–14.
[43]. Gong Y, Han T, Yin X, Yang G, Zhuang R, Chen Y, et al. Prevalence of anxiety and depressive symptoms and related risk factors among physicians in China: a cross-sectional study. *PLoS One*. 2014. 9(7):e103242.
[44]. Woodhead EL, Northrop L, Edelstein B. Violence in the workplace: exploring nursing students' perceptions of safety. *Journal of Nursing Education and Practice*. 2022. 12(5):53–61.
[45]. OSHA. *Guidelines for Preventing Workplace Violence for Healthcare and Social Service Workers*. Washington, DC: Occupational Safety and Health Administration; 2016.
[46]. ILO. *Framework Guidelines for Addressing Workplace Violence in the Health Sector*. Geneva: International Labour Organization; 2020.
[47]. Gillespie GL, Gates DM, Miller M, Howard PK. Workplace violence in healthcare settings: risk factors and protective strategies. *Rehabilitation Nursing*. 2013. 38(1):31–43.
[48]. Arnetz JE, Hamblin L, Ager J, Luborsky M, Upfal MJ, Russell J, et al. Underreporting of workplace violence: comparison of self-report and actual documentation of hospital incidents. *Workplace Health & Safety*. 2015. 63(5):200–10.
[49]. Pompeii LA, Schoenfisch AL, Lipscomb HJ, Dement JM, Smith CD, Upadhyaya M. Physical assault, physical threat, and verbal abuse perpetrated against hospital workers by patients or visitors in six U.S. hospitals. *American Journal of Industrial Medicine*. 2013. 56(11):1262–72.
[50]. Hwang J-I, Park H-A, Lee S-K, Kim J-A. Work-related violence and burnout in nurses. *Journal of Korean Academy of Nursing Administration*. 2006. 12(4):589–98.

ORIGINAL ARTICLE

Assessing Community Knowledge and Attitude towards Cardiopulmonary Resuscitation and Automated External Defibrillator in Ipoh, Perak.

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Abstract

Introduction: Cardiopulmonary resuscitation (CPR) and automated external defibrillator (AED) use are critical interventions for out-of-hospital cardiac arrest (OHCA), significantly improving survival rates. This study assessed the knowledge and attitude towards CPR and AED among the local community in Ipoh, Perak, Malaysia. **Methods:** A cross-sectional study using convenience sampling was conducted from January to February 2024, involving 385 respondents. A self-administered questionnaire, available in English and Malay, collected sociodemographic data and assessed CPR knowledge (12 items) and attitude (10 items). Data were analysed using SPSS version 28. **Results:** Nearly all respondents (99.0%) had heard of CPR, but only 27.8% knew the correct initial step (call for help immediately). Knowledge was moderate (median score: 58.3%, IQR: 41.7-66.7), with significant associations with age group, education level, and employment status ($p<0.05$). While 65.5% were willing to perform CPR on family members, willingness decreased to 43.1% for strangers. Most (61%) had never received CPR training, but 76.4% expressed interest. AED awareness was lower (50.4%), and only 22.9% knew that anyone can use an AED. **Conclusion:** The Ipoh community demonstrates moderate CPR knowledge and attitude, but significant gaps persist, particularly regarding AED. There is a strong need for expanded community-based CPR and AED training, integration into educational curricula, and addressing barriers like legal fears and gender-related concerns to improve bystander intervention in OHCA incidence.

Keywords: *Attitude, automated external defibrillator, cardiac arrest, cardiopulmonary resuscitation, knowledge.*

Introduction

Cardiopulmonary resuscitation (CPR) is a life-saving procedure performed in emergencies when breathing or cardiac activity has ceased, often due to myocardial infarction, suffocation, or drowning. CPR involves a combination of chest compressions, which manually circulate blood, and rescue breaths, delivering oxygen to the lungs. The primary objective is to maintain circulatory flow and oxygenation to preserve brain function and other vital organs until medical assistance becomes available. This is a critical procedure, as within minutes of cardiac arrest, the lack of oxygenated blood can result in irreversible brain damage or death.

An estimated two million individuals globally die from sudden cardiac death each year, with many cases occurring outside of hospitals [1,2]. Some of these could have been avoided if early CPR performed by bystanders had been made possible [3]. The rate of early bystander-initiated CPR in Malaysia remains low. Based on studies among the local communities in a few states in Malaysia, namely Kelantan, Selangor, and Melaka, roughly about 1% to 10% out-of-hospital cardiac arrest (OHCA) cases received CPR from bystanders [3,4,5].

Reluctance to perform bystander CPR has been attributed to several factors, including lack of interest, low confidence, limited time, uncertainty about where to receive training, embarrassment, fear of legal implications, fear of injuring a victim, and concern over the transmission of infections [6,7,8]. Knowledge and skill are among the main influencing factors that contribute to the willingness of public to engage with out of hospital CPR [9,10]. Many of these barriers are linked to insufficient knowledge and a lack of CPR training [11,12].

Training not only improves knowledge but also enhances confidence and preparedness in emergency situations [13]. Studies have shown that individuals who have received CPR training are more likely to perform CPR compared to those without such experience [14,15,16]. In addition, CPR training has been associated with improved survival rates in cardiac arrest cases [17].

An essential concept in improving survival outcomes in OHCA cases is the "chain of survival," a sequence of critical actions including early call for help, initiation of CPR, and defibrillation using an automated external defibrillator (AED). An AED is a portable device that assesses heart rhythm and, when necessary, delivers an electric shock to restore the normal cardiac function while awaiting the arrival of medical personnel [18]. Therefore, along with CPR training, familiarity with the use of an AED forms a critical component of an emergency response. Hence, it is necessary that bystanders are equipped with the knowledge and skills required to operate an AED effectively. Again, studies have suggested that AED use by bystanders is low [3,19,20].

It is evident that knowledge and a positive attitude towards CPR can greatly improve the survival rate in emergency situations involving cardiac arrest. Therefore, it is important to assess the knowledge and attitude towards CPR among the local community in Ipoh. We also assessed AED knowledge as it is a critical component in the chain of survival. In addition, a question addressing the integration of CPR training into the school and university curricula was also included. Currently, CPR training is not part of the national curriculum in Malaysia, and its implementation often depends on individual school principals, who may have limited knowledge about the subject [21]. The findings of this study may contribute valuable data to support the development or enhancement of national policies on basic life support training for Malaysian citizens.

Materials and methods

This cross-sectional study was conducted from 22 January 2024 to 23 February 2024 among the local community in Ipoh, Perak. The minimum required sample size was 384, determined using the Sample Size for a Proportion method on

OpenEpi (Version 3). The anticipated frequency was 50%, with a 5% confidence limit.

A convenience sampling method was employed. The questionnaire was pretested and revised accordingly prior to data collection. The questionnaire was distributed either via Google Form or in hardcopy format for those who were unable to access the Google Form. The questionnaire was made available in English and Malay. The questionnaire consisted of three sections: Section A includes sociodemographic data such as, gender, age group, education level, and employment status; Section B contains 12 questions assessing knowledge of CPR; and Section C contains 10 questions evaluating the attitude towards CPR.

Ethical approval was obtained from the Medical Research Ethics Committee of Universiti Kuala Lumpur Royal College of Medicine Perak (UniKL RCMP/MREC/2023-2024/SSM-008).

Data analysis was performed using SPSS version 28. Descriptive analysis was used to summarise the sociodemographic data as percentages. For the knowledge section, the number of respondents who selected correct and incorrect answers was calculated and presented as percentages: a correct answer was given a score of one, and an incorrect answer a zero. The total knowledge score was calculated by summing the individual scores, converting them into percentages, and categorising them as good ($x \geq 75\%$), moderate ($50 \leq x < 75\%$), or poor ($<50\%$). In the attitude section, the number of 'yes' and 'no' responses was calculated and expressed as percentages: a 'yes' response is given a score of one, and a 'no' a score of zero. An exception is given to one statement: Do you agree that only health providers should perform CPR? for which 'yes was scored as zero and 'no' as one. Similarly, the total attitude score was summed, converted into a percentage, and categorised as good ($x \geq 75\%$), moderate ($50 \leq x < 75\%$), or poor ($<50\%$).

Median scores for knowledge and attitude are presented as median ± interquartile range (IQR). The Mann-Whitney U test and Kruskal-Wallis test were used to compare median scores across sociodemographic variables. Associations between sociodemographic variables and knowledge, as well as between sociodemographic variables and attitude were performed using the chi-square test. A $p<0.05$ is considered statistically significant.

Results

Sociodemographic characteristics of respondents

A total of 385 respondents were obtained, 52.5% female and 47.5% male. The breakdown of their age, educational level, employment status, and ethnicity is shown in Table 1.

Knowledge of CPR

The majority of the respondents had heard of CPR (99.0%) and knew that CPR can be performed outside of a hospital (89.4%). Most of them (79.2%) knew that 999 is the correct contact number for emergency medical services in Malaysia. However, only 27.8% respondents knew that the next step to take when encountering an unresponsive patient is to call for help immediately, with a majority thinking that they should check again for absence of breathing and pulse, then call for help, and subsequently start CPR (60.3%).

The majority of respondents (68.1%) knew the correct location for chest compressions. However, only 35.1% knew the correct chest compression-to-ventilation ratio for adults and children and 52.7% knew the correct depth for chest compression. Less than half of the respondents (41.8%) knew the correct steps in CPR. Nevertheless, the majority of respondents (80.0%) knew that chest compressions should be continued until the rescue team arrives.

Regarding AEDs, 50.4% of the respondents had heard about AEDs, and 41.0% knew about the main purpose of an AED, but only 22.9% of the respondents knew that anyone is allowed to use an AED. The majority of them (77.1%) believed that only emergency personnel or skilled

individuals are allowed to use an AED. The questions and the responses regarding knowledge of CPR are presented in Table 2.

A low percentage of respondents achieved a 'good' knowledge score (Table 3). This was consistent across genders (male: 23.5%; female: 23.3%). These low score in good knowledge is seen across all age groups and education levels. In employment status, a higher percentage is seen among the healthcare workers (44.4%), while a low percentage of good knowledge is seen among the rest of the employment status. The breakdown of this knowledge score is presented in Table 3.

Median score of knowledge of CPR

The median score was 58.3% (IQR: 41.7-66.7) for both male and female respondents with IQRs of 50.0-66.7 and 41.7-66.7, respectively. There was no statistically significant difference in the median scores between genders.

Concerning age, respondents aged 18 to < 30 years and those aged 30 to <45 years had the highest median CPR knowledge score of 58.3% with IQRs of 50.0-75.0 and 41.7-66.7, respectively. A statistically significant difference in median CPR knowledge scores was observed among the age groups ($p<0.01$).

Regarding education level, respondents with postgraduate and bachelor's degrees had higher median score of 66.7% (IQR: 41.7-75.0) and 66.7% (IQR: 50.0-75.0), respectively, compared to those with UPSR/PMR/SPM/STPM qualifications [50.0% (IQR: 41.7-58.3)] [and Diploma holders [50.0% (IQR: 41.7-66.7)] qualifications. The differences in median scores among the education levels were statistically significant ($p<0.01$).

In terms of employment status, students had a median score of 58.3% (IQR: 50.0-75.0), healthcare workers scored 66.7% (IQR: 58.3-75.0), and non-healthcare workers scored 58.3% (IQR: 41.7-66.7). The unemployed, housewives, and retirees had lower median scores of 50.0% (IQR: 29.2-70.8), 50.0% (IQR: 29.2-70.8), and 50.0% (IQR: 41.7-54.2), respectively. The differences in median CPR knowledge scores among employment categories were statistically significant ($p<0.01$) (**Table 4**).

Association between sociodemographic parameters and knowledge of CPR

A significant association was observed between age group, education level, and employment status with knowledge of CPR among the community in Ipoh ($p<0.01$; $p<0.05$) (**Table 5**).

Attitude towards CPR

More than half of the respondents (65.5%) stated that they are willing to perform CPR without hesitation on their family members; this number decreased to 43.1% when it came to performing CPR on strangers. The majority of the respondents (82.1%) had never had an opportunity to perform CPR in their lifetime, and more than half (61%) had never received any CPR training. However, the majority (76.4%) indicated that they would attend free CPR training, while the remaining 23.6% showed no interest. Almost all respondents (98.7%) believed that CPR can significantly increase the chances of saving a person's life in an emergency, and most (82.6%) disagreed that only health providers should perform CPR. An overwhelming majority agrees that CPR training should be mandatory at schools, universities, and workplaces (93.8%) and that CPR training should be integrated into the school and university curriculum (98.4%). Furthermore, more than half (62.3%) agree that CPR training should be a requirement for job applications. The questions and the responses regarding attitude towards CPR are presented in Table 6.

Attitude score of respondents

The distribution of attitude scores across sociodemographic categories is detailed in Table 3. Overall, moderate attitude scores were predominant among most respondent groups. A notably higher proportion of healthcare workers achieved a good score (85.2%) compared to all other employment categories. Similarly, respondents with Bachelor's or Postgraduate

degrees showed a higher tendency towards good scores (47.2% and 45.5%, respectively) than those with lower educational qualifications. In contrast, housewives, retirees, and the unemployed had the highest proportions of poor attitude scores. Across age groups, the proportion of good scores was highest among younger respondents (18 to <45 years) and decreased with advancing age.

The overall median attitude score was 70.0% (IQR: 60.0-80.0). Statistically significant variations in median scores were found across all sociodemographic factors (Table 4). Specifically, scores were significantly higher among male respondents compared to females ($p<0.05$), younger respondents (18-<45 years) compared to older ones ($p<0.01$), and those with higher education (Diploma and above) compared to those with lower qualifications ($p<0.01$). A significant gradient was also evident by employment status ($p<0.01$), with healthcare workers scoring highest, followed by students and non-healthcare workers; the unemployed, housewives, and retirees consistently had the lowest scores.

Association between sociodemographic parameters and attitude towards CPR

A significant association was found between age group, education level, and employment status with attitude towards CPR among the community in Ipoh ($p<0.01$; $p<0.05$) (**Table 5**).

Discussion

This study assessed knowledge of CPR and AED use, as well as attitude towards CPR, among the community in Ipoh, Malaysia. While AED use is rarely incorporated in CPR training, we recognise the ability to use this critical tool in emergencies as its use could be essential in improving survival outcomes in out-of-hospital cardiac arrest (OHCA) cases.

Our findings revealed that most respondents had a moderate level of CPR knowledge, which is slightly higher than that reported by a previous study conducted in Ipoh [22]. This difference may be attributed to variations in the sociodemographic composition, as our study encompassed a wider age range. Notably, we found a significant association between higher education level and better CPR knowledge, a finding consistent with research from Riyadh City, Saudi Arabia [23]. This suggests that while education is a relevant factor, it may not be the sole determinant of CPR knowledge across the entire population.

Age-specific differences were also evident, with respondents above 65 years demonstrating significantly lower CPR knowledge scores - a trend similarly observed in a survey in Münster, Germany [24]. The lower knowledge score among older adults may be due to limited exposure to formal CPR education, reduced access to digital learning platforms, and fewer opportunities to participate in training programs. In Malaysia, it was only in the 1990s that the Ministry of Health began introducing CPR training in the medical and nursing schools [25]. Any public training could have come much later; therefore, the older generation (those 65 and above) may have missed out on the early campaigns. Furthermore, CPR education has only recently been implemented in the secondary school curriculum, embedded within several topics in the Health Education subject [26]. Poor educational attainment among older adults has been suggested to contribute to lower CPR knowledge and reduced confidence in performing resuscitation during emergencies [24].

It is encouraging to find that CPR is almost universally recognized within the community, indicating successful awareness campaigns, likely through media and public health channels. Most respondents correctly understood that CPR can be performed outside hospitals, indicating awareness that cardiac arrest can occur in out-of-hospital environments and that immediate bystander intervention is critical. Of concern, however, approximately 20% of the respondents were unaware of the correct emergency medical services number (999) in Malaysia, possibly due

to confusion with foreign emergency numbers, such as 911, which are frequently mentioned in the Western television series. In this study, employment status showed a significant association with CPR knowledge. Reassuringly, no healthcare workers in our sample had poor CPR knowledge. However, it is noteworthy that a greater number of them had moderate rather than good knowledge scores. This variation could be due to differences in job roles, for example, whether individuals were directly involved in patient care or worked in administrative positions where direct patient care and formal CPR training are limited. Unfortunately, our present study did not obtain these detailed role-specific data. Nevertheless, the level of CPR knowledge among healthcare workers has been reported to vary considerably across different studies; for instance, in some studies, fewer than one-third of healthcare respondents exhibited good CPR knowledge [27,28], whereas a more recent study reported that 89.5% had good knowledge [29]. Unemployed individuals, retirees, and housewives were found to have lower knowledge scores regarding CPR. Again, this may be due to reduced exposure to CPR training or fewer opportunities to attend CPR awareness programmes. For the housewives, their domestic commitments may limit their availability for such programmes. However, one study found that although 90% of young mothers had poor knowledge of infant CPR, they were highly motivated to learn and willing to participate in CPR training [30].

Where attitude is concerned, our study revealed that most respondents had a moderate level of attitude towards CPR, with the median attitude score being higher than the knowledge score. In each category of sociodemographic characteristics, almost all subcategories demonstrated moderate to good attitude among respondents. About 40% of the respondents had received CPR training, and fewer than 20% had experience performing CPR. A similar trend was seen in an earlier study where approximately 48.1% of the participants knew how to perform CPR, and 7.9% had performed it [31]. This indicates a low incidence of OHCA in both study communities. Education was associated with a better attitude towards CPR, with respondents who had a tertiary education showing higher median attitude scores. This difference can be attributed to the more advanced training and exposure that university students receive, particularly those in health-related fields. In addition, healthcare workers also had a good attitude score, which is a response expected of their work environment.

In the present study, gender did not significantly influence CPR knowledge. However, a significant difference was observed in the median attitude scores, with male respondents showing higher scores than females. Fear of being accused of inappropriate touching or sexual assault is a factor that prevents male respondents from performing CPR on female victims [31,32]. Likewise, female respondents have been shown to have a higher willingness to perform CPR on female victims than on male victims [32]. Therefore, female respondents may also experience fear or hesitation in conducting CPR on individuals of the opposite gender, similar to male respondents.

When it comes to performing CPR on family members as opposed to strangers, our respondents are more willing to perform CPR on family members but are more reluctant to do so on strangers. Although we did not explore the reasons for this reluctance, previous research has shown that it may stem from fear of causing unintentional harm or becoming involved in legal complications [33]. The procedure of mouth-to-mouth ventilation may also discourage rescuers, especially due to concerns about hygiene, direct contact with body fluids such as saliva, and the risk of spreading infectious diseases, including COVID-19. Thus, more targeted CPR awareness programmes should be implemented, addressing gender-related concerns and legal fears.

Despite these concerns, most of our respondents agree that performing CPR should not be limited to healthcare professionals, believing that CPR

can significantly increase the chances of survival during cardiac arrest. Many of our respondents expressed interest in attending CPR training. These findings suggest that although practical training and hands-on experience are limited, the overall attitude towards CPR is positive among the population. Furthermore, a majority of our respondents believed that CPR training should be integrated into the education curriculum at schools and universities with many agreeing that such training should be mandatory in these institutions. Indeed, García and Vargas (2025) have shown that students' levels of knowledge and confidence can increase after attending CPR training, highlighting the importance of integrating it into school curricula [34]. Therefore, it is encouraging to note that studies in a couple of states in Malaysia have shown that both students and teachers are open to such an idea [35,36]. In fact, as reported by Haiqal et al. (2024), the majority of secondary school principals in Malaysia agrees that CPR courses should be made mandatory before students complete their studies and were willing to allocate funds to hire certified instructor [21].

Where the use of AED is concerned, the majority of our respondents are unaware of the use of AED or that anyone can use them in an emergency. This finding was observed despite the majority of our respondents having moderate knowledge of CPR. Furthermore, many of our respondents are unaware of AEDs' existence and function; and did not know that anyone can use them, highlighting a critical gap in public education. Prior research has shown that structured educational programmes can effectively improve knowledge and confidence related to AED use. It has been demonstrated that such training significantly improves participants' confidence and willingness to perform CPR and to use AEDs [37].

Lastly, sociodemographic factor aside, while many of our respondents correctly answered technical CPR questions, the overall response pattern indicates that such items may not be easily answered without prior formal training. This highlights the importance of structured CPR education within the community, with more targeted CPR awareness programmes to address gender-related concerns and legal fears. This includes an introduction to AED and its hands-on use and increasing public access to such equipment. These approaches will help bridge current knowledge gaps in the community and enhance emergency preparedness. This is especially relevant given the Malaysian Ministry of Health's plan to make AED installation mandatory in all public facilities by 2025, which may further raise public awareness and encourage educational outreach.

Limitations of the study

This study has several limitations. It was conducted within a single urban community; therefore, the findings may not be generalisable to rural populations or other regions. Although respondents' employment status was categorised, their specific job roles were not identified, especially in the healthcare worker category, where the ability to assess how different types of healthcare workers vary in CPR knowledge and attitude was not identified. Additionally, while hesitancy to perform CPR on strangers was reported, the questionnaire did not include follow-up questions to explore the underlying reason for this reluctance.

Conclusion

In this present study, the majority of respondents from the Ipoh community demonstrated a moderate level of knowledge and attitude towards CPR**.** Both were significantly associated with sociodemographic factors such as age, education, and employment status. Our study highlights the importance of expanding community-based CPR and AED education, integrating CPR and AED training into school and university curricula, and addressing barriers such as legal fears and gender-related concerns among bystanders to improve willingness to assist in OHCA incidence.

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Conflict of interest
The authors declare that no conflict of interst may arise from the research publication.

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Authors' contributions

FZ, NFAAS, NAAMA, IPKS, IAA, AIAZ and BCSC contributed to the study design, data collection, and statistical analysis. FZ, RM and NAL performed the literature search and wrote the manuscript.

Table 1. Sociodemographic parameters of respondents

Variables	Category	N	Percentage (%)
Gender	Male	183	47.5
	Female	202	52.5
Age group	18 - <30	172	44.7
	30 - <45	88	22.9
	45 - 65	99	25.7
	>65	26	6.8
Education level	UPSR/PMR/SPM/STPM	118	30.6
	Diploma	97	25.2
	Bachelor	159	41.3
	Postgraduate (Master/PhD)	11	2.9
Employment status	Student	144	37.4
	Employed in healthcare sector (e.g., hospital, clinic, pharmacy)	27	7.0
	Employed in a non-healthcare sector	126	32.7
	Unemployed	13	3.4
	Housewife	42	10.9

Retired	33	8.6

Table 2. Respondents' responses to knowledge items regarding CPR

Questions	Category	N (%)
Have you ever heard of CPR?	Yes*	381 (99)
	No	4 (1)
Should CPR be done only in the hospital	Yes	41 (10.6)
	No*	344 (89.4)
Number for contacting emergency medical services in Malaysia in case of emergencies.	911	79 (20.5)
	919	0
	999*	305 (79.2)
The next step if you find a patient who is unresponsive.	Check for no breathing and no pulse, call for help then start CPR.	232 (60.3)
	Call for help directly. *	107 (27.8)
	Start CPR.	33 (8.6)
	Turn the patient towards the lateral side.	13 (3.4)
If we need to do chest compression for resuscitating an unconscious patient, what will be the location for the chest compressions?	Right side of the chest	26 (6.8)
	Left side of the chest	97 (25.2)
	In the centre of the chest, below breastbone*	262 (68.1)
While doing resuscitation, what will be the ratio of chest compression and ventilation in adult and children?	10:2	135 (35.1)
	20:2	95 (24.7)
	30:2*	135 (35.1)
	40:2	20 (5.2)
What is the depth for chest compression?	2 cm	107 (27.8)
	5 cm*	203 (52.7)
	8 cm	52 (13.5)
	10 cm	23 (6.0)
What are the steps in CPR?	Check for a response, call for help, open the airway, give two rescue breathing, and check for the pulse, if there is no pulse start chest compression*	161 (41.8)
	Check for response and simultaneously check for no breathing, call for help, check for pulse, and start chest compression if there is no pulse.	124 (32.2)
	Tap and shout for checking response, check for pulse, start chest compression, and give him ventilation by	61 (15.8)

	mouth-to-mouth or bag valve mask	
	Tap and shout for checking response, open the airway, check for pulse, and start chest compression.	39 (10.1)
Is it necessary to continue chest compression until rescue team arrive?	Yes*	308 (80)
	No	77 (20)
Have you heard about AED?	Yes*	194 (50.4)
	No	191 (49.6)
What is the purpose of the automated defibrillator (AED)?	To analyse the heart rhythm	38 (9.9)
	To analyse the heart rhythm and if necessary to give an electric shock*	158 (41.0)
	To give cardiac massage	19 (4.9)
	I do not know	170 (44.2)
Who is allowed to use an automated external defibrillator (AED)?	Every citizen*	88 (22.9)
	Only emergency personnel	139 (36.1)
	Only skilled people	158 (41.0)

*indicates the correct answer

Table 3. Categories of scores for respondents' knowledge and attitude towards CPR based on sociodemographic parameters

Sociodemographic parameters	Knowledge levels category			Attitude levels category		
	Good N (%)	Moderate N (%)	Poor N (%)	Good N (%)	Moderate N (%)	Poor N (%)
Gender:						
Male	43 (23.5)	96 (52.5)	44 (24.0)	76 (41.5)	93 (50.8)	14 (7.7)
Female	47 (23.3)	95 (47.0)	60 (29.7)	60 (29.7)	122 (60.4)	20 (9.9)
Age group:						
18 - < 30	47 (27.3)	85 (49.4)	40 (23.3)	67 (39.0)	94 (54.7)	11 (6.4)
30 - < 45	20 (22.7)	45 (51.1)	23 (26.1)	36 (40.9)	45 (51.1)	7 (8.0)
45 - 65	23 (23.2)	50 (50.5)	26 (26.3)	29 (29.3)	60 (60.6)	10 (10.1)
> 65	0	11 (42.3)	15 (57.7)	4 (15.4)	16 (61.5)	6 (23.1)
Educational level:						
UPSR/PMR/SPM/STPM	14 (11.9)	56 (47.5)	48 (40.7)	27 (22.9)	69 (58.5)	22 (18.6)
Diploma	21 (21.6)	46 (47.4)	30 (30.9)	29 (29.9)	61 (62.9)	7 (7.2)
Bachelor	52 (32.7)	84 (52.8)	23 (14.5)	75 (47.2)	79 (49.7)	5 (3.1)
Postgraduate (Master/PhD)	3 (27.3)	5 (45.5)	3 (27.3)	5 (45.5)	6 (54.5)	0
Employment status:						
Student	44 (30.6)	68 (47.2)	32 (22.2)	59 (41.0)	79 (54.9)	6 (4.2)
Employed in healthcare sector (e.g., hospital, clinic, pharmacy)	12 (44.4)	15 (55.6)	0	23 (85.2)	3 (11.1)	1 (3.7)
Employed in a non-healthcare sector	27 (21.4)	66 (52.4)	33 (26.2)	38 (30.2)	78 (61.9)	10 (7.9)
Unemployed	3 (23.1)	4 (30.8)	6 (46.2)	5 (38.5)	3 (23.1)	5 (38.5)
Housewife	2 (4.8)	21 (50.0)	19 (45.2)	4 (9.5)	30 (71.4)	8 (19.0)
Retired	2 (6.1)	17 (51.5)	14 (42.4)	7 (21.2)	22 (66.6)	4 (12.1)

Table 4. Median scores of knowledge and attitude towards CPR across sociodemographic parameters

Sociodemographic parameters	**Knowledge** Median score (IQR) (%)	p-value	**Attitude** Median score (IQR) (%)	p-value
Gender:				
Male	58.3 (50.0-66.7)	0.771	70.0 (60.0-80.0)	0.015**
Female	58.3 (41.7-66.7)		60.0 (50.0-80.0)	
Age group:				
18 - < 30	58.3 (50.0-75.0)		70.0 (60.0-80.0)	
30 - < 45	58.3 (41.7-66.7)	0.002*	70.0 (60.0-80.0)	0.001*
45 - 65	50.0 (41.7-66.7)		60.0 (50.0-80.0)	
> 65	41.7 (41.7-50.0)		55.0 (47.5-70.0)	
Educational level:				
UPSR/PMR/SPM/STPM	50.0 (41.7-58.3)		60.0 (50.0-70.0	
Diploma	50.0 (41.7-66.7)	< 0.001*	70.0 (60.0-80.0)	< 0.001*
Bachelor	66.7 (50.0-75.0)		70.0 (60.0-80.0)	
Postgraduate (Master/PhD)	66.7 (41.7-75.0)		70.0 (70.0-90.0)	
Employment status:				
Student	58.3 (50.0-75.0)		70.0 (60.0-87.5)	
Employed in healthcare sector (e.g., hospital, clinic, pharmacy)	66.7 (58.3-75.0)		80.0 (80.0-100.0)	
Employed in a non-healthcare sector	58.3 (41.7-66.67)	< 0.001*	70.0 (50.0-80.0)	< 0.001*
Unemployed	50.0 (29.2-70.83)		60.0 (40.0-80.0)	
Housewife	50.0 (29.2-70.8)		60.0 (50.0-70.0)	
Retired	50.0 (41.7-54.2)		60.0 (50.0-70.0)	

*p<0.01;**p<0.05: indicates a significant difference between groups; IQR: interquartile range (Q1-Q3); p>0.05: no significant difference; p<0.05: have significant difference

Table 5. Association of sociodemographic parameters with knowledge and attitude towards CPR

		X^2	p-value
Knowledge	Gender	1.716	0.424
	Age group	21.414	0.002*
	Education level	32.951	< 0.001*
	Employment status	48.220	< 0.001*
Attitude	Gender	5.937	0.051
	Age group	12.752	0.047**
	Education level	34.594	< 0.001*
	Employment status	66.697	< 0.001*

*p<0.01;**p<0.05: indicates a significant difference between groups;

Table 6. Respondents' responses to attitude items regarding CPR

Question	Category	N (%)
Can you provide CPR without hesitation to your family?	Yes	252 (65.5)
	No	133 (34.5)
Can you provide CPR without hesitation to strangers?	Yes	166 (43.1)
	No	219 (56.9)
Have you ever had the opportunity to perform CPR during your lifetime?	Yes	69 (17.9)
	No	316 (82.1)
Have you ever received any training in CPR?	Yes	150 (39.0)
	No	235 (61.0)
Would you be interested in attending CPR training if it were offered at no cost?	Yes	294 (76.4)
	No	91 (23.6)
Do you believe CPR can significantly increase the chances of saving a person's life in an emergency?	Yes	380 (98.7)
	No	5 (1.3)
Do you agree that only health providers should perform CPR?	Yes	67 (17.4)
	No	318 (82.6)
In your opinion, should CPR training be mandatory at school/ university/ workplace?	Yes	361 (93.8)
	No	24 (6.2)
Do you believe CPR training should be integrated into the educational curriculum at school/ universities?	Yes	365 (94.8)
	No	20 (5.2)
In your perspective, should CPR training be a requirement for job applications?	Yes	240 (62.3)
	No	145 (37.7)

References

[1]. Markwerth P, Bajanowski T, Tzimas I, Dettmeyer R. Sudden cardiac death—update. International journal of legal medicine. 2021 Mar;135(2):483-95.

[2]. Ha AC, Doumouras BS, Wang CN, Tranmer J, Lee DS. Prediction of sudden cardiac arrest in the general population: review of traditional and emerging risk factors. Canadian Journal of Cardiology. 2022 Apr 1;38(4):465-78.

[3]. Chew KS, Mohd Idzwan Z, Nik Hishamuddin NA, Wan Aasim WA, Kamaruddin J. How frequent is bystander cardiopulmonary resuscitation performed in the community of Kota Bharu, Malaysia?. Singapore medical journal. 2008 Aug 1;49(8):636.

[4]. Ismail AK, Md Jawi MI, Mohd Salleh NI, Hamdan NA, Md Jamal S, Shah SA, Abdul Razak SN. Outcome of early cardiopulmonary resuscitation in out-of-hospital cardiac arrest managed in Universiti Kebangsaan Malaysia Medical Centre. Medicat Heal. 2016;11(1):38-46.

[5]. Yasin S, Bakar SA, Nurumal MS, Arifin SA. Cardiopulmonary resuscitation performed by bystanders: A systematic review. International Journal of Care Scholars. 2023 Mar 31;6(1):71-91.

[6]. Huang EP, Chiang WC, Hsieh MJ, Wang HC, Yang CW, Lu TC, Wang CH, Chong KM, Lin CH, Kuo CW, Sun JT. Public knowledge, attitudes and willingness regarding bystander cardiopulmonary resuscitation: A nationwide survey in Taiwan. Journal of the Formosan Medical Association. 2019 Feb 1;118(2):572-81.

[7]. Myo T, AR MK, Muhammad Y, Adani N. Knowledge and attitude towards basic life support among medical and nursing students in Universiti Kuala Lumpur Royal College of Medicine Perak. Asian Journal of Medicine & Health Sciences. 2020 Jun 1;3(1):36-43.

[8]. Daud A, Nawi AM, Aizuddin AN, Yahya MF. Factors and barriers on cardiopulmonary resuscitation and automated external Defibrillator willingness to Use among the community: a 2016–2021 systematic review and data synthesis. Global Heart. 2023 Aug 25;18(1):46.

[9]. Tian X, Zhang Y, Dou D. Training experience is an important factor affecting willingness for bystander CPR and awareness of AED: a survey of residents from a province in Central China in 2023. Frontiers in Public Health. 2024 Sep 2;12:1459590.

[10]. Cheng W, Liu J, Zhou C, Wang X. Factors analysis of lower probability of receiving bystander CPR in females: a web-based survey. BMC Cardiovascular Disorders. 2025 Dec;25(1):1-3.

[11]. Matsuyama T, Scapigliati A, Pellis T, Greif R, Iwami T. Willingness to perform bystander cardiopulmonary resuscitation: A scoping review. Resuscitation Plus. 2020 Dec 1;4:100043.

[12]. Riccò M, Berrone M, Vezzosi L, Gualerzi G, Canal C, De Paolis G, Schallemberg G. Factors influencing the willingness to perform bystander cardiopulmonary resuscitation on the workplace: a study from North-Eastern Italy. Acta Bio Medica: Atenei Parmensis. 2020 Nov 10;91(4):e2020180.

[13]. Jaskiewicz F, Kowalewski D, Kaniecka E, Kozlowski R, Marczak M, Timler D. Factors influencing self-confidence and willingness to perform cardiopulmonary resuscitation among working adults—A quasi-experimental study in a training environment. International Journal of Environmental Research and Public Health. 2022 Jul 7;19(14):8334.

[14]. Lešnik D, Lešnik B, Golub J, Križmarić M, Mally Š, Grmec Š. Impact of additional module training on the level of basic life support knowledge of first year students at the University of Maribor. International Journal of Emergency Medicine. 2011 Apr 19;4(1):16.

[15]. Tanigawa K, Iwami T, Nishiyama C, Nonogi H, Kawamura T. Are trained individuals more likely to perform bystander CPR? An observational study. Resuscitation. 2011 May 1;82(5):523-8.

[16]. Cheng-Yu C, Yi-Ming W, Shou-Chien H, Chan-Wei K, Chung-Hsien C. Effect of population-based training programs on bystander willingness to perform cardiopulmonary resuscitation. Signa Vitae. 2016 Oct 5;12(1):63-9.

[17]. Birkun A, Gautam A, Trunkwala F. Global prevalence of cardiopulmonary resuscitation training among the general public: a scoping review. Clinical and experimental emergency medicine. 2021 Dec 31;8(4):255.

[18]. Malathy NB, Dhaarani S, Bairavi N, Niranjhana V. A Study of Automated External Defibrillator with the Help of Monophasic and Biphasic Pulse. Int. J. Innov. Res. Comput. Commun. Eng. 2015;3(2).

[19]. Sheng CK, Zakaria MI, Rahman NH, Jaalam K, Adnan WA. Cardiopulmonary resuscitation: the short comings in Malaysia. The Malaysian Journal of Medical Sciences: MJMS. 2008 Jan;15(1):49.

[20]. Krammel M, Schnaubelt S, Weidenauer D, Winnisch M, Steininger M, Eichelter J, Hamp T, van Tulder R, Sulzgruber P. Gender and age-specific aspects of awareness and knowledge in basic life support. PloS one. 2018 Jun 12;13(6):e0198918.

[21]. Haiqal MH, Fariduddin MN, Siau CS. Readiness and Challenges in Cardiopulmonary

Resuscitation Teaching: A Preliminary Perspective Amongst Malaysian Secondary School Principles. Malaysian Journal of Medicine and Health Sciences. 2024 Jan 31;20(1):12-20.

[22]. Muhammad NS, Govindan SN, Ghani BA, Shet D. Community's Knowledge, Perception, and Attitude Towards Cardiopulmonary Resuscitation in Ipoh, Perak, Malaysia: A Cross-sectional Study. Malaysian Journal of Medicine & Health Sciences. 2025 Jan 1;21(1).

[23]. Alhussein RM, Albarrak MM, Alrabiah AA, Aljerian NA, Bin Salleeh HM, Hersi AS, Wani TA, Al Aseri ZA. Knowledge of non-healthcare individuals towards cardiopulmonary resuscitation: a cross-sectional study in Riyadh City, Saudi Arabia. International journal of emergency medicine. 2021 Dec;14(1):1-9.

[24]. Brinkrolf P, Bohn A, Lukas RP, Heyse M, Dierschke T, Van Aken HK, Hahnenkamp K. Senior citizens as rescuers: Is reduced knowledge the reason for omitted lay-resuscitation-attempts? Results from a representative survey with 2004 interviews. PLoS One. 2017 Jun 12;12(6):e0178938.

[25]. Guidelines For Resuscitation Training In Ministry of Health Malaysia Hospitals and Healthcare Facilities. January 2012 (1st Edition) by Medical Development Division Ministry of Health, Malaysia. https://www.moh.gov.my/moh/images/gallery/Garispanduan/NCORT_Book.pdf

[26]. Fariduddin MN, Mohamed M, Jaafar MJ, Baharin K, Siau CS, Bashah K. Compression-only cardiopulmonary resuscitation and automated external defibrillator course for primary school students: a Malaysian pilot study. Children. 2022 Dec 27;10(1):58.

[27]. Mersha AT, Egzi AH, Tawuye HY, Endalew NS. Factors associated with knowledge and attitude towards adult cardiopulmonary resuscitation among healthcare professionals at the University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia: an institutional-based cross-sectional study. BMJ open. 2020 Sep 1;10(9):e037416.

[28]. Khatun R, Chowdhury S, Goni O. Knowledge and attitudes towards cardiopulmonary resuscitation: a cross sectional survey on health care providers in clinical practice. Health Sciences Quarterly. 2021 Oct 15;1(3):87-93.

[29]. Chik M, Ahmad A, Kunjukunju A, Omar M, Fariza N, Yusof P. Knowledge and practice of cardiopulmonary resuscitation (CPR) among registered nurses. Open Access J Nurs. 2023;6(2):30-6.

[30]. Alenezi F, Mohan SK, Almutairi RM, Altheyab HA, Alkhaldi AA, Alanazi BM. The knowledge of infant CPR among mothers in King Abdulaziz medical city (KAMC). ARC J

Pediatr. 2018;4:6-12.

[31]. Shelton SK, Rice JD, Knoepke CE, Matlock DD, Havranek EP, Daugherty SL, Perman SM. Examining the impact of layperson rescuer gender on the receipt of bystander CPR for women in cardiac arrest. Circulation: Cardiovascular Quality and Outcomes. 2024 Apr;17(4):e010249.

[32]. Cheng W, Liu J, Zhou C, Wang X. Factors analysis of lower probability of receiving bystander CPR in females: a web-based survey. BMC Cardiovascular Disorders. 2025 Dec;25(1):1-3.

[33]. Ali KU, Ali KA, Ali KZ, Hinna RE, Bilal KM, Saad AK. Public perception and willingness towards bystander cardiopulmonary resuscitation (CPR) training and performance in Pakistan. Scripta Medica. 2023;54(4):371-8.

[34]. García NA, Vargas M. CPR and AED Use Training: Strengthening Emergency Response in High School Students. SCT Proceedings in Interdisciplinary Insights and Innovations. 2025;3:479.

[35]. Fariduddin MN, Siau CS. Readiness to Teach and Perform CPR: A Survey Amongst Secondary School Teacher in Malaysia. J Public Hlth Dev. 2022;20(1):267-76.

[36]. Kavetha C, Khor J, Ardini N, Haziq M, Hanis A. CPR Knowledge and Attitude among Secondary School Students in Negeri Sembilan, Malaysia. Ameri J Clin Med Re: AJCMR-208. 2025.

[37]. Liaw SY, Chew KS, Zulkarnain A, Wong SS, Singmamae N, Kaushal DN, Chan HC. Improving perception and confidence towards bystander cardiopulmonary resuscitation and public access automated external defibrillator program: how does training program help?. International journal of emergency medicine. 2020 Dec;13(1):13.

ORIGINAL ARTICLE

Idiopathic Inflammatory Myopathy: A Hospital-based Case Review in the State of Perak, Malaysia.

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Abstract

Background: Idiopathic inflammatory myopathy (IIM) is a rare condition characterized by proximal muscle weakness and myositis. It includes dermatomyositis (DM), polymyositis (PM), inclusion body myositis (IBM), and juvenile dermatomyositis (JDM). They may share clinical and histological features but differ in underlying pathophysiology. **Objective:** To assess the diagnostic probabilities, and clinical characteristics of IIM. **Methods:** Clinical data from 50 IIM patients were retrospectively reviewed from Rheumatology and Dermatology clinics across four centres in Perak, Malaysia (2013–2023) and were evaluated using the 2017 The European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) classification criteria for adult and juvenile IIM. **Results:** According to the EULAR/ACR criteria, 98.2% of cases were classified as definite IIM (mean score 10.6), 74.1% as probable (mean score 6.6), and 47.8% as possible (mean score 6.4). IIM was excluded in 36% of patients (mean score 3.9; probability 20.8%). Eighty-four percent had DM, 8% had ADM or PM, with a mean age of 45.9±18.1 years. 95.6% were diagnosed within a year of symptom onset, and 72% showed proximal myopathy, significantly common in DM (P=0.001). Ethnic breakdown showed 46% Chinese, 42% Malay, and 8% Indian patients, with Malays developing DM at a younger age (39.8±16.9 years). The shawl sign and telangiectasia were more common in Chinese (P=0.018) and Malay (P=0.023) patients, respectively. **Conclusion:** The EULAR/ACR scoring system effectively identified IIM subgroups. Despite varying probabilities, cases of both DM and ADM were classified into definite, probable, and possible categories, with or without biopsy data. DM was more prevalent than ADM, primarily affecting Chinese patients, while Malays had earlier onset.

Keywords: *Amyopathic dermatomyositis, clinical characteristics, dermatomyositis, EULAR/ACR criteria, idiopathic inflammatory myopathy, polymyositis.*

Introduction

Idiopathic inflammatory myopathy (IIM) is a rare group of chronic immune-mediated inflammatory myopathies that characteristically present with myopathy or myositis and a spectrum of clinical manifestations. It is classified into dermatomyositis (DM), amyopathic dermatomyositis (ADM), polymyositis (PM), inclusion body myositis (IBM), and juvenile dermatomyositis (JDM). The exact pathogenetic process of IIM is still unknown, but it is believed to involve genetic and environmental factors, including HLA alleles and viral triggers [1]. They may share clinical features but may be distinguished by certain specific presentations and histopathology findings. Nevertheless, cutaneous involvement is more common in DM. The patients may present with classical cutaneous lesion alone or with concomitant progressive myopathy and may develop complications such as pulmonary fibrosis and malignancy. Cutaneous manifestations may precede myositis by three to six months in 30-50% of patients, and 10% may present with myositis prior to the onset of cutaneous lesions [2,3]. DM with predominantly cutaneous phenotype without myopathy is classified as clinically amyopathic DM (CADM) which includes the amyopathic DM (ADM) and hypomyopathic DM (HDM) [3, 4, 5]. Due to the heterogeneity of IIM, the Bohan and Peter and the 2017 American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) criteria in the classification of myositis are widely used [6,7]. These criteria classify IIM into 'definite', 'probable' and 'possible' categories. Developed by EULAR/ACR in 2017, they enable better identification of IIM subgroup including juvenile IIM.

DM commonly affects middle-aged adult female. The prevalence and incidence of DM, however, vary widely with different geographical distributions and research methodology from previous reports [8,9,10]. Myositis-specific antibodies (MSA) and myositis-associated antibodies (MAA) such as the anti-melanocyte differentiation-associated gene 5 (MDA5) and anti-transcriptional intermediary factor 1 gamma (TIF1-γ) antibodies are important markers in determining the risk of DM or ADM developing interstitial lung disease (ILD) and malignancy.

Methods

This is a descriptive study analysing the clinical presentation of DM and PM patients in Perak state, Malaysia. The DM/PM patients in this study were ascertained based on a confirmed diagnosis by the rheumatologist according to the 2017 European League Against Rheumatism/
American College of Rheumatology (EULAR/ACR) classification criteria for adult and juvenile idiopathic inflammatory myopathies (IIM) [7]. Subgroups of IIM were determined by using scoring systems according to the criteria. Since DM is a considerably rare disease, all patients with confirmed diagnoses by the rheumatologist in the 10-year study period between 2013 and 2023 and currently still on follow-up were included in this study. Patients with myositis secondary to other causes such as drug-induced, electrolyte derangement (hypokalaemia), diabetes, thyroid disease, and neurological disorders as well as patients with no documented clinical and laboratory evidence of DM or PM were excluded.

Clinical data were retrieved from the patient medical records. The diagnostic criterion for DM includes classical cutaneous lesions, skin biopsy, clinically significant myopathy evaluated by electromyography (EMG), muscle enzymes i.e., creatine kinase ([CK], 24-173 IU/L), lactate dehydrogenase ([LDH], 20-350 IU/L), alanine aminotransferase ([ALT],10-36 IU/L), aspartate aminotransferase ([AST], 10-36 IU/L), muscle biopsy, myositis-specific or myositis-associated autoantibodies (MSA, MAA). The MSA profiles (anti-Jo-1 (histidyl-), anti-PL-7 (threonyl-), anti-PL-12 (alanyl-), anti-EJ (glycol-), anti-OJ (isoleucyl-tRNA synthetase), anti-KS (asparaginyl-), anti-SRP (signal recognition particle), anti-Mi-2, anti-TIF1-γ, anti-SAE (small ubiquitin-like modifier activating enzyme), anti-NXP-2 (nuclear matrix protein 2), anti-MDA5

(anti-melanoma differentiation-associated protein 5), and MAA profiles (anti-PM-Scl 75, anti-PM-Scl 100, anti-Ku, and anti-SS-A/Ro-52 kDa) were done by outsourcing the tests due to unavailability in public hospitals. Data extracted from the patient's clinical notes were demographics, cutaneous features, comorbidities (including malignancy, ILD), muscle enzymes, erythrocyte sedimentation rate ([ESR], <20 mm/1st hour), high sensitivity C-reactive protein ([CRP], <5 mg/L), serological and immunological markers (antinuclear antibody [ANA], extractable nuclear antigen panel [ENA], MSA, MAA), skin and muscle biopsy, electromyography (EMG), and imaging report (magnetic imaging resonance, MRI and high-resolution computed tomography (HRCT) if available.

Statistical analysis

Statistical analysis was performed using RStudio version 2023.06.1+524 (Mountain Hydrangea). Descriptive analysis was performed and presented as frequencies and proportions. The Fisher exact test was used to determine the significant association between the exploratory variables (i.e., the demographic and the clinical characteristics) and the type of myositis (i.e., DM or ADM). A p-value of less than 0.05 was considered statistically significant.

Results

Table 1 and 2 show distinct clinical features between Dermatomyositis (DM) and Amyopathic Dermatomyositis (ADM), with DM typically presenting with more significant muscle involvement, higher CK levels, positive ANA, and a greater risk for associated malignancy and ILD. Overall, the clinical features vary across gender and ethnicity in IIM patients. MSA and MAA show a variety of autoantibodies across ethnic groups and genders.

Most patients were diagnosed in adulthood, with a mean age of 45.9 years (SD = 18.1). However, seven patients were diagnosed during childhood (under 18 years of age). Among the DM (Dermatomyositis) patients, the majority were female, with a male-to-female ratio of 1:4. The largest proportion of patients were of Chinese descent, accounting for nearly half of the total (46.0%), followed by Malays at 42.0%, Indians at 8.0%, and others at 4.0%. There was no significant difference in the cutaneous features between DM and ADM. Shawl sign was the most common cutaneous lesion observed in Chinese ethnic group (P=0.018). There was a statistically significant difference in mean CK levels between DM, ADM and PM (P=0.016).

The probability scores for the IIM subgroups in Table 3 suggest that DM patients are more likely to meet the Definite IIM criteria, followed by ADM patients. There is also a notable portion of DM patients (n = 14) classified as non-IIM, indicating some overlap or uncertainty in the classification. PM patients are less represented in the table, but those included are close to the Definite IIM category. The EULAR/ACR classification criteria help stratify patients based on the likelihood of having IIM, with most patients falling into the Definite or Probable IIM categories.

Table 4 shows that the Definite and Probable IIM groups predominantly received a mix of traditional DMARDs and steroids. Non-IIM patients received more specialized treatments like rituximab and IV immunoglobulin. The Possible group received fewer treatments, with no patients in this category receiving multiple DMARDs, steroids, or NSAIDs. This treatment approach reflects a focus on controlling the autoimmune response in confirmed cases of IIM while more targeted therapies are employed in ambiguous or non-IIM diagnoses.

Discussion

The incidence of IIM has been reported as 11 per million person-years (10 for men and 13 for women) and a prevalence of 14/100,000 [11]. Whereas the global incidence and prevalence of DM vary widely from 1.97 to 21.5 per 100,000 population respectively [4,8,10,12].

In this study, the 2017 EULAR/ACR criteria for IIM were successfully used to classify IIM into subgroups according to the scores based on the suggested domains in the criteria. The probability of being classified as 'definite' for DM, ADM, and PM were 98.2%, 99.5%, and 97%, corresponding to scores of 10.4, 10.6, and 10.2, respectively. These results were consistent with the EULAR/ACR criteria, which define 'definite IIM' as a probability of ≥90%, with a score of ≥7.5 (≥8.7 with muscle biopsy). For 'probable' IIM, the probabilities for DM and ADM were 72.3% and 87.8%, corresponding to scores of 6.5 and 7.3, respectively, consistent with the criteria, which set the probability cut-off at 55%, corresponding to a score of 5.5 (6.7 with muscle biopsy). For DM, the probability of being classified as 'possible' was 47.8%, corresponding to a score of 6.4, which falls within the probability range of ≥50% to <55%.

IIM was ruled out in 18 patients, as their calculated probabilities were 21.2% and 17.3%, with scores of 3.9, 4.2 and 3.6 for DM, ADM and PM, respectively. These scores were below the 50% probability threshold, with scores lower than 5.3 (<6.5 with muscle biopsy) according to the criteria. These patients were categorized as non-IIM due to insufficient evidence in the criteria. However, despite the absence of certain criteria features, these patients were still treated as IIM cases, as they presented other signs such as myopathy, shawl sign, poikiloderma, and arthritis, which are not included in the scoring criteria. Therefore, while their probability scores did not meet the criteria for IIM, clinical judgment led to their continued treatment.

Females were found to have a greater risk of developing IIM, with a 2:1 female-to-male ratio, and the mean age of diagnosis among adults is between 40 and 60 years in other studies [4,13,14]. However, in this study, although a female preponderance is consistent with previous reports, the ratio was higher i.e., 4:1, which is almost similar to that in the study by Dourmishev i.e., 3.75:1[15]. This discrepancy is likely attributable to the multiethnic nature of this cohort. The mean age at diagnosis were 45.9±18.0 year for DM in this cohort, consistent with most reports in the literature [16, 17]. The age onset for JDM was 11 years old. DM was found to be common in Chinese ethnic group which is consistent with the study by Tong in Malaysia although the number was very small i.e., only eight patients [18]. The mean duration from birth to the onset of development of cutaneous manifestations was 11.2±6.4 years in JDM. The majority of patients were diagnosed in the same year when they developed the symptoms.

The term ADM was first coined by Carl Pearson [19] and recognized as a subtype of DM characterized by biopsy-confirmed cutaneous lesions, which are the hallmarks of DM, occurring for six months or longer with no clinical evidence of proximal myopathy and no serum muscle enzyme abnormalities [20]. It had been regarded and classified as a distinct entity among the spectrum of IIMs by Hoogendijk *et al*. in 2004 [21]. The incidence of ADM had been reported at 10% to 20% [4, 22] and was higher in Asian population (10% of DM cases) [5,23]. ADM is more often associated with fatal rapidly progressive interstitial lung disease (RP-ILD) and malignancy as compared to DM [4]. One ADM patient in this cohort with the presence of anti-MDA-5 antibodies had developed RP-ILD. This patient remains in clinical remission without development of malignancy over more than a three-year period.

In this study, the classical cutaneous manifestations i.e., heliotrope rash, Gottron's papules, poikiloderma, and photosensitivity occurred in both DM and ADM. Among the cutaneous lesions, Shawl's sign was commonly seen in Chinese ethnic group in this study (P = 0.018) compared to other ethnic groups. Although JDM and DM share common characteristics, cutaneous lesions especially calcinosis with skin ulceration were commonly found in JDM [24].

However, in the cohort of this study, these skin lesions were not documented in detail in the medical record.

Antinuclear antibody (ANA) is positive in more than 50% in confirmed cases of DM from previous report [25]. In this study, ANA was positive in 58% of patients. The relevancy of ANA in DM is still uncertain. There was no significant association between positive ANA with the cutaneous lesions of DM or the risk of malignancy in this study, similar to findings by Hoesly *et. al.* [25]. Four patients with DM were overlapped with systemic lupus erythematosus with positive anti-dsDNA.

DM has been recognized as paraneoplastic in established studies, estimated between 7% to 33% of DM patient particularly of adult onset [26,27]. MSA has been considered as important biomarker which provides guidance to the classifications of the disease and organ-specific involvement as well as the risk of malignancy [28]. However, it has been shown to be a poor diagnostic tool in DM patients [29] a finding supported by the present cohort. The presence of MSA i.e., anti-NXP-2 or anti-TIF1-γ antibodies, were found to be associated with the risk of malignancy [30, 31]. The prevalence of anti-TIF1-γ antibody is estimated to be between 18-35% in JDM [32]. The anti-TIF1-γ was positive in one of the juvenile-onset ADM and two DM patients in this study. Presence of anti-TIF1-γ in JCADM has been shown to have no association with risk of malignancy compared to adult DM or ADM [33] and the cutaneous lesions may take longer time to resolve. Meanwhile, among patients with the MSA test performed in this cohort, anti-Mi-2 autoantibodies were present in five (10%) of the CDM cases and none of them demonstrated any evidence of malignancy. The prevalence of anti-Mi-2 autoantibodies is estimated from 2% to 38% in adults with DM [26]. In contrast to anti-NXP-2 or anti-TIF1-γ, patients with anti-Mi-2 autoantibodies in general, had shown a lower risk of malignancy and a better response to treatment with better prognosis [34]. Adult DM had been reported to be commonly associated with occurrence of malignancy and interstitial lung disease (ILD) compared to JDM [35]. These complications of adult DM (ILD 83.3%, malignancy 10%) in this study had demonstrated similar incidence although the number was small and limited. However, among the patients with malignancy in this study who had the MSA test done, the antibodies were found to be negative.

In this study, skin biopsies were performed in 34% of patients as compared to muscle biopsies (20%). The majority of patients did not consent to or were not keen on muscle biopsy due to logistic problems. For those who had skin or muscle biopsies, the results were consistent with dermatomyositis and inflammatory myopathy changes, respectively. Electromyography (EMG) study findings were indicative of the disease in 24% of patients who underwent the procedure. However, EMG findings in DM are neither specific nor sensitive and may be negative or normal in 11% of patients [12]. A study by Constantinides *et al* revealed that muscle biopsy yielded excellent diagnostic accuracy compared to EMG (90% vs 70% respectively) [36]. In this study, the discordance between EMG and muscle biopsy findings was likely due to a significant number of patients who did not undergo these investigations and for those who had these tests done, there were normal biopsy findings despite myopathic EMG changes.

Corticosteroid and immunosuppressant had been the mainstay of treatment in all DM patients at any time period during the course of the disease, similar to all reviewed studies [37]. Anti-malarial drug (hydroxychloroquine) in combination with corticosteroid were used in majority of patients. Azathioprine (AZA) and methotrexate (MTX) were prescribed as corticosteroid-sparing agent and for patient who failed to respond to corticosteroid alone. MTX was more often used compared to AZA. It is evident that methotrexate is an effective corticosteroid-sparing agent to

treat the cutaneous lesions in DM [38]. Pulse intravenous (IV) cyclophosphamide (CYC) monthly was given to patients who were refractory to other immunosuppressants including corticosteroids especially those with ILD. Study by Shahin *et al* had indicated that CYC improves clinical response especially in refractory myositis [39]. Nine patients with severe cutaneous DM were administered with IV immunoglobulin (Ig) and better response to treatment was observed. However, due to its high cost, IVIg was only administered for short periods of time. Three patients who were resistant to steroid and other standard treatment were given rituximab (RTX).

