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RUMC INTERNATIONAL
MEDICAL RESEARCH
CONFERENCE

2ND RUMC INTERNATIONAL MEDICAL RESEARCH CONFERENCE (RIMRC 2025)

29TH NOVEMBER 2025

INNOVATION AND PROGRESS IN MEDICAL SCIENCE

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Extended Abstracts



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RCSI
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Foreword from



President & CEO RCSI & UCD Malaysia Campus

Distinguished Keynote Speakers, esteemed colleagues, researchers, clinicians, students, ladies and gentlemen,

It is a profound pleasure to welcome you to the 2nd RUMC International Medical Research Conference (RIMRC 2025). As President of RCSI & UCD Malaysia Campus (RUMC), I am delighted that we can host this premier, face-to-face platform for intellectual exchange and collaboration.

Our theme, “*Innovation and Progress in Medical Science*,” perfectly captures the spirit of this event. This conference is a vital opportunity to showcase cutting-edge advancements and highlight the innovations that are truly shaping the future of healthcare. We are here to explore breakthroughs across clinical and translational research, precision medicine, and regenerative medicine.

I wish all participants, especially our early-career researchers and students, a successful and inspiring day of presentations and networking. I encourage you to seize this opportunity to foster interdisciplinary collaboration and explore the global impact of your work.

Thank you.

Professor Dr. Karen Morgan
President & CEO,
RCSI & UCD Malaysia Campus (RUMC)

Foreword from



Dean

RCSI & UCD Malaysia Campus

To our respected Keynote Speakers, the Organising and Scientific Committees, dedicated researchers, students, and all participants,

As the Dean of RCSI & UCD Malaysia Campus (RUMC), I extend a warm welcome to everyone attending the 2nd RUMC International Medical Research Conference (RIMRC 2025).

This conference is a testament to RUMC's commitment to academic excellence and research discovery. Our objectives are clear: to highlight groundbreaking research in medical and biomedical sciences and to provide a robust platform for presenters to share their work and exchange knowledge.

Today, we will explore a wide scope of research structured into three major pillars: Non-Clinical Research Areas, Clinical Research Areas, and Biomedical Research Areas. The breadth of these topics reflects the dynamic nature of our field, covering everything from drug discovery and pharmacology to advancements in personalised medicine and targeted therapies.

I am especially looking forward to the oral and poster presentations by our undergraduate and postgraduate students, which form a core component of today's scientific programme. May this conference be filled with insightful discussions, meaningful connections, and new collaborations that further the progress of medical science.

Thank you.

Professor Dato' Dr. Abdul Rashid Khan
Dean,
RCSI & UCD Malaysia Campus (RUMC)

Welcoming Message from

Chairman of RIMRC 2025

RUMC Vice Dean of Research



It is my great pleasure to welcome all esteemed speakers, members of the faculty, researchers, and students to the RIMRC 2025.

This year's theme, "*Innovation and Progress in Medical Science*", reflects our commitment to advancing knowledge and embracing emerging frontiers in healthcare. The Scientific Committee has meticulously curated a programme designed to inspire, challenge, and showcase the breadth of contemporary medical research.

RIMRC 2025 features keynote lectures alongside parallel oral and poster presentations held across three lecture theatres. The research presented spans several pivotal areas, including artificial intelligence and big data in healthcare, regenerative medicine, and immunology and vaccine development. We aim to foster an enriching environment where ideas can be exchanged, debated, and refined.

We extend our best wishes to all presenters. Awards will be presented across six categories, recognising excellence in both clinical and non-clinical oral and poster presentations.

Thank you for contributing your work to this conference.

Dr. Gobinath Ramachawolran
Chairman of RIMRC 2025
Vice Dean of Research
RCSI & UCD Malaysia Campus (RUMC)

KEYNOTE SPEAKER 1

Professor Dr. Michael P. Keane

*Professor of Medicine and Therapeutics
University College Dublin (UCD), Dublin, Ireland*



Professor Keane is a distinguished respiratory physician who is a fellow of the Royal Colleges of Physicians of Ireland and London as well as American College of Chest Physicians. His long association with University College Dublin began as a medical student, and has culminated in his appointment as Professor of Medicine and Therapeutics, as well as Principal of the College of Health and Agriculture Science. He was also formerly Dean of Medicine and Head of the School of Medicine. His other notable academic appointments have been at University of Michigan Medical Center and University College Los Angeles.

Professor Keane's widespread research interests include the biology of idiopathic pulmonary fibrosis, the function and regulation of IL-13 receptors, regulation of fibrocytes differentiation and the potential of mesenchymal cells to attenuate fibrosis. He has authored over 25 book chapters as well as 160 peer reviewed papers in relation to respiratory disease. He is a reviewer with numerous prestigious international journals including American Journal of Respiratory and Critical Care Medicine, and is an Associate Editor for Journal of Immunology.

KEYNOTE SPEAKER 2

Dr. Yoon Chee Kin

*Acute Medicine Physician
Head of Acute Medicine
Head of Clinical Research Centre (CRC)
Pulau Pinang Hospital*



One of Penang Medical College's earliest graduates, Dr Chee Kin is an Advanced Acute Internal Medicine specialist in Hospital Pulau Pinang. He is a member of the Royal College of Physicians of Ireland and the United Kingdom and is vice-president of the Malaysian Advanced Acute Internal Medicine Ultrasound Society. Dr Chee Kin actively participates in a broad range of undergraduate and postgraduate medical training. He is a supervisor for Masters programs in both internal medicine and family medicine, including the Malaysia-Ireland Training Programme for Family Medicine (or MInTFM) based in RUMC. He sits on multiple committees within HPP and nationally, including the National Curriculum for Specialist Training in Internal Medicine and National Committee for Resuscitation Training.

Dr Chee Kin is head of HPP's Clinical Research Centre which coordinates and oversees the hospital's major studies. His research interests include a wide range of conditions within internal medicine including asthma, diabetes mellitus and infectious diseases. He has helped many recent clinical practice guidelines in Malaysia, including for asthma, Hepatitis B and systemic lupus erythematosus.

KEYNOTE SPEAKER 3

Professor Dr. Manickam Ravichandran

Chief Scientific Officer at Mygenome



Prof Manickam is an accomplished microbiologist and biotechnologist from Tamil Nadu, India whose who is currently Chief Scientific Officer in Mygenome, a biotechnology firm that specialises in precision genomic medicine. He was previously the Chief Executive and Vice Chancellor of AIMST, Kedah, as well as its Dean of Faculty of Applied Sciences. He has also been an associate professor for Universiti Sains Malaysia's Department of Microbiology and Parasitology, and was a founding member of its nationally acclaimed Department of Microbiology and Parasitology.

Prof Manickam's extensive list of journal and book publications encompass both his major career paths. These are particularly in the areas of treatment for lymphatic filariasis, detection of methicillin-resistant *Staphylococcus aureus* and cholera vaccine development. He has been a dedicated supporter of student research, including supervising over 100 postgraduate studies and theses in multiple institutions. His research projects have won 50 international awards over decades in multiple countries. Among the more recent ones is a Gold Medal at the International Invention, Innovation and Technology Exhibition in 2019, related to a thermostable prototype for a live cholera vaccine.

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UC1

HUMAN RIGHTS AND VULNERABLE GROUP INCLUSION IN NATIONAL HIV/AIDS STRATEGIES: A COMPARATIVE EQUIFRAME ANALYSIS OF MALAYSIA'S PAST AND CURRENT APPROACHES

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Abstract

Background: Malaysia's HIV response has advanced through policy reforms, yet gaps remain in integrating rights-based and inclusive approaches. Stronger protection of key populations is needed to ensure equitable access, address stigma, and improve health outcomes.

Aim: To assess how human rights principles, equity, and inclusion are integrated in Malaysia's past and current national HIV strategies using the EquiFrame framework, and to identify gaps to guide future policy development.

Methods: Using the EquiFrame framework, we analyzed Malaysia's National Strategic Plan for Ending AIDS 2016–2030 and the National Strategic Plan on HIV and AIDS 2011–2015. NVivo-12 was used to code the documents for 21 core concepts and 14 vulnerable groups. Analysis focused on core concept presence, vulnerable group coverage, and quality of commitment—reflecting whether policies outlined actions or mechanisms for monitoring—culminating in an overall summary ranking.

Results: The National Strategic Plan on HIV and AIDS 2011–2015 demonstrated coverage of 76% of core concepts and 50% of vulnerable groups, with a quality rating of 48%, resulting in a moderate overall ranking. The National Strategic Plan for Ending AIDS 2016–2030 addressed 81% of core concepts, 50% of vulnerable groups, and achieved a 57% quality rating, therefore attaining a high overall ranking. Despite this improvement, both strategies continued to show limited inclusion of several vulnerable populations. Quality ratings indicate insufficient inclusion of actions or monitoring intentions for several core concepts.

Conclusion: Our study highlights the urgent need for inclusive, rights-based HIV policies in Malaysia to ensure equity, participation, and accountability for all vulnerable populations.

Keywords: *HIV policy, human rights, health equity, vulnerable populations, Malaysia, rights-based approach*

INTRODUCTION

Health is recognized globally as a fundamental human right, as affirmed in the World Health Organization's Constitution and numerous international treaties. Malaysia's HIV response has evolved through significant policy efforts, including the expansion of harm reduction programs and collaboration with civil society. However, persistent structural barriers and stigma continue to limit equitable access to services for key populations such as people who use drugs, sex workers, men who have sex with men, transgender individuals, migrants, and refugees. The 2014 report of the UN Special Rapporteurs on the Right to Health highlighted ongoing discrimination and selective application of rights protections, underscoring the need for more comprehensive, inclusive, and rights-based HIV policies [1]. Ensuring that national HIV strategies meaningfully address human rights is critical not only to upholding ethical and legal commitments, but also to achieving effective epidemic control through improved engagement, retention, and treatment outcomes.

This study applies the EquiFrame framework to assess the extent to which Malaysia's past and current national HIV strategic plans incorporate principles of human rights, equity, and inclusion of vulnerable groups. By systematically assessing the presence, coverage, and quality of commitments to key populations and core rights concepts, this research identifies strengths, gaps, and areas requiring policy attention. The relevance of this study aligns with ongoing public health priorities and regional calls for health systems that promote dignity, inclusivity, and access for marginalized communities. The findings offer guidance to support a more equitable and rights-based national HIV response in Malaysia, contributing to broader goals of ending AIDS as a public health threat while ensuring that no population is left behind.

OBJECTIVES

1. To assess the inclusion of core concepts of human rights and vulnerable groups in the National Strategic Plan on HIV and AIDS 2011–2015 and the National Strategic Plan for Ending AIDS 2016–2030.
2. To provide an objective assessment of the policies' quality in terms of core concept presence, vulnerable group coverage, and core concept quality ratings.
3. To generate actionable insights from the policy analysis, directing attention to areas requiring improvement for the formulation of more inclusive and effective HIV policies and strategies in Malaysia.

METHODOLOGY

This study employed the EquiFrame policy analysis framework to assess the extent to which Malaysia's national HIV strategies incorporate human rights principles and target key affected populations. The analysis focused on two national policy documents, the National Strategic Plan on HIV and AIDS 2011–2015 and the National Strategic Plan for Ending AIDS 2016–2030.

EquiFrame comprises 21 core concepts and 12 vulnerable groups. In this study, all 21 core concepts were retained without modification. However, as the framework allows contextual adaptation, the list of vulnerable groups was reviewed and revised to reflect those most relevant to Malaysia's HIV context. Two groups (female-headed households and children with special needs) were removed due to minimal direct relevance, and four key affected populations (sex workers, gender-diverse communities, prisoners, and people who inject drugs) were added. This resulted in a final set of 14 vulnerable groups used in the analysis.

NVivo 12 was used to code and organize the policy documents. A systematic coding framework was developed based on the 21 core concepts and the 14 vulnerable groups identified. Both HIV strategic plans were reviewed in full, and codes were assigned where core concepts and group-specific references appeared. To facilitate data management, the coded information was then structured into a data extraction matrix, with core concepts listed vertically and vulnerable groups listed horizontally. This allowed for a clear comparison of how each core concept was addressed across different population groups within the policies.

Each core concept was assigned a score from 1 to 4 to reflect the level of policy commitment, where 1 indicated that the concept was mentioned, 2 indicated that the concept was described, 3 indicated that a specific policy action was identified, and 4 indicated a stated intention for monitoring or evaluation. Concepts framed as applying to the general population were recorded as universal. Three summary indices were calculated for each policy. Core Concept Coverage (CC%) reflected the proportion of the 21 concepts referenced. Vulnerable Group Coverage (VG%) reflected the proportion of the 14 identified groups addressed. Core Concept Quality (CCQ%) reflected the proportion of core concepts that scored 3 or 4. Each policy was then assigned an overall ranking: High if it scored at least 50% in all three indices, Moderate if it scored at least 50% in two indices, and Low if it scored below 50% in two or more indices.

MAIN RESULTS

Policy	VG%	CC%	% CC Quality (3-4)	Overall Ranking
National Strategic Plan on HIV and AIDS 2011–2015	50	76	48	Moderate
National Strategic Plan for Ending AIDS 2016–2030	50	81	57	High

Table 1. EquiFrame Summary Indices: National Strategic Plan on HIV and AIDS 2011–2015 and National Strategic Plan for Ending AIDS 2016–2030

The EquiFrame analysis findings for the National Strategic Plan on HIV and AIDS 2011–2015 and the National Strategic Plan for Ending AIDS 2016–2030 are summarized in Table 1. The 2011–2015 plan addressed 16 of the 21 core concepts (76%), with recurring emphasis on access, non-discrimination, prevention, and individualized services. However, concepts such as participation, entitlement, and accountability were limited and rarely supported by specific policy actions. The 2016–2030 plan addressed 17 of the 21 core concepts (81%), again emphasizing access and non-discrimination, while concepts such as privacy, liberty, and family support appeared absent or were broadly stated.

Both policies referenced 7 of the 14 identified vulnerable groups (50%). People who inject drugs, prisoners, sex workers, and gender diverse communities received consistent policy attention. However, several groups, including ethnic minorities, refugees and stateless persons, migrants, and rural populations, were only minimally addressed or not mentioned, indicating notable gaps in inclusivity.

The quality score for the 2011–2015 plan was 48%, indicating that although core concepts were referenced, they were not consistently supported by defined implementation steps or monitoring mechanisms. The 2016–2030 plan demonstrated a higher quality score of 57%, showing some improvement in operational commitment. However, many core concepts continued to lack clear accountability or evaluation pathways.

Taken together, the 2011–2015 plan received a moderate overall ranking, while the 2016–2030 plan achieved a high overall ranking.

DISCUSSION

The analysis indicates that although both national HIV strategies incorporated a wide range of human rights concepts, several key principles and vulnerable populations were insufficiently addressed. Concepts such as participation, privacy, entitlement, and accountability were referenced inconsistently and rarely accompanied by concrete plans for

implementation or monitoring. These concepts are central to ensuring meaningful involvement in care, protection of confidentiality, and clearly defined responsibility within service delivery. Their limited presence suggests that rights-based commitments were not fully implemented in either policy.

The 2016–2030 plan demonstrated a moderate improvement in both core concept coverage and quality compared to the 2011–2015 plan, indicating clearer articulation of commitments. However, rather than expanding the scope of rights-based principles, the newer strategy primarily built on the earlier framework. While it placed greater emphasis on operationalisation and monitoring, the range of rights concepts addressed remained largely the same, reflecting refinement of structure rather than broadening of commitments.

Vulnerable group coverage remained unchanged at 50 percent across both policies. Consistent attention to people who inject drugs, prisoners, sex workers, and gender diverse communities reflects established epidemiological priorities. However, other groups such as migrants, refugees, ethnic minorities, rural communities, and populations experiencing socioeconomic disadvantage were minimally addressed, despite increasing evidence of heightened HIV vulnerability linked to mobility, legal uncertainty, and access barriers. The narrow focus of both strategies suggests that policy inclusion has not evolved in line with changing social contexts and patterns of risk.

While Malaysia has made progress in public health development and law reform, the scope of inclusion within national HIV policy has not expanded to reflect these broader advancements. The continuity of focus across both strategies highlights an opportunity for future policy to adopt a more comprehensive and inclusive approach that strengthens participation, accountability, and equitable access for all populations affected by HIV.

CONCLUSION

This study shows that Malaysia's national HIV strategies incorporate several human rights principles but do not sufficiently operationalize them across all vulnerable and key affected populations. Strengthening future policies will require clearer accountability mechanisms, broader recognition of all groups experiencing disproportionate HIV risk, and structured participation of affected communities to support a more equitable and effective HIV response.

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UC2

Views, Perceptions, and Experiences on the Role of Family Doctors in Malaysia: A Qualitative Study

Lee Onn¹, Cerelia Yoong Yue¹, Kavizha R. Rames¹, Daniel Tai Jun Wen¹,
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Abstract

Malaysia's dual public-private healthcare system allows patients to access both primary and specialist care without referral, promoting flexibility but leading to fragmented care and "doctor shopping." This study explored Malaysians' views, perceptions, and experiences regarding the role of a family doctor to inform future primary care reform. A qualitative grounded theory approach was employed. Semi-structured interviews and small focus groups were conducted with participants from diverse demographic and healthcare backgrounds across both sectors. Data were analysed thematically using an inductive approach, guided by Andersen's Behavioural Model and the Health Belief Model. A total of 23 participants were interviewed. Four major themes emerged: (1) Pragmatic navigation—provider choice was based on convenience, cost, and illness severity; (2) Trust and relational continuity—communication and empathy were key to sustained engagement; (3) Family and social influence—healthcare decisions were shaped by family norms and social recommendations; and (4) Fragmented continuity and parallel care pathways—insurance, employment, and public-private divides disrupted long-term relationships. Participants valued trust and familiarity with doctors but navigated the healthcare system pragmatically. Structural fragmentation, sociocultural norms, and financing barriers limited continuity. Strengthening Malaysia's family doctor system requires structured patient registration, integration of private general practitioners, shared electronic medical records, and public education to promote coordinated, continuous care.

Keywords: *Family doctor, primary care, qualitative study, Malaysia*

1. INTRODUCTION

Malaysia's healthcare operates without a formal gatekeeping or registration system, allowing patients to move freely between public and private providers. This unrestricted access fosters convenience but contributes to fragmented care, inconsistent standards, and "doctor shopping" behaviours [1,2]. The Enhanced Primary Healthcare (EnPHC)

programme, introduced in 2017, aimed to strengthen continuity of care through the Family Health Team model [3,6]. However, the extent to which patients understand and value the family doctor concept remains unclear. This study explored the views, perceptions, and experiences of Malaysians toward the role of family doctors to inform future primary care reform within the dual public–private system.

2. OBJECTIVES

To explore how Malaysian patients conceptualise the role of a family doctor and to identify the social, structural, and behavioural factors influencing healthcare-seeking behaviour and continuity of care.

3. METHODOLOGY

This qualitative study employed a grounded theory approach to derive a patient-informed understanding of the family doctor concept. Participants were recruited using purposive sampling to ensure diversity in age, health status, and utilisation of both public and private healthcare. Data were collected through in-depth interviews and small focus groups, conducted either face-to-face or virtually. Interviews were transcribed verbatim and analysed inductively using open and axial coding. Themes were refined through constant comparison until theoretical saturation was achieved. Ethical approval was granted by the RCSI & UCD Malaysia Campus Research Ethics Committee (Approval Number: RUMCEC 09-24-0004-S01)

4. MAIN RESULTS

Twenty-three participants representing a range of healthcare experiences were interviewed. Four major themes emerged:

1. Pragmatic navigation of the healthcare system – provider choice was guided by convenience, cost, and illness severity rather than continuity.
2. Trust and relational continuity – empathy, good communication, and familiarity fostered loyalty, while negative encounters triggered “doctor hopping.”
3. Family and social influence – healthcare decisions were strongly shaped by family norms, intergenerational continuity, and social recommendations.
4. Fragmented continuity and parallel care pathways – employment-linked insurance, systemic inefficiencies, and public–private divides disrupted long-term relationships, producing parallel streams of care.

5. DISCUSSION

Patients in Malaysia view healthcare as a pragmatic choice shaped by access and affordability rather than relational loyalty. Continuity, while valued, is undermined by structural fragmentation and socio-cultural norms. These findings mirror international patterns observed in Hong Kong and Italy, where system design alone could not drive relational continuity without addressing patient behaviour and trust [4,5]. The study reinforces the importance of trust-based relationships and interpersonal quality as prerequisites for the success of reforms like the Health White Paper [7].

6. CONCLUSION

For Malaysia's family doctor model to succeed, reforms must integrate private general practitioners, implement structured patient registration, and enhance continuity through shared electronic medical records. Building patient trust through communication, empathy, and public education will be critical for fostering sustained, coordinated primary care.

7. ACKNOWLEDGEMENT

This research was conducted as part of the undergraduate research module under the supervision of Associate Professor Dr. Chean Kooi Yau, Department of Family Medicine, RCSI & UCD Malaysia Campus.

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Aetiology of Bone Sarcomas Among Individuals Aged 0–24 Years, 2009–2025: Updated Evidence Synthesis with New Pooled Estimates

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Abstract

This narrative review synthesises evidence from 2009–2025 on the aetiology and incidence of paediatric bone sarcomas (osteosarcoma, Ewing sarcoma) in individuals aged 0–24 years. Searches of MEDLINE, Embase, and Web of Science identified 1,698 records; after screening and full-text assessment, 37 studies met inclusion criteria. Findings were organised into eight aetiological domains spanning genetic, developmental, and environmental factors. The most consistent signals were observed for germline TP53 (Li–Fraumeni) and RB1-related syndromes [1], taller stature and genetic height liability, and congenital hernia associations with Ewing sarcoma [3]. Descriptive incidence analyses using Cancer Incidence in Five Continents Plus (CI5-Plus; 1983–2017) showed a reproducible adolescent peak and male predominance across registries [5]. Overall, the evidence suggests that growth-related biology and inherited susceptibility, rather than time-varying environmental exposures, predominate in the aetiology of early-onset bone sarcomas; environmental exposures show no consistent association in larger population-based analyses (e.g., community fluoride) [4].

Keywords: *Osteosarcoma, Ewing sarcoma, Aetiology, Epidemiology, CI5-Plus*

1. INTRODUCTION

Primary malignant bone tumours such as osteosarcoma and Ewing sarcoma account for a small fraction of paediatric cancers but exhibit distinct developmental and epidemiological signatures. Understanding their aetiology requires integrating genetic predisposition with early-life exposures and growth dynamics.