Limitations of the study

This study's limitations are primarily due to the use of secondary data. A significant amount of missing data was encountered as information was extracted from medical records. Incomplete clinical and laboratory documentation further contributed to discrepancies in the study's results. Although myositis-specific antibodies (MSA) and myositis-associated antibodies (MAA) are crucial for diagnostic evaluation of idiopathic inflammatory myopathies (IIM), these tests have only been available in the Malaysian private hospitals over the past decade. Their high costs had made them inaccessible for many patients, with nearly half declining testing. As a result, only antinuclear antibody (ANA) and extractable nuclear antigens (ENA), which are available in public hospitals, were tested. Additionally, other essential ancillary tests such as muscle biopsy and MRI were also limited due to logistical challenges.

Conclusion

This study shows IIM is relatively uncommon in this region. The utility of the EULAR/ACR criteria is useful for diagnosing idiopathic inflammatory myopathies (IIM), even with its limitations. IIM should still be considered if clinical signs and lab findings suggest it—even if these features are not part of the diagnostic scoring system. DM was most common IIM subtype, more prevalent than polymyositis or inclusion body myositis.

Malay females were diagnosed with DM at a younger age, pointing to potential genetic or environmental factors. Additionally, DM was more common in the Chinese ethnic group, which suggests an ethnic predisposition. Rare complications such as ILD and malignancy were not commonly observed in the study population, indicating that these severe outcomes may not be as prevalent in this specific cohort.

These findings can help guide clinicians in recognizing DM in the Malaysian context and highlight the importance of early diagnosis, particularly in specific ethnic and gender groups. Further research may be needed to explore underlying reasons for the observed ethnic variations and the infrequent complications in this population.

Ethical approval

This study was approved by the Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia (NMRR ID-23-01339-CWA) and the Universiti Kuala Lumpur Royal College of Medicine Perak Ethics Committee.

Authors' contributions

WS, ASSC, AFI, AH, ANZ, MAKHM, SKNAN, OPS, TJJ, LEL, NMH, PVRD, LHS responsible for conceptualizing, collecting clinical data; WS for report writing, and finalizing the manuscript; NAA for statistical analysis.

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Conflict of interest

None.

Table 1. Demographic and clinical characteristics of classical DM and ADM (N=50)

		Total n (%)	DM n (%)	ADM n (%)	PM n (%)	*p*
Patients (n/%)		50 (100)	41(82.0)	5(10.0)	4 (8.0)	
Gender	Male	10 (20)	7(70)	2 (20)	1 (10)	0.305
	Female	40 (80)	34 (85.0)	3 (7.5)	3(7.5)	
Ethnicity	Chinese	23 (46)	20 (87.0)	2 (8.7)	1 (4.35)	0.709
	Malay	21 (42)	16 (79.2)	2 (9.5)	3(14.3)	
	Indian	4 (8)	3 (75.0)	1 (25.0)	0	
	Others	2 (4)	0	2 (100)	0	
Age at diagnosis (Mean ± SD)		45.9 (±18.1)	46.8 (±18.0)	45.8 (±20.5)	37.8 (±18.9)	
Age of Onset	< 18 years old	7 (14.0)	5 (71.4)	1 (14.3)	1 (14.3)	0.185
	18-39.9	9 (18.0)	7(77.8)	0	2 (22.2)	
	40 and above	34 (68.0)	29 (85.3)	4 (11.8)	1 (2.9)	
Duration from onset of symptoms to diagnosis	< 1 year	43 (95.6)	37 (86.1)	4 (9.3)	2 (4.6)	0.290
	1 to 2 years	2 (4.4)	1(50)	1 (50)	0	
Cutaneous manifestations	Gottron's papule	28 (56.0)	22 (78.6)	5(17.9)	1(3.6)	0.061
	Heliotrope	26 (52.0)	21 (80.8)	4 (15.4)	1(3.9)	0.306
	Shawl sign	14 (28.0)	12 (85.7)	2 (14.3)	0	0.502
	Alopecia	10 (20.0)	7 (70.0)	3 (30.0)	0	0.070
	V sign	7 (14.0)	5 (71.4)	2 (28.6)	0	0.220
	Poikiloderma	6 (12.0)	4 (66.7)	2 (33.3)	0	0.165
	Telangiectasia	6 (12.0)	4 (66.7)	2 (33.3)	0	0.165
	Mechanic's hand	1 (2.0)	1	0	-	-
Proximal myopathy		36 (72.0)	32 (88.9)	0	4(11.1)	**0.001**
Skin Biopsy	Done	17 (34.0)	14 (82.4)	3(17.7)	0	-
Muscle Biopsy	Done	10 (20.0)	9 (90)	0	1 (10.0)	
EMG	Done	**12 (24)**	11(91.7)	0	1(8.3)	
Laboratory:	Raised CK	33 (66.0)	29 (87.9)	-	4 (12.1)	**0.002**
	CK (Mean±SD)	3802.7(±6654.6)	3975.3(±6837.6)	113.2(±57.2)	6645.3(±8127.2)	**0.016**
	LDH(Mean±SD)	628.1 (± 610.1)	588.5(± 554.3)	372(±182.4)	2088	0.258
	AST (Mean±SD)	176.1 (± 269.0)	192.2 (±285.2)	17.5(±2.121)	118.25(± 147.2)	0.118
	ESR (Mean±SD)	36.5 (± 25.8)	36.7(±26.0)	27.4 (± 10.73)	45.7 ((± 38.6)	0.816
	Positive ANA	29 (58.0)	28 (96.5)	1 (3.5)	0	**0.001**
Interstitial lung disease (ILD)		6 (12.0)	5 (83.3)	1 (16.7)	0	0.717
Malignancy		5 (10.0)	4 (80.0)	0	1(20.0)	0.407

DM, dermatomyositis; ADM, amyopathic dermatomyositis; PM, polymyositis; EMG, electromyography; CK creatine kinase, ESR, erythrocyte sedimentation rate; ANA, anti-nuclear antibody; ILD, interstitial lung disease
P-value < 0.05 is considered significant.

Table 2. Clinical characteristics by major ethnic groups and genders.

Clinical characteristic	Gender n (%)		P	Ethnicity n (%)				P
	Male	Female		Malay	Chinese	Indian	Others	
Age at diagnosis (Mean±SD)	42.9±20.9	46.7±17.5	-	39.8±16.9	50.4±19.1	48.0±9.1	55.5±23.3	
Cutaneous lesions:								
Gottron's papule	7 (25.0)	21 (75.0)	0.263	11 (39.3)	14 (50.0)	2 (7.1)	1 (3.6)	0.955
Heliotrope	5 (19.2)	21 (80.8)	1.000	12 (46.2)	12 (46.2)	1 (3.9)	1 (3.9)	0.785
Shawl sign	3 (21.4)	11 (78.6)	1.000	2 (14.3)	8 (57.1)	3 (21.4)	1 (7.1)	**0.018**
Alopecia	0	10 (100.0)	0.179	6 (60.0)	3 (30.3)	1 (10.5)	0	0.546
V sign	2 (28.6)	5 (71.4)	0.616	1 (14.3)	4 (57.1)	2 (28.6)	0	0.100
Poikiloderma	0	6 (12.0)	0.327	3 (50.0)	2 (33.3)	1 (16.7)	0	0.546
Telangiectasia	0	6 (100)	0.327	4 (66.7)	0	1 (16.7)	1 (16.7)	**0.023**
Mechanic's hand	0	1 (100)	-	0	1	0	0	-
Laboratory:								
Raised CK	7 (21.2)	26 (78.8)	0.765	15 (45.5)	14(42.4)	3(9.1)	1(3.1)	0.821
ESR (Mean ± SD)	22.1(±19.7)	39.97(±26.1)	**0.021**	42.0(±28.6)	31.9(±25.3)	30.3(±11.9)	38.5(±9.2)	0.606
Positive ANA	3 (10.3)	26 (89.7)	**0.048**	12 (41.4)	13 (44.8)	2 (6.9)	2 (6.9)	0.498

CK, creatine kinase; ESR, erythrocyte sedimentation rate; ANA, anti-nuclear antibody;
P-value < 0.05 is considered significant.

Table 3. Classification of IIM according to EULAR classification criteria scoring.

IIM	n	Mean Score ± SD	Mean Probablity (%) ± SD	Diagnosis	n	Mean_Score ± SD	Mean Probability (%) ± SD
Definite_IIM	19	10.6 ± 2.08	98.2± 2.13	PM	1	10.2	97.6
				DM	16	10.7 ± 2.28	98± 2.28
				ADM	2	10.6	99.5
Probable_IIM	12	6.64 ± 0.71	74.1±10.5	PM	0		
				DM	11	6.58± 0.711	72.8 ± 10
				ADM	1	7.3	87.8
Possible_IIM	1	6.4	47.8	PM	0		
				DM	1	6.4	47.8
				ADM	0		
Non-IIM	18	3.86 ± 1.10	20.8± 15.6	PM	3	3.6±0.87	17.3 ± 13.2
				DM	14	3.89 ± 1.2	21.2 ± 16.9
				ADM	1	4.2	24.4

DM, dermatomyositis; ADM, amyopathic dermatomyositis; PM, polymyositis; IIM, Idiopathic Inflammatory Myositis.

Table 4. Treatment administered.

	Definite		Probable		Possible		Non-IIM	
	n	%	n	%	n	%	n	%
DMARDs								
Methotrexate	5	26.3	6	50	-	-	2	11.1
Cyclosporine	2	10.5	1	8.3	-	-	2	11.1
Hydroxychloroquine	9	47.4	10	83.3	1	100	7	38.9
Mycophenolate mofetil	2	10.3	1	8.3	-	-	1	5.6
Azathioprine	9	47.4	6	50	-	-	5	27.8
≥ 2 cDMARDs	8	42.1	8	66.7	-	-	4	22.2
≥ 3 cDMARDs	1	5.3	4	33.3	-	-	-	-
Steroids	19	100	11	91.7	-	-	15	83.3
NSAIDs	4	21.1	1	8.3	-	-	2	11.1
Combined treatment								
cDMARDs+Steroid	17	89.5	10	83.3	-	-	13	72.2
Other treatment								
Rituximab	2	10.5	-	-	-	-	1	5.6
IV Ig	1	5.3	1	8.3	-	-	7	38.9

Percentage per column total.
NSAIDs, non-steroidal anti-inflammatory drugs; cDMARDs, conventional disease modifying agent for rheumatic diseases; IV Ig, intravenous immunoglobulin.

References

[1]. Mandel DE, Malemud CJ, Askari AD. Idiopathic inflammatory myopathies: A review of the classification and impact of pathogenesis. International journal of molecular sciences. 2017; 18(5):1084.

[2]. Callen JP. Cutaneous manifestations of dermatomyositis and their management. Current rheumatology reports. 2010; 12:192–7.

[3]. Sontheimer RD. The management of dermatomyositis: Current treatment options. Expert opinion on pharmacotherapy. 2004; 5(5):1083–99.

[4]. Bendewald MJ, Wetter DA, Li X, Davis MD. Incidence of dermatomyositis and clinically amyopathic dermatomyositis: A population-based study in Olmsted County, Minnesota. Archives of dermatology. 2010; 146(1):26–30.

[5]. Sontheimer RD. Dermatomyositis: An overview of recent progress with emphasis on dermatologic aspects. Dermatologic clinics. 2002; 20(3):387–408.

[6]. Bohan A, Peter JB. Polymyositis and dermatomyositis: (First of two parts). New England Journal of Medicine. 1975; 292(7):344–7.

[7]. Lundberg IE, Tjärnlund A, Bottai M, Werth VP, Pilkington C, Visser M de, *et al*. EULAR/ACR classification criteria for adult and juvenile idiopathic inflammatory myopathies and their major subgroups. Annals of rheumatic diseases. 2017; 76(12):1955.

[8]. Ohta A, Nagai M, Nishina M, Tomimitsu H, Kohsaka H. Prevalence and incidence of polymyositis and dermatomyositis in Japan. Mod Rheumatol. 2014; 24(3):477-80.

[9]. Osman M, Martins KJB, Wong KO, Vu K, Guigue A, Cohen JW, *et al.* Incidence and prevalence, and medication use among adults living with dermatomyositis: an Alberta, Canada population-based cohort study. Sci Rep 2023; 13**:**16444.

[10]. Kronzer VL, Kimbrough BA, Crowson CS, Davis JM III, Holmqvist M, Ernste FC. Incidence, Prevalence, and Mortality of Dermatomyositis: A Population-Based Cohort Study. Arthritis Care Res 2023; 75:348-355.

[11]. Svensson J, Arkema EV, Lundberg IE, Holmqvist M. Incidence and prevalence of idiopathic inflammatory myopathies in Sweden: a nationwide population-based study. Rheumatology. 2017;56:802–10.

[12]. Tan JA, Roberts-Thomson PJ, Blumbergs P, Hakendorf P, Cox SR, Limaye V. Incidence and prevalence of idiopathic inflammatory myopathies in South Australia: a 30-year epidemiologic study of histology-proven cases. Int J Rheum Dis. 2013;16(3):331-8.

[13]. DeWane ME, Waldman R, Lu J. Dermatomyositis: Clinical features and pathogenesis. J Am Acad Dermatol. 2020; 82(2):267-281.

[14]. Abu Mansor Matardiah NH, Mohd A, Ali RA. A review of idiopathic inflammatory myopathy cases in Terengganu, Malaysia: A single centre experience. The Medical journal of Malaysia. 2012; 76:488-492.

[15]. Dourmishev LA. Dermatomyositis associated with malignancy. 12 case reports. Adv Exp Med Biol. 1999; 455:193-9. doi:10.1007/978-1-4615-4857-7_28.

[16]. Neely J, Ardalan K, Huber A, Kim S; Childhood Arthritis and Rheumatology Research Alliance Investigators. Baseline characteristics of children with juvenile dermatomyositis enrolled in the first year of the new Childhood Arthritis and Rheumatology Research Alliance registry. Pediatr Rheumatol Online J. 2022; 20(1):50. doi:10.1186/s12969-022-00709-3.

[17]. Nitiyarom R, Charuvanij S, Likasitwattanakul S, Thanoophunchai C, Wisuthsarewong W. Juvenile dermatomyositis in Thai children: Retrospective review of 30 cases from a tertiary care center Indian. J Dermatol Venereol Leprol 2022; 88:162-70.

[18]. Tong M. A Review of Dermatomyositis Cases at Hospital Besar Kuala Lumpur 1989 - 1993. Med J Malaysia. 1995; 50(1):32-26.

[19]. Dourmishev LA, Assen Lyubenov Dourmishev, Springerlink (Online Service. Dermatomyositis: Advances in Recognition, Understanding and Management. Berlin, Heidelberg: Springer Heidelberg; 2009. 65-68.

[20]. Euwer RL, Sontheimer RD. Amyopathic dermatomyositis (dermatomyositis sine myositis) Presentation of six new cases and review of the literature. J Am Acad Dermatol. 1991; 24:959–66.

[21]. Hoogendijk JE, Amato AA, Lecky BR, Choy EH, Lundberg IE, Rose MR, et al. 119th ENMC international workshop: trial design in adult idiopathic inflammatory myopathies, with the exception of inclusion body myositis, 10–12 October 2003, Naarden, The Netherlands. Neuromuscul Disord. 2004; 14:337–45.

[22]. Gerami P, Schope JM, McDonald L, Walling HW, Sontheimer RD. A systematic review of adult onset Clinically amyopathic dermatomyositis (dermatomyositis sine myositis): a missing link within the spectrum of the idiopathic inflammatory myopathies. J Am Acad Dermatol 2006; 54(4):597–613.

[23]. Tang K, Zhang H, Jin H. Clinical Characteristics and Management of Patients with Clinical Amyopathic Dermatomyositis: A Retrospective Study of 64 Patients at a Tertiary Dermatology Department. Front Med (Lausanne). 2021; 8:783416.

[24]. Rider LG, Lachenbruch PA, Monroe JB, Ravelli A, Cabalar I, Feldman BM, et al. IMACS Group. Damage extent and predictors in adult and juvenile dermatomyositis and polymyositis as determined with the myositis damage index. Arthritis Rheum. 2009; 60:3425–3435.

[25]. Hoesly PM, Sluzevich JC, Jambusaria-Pahlajani A, Lesser ER, Heckman MG, Abril A. Association of antinuclear antibody status with clinical features and malignancy risk in adult-onset

dermatomyositis. J Am Acad Dermatol. 2019; 80(5):1364-1370.

[26]. Aussy A, Boyer O, Cordel N. Dermatomyositis and immune-mediated necrotizing myopathies: a window on autoimmunity and cancer. Front Immunol. 2017; 8:992

[27]. Chen H, Peng Q, Yang H, Yin L, Shi J, Zhang Y, et al. Increased Levels of Soluble Programmed Death Ligand 1 Associate with Malignancy in Patients with Dermatomyositis. J Rheumatol. 2018; 45(6):835-840.

[28]. Satoh M, Tanaka S, Ceribelli A, Calise SJ, Chan EK. A Comprehensive Overview on Myositis-Specific Antibodies: New and Old Biomarkers in Idiopathic Inflammatory Myopathy. Clin Rev Allergy Immunol. 2017; 52(1):1-19.

[29]. Cassius C, Le Buanec H, Bouaziz JD, Amode R. Biomarkers in Adult Dermatomyositis: Tools to Help the Diagnosis and Predict the Clinical Outcome. J Immunol Res. 2019; 2019:9141420.

[30]. Lu X, Yang H, Shu X, Chen F, Zhang Y, Zhang S, et al. Factors predicting malignancy in patients with polymyositis and dermatomyostis: a systematic review and meta-analysis. PLoS One. 2014; 9(4): e94128.

[31]. Kilinc OC, Ugurlu S. Clinical features of dermatomyositis patients with anti-TIF1 antibodies: A case based comprehensive review. Autoimmun Rev. 2023; 22(12):103464.

[32]. Tansley SL, Simou S, Shaddick G, Betteridge ZE, Almeida B, Gunawardena H, et al. Autoantibodies in juvenile-onset myositis: Their diagnostic value and associated clinical phenotype in a large UK cohort. J Autoimmun. 2017

[33]. Temmoku J, Sato S, Fujita Y, Asano T, Suzuki E, Kanno T, et al. Clinical significance of myositis-specific autoantibody profiles in Japanese patients with polymyositis/dermatomyositis. Medicine (Baltimore). 2019; 98(20):e15578.

[34]. Wolstencroft PW, Fiorentino DF Dermatomyositis clinical and pathological phenotypes associated with myositis-specific autoantibodies. Curr Rheumatol Rep. 2018; 20:28.

[35]. McCann LJ, Juggins AD, Maillard SM, Wedderburn LR, Davidson JE, Murray KJ, et al. Juvenile Dermatomyositis Research Group. The Juvenile Dermatomyositis National Registry and Repository (UK and Ireland) - clinical characteristics of children recruited within the first 5 yr. Rheumatology. 2006; 45:1255–1260.

[36]. Constantinides VC, Papahatzaki MM, Papadimas GK, Karandreas N, Zambelis T, Kokotis P, et al. Diagnostic Accuracy of Muscle Biopsy and Electromyography in 123 Patients with Neuromuscular Disorders. In Vivo. 2018;32(6):1647-1652.

[37]. Dalakas MC, Hohlfeld R. Polymyositis and dermatomyositis. Lancet 2003; 362(9388):971–82

[38]. Kasteler JS, Callen JP. Low-dose methotrexate administered weekly is an effective corticosteroid-sparing agent for the treatment of the cutaneous manifestations of dermatomyositis. J Am Acad Dermatol. 1997; 36(1):67-71.

[39]. Shahin AA, Niazy MH, Haroon MM. Response to cyclophosphamide and rituximab therapy in idiopathic inflammatory myopathies: A single center experience. Egyptian Rheumatologist 2021; 43:247–51.

ORIGINAL ARTICLE

Parental Knowledge, Attitudes, and Concerns Regarding Childhood Febrile Seizures.

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Abstract

Background: Febrile seizures are the most common seizure disorder among young children, often leading to parental anxiety and unnecessary medical interventions. Despite their prevalence, limited research has explored parental knowledge, attitudes, and concerns in Malaysia. **Objective:** This study aimed to assess parental knowledge, attitudes, and concerns regarding febrile seizures among parents in Pahang, Malaysia. **Methods:** A cross-sectional study was conducted among 235 parents of children under five years old in selected kindergartens. Data were collected using a structured questionnaire covering sociodemographic characteristics, knowledge, attitudes, and concerns. Descriptive statistics and chi-square tests were applied. **Results:** The findings revealed that 55.3% of parents had moderate knowledge, with 53.6% believed recurrent febrile seizures could cause brain damage, and 43.8% incorrectly identified them as epilepsy. While 74% demonstrated a positive attitude, a similar proportion (74%) reported high levels of concern, particularly about potential brain damage (mean = 3.54, SD = 0.8) and subsequent epilepsy (mean = 3.38, SD = 0.8). Higher education level ($p < 0.001$) and prior experience with febrile seizures ($p < 0.001$) were significantly associated with better knowledge and attitudes. **Conclusion:** This study highlights persistent misconceptions and significant parental anxiety regarding febrile seizures. Targeted educational interventions are needed to improve parental understanding, alleviate fears, and enhance seizure management at home. Healthcare professionals should implement structured counselling and culturally sensitive communication strategies to support parents effectively.

Keywords: *Febrile seizures, Malaysia, paediatric emergency, parental knowledge.*

Introduction

Febrile seizures are the most prevalent convulsive disorder in young children, primarily affecting those between 6 months and 5 years of age [1]. Fever is one of the most common signs of illness and is the reason for 15-25% of visits to primary health care facilities or emergency departments [1]. In some cases, fever can be managed without medical intervention, but a high fever (temperature exceeding 38 °C), can result in febrile seizures [2].

The prevalence of febrile seizures varies globally and is influenced by a combination of social, economic, environmental, and genetic factors. It is estimated that febrile seizures occur in approximately 4% to 10% of children under the age of six [3]. Roughly one in every 25 children will experience at least one febrile seizure in their lifetime [4]. To date, no published studies in Malaysia have specifically reported the prevalence of febrile seizures. However, existing local data indicate that the average age of affected children is approximately 21 months, with the majority presenting with characteristics typical of simple febrile seizures [5].

Although generally benign and self-limiting, their sudden onset often causes significant distress among parents, frequently leading to misconceptions and undue fear regarding potential long-term neurological consequences [5,6]. These misconceptions contribute to heightened parental anxiety and inappropriate seizure management strategies, resulting in unnecessary emergency department visits and medical interventions, further exacerbating parental anxiety [7-8].

A recent study by Othman et al. [6] assessed the psychological impact of febrile seizures on parents in Malaysia. It indicated that 58.2% of parents experienced anxiety, 29% reported stress, and 23.6% exhibited symptoms of depression. The findings highlight the need for targeted interventions to reduce parental anxiety through education, counselling, and structured support strategies.

Despite the widespread occurrence of febrile seizures, limited research has explored parental knowledge, attitudes, and concerns in Malaysia. Understanding the extent of parental awareness and identifying knowledge gaps is essential for developing targeted educational programs that can empower caregivers with accurate information. By addressing misconceptions and alleviating fears, healthcare professionals can improve parental confidence in managing febrile seizures at home, can ultimately lead to better health outcomes for children. Studies suggest that increased parental education and awareness can lead to better coping mechanisms and reduced anxiety when dealing with febrile seizures [6,8].

Therefore, parental understanding of febrile seizures plays a critical role in shaping their response and management strategies. This study aims to assess the level of knowledge, attitudes, and concerns among parents in Pahang, Malaysia, regarding febrile seizures. By identifying factors influencing parental perceptions, the findings will help inform healthcare professionals on how to structure effective educational interventions that reduce anxiety and enhance parental preparedness in managing febrile seizures.

Materials and methods

This study employed a cross-sectional descriptive design to assess parental knowledge, attitudes, and concerns regarding febrile seizures in children. The study was conducted in selected kindergartens across Pahang, Malaysia, from February to August 2024. The target population was parents of children below five years of age. A total of 235 parents were selected using a simple random sampling method to ensure representativeness. First, a list of registered kindergartens in the selected districts was obtained from the local education department. Several kindergartens were randomly selected, and within each kindergarten, participating parents were chosen through a randomized list provided by the school administrators based on the inclusion criteria.

The study utilized a structured questionnaire consisting of four sections: (i) Sociodemographic

information which collected data on parental age, gender, education level, and employment status, (ii) Parental knowledge, assessing the understanding of febrile seizures, their causes, management, and long-term effects; (iii) Parental attitudes, evaluating perceptions and beliefs regarding febrile seizures, and (iv) Parental concerns, measuring levels of anxiety and worry about seizure episodes and their consequences. The questionnaire was translated into Malay and underwent both reliability and validity assessment. Reliability, measured using Cronbach's alpha, ranged from 0.74 to 0.84 across the sections. Content validity was established through expert evaluation, with a Content Validity Index (CVI) of 0.89, indicating good content relevance and clarity.

Descriptive statistics (mean, standard deviation, frequency, and percentage) were used to analyse sociodemographic characteristics and responses to knowledge, attitude, and concern-related questions. Prior to inferential analysis, the normality of continuous variables was assessed using the Shapiro-Wilk test. Since the data did not meet the assumptions for parametric testing, the chi-square test was used to evaluate associations between sociodemographic factors and levels of parental knowledge, attitudes, and concerns. Statistical significance was set at $p < 0.05$.

Ethical approval was obtained from the International Islamic University Malaysia (IIUM) Research Ethics Committee (IREC), ID number: IREC 2024-130. Participants were informed about the study objectives, assured of confidentiality, and provided written informed consent before participation.

Results

Profile of the parents

Table 1 presents the profile of the parent participants. The study sample consisted of 235 parents, with a higher proportion of mothers (57.0%) compared to fathers (43.0%). A significant majority (75.3%) had attained tertiary education, while 24.7% had secondary education. More than half of the participants (52.8%) were employed in the public sector, 28.9% worked in the private sector, and 18.3% were housewives or unemployed. Regarding past experiences with febrile seizures, 41.7% of parents reported that their child had experienced at least one febrile seizure. However, only 40% of parents were present during the seizure episode, potentially influencing their level of knowledge and concern.

Parents' knowledge on childhood febrile seizure

Table 2 highlights varying levels of understanding and misconceptions among parents regarding the management and implications of febrile seizures in children. The findings revealed a mixed level of knowledge. Although all parents correctly identified that anticonvulsant drugs are not required for every child with febrile seizures, 50.2% were uncertain about this fact. A significant misconception observed was that 53.6% of parents believed recurrent febrile seizures could cause brain damage, while 37.9% were unsure. Similarly, 43.8% of parents incorrectly classified febrile seizures as epilepsy. Additionally, nearly half of the parents (49.4%) were unsure whether children with febrile seizures could receive immunizations on schedule. These findings indicate substantial gaps in knowledge, emphasizing the need for targeted educational interventions to address misconceptions.

Parents' attitudes towards childhood febrile seizure

Overall, parents demonstrated moderate to positive attitudes toward febrile seizures. Parents strongly agreed that children with febrile seizures require extra attention and care (mean = 3.16, ±0.7) and believed that febrile seizures could be outgrown (mean = 3.1, ±0.6). However, concerns persisted regarding the potential for brain damage (mean = 3.2, ±0.7) and the risk of febrile seizures developing into epilepsy (mean = 2.84, ±0.6). Interestingly, traditional beliefs, such as febrile seizures being caused by spirits (mean = 1.22, ±0.8), were largely rejected. However, moderate

reliance on traditional medicine was observed (mean = 3.26, ±0.8), suggesting the importance of culturally sensitive health education to dispel misconceptions while respecting cultural beliefs.

Parents' concerns regarding childhood febrile seizure

Parental concerns in this study were assessed using 10 specific items (as detailed in Table 4). The most frequently cited concerns included fear of potential brain damage (mean = 3.54, ±0.8) and the possibility of subsequent epilepsy (mean = 3.38, ±0.8). Concerns about recognizing seizure attacks early (mean = 3.14, ±0.8) and managing seizures effectively (mean = 3.3, ±0.7) were also significant. Interestingly, parents showed less concern about febrile seizures occurring at night (mean = 1.51, ±1.1) or frequent fever episodes (mean = 1.9, ±0.6).

Level of knowledge, attitude, and concern of parents regarding febrile seizure in children

Figure 1 illustrates the overall distribution of parental knowledge, attitudes, and concerns regarding febrile seizures. To categorize these levels, cut-off scores were used as follows: knowledge was classified as good (scores ≥5) and poor (scores <5); attitude as positive (≥80% of total score) and negative (<80%); concern as high (≥80%) and low (<80%), based on the total concern score.

The findings showed that while a majority of parents demonstrated moderate knowledge (55.3%), misconceptions remain prevalent, particularly concerning the risks and long-term effects of febrile seizures. Attitude scores generally reflect a positive outlook, with parents expressing concern and a willingness to learn more about managing febrile seizures. However, high levels of concern persist (74%), particularly regarding fears of brain damage and epilepsy, highlighting the need for targeted health education initiatives to enhance parental confidence and reduce anxiety.

Association between sociodemographic profile with knowledge, attitude and concern of parents regarding febrile seizure among children

Table 5 presents the associations between selected sociodemographic profile and parental knowledge, attitudes, and concerns regarding febrile seizures. The analysis demonstrated significant associations between certain sociodemographic profile and parental knowledge and attitudes regarding febrile seizures.

Mothers showed significantly better knowledge and more positive attitudes compared to fathers ($p < 0.05$; $X^2 = 10.49$, df = 1). Educational level also played a key role, with parents holding tertiary education showing higher knowledge and attitude scores ($p < 0.001$; $X^2 = 14.53$, df = 2). Similarly, employment in the public sector was associated with better knowledge ($p < 0.001$; $X^2 = 37.26$, df = 2). Prior experience with febrile seizures either through one's own child or another sibling was significantly associated with improved knowledge and attitudes ($p < 0.001$; $X^2 = 40.70$, df = 2). While concern levels were not significantly influenced by most sociodemographic variables, parents who had another child with a history of febrile seizures reported significantly higher levels of concern ($p < 0.05$; $X^2 = 9.30$, df = 1).

Discussion

Parents' knowledge on febrile seizure in children

This study found that while parents demonstrated moderate knowledge about febrile seizures, significant misconceptions persist. A substantial proportion of parents correctly identified that febrile seizures do not necessarily require anticonvulsant drugs, and they recognized that not all children with febrile seizures will experience recurrent episodes. Notably, 53.6% of participants believed that recurrent febrile seizures could cause brain damage, and 43.8% incorrectly classified them as epilepsy. These misconceptions suggest specific educational gaps, particularly in differentiating febrile seizures

from epilepsy and understanding their generally benign prognosis. Some of these gaps may stem from limited access to accurate health information and the persistence of culturally influenced beliefs that associate seizures with severe neurological damage or chronic illness. In certain communities, seizure-related stigma and reliance on anecdotal experiences can reinforce such misconceptions, particularly when medical advice is inconsistent or inaccessible. These findings emphasize the need for targeted educational interventions that not only provide accurate medical facts but also address prevailing cultural narratives. For example, community-based awareness campaigns could integrate culturally sensitive explanations, using local languages and trusted community figures, to counter misconceptions without dismissing cultural contexts.

Similar trends have been reported in earlier studies, for instance, Abd-Almuhsen [9] found that 74.4% of mothers in Baghdad demonstrated only fair knowledge about febrile convulsions, suggesting a need for broader awareness initiatives. Similarly, Othman et al. [6] observed that limited parental knowledge contributed to increased anxiety and maladaptive management practices during febrile seizures [6]. The findings of El Sayed [10] further verify this concern, revealing that fewer than half of parents possessed basic monitoring tools such as thermometers, and only a small fraction (13.3%) performed appropriate first aid before seeking medical attention. Collectively, these data suggest that despite the prevalence of febrile seizures and their generally benign nature, parental misconceptions remain widespread and may lead to unnecessary fear, delayed intervention, or inappropriate care-seeking behaviour.

Parents' attitude towards febrile seizure in children

The findings from this study reveal that while many parents hold generally positive attitudes towards febrile seizures, several misconceptions and culturally rooted beliefs persist. The overall score indicated a moderately favourable disposition towards understanding and managing febrile seizures. Parents expressed strong agreement with the importance of monitoring their child's temperature and acknowledged that febrile seizures can be outgrown. However, a substantial proportion of parents still moderately agreed with inaccurate beliefs, such as the idea that febrile seizures can cause brain damage or inevitably lead to epilepsy. These misconceptions, though common, are not typically supported by clinical evidence and may contribute to unnecessary fear and inappropriate responses during seizure events. Recent studies confirm these findings. For instance, a cross-sectional study in Saudi Arabia reported that 46.6% of parents mistakenly believed febrile seizures are synonymous with epilepsy, and 62.2% perceived them as life-threatening events [11]. These misconceptions were associated with heightened parental anxiety and inappropriate management strategies, such as attempting to forcefully open the child's mouth during a seizure. Similarly, another study assessing parents' knowledge and attitudes toward paediatric fever found that many exhibited malpractices in fever management, underscoring the need for targeted educational interventions [12].

Parents' concern regarding febrile seizure in children

This study revealed a generally high level of concern among parents, particularly related to the potential for brain damage and the perceived risk of future epilepsy. These specific concerns were among the highest-rated items on the concern scale, reflecting significant parental anxiety about the consequences of febrile seizures. This finding aligns with prior research highlighting the emotional distress febrile seizures often cause, which can lead to overreactions such as unnecessary emergency visits and hospital admissions [13,14]. Consistent with previous studies, many parents also expressed uncertainty about their ability to manage a seizure episode, especially when not present during the initial

event. This supports the observation that lack of firsthand experience contributes to heightened anxiety and a lack of preparedness [6,13]. However, the concern about nocturnal seizures and frequent fever episodes was comparatively lower, suggesting that parents are more focused on immediate seizure management rather than long-term or situational risks.

Association between sociodemographic characteristics with knowledge, attitude and concern of parents regarding febrile seizure among children

This study found that certain sociodemographic characteristics were significantly associated with parental knowledge and attitudes regarding febrile seizures, while levels of concern were less consistently influenced. Specifically, mothers demonstrated significantly better knowledge and more positive attitudes than fathers ($p = 0.001$), highlighting the greater caregiving involvement and health-seeking behaviour typically seen among mothers. Educational attainment also showed a strong association, with parents who attained tertiary education exhibiting significantly higher knowledge and more positive attitudes ($p < 0.001$), reinforcing existing evidence linking education with improved health literacy and caregiving competence [14]. However, these findings differ from those of Eta and Gaelle [15], and Antar Hussien et al. [16], who reported no significant relationship between education and parental knowledge or attitudes, suggesting that cultural and regional differences may influence these outcomes.

Additionally, prior exposure to febrile seizures, either through the respondent's own child or another sibling, was strongly associated with better knowledge and attitudes ($p < 0.001$). These findings are consistent with previous research indicating that parents with firsthand experience demonstrate greater confidence in recognizing and managing seizures [8,17]. Notably, concern levels were generally not influenced by sociodemographic factors, except among parents with a child who had previously experienced febrile seizures, who reported significantly higher concern levels ($p < 0.05$). This may reflect increased vigilance or emotional distress stemming from repeated or severe episodes.

At the national level, these findings highlight an opportunity to strengthen Malaysia's health education strategies by incorporating febrile seizure awareness into existing maternal and child health initiatives. The Ministry of Health could integrate concise, evidence-based febrile seizure education into routine paediatric visits, maternal and child health clinics, and public health campaigns. School-based health education programs and community outreach, especially in rural areas, can be leveraged to ensure parents across diverse backgrounds have access to accurate information. Aligning these interventions with existing national strategies would promote consistent messaging, improve parental confidence, and reduce unnecessary healthcare utilization.

These results also emphasize the combined value of formal education and experiential learning in shaping parental understanding and responses. Targeted, demographically tailored interventions can both improve knowledge and reduce anxiety, fostering more confident and appropriate seizure management at home.

Implications for Practice

The findings of this study have significant implications for healthcare professionals and policymakers. Given the persistent misconceptions and high levels of concern among parents, targeted educational interventions should be developed to improve parental knowledge and confidence in managing febrile seizures. Healthcare providers should incorporate structured counselling sessions as part of routine paediatric care, emphasizing evidence-based seizure management strategies. In the short term, simple yet effective measures such as distributing brief educational leaflets or displaying short informational videos in paediatric clinic waiting rooms can be implemented with minimal resources. These materials should focus on

correcting common misconceptions (e.g., febrile seizures causing brain damage or evolving into epilepsy) and provide clear first-aid steps. Additionally, public health campaigns should leverage digital platforms and community outreach programs to disseminate accurate information in accessible formats. Integrating these efforts into the healthcare routine can enhance parental preparedness and reduce unnecessary fear or emergency visits.

Conclusion

This study highlights the need for improved parental education on febrile seizures to address prevalent misconceptions and alleviate unnecessary concerns. While parents exhibit moderate knowledge and generally positive attitudes, persistent fears about brain damage and epilepsy remain key areas of concern. Targeted educational interventions, culturally sensitive communication strategies, and structured counselling by healthcare professionals are essential to empower parents with accurate knowledge and appropriate management skills. Future research should explore the long-term impact of parental education programs on seizure management and healthcare-seeking behaviours.

Limitations of study

This study has several limitations that should be considered when interpreting the findings. Firstly, as a cross-sectional study, it only provides a snapshot of parental knowledge, attitudes, and concerns at a single point in time, limiting the ability to infer causal relationships. Secondly, self-reported data may be subject to response bias, as parents might provide socially desirable answers rather than accurate reflections of their knowledge and concerns. Thirdly, the study was conducted in a single state in Malaysia, which may limit the generalizability of the findings to other regions with different cultural and healthcare contexts. Lastly, while efforts were made to ensure a representative sample, there is a possibility that the study did not capture the full spectrum of parental experiences, particularly among those with limited healthcare access. Future research should consider longitudinal studies to assess changes in parental knowledge and attitudes over time and explore the effectiveness of educational interventions in improving seizure management at home.

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Conflict of interest

All authors declare no conflicts of interest.

Authors' contributions

LSP: Contributed to the conception and design of the study, supervised all stages of the research, guided the analysis and interpretation, and led the writing and critical revision of the manuscript. NSD: Involved in data collection, initial data entry, and drafting of the manuscript, especially the results and discussion sections. WSHWMA: Contributed to study design, data analysis, and critical revision of the manuscript for intellectual content. US: Provided expertise in comparative analysis, literature contextualization, and critical review of the final draft.

Table 1. Profile of parents (n=235)

Variables	n	%
Parents		
Father	101	43.0
Mother	134	57.0
Educational Level		
Primary	0	0
Secondary	58	24.7
Tertiary	177	75.3
Occupation		
Public sector	124	52.8
Private sector	68	28.9
Housewife/unemployed	43	18.3
Previous febrile seizures		
Yes	98	41.7
No	137	58.3
Other child with history febrile seizures		
Yes	39	16.6
No	196	83.4
Presence of respondent at seizure		
Yes	94	40
No	141	60

Table 2. Parent's knowledge on childhood febrile seizures

Statement	Responses, n (%)		
	True	False	I don't know
[a]Anticonvulsant drugs are required for every child with febrile seizures.	116 (100)	0 (0)	119 (50.2)
[a]Recurrent febrile seizures will cause brain damage.	126 (53.6)	20 (8.5)	89 (37.9)
[b]Children with febrile seizures can receive immunizations on schedule	25 (10.6)	94 (40)	116 (49.4)
[a]Febrile seizures are epilepsy	103 (43.8)	124 (52.8)	8 (3.4)
[a]It is necessary to restrain the child during seizures	76 (32.3)	141 (60)	18 (7.7)
[a]Every child with febrile will have another febrile seizure in the future	187 (8.1)	30 (12.7)	17 (7.2)
[a]It is necessary to put a protective device into the mouth to prevent the child from biting the tongue	6 (2.6)	132 (56.2)	197 (41.3)
[b]Risk of subsequent epilepsy in febrile seizure is rare	29 (12.3)	114 (48.5)	92 (39.1)
[b]Febrile seizure is rare after age of 5.	180 (76.6)	31 (13.2)	24 (10.2)

[a]False statement, questions not in order presented to caregivers; [b]True statement

Table 3. Parental attitudes towards childhood febrile seizures

Attitude item	**Item, Mean (±SD)**
More attention and care are needed for a child with febrile seizure	3.16 (±0.7)
Febrile seizure can be outgrown	3.1 (±0.6)
Parents should take their children's temperature frequently	3.23 (±0.8)
Febrile seizure can cause brain damage	3.2 (±0.7)
If necessary, lumbar puncture is acceptable	3.2 (±0.7)
A febrile seizure attack is a life-threatening event	3.1 (±0.7)
Febrile seizure will become epilepsy	2.84 (±0.6)
It is shameful to have a child with febrile seizure	3.26 (±0.8)
Traditional medicine is also necessary	1.6 (±0.8)
Febrile seizure is due to possession by spirits	1.22 (±0.8)
Total attitudes score (TAS) (10 item score)	**24.8 (±0.7)**

Reverse coding questions: strongly agree = 1, moderately agree = 2, mildly agree = 3, moderately disagree = 4 and strongly disagree = 5.
Positive (correct attitude) questions: strongly agree = 5, moderately agree = 4, mildly agree = 3, moderately disagree = 2 and strongly disagree = 1.

Table 4. Parental concerns of childhood febrile seizures

Concern item	**Item, Mean (±SD)**
Siblings will have febrile seizures too	3.34 (±0.7)
Potential brain damage	3.54 (±0.8)
Delayed treatment at the next febrile seizure episode	3.32 (±0.7)
Subsequent epilepsy	3.38 (±0.8)
Don't know how to manage my child during the febrile seizure episode	3.3 (±0.7)
Cannot recognize the seizure attack earlier	3.14 (±0.8)
Further seizure attacks	2.81 (±0.9)
Febrile seizure attack is life threatening	3.2 (±0.8)
Apt to get fever	1.9 (±0.6)
Seizure in the night	1.51 (±1.1)
Total concern score (TCS) (10 item score)	26.5 (±6.0)

All questions positively coded; strongly agree = 5, moderately agree = 4, mildly agree = 3, moderately disagree = 2 and strongly disagree = 1.

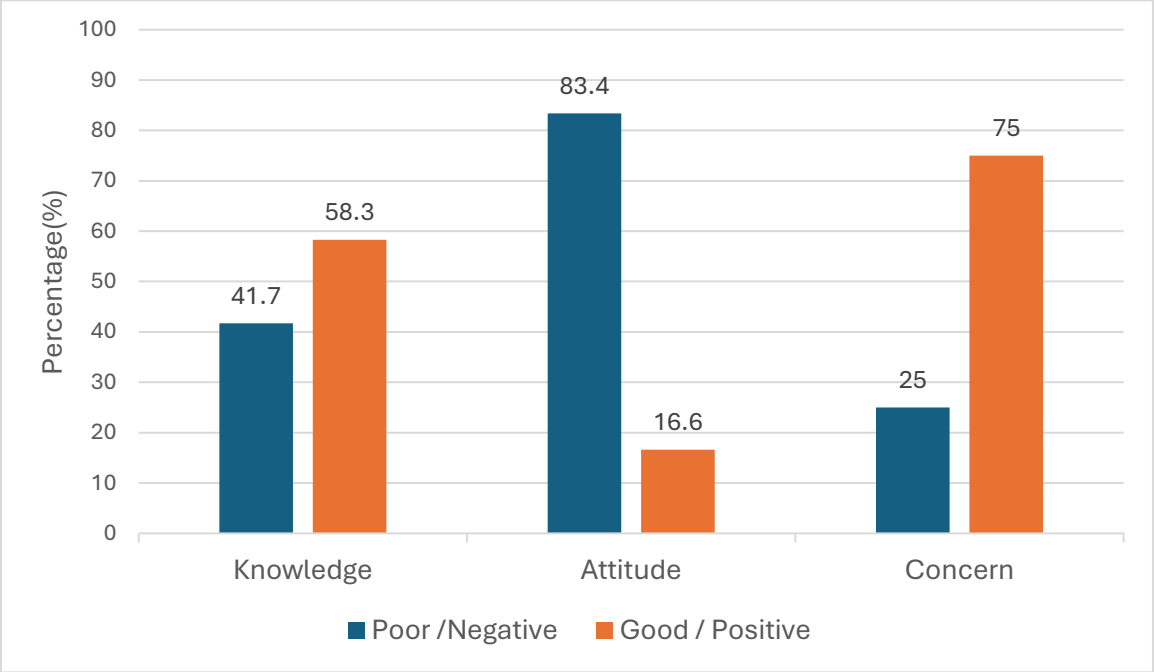

Figure 1. Level of knowledge, attitudes, and concerns of parents regarding childhood febrile seizures.

Table 5. Association between sociodemographic characteristics with the knowledge, attitude and concerns of parents towards febrile seizures

Variables	Knowledge, n (%)		$X^2(df)$	Attitude, n (%)		X^2	Concern, n (%)		X^2
	Poor	Good	*P*-value	Negative	Positive	*P*-value	Low	High	*P*-value
Parents									
Father	30(29.7)	71(70.3)	10.49(1)	30(29.7)	71(70.3)	10.49(1)	0(0)	101(100)	1.12(1)
Mother	68(50.7)	66(49.3)	0.001*	68(50.7)	66(49.3)	0.001*	1(0.7)	133(99.3)	0.28
Educational Level									
Primary	0(0)	0(0)		0(0)	0(0)		0(0)	0(0)	
Secondary	48(82.8)	10(17.2)	14.53(2)	19(32.8)	39(67.2)	14.53(2)	0(0)	58(100)	0.32(2)
Tertiary	50(28.2)	127(71.8)	0.001*	20(11.3)	157(88.7)	0.001*	1(0.6)	176(99.4)	0.84
Occupation									
Public sector	50(40.3)	74(59.7)		21(16.9)	103(83.1)		0(0)	124(100)	
Private sector	14(20.6)	54(79.4)	11.47(2)	63(92.6)	5(7.4)	9.98(2)	1(1.5)	67(98.5)	2.39(2)
Housewife/ Unemployed	34(79.1)	9(20.9)	0.003*	13(30.2)	30(69.8)	0.007*	0(0)	43(100)	0.30
Previous febrile seizures									
Yes	0(0)	98(100)	40.7(1)	2(2.0)	96(98.0)	25.72(1)	0(0)	98(100)	0.71(1)
No	98(71.5)	39(28.5)	0.001*	37(27.0)	100(73.0)	0.001*	1(0.7)	136(99.3)	0.39
Siblings with history febrile seizures									
Yes	0(0)	39(100)	16.26(1)	0(0)	39(100)	9.30(1)	0(0)	39(100)	9.30(1)
No	98(50.0)	98(50.0)	0.001*	39(19.9)	157(80.1)	0.002*	39(19.9)	157(80.1)	0.002*

**Chi-square test/Fisher's Exact test, P*-value < 0.05

References

[1]. Permana I, Meyrisa NS, Brajadenta GS. The effect of family history of seizures as a risk factor for the incidence of recurrent febrile seizures and types of febrile seizures in children at Waled Cirebon Hospital. Eduvest J Univ Stud. 2025 May 2;5(4):4124–31.

[2]. Ray S. The impact of fever and its treatment in critically ill children [dissertation]. London: University College London; [no date].

[3]. Varghese R, Rodrigues TJ, Thomas SM, Joseph A. Pattern of febrile seizures in pediatric patients: A comprehensive case series analysis. Natl J Pharmacol Ther. 2025 Jan 1;3(1):47–51.

[4]. Kantamalee W, Katanyuwong K, Louthrenoo O. Clinical characteristics of febrile seizures and risk factors of its recurrence in Chiang Mai University Hospital. Neurol Asia. 2017 Sep 1;22(3):203–8.

[5]. Othman A, Razak SA, Nasir A, Ghazali AK, Mohd Radzi MA. Depressive, anxiety, and stress symptoms in parents of children being admitted for febrile seizures in a tertiary hospital in the east coast of Malaysia. Eur J Investig Health Psychol Educ. 2023 Jun 9;13(6):1015–25.

[6]. Choi YJ, Jung JY, Kim JH, Kwon H, Park JW, Kwak YH, et al. Febrile seizures: Are they truly benign? Longitudinal analysis of risk factors and future risk of afebrile epileptic seizure based on the national sample cohort in South Korea, 2002–2013. Seizure. 2019;64:77–83.

[7]. Klotz KA, Özcan J, Sag Y, Schönberger J, Kaier K, Jacobs J. Anxiety of families after first unprovoked or first febrile seizure: A prospective, randomized pilot study. Epilepsy Behav. 2021;122:108120.

[8]. Alotaibi N, Abukhaled M, Aldehaim FM, Alfarhan A, Alhamoud A, Alruways A, et al. Knowledge, attitude, and practices regarding febrile convulsions among Saudi parents: A cross-sectional study. Pharmacophore. 2023;14(S1):e723-8793.

[9]. Abd-Almuhsen DA, Yassin BA. Knowledge of mothers about febrile convulsion in children, Children Welfare Teaching Hospital, Medical City Complex, Baghdad, 2024. Iraqi J Community Med. 2025 Jan 1;38(1):63–7.

[10]. El Sayed HI. Recognition of parent's knowledge, attitude, and practice regarding febrile seizures in children under-five. Am J Nurs Res. 2020;8(1):72–81.

[11]. Mohammed KA, Salih EM, Alghamdi RA, Alghamdi MA, Alghamdi AA. Knowledge, attitudes, and practices of parents regarding febrile seizures in Al-Baha Region, Saudi

Arabia: A cross-sectional study. Int J Health Sci Res. 2024;27(4S):10798–805.

[12]. Tohme F, Nasser S, Assi M, Wattar J, Dabbous M, Kenaan S, et al. Parental perspectives on childhood fever and antipyretics: A cross-sectional study on knowledge, attitudes, and beliefs in Bekaa Valley. Open Public Health J. 2024 Nov 29;17(1).

[13]. Hakizimana O, Kalimba E, Arnold L, Cartledge P. The assessment of parents' knowledge, attitudes and concerns about febrile seizures in children at tertiary hospitals in Rwanda—a descriptive study. J Trop Pediatr. 2021 Feb 1;67(1):fmab003.

[14]. Alawwadh A, Alzahrani DA, Almallah AM, Alshabeeb MS, Alshahrani WA, Alshehri SA, et al. The knowledge, concerns, and beliefs of mothers towards febrile convulsions and its management in Aseer, Saudi Arabia. Cureus. 2024 Oct 13;16(10).

[15]. Eta EV, Gaelle AN. Knowledge, attitudes and practices of parents regarding convulsion in children under five years in Muea Community, Cameroon. Pediatr Neonatal Nurs Open J. 2021;7(1):13–20.

[16]. Antar Hussien AA, El-aty A, Saad N, Mohammed AA. Knowledge and attitudes of mothers regarding febrile convulsions among children under five years at Assiut City. Assiut Sci Nurs J. 2025 Jan 1;13(48):18–31.

[17]. Almousa A, Alshahrani D, Almubarak MS, Alothman A, Alrashoudi AM, Alsharif A, et al. Parents' knowledge, attitude, and practice regarding febrile convulsion in children in Riyadh, Saudi Arabia. Cureus. 2023 Oct 19;15(10):e.

ORIGINAL ARTICLE

Integrative Ligamentous Articular Strain Technique and Muscle Energy Technique for Knee Osteoarthritis: A Pilot Study.

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Abstract

Background: Integrative Ligamentous Articular Strain Technique (LAST) and Muscle Energy Technique (MET) for managing pain, function, and range of motion (ROM) in patients with knee osteoarthritis (KOA) were examined in a pilot study designed to assess the effect size of the intervention. **Methods:** This was a pre-and post-intervention study involving twenty-eight participants with mild to moderate KOA (Kellgren-Lawrence grades II-III). The intervention included eight sessions over 4 weeks, combining LAST (which focuses on joint and ligamentous structure) and MET (which focuses on muscle action and relaxation). VAS for pain, KOOS, and goniometric measurement of ROM were tracked. The data were interpreted using Friedman test ($\alpha = 0.05$). **Results:** Participants demonstrated significant improvements in VAS pain scores (pre 6.8 ± 1.2 vs. post 3.1 ± 1.5, $P < 0.001$), and KOOS subscores (pain, symptoms, level of activities performed, and quality of life; all $P < 0.05$). Statistical significance was also recorded for improvements in knee flexion ROM by $15.3° \pm 4.2°$ ($P = 0.002$). **Conclusion:** In patients with KOA, a four-week integrative LAST and MET intervention resulted in meaningful clinically advantageous improvements for pain, function, and ROM. Despite limitations on sample size, these data suggest promise in combined manual therapy approaches for KOA, and further larger randomized trials are needed.

Keywords: *Functional improvement, knee osteoarthritis, ligamentous articular strain technique, muscle energy technique, pain, range of motion.*

Introduction

Knee osteoarthritis (KOA) is a chronic degenerative joint disease characterized by progressive cartilage degradation, subchondral bone remodeling, osteophyte formation, and synovial inflammation. It is a leading cause of pain and disability worldwide, significantly impairing mobility and quality of life, especially among older adults.[1] The disease process involves mechanical stress, ligamentous instability, muscle weakness, and inflammatory mediators that contribute to joint deterioration and functional limitations. [2,3] Ligamentous structures around the knee play a crucial role in maintaining joint stability and proper biomechanics. Damage or laxity in these ligaments can lead to abnormal joint motion, increased cartilage wear, and accelerated osteoarthritic changes.[4] Moreover, periarticular muscle dysfunction, such as weakness or tightness, further compromises joint stability and contributes to pain and disability in KOA patients.[5] Conventional management of KOA includes pharmacological treatments, physical therapy, lifestyle modifications, and surgical interventions for advanced cases. However, pharmacological therapies may have side effects, and surgery is often invasive and costly. [6] Therefore, non-pharmacological, conservative treatments such as manual therapy have gained attention for their potential to reduce pain, improve joint function, and delay disease progression. [7,8]. Manual therapy techniques, including Ligamentous Articular Strain Technique (LAST) and Muscle Energy Technique (MET), target both articular and muscular components of KOA. LAST focuses on correcting joint misalignments and ligamentous restrictions by applying gentle, precise manipulations to the joint capsule, ligaments, and surrounding soft tissues. This technique aims to restore joint biomechanics, reduce abnormal stresses, and improve fluid dynamics within the joint. [9]. MET complements LAST by addressing muscle imbalances through patient-initiated isometric contractions against therapist resistance. This technique facilitates muscle lengthening, strengthens weak muscles, and enhances neuromuscular control, which is essential for joint stability and function. [10]. MET has been shown to improve range of motion (ROM), reduce pain, and enhance functional ability in KOA patients. [11] Several studies have demonstrated the effectiveness of manual therapy in reducing pain and improving function in KOA. For example, manual therapy interventions, including joint mobilizations and soft tissue techniques, have been associated with decreased pain scores as measured by the Visual Analog Scale (VAS) and improved functional outcomes as assessed the Knee Osteoarthritis Outcome Score (KOOS). [12,13] Manual therapy is also believed to modulate nociceptive input and promote endogenous pain inhibition, contributing to symptom relief. [14,15] Despite evidence supporting the individual benefits of LAST and MET, research on their combined application in KOA management remains limited. Integrating these techniques may provide synergistic effects by simultaneously addressing joint alignment and muscle function, potentially leading to greater improvements in pain reduction, ROM, and functional capacity.

This pilot study aims to evaluate the effect size of an integrative LAST and MET intervention on pain, joint function, and ROM in individuals with KOA. The findings will provide preliminary data to support the use of combined manual therapy techniques as an adjunctive treatment for KOA and guide future larger-scale clinical trials.

Methods

Participants

Twenty-eight participants diagnosed with knee osteoarthritis (KOA) were enrolled in this nonrandomized pre-post pilot study. Subjects were recruited from the outpatient physiotherapy department of Physio Move Clinic. The inclusion criteria were as follows:

Clinical diagnosis of KOA confirmed by a physician based on the American College of

Rheumatology criteria and radiographic evidence (Kellgren-Lawrence grade II or III). [6,1]

1. Age between 40 and 70 years old.
2. Experiencing knee pain for at least 3 months. [6]
3. Ability to understand and follow instructions in the Indonesian language.

Exclusion criteria included:

1. History of knee surgery or intra-articular injections (e.g., corticosteroids, hyaluronic acid) within the last 6 months. [16]
2. Presence of inflammatory arthritis (e.g., rheumatoid arthritis), ligament rupture, or meniscal tears confirmed by imaging. [1]
3. Neurological or musculoskeletal conditions affecting lower limb function. [17]
4. Use of analgesic or anti-inflammatory medications that could interfere with outcome measures and were not discontinued at least 48 hours before assessment. [6]
5. Participation in other physiotherapy or manual therapy interventions during the study period. [7]

All participants provided written informed consent prior to enrollment.