2. OBJECTIVES

To update the evidence base for paediatric and young-adult bone-tumour aetiology since 2009, summarise consistent risk factors, and contextualise findings with global incidence trends.

3. METHODOLOGY

Structured searches were conducted in MEDLINE, Embase, and Web of Science (1 Jan 2009 – 1 Jul 2025) for English-language or official English translations were eligible. human studies on osteosarcoma, Ewing sarcoma, or primary bone tumours in individuals aged 0–24 years. Eligible designs included case–control, cohort, registry-linkage, and Mendelian-randomisation studies. Data were extracted by two reviewers and synthesised narratively across eight aetiological domains.

4. MAIN RESULTS

In those aged 0–24 years, inherited predisposition explains a minority of cases: germline TP53 occurs in ~9–10% of unselected young-onset osteosarcoma (OS), while RB1 and rare helicase syndromes together account for <2%; no reproducible common-variant effects of material size have been consistently replicated [5]. Growth-related factors show the most consistent association with OS: compared with ≤ 50 th percentile height, risk is higher at the 51st–89th percentile (OR ≈ 1.35) and at ≥ 90 th (OR ≈ 2.60) [1]. Mendelian randomisation supports a modest causal effect per 1 SD of polygenic height (OR ≈ 1.10 for both adult and childhood height, independent in joint models) [3]. Ewing sarcoma (ES) shows only a minimal mean height difference [1].

For ES, congenital hernias are positively associated (inguinal OR ≈ 1.27 ; diaphragmatic OR ≈ 2.27) and are not observed for OS [4,5]. Large, well-designed studies report no reproducible association with community water fluoride, and pesticide evidence remains heterogeneous without a stable bone-tumour-specific signal [5]. Across registries, CI5-Plus demonstrates a reproducible adolescent peak with male excess, consistent with growth-related mechanisms rather than major time-varying environmental drivers [2,6].

5. DISCUSSION

Findings indicate that bone-sarcoma risk reflects intrinsic growth and genetic susceptibility rather than modifiable environmental exposures. The reproducibility of adolescent peaks and sex differences supports a biological model linked to pubertal skeletal development. Integrating genomic and epidemiological data remains crucial to clarifying causal mechanisms.

6. CONCLUSION

Paediatric bone-sarcoma aetiology is driven primarily by genetic and developmental factors. Cross-registry incidence consistency reinforces the central role of growth-related biology over environmental variability.

7. ACKNOWLEDGEMENT

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UC4

KNOWLEDGE, AWARENESS, AND PERCEPTION TOWARDS GENERIC MEDICINES AMONG MEDICAL AND PHARMACY STUDENTS AT A PRIVATE UNIVERSITY IN KEDAH

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Abstract

Generic medicines are essential for improving access to affordable healthcare by providing therapeutically equivalent alternatives to branded drugs. However, misconceptions regarding their quality, safety, and effectiveness remain, especially among future healthcare professionals. This study assessed the knowledge, awareness, and perception (KAP) of generic medicines among medical and pharmacy undergraduate students at AIMST University, Kedah, Malaysia. A cross-sectional survey was conducted from April to June 2025 using a validated online questionnaire distributed via Google Forms. A total of 292 students (166 pharmacy, 126 medical) participated. The questionnaire included multiple-choice items and Likert scales. Data were analyzed with SPSS Version 27 applying descriptive statistics, Chi-square, and Mann-Whitney U tests, with significance set at $p < 0.05$. Most students showed high knowledge about bioequivalence, API content, and regulatory requirements of generics, but misconceptions persisted about the need for preclinical trials and potential side effects. Pharmacy students scored slightly higher than medical students, though the difference was not significant overall ($p > 0.05$), except for dosage uniformity ($p = 0.027$) and clinical testing requirements ($p = 0.002$). Both groups exhibited positive awareness and perception of generic medicines, recognizing their affordability and clinical value. The findings highlight the need to strengthen educational components on generic medicines, particularly focusing on regulatory science, safety, and clinical application. Integrating structured modules and interprofessional learning could enhance prescribing confidence, patient counselling, and public trust in generics within Malaysia's healthcare system.

Keywords: *Generic medicines, healthcare students, knowledge, awareness, perception*

1. INTRODUCTION

The increasing global emphasis on cost-effective healthcare has positioned generic medicines as a key strategy to enhance access to affordable treatment. Despite their proven bioequivalence, safety, and therapeutic effectiveness compared to branded drugs,

misconceptions and hesitancy toward their use remain prevalent among healthcare professionals and the public. Understanding how future healthcare providers (medical and pharmacy undergraduate students) perceive, understand, and respond to generic medicines is crucial, as these students will soon assume roles that directly influence prescribing, dispensing, and patient education practices. Unfortunately, previous studies have primarily focused on practicing doctors and pharmacists rather than on medical and pharmacy students. This distinction is critical because, while licensed professionals already influence medication use, students represent the next generation of healthcare providers whose knowledge and attitudes are still developing and can be shaped through education. Their understanding of generic medicines will significantly impact future efforts in promoting safe, cost-effective prescribing and patient trust. This study addresses the existing gap by evaluating and comparing the knowledge, awareness, and perception (KAP) of medical and pharmacy undergraduate students toward generic and brand-name medicines, identifying specific areas of misunderstanding or limited awareness.

Their preparedness directly reflects the progress and innovation within medical science education. By focusing on this group, the study identifies educational gaps related to generic medicines that may affect future clinical practice. The findings highlight the need to strengthen university curricula in Malaysia by integrating more comprehensive content on generics, aligning with the conference theme of “Innovation and Progress in Medical Science” through advancing pharmaceutical education and promoting evidence-based, cost-effective healthcare delivery.

2. OBJECTIVES

General Objective:

To evaluate the KAP toward generic medicines among medical and pharmacy undergraduate students at a Private University in Kedah.

Specific Objectives:

1. To assess the level of KAP among medical and pharmacy undergraduate students regarding the effectiveness, safety, and quality of generic medicines compared to brand-name drugs.
2. To compare the differences in KAP toward generic medicines between medical and pharmacy undergraduate students.
3. To assess the self-reported confidence of medical and pharmacy undergraduate students regarding the use and dispensing of generic medicines in clinical practice.

3. METHODOLOGY

This cross-sectional, questionnaire-based study was conducted from April to June 2025 among medical and pharmacy undergraduate students at AIMST University, Kedah, Malaysia, to assess their KAP toward generic medicines. Data were collected using a validated, self-administered online questionnaire developed in Google Forms and distributed via WhatsApp and in-person recruitment. Participation was voluntary, with informed consent obtained prior to completion. Convenience sampling was used to recruit eligible students aged 18 years and above who were enrolled in Bachelor of Pharmacy (Honours) or Bachelor of Medicine and Bachelor of Surgery (MBBS) programs during the 2024/2025 academic session. The questionnaire consisted of four sections: demographic details, knowledge (10 items), awareness (9 items), and perception (10 items), adapted from previous validated studies. Responses were measured using both dichotomous (Yes/No/Not Sure) and five-point Likert scales.

A pilot study involving 30 participants was conducted to evaluate the instrument's clarity and reliability, with those respondents excluded from the final analysis. Data were analyzed using SPSS version 27. Descriptive statistics were used to summarize demographic and response data, while the Shapiro-Wilk and Kolmogorov-Smirnov tests were employed to assess normality. Given that the data were non-normally distributed, non-parametric tests were applied. The Chi-Square test was used to determine associations between course of study and KAP levels. Ethical approval was obtained from the AIMST University Human and Animal Ethics Committee (AUHEC/FoP/12/03/2025/14), ensuring participants' confidentiality and the voluntary nature of their participation.

4. MAIN RESULTS

Chi-square test for independence was conducted to assess the association between undergraduate students' course of study (Pharmacy vs. Medical) and their level of knowledge regarding generic and brand-name medicines. This test is appropriate because both variables are categorical in nature - course of study and knowledge level (classified as high, moderate, or low). The Chi-square test compares the observed frequencies of responses across these categories with the expected frequencies that would occur if no relationship existed between the variables. By doing so, it helps determine whether differences in knowledge levels are likely due to chance or are meaningfully associated with the students' academic background. In this study, the resulting *p*-value of 0.125 indicated no significant association, suggesting that the level of knowledge about generic medicines does not differ significantly between medical and pharmacy students.

Figure 1 presents the percentage of respondents' knowledge based on their course of study.

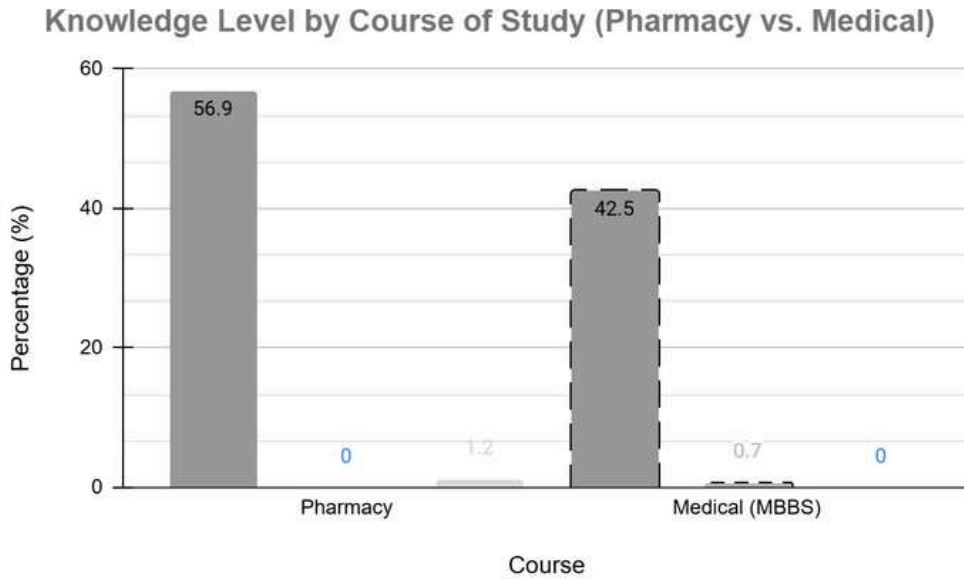


Figure 1: Knowledge Level by Course of Study (Pharmacy vs. Medical)

The Chi-square test results assessing the association between respondents' course of study and their total knowledge level on generic and brand-name medicines, along with individual knowledge domain items, are presented in Table 1. Out of the ten knowledge items analyzed, only two demonstrated statistically significant associations between course of study and knowledge level.

Table 1: Chi-Square Test of Association Between Course of Study and Total Knowledge Level, Including Item-Specific Focus Areas with Significance Values

Pearson Chi - square		Value	p-value
		4.154	0.125
Item	Knowledge Focus Area	p-value	
K1	Bioequivalence	0.292	
K2	API equivalence	0.103	
K3	Dosage uniformity	0.027*	
K4	Safety standards	0.718	
K5	Therapeutic effectiveness	0.384	
K6	Adverse effect similarity	0.178	
K7	Patent and market exclusivity	0.072	
K8	Regulatory requirements - clinical studies	0.002*	
K9	BA/BE regulatory testing	0.079	
K10	Cost-effectiveness	0.735	

* $p < 0.05$ = statistically significant

Since the p-value is greater than the conventional significance level of 0.05, the results do not indicate a statistically significant association between course of study and knowledge level.

5. DISCUSSION

The comparison of knowledge levels between medical and pharmacy undergraduate students revealed no statistically significant association between course of study and knowledge level ($\chi^2 = 4.154$, $p = 0.125$) as shown in Table 1. Overall, both groups demonstrated comparable knowledge of generic and brand-name medicines. However, Figure 1 shows that pharmacy students had a slightly higher proportion of “High” knowledge (56.9%) than medical students (42.5%). This difference, though not significant, may reflect the pharmacy curriculum’s stronger emphasis on pharmaceutical sciences, regulatory guidelines, and pharmacotherapeutics, aligning with Babar and Awaisu (2018), who noted that pharmacists’ education promotes confidence in generics.

More specifically, statistically significant associations were observed for two individual knowledge items in Table 1 namely dosage uniformity ($p = 0.027$) and regulatory requirements for clinical studies ($p = 0.002$). These results are consistent with prior studies showing that pharmacy undergraduate students often outperform their medical counterparts in areas involving technical and regulatory details. Avik et al. (2017) found that while medical undergraduate students generally understood therapeutic equivalence, they lacked knowledge about regulatory processes such as patent expiry and bioequivalence studies. Likewise, Zhao et al. (2021) highlighted that many physicians, and by extension, medical undergraduate students, were unaware of the clinical testing requirements for generics.

For other areas such as API content, safety, and cost, both groups performed similarly, reflecting shared exposure to fundamental pharmacological concepts. These findings, consistent with Davit et al. (2019), indicate that while pharmacy students excel in technical aspects, both disciplines possess a solid foundational understanding. Strengthening regulatory science content in medical programs could help bridge these minor gaps and enhance future clinical practice.

The study highlights the importance of strengthening students’ knowledge and acceptance of generic medicines through curriculum enhancement and interdisciplinary learning. Incorporating topics such as bioequivalence, regulatory standards, cost-effectiveness, and safety early in both medical and pharmacy programs is crucial. Joint workshops, faculty training, and standardized materials can ensure consistent education. Collaboration with health authorities for awareness campaigns and the use of digital learning tools and research opportunities can further improve competence. These initiatives will prepare future healthcare professionals to promote the rational and sustainable use of generic medicines in Malaysia.

6. CONCLUSION

This study found that both medical and pharmacy undergraduate students demonstrated strong overall knowledge and awareness, and positive perceptions toward generic medicines, though minor misconceptions about safety and regulatory aspects persisted. Pharmacy students showed slightly higher knowledge and confidence levels. The results highlight the need for enhanced curriculum content on bioequivalence, regulation, and clinical safety to better prepare future healthcare professionals to advocate for cost-effective generic medicine use.

7. ACKNOWLEDGEMENT

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UC5

Developing Marmoset and Macaque Translational Model to Understand Autism and Social Prediction

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Abstract

Autism Spectrum Disorder (ASD) is a complex neurodevelopmental condition characterized by deficits in communication, social interaction, and adaptive learning. Despite extensive clinical research, the neurobiological mechanisms underlying social prediction remain poorly understood. This study aimed to develop a translational marmoset model to explore associative learning processes that parallel human social prediction in ASD. Four marmosets were trained on stepwise touchscreen tasks of increasing difficulty, and one macaque (Alvar) was used for cross-species comparison. Behavioral responses were recorded during probabilistic reward-based trials where contingency between stimuli and reward shifted dynamically. The Rescorla–Wagner learning model was applied to quantify trial-by-trial learning through prediction-error analysis. Using Sum of Squared Errors (SSE) minimization, optimal learning parameters were determined ($\alpha = 0.462$, $\beta = 0.537$), reflecting balanced attention to cues and sensitivity to rewards. These results indicate a moderate but adaptive learning pattern, mirroring the flexible-yet-imperfect reward prediction often disrupted in ASD. The findings demonstrate that computational modeling can meaningfully interpret behavioral variability in primates, providing a bridge between experimental neuroscience and clinical psychiatry. This pilot work establishes a foundation for future studies integrating behavioral modeling, neural recording, and pharmacological modulation to better understand social cognition deficits in neurodevelopmental disorders.

Keywords: *Autism, Marmoset, Social Prediction, Rescorla–Wagner Model, Computational Neuroscience*

1. INTRODUCTION

Autism Spectrum Disorder (ASD) involves altered social prediction and learning. To probe these mechanisms in a translational framework, we used non-human primates particularly marmosets for task development and a macaque for cross-species validation. Thus, linking behavior to a principled learning model.

UC5

2. AIM

To quantify trial-by-trial learning and prediction error in primate social-prediction tasks and assess translational relevance to ASD.

3. METHODS

Four marmosets completed a stepwise touchscreen paradigm: Step 1 (spatial preference assessment), Step 2 (bias attenuation via 50% reinforcement on the non-preferred side), and Step 3 (probabilistic reversal with 95% correct on one side, reversing every 18 trials). One macaque (“Alvar”) performed Step 3 (n = 2160 trials). Performance was modeled with the Rescorla–Wagner framework; parameters were estimated by minimizing the sum of squared errors (SSE) between observed and predicted accuracies.

The research project was undertaken as part of the CBC Newcastle under the ethics filed by the CTN lab Newcastle.

4. RESULTS

In Step 1, three marmosets showed strong lateral biases (two right, one left; 497 trials each). Step 2 reduced biases over 1 week. In Step 3, consistent usable data were obtained from one marmoset as shown in Figure 1; cross-species validation with Alvar yielded 1244/2160 correct responses (57%). Side contingencies were 53.7% right vs 46.3% left; corresponding average absolute prediction errors were 3.3% and 10.7%. SSE optimization produced balanced learning rates ($\alpha = 0.462$, $\beta = 0.537$), indicating moderate, adaptive updating to cue and outcome.

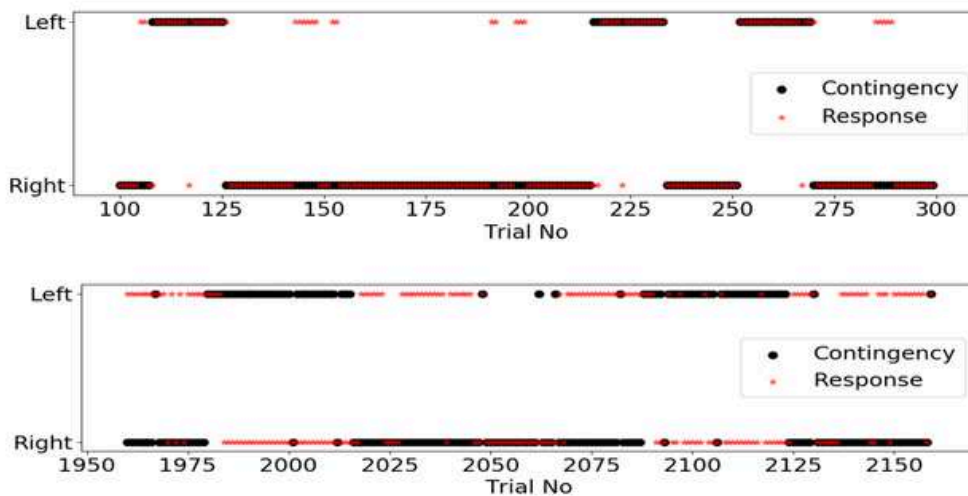
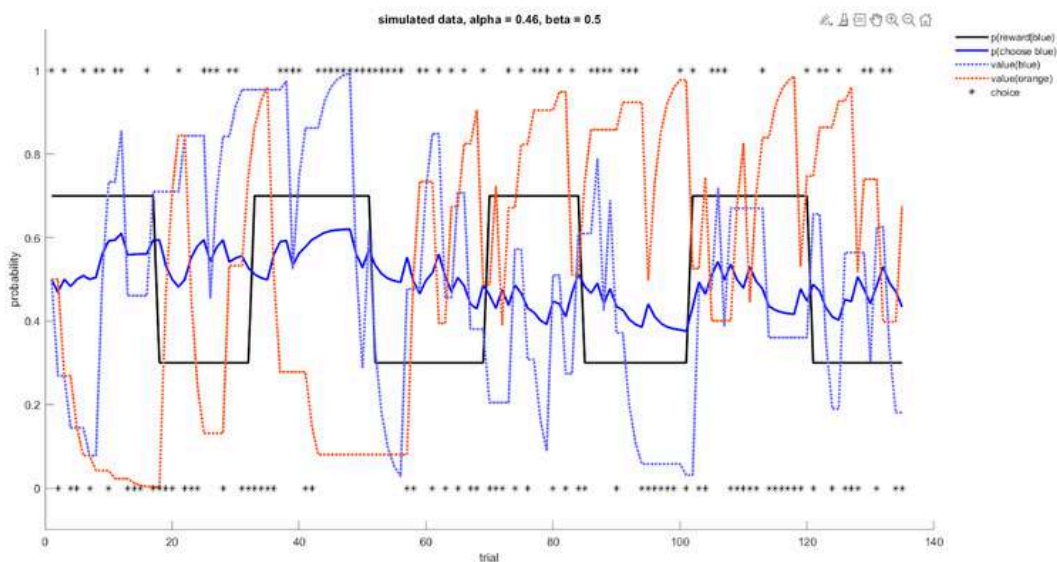


Figure 1: Alvar (Macaque) contingency and response at the start of step 3 versus at the end of step 3

5. CONCLUSION

A stepwise touchscreen task combined with Rescorla–Wagner modeling captures primate prediction-error learning and yields interpretable parameters. This pilot establishes a translational bridge from primate behavior to computational constructions relevant to ASD as demonstrated in Figure 2.



**Figure 2: Computational simulation of trials by using calculated alpha and beta values for Alvar (Macaque);
 Program developed by Jill O'Reilly and Hanneke den Ouden**

6. ACKNOWLEDGEMENT

The author sincerely thanks **Newcastle University** and the **Cognition and Translation Neuroscience (CTN) Lab** for their guidance, resources, and research environment that made this project possible.

UC6

Development and Validation of a Survey questionnaire to assess the public's attitude towards breastfeeding for BFCITY

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Abstract

Introduction: Public opinion influences breastfeeding behaviours, particularly in public settings where negative attitudes can create stigma and pressure to wean early. BFCITY is a novel indicator set of a breastfeeding-friendly city, including an indicator of welcoming community attitude. No validated tool exists to measure public attitudes within this framework.

Objective: To develop, validate, and test a questionnaire to measure the public's attitude towards breastfeeding.

Methods: A two-stage mixed-methods study was conducted. Stage 1 involved questionnaire development through focus group discussions and experts content validation. Stage 2 involved pilot testing among the general public in three languages. Participants completed the questionnaire at baseline and after one week. Content validity was evaluated using content validity index(CVI), internal reliability using Cronbach's alpha, and test-retest reliability using the Intraclass Correlation Coefficient(ICC) and Cohen's kappa.

Results: The 6-item questionnaire assessed knowledge(n=2), attitude(n=3) and practice(n=1). Following expert review(n=10), it achieved an S-CVI/Average of 0.94 and CVI/UA of 0.60. The pilot testing had 130 participants, with 103 completing the second round. Internal consistency for attitude was Cronbach's $\alpha=0.56$. Test-retest reliability was good across all domains: knowledge(ICC=0.89), attitude(ICC=0.87), and practice($\kappa=0.486$).