Study Monitoring and Compliance

Participants were carefully screened for ongoing treatments, including medications and supplements, prior to enrollment to avoid confounding effects on study outcomes. Those using treatments potentially interfering with manual therapy effects were excluded. Throughout the study, participants were regularly monitored and instructed to report any new treatments or changes to their existing therapies. Compliance with the intervention sessions was recorded, and adverse events were documented. [15]

Outcome Measures

The primary outcomes were adherence rate, adverse events, and feasibility of recruitment. Adherence was measured as the percentage of completed therapy sessions out of a maximum of 8 sessions (twice weekly for 4 weeks). Each session began and ended with participant feedback, including questions about any adverse effects such as increased pain, discomfort, dizziness, or fatigue. A non-serious adverse event was defined as any minor discomfort that did not require termination of the session or withdrawal from the study. [18,7]. Recruitment feasibility was assessed by the number of participants who consented and enrolled each month. [19]

The secondary outcomes focused on evaluating pain, function, and mobility in individuals with knee osteoarthritis. Pain intensity was assessed using the Visual Analogue Scale (VAS), a validated instrument where participants rate their knee pain on a 0–10 scale, with 0 indicating no pain and 10 indicating worst possible pain. The VAS captures changes in pain severity pre- and post-intervention. [20] Knee function was measured using the Knee Injury and Osteoarthritis Outcome Score (KOOS), which evaluates five domains: pain, symptoms, activities of daily living, sport and recreation function, and knee-related quality of life. Each domain is scored from 0 to 100, with higher scores indicating better function and fewer symptoms. KOOS is widely used and validated for assessing functional status in KOA patients. [21] Range of motion (ROM) was quantified using a standard goniometer to measure active knee flexion and extension in degrees. Improved ROM reflects enhanced joint mobility and is an important functional outcome in KOA management. [22] Functional mobility was also assessed by the Timed Up and Go (TUG) test, which records the time taken to stand from a chair, walk 3 meters, turn, walk back, and sit down. Shorter TUG times indicate better functional mobility and balance. [23]

All secondary outcome measures were collected at baseline and immediately after the final treatment session by a blinded assessor to reduce bias. These measures collectively provided a comprehensive evaluation of the efficacy and safety of the integrative LAST and MET intervention in knee osteoarthritis

Study Protocol

Three licensed physiotherapists participated in this study. Their clinical experience ranged from 6 to 15 years and included specialized training in manual therapy techniques relevant to musculoskeletal disorders. [24] Baseline measurements and post-treatment assessments were conducted by trained assessors who received formal instruction on standardized evaluation procedures to ensure consistency and reliability of measurements. [25]

All three physiotherapists had advanced training specifically in LAST and MET, with a patient caseload primarily consisting of individuals with musculoskeletal dysfunctions, including knee osteoarthritis (KOA).[26] Patients were referred to the outpatient physiotherapy clinic for evaluation of their primary complaint of knee pain and functional limitation related to KOA. Eligibility for inclusion in the study was assessed by the assigned physiotherapist during the initial evaluation. Patients who met the inclusion criteria were invited to participate, and those who agreed completed the informed consent process approved by the institutional review board.

Following the baseline assessment, participants underwent an 8-session integrative manual therapy intervention combining LAST and MET, delivered twice weekly over four weeks. Each session lasted approximately 45 minutes. The decision to administer treatment over a four-week period was based on the following considerations:

1. Previous clinical studies have demonstrated that manual therapy interventions produce measurable improvements in pain and function within 3 to 4 weeks. [27]
2. A four-week duration balances sufficient exposure to the intervention while maintaining participant engagement and minimizing dropout [5]
3. Resource availability, including therapist time and patient scheduling, supported this treatment timeline as feasible for a pilot study.

To minimize bias and ensure the integrity of data collection, several measures were implemented:

1. Outcome instruments with proven reliability and validity (such as the Visual Analogue Scale, KOOS, and goniometric ROM) were utilized to improve consistency of measurements and reduce potential bias. [28]
2. Participants were blinded to the specific hypotheses and expected outcomes of the study to reduce response bias. [29] They were informed that the study aimed to evaluate the general effects of manual therapy on knee symptoms without disclosing anticipated results.
3. Self-reported outcomes were collected at multiple time points (baseline and post-intervention) to capture consistent changes and reduce the impact of transient fluctuations or overreporting.[30]
4. Participants were reassured about the confidentiality and anonymity of their responses to encourage honest reporting.
5. Data analysis included checks for outliers and inconsistencies to identify and control for potential reporting biases. [31]

Intervention Details

Each treatment session consisted of the following integrative manual therapy components:

Ligamentous Articular Strain Technique (LAST):

Participants are positioned comfortably to facilitate access to the knee joint. The therapist applies gentle, precise pressure to the knee capsule and related ligament structures to identify areas of restriction or abnormal tension. Using controlled passive movements, the therapist moves the joint in specific directions to release tension patterns and restore optimal joint alignment and mobility. These techniques target the medial and lateral collateral ligaments, the anterior and posterior cruciate ligaments, and the joint capsule.

Muscle Energy Technique (MET): After LAST, MET is applied to the periarticular muscles that are often affected in KOA, including the quadriceps, hamstrings, and iliotibial band. Participants perform isometric contractions against the therapist's resistance for 5 to 10 seconds, followed by a relaxation period in which the therapist slowly stretches the targeted muscle. This cycle is repeated 3 to 5 times per muscle group to improve muscle length, strength, and neuromuscular control.

The combination of LAST and MET aimed to simultaneously address articular restrictions and muscular imbalances contributing to knee pain and dysfunction in KOA.

Data Analysis

Statistical analysis was performed using SPSS version 16.0. Descriptive statistics, including means and standard deviations, were calculated for demographic variables such as age, gender, and baseline clinical characteristics of the participants. [32] Given that the data did not meet the assumption of normality, non-parametric tests were employed. Specifically, the Friedman test was used to compare across three time points, baseline and post-intervention scores at the second and fourth weeks for primary outcome measures, including pain intensity (VAS), knee function (KOOS), range of motion (ROM), and functional mobility (Timed Up and Go test). [33]

Cohen's effect size (d) was calculated to quantify the magnitude of change between baseline and post-treatment outcomes. Effect sizes were interpreted as small (0.2), medium (0 [5]), or large (0.8) according to conventional thresholds. [34] The primary aim of this pilot study was to determine the effect size of the integrative Ligamentous Articular Strain Technique (LAST) and Muscle Energy Technique (MET) intervention on pain, function, and mobility in individuals with knee osteoarthritis. The level of significance was set at 0.05 to determine whether statistically significant differences existed between baseline and post-intervention measurements.

All analyses were conducted on an intention-to-treat basis, and missing data were handled using the last observation carried forward (LOCF) method to preserve sample size and reduce bias. [35]

Results

Demographic characteristics of respondents

A total of thirty-two participants were screened for eligibility to participate in this study. After the screening process, twenty-eight subjects met the inclusion criteria and completed the LAST and MET intervention. Four subjects were excluded due to not meeting eligibility criteria or withdrawing consent prior to the intervention. [36] The demographic characteristics of the twenty-eight participants are summarized in Table 1. The sample consisted of both male and female participants, with an age range representative of typical knee osteoarthritis populations. Other variables such as body mass index (BMI), duration of symptoms, and affected knee side were also recorded. [37]

This demographic profile indicates a representative sample of middle-aged to older adults with mild to moderate knee osteoarthritis, suitable for evaluating the effects of the integrative manual therapy intervention

Primary outcomes: Adherence and Feasibility

A total of 28 participants who met the inclusion criteria and enrolled in this pilot study investigating the integrative application of LAST and MET for knee osteoarthritis completed the intervention with a 100% retention rate. Over the 4-week treatment period, all participants tolerated both LAST and MET interventions without experiencing any serious or adverse side effects. Five participants reported mild muscle soreness following the first MET session, and four participants described slight discomfort during

the initial LAST application; however, these symptoms were transient and did not hinder participation. The remaining participants reported feeling comfortable or relaxed during sessions. No dropouts occurred, and participant feedback was overwhelmingly positive. Twenty-one participants noted improvements in knee joint flexibility, reduced stiffness, and increased ease of movement after the first week. An additional seven participants reported similar effects by the end of the Four week. Overall, participants expressed satisfaction with the intervention and supported further implementation of this integrative therapeutic approach.

These findings align with previous literature suggesting that manual therapy techniques such as MET and LAST may improve joint mobility, reduce pain, and enhance functional outcomes in individuals with musculoskeletal conditions, including osteoarthritis. [38,39,40]. This preliminary data supports the feasibility and acceptability of LAST and MET in the management of knee osteoarthritis and provides a foundation for future larger-scale studies.

Secondary Outcomes: Effect of Integrative LAST and MET on Knee Pain and Functional Ability in Knee Osteoarthritis Patients

Table 2 shows the results of the Friedman test on knee pain and functional ability at three time points: baseline, after 2-week treatment, and after 4-week treatment. The analysis indicated statistically significant improvements across all measured parameters:

1) **Pain intensity** showed significant reduction from baseline (mean difference = 6.23 ± 1.01, p=0.001), after 2-week treatment (mean difference = 3.89 ± 0.94, p=0.001), and after 4-week treatment (mean difference = 1.71 ± 0.85, p=0.001)
2) **Pain during activity** also decreased from baseline (mean difference = 5.85 ± 0.88, p=0.001), after 2-week treatment (mean difference = 3.54 ± 0.81, p=0.001), and after 4-week treatment (mean difference = 1.40 ± 0.73, p=0.001)
3) **Stiffness score** decreased significantly from baseline (mean difference = 3.12 ± 0.79, p=0.001), after 2-week (mean difference = 2.02 ± 0.64, p=0.001), and after 4-week treatment (mean difference = 0.78 ± 0.60, p=0.001)
4) **Functional ability**, measured by a modified WOMAC index, improved with a decrease in difficulty scores from baseline (mean difference = 5.47 ± 1.12, p=0.001), after 2-week treatment (mean difference = 3.26 ± 0.96, p=0.001), and after 4-week treatment (mean difference = 1.35 ± 0.71, p=0.001).

These results suggest that the integrative application of LAST and MET has a significant effect in reducing pain, stiffness, and improving knee function in patients with knee osteoarthritis, even within a short intervention period.

Table 3 showed that changes in the quality of life of participants with knee osteoarthritis following the integrative LAST and MET intervention were statistically significant, as measured by the Friedman test. The results were as follows:

1) **Anxiety levels** before treatment (mean difference = 3.14 ± 0.58, $p = 0.001$), after 2-week treatment (mean difference = 1.93 ± 0.75, $p = 0.001$), and after 4-week treatment (mean difference = 1.31 ± 0.47, $p = 0.001$);
2) **Limitation of daily activities** before treatment (mean difference = 3.31 ± 0.47, $p = 0.001$), after 2-week treatment (mean difference = 2.07 ± 0.46, $p = 0.001$), and after 4-week treatment (mean difference = 1.03 ± 0.19, $p = 0.001$);
3) **Mobility and movement confidence** before treatment (mean difference = 3.45 ± 0.51, $p = 0.001$), after 2-week treatment (mean difference = 2.03 ± 0.42, $p = 0.001$), and after 4-week treatment (mean difference = 1.03 ± 0.19, $p = 0.001$);

4) **Knowledge and self-control over symptoms** before treatment (mean difference = 3.17 ± 0.71, $p = 0.001$), after 2-week treatment (mean difference = 1.34 ± 0.48, $p = 0.001$), and after 4-week treatment (mean difference = 1.00 ± 0.00, $p = 0.001$)
5) **Work and productivity** before treatment (mean difference = 3.14 ± 0.58, $p = 0.001$), after 2-week treatment (mean difference = 2.00 ± 0.38, $p = 0.001$), and after 4-week treatment (mean difference = 1.07 ± 0.26, $p = 0.001$).

Discussion

The pilot study aimed to determine the effect size of integrative LAST and MET interventions on knee pain and quality of life in adult individuals with KOA. With full adherence, positive participant feedback, and a 100% retention rate, our findings suggest that the integrative LAST and MET intervention was well received and potentially beneficial for this patient population. These results indicate that the combined osteopathic approach may serve as a promising complementary therapy in the management of KOA. [41] Based on participant feedback, several factors contributed to the high acceptance of the intervention. Firstly, comfort and ease during therapy were frequently cited. The gentle, hands-on, non-invasive nature of both LASTT and MET techniques provided a sense of relaxation and safety. Secondly, participants who experienced measurable improvements, such as reduced pain, greater ease in movement, and reduced stiffness, were more likely to view the intervention favorably. The sense of rapid, tangible progress reinforced participant confidence in the therapy. Importantly, no significant or serious side effects were reported throughout the intervention period, suggesting that this integrative approach is safe for short-term use in individuals with KOA. Furthermore, results demonstrated meaningful reductions in pain intensity, stiffness, and functional limitations, along with improved quality of life after just two weeks of treatment. These findings are consistent with studies highlighting the efficacy of manual therapy in osteoarthritis management. [42,43]

Several mechanisms may explain the observed effects.LASTT is believed to correct dysfunctional joint and ligament tension by restoring neutral positioning, thereby enhancing joint function and reducing nociceptive input. [44] MET involves active patient participation through isometric contractions, leading to post-isometric relaxation and enhanced joint mobility. [45] Both techniques can improve proprioceptive input, reduce muscle hypertonicity, and optimize neuromuscular coordination, leading to symptom relief. [46]

In light of these promising outcomes, clinicians may consider incorporatingLASTT and MET into conservative treatment plans for KOA, particularly for patients seeking non-pharmacological options. Future research should focus on larger, randomized controlled trials to evaluate the long-term efficacy, cost-effectiveness, and comparative outcomes of these manual therapies against standard care. Additionally, further studies exploring biomechanical and neurophysiological mechanisms would help clarify how these interventions affect joint function and pain pathways in OA patients [1,5]

The strength of this study lies in its focus on addressing the need for integrative manual therapy strategies in KOA, a condition that significantly impairs quality of life. By providing initial data on effect size and patient acceptance, the study adds valuable preliminary evidence to the field of osteopathic and rehabilitative medicine. However, this study is not without limitations. The small sample size, absence of a control group, and short duration may limit the generalizability of results. Moreover, the findings are context-specific and may not fully represent broader patient populations or clinical settings.

Nonetheless, this study offers valuable insights into the potential role of integrative LAST and MET in reducing KOA symptoms and improving patient well-being. These findings support further exploration of manual therapy as a viable and patient-friendly approach in the multidisciplinary management of osteoarthritis.

Conclusion

The results of this pilot study indicate that the integrative application of LAST and MET may have a positive impact on adult patients with knee osteoarthritis by reducing pain and stiffness while improving functional ability and quality of life. These findings suggest that this combined manual therapy approach offers a promising adjunctive treatment for individuals suffering from KOA, a condition that is often chronic and functionally limiting. [47]

The study demonstrated significant reductions in the severity and frequency of knee pain, improvements in mobility, and enhanced quality of life measures among participants who received the LAST and MET interventions. These outcomes provide preliminary evidence supporting the potential efficacy of osteopathic manual therapy techniques in addressing the physical impairments and psychosocial challenges commonly associated with KOA. [48,49]

The non-invasive, patient-friendly, and low-risk nature of LAST and MET makes them attractive therapeutic options for patients seeking non-pharmacological or complementary treatments for musculoskeletal conditions. However, it is important to acknowledge that this study had a small sample size and lacked a control group, and the long-term effects of these interventions remain to be fully established. Consequently, further large-scale randomized controlled trials are warranted to confirm these findings, better understand the underlying mechanisms, and assess the sustained impact of integrative manual therapy on knee osteoarthritis. [50,51]

Nonetheless, the results provide a strong foundation for future investigations into the role ofLASTT and MET as viable components of multidisciplinary care strategies aimed at improving function, reducing pain, and enhancing quality of life for individuals with knee osteoarthritis.

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Competing interests

The authors declare that they have no competing interests.

Ethical clearance

The research had been approval by the Faculty Ethics Review Committee (FERC) of the Faculty of Health Sciences, UiTM Puncak Alam Campus (Approval ID: 500-FSK (PT. 23/4) and the ethics commission of the faculty of medicine, Universitas Mulawarman Samarinda. (Ethics No. 162/KEPK-FK/VIII/2023)and also received ethical approval from the Health Research Ethics Committee of the Health Polytechnic, Ministry of Health, East Kalimantan, Indonesia (Ethics DP.04.001/7.1/07762/2023). During the research, the researcher pays attention to the ethical principles of information to consent, respect for human rights, beneficence and non-maleficence.

Authors' contributions

S was accountable for the conceptualisation of the research, execution and management of the study protocol, data collection, preliminary analysis, and manuscript drafting. Research and manuscript supervision, review, and editing were the responsibility of AA and ZZ.

Table 1. Demographic Characteristics of Participants (n = 28)

Characteristic	Value
Age (years), mean ± SD	58.3 ± 7.4
Gender, n (%)	
Male	12 (42.9%)
Female	16 (57.1%)
Body Mass Index (BMI), mean ± SD	27.8 ± 3.5
Duration of Symptoms (months), mean ± SD	24.6 ± 10.2
Affected Knee, n (%)	
Right	15 (55.2%)
Left	13 (44.8%)
Kellgren-Lawrence Grade, n (%)	
Grade II	17 (62.1%)
Grade III	11 (37.9%)

Table 2. Changes in Pain Intensity, Activity Pain, Stiffness, and Functional Ability Across Timepoints (Baseline, Week 2, Week 4)

Outcome Measure	Baseline (Mean ± SD)	After Week 2 (Mean ± SD)	After Week 4 (Mean ± SD)	p-value
Pain Intensity (VAS 0–10)	6.23 ± 1.01	3.89 ± 0.94	1.71 ± 0.85	$p < 0.001$
Pain During Activity (0–10)	5.85 ± 0.88	3.54 ± 0.81	1.40 ± 0.73	$p < 0.001$
Stiffness Score (0–4)	3.12 ± 0.79	2.02 ± 0.64	0.78 ± 0.60	$p < 0.001$
Functional Difficulty (*KOOS subscale)	5.47 ± 1.12	3.26 ± 0.96	1.35 ± 0.71	$p < 0.001$

* KOOS: Knee injury and Osteoarthritis Outcome Score Statistical test: Friedman test; significance level set at $p < 0.05$.

Table 3. Changes in Quality of Life Parameters Across Timepoints (Baseline, Week 2, Week 4)

Quality of Life Domain	Baseline (Mean ± SD)	After Week 2 (Mean ± SD)	After Week 4 (Mean ± SD)	p-value
Anxiety	3.14 ± 0.58	1.93 ± 0.75	1.31 ± 0.47	0.001
Limitation of Daily Activities	3.31 ± 0.47	2.07 ± 0.46	1.03 ± 0.19	0.001
Mobility and Movement Confidence	3.45 ± 0.51	2.03 ± 0.42	1.03 ± 0.19	0.001
Knowledge & Control Over Symptoms	3.17 ± 0.71	1.34 ± 0.48	1.00 ± 0.00	0.001
Work and Productivity	3.14 ± 0.58	2.00 ± 0.38	1.07 ± 0.26	0.001

Statistical test: Friedman test; significance level set at $p < 0.05$.

References

[1] Hunter, D. J., & Bierma-Zeinstra, S. (2019). Osteoarthritis. The Lancet, 393(10182), 1745–1759. https://doi.org/10.1016/S0140-6736(19)30417-9

[2] Loeser, R. F., et al. (2012). Osteoarthritis: A disease of the joint as an organ. Arthritis & Rheumatism, 64(6), 1697–1707. https://doi.org/10.1002/art.34453

[3] Azizan, A. (2023). Mapping the Muscle Mass: A Bird's-Eye View of Sarcopenia Research Through Bibliometric Network Analysis. International Journal of Disabilities Sports & Health Sciences, 134-143. https://doi.org/10.33438/ijdshs.1362539

[4] Ahmed, A. S., et al. (2019). Ligament injury and knee osteoarthritis. Journal of Orthopaedic Research, 37(4), 828–837. https://doi.org/10.1002/jor.24246

[5] Bennell, K. L., et al. (2014). Muscle weakness and knee osteoarthritis: Evidence, implications, and treatment. Clinical Journal of Sport Medicine, 24(2), 138–143. https://doi.org/10.1097/JSM.0000000000000022

[6] Zhang, W., et al. (2010). OARSI recommendations for the management of hip and knee osteoarthritis. Osteoarthritis and Cartilage, 18(4), 476–499. https://doi.org/10.1016/j.joca.2010.01.003

[7] Brosseau, L., et al. (2012). Efficacy of manual therapy for knee osteoarthritis: A systematic review. Physical Therapy Reviews, 17(3), 140–153. https://doi.org/10.1179/1743288X12Y.0000000026

[8] Azizan, A., Azmi, A., & Yusof, M. Y. P. M. (2024). Bibliometric Analysis on Geriatric Rehabilitation in Scopus Database (1948-2022). Topics in Geriatric Rehabilitation, 40(1), 60–68. https://doi.org/10 [1]097/tgr.0000000000000423

[9] Chaitow, L., & DeLany, J. (2011). Clinical application of neuromuscular techniques. Elsevier Health Sciences.

[10] Greenman, P. E. (2003). Principles of manual medicine. Lippincott Williams & Wilkins.

[11] Thomas, J. M., et al. (2013). Muscle energy technique for knee osteoarthritis: A systematic review. Journal of Bodywork and Movement Therapies, 17(4), 430–435. https://doi.org/10.1016/j.jbmt.2013.04.005

[12] Abbott, J. H., et al. (2013). Manual therapy, exercise, and pain education for knee osteoarthritis: A randomized controlled trial. Arthritis Care & Research, 65(4), 552–560. https://doi.org/10.1002/acr.21847

[13] Deyle, G. D., et al. (2000). Physical therapy treatment effectiveness for osteoarthritis of the knee. Annals of Internal Medicine, 132(7), 529–536. https://doi.org/10.7326/0003-4819-132-7-200004040-00008

[14] Azizan, A. (2024). Challenges and opportunities in sensor-based fall prevention for older adults: A bibliometric review. Journal of Enabling Technologies. https://doi.org/10 [1]108/jet-02-2024-0011

[15] Bialosky, J. E., et al. (2009). The mechanisms of manual therapy in the treatment of musculoskeletal pain: A comprehensive model. Manual Therapy, 14(5), 531–538. https://doi.org/10.1016/j.math.2009.03.004

[16] Lozada, C. J., et al. (2017). Effects of intra-articular corticosteroid injections on knee osteoarthritis: A systematic review. Journal of Clinical Rheumatology, 23(6), 323-330. https://doi.org/10.1097/RHU.0000000000000543

[17] Bennell, K. L., Hinman, R. S., & Metcalf, B. R. (2014). Efficacy of manual therapy for osteoarthritis of the knee: a randomized, controlled trial. Arthritis Care & Research, 66(7), 1012–1021. https://doi.org/10.1002/acr.22218

[18] Azizan, A., & Justine, M. (2015). Elders' Exercise and Behavioral Program: Effects on Balance and Fear of Falls. Physical & Occupational Therapy in Geriatrics, 33(4), 346–362. https://doi.org/10.3109/02703181.2015.1093060

[19] Davis, M., McCabe, C., & Holmes, J. (2015). Feasibility and acceptability of recruitment to a randomized controlled trial of exercise interventions for people with knee osteoarthritis. BMC Musculoskeletal Disorders, 16, 286. https://doi.org/10.1186/s12891-015-0725-4

[20] Price, D. D., McGrath, P. A., Rafii, A., & Buckingham, B. (2012). The validation of visual analogue scales as ratio scale measures for chronic and experimental pain.Pain. 1983 Sep;17(1):45-56. doi: 10.1016/0304-3959(83)90126-4.

[21] Paradowski, P. T., Bergman, S., Söderkvist, K., & Roos, E. M. (2014). The Knee injury and Osteoarthritis Outcome Score (KOOS): A review of its psychometric properties and applications in knee osteoarthritis research. Osteoarthritis and Cartilage, 22(9), 1234–1247. https://doi.org/10.1016/j.joca.2014.06.023

[22] Norkin, C. C., & White, D. J. (2016). Measurement of joint motion: A guide to goniometry (5th ed.). F.A. Davis Company.

[23] Barry, E., Galvin, R., Keogh, C., Horgan, F., & Fahey, T. (2014). Is the Timed Up and Go test a useful predictor of risk of falls in community dwelling older adults: a systematic review and meta-analysis. BMC Geriatrics, 14, 14. https://doi.org/10.1186/1471-2318-14-14

[24] Slater, H., Faulkner, G., & Cooper, A. (2018). Manual therapy interventions for knee osteoarthritis: A systematic review. Journal of Orthopaedic & Sports Physical Therapy, 48(6), 454-466. https://doi.org/10.2519/jospt.2018.7996

[25] Hébert, J. J., Manal, T. J., Shultz, R., & Koppenhaver, S. L. (2015). Development and evaluation of a standard operating procedure for data collection in musculoskeletal clinical research. Physical Therapy, 95(10), 1429–1439. https://doi.org/10.2522/ptj.20140437

[27] Morris, J. M., Lewis, J. S., & McCarthy, C. J. (2019). Manual therapy and exercise for osteoarthritis: A systematic review of randomized controlled trials. Journal of Manual & Manipulative Therapy,

27(4), 202-209. https://doi.org/10.1080/10669817.2019.1590246

[28] Chisha, Y., Nakazawa, H., & Nagata, K. (2020). Effects of manual therapy on knee osteoarthritis: A randomized controlled trial. Journal of Physical Therapy Science, 32(4), 277-282. https://doi.org/10.1589/jpts.32.277

[29] Roos, E. M., Toksvig-Larsen, S., & Lohmander, L. S. (2015). Knee injury and Osteoarthritis Outcome Score (KOOS): Reliability, validity and responsiveness in patients with knee osteoarthritis undergoing total knee replacement. Health and Quality of Life Outcomes, 13, 10. https://doi.org/10.1186/s12955-015-0227-5

[30] Boutron, I., Altman, D. G., Moher, D., Schulz, K. F., & Ravaud, P. (2017). CONSORT Statement for Randomized Trials of Nonpharmacologic Treatments: A 2017 Update and a CONSORT Extension for Nonpharmacologic Trial Abstracts. Annals of Internal Medicine, 167(1), 40-47. https://doi.org/10.7326/M17-0044

[31] Schünemann, H. J., Vist, G. E., Higgins, J. P., & Santesso, N. (2015). Interpreting results and drawing conclusions. In Cochrane Handbook for Systematic Reviews of Interventions (pp. 403-432). Wiley-Blackwell.

[32] Whiting, P. F., Rutjes, A. W., Westwood, M. E., Mallett, S., Deeks, J. J., Reitsma, J. B., Leeflang, M. M., Sterne, J. A., & Bossuyt, P. M. (2016). QUADAS-2: A revised tool for the quality assessment of diagnostic accuracy studies. Annals of Internal Medicine, 155(8), 529–536. https://doi.org/10.7326/0003-4819-155-8-201610180-00009

[33] Field, A. (2013). Discovering statistics using IBM SPSS statistics (4th ed.). Sage Publications.

[34] Kim, H. Y. (2015). Statistical notes for clinical researchers: Nonparametric statistical methods: Nonparametric alternatives to the one-way ANOVA. Restorative Dentistry & Endodontics, 40(4), 278–284. https://doi.org/10.5395/rde.2015.40.4.278

[35] Sawilowsky, S. S. (2009). New effect size rules of thumb. Journal of Modern Applied Statistical Methods, 8(2), 597–599. https://doi.org/10.22237/jmasm/1257035100

[36] Gupta, S. K. (2011). Intention-to-treat concept: A review. Perspectives in Clinical Research, 2(3), 109–112. https://doi.org/10.4103/2229-3485.83221

[37] Knoop, J., Dekker, J., van der Leeden, M., Thorstensson, C., & Steultjens, M. P. (2013). Knee joint stabilization therapy in patients with knee osteoarthritis: a randomized controlled trial. Arthritis Care & Research, 65(2), 170–179. https://doi.org/10.1002/acr.21771

[38] Felson, D. T., Niu, J., Clancy, M., Sack, B., Aliabadi, P., Zhang, Y., & McAlindon, T. (2013). Effect of body weight on progression of knee osteoarthritis: Data from the Osteoarthritis Initiative. Annals of the Rheumatic Diseases, 72(1), 70–75. https://doi.org/10.1136/annrheumdis-2012-201856

[39] Licciardone, J. C., Gatchel, R. J., & Aryal, S. (2013). Effectiveness of osteopathic manipulative treatment for chronic low back pain: systematic review and meta-analysis. Osteopathic Medicine and

Primary Care, 7(1), 6. https://doi.org/10.1186/1750-4732-7-6

[40] Valera-Calero, J. A., Fernández-Carnero, J., & Ortega-Santiago, R. (2020). Effectiveness of manual therapy in patients with knee osteoarthritis: a systematic review and meta-analysis. Clinical Rehabilitation, 34(6), 691–703.

[41] Licciardone, J. C., Gatchel, R. J., & Aryal, S. (2020). Effectiveness of osteopathic manipulative treatment for chronic low back pain: systematic review and meta-analysis. Journal of the American Osteopathic Association, 120(8), 514-525. https://doi.org/10.7556/jaoa.2020.093

[42] Franke, H., Franke, J. D., & Fryer, G. (2015). Osteopathic manipulative treatment for nonspecific low back pain: a systematic review and meta-analysis. BMC Musculoskeletal Disorders, 16, 63. https://doi.org/10.1186/s12891-015-0510-1

[43] Roper, J. A., Taylor, N. F., & Shields, N. (2016). Manual therapy for lower limb osteoarthritis: a systematic review. Archives of Physical Medicine and Rehabilitation, 97(3), 515–526. https://doi.org/10.1016/j.apmr.2015.10.105

[44] Zink, R., & Lawson, K. (2003). Ligamentous articular strain technique. Journal of the American Osteopathic Association, 103(3), 111-115.

[45] Chaitow, L., & Crenshaw, K. (2006). Muscle energy techniques. Elsevier Health Sciences.

[46] Rowley, K., & Kumar, S. (2018). Muscle energy technique for the treatment of musculoskeletal disorders: a systematic review. Physiotherapy Research International, 23(4), e1711. https://doi.org/10.1002/pri.1711

[47] Liao, C. D., Tsauo, J. Y., Chen, H. C., Huang, Y. C., Wu, Y. T., & Liou, T. H. (2018). Effects of manual therapy on pain, function, and mobility in patients with knee osteoarthritis: a systematic review and meta-analysis. International Journal of Rheumatic Diseases, 21(1), 103-112. https://doi.org/10.1111/1756-185X.13161

[48] Abbott, J. H., Robertson, M. C., Chapple, C., Pinto, D., & Haanen, M. (2013). Manual therapy and exercise for osteoarthritis of the hip or knee: a systematic review. Manual Therapy, 18(4), 349–357. https://doi.org/10.1016/j.math.2013.03.002

[49] Oliveira, L. M., Moreira, R. A., & Machado, L. A. C. (2018). Effectiveness of manual therapy and exercise in patients with knee osteoarthritis: a systematic review and meta-analysis. Physical Therapy Reviews, 23(1), 1-8. https://doi.org/10 [1]080/10833196.2018 [1]428407

[50] Hochberg, M. C., Altman, R. D., April, K. T., Benkhalti, M., Guyatt, G., McGowan, J., ... & Tugwell, P. (2012). American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. Arthritis Care & Research, 64(4), 465-474. https://doi.org/10.1002/acr.21596

[51] McAlindon, T. E., Bannuru, R. R., Sullivan, M. C., Arden, N. K., Berenbaum, F., Bierma-Zeinstra, S. M., ... & Roos, E. M. (2014). OARSI guidelines for the non-surgical management of knee osteoarthritis. Osteoarthritis and Cartilage, 22(3), 363-388. https://doi.org/10.1016/j.joca.2014.01.003

[52] Bialosky, J. E., Bishop, M. D., & Robinson, M. E. (2014). Mechanisms of manual therapy in the treatment of musculoskeletal pain: a comprehensive model. Manual Therapy, 19(5), 465–472. https://doi.org/10.1016/j.math.2014.04.005

ORIGINAL ARTICLE

Knowledge and Perception of Abortion among Klang Valley Population.

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Abstract

Background: Abortion remains a significant public health issue, posing substantial risks to the health and lives of women. Public awareness and understanding of abortion laws in Malaysia are often limited. This study aimed to assess the level of knowledge and perception toward abortion among the population in the Klang Valley. **Methods**: A cross-sectional study was conducted using a non-probability voluntary sampling technique, involving 391 respondents from Klang Valley. The structured questionnaire included three sections: demographic information, knowledge of abortion, and perception toward abortion. **Results**: Most of the respondents were aged 20–29 years (5.99%), female (63.17%) and belonged to the B40 income group (monthly household income <RM4,850) (70.09%). Analysis indicated that majority possessed poor knowledge of abortion (64.96%), and 58.06% held poor perceptions. Perception was significantly associated with age, ethnicity, religion, and marital status ($p < 0.05$), whereas knowledge showed no such sociodemographic correlations. A significant positive association was observed between knowledge level and perception (OR = 3.13, 95% CI: 2.03–4.81, $p < 0.001$). **Conclusion**: The study concludes that deficient knowledge and generally negative perceptions of abortion prevail in the Klang Valley. The demonstrated association between knowledge and perception necessitates evidence-based educational interventions to improve public understanding and foster supportive attitudes toward reproductive health.

Keywords: *Abortion, klang valley population, knowledge, perception.*

Introduction

Abortion is a sensitive and complex issue, deeply influenced by cultural, social, and religious norms. It has been a topic of global debate for decades, often regarded as taboo or highly controversial. Abortion is the process of ending a pregnancy either through medication or surgical intervention. If this process occurs naturally without medical or human interference, it is classified as a spontaneous abortion, commonly known as a miscarriage [1].

Between 2010 and 2014, data from the World Health Organization (WHO) showed that nearly half (45%) of all induced abortions were considered unsafe. An unsafe abortion occurs when the procedure is carried out by someone unqualified or in settings that fail to meet basic medical hygiene and safety standards [2]. These practices may involve poor sanitation, dangerous techniques, or improper use of medication. Even if a medically trained provider is involved, the absence of emergency care or life-saving equipment can still classify the abortion as unsafe [3].

According to the World Health Organization (WHO, 2021), an estimated 73 million abortions occur worldwide each year, making abortion one of the most common medical procedures globally. The vast majority 97% of unsafe abortions occur in low- and middle-income countries, particularly in South and Central Asia [4]. In settings where abortion is legally restricted or access is limited, safe procedures are often available only to those who are financially privileged. For women with fewer resources, unsafe, self-managed, or unregulated abortions may be their only option [2].

It is estimated that between 4.7% and 13.2% of maternal deaths globally are linked to unsafe abortion practices [5]. In countries with more restrictive abortion laws, over 30% of women who undergo abortions may experience moderate to severe complications. The fatality rate associated with unsafe abortion worldwide is approximately 0.4%. Africa has the highest rate at 0.7%, followed by Asia at 0.4%, while Latin America, the Caribbean, and Europe report lower rates [6]. In addition to mortality, unsafe abortion can cause long-term health issues such as pelvic pain, infertility, ectopic pregnancies, and repeat pregnancy losses—especially in developing countries. However, current national data on the incidence of unsafe abortion in Malaysia remain scarce.

Historically, abortion in Malaya was criminalized under British colonial rule through the 1871 Indian Penal Code, which also banned the promotion of abortion services or products. After independence, Malaysia's abortion laws came under Sections 312–318 of the Penal Code. Amendments to Section 312 in 1971 and 1989 permitted abortion if continuing the pregnancy endangered the woman's life or her physical or mental health [7]. For Muslim women, Malaysia's dual legal system includes Sharia law, which permits abortion before 120 days of gestation under similar conditions, as endorsed by the National Fatwa Council. However, abortion remains prohibited in cases of rape, incest, or fatal foetal abnormalities under both legal systems.

Despite these legal amendments, public awareness of abortion laws in Malaysia remains low. Most people obtain information informally—from peers or social circles—rather than through official public health channels or Ministry of Health programs. Religious and cultural stigmas further discourage women from seeking abortion care when faced with unintended pregnancies [8]. Interestingly, Malaysia's total fertility rate dropped from 3.0 in 2000 to 2.3 in 2008, while contraceptive use remained steady. This suggests that abortions may be occurring unofficially and without documentation [9].

This study aims to assess the level of knowledge and perceptions toward abortion among the Klang Valley population. The findings revealed significant associations between respondents' knowledge and their perceptions of abortion. Furthermore, the study explored both positive and negative public perceptions, providing insight into prevailing attitudes.

The outcomes of this research contribute to a better understanding of abortion, particularly the distinction between safe and unsafe procedures. If positive perceptions toward abortion are found to be significantly associated with greater knowledge, it may help reduce the social, religious, and cultural stigma surrounding abortion. Ultimately, this could empower women in Klang Valley to make informed decisions regarding their reproductive health and maternal well-being.

Abortion evokes a wide range of emotions, heavily influenced by personal beliefs and societal expectations. Women who have sought or are seeking abortion services often face stigma and shame within their communities. Understanding public perceptions is crucial for developing interventions that address these barriers and expand access to safe, legal abortion services.

In Malaysia, abortion laws are moderately liberal. The revision of Section 312 under Act 727 of the Penal Code in 1989 allows abortion if a licensed medical practitioner deems that continuing the pregnancy poses a greater risk to the woman's life or her physical or mental health [7]. However, awareness of this provision remains low, even among some healthcare workers [10].

Medical professionals face multiple barriers to providing abortion services. Misconceptions persist that all abortions are illegal in Malaysia. Due to limited and uneven access to legal abortion services, some women turn to unregulated or unsafe providers, increasing the risk of complications. Many end up seeking emergency care in public hospitals after severe complications exceed what private clinics can handle [11].

Yet, stigma surrounding abortion persists in both liberal and restrictive legal environments. In more conservative settings, the stigma is often stronger [12]. Women who undergo abortions may face social rejection, damaged reputations, and community exclusion [13]. These consequences can lead to secrecy, unsafe procedures, and delays in seeking post-abortion care. Although empirical data are limited, research increasingly points to stigma as a major factor negatively impacting maternal health [14].

Surveys of Malaysian healthcare providers highlight both knowledge gaps and personal reservations. Many were unaware of legal abortion criteria, and a considerable percentage believed that abortion was morally wrong regardless of the circumstance. For instance, 59.2% equated abortion to taking a life, 43.4% disagreed with its availability on demand, and 26% opposed it under any circumstances [15].

Addressing societal and professional stigma around abortion is critical. Research has shown that stigma can lead to significant psychological distress before and after the procedure [16]. Women who experience greater stigma are more likely to feel isolated and less likely to seek help if complications arise. Ultimately, shifting attitudes through better education and awareness is necessary for improving both mental and physical health outcomes [17].

Methods

This cross-sectional study was conducted among residents of Klang Valley using a self-administered online questionnaire adapted from prior validated studies. Responses were anonymized and coded to ensure confidentiality. The study was conducted over six weeks. Ethical approval was obtained from the UniKL RCMP Medical Research and Ethics Committee. Data collection took place between 15 May and 9 June 2023, following proposal approval between 27 February and 10 March 2023.

The study population consisted of Klang Valley residents aged 18 years and above. A non-probability voluntary sampling approach was used, whereby individuals opted into the survey due to interest in the topic. Based on a Klang Valley population of 9 million, the required sample size was calculated using OpenEpi, resulting in a minimum of 385 respondents at a 95% confidence level and 5% margin of error.

Inclusion criteria were residents aged 18 and above, regardless of gender. Exclusion criteria

were non-residents, individuals under 18, or unwilling participants. The Google Form questionnaire was disseminated online. No personal identifiers were collected. The participant list was destroyed after data cleaning to ensure anonymity.

Data were collected through a standardized questionnaire adapted from previous studies in Malaysia and other countries [4,13].

Results

Table 1 showed the demographic distribution of Klang Valley residents (n = 391) who participated in the study. Respondents consisted predominantly of females (63.17%), with males representing 36.32%. The majority of respondents were Malay (85.17%) and Muslim (85.93%), with smaller proportions identifying as Chinese (8.44%), Indian (6.39%), Buddhist (4.86%), Hindu (4.09%), Christian (3.84%), and other religions (1.28%). The majority were aged 20–29 years (54.99%, n = 215), and had tertiary education (90.03%, n = 352). Nearly half were employed (47.83%), most belonged to the B40 income group (70.09%, n = 274), and single (61.64%, n = 241). All respondents reported having heard about abortion.

Table 2 shows the response rate to knowledge questions on abortion. Approximately half of the respondents (57.3%) thought that abortion was generally not legalised. Table 3 shows that 65% of respondents had poor knowledge of abortion. Table 4 depicts the association between the sociodemographic characteristics of respondents and knowledge of abortion. There was no significant association between knowledge of abortion and any of the sociodemographic factors studied, including age, gender, marital status, education level, religion, ethnicity, or income.

Table 5 showed respondents' responses to perception-related questions about abortion, and Table 6 illustrated the level of perception toward abortion using the mean value. Table 7 showed the association between sociodemographic characteristics and perceptions of abortion. There were statistically significant associations between age, ethnicity, religion, and marital status and abortion perception.

Table 8 presents the sources of information about abortion among respondents. The majority (86.7%, n = 339) reported obtaining information from the internet, newspapers, magazines, books, or articles. This was followed by friends or society (43.7%) and doctors (41.7%). The least common source was family, with only 21.5% (n = 84) of respondents indicating they received abortion-related information from family members.

Table 9 presented that among respondents with good knowledge of abortion, 59.85% had a positive perception, while 40.15% had a poor perception. In contrast, among those with poor knowledge, only 32.28% had a good perception, and 67.72% had a poor perception. The odds of having a good perception were significantly higher among those with good knowledge (OR = 3.13, 95% CI: 2.03–4.81, $p < 0.001$), indicating a strong association between knowledge and perception toward abortion.

Discussion

Abortion knowledge and perception are shaped by various factors including culture, religion, education, and socioeconomic background. Cultural and religious beliefs significantly influence attitudes, particularly views on the sanctity of life, reproductive rights, and women's autonomy. Family values, educational exposure, and access to healthcare and information also play critical roles [4].

The study found no statistically significant association between knowledge of abortion and sociodemographic factors such as age, gender, marital status, education level, religion, ethnicity, and income ($p > 0.05$). However, respondents with tertiary education demonstrated better knowledge (36.08%) than those with secondary education (27.78%). Similarly, a cross-sectional study among women in Herat, Afghanistan, found

that 76.9% of participants with high school education had a good knowledge of abortion, compared to 46.7% of illiterate participants [18]. In contrast, perception toward abortion was significantly associated with age ($p < 0.001$), ethnicity ($p < 0.001$), religion ($p = 0.007$), education level ($p = 0.014$), and marital status ($p < 0.001$). Gender, employment status, and income showed no significant associations. These findings partially contradict prior research by Tey and Yew [16], which found no link between perception and ethnicity.

The study revealed that 64.96% of respondents had poor knowledge about abortion, while 35.04% demonstrated good knowledge. These results are consistent with findings from medical students at Melaka Manipal Medical College [7] and a similar study in Trinidad and Tobago [13], where 57% lacked accurate knowledge of abortion laws. While over 77% of respondents correctly answered questions about abortion procedures, awareness of complications related to unsafe abortion—such as the risk of HIV (39.9%) and infertility (28.9%)—was significantly lower. However, 93.86% recognized heavy bleeding as a major complication. These findings mirror results from Nigeria [6].

Perceptions toward abortion were also varied, with 58.06% of respondents holding poor perceptions, and only 41.94% demonstrating a more informed and accepting view. Most supported abortion when the mother's health is at risk, and a notable 62.91% agreed or were neutral on the need to legalize abortion, recognizing that legal reform should be based on public health considerations rather than personal or political beliefs.

However, respondents generally disagreed or remained neutral when abortion was considered for reasons such as poverty, contraception failure, or anticipated birth defects. Those with good perception (41.94%) tended to support a woman's right to information and healthcare services for managing unintended pregnancies, while 58.06% showed limited acceptance.

The primary sources of information were the internet, newspapers, magazines, and articles (86.7%), followed by friends and society (43.7%), healthcare professionals (41.7%), and family (21.5%). This contrasts with findings from low- and middle-income countries where parents and educators are primary sources of information [4].

A chi-square test confirmed a significant association between knowledge and perception toward abortion ($p < 0.001$). Respondents with good knowledge were more likely to have positive perceptions. However, only 20.97% had both good knowledge and perception, while 20.97% had good knowledge but poor perception. Additionally, 3.32% had poor knowledge but good perception, and 40.66% had both poor knowledge and poor perception.

These results highlight that knowledge alone may not directly determine perception. Perception is often shaped by deep-seated beliefs, emotions, and personal experiences. Nevertheless, comprehensive and accurate knowledge can promote more compassionate perception and support informed public discourse and policy-making that protect women's reproductive rights [15,17,19].

Conclusion

This study underscores the urgent need to address the widespread lack of knowledge regarding abortion in the Klang Valley population. Although sociodemographic factors were not significantly associated with abortion knowledge, a strong relationship was observed between knowledge level and perception, with individuals possessing better knowledge generally showing more positive perception. To address these gaps, public awareness campaigns should be launched to disseminate factual, rights-based information about abortion. Comprehensive sexual and reproductive health education must be introduced in both schools and community settings to ensure early and accurate understanding. Safe and non-judgmental platforms should also be created to

provide individuals with reliable information and support.

Healthcare providers should receive proper training to deliver unbiased, evidence-based counselling on abortion and related services. These combined efforts can empower individuals with accurate knowledge, dispel misconceptions, and foster a more informed and supportive environment surrounding abortion in the Klang Valley and beyond.

Conflict of interest

The authors verified that there were no financial or commercial ties that might be viewed as having a potential conflict of interest.

Declaration of competing interests

None

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Authors' contributions

The first seven authors designed, managed, and wrote the paper as the main contributors to this study. The eighth author provided intellectual and technical input to the manuscript for publication purposes.

Table1. Sociodemographic characteristics of respondents

Variable	***Frequency (n)***	***Percentage (%)***
Gender		
Male	144	36.8
Female	247	63.2
Age (years)		
Less than equal to 29	225	57.5
More than 29	166	42.5
Ethnicity		
Malay	333	85.2
Non-Malay	58	14.8
Religion		
Islam	336	85.9
Non-Muslim	55	14.1
Education Level		
No Formal Education	2	0.51%
Primary Education	1	0.26%
Secondary Education	36	9.21%
Tertiary Education	352	90.03%
Employment Status		
Employed	187	47.83%
Unemployed	17	4.35%
Student	149	38.11%
Retired	17	4.35%
Self-employed	21	5.37%
Monthly Income		
<RM2,500	194	49.62%
RM 2,500 – RM4,849	80	20.46%
RM 4,850 – RM10,959	81	20.72%
RM 10,960	36	9.21%
Marital Status		
Married/Divorced/Separated	150	38.4
Single	251	61.6

Table 2. Knowledge questions on Abortion and its response rate

No.	Questions	Option					
		Yes		Not sure		No	
		n	%	n	%	n	%
1.	Is abortion generally legal in Malaysia?	79	20.20	88	22.51	224	57.29
2.	In Malaysia, it is permissible by law to have an abortion to preserve mother's mental health.	193	49.36	115	29.41	83	21.23
3.	Abortion is a medically safe procedure when performed with proper equipment.	304	77.75	57	14.58	30	7.67
4.	Abortion is a medically safe procedure when performed with correct technique.	309	79.03	52	13.30	30	7.67
5.	Abortion is a medically safe procedure when performed with sanitary standards.	314	80.31	49	12.3	28	7.16
6.	Abortion may lead to infertility.	113	28.90	155	39.6	123	31.46
7.	Unsafe abortion can cause heavy bleeding.	367	93.86	22	5.63	2	0.51
8.	Unsafe abortion has high risk of developing HIV or AIDS.	156	39.90	155	39.64	80	20.46

Table 3. Level of Knowledge Towards Abortion among People in Klang Valley, by using mean score

Knowledge Category	***Mean***	***n***	***%***
Good	4.69	137	35.04%
Poor		254	64.96%

Table 4. Association between socio-demographic characteristic of the respondents and level of knowledge towards abortion

Variables	Level of Knowledge				
	High n(%)	Low n(%)	X^2	df	P value
Gender					
Male	56(38.9)	88(61.1)	1.485	1	0.223
Female	81(32.8)	166(67.2)			
Age (year)					
Less than equal to 29	76(33.8)	149(66.2)	0.370	1	0.543
More than 29	61(36.7)	105(63.3)			
Ethnicity					
Malay	114(34.2)	219(65.6)	0.638	1	0.425
Non-Malay	23(39.7)	35(60.3)			
Religion					
Islam	114(33.9)	222(66.1)	1.293	1	0.256
Non-Muslim	23(41.8)	32(58.2)			
Education Level					
No Formal Education	0(0)	2(100)	2.620	3	0.454
Primary Education	0(0)	1(100)			
Secondary Education	10(27.8)	26(72.2)			
Tertiary Education	127(36.1)	225(63.9)			
Employement Status					
Employed	62(33.2)	125(66.8)	2.676	4	0.613
Unemployed	4(23.5)	13(76.5)			
Student	55(36.9)	94(63.1)			
Retired	8(47.1)	9(52.9)			
Self-employed	8(38.1)	13(61.9)			
Monthly income					
<RM2,500	65(33.5)	129(66.5)	0.751	3	0.861
RM 2,500 – RM4,849	31(38.8)	49(61.3)			
RM 4,850 – RM10,959	29(35.8)	52(64.2)			
RM 10,960	12(33.3)	24(66.7)			
Marital status					
Married/Divorced/Separated	54(36.0)	96(64.0)	0.099	1	0.753
Single	83(34.4)	158(65.6)			

Chi-square test was performed, df = degree of freedom

Table 5. Respondent's Response towards Perception Question Regarding Abortion

No.	Question	Strongly Disagree		Disagree		Neutral		Agree		Strongly agree	
		n	%	n	%	n	%	n	%	n	%
1.	Abortion should be legalised.	50	12.79	95	24.30	108	27.62	82	20.97	56	14.32
2.	Abortion should be easily accessible.	60	15.35	122	31.20	75	19.18	79	20.20	55	14.07
3.	Abortion services should be easily affordable.	55	14.07	75	19.18	102	26.09	108	27.62	51	13.04
4.	Abortion services should be made available to the public.	66	16.88	118	30.18	86	21.99	74	18.93	47	12.02
5.	Women should be given the right to decide whether to carry on with their pregnancy.	56	14.32	65	16.62	76	19.44	90	23.02	104	26.60
6.	Abortion should be carried out if the mother's physical health is risk.	8	2.05	4	1.02	27	6.91	143	36.57	209	53.45
7.	Abortion should be carried out if the mother's mental health is risk.	13	3.32	20	5.12	58	14.83	151	38.62	149	38.11
8.	Abortion should be carried out if pregnancy will result in the birth of a child with physical/mental defects.	19	4.86	84	21.48	106	27.11	83	21.23	99	25.32
9	Abortion should be carried out if a couple did not want a family.	84	21.48	133	34.02	85	21.74	41	10.49	48	12.28

Table 6. Level of Perception Towards Abortion among People in Klang Valley, by using mean score

Knowledge Category	***Mean***	***n***	***%***
Good	29.43	164	41.94%
Poor		227	58.06%

Table 7. Association between socio-demographic profile of the respondents and perception towards abortion

Variables	**Level of Perception**							
	Good n(%)	**Poor n(%)**	**X^2**	**df**	**POR**	**95% Confidence Interval**		**P value**
						Lower	**Upper**	
Gender								
Male	60(41.7)	84(58.3)	0.007		-	-	-	0.932
Female	104(42.1)	143(57.9)						
Age (year)								
More than 29	55(33.1)	111(66.9)	9.197	1	1.896	1.251	2.874	**0.002***
Less than equal to 29	109(48.1)	116(51.6)						
Ethnicity								
Non-Malay	40(69.0)	18(31.0)	20.421	1	3.746	2.058	6.818	**<0.001***
Malay	124(37.2)	209(62.8)						
Religion								
Non-Muslim	38(69.1)	17(30.9)	19.370	1	3.725	2.018	6.878	**<0.001***
Islam	126(37.5)	210(62.5)						
Education Level								
No Formal Education	0(0)	2(100)	10.673	3	-	-	-	**0.014***
Primary Education	0(0)	1(100)						
Secondary Education	7(19.4)	29(80.6)						
Tertiary Education	157(44.6)	195(55.4)						
Employment Status								
Employed	79(42.2)	108(57.8)	6.019	4	-	-	-	0.198
Unemployed	4(23.5)	13(76.5)						
Student	66(44.3)	83(55.7)						
Retired	4(23.5)	13(76.5)						
Self-employed	11(52.4)	10(47.6)						
Monthly income								
<RM2,500	82(42.3)	112(57.7)	2.330	3	-	-	-	0.507
RM 2,500 – RM4,849	35(43.8)	45(56.3)						
RM 4,850 – RM10,959	29(35.8)	52(64.2)						
RM 10,960	18(50)	18(50)						
Marital status								
Single	121(50.2)	120(49.8)	17.617	1	2.509	1.624	3.875	**0.001***
Married/Divorced/Separated	43(28.7)	107(71.3)						

Chi-square test was performed, level of significant at p<0.05; POR =Prevalence Odds Ratio, df = degree of freedom*

Table 8. Source of Information about abortion

Source of information	n	%
Doctor	163	41.7
Family	84	21.5
Friends/Society	171	43.7
Internet/Newspaper/Magazine/Book/Article	339	86.7

Table 9. Association between knowledge and perception towards abortion

Level		Perception		P-value	Odd ratio (95% CI)
		Good	Poor		
		n (%)	n (%)		
Knowledge	**Good n (%)**	82 (59.85)	55 (40.15)	**<0.001**	3.127 (2.03 – 4.81)
	Poor n (%)	82 (32.28)	172 (67.72)		

References

[1]. Oxford Bibliographies. Abortion. 2023.

[2]. WHO. Safe abortion: technical and policy guidance for health systems. 2022.

[3]. Shah I, Ahman E. Safe Abortion: Global and Regional Incidence, Trends, Consequences, and Challenges. J Obstet Gynaecol Can. 2009.

[4]. Ganatra B, Gerdts C, Rossier C, et al. Global, regional, and subregional classification of abortions by safety, 2010–14: estimates from a Bayesian hierarchical model. Lancet. 2017.

[5]. Say L, Chou D, Gemmill A, et al. Global causes of maternal death: a WHO systematic analysis. Lancet Glob Health. 2014.

[6]. Okonofua F. Abortion and Maternal Mortality in the Developing World. J Obstet Gynaecol Can. 2006.

[7]. Reproductive Rights Advocacy Alliance Malaysia (RRAAM). 2007.

[8]. Tey NP. Proximate Determinants of Fertility in Peninsular Malaysia. Asia Pac J Public Health. 2011.

[9]. Singh S, Wulf D, Hussain R, Bankole A, Sedgh G. Unintended Pregnancy and Induced Abortion in Uganda. Guttmacher Institute. 2006.

[10]. Nai-peng Tey, Yew SY. Medical students' attitudes towards abortion education: Malaysian perspective. PLoS One. 2012.

[11]. Sedgh G, Henshaw S, Singh S, Ahman E, Shah IH. Induced abortion: estimated rates and

trends worldwide. Lancet. 2007.

[12]. Shellenberg KM, et al. Social stigma and disclosure about induced abortion. Glob Public Health. 2011.

[13]. Levandowski BA, Kalilani-Phiri L, Kachale F, et al. Investigating social consequences of unwanted pregnancy and unsafe abortion in Malawi. BMC Women's Health. 2012.

[14]. Izugbara CO, Egesa CP. Women, stigma and un/safe abortion in Kenya. Soc Sci Med. 2015.

[15]. Low WY, et al. Malaysian healthcare providers' attitudes toward abortion. 2014.

[16]. Major B, et al. Abortion as stigma: Cognitive and emotional implications. 1999.

[17]. Harris LH. Stigma and abortion complications in the United States. 2012.

[18]. Rasoul A, Hashimi S, Sadat SM, Hamdard J, Akbari S, Azimi M. Assessing post-abortion care in health facilities in Afghanistan: A cross-sectional study. *BMC Pregnancy Childbirth*. 2015.

[19]. Mekonnen BD, et al. Knowledge, Attitude, and Associated Factors towards Safe Abortion. 2020.

ORIGINAL ARTICLE

Evaluation of Fitness Levels and Associated Factors among Public Health Pharmacy Staff in Perlis.

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Abstract

Background: Maintaining good fitness levels is vital for healthcare workers due to the physical and mental demands of their roles. This study assessed the fitness levels of pharmacy staff at public health clinics in Perlis and explored associated factors. **Methods:** A cross-sectional study was conducted from April to June 2024 among pharmacy staff in 13 public health facilities in Perlis. Data on sociodemographic characteristics, fitness levels (cardiovascular endurance, muscle strength, and muscle endurance), and mental health symptoms were collected using an English-language questionnaire and analysed with SPSS version 25.0. **Results:** Of the 72 participants (mean age 36.3 years, SD=7.04), most were Malay (95.8%), female (77.8%), and married (70.8%). Obesity (BMI ≥30 kg/m²) was present in 11 participants (15.3%). Cardiovascular endurance was rated average or above in 87.5% of participants, muscle strength in 55.6%, and muscle endurance in 73.6%. Overall, 37.5% were classified as physically fit. Exercising four to five times per week significantly increased the likelihood of being physically fit compared to those who did not exercise (AOR=17.29, p=0.030). **Conclusion:** A considerable proportion of pharmacy staff were not classified as physically fit, highlighting the need for targeted interventions. Regular exercise, particularly four to five times per week, was strongly associated with improved fitness levels.