Discussion: The strong test-retest reliability confirms the questionnaire's consistency over time and across languages. The limited internal consistency assessment is expected due to the small number of questions.

Conclusion: This questionnaire demonstrates acceptable validity and reliability. As the survey is intended to be short, content validation will be used as the main supporting evidence of validity. This questionnaire provides the first practical metric to measure the welcoming community attitude within the BFCITY framework.

Keywords: *Breastfeeding, Maternal and child health, Public attitudes, Questionnaire validation*

1. INTRODUCTION

Breastfeeding is key to the health and well-being of women and children. Throughout the breastfeeding period, the mother-infant dyad interacts within three primary sectors: healthcare, workplace, and community. This continuous network of support is referred to as the "warm chain" of breastfeeding support [1]. The concept of a breastfeeding-friendly city embodies and exemplifies the ideals of the warm chain. Despite the numerous benefits of breastfeeding, global breastfeeding rates currently stand at approximately 40%, which falls significantly short of the WHO's target of achieving 70% of infants under 6 months exclusively breastfeeding by the year 2030 [2]. This gap highlights that the success of breastfeeding does not depend on workplace and healthcare policies alone, but also on the attitudes of the public.

BFCITY is a newly developed tool which aims to measure the breastfeeding friendliness of a city. This evidence-based tool was developed by an international team from Malaysia, Ireland and Sweden. BFCITY is divided into 5 sectors (city administration, healthcare, community, workplace, and collaboration) with a total of 16 indicators. Each indicator is subject to its unique method of measurement. To measure the Community Sector indicator for "A welcoming attitude", a survey of the residents of the city is needed. However, we do not have a ready-made survey for this purpose.

A literature review identified several existing questionnaires that could potentially be adapted (which broadly fall into two categories: those targeting the general public and those targeting breastfeeding mothers [3-9]). The limitation of these questionnaires is their length. Therefore, we decided to develop a concise questionnaire tailored to fit the BFCITY framework.

2. OBJECTIVES

To develop, validate, and test a questionnaire to measure the public's attitude towards breastfeeding.

3. METHODOLOGY

We conducted a two-stage mixed-method study from July to August 2025. Stage 1 involved focus-group discussions (FGD) with breastfeeding mothers and expert content validation of the draft questionnaire. Stage 2 (quantitative) involved a pilot study to assess feasibility and reliability of the final questionnaire.

Mothers with sufficient personal experience with breastfeeding (currently breastfeeding a child aged one year or older or having breastfed an infant for at least one year within the past three years) were invited to participate in the FGD. During the FGD they were asked: "What are the most important actions or gestures by a member of the public to show that

they support or welcome you as a breastfeeding mother?” “What are the negative actions or gestures that made you feel otherwise?”. They were also shown a list of potential items obtained from prior literature reviews and asked for their comments or thoughts on whether they would demonstrate a welcoming attitude towards breastfeeding.

The findings informed which questions to be included in the new questionnaire, which was then presented to a group of 10 breastfeeding experts. They included lactation consultants, active researchers in breastfeeding, breastfeeding advocates or formally trained medical healthcare professionals. The experts were asked to evaluate the content validity by rating each item on a scale of 1-4.

The final questionnaire was then translated into Malay and Chinese.

In Stage 2, adults aged 18 years old and living in Georgetown, Penang were invited to participate. Recruitment was done using a purposive and snowball sampling method. A sample size of 30 participants per language was used [10]. Participants completed the questionnaire in the language of their choice. After 1 week, the participants were presented with the same questionnaire again. At the end of the second survey, they were asked an additional question regarding how easy/difficult it was to understand and answer the questions.

Data Analysis

Exploratory qualitative analysis of the focus group discussion (FGD) meeting notes was used to identify and refine items for inclusion in the questionnaire. Content validity was evaluated using the Content Validity Index (CVI). For each item, an Item-level CVI (I-CVI) was calculated as the proportion of experts rating the item as either 3 or 4 on a four-point Likert scale, indicating relevance. An overall Scale-level CVI was also calculated using the average of the I-CVI values across all items (S-CVI/Average). Given the involvement of 10 experts, a minimum acceptable I-CVI threshold of 0.78 was applied to guide item retention. Quantitative data from the pilot study were analysed using Stata. Descriptive statistics were used with categorical variables presented as percentages and continuous variables described using means and standard deviations. Internal consistency reliability was assessed using Cronbach's alpha, while test-retest reliability was examined using the Intraclass Correlation Coefficient (ICC) for each language version of the questionnaire.

4. MAIN RESULTS

Ten breastfeeding mothers participated in the focus group discussion (FGD) and confirmed that the selected themes were appropriate for assessing public attitudes toward breastfeeding. Based on these discussions, the final BFCITY public attitudes questionnaire was developed, comprising items assessing knowledge (n = 2), attitude (n = 3), and practice (n = 1).

Content validation was conducted with ten breastfeeding experts, including paediatricians, obstetricians, and lactation consultants. The overall Scale-level Content Validity Index (S-CVI/Average) was 0.94, exceeding the acceptable threshold of 0.8, indicating strong expert agreement on item relevance.

The questionnaire was pilot-tested with 130 participants across three language groups: English (n = 45), Bahasa Melayu (n = 37), and Chinese (n = 48). The median age of respondents was 30–39 years, and 76.2% (n = 99) were female. Following the second round of data collection, a total of 103 responses were received (English n = 39; Bahasa Melayu n = 28; Chinese n = 36). Reliability and test–retest analyses for the questionnaire in each language are presented in Table 1.

Table 1: Summary of the reliability and test-retest analysis results from the pilot study

Reliability Analysis					
	Overall (n=130)	English (n=45)	Malay (n=37)	Chinese (n=48)	Cut-off
Knowledge (ICC)	0.89 (95% CI 0.84–0.93, p < 0.001)	0.87 (95% CI 0.75–0.93, p < 0.001)	0.88 (95% CI 0.74–0.95, p < 0.001)	0.92 (95% CI 0.84–0.96, p < 0.001)	<0.50 (poor) >0.75 (good)
Attitude (Cronbach α)	0.561	0.803	0.317	0.454	<0.60 (poor) >0.70 (Acceptable)
Practice (κ)	0.49 (p < 0.001)	0.30 (p = 0.005)	0.62 (p < 0.001)	0.47 (p = 0.021)	<0.40 (poor) 0.61–0.80 (substantial)
Test-Retest Analysis					
Knowledge (ICC)	0.87 (95% CI 0.81–0.91, p < 0.001)	0.93 (95% CI 0.86–0.96, p < 0.001)	0.86 (95% CI 0.70–0.94, p < 0.001)	0.81 (95% CI 0.63–0.90, p < 0.001)	
Attitude (ICC)	0.87 (95% CI 0.81–0.91, p < 0.001)	0.93 (95% CI 0.86–0.96, p < 0.001)	0.86 (95% CI 0.70–0.94, p < 0.001)	0.81 (95% CI 0.63–0.90, p < 0.001)	
Practice (κ)	0.486 (p < 0.001)	0.302 (p = 0.005)	0.618 (p < 0.001)	0.474 (p = 0.021)	

5. DISCUSSION

This study developed and evaluated a brief questionnaire intended to measure public attitudes toward breastfeeding as part of the BFCITY framework. The mixed-method approach ensured that item generation was grounded in the lived experiences of breastfeeding mothers and guided by expert consensus, consistent with recommendations for questionnaire development in public health tools.

A key finding was the variable psychometric performance of the three domains. Although the knowledge items demonstrated excellent test–retest reliability across all languages, internal consistency was low. This pattern shows high temporal stability but weak inter-item correlation which suggests that the two knowledge items capture stable but distinct aspects of breastfeeding knowledge rather than a single construct.

In contrast, the attitude domain performed more consistently, though with differences among the three languages. The English version demonstrated the strongest internal reliability. Lower internal consistencies in the Bahasa Melayu and Chinese versions likely reflects linguistic or cultural nuances affecting how participants interpret the question. Importantly, test–retest reliability for attitudes remained excellent across all languages, indicating that participants' views were stable over time even if internal consistency varied.

The practice item showed a fair-to-substantial test–retest reliability but weak convergent validity. This is consistent with the theoretical understanding that “practice” in public breastfeeding contexts represents behavioural tendencies that are influenced by situational, cultural, and environmental factors, and therefore may not correlate strongly with knowledge or attitudes. This supports the view that practice should remain a distinct domain within the questionnaire rather than an expectation of internal convergence.

Ultimately, the determination of whether these items are retained requires returning to qualitative insights from the FGDs and expert CVI ratings, which highlighted their conceptual importance despite low internal coherence.

Overall, the findings reinforce the broader literature showing that public breastfeeding support is multifaceted, culturally mediated, and not reducible to a single metric. The excellent test–retest reliability across all domains suggests that the tool is stable over time and appropriate for repeated community assessments. For policymakers and city administrators, this provides a practical method for monitoring public acceptance, a component that is often challenging to measure.

6. CONCLUSION

This questionnaire demonstrates acceptable validity and reliability. Internal consistency testing was limited by the small number of questions. As the survey is intended to be short, content validation will be used as the main supporting evidence of validity. This questionnaire will be used as part of larger BFCITY, which is in the process of being tested in other cities such as Dublin and Kota Bharu.

7. ACKNOWLEDGEMENT

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UC7 Exclusive expressed breast milk feeding versus exclusive direct breastfeeding: A scoping review of maternal and infant outcomes

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Abstract

The milk delivery method (direct breastfeeding [DBF] versus exclusive expressed breast milk [EBM]) may influence maternal, infant, and feeding outcomes, yet evidence remains limited and scattered. To map and describe current evidence that compares exclusive DBF and EBM, focusing on infant, maternal, and breastfeeding outcomes. Methods: We used the PCC framework (Population: term infants and mothers; Concept: exclusive DBF versus EBM; Context: all settings) and searched CINAHL, EMBASE, PubMed, and Cochrane Library for studies that compared the two feeding methods. Two reviewers screened the studies independently for inclusion. Any disagreements were resolved by discussion with a third reviewer. Data extraction included methods, outcomes and findings (whether favouring DBF or EBM) from primary studies. Outcomes of interest included infant (growth, neurodevelopment, infection, asthma, eczema), maternal (mastitis, mental health, satisfaction) and breastfeeding practices (duration, exclusivity). From the database search on 9th October 2025, we found 1,228 articles. After screening, 12 studies were included (8 prospective cohorts, 2 observational studies, 1 controlled clinical study, 1 randomized-controlled trial [RCT]) with 4 ongoing studies (2 prospective cohorts, 1 open-label parallel trial, 1 RCT). Of the included studies, two reported maternal outcomes (eg, confidence); six on infant outcomes (eg, asthma/allergies); four on breastfeeding outcomes. Some of the outcomes in infants and mothers were related to the physiology of breastfeeding with unclear clinical relevance. DBF showed advantages over EBM (e.g., healthier microbiota, higher self-efficacy, less nipple pain) with similar cognitive results, while several outcomes (growth, maternal mental health, process factors) were unreported. Research comparing exclusive EBM and DBF is limited and varied. While some outcomes have been studied, many areas remain underexplored. Further research is required, such as determining the important outcomes, to aid guideline development related to breastfeeding methods.

Keywords: *Exclusive breastfeeding, expressed breast milk, JBI methodology, scoping review*

1. INTRODUCTION

Milk delivery methods (exclusive direct breastfeeding [eDBF] versus expressed breast milk [eEBM]) may influence maternal, infant, and breastfeeding outcomes, yet evidence remains unclear.

2. OBJECTIVES

To map the extent, nature, and characteristics of studies explicitly comparing eEBM with eDBF.

3. METHODS

We used the PCC framework (Population: term infants and mothers; Concept: eDBF versus eEBM; Context: all settings) and searched CINAHL, EMBASE, PubMed, and Cochrane Library for studies comparing both feeding methods. Two reviewers independently screened primary studies for inclusion, with a third resolving disagreements. Data extraction included methods, outcomes and findings. Outcomes of interest included infant (growth, neurodevelopment, infection, asthma, eczema), maternal (mental health, mastitis, satisfaction) and breastfeeding (duration, exclusivity) outcomes.

4. MAIN RESULTS

Of 1,228 articles found (9th October 2025), 12 studies were included (7 cohort¹⁻⁷, 3 randomized-controlled trials[RCT]⁸⁻¹⁰, 2 cross-sectional¹¹⁻¹²) with 4 ongoing studies (2 prospective cohort¹³⁻¹⁴, 2 RCTs¹⁵⁻¹⁶). Amongst included studies, two reported maternal outcomes(eg, confidence)^{8,12};six reported infant outcomes(eg, asthma/allergies)²⁻⁷; four reported breastfeeding outcomes¹⁰⁻¹³. Some infant and maternal outcomes were related to breastfeeding physiology with unclear clinical relevance.

5. DISCUSSION

Reported maternal, infant, and breastfeeding outcomes are mainly short-term, with long-term outcomes (i.e. infant growth) largely unstudied^{7,9-11}. eDBF may have some advantages over eEBM (e.g., healthier microbiota, higher self-efficacy, less nipple pain) however, cognitive results were similar.^{6,8,9,12}

6. CONCLUSION

Research comparing eEBM and eDBF is limited and varied. Further research is required to determine important outcomes, aiding in developing intervention.

7. ACKNOWLEDGEMENT

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Exposure, experience, and expectations of people residing in Malaysia regarding the provided telemedicine services

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Abstract

Telemedicine has emerged as a key component of Malaysia's healthcare delivery, especially after the COVID-19 pandemic where remote care options became necessary. While prior studies have explored healthcare professionals' attitudes toward telemedicine, limited research has examined the exposure, experience, and expectations of individuals residing in Malaysia regarding these services. This study aims to assess the level of exposure to, experiences with, and expectations of telemedicine among people residing in Malaysia, providing insight into public awareness and acceptance of telemedicine as a sustainable healthcare option. This cross-sectional research was conducted from September 2024 until October 2025, and data analysis was conducted from May 2025 until August 2025 using an online Google questionnaire distributed via snowball sampling. Inclusion criteria were Malaysian residents aged 18 years and above who had resided in Malaysia for at least six months. Participants were recruited through social media platforms. Data were analyzed descriptively to evaluate exposure, experiences, and expectations. We obtained Ethical approval from the RUMC Ethics Committee. A total of 197 responses were obtained, with participants aged 18-66 years (mean age 35.9). 65% were female and 39.1% from Selangor. Only 9.6% (n=19) had used telemedicine services, through Google Meet (42.1%) or Zoom (10.5%). Among users, 57.9% reported satisfactory experiences. Among non-users (90.4%), 64.6% had heard of telemedicine, 86.5% believed they could benefit from it in the future, and 73.8% expressed positive expectations for future use. There is growing public openness toward telemedicine despite low current utilization, emphasizing the need for awareness, accessibility, and infrastructure improvements. Telemedicine in Malaysia demonstrates high potential for acceptance among the general population. While exposure remains limited, satisfaction and expectations are encouraging, suggesting that strategic promotion and integration could enhance equitable healthcare access nationwide.

Keywords: *Telemedicine, Malaysia, Telehealth Expectations, Medical Accessibility*

1. INTRODUCTION

Telemedicine is described as a scheduled online consultation between healthcare professionals with their patient when distance or other factors are limiting the ability for patients to meet face-to-face with their healthcare providers¹. The Movement Control Order (MCO) implemented in the early year of 2020 during the COVID-19 pandemic in Malaysia has limited the ability for people to travel to hospital to receive necessary treatment for their medical conditions. Due to the physical barrier of this MCO, telemedicine became more recognised for some physicians to utilize to solve this physical barrier between doctor-patient consultations.

A research study by Thong et al, 2021² showed that healthcare professionals in Malaysia who are using telemedicine services during the COVID-19 period in 2020 have an overall positive response towards the usage of telemedicine service in Malaysia. However, there is not much research done regarding the usage of telemedicine services from the point of view of users in Malaysia. Hence, we decided that we will be conducting research to explore the acceptability of telemedicine services in Malaysia from the perspective of users in Malaysia.

2. AIMS & OBJECTIVES

This study aims to assess the level of exposure to, experiences with, and expectations of telemedicine among people residing in Malaysia, providing insight into public awareness and acceptance of telemedicine as a sustainable healthcare option.

3. METHODS

From September 2024 to October 2025, this cross sectional study was conducted via online Google questionnaire and participants were recruited via snowball sampling. Participants were Malaysian residents of at least 18 years old and lived in Malaysia for at least 6 months. Recruitment posters were distributed via social media platforms and all data collected were evaluated for exposure, experience and expectations of Malaysians for Telemedicine services. Ethical approval was applied and obtained from the RUMC Ethics Committee.

4. RESULTS & DISCUSSION

From our data collection period of May 2025 to August 2025, we received a total of 197 responses for our research. We received responses from almost all of the states in Malaysia, with Selangor representing a majority of our respondents, at 39.1% (n=77), followed by Perak at 14.2% (n=28), Penang at 12.2% (n=24), and Kuala Lumpur at 9.1% (n=18). As for the race of our participants, Malays represents 48.2%, Chinese represents 45.2%, Indians represents 3%, while the remaining 3.6% represents other races.

A total of 19 out of 197 participants (9.6%) have been given telemedicine services before, with the majority of this service being provided in the state of Selangor and Kuala Lumpur. Among these users of telemedicine service, 57.9% of participants reported an overall satisfactory use of the telemedicine service being provided in Malaysia, and the remaining 42.1% had a moderate or neutral satisfactory use of the service.

The remaining 178 participants (90.4%) of our research have never used this telemedicine service before. Out of these 178 participants, 115 of them (64.6%) have heard of this service before, but out of these 178 participants, only 45 of these participants (25.3%) know where they could be offered this service. 154 of the participants (86.5%) think they could benefit from this service being provided to them, and a total of 145 participants (81.5%) would like this service to be provided to them. Analysing the expectations of the telemedicine service in Malaysia of these 145 participants, we report that 1.4% of them had an overall negative expectation of this service, 24.8% of them had an overall moderate or neutral expectation of this service, while a high percentage of 73.8% of the respondents had an overall positive expectation of this service if they were provided with it.

Consequently, the established findings suggest that while public receptiveness is increasing, the transition from awareness to utilization is currently hindered. To bridge this gap, future efforts must prioritize the enhancement of digital infrastructure and the accessibility of services to meet the growing public demand.

6. CONCLUSION

The evidence strongly suggests that the Malaysian landscape is primed for the widespread adoption of telemedicine, revealing a high potential for acceptance among the general populace. Although the current level of public exposure to these services remains in its nascent stages, the underlying sentiment is robust; the combination of reported satisfaction among early adopters and the optimistic expectations of potential users paints an encouraging picture.

7. ACKNOWLEDGEMENT

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KNOWLEDGE, AWARENESS, AND PERCEPTION OF UNIVERSITY STUDENTS ON THE USE OF OVER-THE-COUNTER MEDICATION AS A RESPONSE TO ACADEMIC STRESS

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Abstract

Academic pressure among university students is often managed through various coping strategies, including the use of over-the-counter (OTC) medications. While OTC drugs are easily accessible and widely used for minor ailments, inappropriate use for stress relief poses health risks. Understanding students' knowledge, awareness, and perception (KAP) of OTC medication is vital to promote safe self medication and effective health education. This study aimed to assess university students' KAP toward OTC medication use for academic stress relief across gender, academic year, and field of study; identify the main academic-related stressors driving OTC medication use; and explore alternative coping strategies. A cross-sectional quantitative study was conducted among 448 AIMST University students from various faculties using a validated, self-administered questionnaire via Google Forms. The questionnaire covered demographics, knowledge, awareness and perception. Data were analysed using descriptive analysis, with $p < 0.05$ considered as statistically significant. Students demonstrated high knowledge, strong awareness, and moderately cautious perceptions regarding OTC medication use. Significant differences in KAP were observed by academic year and field of study, with partial significance for gender. Senior students and pharmacology-related faculty students showed better understanding and safer perceptions toward OTC medications. Exams and workload were the main academic stressors driving OTC medication use (92.2%), while 87.7% practised non-medication alternatives such as exercise or relaxation. Most students exhibited responsible attitudes toward OTC medication use, though some misconceptions persisted. Universities should strengthen health literacy and stress management initiatives through peer-led and digital outreach to encourage safe, informed coping behaviours.

Keywords: *KAP, OTC medication, academic stress, self-medication*

1. INTRODUCTION

The growing accessibility of higher education has led to increased academic expectations and psychological distress among university students. Stress is now widely recognised as a major concern in tertiary education [1]. Studies in Malaysia have shown that over half of university students experience moderate to severe levels of stress, anxiety and depression

due to academic workload and social adjustment difficulties [2,3]. To cope with these pressures, many students adopt various strategies, including self-medicating with over-the-counter (OTC) medications for quick symptom relief. Although OTC drugs are considered safe when used appropriately, their misuse for stress management without proper medical guidance poses a significant health risk [4,5].

Recent research has reported a rising trend of OTC medication use among university students, driven by accessibility, affordability and perceived safety [5,6]. However, gaps in students' knowledge, awareness and perception (KAP) of OTC medications may lead to misuse and potential adverse effects [7]. This study addresses these gaps by examining the KAP of AIMST University students toward OTC medication use for academic stress relief and its association with demographic and academic factors. Understanding these aspects is crucial to promote safe self-care, strengthen health literacy and guide appropriate health education initiatives such as informative sessions or counselling to improve clinic access and promote responsible OTC medication use among Malaysian university students [7]. In line with the conference theme "Innovation and Progress in Medical Science," this research contributes to advancing preventive healthcare through innovative, student-centred wellness strategies and informed medication practice that support academic and mental well-being.

2. OBJECTIVES

Main Aim: To study the KAP of university students regarding the use of OTC medication for managing academic stress.

Specific Objectives:

- To evaluate university students' KAP of OTC medication use for academic stress relief with demographic analysis including gender, academic year and field of study.
- To examine the main academic-related stress factor that drives university students to use OTC medications.
- To explore the use of alternative stress management strategies among university students, either alongside or in place of OTC medications.