Keywords: *Cardiovascular endurance, healthcare workers, muscle endurance, muscle strength, physical fitness.*

Introduction

The World Health Organization (WHO) defines physical activity as any energy-driven movement initiated by skeletal muscles, encompassing a wide range of daily activities such as commuting, working, and leisure activities like walking, cycling, sports, and active recreation [1]. Regular physical activity is vital for maintaining health, significantly reducing the risk of noncommunicable diseases like diabetes, heart disease, stroke, and certain cancers. It aids in managing blood pressure, maintaining a healthy body weight, and preventing obesity-related conditions [1]. Beyond its physical benefits, physical activity also enhances mental health by reducing anxiety and depression, contributing to an overall sense of well-being [2].

Fitness levels, which are directly linked to consistent physical activity, encompass improvements in cardiovascular endurance, muscular strength, muscle endurance, and body composition [3]. Activities such as walking, running, and cycling boost cardiovascular health and stamina, while strength training builds muscle and supports joint stability. Muscle endurance exercises are essential for maintaining performance during prolonged activities, and flexibility exercises help preserve a full range of motion, reducing the risk of injury [4]. Higher fitness levels also correlate with improved cognitive function, greater focus, and increased productivity, making physical activity a key contributor to both physical and mental resilience [5].

The importance of maintaining good fitness levels is particularly evident in healthcare workers, whose roles require physical endurance, strength, and mental resilience. High fitness levels enable healthcare workers to perform physically demanding tasks, such as moving patients or standing for long hours, while also reducing fatigue and preventing work-related injuries [6]. Evaluating fitness levels through assessment of cardiovascular endurance, muscle strength, and muscle endurance provides a comprehensive understanding of healthcare workers' physical capabilities, helping to identify areas for improvement [7]. Moreover, healthcare workers with better fitness often report improved mental clarity, focus, and stress management, which are critical qualities for delivering high-quality care in demanding environments [8].

A lack of physical fitness has been associated with several occupational concerns, including reduced work productivity, increased rates of absenteeism, and a higher incidence of medication errors in healthcare settings [9]. Physically inactive workers are more likely to experience musculoskeletal problems, fatigue, and chronic diseases, all of which contribute to workplace inefficiencies and safety concerns. In pharmacy practice specifically, where precision and sustained concentration are essential, these negative outcomes can impact on both staff well-being and patient safety.

Despite the well-documented benefits of physical activity, a significant portion of the global population, including healthcare workers, fails to engage in sufficient physical activity. According to the WHO, 1.4 billion adults, which is over 25% of the global adult population, fail to meet the recommended activity levels, with one in three women and one in four men affected [1]. This inactivity is also prevalent in the healthcare sector, where many employees lead sedentary lifestyles. A study conducted in Perak revealed that 45.6% of primary healthcare personnel were physically inactive, averaging five hours of sedentary behavior per day [10]. Additionally, the same study found that 51% of healthcare workers were at risk of abdominal obesity, 49.9% were overweight or obese, and 79.6% had excessive body fat percentages [11]. Further research by Kunyahamu et al. showed that only 43% of healthcare workers had a normal BMI, while 33.1% were classified as overweight and 21.1% as obese [12].

Pharmacists and pharmacy assistants play crucial roles in healthcare delivery, ensuring that patients receive accurate medication management and counseling. Despite the evident importance of assessing healthcare workers' fitness status, the literature on the fitness levels of pharmacists and

pharmacy assistants in Malaysia remains relatively scarce [13]. Understanding and evaluating their fitness levels is essential as it can significantly promote their health and well-being, potentially leading to reduced absenteeism and enhanced job satisfaction [9]. A healthy workforce is vital for maintaining high standards of care, reducing the risk of errors, and improving overall productivity [14]. Moreover, encouraging physical fitness among these healthcare professionals not only benefits their personal health but also sets a positive example for patients, reinforcing the importance of a healthy lifestyle [15].

This study focused specifically on pharmacy staff at public health clinics in Perlis rather than including those from hospitals. The rationale for this decision lies in the distinct work environments and service demands between the two settings. Public health clinic pharmacy staff often handle high outpatient volumes, provide community health outreach, and work in smaller teams, potentially placing them at greater risk of sedentary behavior and physical inactivity. In contrast, hospital pharmacy staff may operate within larger teams with more role division and a different workflow. Furthermore, the public health setting in Perlis offered consistent access across facilities, making data collection more feasible and representative of primary care services.

Given these concerns, this study aims to evaluate the fitness levels of pharmacy staff at public health clinics in Perlis, focusing on key components of physical fitness, including cardiovascular endurance, muscle strength, and muscle endurance. By assessing these parameters, the study will provide a comprehensive understanding of the overall fitness levels of pharmacy staff, highlighting their physical health in relation to their ability to perform tasks that require sustained energy, strength, and stamina. In addition to evaluating these fitness components, the study will explore factors influencing physical activity among this group. Identifying these factors will help pinpoint barriers to physical activity and offer insights into potential strategies for promoting a healthier, more active lifestyle among pharmacy staff.

Methods

This was a cross-sectional study that targeted all pharmacy staff (including pharmacists and pharmacy assistants) from all 13 public health facilities in Perlis from April to June 2024. The study population included those who were on duty (not on long-term or extended leave) and performing their usual work roles during the study period. Staff members on extended leave (e.g., maternity, study, or unpaid leave exceeding two weeks) were excluded.

A universal sampling method was employed to invite all eligible pharmacy staff to participate. Although the study aimed to include all staff members, the estimated minimum required sample size was calculated using the single proportion formula. Using a 95% confidence interval ($Z = 1.96$), an estimated prevalence (P) of physical inactivity at 0.456 based on previous findings [10], and a margin of error (d) of 0.10, the calculated minimum sample size was 95 participants. The universal approach ensured that the entire accessible population was approached to minimize sampling bias.

This study was registered with the National Medical Research Register (NMRR ID-24-00117-07L) with ethical approval. Before data collection, permission to conduct this study was obtained from the Kangar District Health Officer. Investigators recruited participants for the study by scheduling appointments at each facility for data collection. During each visit, all eligible participants received detailed information about the study and had the opportunity to ask questions for clarification. Only individuals who provided consent received a paper-based questionnaire. The questionnaire, available in English, consists of two parts.

Sociodemographic and lifestyle information

The first part collected sociodemographic information, including weight, height, BMI, age, gender, race, marital status, number of children, education level, and number of shifts per month. Number of shifts per month, defined in this study as any work assignment outside regular weekday hours (8 am–5 pm), including on-call duty, night shifts, weekend duties, or extended overtime hours. It also gathered data related to exercise routines, and dietary plans (e.g., Keto diet, fasting, intermittent fasting).

Medical history and symptoms of mental health

Medical history (asthma, diabetes mellitus, hypertension, and dyslipidemia) and symptoms of mental health (depression, stress, and anxiety) were also recorded. The questionnaire utilized the Depression, Anxiety, and Stress Scale (DASS-21), which is a shorter version of the DASS-42 survey [16]. Each of the three components contains seven items rated on a 4-point Likert scale from 0 ("Did not apply to me at all") to 3 ("Applied to me very much or most of the time"). The following conventional cut-off scores were used to interpret the severity levels of depression, anxiety, and stress in the DASS-21: for depression, scores of 0–9 were considered normal, 10–13 mild, 14–20 moderate, 21–27 severe, and 28 or above extremely severe; for anxiety, scores of 0–7 were normal, 8–9 mild, 10–14 moderate, 15–19 severe, and 20 or above extremely severe; and for stress, scores of 0–14 were normal, 15–18 mild, 19–25 moderate, 26–33 severe, and 34 or above extremely severe [16].

Fitness assessment

Three fitness components were measured:

- Cardiovascular Endurance was assessed by using the YMCA 3-Minute Step Test. Participants stepped up and down on a 12-inch bench at a consistent pace for 3 minutes. Heart rate was recorded immediately after the post-test. Fitness classification was based on heart rate recovery benchmarks by age and gender following the YMCA norms [17].
- Muscle strength was assessed using the Five-Level Sit-Up Test. Participants were required to perform sit-ups with increasing levels of difficulty, and the highest level successfully completed was recorded. Those who were unable to perform even the easiest movement were classified as 'Very Weak', while participants who could place both hands behind the head and perform a sit-up until the chest touched the thighs were classified as 'Excellent' [18].
- Muscle Endurance was measured by the Push-Up Test (standard push-ups for men; modified/knee push-ups for women). The number of correct repetitions performed in one minute was used. Classification of fitness level was based on established ACSM normative data [19].

Participants who scored “below average” or “poor” in any fitness categories were classified as “unfit,” while those who scored “average” or higher in all categories were classified as “fit.”

Data analysis

The data were analyzed using SPSS version 25.0 [20]. Descriptive statistics were employed to measure the sociodemographic characteristics of participants. The Chi-square test or Fisher’s Exact Test was used for associations between categorical variables and fitness classification. The Independent t-test was used for continuous variables after checking assumptions of normality (Shapiro-Wilk test) and homogeneity of variance (Levene’s test).

Variables with p-values < 0.25 in univariate analysis were entered into multiple logistic regression to identify predictors of fitness level. Multicollinearity was assessed using Variance Inflation Factor (VIF), with values <5 indicating no concern. Model fit was evaluated using the Hosmer-Lemeshow goodness-of-fit test, and the Nagelkerke R^2 was reported to indicate the proportion of variance explained [21].

Results

Participants' characteristics and lifestyle behaviours

The questionnaire was distributed to 97 eligible participants at public health clinics, and 72 pharmacy staff responded, resulting in a response rate of 74.2%. The sociodemographic characteristics and lifestyle behaviors of the respondents are shown in Table 1. Overall, participants were predominantly Malay (n=69, 95.8%), female (n=56, 77.8%), and married (n=51, 70.8%). The average age was 36.3 years (SD = 7.04). Nearly two-thirds of respondents were pharmacists, while the remainder were pharmacy assistants. More than half (58.3%) reported having one to three shifts per week.

Notably, eleven participants (15.3%) were classified as obese, with a body mass index (BMI) of 30 kg/m² or higher. Only 26.4% reported following a specific diet plan, such as the Keto diet or intermittent fasting. Physical activity levels were generally low, with nearly 40% reporting no regular exercise. Another quarter of the participants (n=18) engaged in physical exercise two to three times per week. Only a small minority (5.6%, n=4) reported exercising four to five times per week.

Medical history and symptoms of mental health

Table 2 summarises the self-reported medical history of participants. The majority reported no chronic health conditions. Hypertension (8.3%) and diabetes mellitus (5.6%) were the most commonly reported conditions, followed by dyslipidemia (4.2%) and asthma (2.8%). Table 3 summarises the prevalence of depression, anxiety, and stress symptoms among participants. Most participants reported normal levels across all three domains. However, symptoms of anxiety were more commonly reported (22.2%) compared to depression (13.9%) and stress (9.7%). Severe or extremely severe symptoms were rare across all categories.

Assessment of fitness level

Table 4 presents the assessment of participants' physical fitness across multiple domains. In terms of cardiovascular endurance, most participants rated within the "good" to "excellent" range, accounting for over half of the respondents. Muscle strength assessments revealed a broader distribution, with a notable proportion falling in the "poor" to "very poor" categories (44.4%). Muscle endurance was generally better, with the majority achieving "average" or "good" levels. Despite some positive indicators in individual components, overall fitness classification showed that 62.5% of participants were considered unfit, while only 37.5% were categorised as fit.

Factors associated with fitness level

Univariate analysis indicated that only one factor, frequency of exercise, was significantly associated with overall fitness level (Table 5). After adjusting for confounding variables in the multiple logistic regression (Table 6), it was found that individuals who engaged in frequent physical exercise showed higher fitness levels. Specifically, those who exercised two to three times per week had 4.49 times the odds of being fit compared to non-exercisers (p=0.030). Furthermore, individuals who exercised four to five times per week had 17 times the odds of achieving fitness compared to those who did not exercise (p=0.030).

Discussion

Similar to a previous study, the current study found that less than half of the participants were categorized as physically fit, highlighting a concerning trend of suboptimal fitness levels among pharmacy staff [10]. This finding suggests that a significant portion of the participants may not be meeting the recommended levels of physical activity and fitness. Studies have attributed low fitness levels in similar populations to sedentary work, long or irregular hours, and limited opportunities for physical activity during the workday [22]. The occupational implications

are noteworthy, as poor physical fitness among healthcare professionals can lead to increased fatigue, decreased productivity, and higher rates of absenteeism [22]. Addressing this issue requires workplace-level strategies, such as integrating wellness programs, providing access to on-site or subsidised fitness facilities, scheduling protected time for exercise, and promoting active commuting.

The present study found that none of the demographic factors, including age, gender, and BMI, were significantly associated with overall fitness level, even in the univariate analysis. This suggests that demographic characteristics alone may not adequately predict physical fitness among pharmacy staff. One possible explanation is that the homogeneity of the study population, in terms of occupation, work setting, and potentially shared health awareness which may reduce variability in fitness determinants typically observed in more heterogeneous populations. Additionally, the lack of association might reflect the overriding influence of modifiable lifestyle behaviours, particularly physical activity levels, which showed a strong and statistically significant relationship with fitness. These findings align with some previous research that highlights behaviour over background as a key determinant of fitness [23]. Individuals who engage in regular exercise and lead active lifestyles tend to exhibit higher fitness levels through improvements in cardiovascular health, muscular strength, and overall physical performance [24].

The frequency of exercise plays a significant role in determining an individual's fitness level, serving as a cornerstone for maintaining and enhancing overall health. Regular physical activity is essential for cardiovascular health and muscle strength [25]. The current study has shown that individuals who exercise four to five times per week exhibit significantly higher fitness levels compared to those who do not exercise, suggesting that regular physical activity has a strong and measurable impact on fitness outcomes. This finding is consistent with prior studies among healthcare professionals, where higher physical activity levels were positively associated with better health indicators [26]. However, among pharmacy staff, engaging in regular exercise may be particularly challenging due to job-related barriers such as prolonged standing, fixed schedules, or limited time for physical activity during or after work hours. Compared to other healthcare professions, pharmacists may have fewer structured wellness initiatives integrated into their workplace settings. This highlights the need for targeted interventions such as incorporating short activity breaks during shifts, promoting active commuting, or providing incentives for gym memberships to support regular exercise among pharmacy personnel. Addressing these occupational barriers can help improve physical fitness and contribute to long-term health and productivity in this essential workforce.

While previous literature supports a positive relationship between physical activity and mental health, particularly in reducing symptoms of depression, anxiety, and stress, the current study found no significant association between mental health status as measured using the DASS-21 and fitness levels among participants. This finding aligns with other studies that have also reported mixed or non-significant results in healthcare populations, suggesting that the relationship may be more complex than direct cause and effect [27]. Several factors may explain this, including the potential influence of occupational stressors, coping mechanisms unrelated to physical activity, or the presence of latent confounding variables such as sleep quality, workload, or social support [28]. Additionally, pharmacy staff may experience stress that is not alleviated solely by physical activity, especially if time constraints or job demands prevent consistent exercise. These findings underscore the need for more nuanced, multifactorial approaches to promoting mental well-being in healthcare workers, rather than relying solely on physical fitness interventions.

One of the primary limitations of the study was its small sample size, which may have reduced the statistical power to detect significant associations, increased the risk of type II errors, and affected the stability and generalizability of the multivariate models. Additionally, the study's regional focus on pharmacy staff in Perlis limits the applicability of the findings to other populations or healthcare settings. Future research efforts could benefit from conducting larger-scale, multicenter studies across Malaysia to improve representativeness and provide a more comprehensive national picture.

Further studies should also consider collecting additional data on factors that may influence fitness, such as physical activity measurements using wearable devices, occupational workload, sleep patterns, dietary habits, and organisational factors like access to wellness programmes or time allocated for physical activity. Including these parameters would allow for a more nuanced analysis of contributors to fitness and enable the development of tailored, evidence-based interventions.

Conclusion

The study revealed a significant portion of participants were not categorized as fit, indicating a concerning trend among pharmacy staff. The frequency of exercise significantly impacts fitness, with those exercising four to five times per week demonstrating higher levels of physical fitness. Given the sedentary nature of pharmacy work and long working hours, tailored interventions such as workplace wellness programs, flexible exercise opportunities, and community-based fitness initiatives are essential to support active lifestyles among pharmacy personnel. Promoting regular physical activity and healthy behaviours within the occupational context can improve overall health and work performance. Future research should explore specific occupational barriers to physical activity and inform the design of targeted strategies to enhance fitness outcomes in this professional group.

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Conflict of interest

All authors declared that no conflict of interest may arise from this research.

Ethics clearance

The Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia (MOH) has provided ethical approval for this study (NMRR ID-24-00117-07L (IIR)).

Authors' contributions

SPP, MHFSH and SM came out with the study design. SPP, MHFSH, SM and NM performed the literature search and data collection SPP and NYH were involved in the statistical analysis and manuscript preparation. All authors agreed and approved the manuscript for publication.

Table 1. Participants' sociodemographic data and lifestyle behaviors, n=72

Variable	Category	n (%)	Mean (SD)
Age (years)			36.30 (7.04)
Gender	Male	16 (22.2)	
	Female	56 (77.8)	
Ethnicity	Malay	69 (95.8)	
	Chinese	1 (1.4)	
	Indian	1 (1.4)	
	Others	1 (1.4)	
Marital status	Single	19 (26.4)	
	Married	51 (70.8)	
	Divorced	2 (2.8)	
Number of children	None	26 (36.1)	
	1-3	35 (48.6)	
	>3	11 (15.3)	
Education level	Diploma	26 (36.1)	
	Degree	46 (63.9)	
Occupation	Pharmacist	46 (63.9)	
	Pharmacist assistant	26 (36.1)	
Number of shifts per week	None	16 (22.2)	
	1-3/week	42 (58.3)	
	>3/week	14 (19.4)	
BMI (kg/m^2)	Non-obese	61 (84.7)	
	Obese (≥ 30 kg/m^2)	11 (15.3)	
Diet plan	Yes	19 (26.4)	
	No	53 (73.6)	
Exercise	None	28 (38.9)	
	1/week	22 (30.6)	
	2-3/week	18 (25.0)	
	4-5/week	4 (5.6)	

SD=Standard deviation

Table 2. Medical history, n=72

Variable	Category	n (%)
Asthma	Yes	2 (2.8)
	No	70 (97.2)
Diabetes mellitus	Yes	4 (5.6)
	No	68 (94.4)
Hypertension	Yes	6 (8.3)
	No	66 (91.7)
Dyslipidemia	Yes	3 (4.2)
	No	69 (95.8)

Table 3. Prevalence of depression, anxiety and stress symptoms among pharmacists and pharmacist assistants in Perlis, n=72

Variable	Category	n (%)
Depression	Normal	62 (86.1)
	Mild	3 (4.2)
	Moderate	6 (8.3)
	Severe	1 (1.4)
	Extremely severe	0
Anxiety	Normal	56 (77.8)
	Mild	6 (8.3)
	Moderate	7 (9.7)
	Severe	1 (1.4)
	Extremely severe	2 (2.8)
Stress	Normal	65 (90.3)
	Mild	4 (5.6)
	Moderate	2 (2.8)
	Severe	1 (1.4)
	Extremely severe	0

Table 4. Assessment on fitness level, n=72

Variable	Category	n (%)
Cardiovascular endurance	Very poor	1 (1.4)
	Poor	8 (11.1)
	Average	12 (16.7)
	Above average	14 (19.4)
	Good	17 (23.6)
	Excellent	20 (27.8)
Muscle strength	Very poor	15 (20.8)
	Poor	17 (23.6)
	Average	8 (11.1)
	Above average	9 (12.5)
	Good	10 (13.9)
	Excellent	13 (18.1)
Muscle endurance	Very poor	9 (12.5)
	Poor	10 (13.9)
	Average	27 (37.5)
	Good	20 (27.8)
	Excellent	6 (8.3)
Overall fitness level	Fit	27 (37.5)
	Unfit	45 (62.5)

Table 5. Univariable analysis on factors associated with fitness level, n=72

Variable	Category	Fit n=27	Unfit n=45	Test-statistics	*p*-value
Demographic data					
Age		35.3 (5.50)	36.9 (7.81)	t (70) = -0.93	0.356
Gender	Male	6 (37.5)	10 (62.5)	X^2 (1) = 0.00	1.000 [a]
	Female	21 (37.5)	35 (62.5)		
Ethnicity	Malay	27 (39.1)	42 (60.9)		
	Chinese	0 (0)	1 (100)	X^2 (3) =3.56	0.313 [b]
	Indian	0 (0)	1 (100)		
	Others	0 (0)	1 (100)		
Marital status	Married	17 (33.3)	34 (66.7)	X^2 (1) =1.30	0.255 [a]
	Unmarried	10 (47.6)	11 (52.4)		
Number of children	None	12 (46.2)	14 (53.8)	X^2 (2) =1.48	0.478 [a]
	1-3	12 (34.3)	23 (65.7)		
	>3	3 (27.3)	8 (72.7)		
Education level	Secondary school	0 (0)	3 (100)	X^2 (3) =-3.87	0.276 [b]
	Diploma				
	Degree	9 (39.1)	14 (60.9)		
		18 (39.1)	28 (60.9)		
Occupation	Pharmacist	18 (39.1)	28 (60.9)	X^2 (1) =0.14	0.704 [a]
	Pharmacist assistant	9 (34.6)	17 (65.4)		
		31 (39.2)	48 (60.8)		
Number of shifts per month	None	8 (50.0)	8(50.0)	X^2 (2) =1.40	0.497 [a]
	1-3/week	14 (33.3)	28 (66.7)		
	>3/week	5 (35.7)	9 (64.3)		
BMI (kg/m^2)		24.7 (5.74)	26.5 (5.92)	t (70) = -1.26	0.211
Diet plan	Yes	7 (36.8)	12 (63.2)	X^2 (1) =0.005	0.945 [a]
	No	20 (37.7)	33 (62.3)		
Exercise	None	5 (17.9)	23 (82.1)	X^2 (3) =8.80	0.032 [b]
	1/week	10 (45.5)	12 (54.5)		
	2-3/week	9 (50.0)	9 (50.0)		
	4-5/week	3 (75.0)	1 (25.0)		
Emotional states					
Depression	Without symptom	23 (37.1)	39 (62.9)	X^2 (1) =0.03	0.860 [a]
	With symptom[#]	4 (40.0)	6 (60.0)		
Anxiety	Without symptom	22 (39.3)	34 (60.7)	X^2 (1) =0.34	0.558 [a]
	With symptom[#]	5 (31.3)	11 (68.8)		
Stress	Without symptom	23 (35.4)	42 (64.6)	X^2 (1) =1.28	0.413 [b]
	With symptom[#]	4 (57.1)	3 (42.9)		

SD=standard deviation; t=t-statistic; X^2= X^2 statistic; a = chi-square; b = fisher exact; *=statistically significant at $p<0.05$; All variables of $p<0.25$ were included for multivariable analysis; #the cut-off score for depression, anxiety, and stress were ≥10, ≥8, and ≥15, respectively.

Table 6. Multiple logistic regression on factors associated with fitness level, n=72

Variable	Category	Adjusted OR (95% CI)	*p*-value
BMI		0.94 (0.85, 1.04)	0.227
Exercise	None (R)		0.128
	1/week	3.43 (0.94, 12.53)	0.062
	2-3/week	4.49 (1.16, 17.41)	0.030*
	4-5/week	17.29 (1.31, 227.98)	0.030*

OR=odds ratio; 95% CI=95% confidence interval; (R)=reference group; *=$p<0.05$, $R^2 = 0.19$

References

[1]. World Health Organization. Physical activity. WHO. 2022. Available from: https://www.who.int/news-room/fact-sheets/detail/physical-activity

[2]. Warburton DER, Bredin SSD. Health benefits of physical activity: a systematic review of current systematic reviews. Curr Opin Cardiol. 2017;32(5):541-56. https://doi.org/10.1097/HCO.0000000000000437

[3]. Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. Public Health Rep. 1985;100(2):126-31. https://pubmed.ncbi.nlm.nih.gov/3920711/

[4]. Garber CE, Blissmer B, Deschenes MR, et al. American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. Med Sci Sports Exerc. 2011;43(7):1334-59. https://doi.org/10.1249/MSS.0b013e318213fefb

[5]. Hillman CH, Erickson KI, Kramer AF. Be smart, exercise your heart: exercise effects on brain and cognition. Nat Rev Neurosci. 2008;9(1):58-65. https://doi.org/10.1038/nrn2298

[6]. Togashi, K., Nakashima, T., & Sato, K.. The influence of physical fitness on work-related injuries and performance in healthcare workers. Journal of Occupational Health. 2016;58(5), 379-384. https://doi:10.1539/joh.16-0196-OA

[7]. Stults-Kolehmainen MA, Sinha R. The effects of stress on physical activity and exercise. Sports medicine. 2014;44:81-121. https://doi:10.1007/s40279-013-0090-5

[8]. Magnavita N, Garbarino S. Sleep, health and wellness at work: A scoping review. Int J Environ Res Public Health. 2017;14(11):1347. https://doi.org/10.3390/ijerph14111347

[9]. Jakobsen MD, Sundstrup E, Brandt M, Jay K, Aagaard P, Andersen LL. Physical exercise at the workplace prevents deterioration of work ability among healthcare workers: cluster randomized controlled trial. BMC public health. 2015;15:1-9. https://doi:10.1186/s12889015-2448-0

[10]. Abu Saad H, Abdullah N, Mohd Nor NA, et al. Level of Physical Activity and Its Associated Factors among Primary Healthcare Workers in Perak, Malaysia. Int J Environ Res Public Health. 2020 Aug

16;17(16):5947. https://doi:10.3390/ijerph17165947

[11]. Kit LP, Abu Saad HA, Jamaluddin R, Phing CH. Prevalence of overweight and obesity among primary healthcare workers in Perak, Malaysia. IIUM Med J Malaysia. 2020 Nov 4;19(1):1327. https://doi:10.31436/imjm.v19i1.1327

[12]. Kunyahamu MS, Daud A, Jusoh N. Obesity among Health-Care Workers: Which Occupations Are at Higher Risk of Being Obese? International Journal of Environmental Research and Public Health [Internet]. 2021; 20;18(8):4381. https://doi.org/10.3390/ijerph18084381

[13]. Soleimani E, Tahmasebi R, Daneshmandi H, Salimi SH, Aliasghari F. Work-life balance and health among pharmacists: physical activity, sleep quality, and general health. BMC Health Services Research. 2024. 11;24(1):1217. https://doi.org/10.1186/s12913-024-11701-w

[14]. Edem MJ, Akpan EU, Pepple NM. Impact of workplace environment on health workers. Occup Med Health Aff. 2017 Jul;5(2):1-5. https://doi.10.4172/2329-6879.1000261

[15]. Oberg EB, Frank E. Physicians' health practices strongly influence patient health practices. The journal of the Royal College of Physicians of Edinburgh. 2009;39(4):290. https://doi: 10.4997/JRCPE.2009.42

[16]. Lovibond SH, Lovibond PF. Manual for the Depression Anxiety Stress Scales. 2nd ed. Sydney: Psychology Foundation; 1995. https://doi.org/10.1037/t01004-000

[17]. Golding LA. YMCA Fitness Testing and Assessment Manual. 4th ed. Champaign: Human Kinetics; 2000.

[18]. Garberr CE, Blissmeer B, Descheness MR, et al. American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults. Med Sci Sports Exerc. 2011;43(7):1334-59. https://doi.org/10.1249/MSS.0b013e318213fefb

[19]. American Council on Exercise (ACE). ACE Personal Trainer Manual. 5th ed. San Diego: American Council on Exercise; 2014.

[20]. SPSS Inc. SPSS Statistics for Windows, Version 25.0. Armonk (NY): IBM Corp.; 2017.

[21]. Hosmer D, Lemeshow S. Applied logistic regression. 3rd ed. New York (NY): Wiley; 2013.

[22]. Cohen C, Pignata S, Bezak E, Tie M, Childs J. Workplace interventions to improve well-being and reduce burnout for nurses, physicians and allied healthcare professionals: a systematic review. BMJ Open. 2023;13(6):e071203. https://doi.org/10.1136/bmjopen-2022-071203

[23]. Wannamethee SG, Shaper AG, Whincup PH. Modifiable lifestyle factors and the metabolic syndrome in older men: effects of lifestyle changes. Journal of the American Geriatrics Society. 2006 ;54(12):1909-14. https://doi.10.1111/j.1532-5415.2006.00974.x

[24]. Warburton DER, Bredin SSD. Health Benefits of Physical activity: a Systematic Review of Current Systematic Reviews. Curr Opin Cardiol. 201;32(5):541–56.

https://doi:10.1097/HCO.0000000000000437

[25]. Pinckard K, Baskin KK, Stanford KI. Effects of Exercise to Improve Cardiovascular Health. Frontiers in Cardiovascular Medicine [Internet]. 2019 Jun 4;6(69). Available from: https://doi.org/10.3389/fcvm.2019.00069

[26]. Abu Saad H, Low PK, Jamaluddin R, Chee HP. Level of physical activity and its associated factors among primary healthcare workers in Perak, Malaysia. International journal of environmental research and public health. 2020;17(16):5947. https://doi: 10.3390/ijerph17165947

[27]. Kua Z, Hamzah F, Tan PT, Ong LJ, Tan B, Huang Z. Physical activity levels and mental health burden of healthcare workers during COVID-19 lockdown. Stress and Health. 2022 Feb;38(1):171-9. https://doi. 10.1002/smi.3078 [27]. Salgado de Snyder VN, Villatoro AP, McDaniel MD, Ocegueda AS, Garcia D, Parra-Medina D. Occupational stress and mental health among healthcare workers serving socially vulnerable populations during the COVID-19 pandemic. Frontiers in public health. 2021 9;9:782846. https://doi.10.3389/fpubh.2021.782846

ORIGINAL ARTICLE

The Satisfaction-Success Paradox: Online Distance Learning Outcomes among Nursing Students during the COVID-19 Pandemic.

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Abstract

Introduction: The COVID-19 pandemic triggered an abrupt global transition to Online Distance Learning (ODL), posing significant challenges for nursing education, which depends heavily on hands-on clinical experiences. Although nursing students reported varying degrees of satisfaction with online learning, the extent to which these perceptions influenced academic success remained unclear. **Methods:** A cross-sectional study was conducted among 164 undergraduate nursing students at Universiti Kuala Lumpur Royal College of Medicine Perak (UniKL RCMP) between August 2023 and January 2024. Participants completed a sociodemographic questionnaire, a validated 20-item Learning Satisfaction Scale, and provided their cumulative Grade Point Average (GPA).. Descriptive statistics were used to summarise participant characteristics and satisfaction levels, while Spearman's rank-order correlation assessed the relationship between learning satisfaction and academic performance. **Results:** Most participants were female (82.3%) and aged between 18 and 25 years (93.3%). The majority reported average internet stability (62.2%) and financial burden (63.4%) during ODL. Overall, 70.7% of students demonstrated moderate learning satisfaction, while 29.3% expressed low satisfaction. The mean GPA was 3.37 ± 0.32, with 60.4% achieving satisfactory and 34.7% excellent performance. Correlation analysis revealed no significant association between total learning satisfaction and GPA ($r_s = 0.033$, $p = 0.672$), indicating that satisfaction did not influence academic performance. **Conclusion:** Although nursing students maintained satisfactory academic results, their overall learning satisfaction remained moderate. Academic performance during ODL may have been shaped more by motivation, adaptability, and institutional support. Continuous improvement in instructional design, interaction, and learner support is vital to enhance satisfaction and academic outcomes in future blended or online nursing education.

Keywords: *Academic performance, COVID-19, GPA, nursing education, online distance learning, student satisfaction.*

Introduction

The COVID-19 pandemic forced a sudden and seismic shift in higher education, pushing institutions globally to abandon traditional classrooms for Online Distance Learning (ODL) almost overnight [1]. This posed a particular challenge for nursing education, a field deeply rooted in clinical practice, hands-on simulation, and direct patient interaction—elements profoundly difficult to deliver in a virtual environment [2]. In Malaysia, the imposition of the Movement Control Order (MCO) from 2021 to 2022 formally suspended all in-person instructions, including essential clinical training. In response, the government leveraged its pre-existing investments in Learning Management Systems (LMS), to facilitate the rapid implementation of ODL and emergency remote teaching (ERT).

Student satisfaction has long been considered a barometer of educational quality and program effectiveness [3]. It encompasses a student's perception of everything from course design and technological ease to their interactions with instructors and peers. On the other hand, academic performance, typically measured by Grade Point Average (GPA), remains the primary, though imperfect, benchmark for student success [4].

The link between a student's satisfaction with their learning environment and their subsequent academic performance in ODL settings is not straightforward. Some studies suggest a positive cycle, where satisfied students perform better [1]. However, other evidence points to a troubling trend where dissatisfaction with ODL contributes to academic struggles, raising urgent questions about how the quality of the learning experience impacts achievement in practice-intensive fields like nursing [5].

This study, therefore, sought to delve into this complex dynamic by aiming to: (i) gauge the level of learning satisfaction with ODL among nursing students, (ii) assess their academic performance via GPA, and (iii) critically examine the relationship between the two to determine if lower satisfaction could predict weaker academic outcomes during the pandemic.

Materials and methods

Study design

A cross-sectional study was conducted between August 2023 and January 2024 at Universiti Kuala Lumpur Royal College of Medicine Perak (UniKL RCMPThe study population comprised of nursing students enrolled in Semesters 2 to 6, who had completed at least one semester of ODL during the COVID-19 pandemic.

Samples and Samplings

The minimum required sample size was estimated using the Raosoft calculator, based on a 95% confidence level and a 5% margin of error. The calculation yielded 137 participants; however, anticipating a 20% attrition rate, the target sample was adjusted to 164, which was achieved. Participants were selected through convenience sampling.

Data Collection Instruments

The instrument used in this study consists of two sections:

Section A: Sociodemographic and Academic Data

Data on age, gender, semester level, primary device used for ODL (laptop, tablet, or smartphone), perceived financial burden (yes/no), and internet stability (good, average, poor) were collected. Academic performance was measured using the cumulative GPA on a 4.00 scale, verified against institutional records.

Section B: Learning Satisfaction

Learning satisfaction was measured using a 20-item modified instrument adapted from previously validated tools by Wan Mamat, et al (2022) and Bolliger, et al (2009) [5,6]. The scale assessed four domains: student readiness and perceptions of the learning environment,

technological and institutional support, educator–student interaction, and course content and critical challenges. Items were rated on a 5-point Likert scale (1 = Strongly Disagree to 5 = Strongly Agree) and reverse-scored for negatively worded items. The instrument was first validated through a pilot study with 30 students, and the survey items were finalised based on its results. The instrument demonstrated strong reliability (Cronbach's $\alpha = 0.91$). For negatively phrased statements (Items 17, 18, and 20), reverse scoring was applied before data analysis to ensure that higher scores consistently reflect a more positive perception of the online learning environment.

Data Collection and Processing

Eligible students were invited to participate via WhatsApp. Data were collected using a Google Forms survey after consent. All participants were provided with detailed information regarding the study's aims, procedures, and the confidentiality of their responses. Informed consent was obtained electronically, and students retained the right to withdraw at any stage without penalty. A total of 164 nursing students participated in the study, yielding a 100% response rate.

Data Analysis

Data were analysed using SPSS version 25 (IBM Corp., 2017). IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp. Descriptive statistics (frequencies, percentages, means, and standard deviations) summarised participant characteristics, learning satisfaction, and GPA. Since the data were not normally distributed, the relationship between learning satisfaction and GPA was examined using Spearman's rank correlation coefficient. A p-value of less than 0.05 was considered statistically significant.

To categorise continuous satisfaction and GPA scores into meaningful groups, Bloom's Cut-Off Point framework [7] was employed in this study (see Table 1). For evaluating academic performance, students' final course GPAs (on a 4.0 scale) were classified as follows: Excellent (above 3.50), Satisfactory (2.80–3.50), and Poor (below 2.80). This approach enabled a more nuanced assessment of academic achievement, moving beyond a simple pass/fail distinction. It also allowed for identifying students who may benefit from additional educational support, as well as those excelling academically.

Similarly, learning satisfaction was assessed using the Bloom's Cut-Off Point framework, which grouped responses into three categories: high satisfaction (80%–100%), moderate satisfaction (60%–79%), and low satisfaction (below 60%). This method provided clearer insight into students' perceptions of their online learning experiences and helped pinpoint areas where instructional quality and engagement could be improved.

Ethical consideration

Ethical approval for this study was granted by the Universiti Teknologi MARA (UiTM) Research Ethics Committee (Reference: 500-FSK/PT.23/4). Participation was entirely voluntary, with informed consent obtained from all participants prior to their involvement. All procedures in this study adhered to ethical standards, and participants' anonymity was maintained. Informed consent was secured from all, ensuring their voluntary participation and confidentiality of their responses.

Results

The majority of participants were female (82.3%, n = 135) with a male-to-female ratio of 1:5 (Table 2). Most participants reported using laptops (26.2%, n = 43) or tablets (21.3%, n = 35) as their primary device for online learning. More than half (63.4%, n = 104) experienced a financial burden due to ODL, and most rated their internet connection as average (62.2%, n = 102).

Level of Learning Satisfaction

The findings in Table 3 provide a detailed overview of students' level of learning satisfaction with their online distance learning (ODL) experiences. Overall, the results indicate that most students reported moderate satisfaction across various aspects of learning, with certain areas showing clear challenges.

Domain 1: Student Readiness and Perception of the Learning Environment

In the student readiness and perception of the learning environment, a large majority of students (78.7%) agreed that they could organise their time effectively for learning, while 69.5% felt that ODL helped them become more organised. However, many students (76.2%) also expressed the need for a tutor to explain difficult concepts, suggesting that independent learning through ODL may not fully meet their academic needs. When asked about safety and comfort, 61% agreed that they felt safer learning online than in a traditional classroom, while 71.3% reported that studying from home improved their academic performance. This reflects a positive adaptation to online learning, though it may also indicate that comfort does not necessarily translate to higher satisfaction or engagement.

Domain 2: Technological and Institutional Support

In terms of technological and institutional support, most students were generally satisfied with the university's preparedness and accessibility. For example, over 80% agreed that registration procedures, course organisation, and website navigation were satisfactory. However, some respondents still perceived limitations in system design and accessibility, which may have affected their overall satisfaction.

Domain 3: Educator–Student Interaction

Regarding educator–student interaction, 61% agreed that there was adequate interaction among participants, although about one-fourth (25%) felt that digital learning tools contributed to lower academic performance.

Domain 4: Course Content and Critical Challenges

Finally, under course content and critical challenges, nearly all respondents (95.1%) agreed that the high volume of online assignments and assessments caused confusion and frustration. Similarly, most students found online quizzes and exams stressful and less comfortable than in-person assessments. Many (78%) also emphasized that face-to-face interaction significantly enhances learning outcomes.

Students' Learning Satisfaction Level and Academic Performance

Most students reported a moderate level of learning satisfaction (70.7%), while nearly one-third (29.3%) expressed low satisfaction with their online distance learning experience. The overall mean score of 1.71 ± 0.46 supports this finding, indicating that students generally felt only moderately satisfied with the quality and effectiveness of their learning during the ODL period (Table 4). These results suggest that while many students were able to adapt to online learning, a considerable proportion still faced challenges that affected their satisfaction. Factors such as limited interaction, increased workload, or technological difficulties may have contributed to this outcome. Overall, the findings highlight the need for ongoing improvements in instructional design, communication, and support systems to enhance students' learning experiences in future online or blended learning environments.

The majority of students achieved a satisfactory GPA (60.4%), while 34.7% achieved an excellent GPA. Only 4.9% of students were categorised as having poor academic performance. The overall mean GPA was 3.37 ± 0.32, indicating that most students maintained good academic standing during the online distance learning period (Table 4)

Association between Learning Satisfaction and Grade Point Average (GPA)

An analysis utilising Spearman's rank-order correlation was performed to investigate the association between students' learning satisfaction and their academic performance, as indicated by GPA. The findings demonstrated a very weak positive correlation between overall learning satisfaction and GPA ($rs = 0.033$, $p = 0.672$); however, this association was not statistically significant (Table 5).

Further analysis of the four satisfaction domains also showed no significant associations with GPA. Domain 1 (student readiness and perception of the learning environment) demonstrated a weak negative correlation ($rs = –0.055$, $p = 0.484$), Domain 2 (technological and institutional support) a weak positive correlation ($rs = 0.081$, $p = 0.304$), Domain 3 (educator–student interaction) a negligible negative correlation ($rs = –0.021$, $p = 0.789$), and Domain 4 (course content and critical challenges) a weak positive correlation ($rs = 0.024$, $p = 0.759$).

Since all p-values were above 0.05, these findings indicate no statistically significant associations between learning satisfaction and GPA across all domains. This means that while students' satisfaction levels varied, these differences did not correspond to changes in academic performance. Other factors, such as motivation, learning environment, personal adaptability, and external stressors during the COVID-19 pandemic, may have had a greater impact on students' academic outcomes than satisfaction alone.

Discussion

Overview of findings

This study investigated the impact of online distance learning (ODL) on nursing students' learning satisfaction and academic performance during the COVID-19 pandemic. The results revealed that while most students achieved satisfactory academic outcomes, their overall learning satisfaction was only moderate. The findings suggest that although nursing students adapted to online learning, several challenges limited their satisfaction with the ODL experience. In contrast, a study conducted in South Korea reported that nursing students' satisfaction with online classes was a significant predictor of their academic achievement, indicating that higher satisfaction levels were associated with better performance outcomes [8]. This finding differs from the present study, where no significant association was observed between satisfaction and academic performance, suggesting that contextual and cultural factors may influence how satisfaction translates into learning success.

Sociodemographic Profile and Learning Context

Most participants were young female nursing students aged 18–25 years, which aligns with the typical demographic profile of nursing programs. The majority relied on laptops or tablets as their primary learning devices, and many reported average internet stability. More than half also experienced financial strain due to ODL, reflecting the economic challenges students faced during the pandemic.

These contextual factors may have influenced students' perceptions of ODL. Financial difficulties and unstable internet connections could lead to stress and learning disruptions, potentially lowering satisfaction levels. Similar findings were reported in other studies, where socioeconomic and technological barriers significantly influenced students' engagement

and satisfaction with online learning. In an Indian study, nursing students identified poor internet connectivity and limited access to reliable devices as major obstacles that hindered effective participation and reduced satisfaction with online learning [9]. Likewise, an Iranian study found that most nursing students relied on personal mobile phones for classes and frequently experienced moderate internet instability and physical strain, all of which contributed to lower satisfaction levels [10].

Learning Satisfaction and Perceived Challenges

The overall moderate satisfaction level (70.7%) suggests that students recognised certain benefits of ODL, particularly its flexibility and safety. Most students agreed that ODL allowed them to organise their learning time and feel safer studying from home. However, the results also highlight several issues that hindered satisfaction. A large proportion (77.2%) indicated the need for a tutor to clarify difficult topics, showing that independent online learning may not fully meet the academic demands of nursing education. The majority also expressed frustration with the volume of online assignments and assessments, with 95.1% stating that excessive workload caused confusion and stress. These findings indicate that while ODL enabled learning continuity during the pandemic, its design may not have been fully optimized for nursing students, who require practical, interactive, and guided learning experiences.

Overall, these findings suggest that while students adapted reasonably well to ODL and recognized its benefits in flexibility and safety, they also encountered challenges related to workload, interaction quality, and the need for stronger academic and emotional support. Additionally, although most respondents were satisfied with the university's technological preparedness and accessibility, some still reported challenges related to system usability and course navigation [11,12]. These technical barriers could contribute to reduced engagement and motivation.

Educator–Student Interaction

Interaction is a crucial component of effective nursing education. In this study, 61% of students agreed that there was adequate interaction during ODL. However, nearly one-fourth believed that the use of digital learning tools contributed to lower academic performance [13]. This suggests that while online communication existed, it may not have been as effective or personal as traditional classroom engagement.

Previous research supports this finding, emphasising that the quality, not just the frequency of online interaction, affects satisfaction and performance. Limited real-time discussions, delayed feedback, and reduced peer collaboration can weaken students' connection to their instructors and classmates, ultimately affecting their learning experience. Similarly, Wang et al. (2023) [14] highlighted that the perceived quality of online interaction strongly influences students' satisfaction and overall learning experience.

Academic Performance

Despite moderate satisfaction, most students performed well academically, with a mean GPA of 3.37 ± 0.32. The majority (60.4%) achieved satisfactory performance, and one-third (34.7%) performed excellently. This indicates that students were able to maintain their academic standards despite the challenges of remote learning. The results may reflect nursing students' resilience, discipline, and adaptability in managing academic responsibilities during a crisis.

However, the small proportion (4.9%) with poor performance indicates that certain students may have struggled with online assessments or lacked sufficient support. Institutions should identify these students early and provide targeted

academic assistance to prevent further learning gaps.

These findings suggest that, despite the challenges associated with online distance learning, most students were able to perform well academically. The relatively high mean GPA reflects effective adaptation to online learning environments, although the small percentage of students with poor performance indicates that some may still require additional academic guidance and support.

Association Between Learning Satisfaction and GPA

The correlation analysis found no statistically significant relationship between total learning satisfaction and GPA ($r_s = 0.033$, $p = 0.672$). Similarly, no significant associations were found across the four satisfaction domains. This implies that satisfaction did not predict academic success during ODL.

These results align with other studies, Yılmaz (2023) [13] and Akpen et al. (2024) [15], suggesting that while satisfaction contributes to engagement and persistence, academic performance is more strongly influenced by other factors such as motivation, study habits, self-efficacy, and external stressors. The pandemic environment may have intensified these external factors, making satisfaction less influential on measurable performance outcomes.

This suggests that students' overall satisfaction with online distance learning (ODL) was not meaningfully related to their academic performance.

Comparison with Previous Studies

The findings are consistent with Ruiz-Grao et al. (2022) [16], AlOsta et al. (2023) [17], Kanagaraj et al. (2022) [18], and Ahmed (2022) [19], showing moderate satisfaction levels among nursing students during COVID-19 online learning. For example, research across various institutions reported that while students valued flexibility and safety, they often faced technological challenges, limited interaction, and heavy workloads.

Likewise, the absence of a significant correlation between satisfaction and GPA echoes findings from other higher education studies [13], suggesting that high-performing students may succeed regardless of satisfaction levels due to strong intrinsic motivation and adaptability.

Implications for Nursing Education

Continuous training in digital literacy for both students and educators is essential. Strengthening technological skills can reduce frustration, improve participation, and enhance learning satisfaction in online and blended environments. Enhancing academic and technical support is essential for institutions to provide students with dependable access to technology and a stable internet connection. Academic support mechanisms such as virtual tutoring, peer mentoring, and regular feedback sessions can be invaluable for those who find independent learning challenging.

Educators should aim to improve instructional design and develop online courses that strike a balance between flexibility and structured interaction. By integrating multimedia simulations, case-based learning, and a series of smaller, more manageable assessments, engagement can be increased and student stress reduced.

Regular virtual meetings, engaging discussion forums, and personalised feedback are crucial for fostering a sense of connection among students and their educators. When students feel recognized and supported, their motivation and satisfaction tend to increase, even in online learning. However, it is important to understand that maintaining engagement is just one aspect.

Students' overall well-being also needs attention. Many students struggle with financial challenges and the stress of continuous assessments, which can adversely affect their mental health. Universities can make a significant impact by

providing both emotional and financial assistance. Simple initiatives like accessible counselling services, peer support groups, and wellness programs can greatly help students manage stress and maintain their mental well-being. Additionally, it is important for both students and educators to feel confident and equipped to utilize digital tools effectively.

Ongoing training in digital literacy can reduce frustration, build confidence, and enhance the online learning experience for everyone. When a sense of connection, well-being, and digital proficiency align, online and blended learning can truly promote students' development and success.

Strengths and Limitations of the Study

This study offers important insights into nursing students' academic performance and satisfaction with online distance learning (ODL), providing baseline evidence to support the policy for future endeavours to structure online distance learning programs.

The cross-sectional design limits assessment of changes or causality. One limitation of the study is the use of non-probability sampling for participant selection. This approach may limit the generalisability of the findings, as the sample may not fully represent the broader nursing student population. Consequently, caution should be exercised when interpreting the results and applying them to other contexts. The sample was restricted to certain institutions and regions, affecting generalisability, and uncontrolled factors, such as access to technology and home environments, may have impacted outcomes.

Conclusion

This study revealed that nursing students demonstrated satisfactory academic performance during online distance learning, despite reporting only moderate levels of learning satisfaction. The absence of a significant association between satisfaction and GPA suggests that academic success in ODL may depend more on motivation, adaptability, and institutional support than satisfaction alone.

For future nursing education, integrating well-structured blended learning approaches—combining online and face-to-face methods—may offer the most effective balance between flexibility, engagement, and practical skill development.

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Conflict of interest

The authors declare that there are no conflicts of interest related to this study.

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Authors' contributions

MZA conceptualised the study, led the literature search, data acquisition, data analysis, statistical analysis, manuscript preparation, and manuscript editing. All authors reviewed and approved the final version of the manuscript.

Table 1. Bloom Cut-Off Point

No	Category	Range of Scores
Section A:	**Grade Point Average (GPA)**	
1	Excellent	Above 3.50
2	Satisfactory	2.80-3.50
3	Poor	Below 2.80
Section B:	**Learning Satisfaction**	
No	**Category**	**Range of Scores**
1	High Satisfaction	80 – 100
2	Moderate Satisfaction	60 – 79
3	Low Satisfaction	20 - 59

Table 2. Sociodemographic Profile of Participants (N = 164)

Variable	Category	n (%)
Gender	Female	135 (82.3)
	Male	29 (17.7)
Age	18–25 years	153 (93.3)
	>25 years	11 (6.7)
Semester	3	26 (15.9)
	4	123 (75.0)
	5	15 (9.1)
Device Use for Online Learning	iPad	32 (19.5)
	Tablet	35 (21.3)
	iPhone	29 (17.7)
	Android phone	25 (15.2)
	Laptop	43 (26.2)
Financial burden	Yes	104 (63.4)
	No	60 (36.6)
Stability of the Internet Connection	Good	49 (29.9)
	Average	102 (62.2)
	Poor	13 (7.9)

Table 3. The Level of Learning Satisfaction

No	Statement	Frequency (%)					Mean ± SD
		Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree	
Domain 1: Student Readiness and Perception of the Learning Environment							
1.	I can organize the time for effective learning.		12(7.3)	129 (78.7)	23 (14.0)		15.98 ± 1.75
2.	ODL helped me organise.	2 (1.2)	20(12.2)	114 (69.5)	28 (17.1)		
3.	I need a tutor to explain things I do not understand.		3 (1.8)	125 (76.2)	36 (22)		
4.	I feel safer being able to learn online than in a classroom.			100 (61.0)	64 (39)		
5.	My academic performance is better when I study at home.	2(1.2)	2(1.2)	117(71.3)	43(26.2)		
Domain 2: Technological and Institutional Support							
6.	In my opinion, most people have no problem using the online learning platform.		3 (1.8)	109 (66.5)	52 (31.7)		31.32 ± 2.90
7.	My university well prepared technologically to online teaching.		4 (2.4)	116 (70.7)	44 (26.8)		
8.	I was satisfied with the accessibility of departmental program personnel when needed.		5 (3.0)	139 (84.8)	20 (12.2)		
9.	I was satisfied with course registration procedures.		6 (3.7)	132 (80.5)	26 (15.9)		
10.	I was satisfied with the organizational structure of the course site.		3 (1.8)	137 (83.5)	24 (14.6)		
11.	I was satisfied with the relevance of course information.		7 (4.3)	133 (81.1)	24 (14.6)		
12.	The website was consistent and well-designed.		7 (4.3)	133 (81.1)	24 (14.6)		
13.	I was satisfied with the navigation within the course website.		3 (1.8)	131 (79.9)	30 (18.3)		
14.	I was satisfied with download times of course pages and resources.		6 (3.7)	132 (80.5)	26 (15.9)		
15.	I participated more in the online course than in a traditional classroom setting.	1 (6)	18 (11.0)	122 (74.4)	23 (14.0)		
Domain 3: Educator–Student Interaction							
16.	There was more interaction between all involved parties in the online course.	7 (4.3)	38 (23.2)	100 (61.0)	19 (11.6)		5.87 ± 1.11

17.*	Use of digital learning tools is responsible for my low academic performance	41 (25.0)	123 (75.0)	
Domain 4: Course Content and Critical Challenges				
18.*	The volume of assignments via e-learning led to confusion, frustration, and poor performance.	8 (4.9)	156 (95.1)	
19.	Face-to-face interaction contributes significantly to boosting students' academic achievement.	36 (22.0)	128 (78.0)	8.90 ± 0.99
20.*	Taking quizzes and exams online from home was not comfortable and made me nervous	8 (4.9)	156 (95.1)	

*Footnote: Items with * marks are calculated in reverse scoring*

Table 4. Students' Learning Satisfaction Level and Overall Distribution of Students' Grade Point Average (GPA)

Items	Category	Frequency	Percent	Mean ± SD
Students' Learning Satisfaction Levels	High Satisfaction	0	0	1.71 ± 0.46
	Moderate satisfaction	116	70.7	
	Low satisfaction	48	29.3	
	Poor	8	4.9	
Students' GPA	Satisfactory	99	60.4	3.37 ± 0.32
	Excellent	57	34.7	

Table 5. Association Between Total Learning Satisfaction Score and Grade Point Average (GPA)

Items	N	*rs* (Spearman's rho)	*p*-value
Learning Satisfaction Total Score vs GPA	164	0.033	0.672
Domain 1: Student Readiness and Perception of the Learning Environment	164	-0.055	0.484
Domain 2: Technological and Institutional Support	164	0.081	0.304
Domain 3: Educator–Student Interaction	164	-0.021	0.789
Domain 4: Course Content and Critical Challenges	164	0.033	0.672

Footnote: p-value < 0.05 is statistically significant.

References

[1]. Gopal, R., Singh, V., & Aggarwal, A. (2021). Impact of online classes on the satisfaction and performance of students during the pandemic period of COVID 19. Education and Information Technologies, 26(6), 6923–6947. https://doi.org/10.1007/s10639-021-10523-1

[2]. Oducado, R. M., & Estoque, H. V. (2021). Online learning in nursing education during the COVID-19 pandemic: stress, satisfaction, and academic performance. Journal of Nursing Practice, 4(2), 143–153. https://doi.org/10.30994/jnp.v4i2.128

[3]. Weerasinghe, I. S., Lalitha, R., & Fernando, N. (2017). Students' Satisfaction in Higher Education Literature Review. American Journal of Educational Research, 5(5), 533–539. https://doi.org/10.12691/education-5-5-9

[4]. Yu, Q. (2022). Factors Influencing Online Learning Satisfaction. Frontiers in Psychology, 13. https://doi.org/10.3389/fpsyg.2022.852360

[5]. Wan Mamat, W. H., Mohd Nazry, S. S., & Mohamad Shariff, N. (2022). Impact, Effectiveness, and Satisfaction of E-Learning among Undergraduate Students During Pandemic COVID-19. International Journal of Care Scholars, 5(3), 12–20. https://doi.org/10.31436/ijcs.v5i3.222

[6]. Bolliger, D. U., & Wasilik, O. (2009b). Factors influencing faculty satisfaction with online teaching and learning in higher education. *Distance Education*, *30*(1), 103–116. https://doi.org/10.1080/01587910902845949

[7]. Bloom, B. S. (1968). Learning for mastery. Instruction and Curriculum. Regional Education Laboratory for the Carolinas and Virginia, Topical Papers and Reprints, No. 1.

[8]. Kim, S., Jeong, S. H., Kim, H. S., & Jeong, Y. J. (2021). Academic success of online learning in undergraduate nursing education programs in the COVID-19 pandemic era. Journal of Professional Nursing, 38, 6–16. https://doi.org/10.1016/j.profnurs.2021.10.005

[9]. Kumar, A., Kalal, N., Rana, N., Vyas, H., Choudhary, V., & Rani, R. (2021). Online learning in nursing students. Journal of Education and Health Promotion, 10(1), 411. https://doi.org/10.4103/jehp.jehp_1221_20

[10]. Atashinsadaf, A., Ramezani-Badr, F., Long, T., Imanipour, M., & Amini, K. (2024). Facilities, challenges, attitudes, and preferences of nursing students related to e-learning in the Covid-19 pandemic in Iranian context: a cross-sectional study. BMC Medical Education, 24(1). https://doi.org/10.1186/s12909-024-05029-6

[11]. Isa, A. K. M., Osman, M., & Othman, Z. (2025). Usability Evaluation of digital learning tools for online Assessment: A study of Malaysian technical education Institutions. International Journal of Research and Innovation in Social Science, 2082–2090. https://doi.org/10.47772/ijriss.2025.909000179

[12]. Shanthi, A., Abedin, N. F. Z., Paramasivam, S., Xavierine, J., & Ekalestari, S. (2025). Navigating Success: The impact of website usability and content quality on user satisfaction in online language learning. *International Journal of Research and Innovation in Social Science*, *IX*(IIIS), 1605–1614. https://doi.org/10.47772/ijriss.2025.903sedu0123

[13]. Yılmaz, A. B. (2023). The Relationship between Satisfaction, Interaction, E-learning Readiness, and Academic Achievement in Online Learning. Open Praxis, 15(3), 199–213. https://doi.org/10.55982/openpraxis.15.3.578

[14]. Wang, X., Hassan, A. B., Pyng, H. S., Ye, H., & Aminuddin, A. A. (2024). The impact of perceived quality of online interaction on satisfaction of international student interactions in higher education. Cogent Education, 11(1). https://doi.org/10.1080/2331186x.2023.2293454

[15]. Akpen, C. N., Asaolu, S., Atobatele, S., Okagbue, H., & Sampson, S. (2024). Impact of online learning on student's performance and engagement: a systematic review. Discover Education, 3(1). https://doi.org/10.1007/s44217-024-00253-0

[16]. Ruiz-Grao, M. C., Cebada-Sánchez, S., Ortega-Martínez, C., Alfaro-Espín, A., Candel-Parra, E., García-Alcaraz, F., Molina-Alarcón, M., & Delicado-Useros, V. (2022). Nursing Student Satisfaction with the Teaching Methodology Followed during the COVID-19 Pandemic. Healthcare, 10(4), 597. https://doi.org/10.3390/healthcare10040597

[17]. AlOsta, M. R., Khalaf, I., & Othman, E. H. (2023). Jordanian nursing students' engagement and satisfaction with e-learning during COVID-19 pandemic. International Journal of Nursing Education Scholarship, 20(1). https://doi.org/10.1515/ijnes-2022-0053

[18]. Kanagaraj, P., Sakthivel, R., Christhumary, P. C., Arulappan, J., Matua, G. A., Subramanian, U., Kanagaraj, A., Jacob, J., & Muniyandi, H. (2022). Nursing student's satisfaction with virtual learning during COVID-19 pandemic in India. SAGE Open Nursing, 8. https://doi.org/10.1177/23779608221144933

[19]. A. M. Ahmed, W. . (2022). Nursing Students' Satisfaction with Online Learning Experiences During Covid-19 Pandemic at Albaha University, Saudi Arabia. *Sudan Journal of Medical Sciences*, *17*(4), 589–598. https://doi.org/10.18502/sjms.v17i4.12556

ORIGINAL ARTICLE

Ethnic Disparities in Vitamin B12 and Folate Deficiency Prevalence and their Haematological Correlates in Malaysia.

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Abstract

Introduction: Vitamin B12 and folate deficiency are preventable conditions that can lead to serious haematological and neuropsychiatric complications if untreated. Global prevalence varies, and data from Malaysia is limited. This study aimed to determine the proportion and associated risk factors of these deficiencies in a Malaysian hospital population. **Materials and methods:** A cross-sectional, retrospective study was conducted using data from the Laboratory Information System of Hospital Teluk Intan from June 2023 to May 2024. Demographic data and serum B12/folate levels from 1,463 subjects were analyzed. Deficiency proportions were calculated, and associations with demographic factors and haematological profiles were examined using Chi-square and multinomial logistic regression. **Results:** The proportion of isolated vitamin B12, isolated folate, and combined deficiencies were 3.2%, 14.5% and 2.9% respectively. Indian ethnicity was significantly associated with higher odds of all deficiency types. Chinese ethnicity was associated with isolated B12 deficiency. Males and younger age groups (12-19 and 20-29 years) had significantly higher odds of isolated folate deficiency. A high proportion of macrocytic anaemia was observed in isolated B12 (52.17%) and combined deficiencies (64.28%), as was megaloblastic anaemia (56.52% and 61.90%, respectively). **Conclusion:** Significant racial, age, and gender disparities exist in the prevalence of B12 and folate deficiencies, which are strongly associated with haematological complications. These findings highlight the need for targeted screening and intervention strategies in high-risk groups within the Malaysian population.

Keywords: *Deficiency, folate, macrocytic anaemia, Malaysia, Vitamin B12.*

Introduction

Vitamin B12 and folate are involved in various biosynthesis processes, including DNA synthesis, nucleoprotein, erythropoiesis, myelin synthesis, normal growth and cell reproduction and one-carbon metabolism [1-5]. Carmel et al., (1977) mentioned in their study that average total body stores of vitamin B12 are 3–5 mg, and when there is little or no vitamin B12 replenished from the diet, the stores may last for up to 5–10 years before manifestations of vitamin B12 deficiencies are seen clinically [6]. Deficiency can lead to various consequences such as megaloblastic anaemia, cardiovascular complication, impaired cognitive function, neurological manifestations like peripheral neuropathy, subacute combined degeneration of spinal cord, neural tube defects [4,7]. Megaloblastic anaemia is a type of macrocytic anaemia characterized by high mean corpuscular volume (MCV) > 101 fL and mean corpuscular haemoglobin (MCH) >32 pg [2]. It is distinguished from other macrocytic anaemia by the presence of large red cells precursors in the bone marrow due to asynchronous maturation between the nucleus and cytoplasm caused by impaired DNA synthesis [3-5].

The definition of vitamin B12 deficiency varies globally, depending on the country and the biomarkers used [7]. For instance, the United States (U.S) National Institute of Health (NIH) states that most laboratories define deficiency as serum vitamin B12 less than 148 pmol/L and insufficiency as below 221 pmol/L [7]. In contrast, the United Kingdom's (UK) National Institute for Health and Care Excellence (NICE) guidelines recommend serum B12 level of <133 pmol/L as the cut-off of absolute B12 deficiency with level of B12 between 133-258 pmol/L regarded as possible deficiency [8]. Data from the National Health and Nutrition Examination Survey (NHANES) from 2007–2018 found the national prevalence of vitamin B12 deficiency and insufficiency among US adults (aged ≥ 19 years) was approximately 3.3% and 12.5% respectively [7]. In UK, the estimated prevalence of B12 deficiency was 6% [9] with higher prevalence of 11% seen in vegetarians [9], consistent with study by Pawlak [10]. The highest national prevalence was reported in India which ranges between 35% to 47.19% [11- 12].

World Health Organization (WHO) defines folate deficiency and insufficiency as having serum Folate of <6.8 nmol/L and 6.8−13.4 nmol/L respectively [13]. In comparison the United Kingdom National Diet and Nutrition Survey Rolling Program (NDNSRP) recommends a serum folate of <7nmol/L as the deficiency threshold, a level significantly associated with megaloblastic anaemia [14]. An 8-year study at the Mayo clinic (2010-2018) involving 197,974 samples, found that the prevalence of folate deficiency in the general US population to be 0.7%, a drop from 16% in 1996 [15]. Furthermore, data from UK NDNSRP (2009 - 2019) revealed a folate deficiency prevalence of 11% in adults aged 19- 64 years, with higher rates observed in the elderly group (>65 years old) and adolescents (12-18 years) at 13% and 17%, respectively [14]. The literature on the prevalence of folate deficiency among Malaysian population is scarce, with the latest available study dating back to 2006. Khor et al., (2006) reported a prevalence of 15.1% among healthy non pregnant women of childbearing age in Malaysia, while a parallel study in Indonesia found no folate deficiency in their subjects [16]. A more recent 2017 study in India found a folate deficiency prevalence of 12% among healthy urban Indian adult population [12].

According to the WHO, anaemia in adult is defined as haemoglobin (Hb) less than 13 g/dL in men and Hb less than 12 g/dL in women. Approximately 30% of global population is affected by anaemia, with 60% of cases caused by nutritional deficiency [13]. A prospective study done in St Stephen's Hospital, Delhi found that 24% of hospitalised patients had an Hb value <10 g/dl, and 2.7% were identified as having macrocytic anaemia [17]. Khajuria A et al., (2022) found that among patients with Hb <10 g/dl, 20% had macrocytic anaemia, with pure vitamin B12 deficiency accounted for 55% of these cases, while 8% folate and combined deficiencies each

accounted for 8% [18]. Another Indian study by Mahajan et. Al., (2015) found 37% and 23% of patients with B12, folate and combined deficiencies had macrocytosis and megaloblastic anaemia, respectively [19].

Despite abundant studies on the prevalence of B12 and folate deficiency and their associated risk factors in other countries, the data remained limited in Malaysia. The purposes of our study are to determine the proportion of patients with B12 deficiency, folate deficiency and combined deficiencies among patients tested for serum B12 and folate in our laboratory. Additionally, this study aims to explore the association of age, gender and ethnicity with these deficiencies, and to study the correlation between vitamin B12 and folate levels and haematological profiles.

Materials and methods

Study design and sampling

This cross-sectional, retrospective record review study was conducted in Pathology Laboratory HTI from January 2025 to October 2025. Ethical approval was obtained from the Institutional Ethics Committee. The study aimed to estimate the proportion of vitamin B12, folate, and combined vitamin B12 and folate deficiencies among patients tested for B12 and folate. Census sampling was applied. The largest computed sample size from calculations for different deficiency types was selected; a sample size of 382 was computed using a 95% confidence level, an expected proportion range of 8.2% and 47% [11-12], and a margin of error of 5% [20]. These calculations are summarized in Table 1.

Data collection

The data was extracted from the Laboratory Information System (LIS). The extracted information included demographic data (ethnicity, age and gender), serum vitamin B12 and folate values, full blood count (FBC) and full blood picture (FBP) findings, which were recorded in a pre-tested data collection form. The samples processed in our laboratory were sourced from inpatients and outpatients at Hospital Teluk Intan and Hospital Tapah, as well as from outpatients at public health clinics in Hilir Perak, Bagan Datuk, and Batang Padang districts.

Serum B12 and folate were measured using the fully automated Alinity i machine by Abbott Diagnostic. The test utilizes Chemiluminescent Microparticle Immunoassay technology, utilizing intrinsic factor-coated microparticles for B12 quantification and a Folate Lysis Reagent for serum folate quantification. The samples were all analysed in the Pathology Laboratory HTI and the results were uploaded into the LIS.

Inclusion and exclusion criteria

Data from a total of 1,753 subjects tested for serum vitamin B12, folate, or both between 1 June 2023 and 31 May 2024 were recorded. The inclusion criteria were subjects more than 12 years old with complete demographic data. Exclusion criteria were rejected and redundant samples sent within the study period. A total of 1,463 subjects met the inclusion criteria and were included in the final analysis. Out of 1,463 subjects, 1,434 subjects were tested for both B12 and folate, 20 subjects were tested for B12 only and 9 subjects were tested for folate only.

Independent variables

This study obtained demographic data including gender, age and ethnicity from the subjects. These data were analyzed to determine the factors associated with B12 or folate deficiency status. Ethnicity was classified into four categories: Malays, Chinese, Indians and Orang Asli. Age was categorized into eight groups: 12 to 19 years, 20 to 29 years, 30 to 39 years, 40 to 49 years, 50 to 59 years, 60 to 69 years, 70 to 79 years and more than 80 years. Deficiency status was analyzed to find the association with the presence of macrocytic anaemia and megaloblastic anaemia.

Dependent variables

Deficiency status of the subjects was determined by our laboratory cut off values. Our laboratory defines vitamin B12 and folate deficiency using age-specific cutoff values [21]: for serum B12, deficiency is indicated by levels <138 pmol/L in adults (>19 years), <150 pmol/L for ages 17–19, <180 pmol/L for ages 14–17, and <186 pmol/L for ages 12–14. For serum folate, deficiency is defined as <7 nmol/L in adults, <18 nmol/L for ages 14–19, and <27 nmol/L for ages 12–14. Subjects with normal B12 and folate level were classified into four groups: group A (normal) for subjects with normal B12 and Folate level, group B (isolated B12 deficiency) for subjects with B12 level below laboratory cut off value but with normal folate level, group C (isolated folate deficiency) for subjects with folate level below laboratory cut off value but with normal B12 level were classified into isolated folate deficiency group and lastly group D (combined deficiencies) for subjects with both B12 and folate level below laboratory cut off value.

Haematological profile including haemoglobin level (g/dL), mean corpuscular volume (fL) and mean corpuscular haemoglobin (pg) and full blood picture examination were analyzed to find the presence of macrocytic anaemia and megaloblastic anaemia in the subjects. A haemoglobin (Hb) level of less than 13 g/dL in men and Hb less than 12 g/dL in women is defined as anaemia, while macrocytic anaemia is characterized by the presence of anaemia with high mean corpuscular volume (MCV) > 101 fL and mean corpuscular haemoglobin (MCH) >32 pg. The presence of megaloblastic anaemia is defined by the full blood picture findings of presence of macrocytosis and hypersegmented neutrophils with concomitant B12 or folate deficiency.

Data analysis

Descriptive analysis was carried out to characterise the dependent and independent variables. The overall proportion of B12, folate, and combined deficiencies was calculated. The proportion of each deficiency across all categories of the variables was also calculated to find out which group of the subjects show highest proportion of deficiency. Chi square analysis was performed to assess the associations between each demographic predictors with deficiency status, as well as the association between deficiency status with the presence of macrocytic anaemia and megaloblastic anaemia. Multinomial logistic regression analysis was conducted to examine the association between demographic predictors and vitamin deficiency status, categorized as no deficiency, isolated B12 deficiency, isolated folate deficiency, and combined deficiencies. Predictors included gender, ethnicity and age group.

Ethical approval

Institutional Ethics Committee, with Medical Research & Ethics Committee (MREC) approval number 24-03916- 5RH (1), with permission to publish obtained from the Director General (DG) of Health.

Results

A total of 1,463 subjects were analyzed. The cohort consisted of 57.6% (n=842) females and 42.4% (n=621) males. Ethnically, 55.9% (n=818) were Malay, followed by Indian 24.2% (n=354), Chinese 16.9% (n=247) and Orang Asli 3% (n=44). The mean age was 58.1 ± 18.2 years. Of the total subjects, 79.6% (n=1165/1463) had normal B12 and folate (group A), 3.2% (n=46/1454) of the subjects were found to have isolated B12 deficiency (group B), 14.5% (n=210/1443) had isolated folate deficiency (group C) and 2.9% (n=42/1434) had combined B12 and folate deficiency (group D) (Figure 1), with different proportions of deficiency observed across different categories. The median vitamin B12 and folate for all subjects were 427.0 (IQR 266.0, 756.0) pmol/L and 16.9 (IQR 8.4, 37.7) nmol/L, respectively. Statistically significant differences in median B12 and folate level ($p<0.05$) were observed across all groups. The

baseline demographic distributions and median levels are summarized in Table 1.

A higher proportion of isolated B12 deficiency was observed among females, Indian ethnicity, and of age between 60 to 69 and 70 to 79 years old, which were reported as 71.7% (n=33/46), 54.3% (n=25/46), 21.7% (n=10/46), and 30.4% (n=14/46), respectively. In contrast, the proportion of isolated folate deficiency was highest among Malays (53,8%, n=113/210), with no prominent gender or age group differences. For combined deficiencies, a higher proportion was seen among Indians 73.8% (n=31/42), as well as subjects age 70–79 years 26.2% (n=11/42), with no significant gender differences (Table 1).
Chi-square analysis showed significant associations ($p<0.05$) between ethnicity and all three deficiencies with varying strength of associations (Cramer's V = 0.25, 0.18, and 0.20 for B12, folate and combined deficiencies, respectively). Gender and age were significantly associated only with folate deficiency ($p<0.05$), with associations strength of 0.10 and 0.25 (Table 2).
A multinomial logistic regression analysis was performed to identify the effect of gender, ethnicity, and age on the deficiency status, using Group A (normal) as the baseline reference category. Male were 2.22 times more likely to have isolated folate deficiency (OR=2.22, 95% CI [1.65, 2.99], $p<0.05$), but were not significantly more likely to have combined deficiencies (OR=1.74, 95% CI [0.91, 3.32], p=0.09) or less likely to have isolated B12 deficiency (OR=0.94, 95% CI [0.84, 3.25], p=0.13). Compared to Malay ethnicity, Indian ethnicity was associated with higher odds of having isolated B12 deficiency (OR=11.83, 95% CI [6.36, 22.01], $p <0.05$), folate deficiency (OR=2.63, 95% CI [1.91, 3.62], $p <0.05$) and combined deficiencies (OR=15.88, 95% CI [6.09,41.42], $p <0.05$). Chinese ethnicity had only significantly higher odds of having isolated B12 deficiency (OR=4.60, 95% CI [2.17, 9.74], $p<0.05$). Individuals of age 12-19 were 21.09 times more likely (OR=21.09, 95% CI [9.12,48.76], $p<0.05$), and those aged 20-29 years were 3.01 times more likely (OR=3.0, 95% CI [1.67, 5.43], $p <0.05$) to have isolated folate deficiency. No significant effect of age was found in isolated B12 deficiency and combined deficiencies (Table 3).

The haematological profiles of subjects were analyzed, focusing on the presence of macrocytic and megaloblastic anaemia. The proportion of macrocytic anaemia in vitamin B12 deficiency was 52.17% (n=24/46), 8.09% (n=17/210) in folate deficiency, and 64.28% (n=27/42) in combined deficiencies. The proportion of megaloblastic anaemia in vitamin B12 deficiency was 56.52% (n=26/46), 5.70% (n= 12/210) in folate deficiency, and 61.90% (n= 26/42) in combined deficiencies. Chi-square analysis showed significant associations ($p<0.05$) between B12, folate and combined deficiencies with the presence of macrocytic and megaloblastic anaemia with varying strength of associations (Cramer's V = 0.40, 0.13, 0.35) and (Cramer's V = 0.56, 0.10, 0.47) respectively. These findings suggest that B12 deficiency, alone or in combination with folate deficiency, is more strongly linked to macrocytic or megaloblastic anaemia compared to folate deficiency in both conditions (Table 4).

Discussion

The recognition of vitamin B12 and folate deficiency is important as these deficiencies can present with haematological, neuropsychiatric, and other adverse clinical manifestations [1-2]. One of the most commonly observed complications is megaloblastic anaemia, in which is a key focus of our study. Despite the well-known consequences and healthcare burden of these deficiencies there are very few studies focusing on the prevalence of B12 or folate deficiency in the Southeast Asia region, particularly in Malaysia.
The proportion of vitamin B12 deficiency in our study was 3.2%, based on our laboratory

deficiency threshold of <138 pmol/L. This rate is higher than the 3.3% prevalence reported in the US (using a <148 pmol/L threshold) [7], equivalent to the 6% reported in the United Kingdom (using a <133 pmol/L threshold) [9], but significantly lower than the 35-47.19% reported in India (using a <150 pmol/L threshold) [11, 12, 17]. The high prevalence of B12 deficiency in our study was attributable to the large proportion of Indian subjects, who commonly practice vegetarianism. This is consistent with previous studies, linking high B12 deficiency rates across many regions in India to strict vegetarian diets [11, 17-18]. Hunt and Pawlak also found a higher prevalence of B12 deficiency among vegetarians, attributing it to inadequate B12 intake, as the vitamin is synthesized only by microorganisms and is absent from plant-based foods unless fortified [9, 10].

The proportion of folate deficiency in our centre was 14.5% with a deficiency threshold of <7nmol.L, consistent with a 2006 Malaysian study by Khor et al., (2006) which reported a 15.1% prevalence of folate deficiency among healthy women of childbearing age, with a parallel study done in Indonesia found none of their subjects were folate deficient, owing to the mandatory wheat-flour fortification programme in Indonesia [16]. Our prevalence also aligned with the 11% national prevalence of folate deficiency in the UK, with the same level of folate deficiency threshold [14] as well as higher than the national prevalence of 0.7% in the USA. This is attributed to the voluntary basis of folic acid food fortification in the UK compared to the mandatory folic acid food fortification in the US since 1998 [7]. In comparison to other literature from the eastern countries, the prevalence of isolated folate deficiency in our centre is higher than previous study in India which reported a lower prevalence of folate deficiency of 11.1% among ageing rural community, ascribing to the higher folate deficiency cutoff of 9.5nmol/L as well as socioeconomic background of the population which is known to consume plant-based diets [17]. Another study done in India also found a lower prevalence of isolated folate deficiency of 12% with folate cut off value of <3ng/ml (6.8 nmol/L). This lower prevalence was explained by the study population, who were all healthy urban adults, who have better socioeconomic backgrounds, with access to various types of food, including green leafy vegetables and supplements, as well as better education on methods of food preparation, to retain folate [12].

The proportion of combined deficiencies in our study was 2.9%, lower than the 10% prevalence of previous study by Mahajan et.al, (2015) which was attributed to a high number of strict vegans (33%) in their cohort [19]. Differences in deficiency cut-offs across different countries and laboratories also contributed to variation in reported prevalence around the world, as such, a higher observed prevalence is likely when a less stringent vitamin cutoff is applied. Currently, there is lack of consensus on defining vitamin B12 and folate deficiency due to differences in measurement methods and population characteristics. However, recent studies by Ispir et al. and Kristensen et. al using the data from the national Qualimedlab EQAS showed acceptable concordance across most analytical platforms [22-23].

Our study demonstrated that Indian ethnicity was the most consistent significant factor associated with all deficiencies. This is consistent with previous studies identifying the Indian population as having the highest national prevalence of vitamin B12 and folate deficiencies, largely attributed to the widespread vegetarianism and a preference for well- cooked meal [11,18-19], which can destroy folate. Khor et al., (2006) also found a lower percentage of Indians taking dietary supplements compared to the Malays and Chinese [16]. Similar to previous studies, deficiency in both B12 and folate were largely attributable to inadequate intake while in contrary, analysis of NHANES data from 1999-2006 by Reinstaller et al., (2012) revealed that vitamin B12 deficiency in general population in US and in western population is more commonly due to the intrinsic factor deficiency and hence

malabsorption of vitamin B12 [24]. This leads to uniform guidelines for treating vitamin B12 deficiency with injectable preparations in western literature, while vitamin B12 deficiency in eastern countries is usually recommended to be treated with oral vitamin B12 [11,24].

Additionally, age group 12-19 years and 20-29 years were found to be significant predictors as well as showing the highest proportion of folate deficiency in our study, in line with UK findings reporting a 17% prevalence in adolescents (12-18 years) compared to 11% in the general population, likely due to poor dietary habits [14]. Male subjects had a higher risk of folate deficiency, consistent with findings by Hao et al. (2003) in a Chinese population [25]. This gender difference has been explained by higher rates of cigarette smoking and alcohol consumption among men. Okumura et.al reported that tobacco smoke exerts direct effects on blood folate level through the release of nitrous oxide, which inhibits methionine synthase activation and lowers endogenous B12. This, in turn, prevents the remethylation pathway and results in folate trapping in the form of 5-methyltetrahydrofolate [26]. Halsted et al. (2002) demonstrated that chronic alcoholism contributes to folate deficiency through intestinal malabsorption, decreased hepatic uptake, and increased renal excretion [27][27]. In contrast, studies by Nath et.al and Alaimo et.al found no gender differences in serum folate levels [28-29].

Another factor contributing to variations in prevalence of folate deficiency is genetic variation, which was explored in several studies previously [30-31]. The U.S Centre of Disease Control and Prevention (CDC), as reported by Cider et al. (2012) mentioned the variation in methylenetetrahydrofolate reductase (MTHFR) genes results in different individual's blood folate levels despite similar amount of folate intake [32]. The study reported that people with similar folate intake, the MTHFR TT (MTHFR C677T variant) genotype have an average about 16% lower amount of folate in their blood than those with the MTHFR CC (normal) genotype [30-31].

A statistically significant association and a high proportion of macrocytic anaemia and megaloblastic anaemia were observed in all deficiency types in our study. These findings are consistent with Mahajan et.al., (2015) who reported a prevalence of 37% macrocytosis and 23% megaloblastic anaemia deficient patients [19]. Our findings also aligned with another study, which showed that 80% and 88% of subjects who had megaloblastic anaemia had very low B12 and folate levels, respectively, compared to only 4% and 24% non-megaloblastic anaemia controls [33]. These significant associations and high proportions represent a public health concern, as these anaemic patients may require blood transfusions, an outcome potentially avoidable with earlier B12 or folate supplementation.

The strengths of our study include its time and cost-efficient retrospective cross-sectional design, utilizing data from an electronic laboratory information system (LIS). To the best of our knowledge, this is the first study to explore the prevalence of vitamin B12, folate, and combined deficiencies in the general population of Malaysia, and possibly in Southeast Asia. It may also serve as a pilot study for future research. A key limitation is potential recruitment bias, as our samples were drawn from patients and outpatients seeking medical attention at Hospital Teluk Intan, Hospital Tapah, public health clinics in Hilir Perak, Bagan Datuk, and Batang Padang districts. This may have led to an imbalance in demographic distributions (ethnicity, age, gender), health status, and comorbidities. A prospective study with a specific study population would be more likely to accurately represent the true prevalence of these deficiencies.

Conclusion

This study revealed significant racial disparities in the prevalence of serum vitamin B12, folate, and combined deficiencies among patients in a district hospital. Age and gender were also identified as risk factors for folate deficiency. These differences were likely influenced by

social determinants, which need to be further explored. Additionally, the significant association and high proportion of macrocytic and megaloblastic anaemia across all types of deficiencies raised concerns about the public health burden. Therefore, larger multicentre studies across Malaysia and Southeast Asia are recommended to establish the national prevalence of these deficiencies and identify their associated risk factors. This would, in turn, aid in developing effective screening strategies and targeted supplementation for high-risk groups, ultimately improving clinical outcomes and reducing healthcare disparities.

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Conflict of interest

None

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Authors' contributions

SAII, LPC, NS and CWYS contributed to the research, background writing, literature review, preliminary writing of the manuscript, as well as data collection and analysis. IMAK, NASA, SJS, and NHS contributed to the manuscript review and facilitation of data collection and analysis.

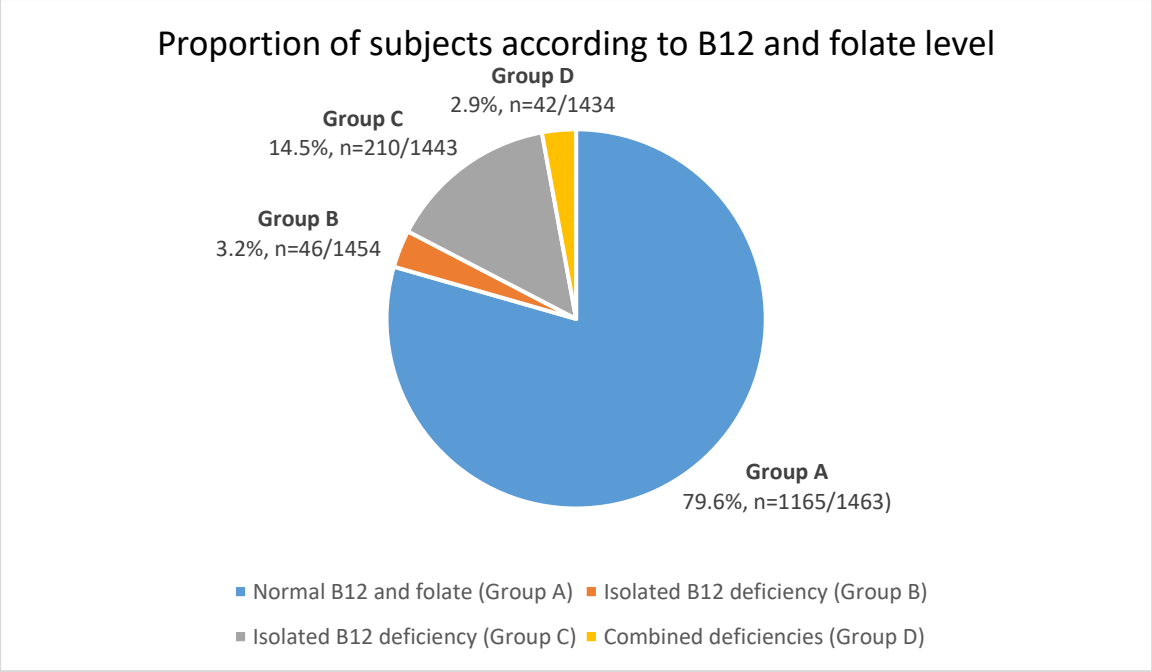

Figure 1. Pie chart showing the proportion of subjects according to B12 and folate level

Table 1. Baseline characteristics of the study population according to serum B12 and Folate level:

Characteristics	Total subject (n=1463) 100%	Group A (n=1165) 79.6%	GroupB (n=46) 3.2%	Group C (n=210) 14.5%	GroupD (n=42) 2.9%	p-value
Gender (%)						
Male	621 (42.4%)	474 (40.7%)	13 (28.3%)	98 (46.7%)	22 (52.4%)	
Female	842 (57.6%)	691 (59.3%)	33 (71.7%)	112 (53.3%)	20 (47.6%)	
Ethnicity (%)						
Malay	818 (55.9%)	692 (59.4%)	8 (17.4%)	113 (53.8%)	5 (11.9%)	
Indian	354 (24.2%)	228 (19.6%)	25 (54.3%)	70 (33.3%)	31 (73.8%)	
Chinese	247 (16.9%)	211 (18.1%)	12 (26.1%)	18 (8.6%)	6 (14.3%)	
Orang Asli	44 (3.0%)	34 (2.9%)	1 (2.2%)	9 (4.3%)	0 (0%)	
Age,year(SD)	58.1 (18.2)	59.3 (17.6)	62.0 (17.6)	51.5 (21.7)	55.0 (17.8)	<0.05[a]
Age group						
12-19, yr	34 (2.3%)	9 (0.8%)	1 (2.2%)	24 (11.4%)	0 (0%)	
20-29, yr	88 (6.0%)	60 (5.2%)	2 (4.3%)	21(10.0%)	5 (11.9%)	
30-39, yr	141 (9.6%)	109 (9.4%)	2 (4.3%)	25 (11.9%)	5 (11.9%)	
40-49, yr	191 (13.1%)	150 (12.9%)	8 (17.4%)	26 12.4%)	7 (16.7%)	
50-59, yr	240 (16.4%)	205 (17.6%)	4 (8.7%)	25 (11.9%)	6 (14.3%)	
60-69, yr	315 (21.5%)	264 (22.7%)	10 (21.7%)	35 (16.7%)	6 (14.3%)	
70-79, yr	301 (20.5%)	240 (20.6%)	14 (30.4%)	36 (17.1%)	11 (26.2%)	
>80, yr	153 (10.5%)	128 (11.0%)	5 (10.9%)	18 (8.6%)	2 (4.8%)	
Median B12 (IQR)	427 .0 (266.0,756.0)	478.0 (311.0, 835.0)	109.0 (109.0,120.7)	307.0 (183.5, 524.5)	109.0 (109.0, 120.7)	<0.05[b]
Median Folate (IQR)	16.9 (8.40,37.7)	23.6 (12.2, 41.5)	7.1 (5.0, 28.7)	5.3 (5.0, 6.2)	5.0 (5.0, 5.65)	<0.05[b]

[*] Group A = Subjects with normal B12 and folate level

Group B = Subjects with isolated B12 deficiency

Group C = Subjects with isolated folate deficiency

Group D = Subjects with combine B12 and folate deficiencies

[a] ANOVA test

[b] Kruskal Wallis-test

Table 2. Chi-square analysis of factors associated with B12, folate or combined deficiencies:

	Pearson's Chi-square	p-value	Cramer's V
Gender			
Isolated B12 deficiency	0.27	0.60[a]	-
Isolated folate deficiency	14.28	<0.05[a]	0.10
Combined deficiencies	1.69	0.19[a]	-
Ethnicity			
Isolated B12 deficiency	91.03	<0.05[a]	0.25
Isolated folate deficiency	47.05	<0.05[a]	0.18
Combined deficiencies	61.27	<0.05[a]	0.20
Age group			
Isolated B12 deficiency	7.86	0.34[b]	-
Isolated folate deficiency	14.28	<0.05[a]	0.25
Combined deficiencies	6.63	0.42[a]	-

[a] Chi-square test | [b] Fisher's Exact test

Table 3. Multinomial logistic regression analysis explaining the factors associated with deficiency status

Variable	Category	Isolated B12 deficiency			Isolated folate deficiency			Combined deficiencies		
		OR (e^B)	95% CI of OR	p-value	OR (e^B)	95% CI of OR	p-value	OR (e^B)	95% CI of OR	p-value
Gender	Female (R)									
	Male	0.94	0.84, 3.25	0.13	2.22	1.65, 2.99	<0.05	1.74	0.91, 3.32	0.09
Ethnicity	Malay (R)									
	Indian	11.83	6.36, 22.01	<0.05	2.63	1.91, 3.62	<0.05	15.88	6.09,41.42	<0.05
	Chinese	4.60	2.17, 9.74	<0.05	0.71	0.43, 1.16	0.17	4.16	1.22, 14.21	0.20
	Orang Asli	1.55	0.19, 12.29	0.67	1.14	0.50, 2.61	0.74	0.00	0.00, 0.00	0.99
Age group	12-19 years	0.57	0.07, 4.71	0.42	21.09	9.12,48.76	<0.05	0.00	0.00,0.00	0.99
	20-29 years	1.65	0.62, 4.39	0.60	3.01	1.67, 5.43	<0.05	3.42	0.96,12.18	0.50
	30-39 years	0.74	0.28, 1.91	0.30	1.83	1.06, 3.16	0.02	1.63	0.47,5.64	0.44
	40-49 years	1.44	0.67, 3.09	0.54	1.42	0.84, 2.38	0.18	1.76	0.56,5.55	0.32
	50-59 years	0.77	0.33, 1.79	0.34	0.92	0.55, 1.53	0.74	1.22	0.38, 3.96	0.73
	60-69 years (R)									
	70-79 years	1.53	0.78, 3.00	0.55	1.31	0.82, 2.09	0.25	1.80	0.64,5.07	0.26
	>80 years	0.85	0.33, 2.17	0.21	1.18	0.65, 2.14	0.56	0.72	0.14, 3.74	0.70

R= reference group for each variable measured

Table 4. Chi-square analysis of association of B12, Folate or combined deficiency with macrocytic and megaloblastic anaemia:

	Pearson's Chi-square	p-value	Cramer's V
Macrocytic anaemia[a]			
Isolated B12 deficiency	128.6	<0.05[c]	0.40
Isolated folate deficiency	45.15	<0.05[c]	0.13
Combined deficiencies	88.2	<0.05[c]	0.35
Megaloblastic anaemia[b]			
Isolated B12 deficiency	199.7	<0.05[c]	0.56
Isolated folate deficiency	86.5	<0.05[c]	0.10
Combined deficiencies	117.9	<0.05[c]	0.47

[a] Based on indices from full blood count or full blood picture

[b] Based on full blood picture morphology

[c] Fisher's Exact test

References

[1]. Food And Agriculture Organization of the United Nations, World Health Organization. Vitamin and mineral requirements in human nutrition. Geneva: World Health Organization; 2005.

[2]. Abali EE, et al. Lippincott Illustrated Reviews: Biochemistry. Philadelphia: Wolters Kluwer; 2022.

[3]. World Health Organization. Vitamin mineral requirements in human nutrition. 2nd ed. Available from:[https://apps.who.int/iris/bitstream/handle/10665/42716/9241546123.pdf] (https://apps.who.int/iris/bitstream/handle/10665/42716/9241546123.pdf)

[4]. NIH Office of Dietary Supplements. Vitamin B12 \[Internet]. no date. Available from: [https://ods.od.nih.gov/factsheets/VitaminB12HealthProfessional/](https://ods.od.nih.gov/factsheets/VitaminB12-HealthProfessional/) Accessed 24 Oct 2024.

[5]. Branch N, Pirkle J, Director. Laboratory Procedure Manual Vitamin B12 (B12) Roche E-170 VitaminB12 'ECLIA'. Available from: https://wwwn.cdc.gov/nchs/data/nhanes/public/2013/labmethods/VITB12_H_MET_VITAIMIN_B12.pdf

[6]. Carmel R, Tatsis B, Baril L. Circulating antibody to transcobalamin II causing retention of vitamin B12 in the blood. Blood. 1977;49(6):987–1000.

[7]. Zhou Y, et al. Folate and vitamin B12 usual intake and biomarker status by intake source in United

States adults aged ≥19 y: NHANES 2007–2018. Am J Clin Nutr. 2023;118(1):241–254. doi:10.1016/j.ajcnut.2023.05.016.

[8]. B12-Folate deficiency NICE. Available at: https://cks.nice.org.uk/topics/anaemia-b12- folate-deficiency/.

[9]. Hunt, A., Harrington, D. and Robinson, S. (2014) 'Vitamin B12 Deficiency', BMJ, 349. Available at: https://doi.org/10.1136/bmj.g5226.

[10]. Pawlak R, Lester SE, Babatunde T. The prevalence of cobalamin deficiency among vegetarians assessed by serum vitamin B12: A review of literature. Eur J Clin Nutr. 2014;68:541–548.

[11]. Singla R, Garg A, Surana V, Aggarwal S, Gupta G, Singla S. Vitamin B12 deficiency is endemic in Indian population: a perspective from North India. Indian J Endocrinol Metab. 2019;23:211. doi:10.4103/ijem.IJEM_122_19

[12]. Sivaprasad, M. *et al.* (2019) 'Prevalence of vitamin deficiencies in an apparently healthy urban adult population: Assessed by subclinical status and dietary intakes', *Nutrition*, 63-64, pp. 106–113. Available at: https://doi.org/10.1016/j.nut.2019.01.017.

[13]. WHO, Serum and red blood cell folate concentrations for assessing folate status in populations, 2015. https://www.who.int/publications/i/item/WHO-NMHNHD- EPG-15.01

[14]. Jones, K.S. et al. (2023) 'National Diet and Nutrition Survey data reveal a decline in folate status in the United Kingdom population between 2008 and 2019', The American Journal of Clinical Nutrition, 118(6). Available at: https://doi.org/10.1016/j.ajcnut.2023.10.006

[15]. Gonzalez-Velez M, et al. Racial/ethnic differences in patients with anemia and folate deficiency. Int J Lab Hematol. 2020;42(4):403–410. doi:10.1111/ijlh.13205

[16]. Khor GL, et al. Dietary and blood folate status of Malaysian women of childbearing age. PubMed. 2006;15(3):341–349.

[17]. Sundarakumar JS, Shahul Hameed SK, Ravindranath V. Burden of Vitamin D, Vitamin B12 and Folic Acid Deficiencies in an Aging, Rural Indian Community. Front Public Health. 2021;9:707036. doi:10.3389/fpubh.2021.707036

[18]. Khajuria A, Das R. Prevalence of megaloblastic anaemia and its causative factors in a tertiary care centre at Western India. Santosh Univ J Health Sci. 2022;8:141–144.

[19]. Mahajan S, Aundhakar S. A study of the prevalence of serum vitamin B12 and folic acid deficiency in Western Maharashtra. J Family Med Prim Care. 2015;4(1):64. doi:10.4103/2249- 4863.152255

[20]. Charan J, Biswas T. How to calculate sample size for different study designs in medical research? Indian J Psychol Med. 2013;35(2):121–126. doi:10.4103/0253-7176.116232

[21]. Caliper Project. Caliper database. Available from: https://caliperproject.ca/caliper/database/

[22]. İspir E, Serdar MA, Ozgurtas T, Gulbahar O, Akın KO, Yesildal F, et al. Comparison of four

automated serum vitamin B12 assays. Clin Chem Lab Med. 2015;53:1205–1213.

[23]. Kristensen GB, Rustad P, Berg JP, Aakre KM. Analytical bias exceeding desirable quality goal in 4 out of 5 common immunoassays: results of a native single serum sample external quality assessment program for cobalamin, folate, ferritin, thyroid-stimulating hormone, and free T4 analyses. Clin Chem. 2016;62:1255–1263.

[24]. Reinstatler L, Qi YP, Williamson RS, Garn JV, Oakley GP. Association of Biochemical B12 Deficiency With Metformin Therapy and Vitamin B12 Supplements: the National Health and Nutrition Examination Survey, 1999–2006. Diabetes Care. 2012;35(2):327–333. doi:10.2337/dc11-1582

[25]. Hao, L. et al. (2003) 'Geographical, Seasonal and Gender Differences in Folate Status among Chinese Adults', The Journal of Nutrition, 133(11), pp. 3630–3635. Available at: https://doi.org/10.1093/jn/133.11.3630.

[26]. Okumura, K. and Tsukamoto, H. (2011) 'Folate in smokers', Clinica Chimica Acta, 412(7-8), pp. 521–526. Available at: https://doi.org/10.1016/j.cca.2011.01.003.

[27]. Halsted, C.H. et al. (2002) 'Metabolic Interactions of Alcohol and Folate', The Journal of Nutrition, 132(8), pp. 2367S2372S. Available at: https://doi.org/10.1093/jn/132.8.2367s.

[28]. Nath, S.D., Samer Koutoubi and Huffman, F.G. (2006) 'Folate and vitamin B12 status of a multiethnic adult population.', PubMed, 98(1), pp. 67–72.

[29]. Alaimo K, McDowell MA, Briefel RR, et al. Dietary intake of vitamins, minerals, and fiber of persons ages 2 months and over in the United States: Third National Health and Nutrition Examination Survey, Phase 1, 1988-1991. Adv Data. 1994;258:1-28.

[30]. Online Mendelian Inheritance in Man, OMIM®. Johns Hopkins University, Baltimore, MD. MIM Number: 236250: 12/11/2014: https://omim.org/entry/236250#genotypePhenotypeCorrelations

[31]. Tsang BL, Devine OJ, Cordero AM, et al. Assessing the association between the methylenetetrahydrofolate reductase (MTHFR) 677C>T polymorphism and blood folate concentrations: a systematic review and meta-analysis of trials and observational studies. Am J Clin Nutr. 2015;101(6):1286-1294.

[32]. Crider KS, Yang TP, Berry RJ, Bailey LB. Folate and DNA methylation: A review of molecular mechanisms and the evidence for folate's role. Adv Nutr. 2012;3(1):21-38

[33]. Yadav MK, Manoli NM, Madhunapantula SV (2016) Comparative Assessment of Vitamin-B12, Folic Acid and Homocysteine Levels in Relation to p53 Expression in Megaloblastic Anemia. PLoS ONE 11(10): e0164559. doi:10.1371/journal.pone.0164559

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ORIGINAL ARTICLE

Exploring Balance as a Determinant of High-Level Mobility After Traumatic Brain Injury.

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Abstract

Traumatic brain injury (TBI) remains a major cause of long-term disability. Individuals with moderate to severe TBI often experience lasting difficulties in balance and mobility. High-level mobility, which includes tasks such as running, stair climbing, and quick directional changes, is frequently impaired in this population and poses significant barriers to independence and community reintegration. Despite the known importance of balance in rehabilitation, its precise contribution to the high-level mobility critical for independence remains poorly understood. This study aimed to determine the relationship between balance performance and high-level mobility in individuals with moderate to severe TBI. A total of 86 participants were assessed using the High-Level Mobility Assessment Tool (HiMAT), the Sensory Organization Test (SOT), and the Limits of Stability (LOS) test. The analysis demonstrated moderate to strong positive correlations between high-level mobility and both SOT and LOS measures, with maximum excursion (MXE) ($r = 0.603$) showing the strongest association. These results advocate for incorporating dynamic balance challenges (e.g., perturbed walking, reactive stepping) into rehabilitation to maximise mobility recovery. By highlighting balance as a modifiable and measurable contributor to mobility, this study offers practical insights for designing more effective rehabilitation strategies that support recovery and independence after TBI.

Keywords: *Balance; high-level mobility; postural control; traumatic brain injury.*

Introduction

Traumatic Brain Injury (TBI) remains a substantial public health concern, with approximately 69 million new cases reported globally each year [1,2]. Among these, moderate to severe TBI is particularly impactful, contributing to long-term disability and reduced quality of life for millions of individuals worldwide. In the United States alone, over 5.3 million people live with disabilities resulting from moderate to severe TBI [3]. The consequences of such injuries often include impairments in motor control, cognitive function, and mobility [4]. Notably, balance dysfunction is among the most significant motor-related challenges, as it affects postural stability and increases the risk of falls and associated injuries [5,6].

The relationship between balance and mobility is a critical area of focus in neurorehabilitation, especially for individuals recovering from moderate to severe TBI. Numerous studies have reported that survivors of TBI commonly experience balance disturbances, which interfere with their ability to resume daily routines and community participation [5,7]. Although conventional clinical assessments of balance provide useful information, they often fall short in capturing the complex and dynamic nature of mobility limitations experienced by individuals with TBI. The High-Level Mobility Assessment Tool (HiMAT), developed specifically for this population, offers a more comprehensive evaluation of higher-level mobility skills and real-world functional performance [8,9]. Recognizing these advantages, the present study employed the HiMAT as it encompasses challenging tasks such as running, jumping, and stair negotiation, activities that closely reflect the demands of community reintegration following TBI.

Growing evidence from rehabilitation research highlights that targeted, goal-oriented interventions can effectively enhance both balance and mobility among individuals recovering from TBI [10]. Interventions that incorporate intensive mobility training, balance-focused exercises, and adapted physical activity have consistently demonstrated improvements in walking ability and postural control [11,12]. Multimodal rehabilitation approaches that combine elements of strength, coordination, and balance training appear particularly effective in addressing the complex functional needs of this population [13,14]. Beyond restoring physical function, these integrated programs also aim to promote autonomy, confidence, and participation in meaningful community activities. Recognising the central role of balance in recovery, it is therefore essential to evaluate balance performance as a key component in developing rehabilitation strategies that foster greater mobility and functional independence.

Despite the growing body of literature linking balance to mobility, the specific relationship between balance performance and high-level mobility remains underexplored in individuals with moderate to severe TBI. Understanding how postural stability influences advanced mobility tasks could guide more effective rehabilitation strategies tailored to the unique challenges faced by this population. This study, therefore, aims to determine the correlation between balance performance and high-level mobility in individuals recovering from moderate to severe TBI. By clarifying this relationship, the findings may provide clinicians with meaningful insights for developing goal-oriented rehabilitation plans. Ultimately, the results could contribute to a broader understanding of how targeted balance interventions can enhance functional mobility and quality of life following TBI.

Materials and methods

Study design and participants

This study employed a cross-sectional design to examine the relationship between balance performance and high-level mobility among individuals with moderate to severe TBI. Participants were recruited using purposive

sampling from the Cheras Rehabilitation Hospital, where they were receiving physiotherapy care following discharge from acute services. Inclusion criteria required participants to be between 25 and 60 years old, with a confirmed diagnosis of moderate to severe TBI based on their initial Glasgow Coma Scale (GCS) scores. Individuals with pre-existing neurological, orthopedic, or vestibular conditions unrelated to TBI were excluded to minimise potential confounding factors. A total of 86 participants who met the criteria agreed to participate. Ethical approval for the study was obtained from the Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia, and written informed consent was obtained from all participants or their legal guardians prior to data collection.

Outcome Measures

The main outcome measures selected for this study were the HiMAT and balance tests derived from the NeuroCom® Balance Master, specifically the Sensory Organization Test (SOT) and Limits of Stability (LOS) protocols. The HiMAT is a 13-item performance-based scale that assesses advanced mobility skills such as running, jumping, hopping, and stair negotiation, making it particularly relevant for individuals recovering from TBI [15]. Validation studies have shown that the HiMAT demonstrates excellent psychometric properties, including high internal consistency ($\alpha = 0.99$) and outstanding interrater and test–retest reliability (ICC = 0.99). Moreover, the tool has proven to be more responsive than traditional functional measures such as the Functional Independence Measure and Rivermead Motor Assessment, making it a robust assessment for evaluating mobility outcomes in individuals with TBI [16]. The SOT provides an overall measure of postural stability by evaluating an individual's ability to maintain balance under six progressively challenging sensory conditions that alter visual, vestibular, and somatosensory input. Previous research has shown that the SOT demonstrates good reliability among adults with traumatic brain injury (ICC = 0.72–0.80) [17]. The LOS test assesses dynamic balance by quantifying parameters such as reaction time (RT), movement velocity (MVL), endpoint excursion (EPE), maximum excursion (MXE), and directional control (DCL) [7]. Prior studies have supported its reliability and validity in evaluating dynamic postural control [18]. Together, these outcome measures provide a comprehensive evaluation of both static and dynamic balance performance and high-level mobility, offering valuable insight into functional recovery following moderate to severe TBI.

Procedure

All assessments were conducted in a standardised clinical environment by qualified physiotherapists trained in the administration of the selected tools. Participants completed a brief warm-up consisting of five minutes of gentle stretching and stepping exercises to ensure physical readiness for testing. The HiMAT was administered first, following standardised instructions and scoring protocols to maintain consistency. A brief familiarisation trial was conducted before the assessment to ensure participants understood the tasks. Each HiMAT item were scored on a 5-point scale ranging from 0 (unable to perform) to 4 (best performance). Items were either timed or measured by distance, and the total score was calculated by summing all item scores, with higher values indicating better mobility performance [15].

Balance assessments were carried out using the NeuroCom® Balance Master system, with participants securely fitted in a safety harness to prevent falls during testing. Two standardised protocols were administered: the SOT and the LOS. In the SOT, participants stood barefoot on a force platform and were asked to maintain an upright posture under six sensory conditions that systematically altered visual, vestibular, and somatosensory inputs. Each trial lasted approximately 20 seconds, and higher equilibrium scores reflected better postural stability. The LOS test assessed dynamic balance

by evaluating how participants shifted their centre of gravity toward eight visual targets displayed on a monitor while keeping their feet in place. The test generated several parameters, including RT, MVL, EPE, MXE, and DCL, which together described the accuracy and control of voluntary weight shifting [7]. A brief practice trial was provided before testing, and rest periods of about three minutes were allowed between assessments to minimise fatigue.

Data Analysis

Data were analyzed using IBM SPSS Statistics version 26. Descriptive statistics were calculated to summarize participant demographics and scores on the HiMAT and balance measures. The primary aim of the analysis was to determine the relationship between high-level mobility and balance performance in individuals with TBI. For this purpose, Spearman's rank-order correlation was employed, given the non-normal distribution of the dataset. This non-parametric method allowed for the identification of associations between HiMAT scores and the SOT composite, RT, MVL, EPE, MXE, and DCL values. A significance level of $P < 0.05$ was applied to all statistical tests.

Results

This study included 86 individuals with moderate to severe TBI who met the eligibility criteria and completed assessments of both balance and high-level mobility. Participants ranged in age from 25 to 57 years, with a mean age of 33.13 years (SD = 8.40). The majority were male (84.9%), and motor vehicle accidents were the primary cause of injury (90.7%), followed by falls (7.0%) and other causes such as acts of violence (2.3%). Most participants sustained severe TBI (83.7%), while the remaining had moderate injuries (16.3%). These demographic and clinical characteristics provide important context for interpreting the observed patterns of balance and mobility. A summary of participant demographics is presented in Table 1.

Balance performance was assessed using two standardised tools: the SOT and LOS test. The mean SOT composite equilibrium score was 69.24% (SD = 10.80), reflecting participants' ability to maintain postural control under varying sensory conditions. For dynamic balance, LOS scores revealed average values of 3.27°/s (SD = 1.05) for MVL, 62.37% (SD = 13.92) for EPE, 79.15% (SD = 14.31) for MXE, and 68.05% (SD = 13.13) for DCL. These outcomes reflect a spectrum of postural stability and dynamic control abilities across the sample.

Correlation analysis using Spearman's rank-order test revealed significant positive associations between HiMAT scores and both static and dynamic balance parameters. A moderate correlation was found between HiMAT and the SOT composite equilibrium score ($r = 0.495$, $P = 0.001$), indicating that individuals with better postural control under altered sensory conditions tended to perform better in mobility tasks. Among the LOS variables, all four parameters demonstrated significant correlations with HiMAT: MVL ($r = 0.321$, $P = 0.001$), EPE ($r = 0.578$, $P = 0.001$), MXE ($r = 0.603$, $P = 0.001$), and DCL ($r = 0.558$, $P = 0.001$). Notably, MXE showed the strongest association with high-level mobility. These findings are summarized in Table 2 and highlight the relevance of dynamic balance measures in predicting functional performance.

Taken collectively, these findings emphasize the critical role of both static and dynamic balance in determining mobility outcomes in individuals with moderate to severe TBI. The SOT offered valuable insights into equilibrium control during sensory conflict, while the LOS test captured dynamic balance abilities essential for navigating real-world environments. The strength of these correlations supports the argument that impairments in balance, particularly in dynamic control, can directly limit one's ability to perform high-level mobility tasks such as running, jumping, or stair navigation. These findings reinforce the need for rehabilitation programs to include specific interventions that target postural control and balance retraining. Enhancing these

domains may be instrumental in optimizing mobility and functional independence among TBI survivors.

Discussion

This study explored the relationship between balance performance and high-level mobility in individuals with moderate to severe TBI. Significant associations were observed between mobility outcomes and both static and dynamic balance parameters, emphasizing the integral role of postural control in functional recovery. These findings are consistent with previous research suggesting that mobility limitations in this population are multifactorial, encompassing not only motor impairments but also cognitive, emotional, and sensory-processing deficits that compromise coordination and independence [19]. This complexity suggests that conventional rehabilitation approaches, which often focus solely on gross motor recovery, may not adequately address the broader mobility challenges faced by this group. Integrating balance-focused strategies into rehabilitation may offer a more effective, targeted approach to improving real-world function.

The observed correlation between HiMAT scores and the SOT composite score highlights the influence of sensory integration on mobility performance. Individuals with greater postural stability in the face of sensory perturbations tended to perform better in dynamic mobility tasks. This finding is consistent with existing evidence showing that disturbances in vestibular, visual, or proprioceptive function can markedly disrupt balance control and overall postural stability [20]. Recent findings have shown that interventions aimed at enhancing multisensory integration, such as galvanic vestibular stimulation, may improve postural control and support mobility gains in neurological populations [21]. These insights underline the value of sensory-based rehabilitation in addressing balance impairments among TBI survivors.

Dynamic balance variables from the LOS test demonstrated particularly strong associations with high-level mobility. The ability to shift and control the centre of gravity reflected in metrics such as MXE, EPE, and DCL was closely linked to performance in complex mobility tasks, including turning, climbing stairs, and obstacle negotiation. These results are supported by recent studies emphasizing the importance of dynamic postural control in safe, efficient community ambulation [22]. Notably, among the LOS parameters, MXE emerged as the most strongly correlated with HiMAT, reinforcing the importance of voluntary control over centre-of-mass displacement as a predictor of mobility function. The quantitative trends observed here support a growing clinical emphasis on training dynamic balance abilities rather than relying solely on traditional static exercises. As suggested by Klima et al. [23], incorporating task-specific, context-rich training such as walking on uneven surfaces or navigating crowded environments may better simulate daily functional demands and improve transferability. Rehabilitation programs that incorporate both anticipatory and reactive balance responses may offer more comprehensive improvements in mobility, confidence, and fall prevention.

Although balance was the primary focus of this investigation, it is essential to recognize that mobility performance is influenced by multiple physical and neurological systems. Prior analysis involving this cohort has shown that muscle strength, gait speed, and endurance also significantly impact HiMAT scores [6]. Nonetheless, the current findings establish balance, especially dynamic balance as a measurable and modifiable component that should be prioritized in rehabilitation planning. These results support a more integrated rehabilitation approach that combines balance training with strength and aerobic conditioning to maximise recovery [24].

Additional insights were gained through the analysis of SOT subcomponents. Specifically, vestibular and visual inputs were significantly

associated with HiMAT performance, whereas somatosensory and preference scores were not. This suggests that individuals with relatively preserved basic balance may still face limitations in high-level tasks requiring multisensory integration. Similarly, the negative correlation observed with RT suggests that delayed postural responses may hinder functional mobility, further highlighting the need to train quick, controlled adjustments during dynamic tasks.

Collectively, these results provide strong support for incorporating dynamic and sensory-based balance training into functional mobility programmes for individuals with moderate to severe TBI. This study adds to the growing understanding of postural control as a key factor in recovery and offers clinicians a practical focus for intervention design.

Despite the valuable insights gained from this study, several limitations should be acknowledged. Firstly, the study employed a cross-sectional design, which limits the ability to establish causality between balance measures and high-level mobility performance. While significant correlations were observed, these findings do not confirm directional or causal relationships. Secondly, the sample size, although adequate for correlation analysis, may not fully represent the broader population. The homogeneity of the sample in terms of age, diagnosis, or functional level may limit the generalizability of the results to other populations such as older adults, individuals with other neurological conditions, or community-dwelling populations with varying levels of physical activity.

Conclusion

This study reinforces the critical role of balance performance, particularly dynamic postural control and sensory integration in determining high-level mobility among individuals with moderate to severe TBI. The evidence supports the inclusion of targeted balance interventions in rehabilitation, as improvements in postural control may directly enhance mobility outcomes. By identifying balance as a measurable and modifiable contributor to function, this study offers a meaningful direction for clinicians seeking to optimise recovery. These findings contribute to a more nuanced understanding of TBI rehabilitation and set the stage for more individualised, function-driven therapeutic approaches. Future studies should explore longitudinal changes and intervention-specific effects to build upon the correlational insights established in this study, thereby advancing evidence-based strategies for improving functional mobility in this population.