3. METHODOLOGY

A cross-sectional quantitative study was conducted among undergraduate students from various faculties at AIMST University, Kedah, Malaysia. The study aimed to recruit a predicted target sample size of 325 students from a total population of 2085 students to maintain a 95% confidence level, 5% margin of error and 50% response distribution. Participants represented different academic years, genders, and were categorised into 3 faculty groups based on their pharmacological academic exposure, Group 1: Faculty of

Pharmacy; Group 2: Faculty of Dentistry & Faculty of Medicine; and Group 3: Faculty of Physiotherapy & Faculty of Business.

The data were collected using a validated, self-administered questionnaire distributed via Google Forms to ensure anonymity and voluntary participation. The questionnaire consisted of 30 questions distributed into 4 sections: (A) Demographic Information, (B) Knowledge, (C) Awareness and (D) Perception toward the use of OTC medications for managing academic stress. The questionnaire items were adapted and refined from previous studies to ensure content validity and reliability. Validation was conducted by experts in the field, including practising pharmacists and clinical lecturers from AIMST University, to confirm relevance, clarity, and accuracy [8]. Furthermore, a pilot study involving 40 students (excluded from the main study) was conducted to evaluate the clarity and reliability of the questionnaire, allowing for refinements to be made before its distribution to participants. Cronbach's Alpha was used as a statistical measure to assess the internal consistency of the questionnaire, and the alpha values obtained demonstrated acceptable reliability across all sections.

Each KAP statement was primarily rated on a 5-point Likert scale ranging from strongly disagree to strongly agree to measure levels of agreement, with additional yes-or-no questions and single-choice questions included where appropriate. Data was analysed using SPSS software. Descriptive statistics were applied to summarise participants' demographic characteristics and KAP scores regarding OTC medication use during academic stress. Inferential analyses, including the Mann-Whitney U test, Kruskal-Wallis test, and Chi-square test, were performed to assess significant associations between KAP levels and sociodemographic variables (gender, academic year, and field of study). All the tests were applied as non-parametric methods, as the normality test p -value < 0.001 , confirming that the data were not normally distributed. A p -value < 0.05 was considered statistically significant. Ethical approval for this study was obtained from the AIMST University Human and Animal Ethics Committee (Ethical Approval References: AUHEC/FoP/12/03/2025/12).

4. MAIN RESULTS

A total of 448 students from different faculties and academic years participated in this study. Overall, students demonstrated high knowledge, strong awareness, and moderately conflicted perceptions regarding the use of OTC medications. Significant associations were found between KAP levels and academic year as well as field of study ($p < 0.001$ for both), whereas gender showed only partial significance in selected KAP items (only statistically significant at knowledge sections). Students from pharmacology-related faculties and those in senior academic years demonstrated a better understanding and safer perceptions of OTC medication use.

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Table 1. Relationship Between Students' KAP on OTC Medication Use and Sociodemographic Factors Based on 5-Point Likert Scale

Sections	Likert Scale					p-value		
	Frequency, n (Percentage, %)					Gender	Academic Year	Field of Study
	SD	D	N	A	SA			
Total Knowledge of the Safety Potential Side Effects of OTC Medications)	15 (3.3)	65 (14.5)	126 (28.1)	171 (38.2)	71 (15.8)	<0.001 ^a	<0.001 ^a	<0.001 ^a
Total Awareness of Risks & Behavioural Influences on OTC Medication Use)	10 (2.2)	26 (5.8)	67 (15.0)	185 (41.3)	160 (35.7)	0.478	<0.001 ^a	<0.001 ^a
Total Perception of Effectiveness and Appropriate Usage of OTC Medication	72 (16.1)	172 (38.4)	129 (28.8)	62 (13.8)	13 (2.9)	0.247	<0.001 ^a	<0.001 ^a

^ap<0.05 (statistically significant)

Note: SD=Strongly Disagree; D=Disagree; N= Neutral, A=Agree, SA=Strongly Agree

Direct academic stress factors such as examinations and workload were the primary triggers for OTC medication use (92.2%), while indirect academic stress factors like social influence or environmental pressure were reported by 7.8% of respondents, showing a statistically significant difference ($p < 0.001$). Furthermore, 87.7% of students indicated that they also used non-medication alternatives to manage academic stress, with a significant preference for non-medication approaches ($p < 0.001$). These findings suggest that most students tend to combine safe self-medication with alternative coping strategies for academic stress relief.

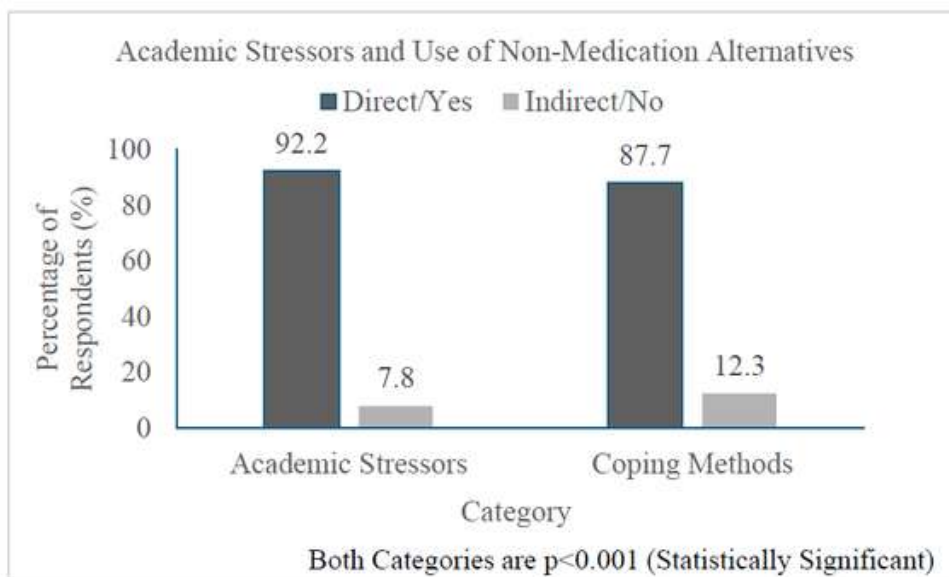


Figure 1. Distribution of Academic Stressors Influencing OTC Medication Use and the Use of Non-Medication Alternatives Reported by AIMST University Students

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5. DISCUSSION

This study revealed that AIMST University students generally possess high knowledge and strong awareness regarding the use of OTC medications, although some misconceptions persist in their perception. These findings are consistent with previous studies reporting that universities students often demonstrate good awareness of medication safety but may still underestimate risks associated with unsupervised self-medication. Many students reported relying on friends' suggestions, perceiving such advice as trustworthy, although this can lead to negative outcomes such as drug allergies or inappropriate medication use [9]. The observed mixed perceptions suggest that while students recognise the convenience and cost-saving benefits of OTC medications, they are also aware of risks such as medication errors or overuse due to misunderstanding labels. However, their confidence in self-treating minor illnesses and the misconception that using expired medications is harmless highlight the need for continuous health education to promote safer medication practices.

Significant differences in KAP based on academic year, field of study, and gender highlight the influence of educational and demographic factors in shaping responsible medication practices. Students in senior academic years demonstrated higher KAP scores, likely due to increased exposure to practical experience and interdisciplinary interactions, which contribute to a broader understanding of drug safety and responsible self-medication [10]. Similarly, students from pharmacology-related faculties exhibited greater awareness of pharmacology principles and rational drug use, aligning with previous findings that pharmacy students tend to possess higher awareness of the risks and benefits of OTC medications [5]. Meanwhile, gender differences were only partially significant, as male and female students showed differences in knowledge, potentially because females are more familiar with analgesics through personal use for menstrual pain, thereby increasing their understanding of OTC drugs [11], but not statistically significant in awareness and perception, where both sections demonstrated comparable awareness on the convenience, effectiveness, and safety of medications. These findings underscore the need for targeted and inclusive health education initiatives across faculties to promote safer and more informed use of OTC medications among university students.

The finding shows that direct academic stressors, such as examinations and workload, were the main academic stressors (92.2%) driving OTC medication use, supporting prior evidence that academic related pressures, such as examinations and academic workload, are key determinants of stress among university students [7,12]. However, it is encouraging that a majority (87.7%) of students also reported using non-medication coping strategies such as exercise, rest, or relaxation. This aligns with previous studies among pharmacy students, which found that non-pharmacological coping strategies, particularly exercise, were associated with lower levels of perceived stress, and that problem solving as well as

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emotional support, were preferred over medication use [13,14]. These findings suggest that while students may rely on OTC medications for quick relief, they also recognise the importance of healthier, long-term coping mechanisms. This implies that many students adopt a multimodal stress-management strategy, combining both medication and non-medication approaches to cope with academic pressure.

From a practical perspective, these findings underscore the importance of integrating stress management education and safe self-care practices within university settings. Health promotion efforts should not only focus on the pharmacological aspects of OTC medication use but also strengthen students' coping capacity through peer-led and faculty-specific programmes. Universities and health professionals can collaborate to design interactive workshops and online campaigns to enhance medication literacy and promote balanced, evidence-based approaches to managing academic stress.

6. CONCLUSION

This study highlights that AIMST University students possess high knowledge and awareness regarding OTC medication use for academic stress, with notable variation across academic years and fields of study. Despite their understanding, certain misconceptions persist, indicating the need for continued emphasis on safe and informed self-medication practices. Overall, the findings underscore the importance of fostering responsible health behaviours among university students.

7. ACKNOWLEDGEMENT

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INTEGRATING PALLIATIVE CARE IN UNDERGRADUATE MEDICAL EDUCATION: A NARRATIVE REVIEW OF STRATEGIES, OUTCOMES, AND CHALLENGES IN MALAYSIA, SOUTHEAST ASIA, AND OTHER LOW- AND MIDDLE-INCOME COUNTRIES

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Abstract

The global need for palliative care (PC) continues to outpace capacity, particularly in low- and middle-income countries (LMICs) such as those in Southeast Asia (SEA), where PC development remains uneven between rural and urban settings. Strengthening undergraduate PC education is essential for preparing future doctors for end-of-life (EOL) care, yet integration across LMICs varies widely. This narrative review aims to explore the challenges, strategies and outcomes in incorporating PC education into undergraduate medical curricula and to inform on such efforts in Malaysia and other LMICs.

A systematic search up to year 2025 was conducted across PubMed, Scopus, Web of Science and ERIC. The search identified 3278 articles, of which 1348 remained after removing duplicates. 34 articles met the eligibility criteria, and 14 were included after full-text screening.

Findings show differing levels of PC integration into undergraduate medical programmes in LMICs. The primary outcome was that even brief exposure to PC consistently improved students' knowledge, attitudes and empathy towards EOL care. Effective strategies include short elective courses and structured modules combining lectures, ward rounds and hospice visits. These approaches emphasised applying theory in practice, multidisciplinary teaching, integration into existing subjects, and using technology to increase access. Key challenges were inadequate trained faculty, limited clinical sites or facilities, inconsistent clinical exposure and cultural discomfort surrounding discussions on death and dying.

Integration of PC into undergraduate medical curricula is feasible and beneficial. Sustained institutional commitment with context-specific adaptation is critical to support PC education amongst medical students and foster PC growth in Malaysia and other LMICs.

Keywords: *Palliative care, end-of-life care, undergraduate medical education, LMIC, Malaysia*

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1. INTRODUCTION

As the world population is both growing and aging rapidly, the healthcare landscape has morphed to serve a bigger number of patients in a wider age spectrum, naturally including more people with life-limiting illnesses. The increasing demand for palliative care (PC) has been acknowledged and brought to the forefront through international publications, such as the World Health Assembly's Resolution on Palliative Care (WHA67.19) and the Worldwide Hospice Palliative Care Alliance (WHPCA)'s Global Atlas of Palliative Care 2020, who have stated unequivocally that a lack of a comprehensive PC education as a barrier to development of PC [1,2]. Building on this, WHA67.19 has also called for basic training and continuing education on PC to be routinely integrated into undergraduate medical education in all member nations, in efforts to increase healthcare equity, fulfill demands and satisfy the ethical responsibility of healthcare systems in alleviating pain and suffering [1]. This is essential as undergraduate medical education represents the earliest and most scalable point of intervention to introduce PC principles, shape attitudes and improve the confidence of future doctors in managing pain and death.

PC is also included in Goal 3.8 of the United Nations Sustainable Development Goals as one of the five key components of Universal Health Coverage (UHC) [3]. Countries with a healthcare system mature enough to fulfill UHC are often high-income or developed nations that consistently rank highly in PC integration into mainstream healthcare, while LMICs may lag in this aspect [1]. Studies have shown that PC development strongly correlates with human development index (HDI), life expectancy, and income level. Therefore, in a Malaysian context, establishing a healthcare system mature enough to fulfill UHC, and hence PC, would signify a step in the right direction in achieving developed nation status – a goal that many LMICs have also been striving to achieve. Reflecting on the strategies, outcomes and challenges documented to date in this endeavour can consequently inform future directions for PC integration into undergraduate medical education in LMICs, including Malaysia. As there is an urgency to produce well-equipped doctors that are capable of driving improvement in PC within healthcare systems, this review aims to facilitate this process by bridging the current literature gap. This would also lay the groundwork for future research on the innovations in PC education worldwide, including how approaches differ across geographical contexts and how LMICs may adapt or adopt these methods to progress a nation through PC development.

2. OBJECTIVES

To explore how PC has been integrated into undergraduate medical education in LMICs by identifying effective strategies, outcomes and challenges, and their implications for strengthening PC education in Malaysia.

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1. To review the integration and teaching approaches of palliative care in undergraduate medical curricula in LMICs.
2. To identify the impacts of a palliative care curriculum on the knowledge, skills and attitudes of students towards palliative care and the challenges to implementation reported among LMICs.
3. To evaluate the current state and gaps in palliative care education in Malaysia.

3. METHODOLOGY

This narrative review was conducted in line with the SANRA (Scale for Assessing Narrative Review Articles) criteria, which provided a structured framework to ensure methodological rigor, transparency and critical appraisal in this narrative review [4]. The literature search was performed across 4 electronic databases (PubMed, Scopus, Web of Science and ERIC) and included articles up until the date of search to ensure an extensive and comprehensive coverage of the existing literature regarding this topic. Search strategies contained keywords and that included 'Palliative Care', 'Medical Education' and 'LMIC'. The retrieved articles were uploaded to the reference management tool Rayyan, where duplicates of articles were removed and subsequently screened to ensure adherence to the inclusion criteria.

Inclusion criteria

- Studies conducted in Malaysia, Southeast Asian countries, or other LMICs (as defined by the World Bank)
- Focus on palliative care education within undergraduate medical curricula
- Includes strategies, models, interventions, program descriptions, curriculum development, implementation processes, or evaluation of palliative care education
- Primary research (qualitative, quantitative, or mixed methods), reviews, policy analyses, case studies, or official reports related to curriculum integration
- Conference proceedings or grey literature that provide substantial information on curriculum strategies or outcomes
- Published in English or Bahasa Malaysia

Exclusion criteria

- Studies focused solely on high-income countries without relevance to LMIC contexts
- Studies addressing postgraduate, nursing, or allied health professional education exclusively
- Studies discussing palliative care service delivery, clinical outcomes, or policy frameworks without any educational component
- Studies analysing undergraduate medical education without palliative care as a focus
- Commentaries, editorials, opinion pieces, or letters with no empirical data or curriculum-related analysis
- Articles not available in full text or published in languages other than English or Bahasa Malaysia

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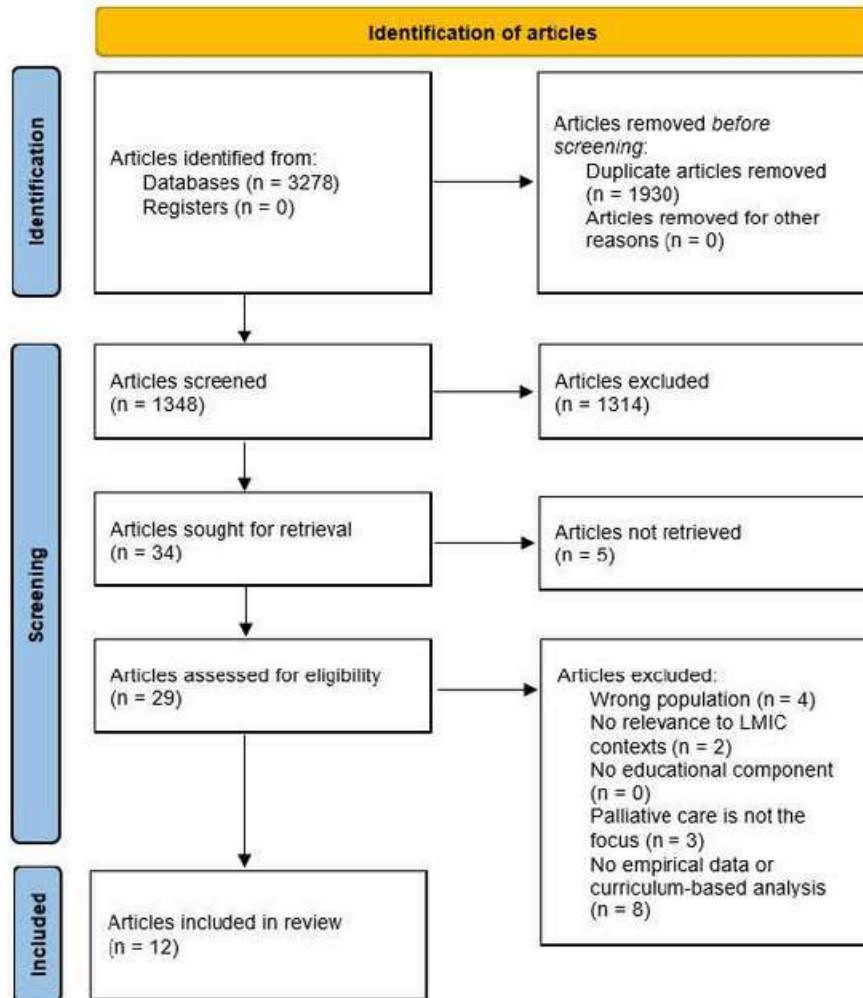


Fig. 1: Overview of Search and Screening Process

4. MAIN RESULTS

Lectures remain a common strategy for delivering PC education in undergraduate medical curricula. In Uganda, teaching helped dispel misconceptions about addiction in the use of morphine in pain management and increased students' confidence in managing pain. However, in many settings, education on pain management, psychosocial support, communication skills and hospice care were found to remain inadequate, leaving future doctors underprepared to offer holistic EOL care. PC content is sometimes embedded within related fields such as oncology and radiotherapy. While integration into these disciplines is important, students may not appreciate the broader scope of PC. Elsewhere, PC has been integrated into the syllabus in some medical colleges by delivery of theory combined with off-site clinical experience, such as ward rounds and hospice visits. Innovative methods, including seminars, problem-based learning (PBL), workshops and social media, have yielded positive outcomes. Multimodal teaching is effective in knowledge integration, with students exposed to self-instructed learning, patient stations and home hospice visits outperforming those taught using fewer methods in OSCE stations. Where PC is not a core subject, it may be offered as a mandatory elective, summer school or workshop. Tools such as the PEACE-Q

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and PCKT questionnaires have been found to be useful in evaluating changes in knowledge and skills following PC education. Making PC examinable through multiple explanatory questions (MEQ) and multiple choice questions (MCQ) further increases confidence in symptom management and clinical skills while fostering greater empathy and understanding of disease pathophysiology. Although short exposures to PC are beneficial to generate interest, at least 2 weeks of combined theory and clinical experience is most effective in building a strong foundation for future application and improved attitudes towards PC. Challenges in implementing PC in undergraduate medical curriculum include determining the optimal year for PC introduction as pre-clinical students may lack clinical context. Cultural and religious diversity also influences comfort levels in discussing death, affecting both teaching and learning. A lack of trained faculty, multidisciplinary involvement and clinical facilities for training have also been identified. However, the greatest barrier remains the lack of a nationwide coordinated effort in integrating a standardised programme, resulting in unequal PC education amongst medical students in many LMICs.

5. DISCUSSION

The integration of PC education in undergraduate medical curricula remains highly variable among LMICs, reflecting broader disparities in PC education on a national and international level. However, the findings of this review suggest that integration is both feasible and impactful, even when implemented on a small scale. The consistent improvement in knowledge, attitudes and empathy following short, structured interventions suggests that meaningful education does not always require extensive curricular restructuring, which is an important consideration for resource-limited settings. Nevertheless, the absence of standardised PC education frameworks in many LMICS is reflected in the wide variation in content and teaching methods across studies. The review also underscores the value of knowledge application through clinical experience, which consistently produced better outcomes than theory alone. This supports the need for blended approaches and the use of technology to extend access where physical PC services are limited. The implementation of PC as a distinct offering also extends to curricula where aspects of PC are introduced through existing disciplines. While a multidisciplinary perspective is important, overall knowledge of PC may be limited and is insufficient to provide satisfactory PC care in practice. This risk is also reflected by the recurrent logistical and cultural challenges identified in LMICs, as these barriers can reduce holistic understanding of PC and decrease confidence in managing future patients. The highly contextual nature of these barriers imply that PC education cannot simply be adopted from high-income settings. Instead, culturally sensitive adaptation and institutional investment is required. Ultimately, these findings suggest that strengthening PC education in Malaysia will require coordinated national efforts to build faculty capacity, establish structured clinical placements and integrate PC longitudinally in all medical schools to ensure baseline competency among future doctors.

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5. CONCLUSION

The integration of PC into undergraduate medical curricula in LMICS is both feasible and necessary to meet the rising demand for PC. Evidence suggests that even short, structured and multimodal courses, when adapted to local cultural and resource contexts, can substantially improve students' competence and attitudes. For Malaysia, progress will require efforts across medical schools, along with collaboration with hospitals and hospice services to ensure consistent clinical exposure and sustained capacity building. Strengthening PC education at the undergraduate level is therefore an essential step towards improving healthcare delivery, while advancing PC and national development.