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Conflict of interest

The authors declare no conflicts of interest in the conduct, authorship, or publication of this study.

Authors' contributions

SA conceptualized the study, collected and analyzed the data, and drafted the manuscript. HM designed the study, reviewed the manuscript, and provided supervision. NAMN conducted the literature review, provided methodological oversight, and edited the manuscript.

Table 1. Participants' demographic data, N=86

	n (%)	Mean	SD
Age	86 (100)	33.13	8.40
Gender			
Male	73 (84.9)	-	-
Female	13 (15.1)	-	-
Mechanism of Injury			
MVA	78 (90.7)	-	-
Acts of violence & others	2 (2.3)	-	-
Fall	6 (7.0)	-	-
Severity of TBI			
Moderate	14 (16.3)	-	-
Severe	72 (83.7)	-	-

Abbreviations: MVA, motor-vehicle accident; n, sample size; SD, standard deviation.

Table 2. Correlation between balance variables and HiMAT scores

Variables	n (%)	Mean	SD	r	*P* value
SOT					
Somatosensory (%)	86 (100)	95.78	4.33	0.140	0.099
Visual (%)	86 (100)	82.06	14.50	0.250	0.010*
Vestibular (%)	86 (100)	54.42	23.04	0.331	0.001*
Preferences (%)	86 (100)	101.16	16.35	0.017	0.437
Composite (%)	86 (100)	69.24	10.80	0.495	0.001*
LOS					
RT (sec)	86 (100)	.72	.24	-0.247	0.011*
MVL (degree/sec)	86 (100)	3.27	1.05	0.321	0.001*
EPE (%)	86 (100)	62.37	13.92	0.578	0.001*
MXE (%)	86 (100)	79.15	14.31	0.603	0.001*
DCL (%)	86 (100)	68.05	13.13	0.558	0.001*
HiMAT (outcome)	86 (100)	25.43	12.80	1.000	-

Abbreviations: DCL, directional control; EPE, end-point Excursion; HiMAT, High-Level Mobility Assessment Tool; MXE, maximum excursion; LOS, Limits of Stability; MVL, movement velocity; n, sample size; r, correlation; RT, Reaction Time; SD, standard deviation; SOT, Sensory Organization Test.
* Significant at $p<0.05$

References

[1]. Righy C, Rynkowski CB, Turon R. Global insights into traumatic brain injury. The low-and middle-income countries' perspective. Vol. 37, Critical Care Science. Associacao de Medicina Intensiva Brasileira - AMIB; 2025.

[2]. Naik A, Bederson MM, Detchou D, Dharnipragada R, Hassaneen W, Arnold PM, et al. Traumatic Brain Injury Mortality and Correlates in Low- and Middle-Income Countries: A Meta-Epidemiological Study. Vol. 93, Neurosurgery. Wolters Kluwer Medknow Publications; 2023. p. 736–44.

[3]. Driver S, Juengst S, McShan EE, Bennett M, Bell K, Dubiel R. A randomized controlled trial protocol for people with traumatic brain injury enrolled in a healthy lifestyle program (GLB-TBI). Contemp Clin Trials Commun. 2019 Jun 1;14.

[4]. Corrigan F, Wee IC, Collins-Praino LE. Chronic motor performance following different traumatic brain injury severity—A systematic review. Vol. 14, Frontiers in Neurology. Frontiers Media S.A.; 2023.

[5]. Tendolkar P, Ibironke O, Marchesi G, De Luca A, Squeri V, Nolan KJ, et al. Relationship between Timed Up and Go performance and quantitative biomechanical measures of balance. Frontiers in Rehabilitation Sciences. 2024;5.

[6]. Cesar GM, Buster TW, Burnfield JM. Lower extremity muscle activity during reactive balance differs between adults with chronic traumatic brain injury and controls. Front Neurol. 2024;15.

[7]. Row J, Chan L, Damiano D, Shenouda C, Collins J, Zampieri C. Balance assessment in traumatic brain injury: A comparison of the sensory organization and limits of stability tests. J Neurotrauma. 2019 Aug 15;36(16):2435–42.

[8]. Clark RA, Weragoda N, Paterson K, Telianidis S, Williams G. A pilot investigation using global positioning systems into the outdoor activity of people with severe traumatic brain injury. J Neuroeng Rehabil. 2014 Mar 19;11(1).

[9]. Williams G, Morris ME, Schache A, McCrory PR. People preferentially increase hip joint power generation to walk faster following traumatic brain injury. Neurorehabil Neural Repair. 2010 Jul;24(6):550–8.

[10]. Shen Y, Jiang L, Lai J, Hu J, Liang F, Zhang X, et al. A comprehensive review of rehabilitation approaches for traumatic brain injury: efficacy and outcomes. Vol. 16, Frontiers in Neurology. Frontiers Media SA; 2025.

[11]. Peters DM, Jain S, Liuzzo DM, Middleton A, Greene J, Blanck E, et al. Individuals with chronic traumatic brain injury improve walking speed and mobility with intensive mobility training. Arch

Phys Med Rehabil. 2014;95(8):1454–60.

[12]. Romanov R, Mesarič L, Perić D, Damiš JV, Filišič YP. The effects of adapted physical exercise during rehabilitation in patients with traumatic brain injury. Turk J Phys Med Rehabil. 2021;67(4):482–9.

[13]. Alashram AR, Annino G, Raju M, Padua E. Effects of physical therapy interventions on balance ability in people with traumatic brain injury: A systematic review. Vol. 46, NeuroRehabilitation. IOS Press BV; 2020. p. 455–66.

[14]. Bland DC, Zampieri C, Damiano DL. Effectiveness of physical therapy for improving gait and balance in individuals with traumatic brain injury: A systematic review. Vol. 25, Brain Injury. Informa Healthcare; 2011. p. 664–79.

[15]. Williams G, Robertson V, Greenwood K, Goldie P, Morris ME. The high-level mobility assessment tool (HiMAT) for traumatic brain injury. Part 1: Item generation. Brain Inj. 2005;19(11):925–32.

[16]. Williams G, Robertson V, Greenwood K, Goldie P, Morris ME. The concurrent validity and responsiveness of the high-level mobility assessment tool for measuring the mobility limitations of people with traumatic brain injury. Arch Phys Med Rehabil. 2006 Mar;87(3):437–42.

[17]. Warren WS. Concurrent Validity and Test Retest Reliability of Three Postural Control Assessments. University of Texas at Arlington; 2013.

[18]. Pickerill ML, Harter RA. Validity and reliability of limits-of-stability testing: A comparison of 2 postural stability evaluation devices. Vol. 46, Journal of Athletic Training. National Athletic Trainers' Association Inc.; 2011. p. 600–6.

[19]. Chan A, Ouyang J, Nguyen K, Jones A, Basso S, Karasik R. Traumatic brain injuries: a neuropsychological review. Vol. 18, Frontiers in Behavioral Neuroscience. Frontiers Media SA; 2024.

[20]. Wagner AR, Akinsola O, Chaudhari AMW, Bigelow KE, Merfeld DM. Measuring Vestibular Contributions to Age-Related Balance Impairment: A Review. Vol. 12, Frontiers in Neurology. Frontiers Media S.A.; 2021.

[21]. Fu W, Bai Y, Wang X. Galvanic vestibular stimulation for postural rehabilitation in neurological disorders: a systematic review. Vol. 19, Frontiers in Neuroscience. Frontiers Media SA; 2025.

[22]. Joubran K, Bar-Haim S, Shmuelof L. The functional and structural neural correlates of dynamic balance impairment and recovery in persons with acquired brain injury. Sci Rep. 2022 Dec 1;12(1).

[23]. Klima D, Morgan L, Baylor M, Reilly C, Gladmon D, Davey A. Physical Performance and Fall Risk in Persons With Traumatic Brain Injury. Percept Mot Skills. 2019 Feb 1;126(1):50–69.

[24]. Sheridan C, Thaut C, Brooks D, Patterson KK. Feasibility of a rhythmic auditory stimulation gait training program in community-dwelling adults after TBI: A case report. NeuroRehabilitation. 2021;48(2):221–30.

CASE REPORT

Kikuchi-Fujimoto Disease Triggered by *Mycoplasma pneumoniae* Infection: A Case Report.

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Abstract
Kikuchi-Fujimoto disease (KFD) is a rare inflammatory disorder which typically presents with cervical lymphadenopathy and pyrexia. It is frequently misdiagnosed as other more common medical conditions which share similar clinical manifestations. The diagnosis of KFD is often established only after a lymph node biopsy and histopathology evaluation that demonstrates the characteristic features of histiocytic necrotizing lymphadenitis. While the aetiology of KFD remains poorly-understood, certain microbial agents have been implicated as triggering factors. Here, we highlight a case of a young Asian woman who developed prolonged fever and cervical lymphadenopathy. She was initially being investigated for possible lymphoma, but was subsequently found to have KFD, alongside a *Mycoplasma pneumoniae* infection. She recovered well following the treatment with azithromycin.

Keywords: *Azithromycin, Kikuchi-Fujimoto disease*, *Mycoplasma pneumoniae.*

Introduction

Kikuchi-Fujimoto disease (KFD) is a rare form of benign lymphadenitis which was first recognized in Japan in year 1972 and since then, has been reported worldwide [1-4]. It mostly affects young adults with varying gender distribution and ethnic background [5,6]. KFD typically presents with localized lymphadenopathy with a predilection to cervical lymph nodes, along with systemic symptoms, notably fever, weight loss, and fatigue [5,6]. Hence, it is difficult to distinguish KFD clinically from other more serious illnesses such as malignant lymphoma, tuberculous lymphadenitis, systemic lupus erythematosus, and certain viral infections like infectious mononucleosis, until a lymph node biopsy is done, which reveals the distinctive features of histiocytic necrotizing lymphadenitis.

Case report

A 19-year-old female boutique assistant, previously healthy and fit, presented with intermittent fever, reduced appetite, and progressive fatigue for three weeks. At the same time, she also noticed small swellings on both sides of her neck. Otherwise, there were no specific respiratory symptoms, night sweats, skin rashes, joint pain, any bleeding tendency, or lumps elsewhere in the body. She had no history of high-risk behaviour, contact with sick people, recent travel abroad, or jungle trekking. She initially took paracetamol to relieve the fever and received a five-day course of antibiotics from a private clinic one week after the onset of her illness. However, the effect of the treatment was short-lived. The fever persisted, and she lost 6 kg of weight before seeking medical attention in the hospital.

Upon review, she appeared pale and had a temperature of 38 °C but otherwise not in distress. Her pulse rate was 102 beats/minute, blood pressure was 112/73 mmHg, and respiratory rate was 18 breaths/minute. Bilateral cervical lymphadenopathy was noted at levels II to IV. The nodes were mobile, firm, with sizes ranging from 1 to 3 cm, and some were mildly tender. Other peripheral lymph nodes were not palpable. No lesions were found in the ears, nose, or oral cavity. Abdominal examination revealed hepatomegaly (liver span 13 cm). The spleen was not enlarged. Examination of other organ systems was unremarkable.

Her initial haematological indices showed leukopenia (total white cell count, TWBC 1.9 x 10^9/L) with absolute neutropenia (0.86 x 10^9/L) and lymphopenia (0.9 x 10^9/L), hypochromic microcytic anaemia (haemoglobin 8.8 g/dL, mean corpuscular volume 60.2 fl, mean corpuscular haemoglobin 18.3 pg), a low reticulocyte count 0.34%, and normal platelet count. No blast cells were seen on the peripheral blood smear but some atypical lymphocytes were present. Considering possible lymphoproliferative disorder with neutropenic sepsis, she was initiated on broad-spectrum antibiotics upon admission, including intravenous piperacillin/tazobactam, tablet doxycycline, and tablet azithromycin. Subsequent laboratory studies revealed a positive direct coombs test, low serum iron 4.6 µmol/L, total iron binding capacity 39.5 µmol/L, and elevated levels of serum ferritin 1626.8 µg/L, C-reactive protein 39.9 mg/L, lactate dehydrogenase 954 U/L, alanine transaminase 173.8 U/L, and aspartate transaminase 249 U/L. Her erythrocyte sedimentation rate, renal profile, serum bilirubin, and alkaline phosphatase were normal.

Extensive microbiological testing was carried out to exclude various infections being considered as the differential diagnoses. A significant titre (1:320) of anti-Mycoplasma immunoglobulin (Ig) M was noted. Both the anti-Epstein-Barr virus and anti-cytomegalovirus IgG were reactive but the IgM were non-reactive, indicating previous exposure. Her chest radiograph was normal. The blood culture, leptospira and parvovirus B19 serology, human immunodeficiency virus test, malaria parasites, viral hepatitis screen, and tuberculosis work-up were negative. Abdominal ultrasound confirmed the enlarged liver with no focal lesions and excluded intraabdominal lymphadenopathy or abscesses. In addition, the

autoantibody screen for systemic lupus erythematosus was negative.

As lymphoma remained the major concern, an excisional lymph node biopsy was performed on day 3 of admission, and the histopathology examination (HPE) findings revealed histiocytic necrotizing lymphadenitis, consistent with Kikuchi-Fujimoto disease (Figure 1 and 2).

Her condition was stable throughout her stay in the hospital. The fever subsided two days after administration of the antimicrobial therapy. The HPE result was obtained one week after her admission, and by that time, she had completed three days of azithromycin, seven days of doxycycline, and five days of piperacillin/tazobactam followed by two days of amoxicillin/clavulanate. Haematinics were prescribed for the iron-deficiency anaemia. She regained her appetite and reported marked improvement in her general well-being. The TWBC and reticulocyte count improved and normalized after one week. The LDH declined steadily following treatment. The transaminases fluctuated but eventually demonstrated a downward trend. She was discharged well and was scheduled for follow-up in the specialist clinic to monitor her haemoglobin level, liver enzymes, and her future outcome.

Discussion

Kikuchi-Fujimoto disease (KFD) is a rare cause of lymphadenopathy, and it frequently poses challenges in the diagnosis. While localized cervical lymphadenitis remains the most classical presentation of KFD, generalized lymphadenopathy and enlargement of the lymph nodes in other regions such as the axilla, groin, and within the abdominal cavity have been described [3,7-9]. The involved nodes are typically mobile, firm, usually small with sizes less than 3 cm, and at times tender [7]. Besides the common associated systemic features which mimic the B symptoms in lymphoma, other unusual extranodal manifestations recognized in KFD include skin rashes, hepatosplenomegaly, arthritis, and neurological dysfunction [10-12]. Laboratory abnormalities commonly observed in KFD, although non-specific, are leukopenia, presence of atypical lymphocytes in the peripheral blood, increased erythrocyte sedimentation rate, elevated lactate dehydrogenase, and elevated transaminases [5,6,13]. In view of the wide range of differential diagnoses, serology tests for viral infections, tuberculosis work-up, and autoantibody panels are frequently carried out as part of the diagnostic evaluation. A definitive diagnosis of KFD requires a histopathological examination of the involved nodes. Excisional biopsy is helpful to exclude lymphoma. A recent study by Park et al indicated that ultrasound-guided core needle biopsy had a 95.6% accuracy in the diagnosis of KFD, making it a suggested diagnostic modality when KFD is a a clinical consideration [14]. In KFD, histologically, patchy areas of necrosis with abundant karyorrhectic nuclear debris are seen at the paracortical region, surrounded by extensive infiltrates of histiocytes, small lymphocytes, immunoblasts, and plasmacytoid dendritic cells [13]. The neutrophils are notably absent [13]. In addition, immunohistochemistry can further contribute to the diagnosis as the histiocytes in KFD are positive for myeloperoxidase, CD163, and CD68; the lymphocytes are predominantly T cells expressing CD3; and CD123 highlights the plasmacytoid dendritic cells [13,15].

The etiopathogenesis of KFD has not been fully elucidated. Li et al had demonstrated that KFD is associated with an aberrant type 1 interferon response, which is likely mediated by the T-lymphocytes and the plasmacytoid dendritic cells [16]. However, the initiating signals of this dysregulated immune response remain undetermined. Various factors have been implicated as the drivers for KFD, particularly the microbial agents and the autoimmune mechanisms [17]. In our patient, the KFD was associated with an acute *Mycoplasma pneumoniae* infection as evidenced by the high anti-mycoplasma IgM titre along with a positive Coombs test. KFD triggered by *Mycoplasma*

pneumoniae infection is uncommon and our literature search identified only four reported cases [18-20]. Interestingly, our patient also had previous contact with cytomegalovirus and Epstein-Barr virus. Although numerous infectious triggers particularly the viruses have been linked to KFD, microbial analysis by RNA sequencing of the biopsied materials in KFD had not identified any specific pathogens and hence, failed to prove a causal relationship between the microorganisms and KFD [21]. The intricate interplay between the microbial agents and the immune system leading to increased susceptibility to, and the onset of, the inflammatory cascade in KFD, would require further research. The development of KFD has been linked to an autoimmune origin, as multiple cases of KFD associated with systemic lupus erythematosus (SLE) and Sjögren's syndrome have been reported [22,23]. KFD could occur simultaneously with, before, or after the onset of the autoimmune disorders. Furthermore, pathological analysis of the lymph nodes in certain patients with active SLE did reveal the presence of necrosis and histiocytic infiltration which were indistinguishable from KFD [24]. This similarity in the histopathological findings further supports the autoimmune process as a trigger of KFD.

KFD is self-limiting and the majority of patients will have a favourable outcome with spontaneous recovery within a few months, although recurrence has been observed in 3 to 4% of cases [6]. The treatment for KFD is primarily supportive. Paracetamol and non-steroidal anti-inflammatory drugs are frequently prescribed as antipyretics and analgesics. In severe cases with a more prolonged course of illness and extensive nodal or extranodal involvement, systemic corticosteroids, immunomodulators, and intravenous immunoglobulin have been utilized [25-27]. Our patient had a dramatic improvement with resolution of fever, which was apparent soon after the administration of the antimicrobial therapy. Although multiple antibiotics were initiated as the diagnosis of her clinical problem was unclear upon admission, we believed that the patient responded to the azithromycin as it was the appropriate treatment for the *Mycoplasma pneumoniae* infection. The outcome of our patient was similar to the reported cases by Yu et al, indicating that macrolide may play a role in the resolution of KFD if it is associated with *Mycoplasma pneumoniae* infection [18].

Conclusion

This case underscores the fact that Kikuchi-Fujimoto disease is easily misdiagnosed. It is crucial that the clinicians should be aware of this rare clinical entity to streamline the diagnostic evaluations and avoid unnecessary interventions. Further research remains highly anticipated to determine the aetiology and the molecular pathways in the pathogenesis. Despite being self-limiting, the specific targeted therapy to the recognized trigger might contribute to early resolution of the disease and improved outcome.

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Conflicts of interest
None to declare.

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Authors contribution
LHS: Ideas, data collection, manuscript writing, and formatting
OPS: Intellectual input to the manuscript
CKY: Analysis of the lymph node biopsy

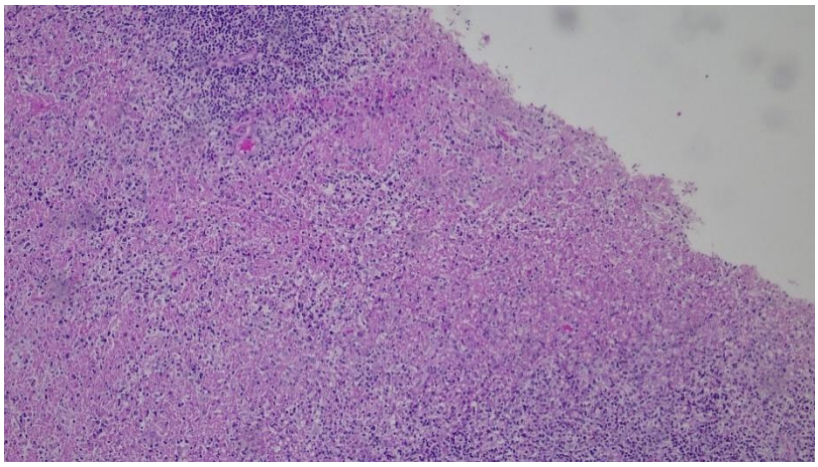

Figure 1. Histopathology of the lymph node showing areas of necrosis consisting of brightly eosinophilic fibrinoid deposits.

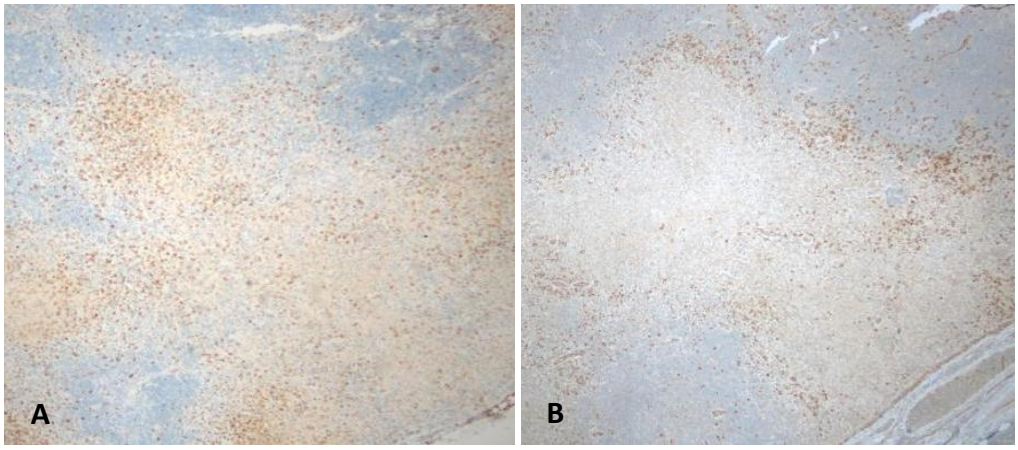

Figure 2. Immunohistochemical staining of the lymph node. **A.** CD163 highlighted the aggregates of histiocytes surrounding the areas of necrosis. **B.** CD123 labeled the plasmacytoid dendritic cells which formed clusters at the edges of the necrotic foci.

References

[1]. Kikuchi M. Lymphadenitis showing focal reticulum cell hyperplasia with nuclear debris and phagocytosis. Nippon Ketsueki Gakkai Zasshi. 1972;35:379-80.

[2]. Fujimoto Y, Kojima Y, Yamaguchi K. Cervical subacute necrotizing lymphadenitis: a new clinicopathological entity. Naika. 1972;20:920-7.

[3]. Deaver D, Naghashpour M, Sokol L. Kikuchi-Fujimoto Disease in the United States: Three Case Reports and Review of the Literature. Mediterr J Hematol Infect Dis. 2014;6(1):e2014001. doi:10.4084/MJHID.2014.001.

[4]. Achappa B, Herath NC, Sebastian B, Dsouza NV, Raghuram PM, Holla R, et al. Kikuchi-Fujimoto disease in a tertiary care teaching hospital in Coastal South India: A 8-year retrospective study. F1000Res. 2022;11:492. doi:10.12688/f1000research.109832.1.

[5]. Deb A, Fernandez V, Kilinc E, Bahmad HF, Camps NS, Sriganeshan V, et al. Kikuchi-Fujimoto Disease: A Case Series and Review of the Literature. Diseases. 2024;12(11):271. doi:10.3390/diseases12110271.

[6]. Mahajan VK, Sharma V, Sharma N, Rani R. Kikuchi-Fujimoto disease: A comprehensive review. World J Clin Cases. 2023;11(16):3664-79. doi:10.12998/wjcc.v11.i16.3664.

[7]. Norris AH, Krasinskas AM, Salhany KE, Gluckman SJ. Kikuchi-Fujimoto disease: a benign cause of fever and lymphadenopathy. Am J Med. 1996;101(4):401-5. doi:10.1016/S0002-9343(96)00231-8.

[8]. Shah S, Vijendren A, Obichere M. Kikuchi--Fujimoto disease: a rare presentation of a groin lump. BMJ Case Rep. 2013;2013:bcr2012006841. doi:10.1136/bcr-2012-006841.

[9]. Mannu GS, Ahmed F, Cunnick G, Sheppard K. A rare cause of axillary lymphadenopathy: Kikuchi's disease. BMJ Case Rep. 2014;2014:bcr2013203100. doi:10.1136/bcr-2013-203100.

[10]. Inamo Y. The Difficulty of Diagnosing Kikuchi-Fujimoto Disease in Infants and Children Under Six Years Old: Case Report and Literature Review. Cureus. 2020;12(3):e7383. doi:10.7759/cureus.7383.

[11]. Nizamuddin, Ubaid A, Waheed F. Arthritis as a Presenting Feature of Kikuchi-Fujimoto Disease: Time to Think Out of the Box in Patients with Arthritis. Hamdan Medical Journal. 2020;13(1):55-6. doi:10.4103/HMJ.HMJ_53_19.

[12]. Iwamoto N, Funahashi M, Shinohara K, Nakaya Y, Motobayashi H, Tochitani K, et al. Two Cases of Kikuchi Disease Presenting with Aseptic Meningitis and Encephalitis. Intern Med. 2022;61(17):2687-9. doi:10.2169/internalmedicine.7724-21.

[13]. Perry AM, Choi SM. Kikuchi-Fujimoto Disease: A Review. Arch Pathol Lab Med. 2018;142(11):1341-6. doi:10.5858/arpa.2018-0219-RA.

[14]. Park SG, Koo HR, Jang K, Myung JK, Song CM, Ji YB, et al. Efficacy of Ultrasound-Guided Needle Biopsy in the Diagnosis of Kikuchi-Fujimoto Disease. Laryngoscope. 2021;131(5):E1519-E1523. doi:10.1002/lary.29160.

[15]. AlShieban S, Masuadi E, Alghamdi R, Alshalfan A, Alessa S, Alqarni AK, et al. Pathological Features and Clinical Characteristics of Kikuchi-Fujimoto Disease: A Tertiary Hospital Experience in Riyadh, Saudi Arabia. Cureus. 2023;15(1):e33683. doi:10.7759/cureus.33683.
[16]. Li EY, Xu J, Nelson ND, Teachey DT, Tan K, Romberg N, et al. Kikuchi-Fujimoto disease is mediated by an aberrant type I interferon response. Mod Pathol. 2022;35(4):462-9. doi:10.1038/s41379-021-00992-7.
[17]. Kucukardali Y, Solmazgul E, Kunter E, Oncul O, Yildirim S, Kaplan M. Kikuchi-Fujimoto Disease: analysis of 244 cases. Clin Rheumatol. 2007;26(1):50-4. doi:10.1007/s10067-006-0230-5.
[18]. Yu RB, Chen YJ, Chang CH, Chen YL, Chen JW. Kikuchi-Fujimoto Disease Associated With Mycoplasma Pneumoniae Infection. Ear Nose Throat J. 2024;103(4):NP223-NP225. doi:10.1177/01455613211044225.
[19]. Kim SH, Lee JM, Gu MJ, Ahn JY. A case of Kikuchi-Fujimoto Disease Associated with Mycoplasma Pneumoniae Infection. Clin Pediatr Hematol Oncol 2019;26(2):83-6. doi:10.15264/cpho.2019.26.2.83.
[20]. Müller CSL, Vogt T, Becker SL. Kikuchi-Fujimoto Disease Triggered by Systemic Lupus Erythematosus and Mycoplasma pneumoniae Infection-A Report of a Case and a Review of the Literature. Am J Dermatopathol. 2021;43(3):202-8. doi:10.1097/DAD.0000000000001764.
[21]. Nelson ND, Meng W, Rosenfeld AM, Bullman S, Sekhar Pedamallu C, Nomburg JL, et al. Characterization of Plasmacytoid Dendritic Cells, Microbial Sequences, and Identification of a Candidate Public T-Cell Clone in Kikuchi-Fujimoto Disease. Pediatr Dev Pathol. 2021;24(3):193-205. doi:10.1177/1093526620987961.
[22]. Baenas DF, Diehl FA, Haye Salinas MJ, Riva V, Diller A, Lemos PA. Kikuchi-Fujimoto disease and systemic lupus erythematosus. Int Med Case Rep J. 2016;9:163-7. doi:10.2147/IMCRJ.S106396.
[23]. Cadório MJ, Oliveira J, Gama J, Duarte C. Kikuchi-Fujimoto disease and primary Sjögren's syndrome coexisting: A case-based literature review. Mod Rheumatol Case Rep. 2025;9(1):110-6. doi:10.1093/mrcr/rxae058.
[24]. Papo M, Cappy P, Degachi A, Woerther PL, Saal C, Charlotte F, et al. Lymphadenopathy in systemic lupus erythematosus: no microbial trigger found by shotgun metagenomics in a retrospective study on 38 patients. Rheumatology (Oxford). 2024;keae578. doi:10.1093/rheumatology/keae578.
[25]. Noursadeghi M, Aqel N, Gibson P, Pasvol G. Successful treatment of severe Kikuchi's disease with intravenous immunoglobulin. Rheumatology (Oxford). 2006;45(2):235-7. doi:10.1093/rheumatology/kei074.
[26]. Hyun M, So IT, Kim HA, Jung H, Ryu SY. Recurrent Kikuchi's Disease Treated by Hydroxychloroquine. Infect Chemother. 2016;48(2):127-31. doi:10.3947/ic.2016.48.2.127.

[27]. Honda F, Tsuboi H, Toko H, Ohyama A, Takahashi H, Abe S, et al. Recurrent Kikuchi-Fujimoto Disease Successfully Treated by the Concomitant Use of Hydroxychloroquine and Corticosteroids. Intern Med. 2017;56(24):3373-7. doi:10.2169/internalmedicine.9205-17.

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CASE REPORT

A Case of Non-Immune Hydrops Fetalis in an HIV-Positive Mother

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Abstract
Mother-to-child transmission (MTCT) remains the primary route of HIV infection in children, with an estimated 30–40% risk in untreated pregnancies. We report a case of a pregnant woman with a high HIV viral load who developed non-immune hydrops foetalis (NIHF), a rare and life-threatening foetal condition characterized by excessive fluid accumulation in at least two compartments. Ultrasound examinations revealed left ventriculomegaly, cardiomegaly with pericardial effusion, pleural effusion, and ascites with an enlarged spleen, confirming NIHF. Extensive investigations ruled out common infectious and non-infectious causes, raising the possibility of a link between maternal HIV and NIHF. This case highlights the need for further investigation into the potential relationship between maternal HIV, congenital HIV, and NIHF, as well as the importance of early detection and multidisciplinary management in high-risk pregnancies.

Keywords: *HIV-Positive Mother, hydrops foetalis, non-immune hydrops foetalis.*

Introduction

Hydrops foetalis (HF) is an abnormal accumulation of fluid in at least two foetal compartments, including the peritoneal cavity (ascites), pleura (pleural effusions), pericardium (pericardial effusion), and generalized skin oedema (defined as skin thickness >5 mm). Additionally, placental thickening (greater than 4 cm in the second trimester or greater than 6 cm in the third trimester) and polyhydramnios are often associated with hydrops foetalis.[1]

Hydrops foetalis can be immune or non-immune. Immune hydrops result from blood type incompatibility between the foetus and the pregnant mother. In contrast, non-immune hydrops foetalis (NIHF) occurs when fluid accumulation is not caused by maternal antibodies attacking foetal blood cells. Due to the widespread use of anti-D immunoglobulin, the prevalence of immune hydrops associated with red cell alloimmunization has declined significantly, making NIHF account for over 90% of all HF cases. The prevalence of NIHF ranges from 1 in 1,500 to 1 in 4,000 births.[2]

We present a case of a neonate born with NIHF who demised shortly after birth. The maternal HIV infection was diagnosed antenatally. An extensive evaluation for known causes of NIHF, both infectious and non-infectious, was negative.

Case report

A 28-year-old Malaysian woman, previously diagnosed as HIV-positive, became pregnant for the third time (gravida 3, para 2). She was diagnosed with HIV seven years ago, having acquired the infection from her first husband. Since then, she had a history of poor adherence, with multiple defaults on follow-up and treatment. At the time of presentation, she was married to her second husband, who was HIV-negative. Her obstetrics history included two previous emergency lower-segment caesarean sections (LSCS). Bothe of her children from previous pregnancies were HIV-negative.

In this pregnancy, she performed a self-urine pregnancy test at six weeks of amenorrhoea due to pregnancy symptoms. After confirming the pregnancy, she visited a healthcare centre, where a medical officer performed baseline viral load and CD4 tests and referred her to the infectious disease team.

At eight weeks of amenorrhea, her initial investigations showed a viral load of 50,322 copies/mL and a CD4 cell count of 205 cells/mm³. Consequently, she was started on highly active antiretroviral therapy (HAART) with Tenofovir-Emtricitabine and Dolutegravir. A repeated blood investigation at 24 weeks of pregnancy showed an improved but still high viral load of 27,290 copies/mL and a CD4 count of 238 cells/mm³. This poor response was likely due to initial poor compliance with medication during the first trimester due to nausea and vomiting. After receiving proper education and counselling, the patient understood the necessity of HAART and adhered to the treatment.

An ultrasound scan (USS) at 27 weeks' gestation identified foetal ascites, prompting referral to a tertiary foetal medicine centre. The USS confirmed the presence of left ventriculomegaly (Figure 1), cardiomegaly with pericardial effusion, hypoplastic ventricles, pleural effusion, and ascites with an enlarged spleen (Figure 2). The Middle Cerebral Artery Doppler peak systolic velocity was within normal limits, ruling out foetal anaemia. The Umbilical Artery Doppler was also normal, excluding increased vascular resistance (Figure 3).

Further investigations to determine the cause of hydrops foetalis were conducted. The patient's blood type was O positive, with negative direct and indirect Coombs tests. Screening tests for syphilis (Venereal Disease Research Laboratory test, VDRL), hepatitis C antibody, and hepatitis B surface antigen were negative. TORCHES screening showed positive IgG but negative IgM ELISA results for toxoplasmosis, rubella virus, cytomegalovirus, herpes simplex virus, and parvovirus, implying a previous infection.

The patient was informed about the diagnosis of hydrops foetalis and its poor prognosis to assist in decision-making. Given her underlying retroviral

disease (RVD) with a high viral load, history of two previous caesarean scars, and the poor prognosis of the foetus, the patient was offered an elective LSCS and bilateral tubal ligation at 32 weeks of pregnancy.

A female baby was delivered, but she was not vigorous, with Apgar scores of 5 at one minute, three at five minutes, and two at ten minutes (Figure 4). No resuscitation was provided due to the poor prognosis. The baby was pronounced dead at 13 minutes of life. The parents declined a post-mortem examination and permission for HIV testing of the newborn.

Discussion

NIHF results from an imbalance in foetal interstitial fluid dynamics due to increased venous pressure and reduced lymphatic return. Even minor increases in venous pressure can impair lymphatic flow, leading to fluid accumulation and NIHF.[3][4]

NIHF has serious perinatal implications, regardless of gestational age at diagnosis. The leading causes include chromosomal anomalies, foetal cardiovascular disorders, and congenital infections.[5]

Standard NIHF assessments include obstetric and family history reviews, infection screenings, maternal red cell antibody testing, and detailed foetal ultrasound. The Middle Cerebral Artery Doppler is used to exclude foetal anaemia. In this case, Doppler findings were normal.[6]

Congenital infections such as parvovirus B19, toxoplasmosis, cytomegalovirus (CMV), congenital syphilis, and herpes simplex virus (HSV) are part of the routine evaluation for infectious causes of NIHF.[6] An extensive infectious workup was negative for our patient. However, congenital HIV infection is not included in routine screening despite mother-to-child transmission being a significant concern in several countries.

To the best of our knowledge, there are very few reported cases of congenital HIV infection associated with NIHF. The first reported case in 2006 described an infant born to an HIV-positive mother with NIHF and hepatitis. The hepatitis resolved after the initiation of HAART, suggesting a secondary cause.[7] Another report, a retrospective review of a case series involving 28 infants with NIHF, identified one case of congenital HIV infection, although the details were not described.[8]

In our case, the mother was HIV-positive, but we were unable to determine whether the baby had congenital HIV as the parents refused testing. However, a case report described a pregnant Zimbabwean woman with HIV and hydrops foetalis whose baby tested negative for HIV.[9] This suggests that NIHF can occur regardless of the infant's HIV status, yet it is distinctly observed in mothers with HIV. This raises an important question regarding the underlying oetiology of NIHF in HIV-negative infants born to HIV-positive mothers.

In this case, the foetal echocardiogram revealed left ventriculomegaly, cardiomegaly with pericardial effusion, and hypoplastic ventricles. After infectious causes, cardiac anomalies represent the next largest oetiological group for NIHF (12.7%).[4] Cardiovascular anomalies can cause haemodynamic disturbances that impair venous return, leading to cardiac failure. Cardiac failure increases central venous pressure and interstitial fluid, which results in NIHF.[10] Interestingly, a study of 173 foetuses from 169 HIV-infected mothers reported that these foetuses can manifest abnormal cardiovascular structure and function and increased placental vascular resistance independent of their HIV status once born. [10] This report suggests that, in infants born to HIV-positive mothers, NIHF may not only be linked to possible congenital HIV infection but also to cardiovascular abnormalities that could be indirectly associated with maternal HIV.

Although our case and other reports provide valuable insights, the link between congenital HIV and hydrops foetalis remains unclear. This case highlights the need for further reporting or investigation into the potential relationship

between maternal HIV, congenital HIV, and NIHF. Since congenital HIV is not part of the routine screening for NIHF, we propose that congenital HIV be considered a possible infectious oetiology of NIHF. Clinicians should also take maternal HIV status into account when evaluating NIHF, as it may contribute to the condition through indirect mechanisms.

Pre-pregnancy counselling is essential to ascertain the optimal medical conditions of HIV-positive women for pregnancy. Aggressive preconception assessment and ART initiation can drastically decrease maternal viral load and mother-to-child transmission (MTCT). In this case, late commencement and inadequate antenatal attendance in early pregnancy resulted in unprecedentedly high viral load, potentially influencing foetal outcomes. Optimal prenatal care that includes adequate planning, achieving viral suppression before conception, and multidisciplinary management is critical to preventing complications and, possibly, associations with non-immune hydrops fetalis (NIHF). This case highlights the need for the integration of HIV care and reproductive planning to optimize safer pregnancies.

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Conflicts of interest

All authors declare no conflicts of interest.

Ethical

The patient provided verbal consent for the use of case details and images for publication.

Authors' contribution:

NKC: conceptualization, data curation, writing – original draft. AHA and CP: supervision, writing – review and editing. All authors have read and agreed to the published version of the manuscript.

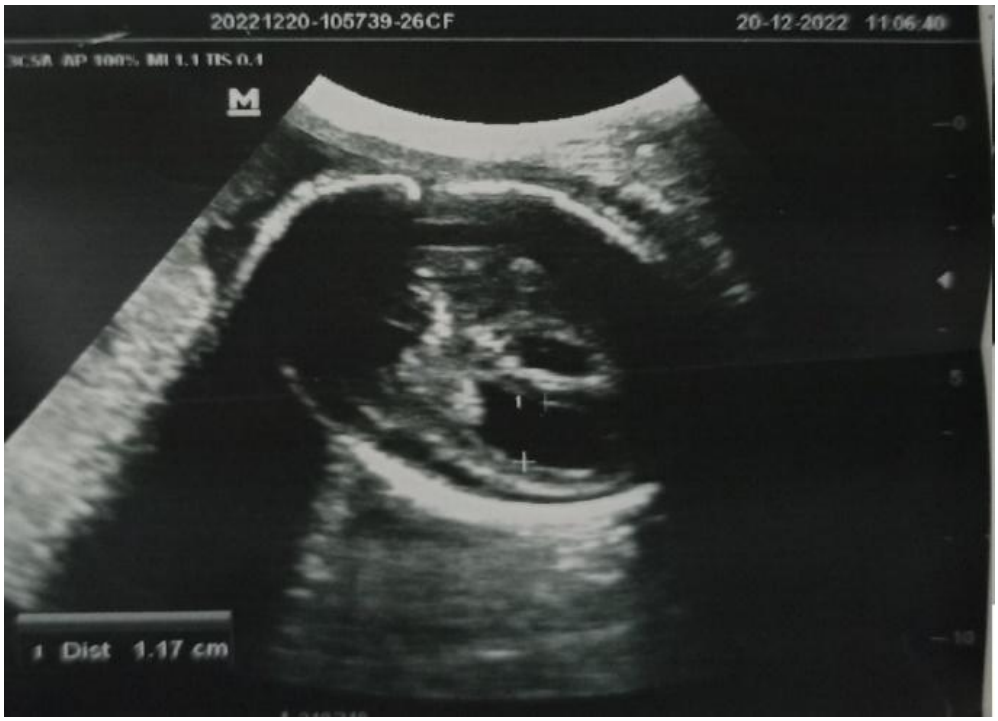

Figure 1. Left ventriculomegaly

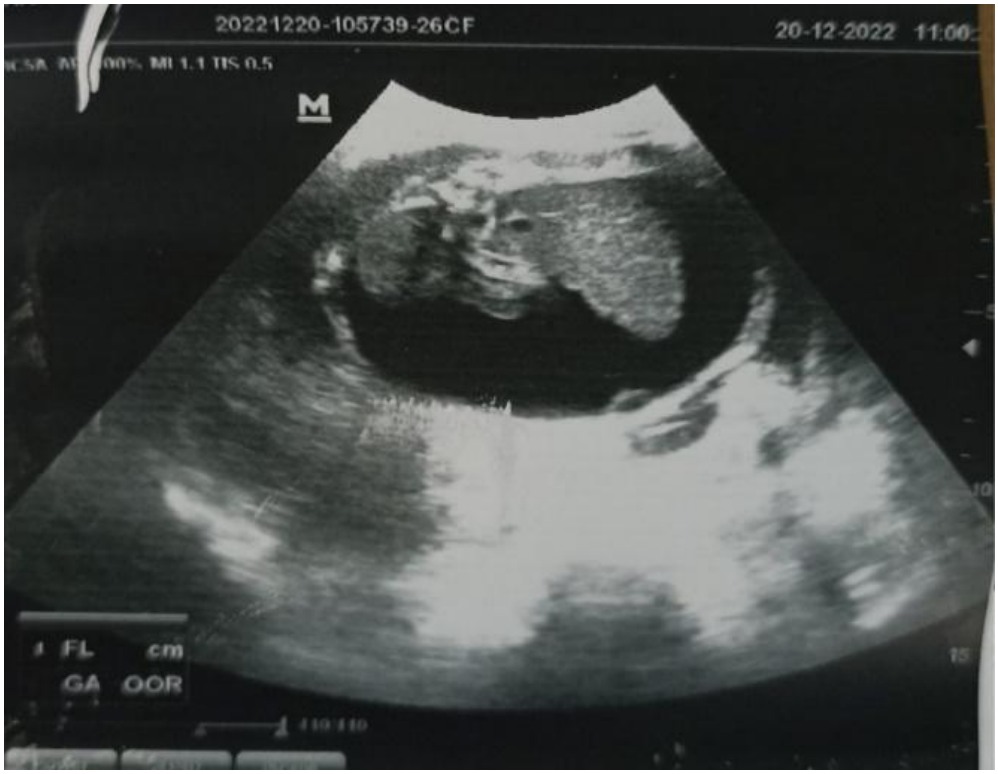

Figure 2. Ascites with enlarged spleen.

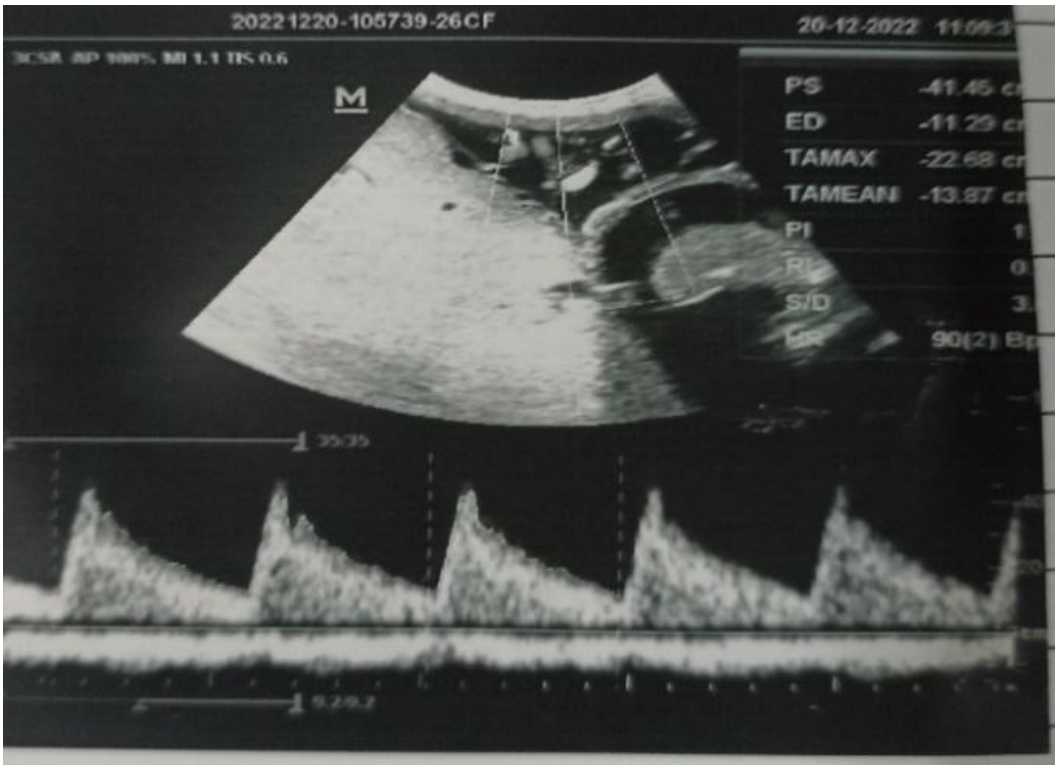

Figure 3. Umbilical artery doppler

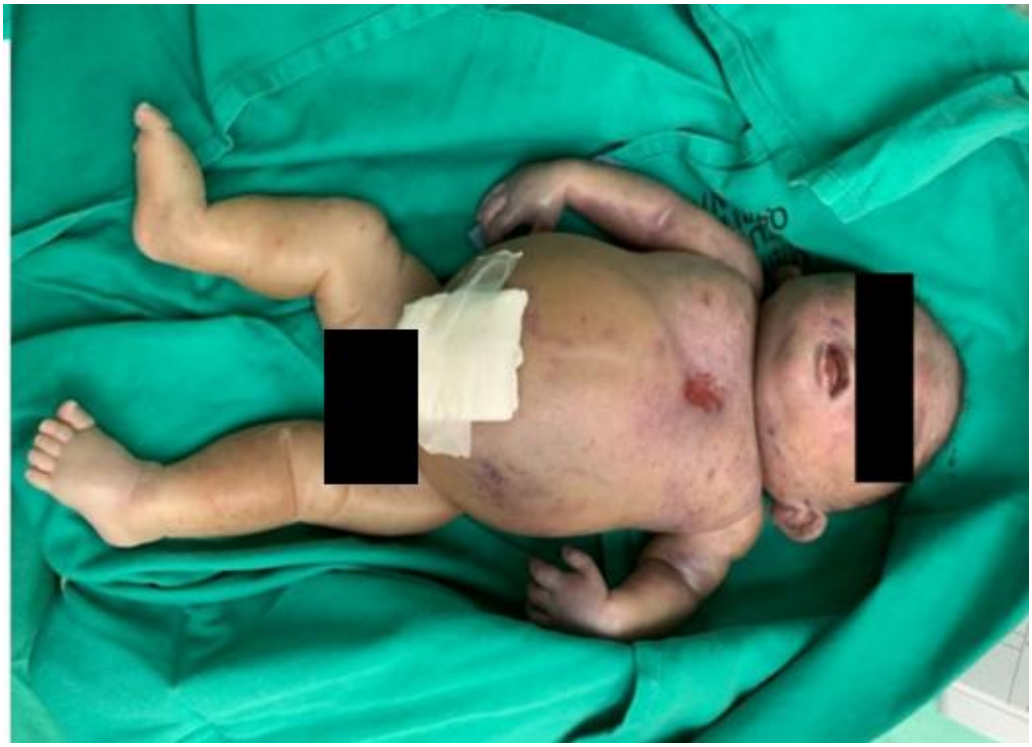

Figure 4. The new-born presented a hydrops fetalis

References

[1] Vanaparthy, R., Vadakekut, E. S. & Mahdy, H. *Nonimmune Hydrops Fetalis*. (2025).

[2] Hall, V., Vadakekut, E. S. & Avulakunta, I. D. *Hemolytic Disease of the Fetus and Newborn*. (2025).

[3] Norton, M. E., Chauhan, S. P. & Dashe, J. S. Society for Maternal-Fetal Medicine (SMFM) Clinical Guideline #7: nonimmune hydrops fetalis. *Am J Obstet Gynecol* **212**, 127–139 (2015).

[4] Khairudin, D., Alfirevic, Z., Mone, F. & Navaratnam, K. Non-immune hydrops fetalis: a practical guide for obstetricians. *The Obstetrician & Gynaecologist* **25**, 110–120 (2023).

[5] Bellini, C. & Hennekam, R. C. Non-immune hydrops fetalis: A short review of etiology and pathophysiology. *Am J Med Genet A* **158A**, 597–605 (2012).

[6] Sileo, F. G. *et al.*Non-immune fetal hydrops: etiology and outcome according to gestational age at diagnosis. *Ultrasound in Obstetrics and Gynecology* **56**, 416–421 (2020).

[7] Kadrofske, M. M. P., Parimi, et al. NONIMMUNE HYDROPS FETALIS AND HEPATITIS IN A. *Pediatr Infect Dis J* (2006).

[8] Wafelman, L. S., Pollock, B. H., et al. Nonimmune Hydrops fetalis: Fetal and Neonatal Outcome during 1983–1992. *Neonatology* **75**, 73–81 (1999).

[9] Davis, J. & Fernando, J. J. R. Successful management of prenatal hydrops fetalis in a mother with HIV. *Int J STD AIDS* **19**, 281–282 (2008).

[10] Hornberger, L. K. *et al. Cardiac Structure and Function in Fetuses of Mothers Infected with HIV: The Prospective P 2 C 2 HIV Multicenter Study*. (2000).

CASE REPORT

Primary Varicella Infection-associated Conjunctivitis: A Case-based Review and Insights into its Pathogenesis.

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Abstract
Primary varicella infection or chickenpox is a very common illness predominantly of childhood caused by the varicella zoster virus (VZV). Ocular involvement in chickenpox is relatively uncommon but is well documented in the literature. We present a case study of a healthy 6-year-old child developing unilateral serous conjunctivitis on day-2 of illness with spontaneous resolution by day-5. We narratively reviewed the findings of 2 larger case series in the English literature, highlighting ocular complications associated with chickenpox. Conjunctivitis is the second commonest ocular complication associated with chickenpox. Conjunctivitis associated with chickenpox generally runs a benign course and spontaneously resolve without anti-viral therapy. We reviewed the potential mechanisms of conjunctival involvement in chickenpox. These include epithelial homology to keratinocytes, the types of carrier T-lymphocyte involved in the secondary viraemic phase and VZV induced T-lymphocyte surface antigenic remodelling favouring ocular homing.

Keywords: *Immune-mediated cytopathy, secondary cell-associated viraemia, Υδ-T cells, T-helper regulatory cells, vesicular conjunctivitis.*

Introduction

The varicella zoster virus (VZV) is a human α-herpesvirus that causes chickenpox (primary infection) and herpes zoster (latent viral reactivation), both common illnesses in childhood and the elderly, respectively.

Primary varicella infection is a very common illness. Epidemiological studies indicate that over 95% of immunocompetent individuals aged 50 years and above are seropositive for this viral infection [1]. Clinically, primary varicella infection is a self-limiting illness characterised by the typical pruritic vesicular rash that erupts in crops over 5 to 7 days before crusting over and resolving within 10 days.

VZV demonstrates tropism for T-lymphocytes and keratinocytes with establishment of latency in neurons. However, the virus can occasionally disseminate to other tissues. The mechanism of this dissemination is still currently obscure.

Ocular involvement in primary varicella infection is uncommon. We report a case of a healthy 6-year-old child who developed a self-limiting unilateral conjunctivitis in the course of a primary varicella infection.

Case presentation

A 6-year-old boy with no chronic illness, achieving all his neurodevelopmental milestones and is fully vaccinated as per immunisation schedule (Ministry of Health Malaysia) presented with a sudden onset polymorphic vesiculo-papular rash. These skin eruptions were pruritic and initially involved the trunk and groin, but rapidly spread to involve the face, including both eyelids, within 24 hours.

Clinical examination on day 1 of the illness revealed multiple vesiculo-papular cutaneous eruptions with surrounding erythematous flare, demonstrating a centrifugal dominant pattern [Figure 1a to c]. He was otherwise reasonably well apart from irritability due to pruritus and a low-grade fever (37.5°C). There were no palpable lymphadenopathies and no mucosal lesions detected. The rest of his physical examination was unremarkable. A diagnosis of primary varicella infection (chickenpox) was made. He was quarantined, and his kindergarten was notified. He was commenced on supportive therapy with paracetamol as required, chlorpheniramine 1mg twice daily, and topical cetrimide 2% lotion body wash followed by calamine lotion (15% calamine, 5% zinc oxide) application once daily.

On the second day (day-2) of illness, new vesiculo-papular lesions appeared, also involving the hands and feet, including bullae on the dorsal right thumb [Figure 3a]. Interestingly, right-sided conjunctivitis was also observed. There was no ocular pain or pruritus, and his visual acuity was intact. Examination revealed right conjunctival inflammation with epiphora [Figure 2a, 2b]. Conjunctival injection mainly involved the bulbar conjunctiva with relative sparing of the palpebral conjunctiva and absence of conjunctival follicles. No pre-auricular nodes were palpable. His cornea was clear with no anterior chamber abnormalities and normal pupillary reflexes. This clinical picture was consistent with an asymptomatic serous conjunctivitis secondary to primary varicella infection. A 'watchful waiting' approach was adopted, and no specific therapy was initiated.

He remained well and by day 5 of illness, the right-sided conjunctivitis completely resolved [Figure 2c]. The final crops of cutaneous lesion also erupted this day, while the right thumb bullae turned haemorrhagic. [Figure 3c]. No cutaneous or mucosal bleeding was identified. Two percent fusidic acid ointment was applied twice daily to the haemorrhagic bullae to cover for secondary bacterial infection for 3 days. All lesions, including this bulla, dried up by day-10 and he made an uneventful recovery.

Discussion

VZV-associated ocular complications are relatively common in the setting of herpes zoster ophthalmicus (viral re-activation affecting the ophthalmic branch of the trigeminal nerve). This is more likely if the nasociliary branch of the

trigeminal nerve is affected (Hutchinson's sign). Ocular complications associated with primary varicella infection are uncommon and are restricted to occasional case series in the literature. The ocular complications of primary varicella infection can be classified into early or late complications:

i. Early complications: These complications occur concurrent with the skin eruptions and are thought to be directly mediated by the virus (secondary viraemia). These include palpebral (eyelid) lesions, conjunctivitis, superficial keratitis, and uveitis.
ii. Delayed complications: These complications occur after a significant period post cutaneous eruption and are more likely to be mediated by an immune process (hypersensitivity or autoimmune) or as a sequela of ocular inflammation. These include conditions such as interstitial keratitis, early cataracts, secondary glaucoma, oculomotor palsy, retinopathy and optic neuritis.

Eyelid and conjunctival lesions are the commonest ocular complications accompanying primary varicella infection. Findings of 2 larger case series are summarised below [Table 1].

In an earlier Canadian case series by Jordan DR *et al* [2], conjunctival pox was identified as the commonest conjunctival manifestation associated with primary varicella infection. Interestingly, the majority (75%) of these pox lesions were peri-limbal. Only one case of conjunctivitis was identified as a unilateral follicular conjunctivitis with pre-auricular lymphadenopathy. All patients experienced spontaneous full resolution within 14 days. Conversely, a later case series by Yap A *et al* conducted in New Zealand identified conjunctivitis as the commonest conjunctival lesion [3]. Duration of the ocular symptoms was not specified, but all patients in this series received topical prophylactic antibiotics and lubricants and none required topical antivirals. An isolated Turkish case reported bilateral serous conjunctivitis in a 9-year-old boy treated with topical 3% acyclovir and prophylactic netilmicin 0.3% [4]. Conjunctivitis developed on day 7 of rash eruption and recovered within 2 weeks.

Based on data from the medical literature combined with our experience, it is inferred that primary varicella-associated conjunctivitis is a benign phenomenon and usually runs an uncomplicated course without requiring specific anti-viral therapy.

The mechanism of ocular involvement in primary varicella infection has not been fully elucidated. The VZV is unique as it is highly cell-associated due to strong interaction between viral surface glycoproteins with intra-cellular receptors (mannose-6-phosphate and insulin-degrading enzyme, which are both abundantly localised in endosomes) [5]. Infective cell-free VZV virions are only found in cutaneous blisters due to downregulation of mannose-6-phosphate receptors in mature keratinocytes [6].