6. CONCLUSION

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DEMOGRAPHIC STUDY OF PATIENTS UNDERGOING CHOLECYSTECTOMY AT HOSPITAL SULTAN ABDUL HALIM

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Abstract

Gallstone disease is a common surgical condition whose prevalence rises with age and is higher in women. Ethnicity is also a factor, with known higher rates in Malays, though data from Sungai Petani is lacking. This study aimed to evaluate the association between demographic factors and gallstone disease among patients undergoing cholecystectomy at Hospital Sultan Abdul Halim (HSAH). Specific objectives were to determine the distribution of age, gender, and ethnicity, and to assess their relationship with gallstone disease. A retrospective, single-centre observational study was conducted at Hospital Sultan Abdul Halim, Sungai Petani, Kedah, reviewing all patients who underwent cholecystectomy between July 2019 and July 2025. Data was analysed using Microsoft Excel. A total of 215 patients' data was analysed. The highest incidence (24.7%) was found in the 46–55 age group with risk increasing with age until fifth decade before declining. Females demonstrated a consistently higher incidence than males. Malays were the majority (82.3%), then Indians (10.7%) and Chinese (6.0%). Indians showed a disproportionately higher prevalence relative to their population size in Kedah. These findings are consistent with previous reports that gallstone risk is strongly associated with female gender, older age, and Indian ethnicity which were identified as significant demographic risk factors for gallstone disease in HSAH patients. These findings highlight the importance of early ultrasonographic screening and targeted preventive strategies in high-risk groups.

Keywords: *Cholecystectomy, gallstone disease, gender, ethnicity, Malaysia*

1. INTRODUCTION

Gallstone disease is one of the most common biliary tract disorders worldwide. It represents a significant cause of morbidity across different populations. The standard treatment for symptomatic gallstones, as well as other gallbladder pathologies such as acute cholecystitis, gallbladder polyps, and gallstone pancreatitis, is cholecystectomy—the surgical removal of

the gallbladder. The burden of gallstone disease varies considerably depending on demographic factors such as age, gender, ethnicity, and geographical location. Globally, gallstones are more common in women than men. The risk rises with age, obesity, pregnancy, and metabolic conditions like diabetes mellitus and dyslipidaemia (Shaffer, 2006)[1]. Regional differences are also evident. In Asia, pigment stones are relatively more frequent, while cholesterol stones dominate in Western countries (Trotman & Soloway, 2013)[2].

In Malaysia, hospital-based studies have shown that gallstone disease is a frequent reason for surgical admission. Laparoscopic cholecystectomy, in fact, ranks among the most performed elective and emergency procedures (Lim et al., 2011)[3]. The ethnic distribution of gallstone disease in Malaysia reflects population diversity. Some studies suggest that Indian and Malay patients are more frequently affected than Chinese patients, although findings differ between regions (Nor et al., 2004)[4]. Lifestyle changes are also shaping disease patterns. With the rising prevalence of metabolic syndrome, obesity, and diabetes in Malaysia, the number of cholecystectomies performed is expected to increase further (Zainal et al., 2013)[5]. Hospital-based demographic studies can therefore provide essential insights. They help to outline patient profiles, understand the burden of disease, and improve healthcare planning, resource allocation, and patient education.

2. OBJECTIVES

Main objective:

To evaluate the association between demographic factors and gallstone disease among patients undergoing cholecystectomy at Hospital Sultan Abdul Halim (HSAH).

Specific objectives:

1. To determine the distribution of age, gender, and ethnicity
2. To assess the relationship of age, gender and ethnicity with gallstone disease

3. NULL HYPOTHESIS

Null Hypothesis (H_0): There is no association between age, gender, or ethnicity and the occurrence of gallstone disease in patients undergoing cholecystectomy at HSAH.

Alternative Hypothesis (H_1): There is a significant association between one or more of the following factors- age, gender, ethnicity and the occurrence of gallstone disease in patients undergoing cholecystectomy at HSAH.

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4. METHODOLOGY

- Study Site: Hospital Sultan Abdul Halim, Sungai Petani, Kedah
- Study Duration: 1st July 2025 to 31th October 2025
- Study Population: All patients who underwent elective or emergency cholecystectomy from July 2019 to July 2025

Data Collection Method

Retrospective review of hospital surgical database.

Inclusion Criteria

Patient who underwent cholecystectomy in HSAH within the specified period.

Exclusion Criteria

Patients with incomplete demographic or surgical data.

Data Analysis

- Simple descriptive analysis using Microsoft Excel
- Age: mean and range
- Gender and ethnicity: frequency and percentage

Ethical approval was obtained from the Hospital Sultan Abdul Halim Research and Ethics Committee.

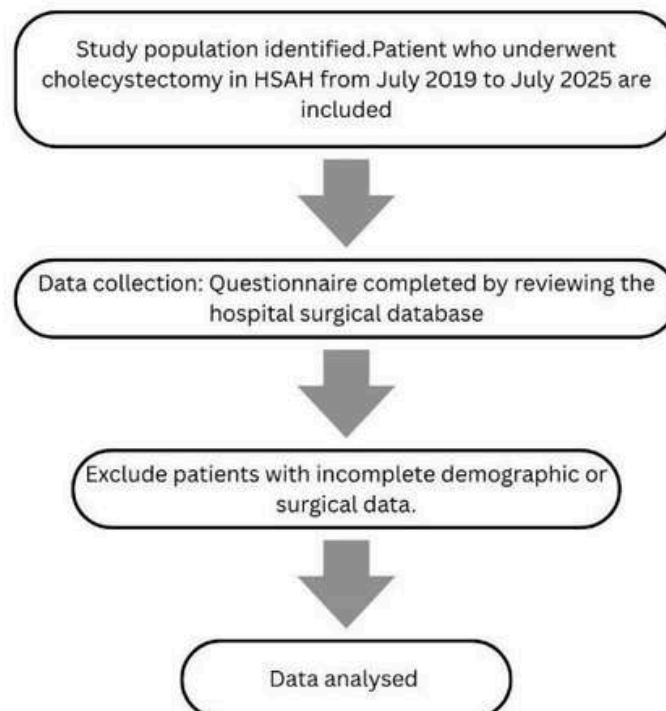


Figure 1. Flowchart of reviewing patient's demographic

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5. RESULTS

AGE

There is gradual increase from 26 – 35 years old age group to 46 – 55 years old age group with the incidence of cholecystitis is found peaked in 46-55 years old (53 out of 215 patients). The incidence also increases with age but gets lower after reaching 5 decades.

ETHNIC

The prevalence for ethnicity is found to be the highest among the Indians (10.7%) as their population in Kedah is less than 6%, followed by Malays (82.3%) although they have the highest cases of cholecystectomy, Chinese (6.0%) and lastly Siamese.

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Figure 2 shows comparison among gender and found that females are more prone to get cholecystitis than males for every year of the study, more than twice as much each year except in 2019.

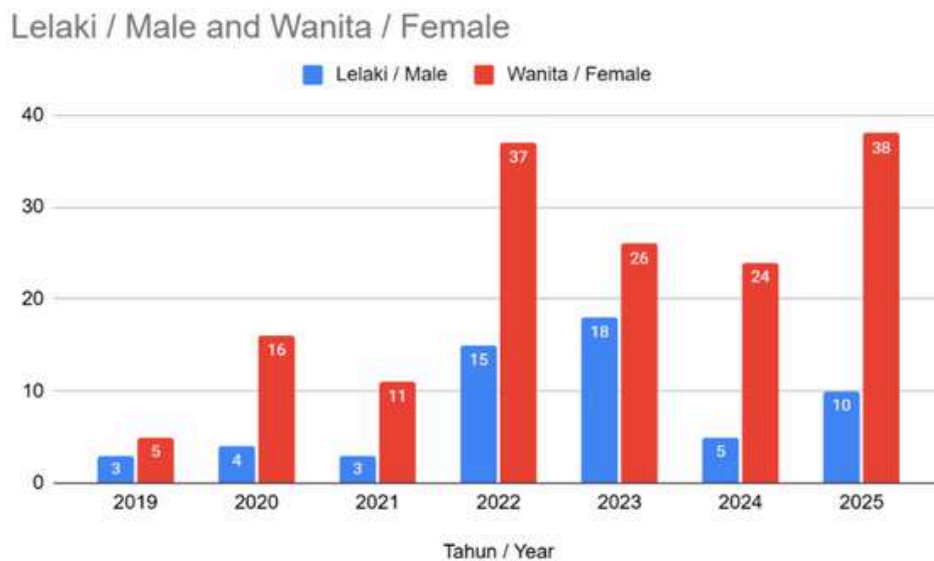


Figure 2. Bar chart of men vs women by year

6. DISCUSSION

There was gradual increase from 26 years old to 55 years old, which reflects the role of ageing within their development. A study by Rahman et al. [6] and Su et al.[7], showed similar result however contrasted with research by Al Atsariyah et al. [8], who reported strong association between cholelithiasis and age. In their opinion, gallstone disease is particularly prevalent among those aged 65 and above.

The result shows that female has higher incidence than male in getting gallstone disease. This aligns with previous research by Shahzad et al. [9], who observed that the incidence of cholelithiasis is high in female and is commonly attributed to sex hormones.

Indian has the highest prevalence compared to Malay and Chinese, this contrasted to the research by Sood et al. (2015)[10], who found that race has no influence in the likelihood of conversion from asymptomatic gallstone to symptomatic. However, according to Tan et al. (2011) [11], Indians have higher prevalence of metabolic disorder compared to Malays and Chinese, which is a risk factor of getting cholelithiasis. They also found that Indians tend to engage in less physical activity and consume fewer fruits and vegetables than Malays and Chinese.

7. CONCLUSION

Female gender, age, race are independent risk factors of cholelithiasis. Understanding the pathophysiology of gallstone disease can aid nurses in providing resources and information to patients who have been diagnosed with gallstones, as well as cholelithiasis prevention.

We strongly recommend ultrasonography as a screening modality in patients with older age group, female gender, and Indian for early detection of gallstones formation.

8. ACKNOWLEDGEMENT

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CLINICAL AND LABORATORY FEATURES OF DENGUE INFECTED PATIENTS IN HOSPITALS IN NORTH JAKARTA

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Abstract

Introduction: Dengue fever is an important endemic disease in tropical countries, with more than 1,000 mortalities were reported in Indonesia annually. The government already imposed several measurements, e.g., mosquito's larvae control and strict reporting systems. Most primary healthcare rely on WHO guidelines to diagnose Dengue infection. However, those were dated in 1997, and clinical and laboratory features of Dengue might change.

Objective: This study evaluated the current features of Dengue infection in Indonesia using RT-qPCR as confirmatory method.

Methods: We conducted a study in two hospitals in North Jakarta during the rainy season. Admitted patients with three or more days of fever without other infections were recruited. We took note of the patient's signs and symptoms, as well as available laboratory data. For confirmatory diagnostic, we used RT-qPCR that detect Dengue, Zika, Chikungunya and West Nile viruses.

Results: Among 135 recruited respondents, 70 were positive for Dengue and 2 for Chikungunya. During analysis with the recorded symptoms, fever with two additional symptoms as in WHO guidelines, is still predictive of Dengue infection. Leukopenia and thrombocytopenia were more common in Dengue cases. Hemoconcentration was not assessed as prior value was unknown. Some respondents had prior serology results of NS1 and IgM/IgG against Dengue virus. Of these tests, NS1 is the preferable alternative diagnostic test for Dengue.

Conclusion: WHO guidelines are still relevant for Dengue infection diagnosis in Indonesia. Leukopenia and thrombocytopenia are also additional signs for Dengue infection. Chikungunya should be considered as another possible causes of fever.

Keywords: *WHO guidelines for Dengue, Leukopenia, Thrombocytopenia, Serology tests*

1. INTRODUCTION

As one of the tropical countries, Indonesia faces many health problems that have yet to be eradicated, including Dengue infection. Indonesia is an endemic hotspot for Dengue virus (DENV) particularly in rainy season and in crowded areas such as Java, Bali, and Lombok [1]. As of October 2025, the national Dengue infection case has reached 131,393 with 544 deaths [2]. Inefficient prevention and treatment of Dengue infection might increase morbidity and mortality nationwide. The Indonesian government has enacted various preventive measurements, including household-based mosquito nests eradication and larvae control [3], a strict and systematic rules for Dengue reporting system [4], and approval of Dengue vaccines [5]. Aside from government's initiative, healthcare service improvement is also crucial. Until now, health workers in Indonesia adapt the Dengue diagnosis guidelines published by WHO: acute fever accompanied by two other signs—headache, myalgia, arthralgia, retro-orbital pain, rash, and bleeding manifestation. Blood results such as leukopenia, thrombocytopenia, and hemoconcentration might also be Dengue infection markers [6,7]. Nonetheless, the interplay of humans and DENV vectors interactions alongside environmental factors might influence the relevancy of WHO-based Dengue diagnostic guidelines for the current condition in Indonesia.

Besides clinical diagnosis, confirmatory diagnosis via laboratory procedures is another important measurement to determine Dengue infection. The common diagnostic tests in Indonesia are rapid test for DENV non-structural protein 1 (NS1) antigen and IgG/IgM antibody for point-of-care setting. However, nucleic acid amplification tests (NAATs), particularly reverse transcription-polymerase chain reaction (RT-PCR), has emerged as the gold standard for diagnosing acute infections of DENV, as it offers highly sensitive and specific performance for confirming Dengue fever [8]. Synergistic association between clinical profiles, haematological data, and accurate diagnostic results will help clinicians and medical personnels in mapping and treating Dengue infections rapidly and precisely.

2. OBJECTIVES

This study aims to analyze the current clinical and laboratory profiles of Dengue-infected patients, with RT-quantitative PCR (RT-qPCR) as the method to determine the infection status.

3. METHODOLOGY

The study was conducted using a case-control design with participants recruited from Atma Jaya Hospital (AJH) and Duta Indah Hospital (DIH) in North Jakarta. The patients' recruitment, conducted in the rainy season between August 2023 and May 2024, has gained permission from the ethical committee of Atma Jaya Catholic University of Indonesia (AJCUI) with referral No. 21/05/KEP-FKIKUAJ/2023 and amendment No. 11/02/KEP-FKIKUAJ/2024. The inclusion criteria included adult patients (≥ 18 years old) experiencing high fever for three days or longer and without any other infections or autoimmune conditions who gave their consent to participate in the study. The clinical symptom data based on WHO guidelines [6,7] were obtained through interview-based questionnaire with patients and further confirmation by the attending physician. Meanwhile, the leftover blood specimens and blood profiles were obtained from laboratories in each hospital. Rapid diagnostic analysis of Dengue infection using NS1 and/or IgG/IgM kit were also obtained from several patients.

For the RT-qPCR analysis, all blood specimens were transported to the Atma Jaya research laboratory and processed to aliquot the plasma. After that, the RNA in plasma specimens were extracted with protocols and reagents from QIAamp Viral RNA Mini Kit (Qiagen). The extracted samples were further undergoing RT-qPCR analysis using CFX96 Touch instrument (Bio-Rad) and multiplex kit (Novaplex Tropical Fever Virus Assay Kit, Seegene) that could detect DENV alongside Chikungunya, Zika, and West Nile viruses. Negative control (nuclease-free water) and positive control (manufactured by the RT-qPCR kit) were always added to each RT-qPCR assignment. The results were subsequently analyzed in Seegene Viewer V3 application, with a cycle threshold (Ct) ≤ 45 considered as positive infection.

The clinical symptoms, hematological results, and RT-qPCR data were compiled in SPSS ver. 25 (IBM SPSS Statistics, Armonk, NY, USA) and statistically evaluated using Pearson's Chi-square or Student's t-test. The association between infection status and clinical or blood profiles of participants were considered significant when the p-value is lesser than 0.05.

4. MAIN RESULTS

A total of 135 patients were analyzed in this study. Based on the RT-qPCR results, 70 (52%) of them had active cases of Dengue infection, while 65 were negative for Dengue infection and considered as control. Among 65 DENV-negative participants, two (1.5%) were positive for Chikungunya infection. No cases of Zika or West Nile infection were found.

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The clinical manifestation profiles revealed that 66, 24, 49, 52, 34, and 34 of DENV-positive respondents showed positive signs of headache, retro-orbital pain, myalgia, arthralgia, rash, and bleeding, respectively. Analysis of each symptom displayed nonsignificant association with Dengue infection status. Despite that, Dengue infection and the WHO guidelines, which is the combination of fever with a minimum of two of those symptoms, showed significant association ($p < 0.011$) in this study. The distribution of clinical manifestation among positive and negative DENV patients was displayed in Figure 1.

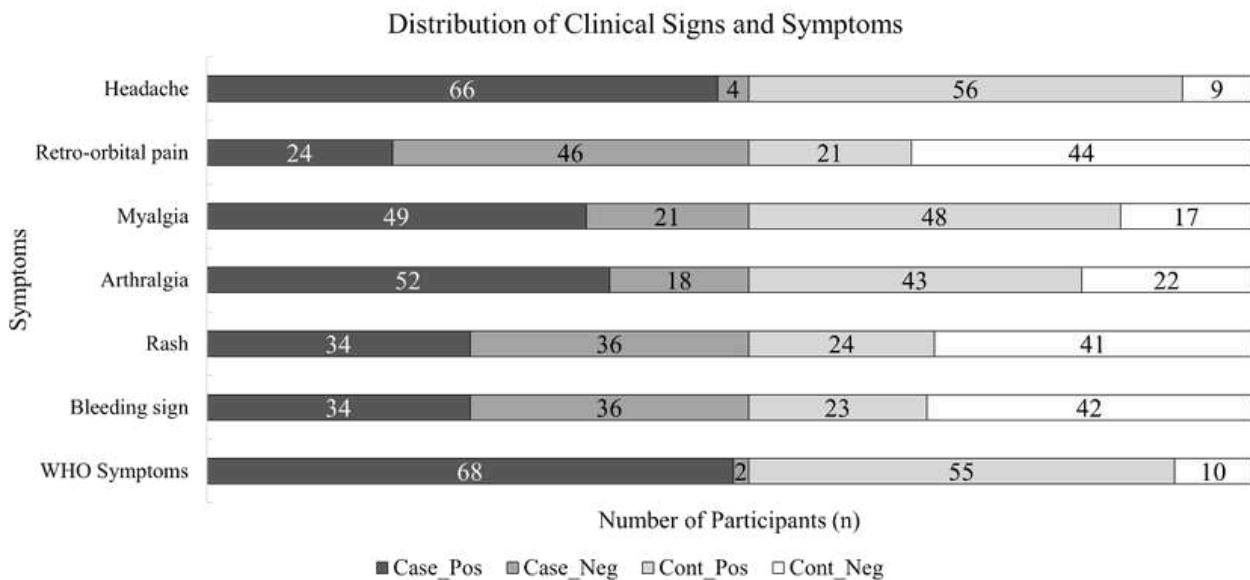


Figure 1. The distribution of clinical symptoms of the participants; Case_Pos: DENV-positive patients with positive clinical manifestation(s); Case_Neg: DENV-positive patients with negative clinical manifestation(s); Cont_Pos: DENV-negative patients with positive clinical manifestation(s); Cont_Neg: DENV-negative patients with negative clinical manifestation(s)

Meanwhile, analysis on the haematological features revealed significant difference between average platelet count ($p=0.019$) and leukocyte count ($p=0.005$) of positive and negative DENV groups, with DENV-positive patients exhibited lower values for both conditions. Further analyses showed that Dengue infection is significantly associated with decreased platelet count or thrombocytopenia and decreased white blood cells (WBCs) or leukopenia ($p < 0.05$). During the data collection, the values for haematocrit increase were not available; therefore, hemoconcentration analysis could not be conducted. Additional data regarding prior rapid diagnostic tests (RDTs) of Dengue infection were also obtained from AJH. Among all types of RDTs, the statistical analysis showed significant correlation between NS1 and RT-qPCR results ($p<0.001$). However, the IgM ($p=0.200$) and IgG ($p=0.644$) analysis do not show significance.

5. DISCUSSION

This study emphasizes the endemicity of Dengue infection in Indonesia [1], as the positive DENV results were higher than the negative ones. Various factors, including the high population density and urbanization, favorable climate conditions, and socio-behavioral aspects (public knowledge and practice), influence Dengue incidence [9]. Based on the clinical signs and symptoms analysis of patients, fever with additional of two or more Dengue-suspected symptoms significantly associated with Dengue infection. Therefore, the WHO guidelines are still appropriate to use in clinical settings in Indonesia [6,7]. A prior systematic review and meta-analysis study regarding diagnostic accuracy of WHO guidelines also revealed its high sensitivity in determining DENV infection (93%; 95% CI=86–96%), albeit low specificity (31%; 95% CI=18–48%) [10]. Another study in Cambodia also supported the importance of WHO clinical guidelines as determinant of DENV infection, especially in resource-limited areas [11].

Additional blood analyses, particularly leukocyte and platelet count analysis, also offer important Dengue diagnostic method. Dengue infection caused leukopenia and thrombocytopenia by directly damaging bone marrow cells, especially hematopoietic stem cells and megakaryocytes, leading to the decreased production of WBC and thrombocytes. Additionally, premature breakdown of platelets due to antibody-mediated lysis further influenced the decrease of platelets [12,13]. Both conditions tend to occur simultaneously, especially around defervescence phase (days 3–8 of illness onset) [13].

The finding of Chikungunya infection showed the ongoing circulation of other arboviruses in Indonesia. Furthermore, the number of CHIKV-suspected individuals reach around 14,000 cases nationally by 2025 [14]. Even though no Zika and West Nile infection were found in this study, the past occurrence of positive seroprevalence for both viruses in Jambi (Zika) [15] and Bandung (West Nile) [16] means that there remains a possibility of these viruses to spread in Indonesia in the future. As these viruses shared similar vector species [17], clinicians and other healthcare personnels should be aware and vigilant of the emergence of other arboviral infections, particularly Chikungunya, beside DENV. In addition, this finding emphasizes the importance of multiplex arbovirus detection using RT-qPCR method. However, for resource-limited areas or point-of-care settings, Dengue NS1 RDT can also be seen as the alternative for RT-qPCR, as this diagnostic method showed rapid result with similar diagnostic accuracy values and easy to perform [18].

6. CONCLUSION

This current study highlights the ongoing applicability of WHO guidelines to diagnose Dengue infection in Indonesia. Additionally, other relevant laboratory analysis, such as leukopenia and thrombocytopenia, are also important additional signs for Dengue infection. Clinicians and health workers must also be aware of other arbovirus with similar clinical symptoms as DENV, especially Chikungunya, as there is ongoing circulation of this virus in Indonesia.

7. ACKNOWLEDGEMENT

This study was supported by internal grant from AJCUI. We thank all participants from both hospitals who were willing to join this study. We would also like to thank doctors from Department of Internal Medicine and laboratory team of AJH, alongside doctors, laboratory team, and other invaluable staffs from DIH for their contribution in patients' recruitment and blood specimen collections. We also thank Helen Kristin, S.Si, Felicia Anggraini, S.Biomed, Angeline Imelda Teguh, and Angelica Michelle Janova for their valuable help in the laboratory work and data verification.

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PREPAREDNESS FOR PRACTICE AMONG FINAL-YEAR MEDICAL STUDENTS: A MIXED-METHODS STUDY

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Abstract

Introduction: The transition from medical school to internship is a critical stage for graduates to demonstrate clinical competence, confidence, adaptability and resilience. Preparedness for practice directly influences professional well-being, patient safety and quality of healthcare delivery.

Objectives: This study explored students' perceptions of readiness for internship, identified strengths and gaps in preparedness, and proposed strategies to enhance transition-to-practice programmes.

Methods: A mixed-methods study was conducted among 96 final-year students in a Malaysian medical school. Quantitative data were collected using a validated modified Clinical Capability Questionnaire (mCCQ). Kendall's tau-b correlation assessed associations between competencies and preparedness, while multivariable linear regression identified independent predictors of preparedness for hospital practice. Qualitative data were obtained from in-depth interviews with 28 students and thematically analysed using NVivo. Ethical approval was obtained (RUMCEC 03-25-0013-S01).

Results: Participants (mean age 24.9 years, 60.4% female, 89.6% Malaysian) reported competence in core clinical skills and preventive care, but lower capability in administration and communication. All clinical capabilities correlated positively with preparedness domains ($\tau=0.151-0.348$, $p<0.05$). Thematic analysis identified four themes: (1) Perceptions of preparedness, (2) Clinical capability and professional development, (3) Systemic and structural influences, and (4) Actionable recommendations to enhance internship preparedness

Discussion: Our findings are consistent with previous studies, demonstrating variable perceived preparedness across clinical and non-clinical domains. Students highlighted bridging programmes, including sub-internship, elective and pre-internship programmes, as vital for enhancing readiness, confidence and adaptability. Innovative approaches such as simulation-based training and digital learning modules have proven effective in facilitating workplace transitions.

Conclusion: Most graduates attained baseline clinical competence but gaps remained in communication, administration and operational management. Targeted curriculum reforms and structured pre-internship programmes, including sub-internships and simulation-enhanced modules, are essential to reinforce readiness, nurture resilience, and ensure high-quality patient care in line with modern medical practice.

Keywords: *Preparedness, Readiness, Clinical Competence, Internship, Medical Students*

1. INTRODUCTION

Transition from medical school to internship is a critical stage. Graduates must demonstrate clinical competence, confidence, adaptability and resilience (1). Readiness for internship directly influences professional well-being, with implications to patient safety and the quality of healthcare (2). This mixed-methods study aims to examine final-year medical students perceived preparedness for internship and propose structured strategies, aligned with evolving healthcare demands to bridge the transition gap. We directly advance the conference theme “Innovation and Progress in Medical Science” through evidence-based approaches that future-proof transition-to-practice experience.

2. OBJECTIVES

2.1 Main objective

A mixed-methods study was conducted using qualitative and quantitative components, to explore the perceived preparedness for practice among final year medical students in Malaysia.

2.2 Specific objectives

- 2.2.1 Identified the perceived preparedness for internship among final year medical students.
- 2.2.2 Identified specific strengths and gaps in preparedness.
- 2.2.3 Proposed targeted strategies to enhance transition-to-practice.

3. METHODOLOGY

A mixed-methods study was conducted among 98 final-year students at a Malaysian medical school. Quantitative data were collected using a validated tool (3), the modified Clinical Capability Questionnaire (mCCQ) which assessed self-perceived clinical capability (clinical, procedural, operational management and administrative skills subscales) and Preparedness for Hospital Practice Questionnaire (PHPQ: confidence, preventive, interpersonal skills and collaboration subscales). Internal consistency was assessed using Cronbach's α . Descriptive statistics summarised demographics and preparedness domains. Inferential statistics used Kendall's tau-b correlation to assess associations between competencies and preparedness, while multivariable linear regression identified independent predictors of preparedness for hospital practice, adjusting for key covariates. Analyses were conducted in IBM SPSS Statistics (v27).

Qualitative data were obtained from in-depth interviews with 28 students, purposively sampled for diversity. Semi-structured interviews were conducted face-to-face or online, audio-recorded with consent, and transcribed verbatim. Transcripts were anonymised and analysed in NVivo (Released 1.7). Three independent investigators conducted deductive coding, developed and applied a thematic framework across the dataset, and refined themes through consensus meeting and peer debriefing to ensure analytic rigour.

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Ethical approval was obtained (RUMCEC 03-25-0013-S01). Written informed consent and data confidentiality procedures were observed throughout.

4. MAIN RESULTS

Ninety-six final-year medical students (response rate of 98%) participated in the quantitative survey (mean age 24.9 years, 60.4% female, 89.6% Malaysian), while 28 were interviewed in the qualitative phase. Students reported strong competence in core clinical (mean 4.03 ± 0.42) and procedural skills (mean 3.80 ± 0.61), with lower confidence in administrative (mean 2.83 ± 0.88) and operational management domains (mean 3.21 ± 0.70). Preparedness scores were highest in preventive care (mean 4.66 ± 0.77) and lowest in interpersonal communication (mean 3.88 ± 1.00). All clinical capability subscales correlated positively with preparedness domains ($\tau = 0.151-0.348$, $p < 0.05$), indicating that students who rated higher in procedural and clinical skills also demonstrated greater confidence, teamwork, and reflective practice.

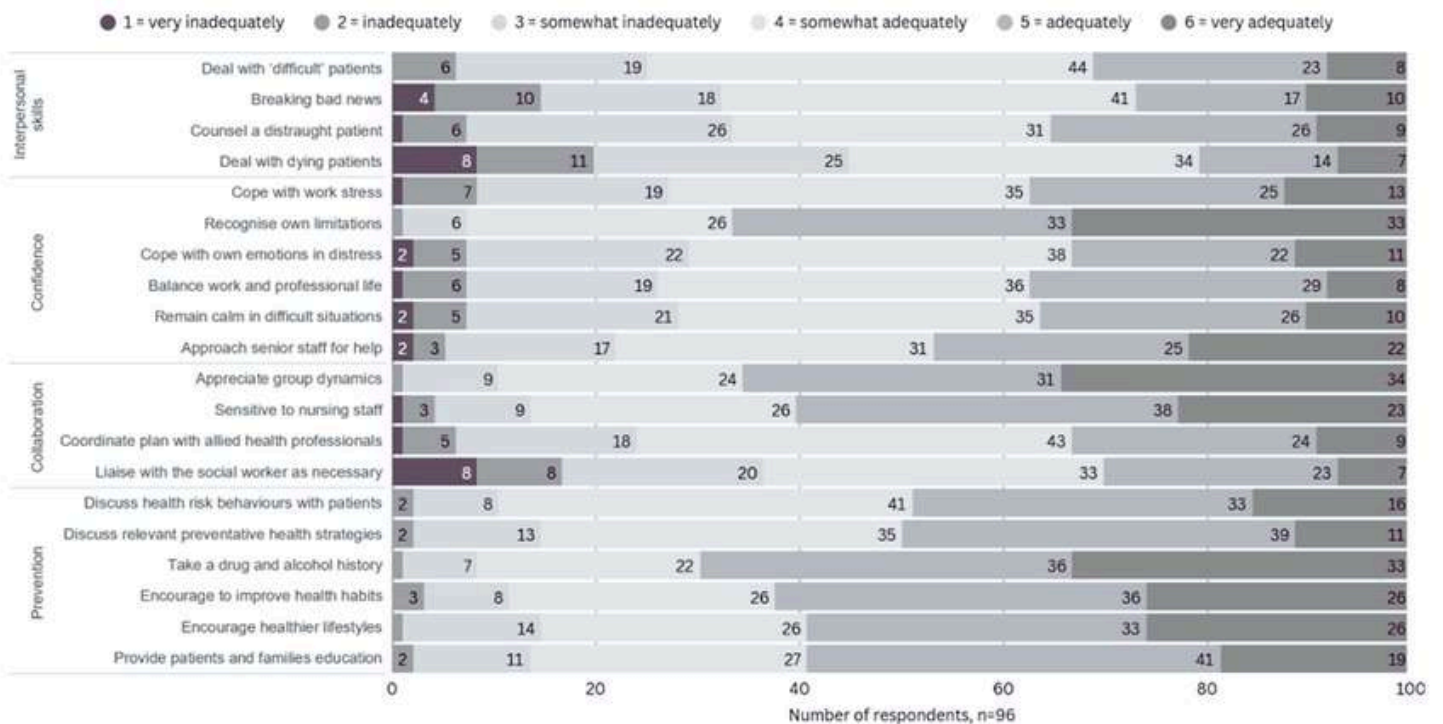


Figure 1. Self-reported Preparedness for Hospital Practice (n=96)

Qualitative interviews were analysed deductively. (1) Perceptions of preparedness; students reflected moderate to high confidence, tempered by anxiety over administrative and documentation duties; (2) Clinical capability and professional development; students highlighted solid theoretical grounding but variability in procedural exposure and interprofessional communication; (3) Systemic and structural influences; strengths in curriculum were bedside teaching and sub-internships alongside gaps in certain specialty rotations, administrative burden, and uneven supervision quality; and (4) Actionable recommendations; students advocated the need for enhanced hands-on training, structured pre-internship programmes, improved mentorship and support systems.

Overall, students demonstrated adequate competence for supervised practice but called for better alignment between academic preparation and real-world clinical expectations to ensure smoother transition into internship.

5. DISCUSSION

Final-year medical students perceived preparedness for internship varied across domains, reflecting earlier studies that reported uneven readiness between clinical and non-clinical domains (1, 4). Consistent with quantitative findings, students who demonstrated stronger clinical and procedural skills also reported greater confidence and overall preparedness for hospital practice from our interviews. These results reinforce the notion that competence, practical and professional domains is foundational to the confidence required for a successful transition into the clinical workplace.

Students consistently identified authentic clinical experiences as central to their preparedness, aligned with Situated Learning Theory (5), which emphasises learning through participation within a community of practice. Sub-internships and elective placements were frequently mentioned as pivotal experiences, offering exposure to real-world clinical expectations and responsibilities (6). Additionally, the expressed need for structured pre-internship programmes and mentoring resonated with Social Constructivist Theory (7) where guided participation within the Zone of Proximal Development enhances the potential competence and confidence. These well-supervised bridging programmes enhance internship readiness and support the formation of professional identity.

Innovative pedagogical strategies such as simulation-based learning, digital modules and use of artificial intelligence in healthcare have been widely recognised as effective in bridging the workplace transition (8-10). These modalities provide safe, realistic environments for practising procedural and communication skills prior to entering high-stakes clinical settings.

Implications: These findings highlight the need for innovative, future-oriented educational strategies that go beyond traditional clinical training. Structured, experiential learning opportunities, integrating longitudinal sub-internships, simulation-based modules and digitally enhances bridging programmes can strengthen both clinical and non-clinical competencies to prepare medical graduates for the evolving complexities of clinical practice. As medical sciences advances, curricula must adapt to foster readiness, resilience and professional identity in future doctors. Future research is needed to evaluate the impact of these interventions on early career performance and well-being.

6. CONCLUSION

Most graduates demonstrated baseline clinical competence; however, gaps persist in communication, administration and operational management domains. Targeted curriculum reforms and structured pre-internship programmes, including sub-internships and simulation-enhanced modules, are essential to strengthen preparedness, nurture resilience and professional confidence. These innovations exemplify progress in medical science education, ensuring future doctors are workplace-ready and equipped to deliver safe, high-quality patient care in an evolving healthcare landscape.

7. ACKNOWLEDGEMENT

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LDL-C TARGET ATTAINMENT RATE AMONG TYPE 2 DIABETES PATIENTS IN PRIMARY CARE

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Abstract

Low-density lipoprotein cholesterol (LDL-C) is a key therapeutic target for cardiovascular disease prevention in patients with Type 2 Diabetes Mellitus (T2DM). Despite guideline-recommended targets based on cardiovascular (CV) risk stratification, LDL-C target achievement remains suboptimal in many settings. Local data on target achievement and contributing factors are limited in Malaysia, particularly in the Klang Valley. To determine LDL-C target achievement rates and associated factors among adults with Type 2 Diabetes Mellitus (T2DM). Methods: A cross-sectional study was conducted among 400 adults with T2DM receiving care at Klinik Kesihatan Bandar Botanik, Klang. Data collected included demographic data, LDL-C levels, cardiovascular risk classification (based on ESC/EAS 2019 guidelines), lipid-lowering therapy patterns, and treatment adherence. Statistical analyses were performed using chi-square tests and logistic regression to identify factors associated with LDL-C target attainment. Only 28.5% (n=114) achieved LDL-C targets, with failure highest in high-risk (70.5%) and very high-risk (81.4%) groups ($p<0.001$). Although comorbidities and diabetes duration (mean 8.99 years) were analysed, adherence was the sole significant predictor (OR=4.59, 95%CI:1.35–15.56, $p=0.014$). Atorvastatin monotherapy predominated (92.8%), with minimal dose escalation (15.8%). LDL-C target attainment remains suboptimal, particularly among high and very high CV-risk groups. Poor adherence is the key modifiable barrier. Findings underscore the importance of personalized adherence strategies and proactive therapy optimization in primary care to improve lipid control and reduce CV risk among patients with T2DM.

Keywords: *Type 2 Diabetes Mellitus, LDL-C, Dyslipidemia, Cardiovascular Risk, Statin Therapy*

1. INTRODUCTION

Malaysia Low-density lipoprotein cholesterol (LDL-C) is a key therapeutic target for cardiovascular disease prevention in patients with Type 2 Diabetes Mellitus (T2DM)(10). Despite guideline-recommended targets based on cardiovascular (CV) risk stratification, LDL-C target achievement remains suboptimal in many settings (2,3,4). Local data on target achievement and contributing factors are limited in Malaysia, particularly in the Klang Valley.

2. OBJECTIVES

To determine LDL-C target achievement rates and associated factors among adults with Type 2 Diabetes Mellitus (T2DM).

3. METHODOLOGY

A cross-sectional study was conducted among 400 adults with T2DM receiving care at Klinik Kesihatan Bandar Botanik, Klang. Data collected included demographic data, LDL-C levels, cardiovascular risk classification (based on ESC/EAS 2019 guidelines), lipid-lowering therapy patterns, and treatment adherence. Statistical analyses were performed using Chi-square tests and logistic regression to identify factors associated with LDL-C target attainment. Ethical approval: MREC (MOH Malaysia, NMRR ID-NMRR ID-24-01454-7II).

4. MAIN RESULTS

Only 28.5% (n=114) achieved LDL-C targets, with failure highest in high-risk (70.5%) and very high-risk (81.4%) groups ($p < 0.001$). Although comorbidities and diabetes duration (mean 8.99 years) were analysed, adherence was the sole significant predictor (OR=4.59, 95%CI:1.35–15.56, $p = 0.014$). Atorvastatin monotherapy predominated (92.8%), with minimal dose escalation (15.8%).



Figure 1: LDL-C Target Achievement among participants.

Table 1 : LDL-C target achievement by patient characteristics (n=400).

Variables		Total, n (%)	LDL-C Target Achieved, n (%)	LDL-C Target Not Achieved, n (%)
Age Group (years)	< 50	44 (11.0)	19 (43.2)	25 (56.8)
	50-59	127 (31.8)	47 (37.0)	80 (63.0)
	60-69	156 (39.0)	32 (20.5)	124 (79.5)
	≥ 70	73 (18.3)	16 (21.9)	57 (78.1)
Gender	Female	229 (57.3)	68 (29.7)	161 (70.3)
	Male	171(42.7)	46 (26.9)	125 (73.1)
Race	Malay	96 (24)	23 (24.0)	73 (76.0)
	Chinese	119 (29.8)	43 (36.1)	76 (63.9)
	Indian	185 (46.3)	48 (25.9)	137 (74.1)
Body Mass Index Category (kg/m ²)	<18.5	5 (1.3)	2 (40.0)	3 (60.0)
	18.5-22.9	57 (14.2)	18 (31.6)	39 (68.4)
	23.0-27.4	152 (38.0)	45 (29.6)	107 (70.4)
	27.5-32.4	126 (31.5)	31 (24.6)	95 (75.4)
	32.5-37.4	46 (11.5)	16 (34.8)	30 (65.2)
	≥37.5	14 (3.5)	2 (14.3)	12 (85.7)
Blood Pressure Control (mmHg)	<140/80	149 (37.3)	45 (30.2)	104 (69.8)
	>140/80	251 (62.7)	69 (27.5)	182 (72.5)
HbA1C (%)	≤ 6.5	173 (43.3)	50 (28.9)	123 (71.1)
	> 6.5	227 (56.8)	64 (28.2)	163 (71.8)
Comorbidity Status	None	85 (21.3)	29 (34.1)	56 (65.9)
	Single	271 (67.8)	74 (27.3)	197 (72.7)
	Multiple	44 (11.0)	11 (25.0)	33 (75.0)
Macrovascular Complications	Nil	330 (82.5)	102 (30.9)	228 (69.1)
	IHD	49 (12.3)	9 (18.4)	40 (81.6)
	Stroke	16 (4.0)	2 (12.5)	14 (87.5)
	PAD	3 (0.8)	0 (0.0)	3 (100.0)
	IHD and Stroke	2 (0.5)	1 (50.0)	1 (50.0)
Microvascular Complication Count	None	254 (63.5)	84 (33.1)	170 (66.9)
	One	125 (31.3)	27 (21.6)	98 (78.4)
	Two	19 (4.8)	3 (15.8)	16 (84.2)
	Three	2 (0.5)	0 (0.0)	2 (100.0)
CV Risk Group	Low risk	0 (0.0)	0 (0.0)	0 (0.0)
	Intermediate risk	46 (11.5)	27 (23.7)	19 (6.6)
	High risk	193 (48.3)	57 (50.0)	136 (47.6)
	Very high risk	161 (40.3)	30 (26.3)	131 (45.8)
Statin Therapy Type	Statin monotherapy	392 (98.0)	112 (28.6)	280 (71.4)
	Statin combination therapy	8 (2.0)	2 (25.0)	6 (75.0)
Statin Intensity	Low Intensity	29 (7.2)	5 (17.2)	24 (82.8)
	Moderate Intensity	291 (72.8)	91 (31.3)	200 (68.7)
	High Intensity	80 (20.0)	18 (22.5)	62 (77.5)

PAD = Peripheral Artery Disease; IHD = Ischaemic Heart Disease; CV = Cardiovascular

5. DISCUSSION

This study found that LDL-C target achievement among adults with Type 2 Diabetes Mellitus was significantly influenced by cardiovascular risk level, age, ethnicity, treatment adherence, and diabetes duration, with poor adherence emerging as the strongest barrier to optimal lipid control.

6. CONCLUSION

LDL-C target attainment remains suboptimal, particularly among high and very high CV-risk groups. Findings underscore the importance of personalized adherence strategies and proactive therapy optimization in primary care to improve lipid control and reduce CV risk among patients with T2DM(5).

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Effectiveness of Cervical Proprioception Training versus Deep Cervical Extensor Training on Cervical Extensor Endurance in Patients with Chronic Non-Specific Neck Pain

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Abstract

Background: Chronic neck pain (CNP) is characterized as persisting pain for more than 3 months, which has a longer expected recovery time, and is one of the individuals most common and debilitating problem. CNP has been linked to abnormalities in cervical proprioception and neck extensor endurance (NEE), two processes that are essential for preserving cervical spine function. Neck pain itself has a clear role in proprioception and neck sensorimotor control, and subsequently influence orientation. The cervical extensor muscles are considered equally important in the recovery of patients with neck pain. Cervical Proprioception Training (CPT) may have the added advantage of facilitating the deep cervical extensor muscles.

Objective: To compare the effectiveness of Cervical Proprioception Training (CPT) versus Deep Cervical Extensor Training (DCET) in patients with chronic non-specific neck pain.

Methods: This was a non-randomized clinical trial that was quasi-experimental in nature. The study population included factory workers in Penang patients of both sexes, aged between 30 and 50 years, diagnosed by GP with a chronic non-specific neck pain for 3 months or more. Two experimental groups, group 1 received Cervical Proprioception Training and while group 2 received Deep Cervical Extensor Training for a duration of 6 weeks. The study included a pre and post intervention assessment of muscle endurance, functional status and pain, using validated measurement tools such as the Cervical Extensor Endurance Test (CEET), Neck Disability Index (NDI) and Visual Analogue Scale (VAS).

Results: Following 6 weeks, concerning VAS there was a statistically significant decline of VAS in the two groups with favor to the CPT group ($p < 0.05$) in comparison with the DCET group. In regards to the NDI levels, there was a statistically significant decline in NDI scores in the two groups with favor to the CPT group (mean decline of 13.48) in comparison with the DCET group (mean decline of 10.17). Concerning CEET levels there was a statistically significant improvement in CEET scores ($p < 0.05$) in the two groups with favor to the DCET group in comparison with the CPT group.

Conclusion: Both groups of patients with chronic non-specific neck pain (CNNP) demonstrated similar outcomes. Both groups were found to reduce pain levels, as assessed using VAS, and enhance functional status, as evaluated using NDI and improve NEE as measured by CEET. The present study also provided evidence to support the idea that Cervical Proprioception Training and Deep Cervical Extensor Training lead to improvements in cervical extensor endurance, as measured by CEET.