For primary varicella infection to spread from the site of inoculation (lymphoid tissue of the Waldeyer's ring), it requires a carrier cell, which are known to be $CD4^+$ T-lymphocytes. Interestingly, memory T-helper cells ($CD4^+$ $CD45RO^+$) are preferentially infected and are highly permissive for VZV invasion and replication [7]. Many of these infected memory T-lymphocytes also express surface homing markers to the skin, namely cutaneous lymphocyte antigen (CLA) and chemokine receptor 4 (CCR-4), which may explain the cutaneous tropism of this virus [7]. Hitchhiking these memory T-lymphocytes enables dissemination of the VZV to host keratinocytes in an asymptomatic phase of primary cell-associated viraemia. Once disseminated to keratinocytes, the VZV is initially suppressed by interferon-β produced by neighbouring keratinocytes. After a period of 7 to 10 days, VZV specific proteins (including IE62 and ORF61) overwhelms interferon-β suppression, allowing rapid viral replication, subsequently leading to a symptomatic phase of secondary cell-associated viraemia [8][9]. This phase is clinically recognised as the classic vesiculo-papular skin eruption of chickenpox. It is during this eruptive

phase that the VZV may potentially disseminate to other organs such as the lungs, nervous system and eyes.

- Mechanism of ocular involvement:

The pathophysiology of primary varicella-associated conjunctivitis in our case is more likely to be bystander inflammation rather than direct viral cellular invasion. There were eyelid vesicles in our case. Interferon-ϒ released by cytotoxic T-lymphocytes infiltrating the eyelid can signal in a paracrine fashion, inducing inflammatory monocytes to cause surrounding conjunctival inflammation. Conjunctival pox or vesicular conjunctivitis is clinically consistent with cellular conjunctival infection and VZV induced cytolysis. Altered conjunctival vesicles may take on an atypical appearance. This was highlighted by an American case report describing multiple pale tarsal conjunctival lesions secondary to ruptured conjunctival vesicles [10]. Other possible mechanisms of conjunctivitis in primary varicella infection:

i. Homology of conjunctival epithelial cells to keratinocytes:

Conjunctival involvement is the second commonest ocular manifestation (after the eyelid) of primary varicella infection. Many areas of the conjunctiva (particularly limbal, bulbar and outer palpebral) are lined by stratified squamous epithelia. Keratinocytes are also stratified squamous cells but are fortified with keratin (keratinized). This cellular homology may allow for skin homing memory T-lymphocytes to migrate to the conjunctiva. This may explain the predominant bulbar inflammation in our case.

ii. Type of T-lymphocytes infected in the secondary viraemic phase

The nature of T-lymphocytes involved in the secondary viraemic phase has not been scientifically characterised. Since most primary varicella infection is limited to the skin, they can be deduced to be memory $CD4^+$ T-lymphocytes with skin homing markers, identical to cells involved in the primary viraemic phase. This is consistent with the observation that children (predominantly harbouring naïve T-lymphocytes) have relatively few skin lesions compared to adults (predominantly harbouring memory T-lymphocytes) who usually present with several hundred skin lesions [11].

However, it is possible that other types of T-lymphocytes may also harbour the VZV to allow spread to distant organs. The conjunctiva associated lymphoid tissue (CALT) is predominantly populated by tissue-resident memory T-lymphocytes (TRM of both $CD4^+$ and $CD8^+$ cells). However, these cells are unlikely to be the VZV carriers as they are non-migratory cells. Interestingly, the limbal conjunctiva is populated by an unusual population of T-cells predominantly ϒδ-T cells and a small population of Tregulatory cells (Tregs).

Based on the observations by Jordan *et al* that majority of conjunctival pox lesions were peri-limbal, it is likely that ϒδ-T cells may be the VZV carrier-cells. Other possibilities would include transient surveillance naïve T-cells ($CD4^+$ $CD45RA^+$) entering the CALT and conjunctival Tregs ($CD4^+CD25^+$). Similarly, other types of carrier T-lymphocytes may allow dissemination to different organs. Predominant tissue T-lymphocyte populations are characterised below [Table 2]

iii. Induction of ocular homing cell surface molecule expression

Human tonsillar T-lymphocytes experimentally infected with VZV has been demonstrated to induce alterations in their surface membrane protein expression [11]. Sen *et al* utilized single cell mass cytometry, demonstrating surface expression downregulation of CCR7 and upregulation of CD11a and CD49d in both infected memory and naïve T-cells [11]. This surface antigenic profile indicates cellular reconfiguration favouring tissue migration. Furthermore, approximately 35 to 40% of infected T-cells in this study expressed skin homing markers (CLA and CCR4). This study did not investigate presence of other tissue homing markers such as α4β7 (gut) and CD44 (extra-

cellular matrix). Induction of ocular specific tissue homing receptors on VZV infected cells is theoretically a possible explanation for ocular involvement in primary VZV infection. However, further studies are required to corroborate this hypothesis.

Conclusion

Although uncommon, conjunctivitis is one of the commonest ocular manifestations of primary varicella infection. The pathogenic mechanism underlying this condition is still obscure. Primary varicella-associated conjunctivitis is a benign phenomenon and usually runs an uncomplicated course of spontaneous recovery without requiring anti-viral therapy. It's prudent for physicians to monitor for the appearance of further complications such as keratitis (pseudo-dendrites or stromal infiltrates) and anterior uveitis, which may then require anti-viral therapy.

Ethical declaration

Verbal informed consent was obtained from the patient's parents for the publication of this case report and any accompanying images. The parents were assured of the patient's anonymity.

Acknowledgements

The author would like to express his gratitude to the patient and his parents for their permission in writing this case report.

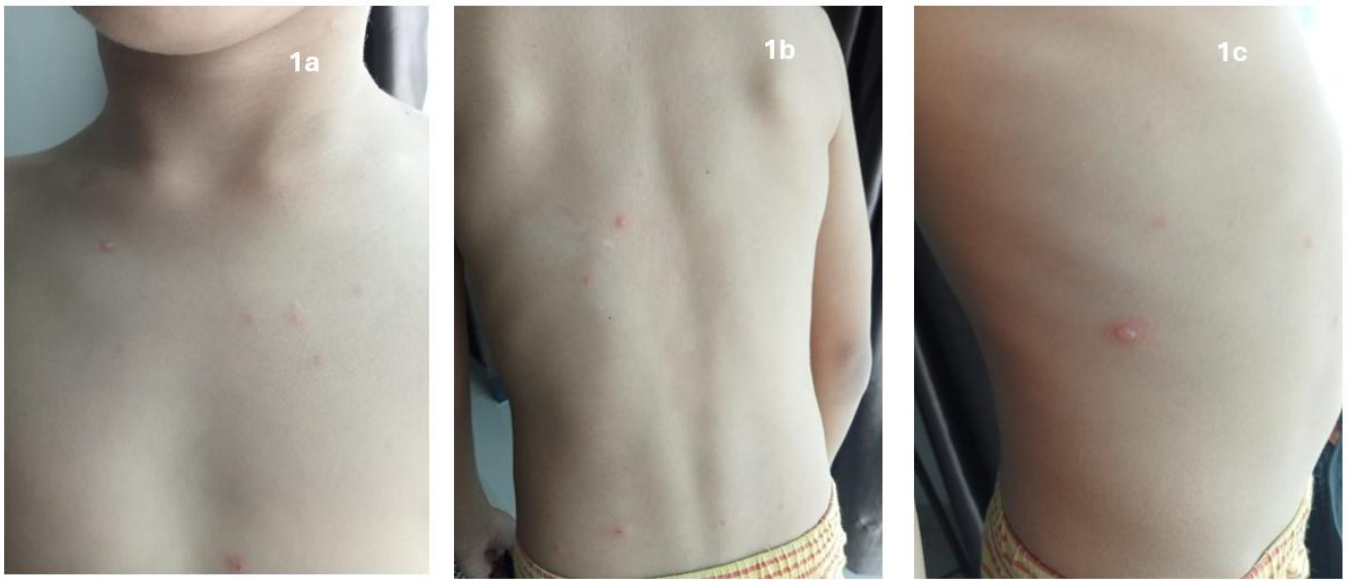

Figure 1a: Multiple vesiculopapular lesions in the anterior chest. Figure 1b: skin lesions of the posterior trunk Figure 1c: bullae of right lower chest with typical erythematous flare. All pictures were taken on day-1.

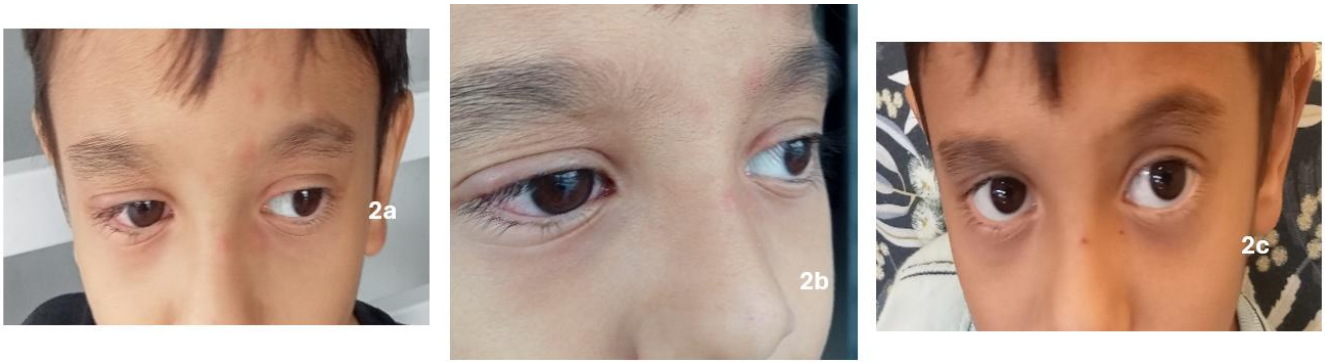

Figure 2a: Right sided conjunctivitis with epiphora noted on day-2. Figure 2b: Close up of the right-sided conjunctivitis. Note the conjunctival injection and bilateral eyelid lesions. Figure 2c: Spontaneous resolution of the right-sided conjunctivitis on day-5. Note the resolution of facial skin lesions with crusting.

Figure 3a: Right dorsal thumb bullae on day-2. Figure 3b: the same bullae turned haemorrhagic on day-5. Figure 3c: Note the bullae resolution leaving a hypopigmented scar, typical of dermo-epidermal skin lesions. This picture was taken on day-28.

Table 1. Ocular complications reported in larger case series.

Ocular complications	Jordan DR *et al* 1984 [3]		Yap A *et al* 2020 [4]	
	Frequency	therapy	Frequency	therapy
Conjunctival lesions	9		15	
• conjunctivitis	1	nil	10*	Top antibiotics and lubricants
• conjunctival pox	8	nil	5	Top antibiotics and lubricants
Eyelid lesions	15		5	
• vesicular lesions	14	nil	3	Top antibiotics
• preseptal cellulitis	1	PO cloxacillin	2	IV antibiotics
Uveitis	6	TCS	7- 12*	TCS ± antiviral
Keratitis	2	nil	3	TCS ± antiviral

Abbreviations: PO (oral), Top (topical), IV (intravenous), TCS (topical corticosteroids). * Yap *et al* reported the frequency as 'number of eyes' instead of number of patients.

Table 2. Predominant T-lymphocyte population of some organ tissues known to be affected in primary varicella infection.

Tissue	Predominant T-lymphocyte population	Remarks
Skin	TRM (both $CD4^+$ and $CD8^+$)	Commonest tissue involved in primary VZV infection
Lung	TRM (both $CD4^+$ and $CD8^+$)	Commonest extra-cutaneous tissue involved in primary VZV infection (commoner in adults) [12].
Liver	MAIT cells	Significant in primary VZV infection involving immunosuppressed patients. Particularly in ALL patients' post-chemotherapy [13].
Conjunctiva (CALT)	TRM (both $CD4^+$ and $CD8^+$)	Cellular densities significantly higher in the adenoid layer with a $CD4^+$ predominance over $CD8^+$ cells by a ratio of 12:1 [14].
Conjunctiva (limbus)	ϒδ-T cells	Limbal T-cells guard and preserves the corneal stem cell population.
Brain/meninges	TRM ($CD4^+$)	Rarely involved in primary varicella infection but carries a high mortality if untreated.

Abbreviations: TRM (tissue-resident memory T-cells) MAIT (mucosal-associated invariant T-cells) ALL (acute lymphoid leukaemia)

References

[1]. Johnson RW, Alvarez-Pasquin MJ, Bijl M, Franco E, Gaillat J, Clara JG *et al*. Herpes zoster epidemiology, management, and disease and economic burden in Europe: a multidisciplinary perspective. Ther Adv Vaccines. 2015 Jul; 3(4):109-20.

[2]. Jordan DR, Noel LP, Clarke WN. Ocular involvement in varicella. Clin Pediatr (Phila). 1984; 23(8): 434-6.

[3]. Yap A, Sims JL, Niederer RL. Ocular complications from primary varicella infection. N Z Med J. 2020 Jun 26;133(1517): 117-122.

[4]. Yüce GA, An I, Alpfidan I. Conjunctivitis secondary to chickenpox: A case report. Arch Clin Exp Med. 2018; 3(2): 97-99.

[5]. Li Q, Ali MA, Cohen JI. Insulin degrading enzyme is a cellular receptor mediating varicella-zoster virus infection and cell-to-cell spread. Cell. 2006 Oct 20; 127(2): 305-16.

[6]. Zuckerman AJ, Banatvala JE, Schoub BD, Griffiths PD, Mortimer P. Principles and practice of clinical virology [6th edition]. West Sussex: Wiley-Blackwell; 2009.

[7]. Ku CC, Padilla J, Grose C, Butcher EC, Arvin AM. 2002. Tropism of varicella-zoster virus for human tonsillar CD4^{+} T lymphocytes that express activation, memory, and skin homing markers. J. Virol. 76**:** 11425-11433.

[8]. Sen N, Sommer M, Che X, White K, Ruyechan WT, Arvin AM. Varicella-zoster virus immediate-early protein 62 blocks interferon regulatory factor 3 (IRF3) phosphorylation at key serine residues: a novel mechanism of IRF3 inhibition among herpesviruses. J Virol. 2010 Sep; 84(18): 9240-53.

[9]. Zhu H, Zheng C, Xing J, Wang S, Li S, Lin R *et al*. Varicella-zoster virus immediate-early protein ORF61 abrogates the IRF3-mediated innate immune response through degradation of activated IRF3. J Virol. 2011 Nov; 85(21): 11079-89.

[10]. Grassmeyer JJ, Bellsmith KN, Bradee AR, Pegany RB, Redd TK. Conjunctival Lesions Secondary to Systemic Varicella Zoster Virus Infection. Cornea Open. 2023 Oct 19;2(4): e0022.

[11]. Sen N, Mukherjee G, Sen A, Bendall SC, Sung P, Nolan GP *et al*. Single-cell mass cytometry analysis of human tonsil T cell remodeling by varicella zoster virus. Cell Rep. 2014 Jul 24; 8(2): 633-45.

[12]. Mohsen AH, McKendrick M. Varicella pneumonia in adults. Eur Respir J. 2003 May; 21(5): 886-91.

[13]. Wiegering V, Schick J, Beer M, Weissbrich B, Gattenlöhner S, Girschick HJ *et al*. Varicella-zoster virus infections in immunocompromised patients - a single centre 6-years analysis. BMC Pediatr. 2011 May 10; 11:31.

[14]. Arnous R, Arshad S, Sandgren K, Cunningham AL, Carnt N, White A. Tissue resident memory T cells inhabit the deep human conjunctiva. Sci Rep. 2022 Apr 12;12(1):6077.

CASE REPORT

Recovery from Knee Strain in a Young Athlete: A Case Study on Gluteal Activation and Core Stabilization.

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Abstract
Knee strain is a common cause of knee injury, particularly among rugby players, due to the high physical demands and frequent contact involved in the sport. Such injuries typically affect the soft tissues, including muscles and tendons around the knee joint. Delayed intervention can negatively impact mobility and interfere with daily activities, potentially leading to compensatory movement patterns and secondary complications. This case study focused on a 20-year-old rugby player with a history of left knee strain who received treatment approximately three months after the initial injury. He experienced difficulty with stair climbing and achieving cross-leg position during prayer. The objective of this case study was to demonstrate how targeted rehabilitation; specifically gluteal muscle activation and core stabilization exercises, can improve function and postural control. Notably, the patient showed measurable improvement as early as the first day of intervention, highlighting the effectiveness of timely physiotherapy assessment and appropriate exercise prescription.

Keywords: *Core stabilization, gluteal muscle activation, knee strain.*

Introduction

Knee injuries are common sports injuries, predominantly in football and rugby. Ligament injuries account for approximately 40% of knee injuries, meniscal injuries for about 10% and the remaining cases are due to other conditions, including knee strains [1]. Knee strains involve damage to the soft tissues, such as tendons or muscles, around the knee joint. They can occur as a result of twisting, overstretching or overuse of the muscles [1,2]. Early clinical assessment by appropriately trained physiotherapists is essential for prescribing suitable exercises to support the patient's recovery and return to sport [3]. Improper management of prolonged inactivity can lead to compensations, weakness or other chronic issues. This case study presents a 20-year-old rugby player with a history of left knee strain who received treatment approximately three months after the initial injury. The aim of this case study is to highlight the importance of proper assessment and targeted treatment, as these may facilitate recovery when appropriate interventions are provided.

Case description

Subjective examination

On January 11, a 20-year-old male patient presented to the physiotherapy clinic, reporting an inability to bend his left knee normally, as he was unable to sit for *tahiyyatul awal* and *akhir,* following a knee injury sustained during a rugby tournament last October. He was diagnosed with a left knee strain, and was prescribed painkillers by a physician, along with a knee bandage for a month, which subsequently led to hypomobility of the left knee. No pain was reported in the left knee during activities of daily living, except during prayers. His pain score was 5 out of 10 during knee flexion, which reduced to 2 out of 10 within a minute of straightening the left knee.

Physical examination

The patient presented with an abnormal gait upon entering the physiotherapy clinic. The pelvis was rotated to the left, and the trunk leaned slightly to the left during right leg swing. No postural deformity was observed during left leg swing. During quiet standing, no bodyweight shifting was noted; however, a slight forward head posture and a mild posterior pelvic tilt were observed. During the sport movement assessment, the body shifted slightly to the right during squatting. He was unable to perform lunges when the left leg was positioned posteriorly. During stairs assessment, a slight drop of the left pelvis was observed when stepping up with the left leg, and poor control was noted when stepping down with the left leg, indicating reduced muscle power of left gluteus maximus. He also demonstrated impaired balance in both lower limbs, being unable to maintain a single-leg stance for more than 3 seconds bilaterally. There was no limitation in the range of motion of the knee flexion, knee extension, hip flexion and hip extension.

Several positions were included during physical examination; sitting, prone lying and bridging. In sitting position, alternate hip flexion and knee extension were assessed. Flickering of erector spinae was observed during that hip flexion, indicating reduced motor control of erector spinae. A slump was noted during knee extension, suggesting tightness or hamstring or erector spinae. In prone lying position, the right pelvis was observed to be higher than the left, and a deviation of the left tibia was noted. Reduced control during knee flexion and extension was observed, along with hyperactive of erector spinae during left extension, indicating reduced muscle power of left gluteus maximus. In bridging position, he was able to maintain the spine in a straight line, however complained of discomfort in the erector spinae, suggesting overactive of erector spinae and underactive of gluteus maximus muscle.

Treatment and evaluation

There was evident weakness of gluteus maximus and reduced control of erector spinae, hence, the treatment would focus on increasing muscle power of gluteus maximus and improving core

control of the erector spinae. Bridging, squatting and kneeling-to-half-kneeling exercises are aimed at strengthening the gluteus maximus, while lumbar stabilization in four-point kneeling is aimed at improving control of the erector spinal. Table 1 illustrates the details of the exercises, and Table 2 illustrates the pre- and post-intervention data. The evaluation of exercises is also illustrated in Figure 1 to Figure 6. Figure 1 and 2 show the pelvic level during prone lying, Figure 3 and 4 show position of *tahiyyatul awal* during prayer from posterior view and Figure 5 and 6 show position of *tahiyyatul awal* during prayer from lateral view.

Discussion

There was an improvement in posture during prone lying and sitting *tahiyyatul awal* after the first day of exercise. Figure 2 shows that the pelvic levels were symmetrical both left and right compared to before the exercises. Figures 4 and 6 also demonstrate improvement during sitting *tahiyyatul awal,* as the patient was able to cross his legs and sit slightly on his heel, and maintain a more relaxed back compared to the pre-exercise condition. These findings indicate that the prescribed exercises appeared to contribute to initial improvements in posture and spinal alignment, following a single day of intervention. From this case study, it was found that the patient had weakness of the gluteus maximus muscles; therefore, bridging, squatting, and kneeling-to-half-kneeling exercises were prescribed. Gluteal muscles play a significant role during many upright activities and lower extremity function, such as walking as they help transmitting forces from the legs to the pelvis [4,5]. Gluteal muscles also act as a stabilizer of pelvis in a single-leg-stance position, including stepping up and down stairs [5,6]. Hence, the gluteal strengthening exercise would help the patient in controlling pelvic and knee control when stepping up and down stairs.

This case study also reported no limitation in the range of motion of knee flexion and extension, indicating that the soft tissue around the knee had fully recovered. However, the patient was unable to perform weight-bearing activities such as stairs climbing and the cross-legged position during prayer. The primary contributing factor to these limitations was weakness of the gluteal muscles. Gluteal muscles are often inhibited or weaken, increasing the risk of chronic injury and limiting athletic performance [7]. Many studies have found that the gluteal muscles contribute to the prevention of knee sprains, as the hip muscles help absorb impact forces during landing; therefore, weakening of the gluteal muscles may predispose individuals to knee injuries [4].

Besides treating the symptoms, for instance, gluteal muscles weakness, it is important for the therapist to understand the underlying causes; for example, lifestyle factors, which are thought to be major role in reducing gluteal muscles activation [7,8]. Prolonged sitting and reduced physical activity may contribute to decreased activation of the lower extremity muscles [7], as the patient was unable to play due to his injury. This sedentary lifestyle also reduces the activation of the core muscles, leading to improper posture during walking and standing [9].

This case study also showed weakness of the core muscles, as the patient leaned his body to the left side while walking and was unable to maintain an erect posture. In addition, the patient demonstrated flickering of the erector spinae muscle during hip flexion in the sitting position, indicating core weakness. Therefore, lumbar stabilization exercises in a four-point kneeling position were prescribed to increase core activation and improve trunk stability. Besides, core exercise can enhance the stability in the pelvis, hip, and knee by stimulating periarticular muscle of the knee and lumbopelvic hip complex [10].

This case study demonstrated initial improvement after the first day of intervention. However, as a single-case report, the findings are limited in generalizability. Long-term follow-up and studies involving larger samples are needed to provide deeper insight into sustained recovery.

Conclusion

Managing knee strain in athletes can be complex, as prolonged muscle inactivation may contribute to a secondary problem. Therefore, suitable assessments are essential, particularly for athletes; for example, sport movement assessments and postural evaluations in positions such as sitting, prone lying, and standing. The physiotherapist must carefully observe for deformities, as even small flickers of muscle activity may contribute to postural deviation. This case study demonstrated that accurate assessment can lead to targeted exercises prescription, resulting in observed initial improvements after the first day of intervention.

Implication of the study

The case study demonstrates to readers that knee strain can affect gluteal muscles and core stabilization. These secondary complications may interfere with posture, mobility, and overall lower limb functions. Therefore, accurate assessment is essential to determine the suitable exercises targeting the affected muscles, ultimately improving patient's condition.

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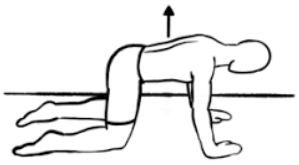
Conflict of interest statement

The author agree that this research was conducted in the absence of any self-benefits, commercial of financial conflicts and declares absence of conflicting interest.

Table 1. Treatment for patient with knee strain at Day 1.

Goals	**Exercises**		**Dosage**
Strengthening gluteus maximus	Bridging		I: 10 seconds hold, 30 times, 3 sets T: Isometric exercise
	Squatting		I: 10 seconds hold, 30 times, 3 sets T: Isometric exercise
	Kneeling-to-half-kneeling		I: 30 times, 3 sets T: Concentric exercise
Improving control of erector spinae	Lumbar stabilization in four-point kneeling		I: 10 seconds hold, 30 times, 3 sets T: Isometric exercise

I: Intensity of exercises; T: Type of exercise

Table 2. Pre- and post-intervention data

Items	**Pre-intervention**	**Post-intervention**
Pain scale	5/10	2/10
Static balance test	< 3 seconds	> 3 seconds
Pelvic alignment	Right pelvic is higher than left in prone lying position	Right and left pelvic are symmetrical
Functional activity	Unable to cross his leg while sitting *tahiyyatul awal*	Able to slightly cross his leg during *tahiyyatul awal*

Figure 1. Pelvic level during prone lying before exercise

Figure 2. Pelvic level during prone lying after exercise

Figure 3. Position of *tahiyyatul awal* during prayer from posterior view before exercise.

Figure 4. Position of *tahiyyatul awal* during prayer from posterior view after exercise.

Figure 5. Position of *tahiyyatul awal* during prayer from lateral view before exercise.

Figure 6. Position of *tahiyyatul awal* during prayer from lateral view after exercise.

References

[1]. Yasen SK. Common knee injuries, diagnosis and management. Surgery (Oxford). 2023 Apr;41(4):215–22.

[2]. Gray AM, Buford WL. Incidence of Patients With Knee Strain and Sprain Occurring at Sports or Recreation Venues and Presenting to United States Emergency Departments. J Athl Train. 2015 Nov 1;50(11):1190–8.

[3]. Campbell P, Pope R, Simas V, Canetti E, Schram B, Orr R. The Effects of Early Physiotherapy Treatment on Musculoskeletal Injury Outcomes in Military Personnel: A Narrative Review. Int J Environ Res Public Health. 2022 Oct 17;19(20):13416.

[4]. Rinaldi VG, Prill R, Jahnke S, Zaffagnini S, Becker R. The influence of gluteal muscle strength deficits on dynamic knee valgus: a scoping review. J Exp Orthop. 2022 Jan 17;9(1).

[5]. Ahn SE, Lee MY, Lee BH. Effects of Gluteal Muscle Strengthening Exercise-Based Core Stabilization Training on Pain and Quality of Life in Patients with Chronic Low Back Pain. Medicina (B Aires). 2024 May 23;60(6):849.

[6]. Nascimento MB, Vilarinho LG, Lobato DFM, Dionisio VC. Role of gluteus maximus and medius activation in the lower limb biomechanical control during functional single-leg Tasks: A systematic review. Knee. 2023 Aug;43:163–75.

[7]. Buckthorpe M, Stride M, Villa F Della. ASSESSING AND TREATING GLUTEUS MAXIMUS WEAKNESS - A CLINICAL COMMENTARY. Int J Sports Phys Ther. 2019 Jul;14(4):655–69.
[8]. Chandran A, Madhuripu, Premkumar M, Menezes CR. Association between genu recurvatum and gluteus maximus muscle strength in college students - Case control study. Journal of Orthopaedic Reports. 2024 Mar;3(1):100229.
[9]. Jung KS, Jung JH, In TS, Cho HY. Effects of Prolonged Sitting with Slumped Posture on Trunk Muscular Fatigue in Adolescents with and without Chronic Lower Back Pain. Medicina (Kaunas). 2020 Dec 23;57(1).
[10]. Thomas DT, Eapen C, Hegde AS, Prabhudev Mane P, Mehta SP. Impact of core muscle strengthening on knee pain, patient outcomes, physical function, and cartilage thickness in knee osteoarthritis: Protocol for a randomized controlled trial. MethodsX. 2024 Dec;13:103008.

CASE REPORT

Subtherapeutic Target Attainment of Intermittent Vancomycin in a Paediatric Burn Patient: A Case Report.

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Abstract
Vancomycin pharmacokinetics in pediatric burn patients can be significantly altered compared to non-burned children due to the physiological changes caused by burn injuries, especially in the hypermetabolic and hyperdynamic phases. Subtherapeutic serum vancomycin concentrations and the consequent need for drastic modification of vancomycin dosage regimen has been reported. This is a case report of a paediatric patient with a Total Body Surface Area (TBSA) of 50 percent with subtherapeutic vancomycin target attainment even with a total daily dose of more than 80 mg/kg/day and the use of prolonged vancomycin infusion.

Keywords: *Burn, paediatric, pharmacokinetics, therapeutic drug monitoring, vancomycin.*

Introduction

Burns constitute a major global public health concern. The World Health Organization (WHO) estimated that burn injury has led to 180,000 deaths yearly, and two-thirds of the occurrence were in the African and South-East Asia regions. Children are more vulnerable to burn injury, and it is the fifth most common cause of non-fatal childhood injuries [1]. A study done by Collier Z. J. et.al. (2022) concluded that Asian children aged below five years old were the most impacted by disability-adjusted life years (DALYs); 314 years/100,000 people. Other findings reported that children aged between 5 and 14 years old had the highest burn rate (219 cases/100,000) [2].

In Malaysia, a cohort of 255 paediatric patients was admitted between 2016 to 2018 to a paediatric burn referral centre in Peninsular Malaysia. The study reported that blood and wound cultures showed growth of methicillin-resistant *Staphylococcus aureus* (MRSA), *Staphylococcus aureus*, *Enterococcus* sp., *Pseudomonas* sp., *Streptococcus* sp., *Escherichia coli*, *Acinetobacter baumannii*, and *Enterobacter* sp. [3]. Similar pathogens have also been isolated in paediatric burn patients from other regions [4,5].

Vancomycin is a glycopeptide antibiotic widely used in paediatric patients to treat serious Gram-positive infections, including those caused by MRSA. The area under the concentration-time curve over 24 hours relative to the minimum inhibitory concentration (AUC_{24}/MIC) of 400 - 600 mg.h/L is the best predictor of vancomycin efficacy and toxicity. Trough concentration is commonly used as an alternative measure of obtaining the AUC_{24}/MIC [6]. In paediatric burn patients, physiological changes including increased cardiac output, capillary leak, and altered renal clearance significantly affect vancomycin pharmacokinetics. The body's physiological reaction to a major burn injury can be divided into two main stages: an acute phase lasting about 48 hours, followed by a hypermetabolic phase that can continue for several weeks [7,8].

The acute phase begins immediately after the burn, characterized by a state of shock. During this period, small blood vessels in both affected and unaffected tissues become increasingly permeable, allowing fluids and proteins to leak out of the circulatory system, resulting in extensive tissue swelling. This fluid shift, along with circulating mediators, leads to decreased cardiac output, increased vascular resistance, and reduced blood flow to organs. These physiologic changes will lead to slower absorption of oral drugs, larger drug volume of distribution (Vd), changes in the amount of free drug, and reduction of drug clearance. The hypermetabolic phase begins around 48 hours post-injury. In this phase, inflammatory and circulating factors trigger a heightened metabolic response, cardiac output rises, vascular resistance decreases, and blood flow to various organs improves. Better absorption of oral drugs, changes in drug distribution patterns, and an increase in drug clearance, as well as drug loss via burn wounds, are expected [8].

Vancomycin pharmacokinetics in paediatric burn patients are significantly altered from those in non-burned children due to the physiological changes caused by burn injuries, especially in the hypermetabolic and hyperdynamic phases [8]. Shorter vancomycin elimination half-life ($t_{1/2}$) was reported in burn patients, which resulted in a one-third increment in vancomycin clearance (CL_v). This will subsequently lead to subtherapeutic serum vancomycin concentrations and drastic modification of vancomycin dosage regimen [9,10]

To our knowledge, few reports have described the use of vancomycin in Malaysian paediatrics; nevertheless, no published data comprehensively address the optimization of initial dosing and therapeutic drug monitoring outcomes in burn cases. Studies done in the Malaysian indigenous

population mainly focus on pharmacogenetics variation and pharmacokinetics of other drugs such as clopidogrel [11,12]. Therefore, this case report aims to offer insights into optimizing vancomycin dosing in pediatric burn patients.

Case report

A 9-year-old indigenous Malaysian boy, weighing 21 kilograms (kg), was admitted to the Burn Unit on 21st September 2024 (Day 1) with scalds burns caused by hot water around 5 pm. He suffered burns on bilateral upper limbs, anterior and posterior trunk, bilateral thighs, buttocks, and genital area with a Total Body Surface Area (TBSA) of 50 percent. The burn injury involved varying depths of skin damage, ranging from superficial dermal to deep dermal layers.

Despite being treated with appropriate antibiotics following reported culture and sensitivity reports, there were still episodes of temperature spikes (ranging between 37.8 to 38.1 °C) and increasing C-reactive protein values (105 mg/L to 143.9 mg/L). Intravenous (IV) vancomycin 15 milligram per kilogram (mg/kg) every 8 hours was initiated on Day 20 post-burn as empirical coverage against MRSA infection. Nevertheless, no positive culture for Gram-positive organisms was obtained during the hospital stay. Patient was stable during the hospital stay with no desaturation episodes. Glomerular filtration rate (GFR) was estimated by using the Bedside Schwartz formula, ranging between 155 and 466 mL/min/1.73 m^2, with a urine output of 3 to 5 mL/kg/hour, during the vancomycin course. Augmented renal clearance (ARC), defined as GFR greater than or equal to 130 ml/min/1.73 m^2, was seen in this case [13].

Table 1 shows a summary of vancomycin regimes, obtained vancomycin concentrations, and computed pharmacokinetic profiles. The patient's Vd was approximately twice the normal reference range for paediatric patients (0.63 ± 0.16 L/kg), and a shorter vancomycin $t_{1/2}$ was observed in this patient compared to the normal paediatric range of 5.6 ± 2.1 hours [6]. Only a single therapeutic AUC_{24}/MIC measurement was obtained during treatment, even though the dose had been adjusted. The obtained trough concentrations were predominantly below 10 mg/L. A total daily dose of 86 mg/kg/day was recommended, representing an estimated 91% increase from the initial dose. However, no concentration monitoring was performed following this dose adjustment.

Discussion

Limited studies have been done in paediatric burn populations. Most studies focused on adult burn patients with variations in the degree of burns, and some included all age ranges in the study design. Several studies reported subtherapeutic trough vancomycin concentration following the standard initiation dose of vancomycin. Gomez D.S. et al. (2013) found that only 15% of pediatric burn patients receiving vancomycin at 10–15 mg/kg per dose every 6 hours, infused over one hour, achieved a trough concentration above 10 mg/L [10]. In a previous report, an average initial vancomycin dose of 31.5 ± 9.3 mg/kg/day, administered every six to eight hours, resulted in subtherapeutic trough concentrations averaging 1.4 ± 1.2 mg/L [14]. This was observed in a case report of an 8-year-old male patient with burns covering 20% of his total body surface area, including 8% third-degree burns on the lower limbs, who was started on intravenous vancomycin at 37 mg/kg/day every 6 hours and achieved a subtherapeutic trough concentration of 1.7 mg/L [15].

Subtherapeutic target attainment was also found in several studies involving adult burn patients. Adult burn patients treated with the standard regimen of intravenous vancomycin 1 gram administered every 12 hours yielded lower trough concentration compared to control non-burned patients (6.4 versus 9.2 mg/L) [16]. Similar findings were reported in adult Chinese burn

patients, in which 83% of the subjects had with subtherapeutic trough vancomycin concentration of less than 10 mg/L [17].

A study reported a statistically significant increase averaging 108.2% from the initial standard vancomycin dose, resulting in a trough concentration of 7.3 ± 4.7 mg/L ($p < 0.001$). The mean adjusted dose was 58.3 $\pm$ 5.4 mg/kg/day administered every four to eight hours [14]. Similarly, another study found that burn patients had a shorter half-life and 33% faster vancomycin, requiring a dose of 46.6 ± 20 mg/kg/day compared to 26.1 ± 5.9 mg/kg/day in control patients to achieve nearly identical peak and trough serum concentrations. This study also found that a more frequent dosing interval was required in burn patients compared to controls to maintain the trough concentration within 5 to 10 mg/L. However, the study subjects consisted of burn patients aged between 5 and 47 years old [18]. A recent study by Gomez D.S. et al. (2013) involving paediatric burn patients aged one to eleven years suggested that a vancomycin dose of 90 to 100 mg/kg/day is necessary to achieve optimal pharmacokinetic and pharmacodynamic (PK/PD) target attainment in this population (AUC_{24}/MIC > 400 mg.h/L, trough concentration > 10 mg/L). This higher dose recommendation closely aligns with the vancomycin dosing given in this case report.

In this case, a strategy of prolonging the vancomycin infusion time to three hours was utilized. Though the vancomycin trough concentrations were subtherapeutic, the levels obtained in this case were promising, indicating progress toward target attainment. The effectiveness of using prolonged vancomycin infusion in order to obtain therapeutic targets was supported by a study done by Li J. et.al. (2024). This retrospective study found that prolonging vancomycin infusion to three hours (PI) leads to significantly higher trough concentrations compared to standard intermittent infusion of one hour (SI). The median trough concentration was statistically significant between these two groups (11.2 versus 7 mg/L, p-value: 0.02). The target concentration attainment rate in the PI group and SI group was 59.4% and 19.3%, respectively (p-value: 0.001). There were no significant differences between the groups regarding the safety profile [19].

Continuous vancomycin infusion (CI) has been practiced in hospital settings, even in paediatric patients. To date, no published data on paediatric burn patients with vancomycin CI. One study done in critically ill burn adult patients observed comparable overall clinical outcomes with CI Vancomycin dosing compared to intermittent infusion (II). Toxicity was minimal with both infusion methods, although patients receiving CI showed a higher frequency of Vancomycin levels exceeding 25 mg/L. Despite this increased incidence of elevated levels, no significant increase in adverse effects was noted, suggesting that both dosing strategies maintain a favourable safety profile. Additionally, CI resulted in more frequent attainment of therapeutic vancomycin concentrations and fewer instances of subtherapeutic concentrations compared to II [5]. Use of CI vancomycin was found beneficial in paediatrics practice in terms of time to therapeutic attainment [20,21]. However, evidence comparing CI to PI specifically is limited, with most research contrasting continuous versus standard intermittent strategies. Both prolonged and continuous infusions seem to provide similar safety profiles, with no significant difference in nephrotoxicity [5,19].

In paediatric burn patients, physiological changes such as hyperdynamic circulation and increased cardiac output enhance renal blood flow, contributing to ARC. This leads to faster vancomycin clearance and often necessitates higher dosing regimens to achieve PK/PD targets. Studies have shown that standard vancomycin doses (60 mg/kg/day) often fail to reach optimal exposure in patients with ARC, while increased doses of 70-80 mg/kg/day or more may be

required. Modeling studies emphasize the importance of individualized dosing in this population to avoid underdosing and treatment failure [22]. Vancomycin treatment failure is associated with significantly increased 30-day mortality and can negatively impact long-term survival [23].

Conclusion

Interpatient variability and enhanced vancomycin clearance identified in burns patients will lead to subtherapeutic vancomycin target attainment. Standard initial dosing may not be sufficient for therapeutic attainment. Clinicians should anticipate increased vancomycin requirements in pediatric burn patients due to altered pharmacokinetics. Early therapeutic drug monitoring and individualized dosing strategies are essential to achieve optimal target concentrations and ensure treatment efficacy. Multicenter pharmacokinetic studies focusing on pediatric burn populations in Southeast Asia are warranted to address regional variations and improve evidence-based dosing guidelines.

Conflicts of interest

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Authors' contribution

SNNAJ contributed to manuscript preparation, data collection, and revisions. SM contributed to manuscript review, editing, and approved the final version.

References

[1]. World Health Organization. Burns [Internet]. WHO. World Health Organization: WHO; 2023. Available from: https://www.who.int/news-room/fact-sheets/detail/burns

[2]. Collier ZJ, McCool K, Magee WP, Potokar T, Gillenwater J. 58 Burn Injuries in Asia: A Global Burden of Disease Study. Journal of Burn Care & Research. 2022 Mar 23;43(Supplement_1):S40–1.

[3]. Low CX, Kok YQ, Loo XS, Ngim CF, Lim RZM, Quah SY. Three-year epidemiology of hospitalised paediatric burn patients in a Malaysian tertiary hospital 2016–2018. Med J Malaysia. 2023 Sep;78(5):661-668.

[4]. Christie M, Theunis Avenant, Masindi Nembudani, Anelisa Mnqandi, Muller C, Villiers M de, et al. Insights into bloodstream infections in South African paediatric burn patients: implications for antimicrobial stewardship. BMC Infectious Diseases. 2025 Mar 14;25(1).

[5]. Akers KS, Cota JM, Chung KK, Renz EM, Mende K, Murray CK. Serum Vancomycin Levels Resulting From Continuous or Intermittent Infusion in Critically Ill Burn Patients With or Without Continuous Renal Replacement Therapy. Journal of Burn Care & Research. 2012;33(6):e254–62.

[6]. Murphy JE, American Society of Health-System Pharmacists. Clinical pharmacokinetics. Bethesda, Md: American Society of Health-System Pharmacists; 2017.

[7]. Patel S, Preuss CV, Bernice F. Vancomycin [Internet]. National Library of Medicine. StatPearls Publishing; 2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK459263/

[8]. Cox IR. Pharmacokinetics in Patients with Burns. Journal of Pharmacy Practice and Research. 2005 Mar;35(1):53–5.

[9]. Carter BL, Damer KM, Walroth TA, Buening NR, Foster DR, Sood R. A Systematic Review of Vancomycin Dosing and Monitoring in Burn Patients. Journal of Burn Care & Research: Official Publication of the American Burn Association [Internet]. 2015 [cited 2023 Aug 22];36(6):641–50. Available from: https://pubmed.ncbi.nlm.nih.gov/25423436/

[10]. Gomez DS, Campos EV, de Azevedo RP, Silva-Jr JM da, Ferreira MC, Sanches-Giraud C, et al. Individualised Vancomycin doses for paediatric burn patients to achieve PK/PD targets. Burns. 2013 May;39(3):445–50.

[11]. Zakaria Z, Fong A, Badhan R. Clopidogrel Pharmacokinetics in Malaysian Population Groups: The Impact of Inter-Ethnic Variability. Pharmaceuticals. 2018 Jul 26;11(3):74.

[12]. Ang GY, Yu CY, Subramaniam V, Abdul Khalid MIH, Tuan Abdu Aziz TA, Johari James R, et al. Detection of CYP2C19 Genetic Variants in Malaysian Orang Asli from Massively Parallel Sequencing Data. Vrana KE, editor. PLOS ONE. 2016 Oct 31;11(10):e0164169.

[13]. Rhoney DH, Metzger SA, Nelson NR. Scoping review of augmented renal clearance in critically ill pediatric patients. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy. 2021 Aug 30;41(10):851–63.

[14]. Bailie GR, Ackerman BH, Fischer J, Solem LD, Rotschafer JC. Increased Vancomycin Dosage Requirements in Young Burn Patients. Journal of Burn Care & Rehabilitation. 1984 Sep 1;5(5):376–8.

[15]. A.M Dell'Aquila, McCulloch JA, E.M Mamizuka, Santos SRCJ, Pereira CAP. Serum levels of Vancomycin should be monitored in burn patients. Burns. 2004 Apr 23;30(4):386–7.

[16]. Dolton M, Xu H, Cheong E, Maitz P, Kennedy P, Gottlieb T, et al. Vancomycin pharmacokinetics in patients with severe burn injuries. Burns. 2010 Jun;36(4):469–76.

[17]. Shi Y, Yin Z, Zhang Q, Yi L, Dou Y. Factors influencing Vancomycin trough concentration in burn patients: a single center retrospective study. Frontiers in Pharmacology [Internet]. 2024 Dec 12 [cited 2025 Jul 10];15. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC11672795/

[18]. Garrelts JC, Peterie JD. Altered Vancomycin dose vs. serum concentration relationship in burn patients. Clinical Pharmacology & Therapeutics [Internet]. 1988 Jul 1 [cited 2024 Sep 8];44(1):9–13. Available from: https://pubmed.ncbi.nlm.nih.gov/3292106/

[19]. Li J, Zhu Y, Zhu X, Kong X. Association between prolonged Vancomycin infusion and trough concentrations in children. Retrospective study. Archivos Argentinos de Pediatría. 2024;122(6):e07.

[20]. Junker A, Howe Z, Schneider JG, Bhumbra S, Kussin ML. Continuous Infusion Vancomycin Dosing and Area Under the Curve Target Attainment in a Freestanding Children's Hospital. Journal of the Pediatric Infectious Diseases Society. 2024 Oct;13(Supplement_3):S12–3.

[21]. Girand HL. Continuous Infusion Vancomycin in Pediatric Patients: A Critical Review of the Evidence. 2020 Apr 1 [cited 2023 Jul 10];25(3):198–214. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7134591/

[22]. Chuphan C, Sukarnjanaset W, Puthanakit T, Wattanavijitkul T. Population Pharmacokinetics and Pharmacodynamics of Vancomycin in Pediatric Patients With Various Degrees of Renal Function. The Journal of Pediatric Pharmacology and Therapeutics. 2022 May 1;27(5):419–27.

[23]. Lodise TP, Graves J, Evans A, Graffunder E, Helmecke M, Lomaestro BM, et al. Relationship between Vancomycin MIC and Failure among Patients with Methicillin-Resistant Staphylococcus aureus Bacteremia Treated with Vancomycin. Antimicrobial Agents and Chemotherapy. 2008 Jun 30;52(9):3315–20.

Table 1. Summary of Vancomycin regimes, obtained Vancomycin concentrations and computed pharmacokinetic profiles.

Days post burn (Day)	Vancomycin regime	Infusion Duration (hour)	Vancomycin daily dose (mg/kg/day)	Vancomycin concentration (mg/L)		Computed pharmacokinetic profiles				Suggested regime
				Trough[a]	Peak[b]	Ke[c] (/hr)	$t_{1/2}$[c] (hr)	Vd[c] (L/kg)	AUC24/MIC[d] Target: 400-600 (mg.h/L)	
22	315 mg every 8 hours	1	45	< 2	8.4	Unable to be computed			Unable to be computed	315 mg every 6 hours
25	315 mg every 6 hours	1	60	2.5	7.8	0.38	1.83	1.55	**128 (Subtherapeutic target attainment)**	400 mg every 6 hours
28	400 mg every 6 hours	2	76	3.3	NM	0.26	2.67	1.55	**265 (Subtherapeutic target attainment)**	400 mg every 6 hours
31	400 mg every 6 hours	3	76	6.5	NM	0.18	3.91	1.55	425 (Therapeutic target attainment)	400 mg every 6 hours
34	400 mg every 6 hours	3	76	3.5	NM	0.25	2.77	1.55	**313 (Subtherapeutic target attainment)**	450 mg every 6 hours
35	450mg every 6 hours	3	86	NM	NM	Unable to be computed			Unable to be computed	OFF

Ke: Elimination rate constant; $t_{1/2}$: Elimination half-life; Vd: Volume of distribution; AUC_{24}/MIC: Area under the concentration-time curve over 24 hours relative to minimum inhibitory concentration; NM: not measured.

[a] Trough was measured concentration obtained within 0-60 minutes before dose served.

[b] Peak was measured concentration obtained 2 hours after dose served, alternatively, 1 hour after Vancomycin infusion completed.

[c] Estimated via the Sawchuk-Zaske calculation method.

[d] Estimated via the trapezoidal approach, assuming MIC of 1 mg/L.

CASE REPORT

Erythema Nodosum Leprosum in a Treatment-Naïve Patient: Clinical Clues Not to Miss in Primary Care.

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Abstract
Leprosy is known as a "great mimicker" due to its broad spectrum of clinical presentations. Erythema nodosum leprosum (ENL), a Type 2 lepra reaction, typically manifests as acute, painful erythematous nodules during or after initiation of multidrug therapy (MDT) in multibacillary patients. We report a case of a 66-year-old treatment-naïve man who presented to primary care with chronic and painless nodules in the absence of classical lepromatous features or prior therapy. Slit-skin smear (SSS) confirmed multibacillary leprosy with a moderate bacterial index (BI) and an inactive morphological index (MI), supporting the diagnosis of chronic ENL. The patient responded well to a second-line MDT regimen and corticosteroids. This case highlights an unusual presentation of ENL preceding treatment and underscores the diagnostic challenges faced in primary care, particularly when classical signs of leprosy are absent. We discuss key differential diagnoses and the importance of early recognition to avoid misdiagnosis and prevent complications.

Keywords: *Clofazimine, erythema nodosum, multibacillary leprosy, Mycobacterium leprae.*

Introduction

Leprosy, or Hansen's disease, is a chronic granulomatous infection caused by *Mycobacterium leprae* and *Mycobacterium lepromatosis,* primarily affecting the skin and peripheral nerves. The incubation period is notably long, ranging from 2 to 20 years, which can obscure early diagnosis and contribute to ongoing transmission [1]. Although the global burden has declined significantly with the widespread implementation of multidrug therapy (MDT), more than 200,000 new cases are still reported annually, particularly in endemic regions such as Southeast Asia, Africa, and South America [2]. Malaysia achieved the World Health Organization's (WHO) leprosy elimination target in 1994 (defined as <1 case per 10,000 population). However, sporadic cases continue to be reported, including in urban populations, partly due to migration and socioeconomic disparities [3]. This highlights the importance of clinical vigilance and awareness of atypical presentations among healthcare providers, particularly in primary care.

Leprosy is classified under the Ridley-Jopling system, with multibacillary forms—lepromatous and borderline lepromatous—carrying the highest bacillary load. A substantial number of these patients experience lepra reactions. Type 2 lepra reactions (ENL) are immune complex-mediated and commonly present with painful nodules, fever, neuritis, or arthritis. ENL occurs in multibacillary leprosy and approximately 50% of lepromatous leprosy patients and 5–10% of those with borderline lepromatous leprosy. ENL is typically observed during or after the commencement of MDT. Only a minority (2–10%) of patients develop ENL as the initial manifestation of leprosy [4]. These uncommon presentations, particularly in treatment-naïve individuals, pose diagnostic dilemmas in primary care settings. Recognizing these cases in the primary care setting is essential to avoid mismanagement, delayed treatment, and irreversible nerve damage.

Case report

A 66-year-old Malay man with underlying glucose-6-phosphate dehydrogenase (G6PD) deficiency and hypertension on amlodipine, presented with a one-year history of painless erythematous nodular lesions on the face, trunk, and upper limbs. The lesions began as periorbital oedema and nodules on the face, initially treated as an allergic reaction. He received both systemic and topical steroids, but the symptoms did not resolve. Over time, the lesions progressively spread and were associated with fatigue, bilateral lower limb oedema, and distal numbness of the hands and feet. He denied having fever, joint pain, or other systemic symptoms. Although he had resided in a leprosy-endemic area, he denied any known contact with leprosy patients, and all family members were reported to be healthy.

Examination revealed multiple symmetric erythematous to violaceous nodules and plaques on the face, trunk, and upper limbs, accompanied by bilateral lower limb pitting oedema (Figure 1). There was distal sensory loss without palpable nerve thickening. Slit skin smear (SSS) from the earlobes, elbows, and active lesions showed a bacterial index (BI) of 1.67 and a morphological index (MI) of 0.0, indicating moderate bacillary load with nonviable bacilli (Figure 2). These findings, together with the diffuse lesion distribution with systemic symptoms, are more suggestive of chronic ENL.

Laboratory investigations, including full blood count, renal and liver profiles, were normal, indicating no evidence of systemic organ involvement. Due to underlying G6PD deficiency, the patient was started on a second-line MDT regimen consisting of ofloxacin 400 mg daily, rifampicin 600 mg daily, clofazimine 50 mg daily and 300 mg monthly, along with pentoxifylline 400 mg three times per day and prednisolone 30 mg daily and tapering down. Regular follow-up was scheduled to monitor treatment response and manage potential side effects. After six months, repeat SSS showed a BI of 0.0. Lesions and lower limb oedema resolved completely (Figure 3).

Discussion

ENL typically presents with acute, tender erythematous papules, plaques, or nodules, often accompanied by systemic symptoms such as fever, malaise, or neuritis. Although pain is considered a hallmark of ENL [5], painless nodules may occur, particularly in chronic or recurrent ENL. Atypical presentations of ENL have also been reported, featuring a range of lesion morphologies, including pustular, vesiculobullous, ulcerative, necrotic, and erythema multiforme–like variants [6]. These uncommon forms can be easily overlooked in primary care settings, underscoring the importance of clinical vigilance and a high index of suspicion in endemic or high-risk populations. In many endemic regions, primary care is often the first point of contact for patients presenting with skin or neurological symptoms. Unfortunately, early signs of leprosy can resemble common benign dermatological or allergic conditions. In the absence of classical features such as hypopigmented or reddish skin lesions with sensory loss and nerve thickening, leprosy may be overlooked in the differential diagnosis. The delayed presentation in our patient highlights this diagnostic challenge and reinforces the importance of heightened clinical awareness and suspicion in primary care settings. In this case, the patient presented with generalised nodular lesions for a year before referral to dermatology, which were initially treated as allergic reactions without improvement. The chronicity and lack of response to therapy warranted an earlier skin biopsy to exclude other diagnoses. Although the slit-skin smear (SSS) ultimately confirmed lepromatous leprosy, the delay underscored the importance of early biopsy in persistent nodular dermatoses. Several differential diagnoses should be considered, including ENL, cutaneous sarcoidosis, lupus panniculitis, and erythema induratum [7]. ENL, in particular, can be easily misdiagnosed, resulting in delayed treatment that may lead to irreversible nerve damage, physical disability, and significant psychological distress. In primary care, thorough history-taking and examination are critical not only to suspect leprosy but also to systematically rule out other causes of chronic skin lesions.

Risk factors for leprosy include prolonged close contact with untreated individuals, residence in endemic regions, and genetic susceptibility, as certain host genes are known to influence immune response to *Mycobacterium leprae.* In this case, the patient had resided in a leprosy-endemic area for several decades but only developed clinical symptoms later in life. The long incubation period of leprosy is explained in this current presentation. This is due to the extremely slow replication rate of *Mycobacterium leprae* and its ability to persist within host macrophages and Schwann cells, evading immune surveillance for extended periods.

The clinical spectrum of leprosy is shaped by the host's immune response. Lepromatous leprosy is marked by a Th2-dominant humoral response, which fails to contain Mycobacterium leprae, resulting in a high bacillary load, minimal inflammation, and widespread skin lesions. In contrast, paucibacillary leprosy involves a Th1-driven cellular response, producing localised granulomatous inflammation. Erythema nodosum leprosum (ENL) is a Type III hypersensitivity reaction associated with multibacillary forms, triggered by immune complex deposition and characterised by neutrophilic vasculitis, which leads to painful erythematous nodules with systemic symptoms [11].

The slit-skin smear (SSS) examination played a pivotal role in confirming the diagnosis. While often underutilised in primary care due to a lack of expertise or facilities, SSS remains a cornerstone diagnostic tool for multibacillary leprosy. It allows direct visualisation of *Mycobacterium leprae* as acid-fast bacilli under microscopy, and provides both the bacterial index (BI) and morphological index (MI). These indices are critical for determining the bacillary load and viability, guiding treatment duration and prognostication. SSS has high specificity

(approaching 100%) for multibacillary leprosy but variable sensitivity (10–50%) depending on sampling site, technique, and disease stage [12]. Sampling multiple high-yield sites (such as earlobes and elbows) improves detection rates. While skin biopsy is the gold standard, providing histological confirmation through findings such as dermal granulomas, foamy histiocytes, and perineural involvement, it was not indicated in this case due to the clear clinical picture and positive bacteriological confirmation. Biopsy is indicated in smear-negative cases or when diagnostic uncertainty persists, especially in differentiating leprosy from other granulomatous or nodular dermatoses.

According to WHO guidelines, the standard MDT regimen for multibacillary leprosy includes rifampicin, dapsone, and clofazimine [1]. However, dapsone poses a significant risk of haemolysis in G6PD-deficient individuals. Our patient was G6PD-deficient and was therefore initiated on a second-line MDT regimen including ofloxacin, rifampicin, and clofazimine, along with pentoxifylline and tapering doses of prednisolone. Pentoxifylline, a phosphodiesterase inhibitor, has shown adjunctive benefit in ENL management due to its anti-inflammatory and vascular protective effects [13]. Corticosteroids effectively controlled the inflammatory manifestations of ENL in this patient. This case emphasises the need for individualised treatment regimens in patients with coexisting conditions. Screening for G6PD deficiency before initiating dapsone is essential to avoid life-threatening haemolysis.

Although Malaysia achieved the WHO's leprosy elimination target in 1994, sporadic cases are still reported [3]. Factors such as migration, urban overcrowding, and limited healthcare access continue to contribute to ongoing transmission. Early diagnosis remains essential to prevent irreversible nerve damage, deformities, and further spread. In this context, primary care practitioners play a crucial role as the first point of contact. Timely referral for dermatological and microbiological evaluation is essential to break the chain of delayed diagnosis and improve patient outcomes.