Keywords: Neck Pain, Proprioception, Muscle, Functional Status, Visual Analogue Scale, Chronic, Chronic Neck Pain, Cervical Spine

1. INTRODUCTION

The prevalence of neck pain is such that by 2050, the anticipated global incidence of neck pain cases is expected to reach 269 million, reflecting a 32.5% rise from 2020 to 2050, one of the most usually occurring musculoskeletal disorders.¹ Among the most prevalent and incapacitating conditions affecting people is Chronic Neck Pain (CNP), which is defined as pain that persists more than three months and requires a longer estimated recovery period. A diagnosis of "non-specific" neck pain (NSNP) can be made solely based on clinical evidence, provided that there are no features that imply a more severe condition and/or a specific underlying disease that is causing the pain.³ The majority of guidelines for diagnosing and treating neck pain suggest that the best evidence-based physiotherapy therapies for treating people experiencing neck pain call for a combination of education, exercise, and manual therapy.⁴

The cervical muscle spindles play a crucial role as proprioceptors in the neck, Modifications in the operation of the cervical muscles have an impact on cervical proprioception by modifying the release of muscle spindles.⁵ Chronic pain has the ability to modify the sensitivity of the muscle spindle receptors and disrupt the incoming proprioceptive signals. Diminished proprioception has been linked to reduced engagement in the deep muscle group, which encompasses the proprioceptive network.⁶ Neck muscle fatigue causes changes in the sensitivity of sensory receptors and muscle spindles, which in turn affects the input of proprioceptive information to the higher centers of the body.⁷ Neck-based cervical proprioception is essential for maintaining postural stability, synchronizing head movements, and guaranteeing ideal spatial awareness.⁸ Previous study demonstrated that individuals with CNP exhibited impaired cervical proprioception in comparison to those who were asymptomatic. which signifies the strong correlation between neck pain and cervical proprioception.⁹ Therefore, engaging in proprioceptive exercises that target the restoration of the muscular tone in the deep neck muscles can be a successful approach to alleviate pain and enhance both the range of motion and functional limitations.¹⁰

The Deep Neck Extensors (DCE) contribute to maintaining the cervical lordosis, by working together with the deep neck flexors and preventing the head from tilting forward. Patients with neck pain are thought to benefit equally from strengthening their cervical extensor muscles highlighting the significance of exercise in enhancing function.¹¹ CNP has been linked to abnormalities in cervical proprioception and Neck Extensor Endurance (NEE), two processes that are essential for preserving function of the cervical spine. In comparison to individuals who did not exhibit any symptoms, CNP subjects displayed reduced endurance capacity and poor proprioception.¹³ The relationship between neck muscle endurance and proprioception in people with chronic neck pain is insufficiently studied. The effectiveness of deep cervical extensor muscle training in comparison with cervical proprioception training remains also unclear.

2. OBJECTIVES

This study aims to evaluate whether in patients with chronic non-specific neck pain, whether cervical proprioception training can have a positive impact on the neuromuscular control of the cervical region extensor muscles. The objective of the current study is to compare the effectiveness of cervical proprioception training versus deep cervical extensor training in patients with chronic non-specific neck pain on Neck Extensor Muscle Endurance, Neck Pain and Functional Status.

3. METHODOLOGY

All subjects were recruited from diverse private manufacturing workers in Penang (Malaysia) who had Chronic Non-Specific Neck pain. This study was conducted in a non-blinded manner, a quasi experimental clinical trial from May to July 2024. A total of 65 chronic non-specific neck pain patients were considered for eligibility in the current study. 60 eligible patients (women and men) ranging in age from 30 to 50 were divided equally into two groups by means of a convenience sampling method. The Cervical Proprioception Training group consisted of 15 males and 15 females, while the Deep Cervical Extensor Training group consisted of 16 males and 14 females. 5 subjects were eliminated as they did not meet inclusion criteria. The Ethical Committees of the AIMST University gave their permission to this study (Ref No: AUHEC/SOP/FAHP/05/07/2024). Once the participant agreed to take part in the research, they were informed and obtained consent in the verbal and written form. They were also informed that they were allowed to withdraw from the study at any moment. Both workout regimens lasted for a duration of 6 weeks, with a frequency of 3 days each week. Prior to commencing the trial, baseline measurements were taken. Each session typically lasted for around 15 to 20 minutes. All the outcome measures were reassessed at the conclusion of the 6-week period. The participants were instructed to abstain from utilizing alternative therapies throughout the duration of the trial.

The inclusion criteria were as follows: patients of both sexes, age between 30 and 50 years, confirm diagnosed with chronic non-specific neck pain grade I and II (according to Task Force on Neck Pain classification Grade), a positive finding for weakness of the deep neck extensors (unable to sustain a chin tuck position in neutral for 20 seconds) measured through the Cervical Extensor Endurance Test (CEET), pain intensity of 1-7 on VAS score and scores mild or moderate disability (15- 24 points) or (10% - 48 %) in Neck Disability Index (NDI) score.

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Interventions

Cervical Proprioception Training (CPT)

The components of Cervical Proprioception Training (CPT) that are considered to be relevant have been adapted here. Oculomotor control exercises, also known as gaze stability exercises, eye-head coordination exercises, and head relocation practice were all included in this regimen. Each regimen conducted involved performing 3 sets of 5 repetitions, thrice each week for a duration of 6 weeks, under the supervision of the therapist.



Fig 1.1 : Cervical Proprioception Training group: Eye-Head coordination exercise

Deep Cervical Extensor Training (DCET)

This technique focused on semispinalis cervicis activation with resisted extension. Participants were instructed to exert their maximum voluntary force in the direction of extension, while ensuring that no neck pain was triggered (Figure 1.2). The workout programme involved maintaining resistance for a duration of 10 seconds, repeated ten times per set, and completing three sets per day. A 30-second interval was permitted between sets. Each participant engaged in this workout thrice weekly for a duration of 6 weeks under the guidance of a physical therapist.²¹



Fig 1.2: Hand positioning for the Deep Cervical Extensor Training group

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4. RESULTS

The Shapiro-Wilk test was utilized to assess the normality of the variables of interest. The Paired Samples t-test was employed for comparing results within the same group, while the Independent Samples t-test was used for contrasting the dependent variables.(VAS, NDI, and CEET) between the two treatment groups (CPT and DCET) at both the baseline and sixth week of intervention. Both groups showed significant pain reduction (VAS) and functional improvement (NDI), with CPT outperforming DCET in pain and disability reduction (mean NDI decline 13.48 vs. 10.17) . DCET yielded greater gains in cervical extensor endurance (CEET) than CPT (mean difference 3.38).

Between Group Analysis

Between-group comparison of patients' mean score of pain intensity (VAS scores), functional status (NDI scores), neck extensor muscle endurance (CEET scores) is outlined in fig (1.3). Concerning VAS there was a statistically significant decline of VAS in the two groups with favor to the CPT group in comparison with the DCET group . Concerning NDI levels there was a statistically significant decline in NDI scores in the two groups with favor to the CPT group (mean decline of 13.48) in comparison with the DCET group (mean decline of 10.17) .Concerning CEET levels there was a statistically significant improvement in CEET levels in the two groups with favor to the DCET group in comparison with CPT group . Thereby, it can be concluded that the null hypothesis is rejected and the alternative hypothesis is accepted.

Table 1.1 : Results of Visual Analogue Scale, Neck Disability Index and Cervical Extensor Endurance Test before and after intervention in group 1- Cervical Proprioception Training

	Mean (SD)	SEM	95% CI of the difference		t	P
			Lower	Upper		
VAS						
Pre-intervention	5.21 (1.37)	0.25	1.74	2.81	8.682	0.000
Post-intervention	2.93 (1.53)	0.28				
NDI						
Pre-intervention	36.72 (10.73)	1.99	10.29	16.67	8.662	0.000
Post-intervention	23.24 (10.64)	1.98				
CEET						
Pre-intervention	15.21 (2.80)	0.52	-4.63	-2.82	-8.395	0.000
Post-intervention	18.93 (4.00)	0.74				

Note: SD: Standard Deviation; SEM: Standard Error of Mean; CI: Confidence Interval;
VAS: Visual Analogue scale; NDI: Neck Disability Index; CEET: Cervical Extensor Endurance Test

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Table 1.2: Results of Visual Analogue Scale, Neck Disability Index and Cervical Extensor Endurance Test before and after intervention in group 2- Deep Cervical Extensor Training

	Mean (SD)	SEM	95% CI of the difference		t	P
			Lower	Upper		
VAS						
Pre-intervention	5.24 (1.30)	0.24	1.68	2.80	8.157	0.000
Post-intervention	3.00 (1.60)	0.30				
NDI						
Pre-intervention	33.97 (8.34)	1.55	8.01	12.33	9.651	0.000
Post-intervention	23.79 (9.18)	1.70				
CEET						
Pre-intervention	14.90 (2.92)	0.54	-8.36	-5.84	-11.558	0.000
Post-intervention	22.00 (4.81)	0.89				

Note: SD: Standard Deviation; SEM: Standard Error of Mean; CI: Confidence Interval; VAS: Visual Analogue Scale; NDI: Neck Disability Index; CEET: Cervical Extensor Endurance Test.

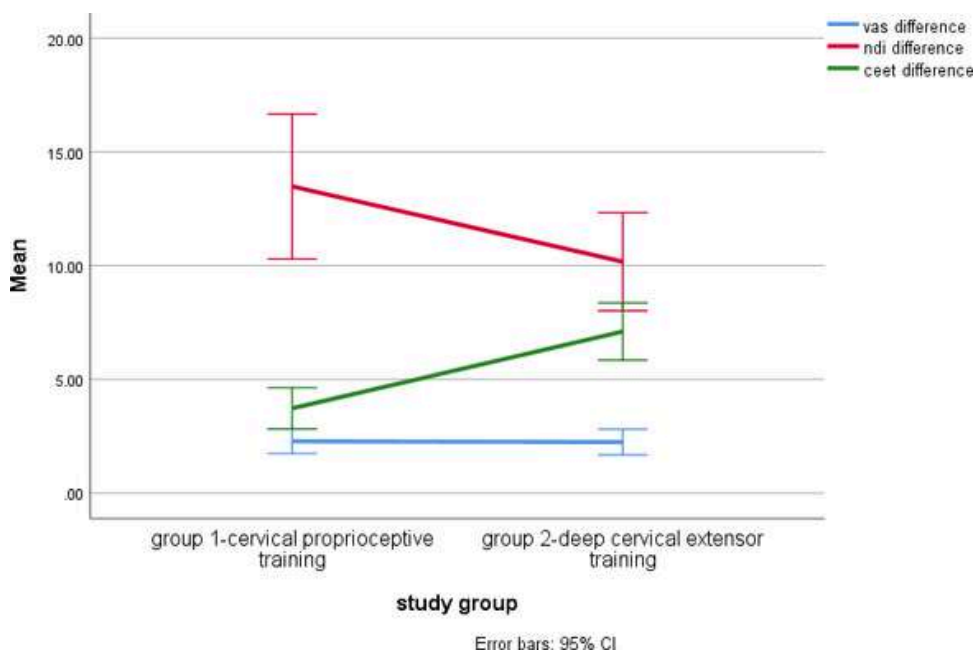


Fig 1.3 : Outcomes of Visual Analogue Scale, Neck Disability Index and Cervical Extensor Endurance Test difference between group 1-Cervical Proprioception Training and group 2-Deep Cervical Extensor Training



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5. DISCUSSION

Both Cervical Proprioception Training (CPT) and Deep Cervical Extensor Training (DCET) led to improvements in pain intensity, neck extensor muscle endurance, and functional status after a 6-week intervention in patients with chronic non-specific neck pain. CPT may benefit not only proprioceptive awareness but also contribute to the strengthening of deep cervical extensor muscles. The findings suggest that exercise training should prioritize modifying specific muscle dysfunction, especially targeting the deep cervical extensor muscles as identified during evaluation. Both interventions resulted in similar outcomes regarding pain reduction (VAS), functional status improvement (NDI), and increased neck extensor endurance (CEET). The study provides evidence that both CPT and DCET improve cervical extensor endurance, supporting their use in rehabilitation for chronic neck pain. The improvements in VAS, NDI, and CEET scores were statistically significant within both groups from pre- to post-intervention. Between-group comparisons revealed that CPT was superior in reducing pain and disability. DCET was superior in increasing cervical extensor muscle endurance. CPT likely improves neuromuscular control and proprioceptive feedback, which may explain its greater effect on pain and disability. DCET directly targets the deep cervical extensors, leading to more robust gains in muscle endurance.

Chronic neck pain (CNP) is associated with abnormalities in cervical proprioception and neck extensor endurance (NEE), both of which are essential for maintaining cervical spine function. Individuals with CNP demonstrate reduced endurance capacity and poor proprioception compared to asymptomatic individuals, highlighting the importance of addressing both factors in rehabilitation. The relationship between neck muscle endurance and proprioception in people with chronic neck pain is not well studied, and the comparative effectiveness of deep cervical extensor muscle training versus cervical proprioception training remains unclear, indicating a gap in the literature. The study's findings align with previous research suggesting that training focused on proprioceptive awareness can also benefit the strengthening of deep cervical extensor muscles, supporting the integration of proprioceptive exercises in clinical practice. The use of validated measurement tools such as the Visual Analogue Scale (VAS) for pain, Neck Disability Index (NDI) for functional status, and Cervical Extensor Endurance Test (CEET) for muscle endurance strengthens the reliability of the study's outcomes and is consistent with established research methodologies. DCET too indicated the presence of the treatment impact in lowering pain and improving functional status, which was one of our study outcomes. Prior discoveries aligned with our observations, indicating that a 6 week regimen targeting the semispinalis cervicis yields notable benefits in reducing pain severity, can effectively decrease functional disability and significantly improve neck-extensor muscle



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endurance compared to the CPT group. The mean difference between the two groups was 3.38, which was the highest among the three outcome measures. The results showed that the DCET group demonstrated more significant training effects. This suggests that CPT demonstrated advantages in enhancing the motor control of cervical extensor muscles. Parallel findings were reported in which they explored the effects of cranio-cervical flexion training versus proprioception training on the cranio-cervical flexion test outcomes, a measure of the deep cervical flexors' neuromuscular control. A systematic review indicated that proprioceptive training has the potential to result in substantial enhancements in both proprioceptive and motor function among various healthy and clinical groups. Experimental data suggests that therapies targeting the enhancement of somatosensory function not only enhance proprioception but also motor function.²⁴

6. CONCLUSION

Both CPT and DCET significantly reduce pain and disability while improving cervical extensor endurance in chronic neck pain patients, with CPT showing superior pain and functional benefits and DCET excelling in muscle endurance enhancement. Both training types effectively improve CNP symptoms; CPT also benefits muscle endurance, suggesting proprioceptive exercises support deep muscle function. This suggests that training focused on proprioceptive awareness could also benefit the strengthening of the deep cervical extensor muscles. Consequently, exercise training should prioritize modifying particular muscle dysfunction, particularly the deep cervical extensor muscles as determined by evaluation. Therefore, it is essential to treat the limitations of the neck musculature using an endurance test as part of problem-based care for patients with CNP. There is no single test that can definitively or comprehensively assess cervical muscle function. However, a simple endurance test, such as the cervical extensor endurance test, can be readily performed in a typical clinical setting due to its minimal time requirements, enhanced efficiency, and increased effectiveness.

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Well-Being and Mobility Status Among Senior Club Members in Klinik Kesihatan Jinjang - A Cross-Sectional Study

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Abstract

Malaysia is projected to become an aging nation by 2030, with 15% of its population aged 60 years and above. The growing older population faces increasing physical and psychosocial challenges. This study aimed to assess the quality of life (QOL), physical performance, and their associations with demographic and clinical factors among senior citizen club members in Klinik Kesihatan Jinjang. A cross-sectional study was conducted among senior club members at Klinik Kesihatan Jinjang. Data collected included demographics, fall history, hand grip strength, and physical performance using the Short Physical Performance Battery (SPPB). Quality of life was assessed using the WHOQOL-BREF questionnaire. Descriptive statistics, *t*-tests, ANOVA, and regression analyses were used to explore associations. A total of 60 community-dwelling older adults participated (mean age 75.4 ± 6.65 years). Most were female (91.7%), married (71.7%), and of Chinese ethnicity (65.0%). Mean club membership duration was 9.7 ± 5.8 years. Eight participants (13.3%) reported a fall in the past year, and most (91.7%) did not use walking aids. Most participants rated their QOL as good (58.3%) or very good (30.0%), and were satisfied with their health (78.3%). About 51.7% had normal hand grip strength, while 66.7% were classified by SPPB as having good functional status. No significant associations were found between SPPB and age, club duration, or exercise level ($p > 0.05$). Mean WHOQOL-BREF scores were physical 76.4, psychological 76.7, and environmental 75.8, reflecting favorable well-being. Exercise significantly influenced the environmental domain ($p = 0.028$), suggesting active seniors perceive better environmental support. Senior club participation is linked to good QOL and functional independence. Interventions emphasizing mobility, exercise, social engagement, and fall prevention are recommended. Larger longitudinal studies are needed to explore causal relationships.

Keywords: *Aging, Older Adults, Senior Citizen Club, Primary Care, Malaysia*

1. INTRODUCTION

Malaysia is projected to become an aging nation by 2030, with 15% of its population aged 60 years and above. Understanding both the physical (mobility) and psychosocial (well-being) dimensions among senior club members at a local health clinic offers actionable insights for preventive geriatrics.

2. OBJECTIVES

To evaluate the well-being and functional status of senior club members at Klinik Kesihatan Jinjang and identify influencing factors. Specifically, to examine how socio-demographic factors affect well-being and functional ability, and to assess physical, mental, and social well-being, as well as mobility using standardized tools.

3. METHODOLOGY

A cross-sectional study was conducted among 60 senior club members. Data included socio-demographics, fall history, handgrip strength, and physical performance using the Short Physical Performance Battery (SPPB). Well-being was measured using the WHOQOL-BREF, while functional status was evaluated using the SPPB and handgrip strength. Data were analyzed using descriptive statistics, t-tests, ANOVA, and multivariate regression. Ethical approval: MREC (MOH Malaysia, NMRR ID-25-01192-QXS).

4. MAIN RESULTS

Participants' mean age was 75.4 ± 6.65 years; 91.7% were female. Most rated their QOL as good (58.3%) or very good (30.0%). Mean WHOQOL-BREF scores were physical 76.4, psychological 76.7, and environmental 75.8. Exercise significantly influenced the environmental domain ($p = 0.019$), suggesting active seniors perceive better environmental support.



Table 1: Baseline Characteristic

Variables		Frequency, N (%)
Sex	Female	55 (91.7)
	Male	5 (8.3)
Age	60-69	11 (18.3)
	70-79	34 (56.7)
	80-89	14 (23.3)
	>90	1 (1.7)
Ethnicity	Malay	12 (20.0)
	Chinese	39 (65.0)
	India	9 (15.0)
Marital Status	Married	42 (70.0)
	Single	2 (5.0)
	Widowed	14 (23.3)
	Divorced	1 (1.7)
Education Level	No formal education	10 (16.7)
	Primary education	21 (35.0)
	Secondary education	22 (36.7)
	Tertiary education	7 (11.7)
Presence of comorbidities	No	8 (13.3)
	Yes	52 (86.7)
History of fall	No	52 (86.7)
	Yes	8 (13.3)
Exercise	Daily	33 (55.0)
	1-2 times per week	16 (26.7)
	3-5times per week	11 (18.3)
Weight (BMI)	Underweight	4 (6.7)
	Normal	12 (20.0)
	Overweight	27 (45.0)
	Obese	17 (28.3)
Duration participation in Senior Club	< 1 year	5 (8.3)
	1-5 years	12 (20.0)
	6-10 years	18 (30.0)
	>10 years	25 (41.7)
Employment status	Employed	38 (63.3)
	Unemployed	20 (33.3)
	Retired	2 (3.4)
Assisted walking	None	55 (91.7)
	Walker	5 (8.3)
Hand Grip Score	Normal	31 (51.7)
	Low	29 (48.3)

Table 2: WHOQOL-BREF Scale Results

Variables		WHOQOL-BREF Scale							
		Physical Health		Psychological		Environment		Social Relationship	
		M	SD	M	SD	M	SD	M	SD
Sex	Female	76.29	12.07	76.97	13.49	75.57	78.75	71.51	8.59
	Male	77.14	13.50	74.17	23.82	10.93	11.35	71.67	15.14
		Z = 120.5 p = 0.648		Z = 126 p = 0.757		Z = 107.5 p = 0.419		Z = 127.5 p = 0.775	
Age	60-69 years	74.67	13.31	76.13	10.88	76.70	12.93	71.96	13.67
	70-79 years	75.52	12.12	75.49	14.17	73.80	10.06	70.09	8.24
	80-89 years	79.59	11.67	79.17	17.45	79.91	10.16	73.81	6.42
	H = 1.807 p = 0.613		H = 2.775 p = 0.428		H = 2.964 p = 0.397		H = 4.333 p = 0.228		
Education	No Education	72.50	18.90	70.00	23.96	76.25	14.89	69.17	12.45
	Primary	75.17	11.76	77.18	14.17	72.76	11.01	70.24	6.22
	Secondary	77.11	7.99	75.95	7.10	76.28	8.11	72.35	9.41
	Diploma	83.33	12.30	86.11	8.19	83.85	11.07	75.00	10.54
	H = 2.348 p = 0.309		H = 4.67 p = 0.097		H = 4.324 p = 0.115		H = 0.972 p = 0.615		
Exercise	Daily	78.25	9.88	80.30	11.33	79.17	9.87	72.72	9.38
	1-2 times per week	76.56	14.10	72.14	15.17	72.27	13.15	71.87	8.54
	3-5 times per week	70.45	14.11	72.72	19.13	71.02	7.00	67.42	8.70
	H = 2.216 p = 0.330		H = 4.052 p = 0.132		H = 7.932 p = 0.019		H = 7.932 p = 0.282		
Marital status	Single	72.62	21.53	68.06	31.82	77.08	17.77	72.22	9.43
	Married	76.11	11.55	77.28	13.81	75.60	10.78	70.93	9.43
	Widowed	79.08	11.79	78.27	11.34	77.01	10.66	73.81	8.56
	H = 2.297 p = 0.513		H = 2.162 p = 0.540		H = 1.858 p = 0.602		H = 1.321 p = 0.602		
Participation	<1 year	72.86	9.97	72.50	9.59	67.50	7.19	69.33	3.73
	1-5 years	82.44	7.53	81.25	9.15	80.73	10.73	75.69	9.70
	6-10 years	73.61	13.59	74.30	16.18	73.78	8.31	69.91	9.95
	>10 years	76.14	12.57	77.17	15.73	76.62	12.31	71.33	8.70
	H = 3.880 p = 0.275		H = 2.627 p = 0.453		H = 6.318 p = 0.097		H = 3.014 p = 0.389		

M – mean; SD – standard deviation; Min. – minimal value; Max. – maximal value; Z – Mann-Whitney test; F – ANOVA; H – Kruskal-Wallis ANOVA. Bold text indicates a statistically significant comparison.

5. DISCUSSION

This High WHOQOL-BREF and SPPB scores mirror findings that structured activity and mobility improve older adults' quality of life.¹⁻³ Functional decline with age remains evident, emphasizing early intervention and sustained activity to preserve independence.

6. CONCLUSION

Senior club participation is linked to good QOL and functional independence. Interventions emphasizing mobility, exercise, social engagement, and fall prevention are recommended. Larger longitudinal studies are needed to explore causal relationships.