Conclusion

This case highlights the need for heightened clinical suspicion in primary care settings when encountering chronic, unexplained nodular skin lesions—particularly in patients with neuropathy or a history of exposure in endemic areas. The slit-skin smear, though often underutilised, is a simple and cost-effective diagnostic tool that can be employed even in primary care. By recognising presentations early, primary care practitioners can play a vital role in early detection, disability prevention, and supporting national leprosy elimination efforts.

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Conflicts of interest

All authors declare no conflicts of interest.

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Nil

Authors contribution

FH contributed to manuscript preparation, data collection, and revisions. SS contributed to the manuscript review, editing, and final approval.

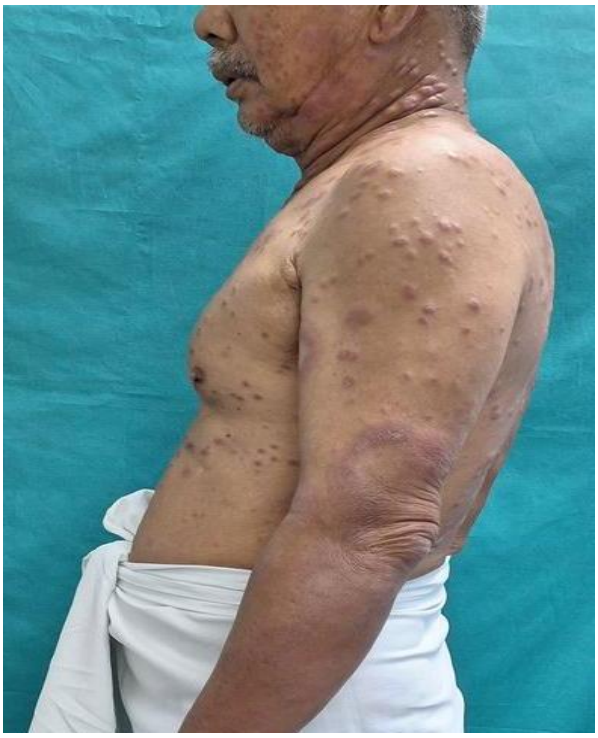

Figure 1. Multiple erythematous to violaceous nodules or plaques of varying sizes at upper part of body.

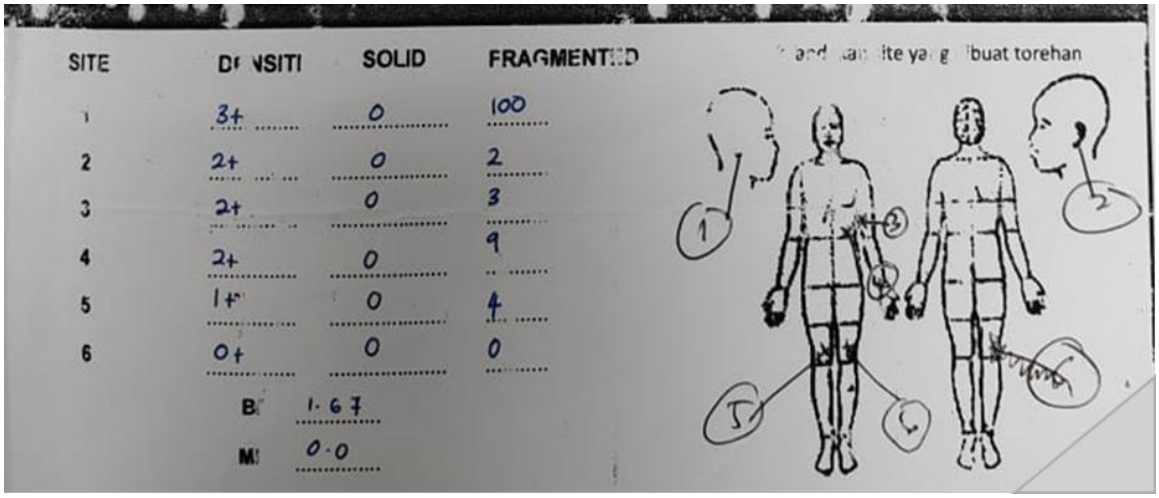

Figure 2. Slit skin smear results with bacterial and morphological indices across multiple body sites.

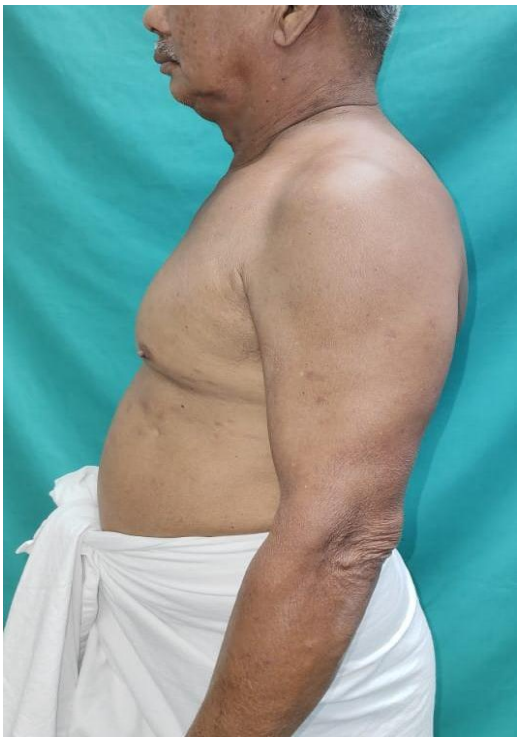

Figure 3. 6 months on treatment showed resolution of nodules.

Table 1. Features of Differential Diagnosis of Chronic Nodular Skin Lesions

Condition	Lesion Appearance	Associated Symptoms	Diagnostic Tests
ENL [4]	Tender erythematous subcutaneous nodules, typically on face and extremities	Fever, neuritis, arthralgia, oedema	Slit-skin smear (AFB), skin biopsy (neutrophilic infiltrate/vasculitis)
Cutaneous Sarcoidosis [8]	Firm, non-tender papules, nodules, or plaques; may be skin-coloured or violaceous	Cough, dyspnoea, lymphadenopathy, fatigue	Skin biopsy (non-caseating granulomas), chest radiograph, serum ACE
Erythema Induratum [9]	Nodules or lumps usually on posterior legs; red purple discolouration, may ulcerate	History of Tuberculosis contact	Skin biopsy (lobular panniculitis with vasculitis), TST/ IGRA,
Lupus Panniculitis [10]	Deep, firm subcutaneous nodules with overlying erythematous or atrophic skin	Photosensitivity, arthralgia, fatigue, systemic lupus erythematosus signs	ANA, anti-dsDNA, skin biopsy (hyaline fat necrosis)

Abbreviations:
AFB – Acid-Fast Bacilli; ANA – Antinuclear Antibody; anti-dsDNA – Anti–double-stranded DNA.
ACE – Angiotensin-Converting Enzyme; IGRA – Interferon Gamma Release Assay. TST – Tuberculin Skin Test

References

[1]. World Health Organization. Guidelines for the diagnosis, treatment, and prevention of leprosy. New Delhi: WHO Regional Office for South-East Asia; 2018.

[2]. World Health Organization. Global leprosy (Hansen disease) update, 2023: elimination of leprosy disease is possible – time to act. Wkly Epidemiol Rec. 2024 Sep 13;99(37):497–522.

[3]. Kwan Z, Pailoor J, Tan LL, Robinson S, Wong SM, Ismail R. Leprosy—an imported disease. Lepr Rev. 2014 Sep;85(3):170–6. PMID: 25509717

[4]. Walker SL, Lockwood DNJ. The clinical and immunological features of leprosy. Br Med Bull. 2006:77-78:103-21. doi: 10.1093/bmb/ldl010.

[5]. Walker SL, Balagon M, Darlong J, Doni SN, Hagge DA, Halwai V, et al. ENLIST 1: An International Multi-centre Cross-sectional Study of the Clinical Features of Erythema Nodosum Leprosum. PLoS Negl Trop Dis. 2015 Sep 9;9(9). doi: 10.1371/journal.pntd.0004065

[6]. Alakad R, Nofal A, Assaf M. Atypical presentations of erythema nodosum leprosum: Diagnostic and therapeutic aspects. J Dtsch Dermatol Ges. 2021 Aug;19(8):1133-1143. doi: 10.1111/ddg.14449

[7]. Akpolat ND, Akkus A, Kaynak E. An update on the epidemiology, diagnosis and treatment of leprosy. In: Ribón W, editor. Hansen's disease: the forgotten and neglected disease. London: IntechOpen; 2018. doi:10.5772/intechopen.82427

[8]. Koneti J, Cherukuri SP, Gadde S, Kalluru R, Chikatimalla R, Dasaradhan T. Sarcoidosis and Its Dermatological Manifestations: A Narrative Review. Cureus. 2022 Aug 16;14(8)

[9]. Irifune S, Yamamoto K, Ishijima S, Koike Y, Fukuoka J, Mukae H. Erythema induratum of Bazin: a subcutaneous granulomatous vasculitis that caused difficulty in walking. Int J Infect Dis. 2021 May; 106:183–4. doi: 10.1016/j.ijid.2021.03.077

[10]. Koley S, Sarkar J, Choudhary SV, Choudhury M, Banerjee G, Bar C, et al. Lupus erythematosus panniculitis: a case report. J Pak Assoc Dermatol. 2011;21(1):63–6.

[11]. Dewi DAR, Djatmiko CBP, Rachmawati I, Arkania N, Wiliantari NM, Nadhira F. Immunopathogenesis of Type 1 and Type 2 Leprosy Reaction: An Update Review. Cureus 2023 Nov 21;15(11): e49155.

[12]. Mahajan VK. Slit-skin smear in leprosy: lest we forget it! Indian J Lepr. 2013 Oct-Dec;85(4):177-83. PMID: 24834639

[13]. Roy K, Sil A, Das NK, Bandyopadhyay D. Effectiveness and safety of clofazimine and pentoxifylline in type 2 lepra reaction: a double-blind, randomized, controlled study. Int J Dermatol. 2015 Nov;54(11):1325-32. doi: 10.1111/ijd.12793.

CASE REPORT

Transcending the Red Eye: A Nearly Missed Case of Adult Gonococcal Conjunctivitis.

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Abstract
Gonorrhoea is a sexually transmitted disease with a rising incidence worldwide. Adult gonococcal conjunctivitis is relatively uncommon but poses significant risks, including corneal perforation if not treated promptly. Diagnosis can be challenging, and delayed or misdiagnosis may occur due to its resemblance to other common forms of conjunctivitis. We reported a case of a 35-year-old sexually active male with persistent unilateral conjunctivitis that did not respond to standard topical antibiotics. Further investigation revealed *Neisseria gonorrhoeae* as the causative organism. Despite developing corneal thinning, the patient responded well to prompt systemic and topical antibiotics, with preservation of vision. This case highlights the importance of taking a comprehensive history, including sexual history, to facilitate early detection and treatment, which can help prevent complications.

Keywords: *Gonorrhoea, gonococcal conjunctivitis, Neisseria gonorrhoeae, red eye.*

Introduction

N. gonorrhoeae is a Gram-negative diplococcus that is responsible for sexually transmitted infections, but it rarely causes acute conjunctivitis in adults. However, the global prevalence of gonorrhoea is rising, particularly among vulnerable populations such as men who have sex with men, sex workers, transgender individuals, and young populations. Ocular transmission typically occurs through direct contact with infected genital or urinary secretions. [1] Copious purulent discharge, severe conjunctival injection, marked oedema, and hyperaemia of the eyelids are the hallmarks of gonococcal conjunctivitis. Due to its rapid progression and resemblance to other bacterial or viral conjunctivitides, it can be easily misdiagnosed. A high index of suspicion is warranted in case of persistent, unilateral conjunctivitis that has not responded to standard treatment. Accurate diagnosis relies on a comprehensive clinical evaluation, excellent history-taking, and microbiological testing, which includes a conjunctival swab for Gram stain, which may reveal gram-negative diplococci. *N. gonorrhoeae* is one of the rare bacteria that can penetrate intact corneal epithelium, making it a potentially vision-threatening pathogen. Complications may include corneal thinning, scarring, and even perforation. Initiation of both parenteral and topical antibiotics is essential to prevent irreversible ocular damage.

Case report

A 35-year-old male with no known chronic medical illness presented with a one-week history of progressive left eye symptoms, including redness, pain, swelling, blurred vision, and profuse mucopurulent discharge. He had a history of a left corneal ulcer one year ago, which required hospital admission and resolved with residual thinning. At presentation, he was diagnosed with left eye pseudomembranous conjunctivitis.

On day two of his illness, he sought treatment at a private clinic and was prescribed topical antibiotics. However, his symptoms persisted. Two days later, he presented to the emergency department at a tertiary hospital, where he was again diagnosed with left eye pseudomembranous conjunctivitis. At that time, his visual acuity was 6/6 in the right eye and 6/24 (pinhole 6/15) in the left eye. Examination revealed swollen, erythematous eyelids with copious mucopurulent discharge and pseudomembranes over both upper and lower palpebral conjunctivae, which were removed under local anaesthesia. A faint inferior corneal opacity was noted at the 7 o'clock position, with no epithelial defect or fluorescence uptake. He was started on Maxitrol (neomycin, polymyxin B, and dexamethasone) ointment and chloramphenicol eye drops under the working diagnosis of viral or allergic conjunctivitis with membrane formation.

Despite treatment, the symptoms persisted. The patient was referred to us for further evaluation and continuation of care due to logistical reasons. Upon presentation at our clinic, his left eye vision remained 6/24 (no improvement with pinhole). Slit-lamp examination revealed thick purulent discharge actively exuding from the lower fornix (Figure 1), accompanied by conjunctival hyperaemia and chemosis (Figure 2). A localised inferior corneal epithelial defect measuring 2.0 x 1.4 mm (Figure 3) was now noted, without infiltrate or fluorescein uptake. The anterior chamber was deep and quiet, and the fundus appeared normal.

The diagnosis was revised to pseudomembranous conjunctivitis with a secondary epithelial defect over an old corneal thinning. Maxitrol was discontinued, and the patient was on ciprofloxacin eye drops every four hours and preservative-free artificial tears.

Due to poor clinical response, conjunctival swabs for culture and sensitivity were taken. By the second week of follow-up, the epithelial defect persisted, and inferior corneal thinning was more pronounced. Although there was no hypopyon or stromal infiltrate, the ongoing mucopurulent discharge raised concern for hyperacute bacterial conjunctivitis.

The conjunctival culture-confirmed *Neisseria gonorrhoeae*. A detailed sexual history was obtained after the swab cultures result. The patient is married with one child and has a long-distance relationship. The patient admitted to unprotected oral sexual contact with unfamiliar partners about one month before the onset. He denied any history of urogenital symptoms or systemic complaints.

He was admitted for inpatient management and started on:

- IV ceftriaxone: 2 g stat, followed by 500 mg daily
- Oral doxycycline: 100 mg twice daily for 7 days
- Fortified gentamicin 0.9% and ceftazidime 5% eye drops hourly
- Preservative-free artificial tears and vitamin C
- Timolol eye drops to manage mild IOP elevation

Full sexually transmitted disease screening was conducted. The HIV test was reactive, while VDRL, HBsAg, and anti-HCV were negative. He was co-managed with the infectious disease team, who provided the following:

- Post-HIV diagnosis counselling
- Partner notification and safe sex education
- Coordination for outpatient HAART initiation

The case was reported to the Public Health Unit. His spouse was referred for screening.

During admission, the patient's symptoms improved significantly. The conjunctival inflammation and discharge resolved, and the epithelial defect closed with residual corneal thinning. Upon review, three days post-discharge, the left eye's visual acuity has improved to 6/12, and he has remained stable on topical lubricants. Regular follow-ups with the ophthalmology and infectious disease teams were continued.

Discussion

Gonococcal conjunctivitis is typically associated with neonates but is becoming more prevalent among adults due to the increasing number of urogenital gonococcal infections worldwide.[2] Adult gonococcal conjunctivitis is rare, but it is a sight-threatening condition that can rapidly progress and lead to serious ocular complications if not recognised and treated promptly.

In adults, gonococcal conjunctivitis is typically transmitted through direct inoculation of the eye with infected genital secretions during sexual contact. [3] It is often associated with other sexually transmitted infections (STIs, but can present independently, without any obvious sign of genital involvement, as seen in this case. The absence of urogenital symptoms often leads to a delay in the diagnosis. Even so, early recognition and timely treatment are critical to avoid complications such as corneal thinning or, in severe cases, vision loss. [3]

This case highlights the importance of primary care doctors in identifying atypical presentations and initiating early referrals. For the first week, the patient's ocular symptoms, including pain and visual impairment, worsened. Since the cornea and visual axis are typically spared in simple conjunctivitis, these are the red flag features. Such symptoms should immediately raise suspicion for more serious pathology.

In this case, the initial diagnosis was delayed because of a lack of a comprehensive sexual history. This step, though simple, is often neglected due to time constraints, discomfort discussing sexual behaviour, or assumptions about the patient's risk profile. However, it is essential for a proper history taking, including sexual history, to identify underlying sexually transmitted infections and ensure appropriate management.

Although specific data on the prevalence of gonococcal conjunctivitis in Malaysia is limited, isolated cases have been documented locally. For example, a case reported by Anuar et al. in 2018 [4] described similar clinical features. Recently, Azmi et al. (2025) reported three cases of delayed treatment, resulting in corneal perforation, all of which were due to misdiagnosis or late referral.[5]

Our case report emphasises the importance of maintaining a high index of suspicion for non-resolving unilateral conjunctivitis, characterised by significant chemosis and purulent exudate.[6] Early microbial testing, including conjunctival swabs, should be performed if standard treatment fails. Prompt initiation of treatment is crucial in preventing ocular complications and vision-threatening conditions, such as keratitis, corneal ulcer and perforation, endophthalmitis, uveitis, and, ultimately, blindness.[7]

Additionally, our patient tested positive for HIV following the diagnosis. While he had no urogenital symptoms, his presentation underscores the syndemic relationship between gonorrhoea and HIV. Gonorrhoea facilitates HIV transmission through mucosal disruption and inflammation, which reinforces the need for comprehensive STI screening in such cases. [8] A multidisciplinary approach, including the ophthalmology, infectious disease, and public health teams, is important for effective management and contact tracing.

Currently, there are no specific Malaysian guidelines for adult gonococcal conjunctivitis in primary care, but clinicians can adopt a general framework when evaluating conjunctivitis. Features such as profuse mucopurulent discharge, visual loss, ocular pain, pseudomembrane formation, or corneal involvement should raise concern and need early referral to ophthalmology. The following practical approach may be helpful:

1. Suspect gonococcal or atypical conjunctivitis in severe, persistent, unilateral cases with corneal signs.
2. Start empirical topical antibiotics, while acknowledging the limitations of primary care settings.
3. Elicit a complete sexual history to identify STI risk, even when urogenital symptoms are absent.
4. Refer urgently to ophthalmology if red flags are present, which include reduced visual acuity, pseudomembranous formation, signs of corneal involvement, or worsening symptoms despite 24–48 hours of empirical therapy, to prevent sight-threatening complications.
5. Ensure proper follow-up and documentation. The patient should be reviewed in 2-3 days to asses clinical response. A lack of improvement should prompt a reevaluation and escalation of care.

In summary, primary care providers play a vital role in the early recognition and management of eye complaints. While most cases of conjunctivitis are self-limiting, this case highlights the importance of having a high index of suspicion for red eye to be able to recognize the warning signs that may indicate a more serious condition, such as gonococcal infection. Taking a comprehensive history, including a sexual history, and closely monitoring the treatment response can make the difference between timely intervention and permanent vision loss.

Conclusion

Adult gonococcal conjunctivitis is rare but potentially sight-threatening. This case highlights the importance of early recognition, thorough sexual history-taking, and timely referral in primary care. Prompt diagnosis and appropriate treatment can prevent serious complications and preserve vision.

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Conflicts of interest

All authors declare no conflicts of interest.

Authors contribution

NEE wrote the first and final drafts. AHS and FSS reviewed, edited, and finalized the final draft. All authors agreed with the results and conclusions.

Patients' consent for the use of images and content for publication

The patient provided consent for the use of images and content for publication.

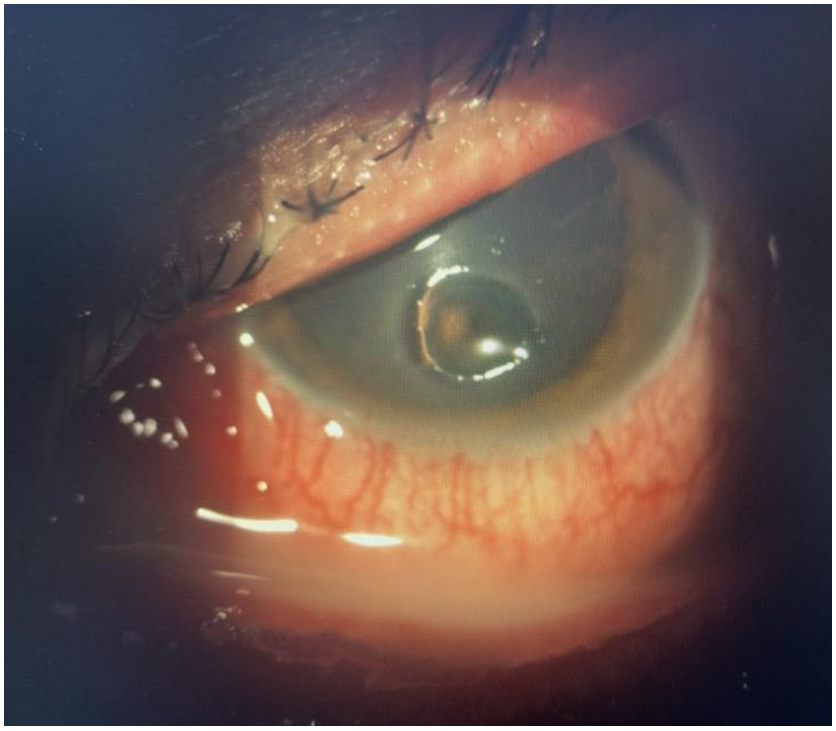

Figure 1. Slit-lamp photograph of the left eye showing thick purulent discharge actively exuding from the lower fornix along with conjunctival hyperaemia.

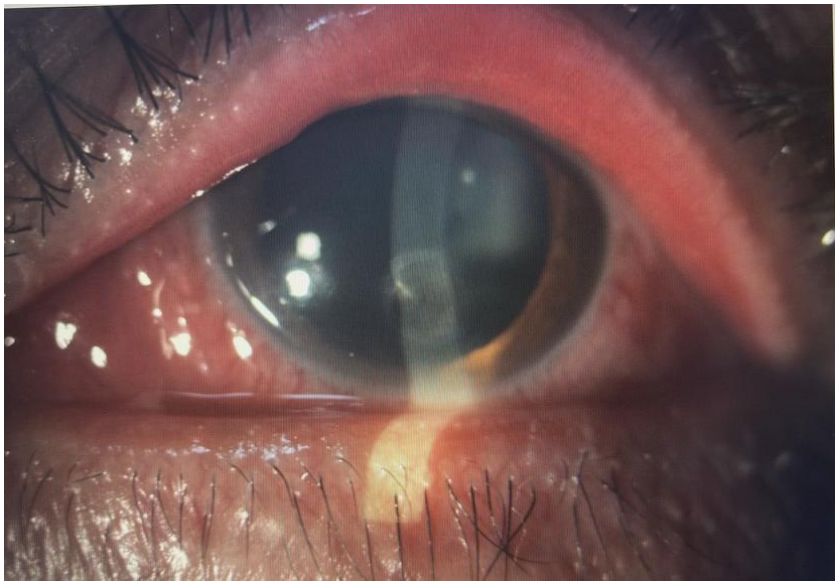

Figure 2. Slit lamp image of the same eye demonstrating conjunctival chemosis, central corneal epithelial defect with mild stromal haze.

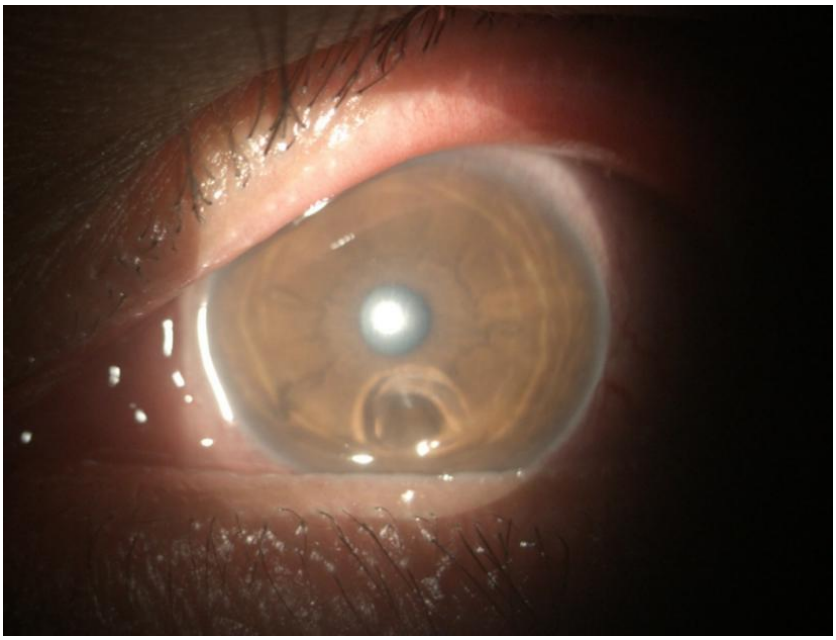

Figure 3. Slit lamp photograph demonstrating residual central corneal thinning post-infection—a well-demarcated area of stromal thinning, measuring 2.0 mm vertically x 1.8 mm horizontally.

Table1. Red flags in red eye presentation

Red Flag	Explanation / Reason for urgent referral
Visual Impairment	Not typical in simple conjunctivitis; may indicate corneal involvement
Ocular Pain	Suggests deeper involvement (e.g., uveitis, keratitis, glaucoma)
Pseudomembrane Formation	Seen in more severe infections like gonococcal conjunctivitis
Profuse Mucopurulent Discharge	Highly suggestive of hyperacute bacterial conjunctivitis
Corneal Involvement	Risk of ulceration or perforation; requires urgent ophthalmology review

References

[1]. Lee JS, Choi HY, Lee JE, Lee SH, Oum BS. Gonococcal keratoconjunctivitis in adults [5]. Eye 2002;16:646–9. https://doi.org/10.1038/sj.eye.6700112.

[2]. Mcanena L, Knowles SJ, Curry A, Cassidy L. Prevalence of gonococcal conjunctivitis in adults and neonates. Eye 2015;29:875–80. https://doi.org/10.1038/eye.2015.57.

[3]. Belga S, Gratrix J, Smyczek P, Bertholet L, Read R, Roelofs K, et al. Gonococcal conjunctivitis in adults: Case report and retrospective review of cases in Alberta, Canada, 2000-2016. Sex Transm Dis 2019;46:47–51. https://doi.org/10.1097/OLQ.0000000000000897

.

[4]. Anuar N, Suhaila Idris N. Gonococcal conjunctivitis: A case report. Number 3 Malaysian Family Physician. vol. 13. 2018.

[5]. Azmi NH, Alias R, Vaiyavari V, Ch'ng H, Nasaruddin RA. Perforated Corneal Ulcer Arising From Gonococcal Keratoconjunctivitis: A Report of Three Cases. Cureus 2025. https://doi.org/10.7759/cureus.82150.

[6]. Walensky RP, Jernigan DB, Bunnell R, Layden J, Kent CK, Gottardy AJ, et al. Morbidity and Mortality Weekly Report Sexually Transmitted Infections Treatment Guidelines, 2021 Centers for Disease Control and Prevention MMWR Editorial and Production Staff (Serials) MMWR Editorial Board. 2021.

[7]. Wang M-F, Wang L, Li L-F. Gonococcal conjunctivitis after incomplete treatment of gonococcal urethritis 2019. https://doi.org/10.2147/IDR.S199163.

[8]. Ghassabi F, Malekzadegan Y, Ebrahim-Saraie HS, Heidari H, Sabet M, Bagheri A, et al. Gonorrhea and syphilis co-infection and related risk factors in HIV patients from Shiraz, South of Iran. Caspian J Intern Med 2018;9:397–402. https://doi.org/10.22088/cjim.9.4.397.

CASE REPORT

Healthy Gums does it Matter? Amlodipine-Induced Gingival Overgrowth (AIGO): A Case Report.

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Abstract
In Malaysia, more than half a million adults, representing 2.5% of the population, are living with four major non-communicable diseases (NCDs): diabetes, hypertension, hypercholesterolemia, and obesity. As for hypertension, 29.2% or 1 in 3 adults in Malaysia has hypertension and 91% are on blood pressure medications. This includes dihydropyridine calcium channel blockers such as amlodipine, which is commonly used in primary care. We report a case from our primary care clinic involving a 70-year-old man with a known history of primary hypertension who developed painless gum swelling and discomfort while the patient was on T. amlodipine 10 mg. Oral examination showed diffuse gingival hypertrophy involving the upper and right lower gums. The condition resolved completely after discontinuation of the offending drug and substitution with an angiotensin-converting enzyme inhibitor. This case is notable because the gingival overgrowth developed only after 4 years of amlodipine 10 mg therapy. This paper aims to bring clinicians' attention to these adverse effects of amlodipine, so that timely and effective management can be given to the patient, avoiding complications and unnecessary treatment.

Keywords: D*ihydropyridine calcium channel blocker, gingival overgrowth, hypertension.*

Introduction

Gingival overgrowth (also referred to as enlargement or hyperplasia) is a benign, painless condition characterized by a marked increase in the size of the interdental papillae, with severity ranging from mild to very extensive. [1,2] Terms such as gum hypertrophy and gum hyperplasia are synonymous, describing the same histological finding of enlarged gingival tissue. The causes of gum overgrowth are multifactorial; however, genetic predisposition has been shown to play a key role in drug-induced cases. To date, more than 20 medications have been implicated in the development of gingival hypertrophy. [3] Calcium channel blockers are one of the recognizable drug-induced gingival hypertrophies, along with anticonvulsants and immunosuppressants. [4] Among calcium channel blockers, the dihydropyridine group (e.g., nifedipine, felodipine, amlodipine) is most often linked to gingival enlargement. [5] Amlodipine, a third-generation dihydropyridine, is widely prescribed for the management of hypertension and angina pectoris. [1] The reported prevalence of amlodipine-induced gingival overgrowth is around 3.3%, which is considerably lower than the prevalence associated with nifedipine, estimated between 14% and 83%. [6] Amlodipine is commonly administered in this class and is frequently used in the management of hypertension, especially in primary care settings.

Case report

A 70-year-old man presented with painless, progressively enlarging swelling of the upper and right lower gums over the past three months. The swelling was associated with gum discomfort, difficulty chewing, malalignment and, loosening of the affected teeth. His medical history included hypertension and dyslipidemia, for which he had been taking amlodipine 10 mg and simvastatin 10 mg daily for four years.

On physical examination, he appeared moderately built, well-nourished and showed no signs of anaemia. His vital signs were stable. Gingival overgrowth was noted throughout the maxilla, as shown in Figure 1(a), and over the right mandible as shown in Figure 1(b), predominantly in the right buccal region. The enlargement was firm, generalized, and outwardly expanded, without periodontal pockets, gingival inflammation, bleeding, or purulent discharge. Poor oral hygiene was evident, with local irritants observed around the teeth. Otherwise, laboratory results as shown in Table 1, including full blood count, C-reactive, protein and renal profile, were normal.

After correlating the clinical history and examination, other potential causes such as the use of alternative medications, nutritional deficiencies, and malignancies were excluded. Based on the clinical findings, a diagnosis of amlodipine-induced gingival overgrowth was made. Amlodipine was discontinued and replaced with an angiotensin-converting enzyme (ACE) inhibitor. Disease progression halted within a few days following the medication change. One month after switching to perindopril 4 mg daily, gingival swelling improved, however, the severe overgrowth and malposition required full dental extraction with denture replacement. The patient declined follow-up photos due to a reluctance to wear dentures.

Discussion

AIGO is considered a multifactorial condition, with its onset and severity influenced by factors such as the dose, duration, and plasma concentration of amlodipine, along with patient-specific elements including sex, genetic predisposition (fibroblasts with abnormal drug susceptibility and/or functional heterogeneity), oral hygiene status, preexisting gingival inflammation, and activation of growth factors. [7,8,9] The exact pathogenesis of AIGO remains unclear, but it is generally explained through a multifactorial model involving both noninflammatory and inflammatory pathways. [7,8] Proposed noninflammatory mechanisms include impaired collagenase activity due to reduced secretion of matrix metalloproteinases-1

and -3, decreased folic acid uptake, inhibition of aldosterone synthesis in the adrenal zona glomerulosa, and upregulation of keratinocyte growth factor. [1] Inflammatory processes may also play a role, triggered by the direct toxic effect of high drug concentrations in gingival crevicular fluid, which can reach levels up to 292 times higher than those measured in plasma. [9] This inflammation could lead to the upregulation of several cytokine factors such as fibroblast growth factor-2 (FGF-2), transforming growth factor-β1 (TGF-β1), interleukin-6 and interleukin-1β (IL-6, IL-1β), and platelet-derived growth factor-β (PDGF-β), predisposing the tissue to a localized toxic effect and the development of fibrotic gingival hyperplasia. [10] Released proinflammatory cytokines are also involved in mast cell migration, influencing fibroblast proliferation, extracellular matrix synthesis, and degradation. Furthermore, amlodipine may stimulate the production of IL-2 by T-cells, causing fibrosis. [9]

Amlodipine-induced gingival overgrowth (AIGO) typically occurs within the first three months of starting a dose of 10 mg/day and often begins as enlargement of the interdental papilla. [9] In our patient, however, gingival enlargement developed only after four years of continuous amlodipine therapy at 10 mg daily. The variable time course of gingival hypertrophy in this patient may be influenced by multifactorial causes, including genetic susceptibility and host response to drug-induced gingival fibroblasts, interleukins, and matrix metalloproteinases. In addition to these known risk factors, our patient did not practice daily tooth brushing, leading to poor oral hygiene. This was supported by a recent dental evaluation showing generalized periodontitis, which likely played an important role in the progression of gingival overgrowth. The strong relationship between inflammation and AIGO is highlighted by evidence that the condition can often be controlled, even with ongoing amlodipine use, through meticulous professional and individual oral hygiene. [6,11] Another possible contributing factor in our case is the patient's male gender, as AIGO occurs about three times more frequently in men than women. [12] This case highlights that AIGO can significantly impair quality of life if not addressed early, as seen in our patient who required extensive dental extractions and dentures despite resolution of gingival overgrowth after discontinuing amlodipine.

Medical doctors and dentists/periodontists should therefore be aware of the potential of amlodipine and other medications to cause or worsen gingival overgrowth, particularly as the condition may progress if left untreated. The gingival enlargement can create periodontal pockets inaccessible to normal brushing or flossing, impairing oral hygiene and predisposing patients to infections, caries, and periodontitis. [13] Hence, it is crucial to explain this adverse effect to patients, emphasizing the importance of maintaining good oral hygiene, especially since amlodipine remains one of the most commonly prescribed anti-hypertensive agents in long-term primary care.

Conclusion

AIGO is a rare but important side effect that can be easily missed, especially in primary care, It often develops within the first three months of starting a 10 mg/day dose, but in some cases, it may appear years later. This delayed onset is linked to several factors, including dosage, duration of use, individual genetics, and most importantly, poor oral hygiene — which can significantly worsen the condition. AIGO can be prevented and reversed with early recognition, proper dental care, and medication adjustments when necessary. It is vital for healthcare providers to stay alert, advise patients on good oral hygiene, and promote regular dental visits — especially for those using amlodipine long-term.

Acknowledgements

The authors would like to thank the patient for his permission and cooperation in writing this case.

Conflicts of interest
None to declare.

Ethical consideration
The patient provided verbal consent before the use of images and the case for publication.

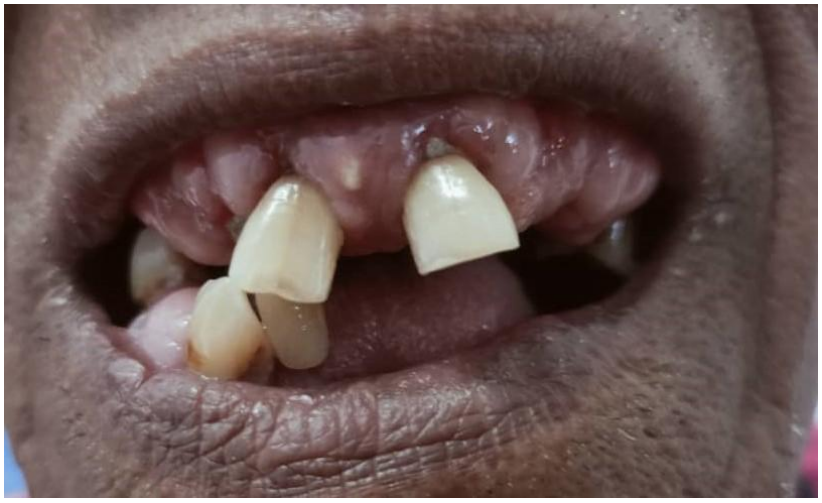

Figure 1(a) Gingival Overgrowth over maxilla area

Figure 1(b). Gingival Overgrowth over the right mandible near the buccal area

Table 1. Laboratory results

Parameter	Result	Reference Range
Urea	3.3	2.8 -7.2 mmol/L
Creatinine	69	59 -104 umol/L
Total white cells	6.4	4.08 – 11.37 10^9/L
Platelets	279	142 – 350 10^9/L
Hemoglobin	12.4	11.8 – 16.9 g/L
C-Reactive protein	0.1	< 0.5 mg/dL

References

[1]. Nyska A., Shemesh M., Tal H., and Dayan D., Gingival hyperplasia induced by calcium channel blockers: mode of action, Medical Hypotheses. (1994) 43, no. 2, 115–118, https://doi.org/10.1016/0306-9877(94)90061-2, 2-s2.0-0028141631

[2]. Lafzi A., Farahani R. M. Z., and Shoja M. A. M., Amlodipine-induced gingival hyperplasia, Medicina Oral, Patología Oral y Cirugía Bucal. (2006) 11, no. 6, E480–E482, 2-s2.0-39049182497.

[3]. Amlodipine-induced gingival hyperplasia. Lafzi A, Farahani RM, Shoja MA. https://pubmed.ncbi.nlm.nih.gov/17072250/ Med Oral Patol Oral Cir Bucal. 2006;11:0–2.

[4]. Brown, R.S.; Arany, P.R. Mechanism of Drug-Induced Gingival Overgrowth Revisited: A Unifying Hypothesis. Oral Dis. 2015, 21, e51–e61.

[5]. Srivastava A. K., Kundu D., Bandyopadhyay P., and Pal A. K., Management of amlodipine-induced gingival enlargement: series of three cases, Journal of Indian Society of Periodontology. (2010) 14, no. 4, 279–281, https://doi.org/10.4103/0972-124x.76931.

[6]. Livada R. and Shiloah J., Calcium channel blocker-induced gingival enlargement, Journal of Human Hypertension. (2014) 28, no. 1, 10–14, https://doi.org/10.1038/jhh.2013.47, 2-s2.0-84889671323.

[7]. Joshi S. and Bansal S., A rare case report of amlodipine-induced gingival enlargement and review of its pathogenesis, Case Reports in Dentistry. (2013) 2013, 3, 138248, https://doi.org/10.1155/2013/138248.

[8]. Nishikawa S., Nagata T., Morisaki I., Oka T., and Ishida H., Pathogenesis of drug-induced gingival overgrowth. A review of studies in the rat model, Journal of Periodontology. (1996) 67, no. 5, 463–471, https://doi.org/10.1902/jop.1996.67.5.463, 2-s2.0-0030139665.

[9]. Banthia R., Gupta S., Banthia P., Singh P., Raje S., and Kaur N., Is periodontal health a predictor of drug-induced gingival overgrowth? A cross-sectional study, Dental Research Journal. (2014) 11, no. 5, 579–584.

[10]. Seymour R. A., Ellis J. S., and Thomson J. M., The pathogenesis of drug-induced gingival overgrowth, Journal of Clinical Periodontology. (1996) 23, no. 3, 165–175, https://doi.org/10.1111/j.1600-051x.1996.tb02072.x, 2-s2.0-0030095969.
[11]. Triveni M. G., Rudrakshi C., and Mehta D. S., Amlodipine-induced gingival overgrowth, Journal of Indian Society of Periodontology. (2009) 13, no. 3, 160–163, https://doi.org/10.4103/0972-124x.60231.
[12]. Tavassoli S., Yamalik N., Çağlayan F., Çağlayan G., and Eratalay K., The clinical effects of nifedipine on periodontal status, Journal of Periodontology. (1998) 69, no. 2, 108–112, https://doi.org/10.1902/jop.1998.69.2.108, 2-s2.0-0031935781.
[13]. Morikawa S, Nasu M, Miyashita Y, Nakagawa T: Treatment of calcium channel blocker-induced gingival overgrowth without modifying medication. BMJ Case Rep. 2021, 14:e238872. 10.1136/bcr-2020-238872.

CASE REPORT

Phacoanaphylactic Endophthalmitis: A Rare Cause of Postoperative Intraocular Inflammation.

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Abstract
Phacoanaphylactic endophthalmitis (PE) is an uncommon and rare immune response to retained lens material after cataract surgery. This case involves a 71-year-old diabetic man who developed PE following a complicated cataract surgery with posterior capsule rupture (PCR) and retained lens fragments. The patient initially presented with mild postoperative inflammation, but eventually developed granulomatous uveitis, vitritis, and vasculitis.
The diagnosis was made based on clinical findings and intraoperative evidence of retained lens material during pars plana vitrectomy (PPV) and anterior chamber washout, which led to resolution of inflammation and improvement in vision, though anterior chamber and vitreous chamber tap were not performed. Early recognition and timely surgical intervention are crucial in managing PE, especially in diabetic patients prone to postoperative complications.

Keywords: *Cataract surgery, diabetes mellitus, lensectomy, phacoanaphylactic endophthalmitis, vitrectomy surgery.*

Introduction

Phacoanaphylactic endophthalmitis is rare autoimmune inflammatory response to lens protein that occurs under special conditions and involves an abrogation of tolerance to lens protein [1]. It most often occurs after traumatic or surgical lens injury [2]. The clinical features of PE are not easily distinguished from other forms of postoperative uveitis. [3] PE can be diagnosed clinically through a thorough history and clinical findings.[2] Diagnostic confirmation can be achieved with a needle biopsy histopathological examination or aqueous humor cytology [4]. Cytological analysis typically demonstrates a granulomatous inflammatory response characterized by macrophages, epithelioid cells, and polymorphonuclear leukocytes surrounding fragments of lens material, a finding highly suggestive of lens-induced uveitis [5].

Case presentation

A 71-year-old man with moderate non-proliferative diabetic retinopathy (NPDR) and macular oedema, previously treated with intravitreal ranibizumab, underwent left eye phacoemulsification complicated by posterior capsule rupture during fragment removal. An anterior chamber intraocular lens (ACIOL) was implanted following anterior vitrectomy. On postoperative day 7, his intraocular pressure (IOP) was elevated at 25 mmHg with corneal haze, anterior chamber cells (2+), and a small retained nuclear fragment was observed near the pupil. He was started on 4-hourly topical steroids, antibiotics, and antiglaucoma drops including oral prednisolone 40 mg (0.5 mg /kg/day) in tapering dose.

One month after cataract surgery, the patient presented with left eye redness and a curtain-like visual defect, with a visual acuity of counting fingers (CF), and not improved with pinhole. Examination revealed granulomatous anterior uveitis with mutton-fat keratic precipitates, vitreous haze, and sclerosed retinal vessels. A series of blood investigations, including full blood count, renal profile, Venereal Disease Research Laboratory (VDRL) test, antinuclear antibody (ANA), rheumatoid factor, chest X-ray, and Mantoux test, were performed to exclude infectious and autoimmune causes, all of which yielded unremarkable results. A retained lens fragment was noted behind the anterior chamber intraocular lens (ACIOL), and a diagnosis of phacoanaphylactic endophthalmitis was made. Pars plana vitrectomy (PPV), lensectomy, and anterior chamber washout were performed, revealing dense vitritis, retained nuclear material within the vitreous cavity and at the ciliary body, vitreous haemorrhage, and a retinal tear with surrounding scarring. Cryotherapy and 360-degree endolaser were applied. Postoperatively, the patient was restarted on high-dose oral corticosteroids (40 mg, 0.5 mg/kg/day) with a tapering regimen to control postoperative inflammation and prevent reactivation of immune-mediated uveitis following surgical removal of the retained lens material. On postoperative day 1 following PPV, lensectomy, and anterior chamber washout (Fig. 1A, 1B), the findings were similar to those observed preoperatively. One week later, the vision improved to 6/60 (pinhole 6/24), with resolution of anterior uveitis and keratic precipitates (Fig. 1C). Left eye funduscopic examination showed a pink optic disc, improved sclerosed vessels, and visible laser marks (Fig. 1D). This case highlights a classic course of PE with anterior and posterior segment involvement in a diabetic eye. The delayed onset, granulomatous inflammation, and retained lens material support the diagnosis. However, definitive management would require surgical removal of all lens fragments.

Discussion

Phacoanaphylactic endophthalmitis is often misdiagnosed with infectious endophthalmitis, iritis, and sympathetic ophthalmitis [6]. Diabetic patients, especially those with diabetic retinopathy, are at an increased risk of postoperative inflammation and macular oedema, which can further complicate the diagnosis and

management of phacoanaphylactic endophthalmitis. In such patients, differentiating phacoanaphylactic endophthalmitis from infectious or non-infectious uveitis is crucial to guiding appropriate treatment strategies. Diabetes mellitus causes chronic microvascular breakdown and endothelial dysfunction, which disrupts the blood-aqueous and blood-retina barriers even before surgery. As a result, during or after cataract extraction, inflammatory mediators such as prostaglandins, vascular endothelial growth factor (VEGF), and cytokines can easily penetrate intraocular tissues, amplifying the inflammatory response. This accelerated response predisposes diabetic eyes to a prolonged anterior chamber reaction and an increased risk of cystoid macular oedema (CME) in the postoperative phase [7]. The incidence of phacoanaphylactic endophthalmitis is unclear. [8] The incidence of dropped lens fragments during phacoemulsification is reported to range from 0.3% to 1.8%. With the increasing popularity of phacoemulsification for cataract surgery, the overall number of cases involving retained lens material has consequently risen [9]. Lens fragments may also be retained in the anterior or posterior chambers during seemingly uncomplicated cataract surgery [10]. Ocular inflammation can develop when there is residual cortex after cataract excision, regardless of whether the posterior capsule is intact [4].

This patient, a 71-year-old man with diabetic retinopathy, initially presented with mild anterior segment inflammation and borderline elevated intraocular pressure (IOP) following cataract surgery. The condition subsequently progressed from granulomatous anterior uveitis to panuveitis, with vitreous and retinal vascular involvement. Despite an initial response to topical steroids and anti-glaucoma medications, the persistence of inflammation led to further evaluation and surgical intervention. The presence of a retained nuclear fragment raised suspicion of a phacogenic inflammatory response. A crucial diagnostic clue was the progression to granulomatous anterior uveitis with posterior segment involvement (vasculitis and vitritis). The delayed onset of symptoms, history of a complicated surgery, and presence of retained lens material helped distinguish PE from infectious endophthalmitis, which typically presents more acutely with severe pain, hypopyon, and more fulminant inflammation. The most definitive treatment for lens-related uveitis is to remove inflammatory cells and lens fragments within the anterior chamber or vitreous by anterior chamber irrigation or vitrectomy [9]. Early diagnosis and timely treatment typically result in a positive visual outcome. Untreated chronic intraocular inflammation carries a poor prognosis due to multiple complications, including corneal oedema, endothelial damage secondary to uveitis, rubeosis iridis, secondary glaucoma, cystoid macular oedema, vitreous traction bands, retinal vasculitis, and, in severe cases, phthisis bulbi [9]. In the published case reports [2 -4, 6, 8-10], the most frequently observed presentations comprised anterior chamber inflammation accompanied by hypopyon, ocular discomfort, and diminished visual acuity, characteristics that could closely resemble infectious endophthalmitis, thus complicating the initial clinical assessment [2, 8]. This overlap frequently required meticulous diagnostic evaluation, which included anterior chamber tap or cytological analysis, to differentiate sterile phacoanaphylactic inflammation from genuine infection [3, 4]. The initial management outlined in most reports highlighted the aggressive control of intraocular inflammation through the use of topical or systemic corticosteroids, along with the reduction of intraocular pressure utilizing aqueous suppressants, aimed at minimizing structural damage and preserving visual potential [2, 3, 6]. Surgical intervention, particularly the extraction of residual or disrupted lens material, was reserved for instances where inflammation continued despite medical treatment or when retained cortical or nuclear fragments were distinctly identified [2, 9]. The outcomes reported across these cases were generally positive when recognition was prompt and both medical and

surgical interventions were implemented in a timely manner, often leading to significant visual recovery [2, 8]. In contrast, outcomes were unfavourable in cases that were delayed or unsuspected, especially those linked with long-standing retained lens material, where irreversible ocular damage and even enucleation were documented [9]. These findings highlight the critical importance of early clinical suspicion, timely differentiation from infectious endophthalmitis, and the definitive removal of antigenic lens proteins to optimize prognosis [2, 3].

Conclusion

Phacoanaphylactic endophthalmitis should be addressed if intraocular inflammation persists or worsens after cataract surgery, particularly if there are posterior capsule rupture or residual lens fragments. PE differs from infectious endophthalmitis in that it develops gradually with granulomatous uveitis, vitritis, and vasculitis rather than immediately with severe pain, hypopyon, and purulent inflammation. While corticosteroids and intraocular pressure control may be beneficial, definitive treatment frequently necessitates pars plana vitrectomy (PPV) and anterior chamber washing to remove residual lens material. Diabetic patients are at higher risk of postoperative inflammation and macular oedema, therefore early identification and appropriate care are critical to preventing vision loss.

Ethical considerations

Consent was obtained or waived by all participants in this study.

Conflicts of interest

In compliance with the ICMJE uniform disclosure form, all authors declare the following

Funding info

All authors have declared that no financial support was received from any organization for the submitted work.

Financial relationships

All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work.

Other relationships

All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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Authors' contributions

L.K.A. was responsible for collecting the clinical information, performing the literature review, preparing the images, and drafting the manuscript. K.A.I. and Z.A.R. provided clinical guidance, critically revised the manuscript, and provided overall supervision. All authors read and approved the final manuscript.

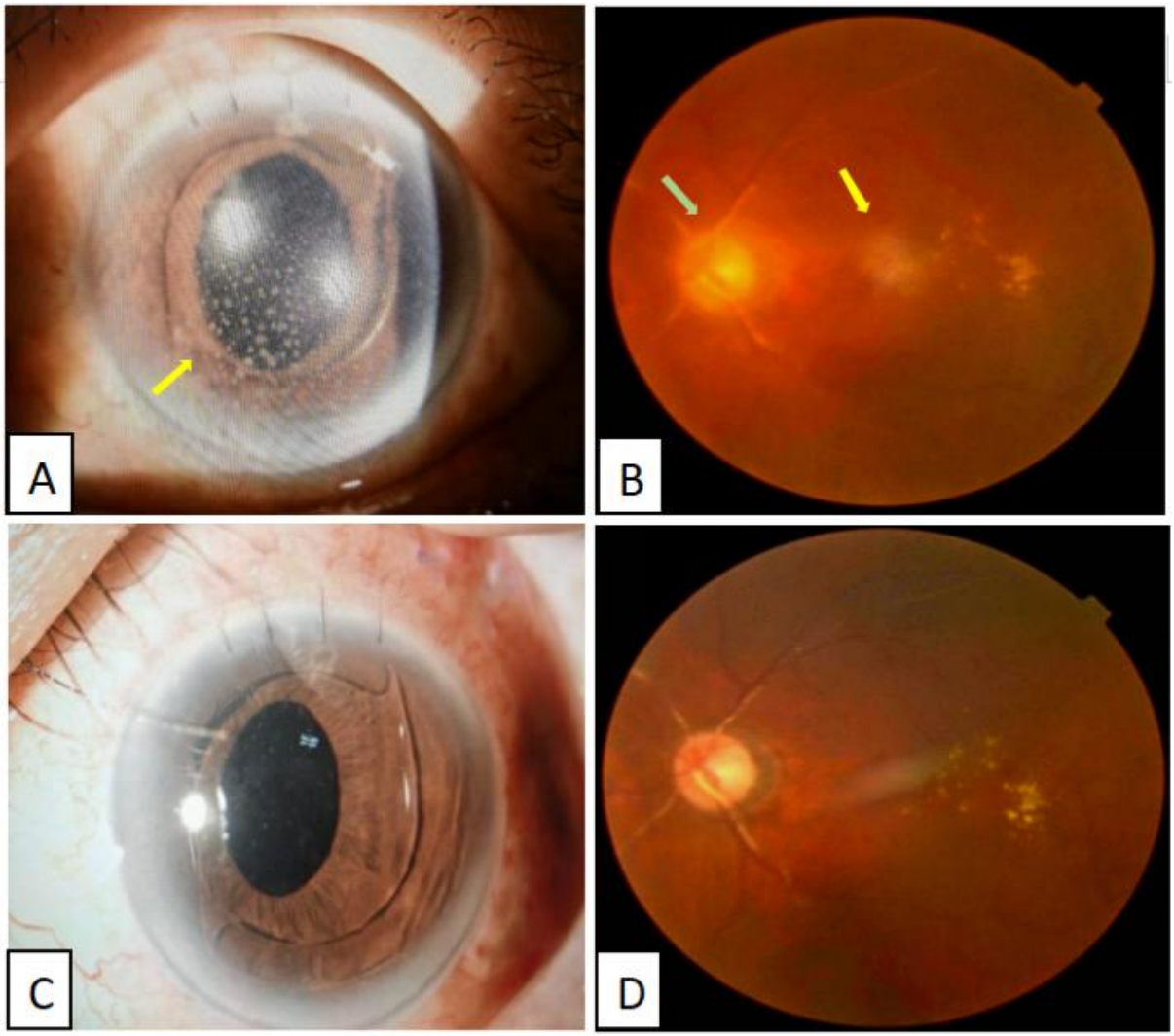

Figure 1. Multimodal images of the patient with postoperative left eye pars plana vitrectomy (PPV), lensectomy, and anterior chamber (AC) washout.
Day 1: (A) Slit-lamp photograph showing multiple keratic precipitates (yellow arrow) and corneal haze following PPV, lensectomy, and AC washout.
(B) Widefield fundus photograph demonstrating an indistinct optic disc (green arrow) with extensive exudates (yellow arrow) and diffuse retinal involvement.
Day 7: (C) Slit-lamp photograph showing improved corneal clarity with complete resolution of keratic precipitates.
(D) Widefield fundus photograph showing a clearer view of the optic disc and retinal details, indicating partial resolution of the inflammatory process.

References

[1]. Phacoanaphylactic endophthalmitis - EyeWiki [Internet]. 2024 Nov 12 [cited 2024 Nov 12]. Available from: https://eyewiki.org/Phacoanaphylactic_Endophthalmitis

[2]. Marak GE. Phacoanaphylactic endophthalmitis. Surv Ophthalmol. 1992;36(5):325–39. doi:10.1016/0039-6257(92)90109-7

[3]. Sridhar U, Tripathy K. Lens-induced inflammation. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 [cited 2022 Feb 8]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK576439

[4]. Kalogeropoulos C, Malamou-Mitsi V, Asproudis I, Psilas K. The contribution of aqueous humor cytology in the differential diagnosis of anterior uvea inflammations. Ocul Immunol Inflamm. 2004;12(3):215–25. doi:10.1080/092739490500165

[5]. Rao NA, Nerenberg AV, Foster DJ. Torulopsis Candida (Candida formata) endophthalmitis stimulating Propionibacterium acnes syndrome. Arch Ophthalmol. 1991;109(12):1718–24

[6]. Castellanos MJ. Endophthalmitis: background, pathophysiology, epidemiology [Internet]. [cited 2024 Nov 12]. https[10]

[7]. Cheema RA, Al-Mubarak MM, Amin YM, Cheema MA. Role of combined cataract surgery and intravitreal bevacizumab injection in preventing progression of diabetic retinopathy. Journal of Cataract & Refractive Surgery. 2009 Jan;35(1):18–25. ://emedicine.medscape.com/article/799431-overview

[8]. Kim JH, Yoo WS, Kong MG, Han YS, Kim SJ. A case of phacoanaphylactic uveitis presenting as endophthalmitis. J Korean Ophthalmol Soc. 2016;57(9):1480. doi:10.3341/jkos.2016.57.9.1480

[9]. Rao S, Murthy S, Geethamala K. An unsuspected case of lens-induced uveitis: a case report. J Clin Ophthalmol Res [Internet]. 2015 [cited 2025 Mar 21];3(2):100. Available from: https://journals.lww.com/jcor/pages/articleviewer.aspx?year=2015&issue=0.020&article=00009&type=Fulltext

[10]. Sridhar U, Tripathy K. Lens-induced inflammation [Internet]. StatPearls Publishing; 2023 [cited 2025 Mar 21]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK

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