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STRESS AMONGST PARENTS OF CHILDREN WITH ORTHOPEDIC DISABILITY ATTENDING THE PEDIATRIC ORTHOPEDIC OUTPATIENT CLINIC IN A TERTIARY HOSPITAL

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Abstract

Introduction: Parental stress is a significant concern among families with children suffering from orthopedic disabilities, which include upper limb, lower limb, and spinal impairments. These disabilities often have long-term implications for the child's mobility, independence, and overall quality of life. This study aims to address this gap by evaluating the levels of stress among parents of children with orthopedic disabilities in a tertiary care hospital setting. Identifying these challenges faced by these parents is an important step towards providing holistic management to alleviate caregiver burden and improve family well-being. **Methodology:** A cross-sectional study was conducted to determine the level of parenting stress amongst parents of children with orthopaedic disability attending the paediatric orthopaedic outpatient clinic in Penang General Hospital. We used the Parenting Stress Index Short Form (PSI-SF), Patient Health Questionnaire (PHQ-2) and parent and children background questionnaire to identify the socio-demographic background. **Results:** A total of 100 parents of children with orthopaedic disabilities were recruited, and the mean Total Scale (TS) of PSI-SF score was 147.37 ± 21.56 , reflecting moderate to high stress levels. Overall, 16% of parents experienced high stress, while 63% reported adequate stress. A significant positive correlation was found between total PSI-SF and PHQ-2 scores ($r = 0.311$, $p = 0.002$), indicating that higher depressive symptoms were associated with greater parental stress. There were no statistically significant differences observed across most parental characteristics. **Conclusion:** Parental stress was common among the caregivers and higher depressive symptoms were strongly linked to greater stress levels. These findings underscore the importance of early psychological screening and supportive interventions to promote caregivers' well-being.

Keywords: *Parental Stress, Pediatric-Orthopaedic Disability, Mental Health, Parenting Stress-Index (PSI-SF)*

1. INTRODUCTION

Parents caring for children with orthopedic disabilities often face prolonged caregiving demands due to the child's physical limitations, which may negatively affect both parental well-being and child development [1,2]. Functional challenges arising from conditions such as congenital limb deformities, cerebral palsy, or spinal disorders contribute to dependency in daily living activities and long-term rehabilitation burden [3]. These responsibilities, combined with financial strain and emotional stress, may result in heightened parental stress [4,5].

Limited research exists regarding stress among parents of children with orthopedic disabilities in Malaysia [3]. Understanding the extent of stress and its association with depressive symptoms is essential to develop caregiver support strategies [2,4]. This study evaluated stress levels among parents attending a tertiary pediatric orthopedic clinic and examined the relationship between stress and depressive symptoms using validated screening tools.

2. OBJECTIVES

- General Objective: To evaluate the level of stress amongst parents of children with orthopedic disabilities attending the pediatric orthopedic outpatient clinic in a tertiary hospital.
- Specific Objectives:
 - To determine the socio-demographic characteristics of the parents.
 - To determine the stress amongst parents of children with orthopedic disability.
 - To assess the dysfunctional parent-child interaction.
 - To determine the challenges faced by the parents in handling a difficult child.

3. METHODOLOGY

This cross-sectional study was conducted from February 2025 until October 2025 at the Pediatric Orthopedic Outpatient Clinic at Penang General Hospital in Malaysia. Pediatric orthopedic clinic takes place every Friday of the week. The study population consisted of parents or primary caregivers of children attending the Paediatric Orthopaedic Outpatient Clinic. A total of 100 participants were recruited using purposive sampling based on attendance at the Friday pediatric-orthopaedic clinic sessions. Eligible parents were identified by the researcher and invited to participate upon registration at the clinic. The purpose and procedures of the study were clearly explained, and written informed consent was obtained prior to participation. Each participant was interviewed and given a set of questionnaires individually in a private area to ensure confidentiality and comfort.

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Completion of both questionnaires required approximately 10–15 minutes. For participants showing signs of emotional distress, immediate psychological support and referral information were provided. Two instruments were used for data collection: the Parent and Children Background Questionnaire and Parenting Stress Index-Short Form (PSI-SF); the questionnaires were both available in English and Bahasa Malaysia, which had been established and validated in previous research conducted [3,7,8,10]. Ethical approval for this study was obtained from the Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia (NMRR ID-24-03593-ANE (IIR)).

Parent and Children Background Questionnaire: This structured form obtained socio-demographic data of the parent (age, gender, education level, employment status, and income) and relevant clinical information of the child (type and duration of disability). It also included the PHQ-2 (Patient Health Questionnaire-2) to screen for depressive symptoms among parents.

Parenting Stress Index–Short Form (PSI-SF): The PSI-SF is a validated 36-item self-report instrument that measures parental stress across three domains: Parental Distress (PD) – 12 items; Parent–Child Dysfunctional Interaction (P-CDI) – 12 items; Difficult Child (DC) – 12 items. Each item was rated on a 5-point Likert scale (1 = strongly disagree, 5 = strongly agree). Subscale scores were summed to yield a Total Scale (TS) score. Scoring followed the standard PSI-SF manual guidelines, including prorating for missing items (if one item per subscale was missing, scores were prorated; two or more missing items invalidated the subscale). Higher scores indicated higher parental stress.

Data Analysis

Data was entered and analyzed using IBM SPSS Statistics version 27. Descriptive statistics (mean, standard deviation, frequency, and percentage) were used to summarize the socio-demographic characteristics and PSI-SF subscale scores. For inferential analysis: Independent *t*-tests, ANOVA, and Kruskal–Wallis tests were used to compare mean PSI-SF scores across categorical demographic variables (e.g., education, income, and child disability type). Pearson's correlation was used to assess the relationship between total PSI-SF scores, parental age, and PHQ-2 scores. Multiple linear regression analysis was performed to identify independent predictors of total parental stress. A *p*-value of <0.05 was considered statistically significant. Results were presented in tables and figures showing descriptive distributions, correlation plots, and regression summaries.

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4. MAIN RESULTS

A total of 100 parents participated in this study. The mean parental age was 38.1 ± 7.2 years, with most being mothers (70%) and married (95%). The majority were Malay (72%) and had completed at least secondary education (53%), with 44% holding tertiary qualifications. Most families had two to three children. Children had a mean age of 8.0 ± 5.1 years, with 62% presenting with congenital disabilities. The most common conditions were congenital talipes equinovarus (CTEV) (26%) and cerebral palsy (12%).

The mean Total Scale (TS) score of the PSI-SF was 147.37 ± 21.56 , indicating moderate levels of parental stress. Based on established score thresholds, 16% of participants were categorized as experiencing high stress, 63% reported adequate stress, and 21% were classified as having low stress (Table 1). A significant positive correlation was observed between parental stress (TS) and depressive symptoms (PHQ-2) ($r = 0.311, p = 0.002$), indicating that higher depressive symptom severity was associated with increased parenting stress (Figure 1). No statistically significant associations were found between stress levels and parental demographic variables such as age, education level, financial status, or number of children.

Category	Count (N =100)	Percent (%)
Low	21	21.00%
Adequate	63	63.00%
High	16	16.00%

Table 1: Stress category frequency

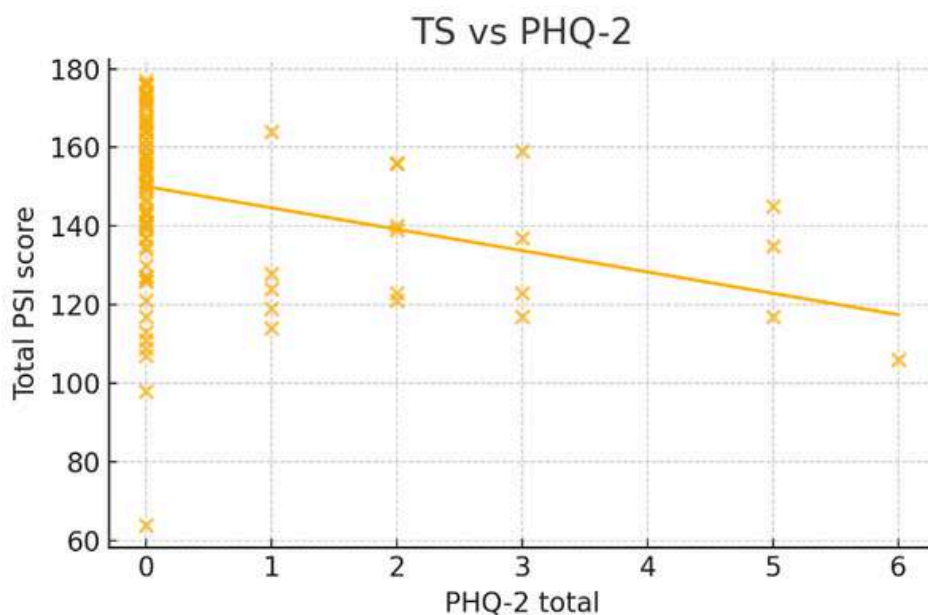


Figure 1: Scatter plot of Total PSI score vs PHQ-2 score

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5. DISCUSSION

Findings indicate moderate levels of stress among parents, with 16% experiencing high stress requiring further support. The positive correlation between stress and depressive symptoms aligns with existing literature, which highlights that psychological strain is common among caregivers of children with chronic disabilities [2,5]. Previous studies have shown similar patterns, where higher stress was associated with reduced coping capacity and greater depressive symptoms [1,4].

The absence of significant associations between demographic characteristics and stress levels suggests that psychosocial factors such as coping strategies and perceived support may be more influential [3]. This is consistent with research indicating that family resilience and adequate psychosocial intervention play vital roles in reducing parenting stress [4,5]. Therefore, early screening and structured mental health support within pediatric orthopedic settings are recommended.

6. CONCLUSION

This study highlights that while most parents of children with orthopedic disabilities experience manageable stress, a notable minority report high stress levels closely associated with depressive symptoms. These findings underscore the need for early psychological screening and incorporation of targeted psychosocial support within pediatric orthopedic care. Integrating family-centered interventions may help improve parental resilience, promote caregiver well-being, and ultimately enhance treatment outcomes for affected children.

7. ACKNOWLEDGEMENT

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EARLY POST-DISCHARGE GROWTH IN PRETERM INFANTS: DISCHARGE TO ONE MONTH CORRECTED AGE TRAJECTORIES

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Abstract

Introduction: The first month after neonatal intensive care unit (NICU) discharge is a critical period for preterm infants as feeding routines and care environments transition. Assessing growth patterns during this interval helps clarify early growth trajectories.

Aims & Objectives: To describe trajectories in weight-for-age (WAZ), length-for-age (LAZ), and head-circumference-for-age (HCZ) z-scores from birth in a Malaysian NICU to discharge and to one-month corrected age (CA).

Methods: A prospective longitudinal observational cohort study involving preterm infants (≤ 34 weeks gestation or ≤ 1800 g birth weight) admitted to a tertiary NICU with a minimum stay of 14 days and reviewed at one-month CA. Weight, length, and head circumference were recorded at birth, discharge, and one-month CA. z-scores at birth and discharge were assessed using the Fenton 2013 growth charts, while the one-month CA measurements were evaluated using the WHO 2006 standards. Descriptive statistics summarized anthropometry, and changes between time points were analyzed using paired t tests or Wilcoxon signed-rank tests.

Results & Discussion: Seventy-seven infants were enrolled (median GA 32 weeks; mean birthweight 1.72kg), and 51 had one-month CA measurements. Mean WAZ, LAZ, and HCZ were -0.34 ± 1.00 , -0.60 ± 1.03 , and 0.11 ± 1.27 at birth, declining to -1.58 ± 0.99 , -2.10 ± 1.31 , and -0.75 ± 1.3 by discharge. At one-month CA, mean scores improved to approximately 0.21 ± 1.29 (WAZ), -0.11 ± 1.39 (LAZ), and 0.27 ± 1.27 (HCZ). From birth to discharge, mean changes were -1.23 ± 0.54 , -1.50 ± 1.23 , and -0.84 ± 1.02 (all $p < 0.001$); from discharge to one-month CA, corresponding increases were 1.72 ± 1.04 , -1.82 ± 1.12 , and -0.92 ± 1.24 (all $p < 0.001$).

Conclusion: Preterm infants showed in-hospital growth faltering, followed by rapid recovery of weight and head size and partial catch up in length by one month CA. Early follow-up should track z-score trajectories to guide nutrition care.

Keywords: *preterm; post-discharge; growth faltering; catch-up growth.*

1. INTRODUCTION

Infants born before term miss the late gestation period when most fetal weight, linear growth, and brain volume accrue, and they often begin life with low nutrient reserves, immature gastrointestinal function, and high illness burden. International recommendations, including position papers from European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) [1] and related expert groups recommend early parenteral nutrition (PN) followed by cautious advancement of fortified human milk or specialized preterm formula via enteral feeding (EN) so that energy and protein intakes approach fetal requirements while minimizing complications [2]. Routine monitoring of weight, length, and head circumference z-scores is central to this strategy because bedside anthropometry enables early detection of growth faltering and guides feeding adjustment and clinic follow-up [3]. Nutrition care for preterm infants therefore remains a key clinical priority, with ongoing efforts to translate scientific advances into improved long-term growth and developmental outcomes. However, extrauterine growth restriction (EUGR) or postnatal growth failure (PGF) during NICU admission remains widely reported. Multicenter and single-center cohorts consistently report downward shift in weight-for-age (WAZ), length-for-age (LAZ), and head-circumference-for-age (HCZ) z-scores from birth to discharge, followed by catch-up of varying speed, with implications for later height, adiposity, and neurodevelopment [4–6]. Early head growth appears especially important, as first-month head-size trajectory groups relate to cognitive outcomes at two years of age [7]. In our Malaysian tertiary NICU, previous work described growth patterns during NICU admission and reported substantial declines in WAZ between birth and discharge and a high proportion of infants meeting criteria for postnatal growth failure at discharge, but post-discharge anthropometric change has not yet been prospectively described [8]. Without local data on how WAZ, LAZ, and HCZ shift from birth to discharge and then to one-month corrected age, clinicians and dietitians have limited reference points when assessing early post-discharge growth or identifying where growth is lagging during nutrition counselling.

2. OBJECTIVES

This study aims to describe trajectories in weight-for-age, length-for-age, and head-circumference-for-age z-scores from birth to discharge and to one-month CA in a Malaysian preterm cohort, with the goal of informing early post-discharge assessment and nutrition care.

3. METHODOLOGY

A prospective longitudinal observational cohort study was conducted in the Neonatal Intensive Care Unit (NICU) of Hospital Canselor Tuanku Muhriz (HCTM) and the dietetics outpatient clinic at Hospital Tunku Ampuan Besar Tuanku Aishah Rohani Hospital Pakar Kanak-Kanak (HPKK), Universiti Kebangsaan Malaysia (UKM). Preterm infants who received care in the NICU survived to discharge, and attended the follow-up visit at one month CA were eligible. Infants with major congenital anomalies were excluded. Ethical approval was obtained from the Research Ethics Committee, National University of Malaysia (UKM) (Approval No: JEP-2024-519), and written informed consent was obtained from parents or legal guardians.

Trained neonatal nurses measured weight, length, and head circumference at NICU discharge, and one month CA according to unit protocols. Measurements were converted to sex-specific z-scores at each time point. At birth and NICU discharge, weight-for-age, length-for-age, and head-circumference-for-age z-scores were calculated with the Fenton 2013[9] preterm growth charts which provide gestational-age and sex specific medians and standard deviations. At one month CA, z-scores were derived from the WHO 2006 Child Growth Standards [10].

Data were analyzed with IBM SPSS Statistics Version 29.0.1.0(171). Continuous variables were summarized as mean and standard deviation when distributions were approximately normal, and as median and interquartile range when skewed. Categorical variables were presented as counts and percentages. For the main objective, change in weight-for-age, length-for-age, and head-circumference-for-age z-scores from birth to NICU discharge and from discharge to one month corrected age was examined within infants. Normality was checked with Shapiro–Wilk tests. Paired t-tests were used for normally distributed z-score changes, and Wilcoxon signed-rank tests were used when distributions were non-normal. Mean z-score trajectories across the three time points and the proportion of infants with z-scores below -2 at each time point were plotted to describe early post-discharge growth patterns.

4. RESULTS

A total of 77 preterm infants were enrolled. The median (IQR) GA at birth was 32 weeks (24–34) and the mean \pm SD birthweight was 1.72 ± 0.46 with most infants classified as moderate to late preterm (59.7 %) and appropriate for gestational age (81.6 %). There were 12 (15.7%) SGA infants in this study (Table 1). Only 51 infants had measurements at one-month CA.

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At birth, mean WAZ, LAZ and HCZ were -0.34 ± 1.00 , -0.6 ± 1.03 , and 0.11 ± 1.27 . However, during the NICU stay, all three growth indices declined, with the largest fall seen in length. By discharge, mean WAZ, LAZ, and HCZ had decreased to -1.58 ± 0.99 , -2.10 ± 1.31 , and -0.75 ± 1.30 , demonstrating marked in-hospital growth faltering. From birth to discharge, mean changes were -1.23 ± 0.54 , -1.50 ± 1.23 , and -0.84 ± 1.02 (all $p < 0.001$); from discharge to one-month CA, and corresponding increases were $+1.72 \pm 1.04$, -1.82 ± 1.12 , and -0.92 ± 1.24 (all $p < 0.001$) (Figure 1).

Table 1. Baseline characteristics and growth outcomes of included infants

Baseline characteristics at birth	
Variable (n=77)	n (%) or summary
Sex	
Male	41 (53.2)
Female	36 (46.8)
GA at birth, weeks (Median (IQR))	32.0 (24–34)
GA category, weeks	
<32	28 (36.36)
32–34	46 (59.74)
≥35	3 (3.9)
Weight, kg (Mean ±SD)	1.72 ± 0.46
Length, cm (Mean ±SD)	40.61 ± 3.65
Head circumference, cm (Mean ±SD)	29.55 ± 2.55
Weight-for-age z-score (Mean ±SD)	-0.34 ± 1.00
Length-for-age z-score (Mean ±SD)	-0.60 ± 1.03
Head circumference-for-age z-score (Mean ±SD)	0.11 ± 1.27
Birthweight status	
AGA	63 (81.8)
LGA	2 (2.6)
SGA	12 (15.7)
Length of NICU stay, (days) (Median (IQR))	25(14-95)
Anthropometry at discharge	
Variable	Mean ± SD
Weight, kg (n=77)	2.18 ± 0.34
Length, cm (n=59)	42.25 ± 3.44
Head circumference, (n=74)	31.82 ± 1.59
Weight-for-age z-score, (n=77)	-1.58 ± 0.99
Length-for-age z-score, (n=59)	-2.10 ± 1.31
Head-circumference-for-age z-score, (n=74)	-0.75 ± 1.30
Change in WAZ, (n=77)	-1.23 ± 0.54
Change in LAZ, (n=59)	-1.50 ± 1.23
Change in HCZ, (n=74)	-0.84 ± 1.02
Anthropometry at 1-month corrected age	
Variable	Mean ± SD
Weight, kg (n=51)	4.53 ± 0.80
Length at 1-month CA, cm (n=45)	54.07 ± 2.72
Head circumference, cm (n=42)	37.27 ± 1.48
Weight-for-age z-score, (n=51)	0.21 ± 1.29
Length-for-age z-score, (n=45)	-0.11 ± 1.39
Head-circumference-for-age z-score, (n=42)	0.27 ± 1.27
Change in WAZ, (n=51)	1.72 ± 1.04
Change in LAZ, (n=45)	-1.82 ± 1.12
Change in HCZ, (n=42)	-0.92 ± 1.24

Values are mean ± standard deviation (SD) or median (interquartile range, IQR) as indicated. Percentages are based on non-missing data. corrected age (CA). n varies by row because of missing measurements at discharge and/or follow-up.

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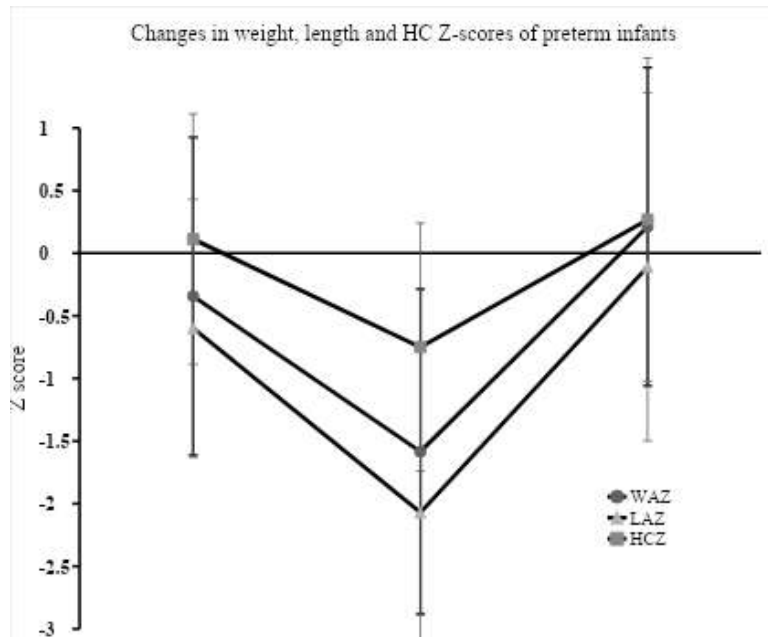


Figure 1: Change in weight-for-age (WAZ), length-for-age (LAZ), and head-circumference-for-age (HCZ) Z-scores of preterm infants from birth to discharge and follow-up. All changes across time points were statistically significant ($p < 0.001$).

5. DISCUSSION

During the NICU stay, all three indices declined, with WAZ falling by approximately 1.2 SD and slightly larger reductions observed in LAZ, while HCZ also decreased. This pattern matches reports from very preterm cohorts in high-income settings, where early hospital period is marked by postnatal growth failure and a downward shift in weight and head-circumference z-scores before term age [4,5,11]. Early catabolism, delays in reaching full enteral feeds, frequent feed interruptions for illness or procedures, and the limits of standard fortification for meeting protein and mineral requirements are likely contributors [2,3]. The magnitude of the WAZ decline (-1.23 ± 0.54) is similar to the ≥ 1.2 SD threshold proposed for postnatal growth failure in Indonesian preterm infants. This alignment with findings from a neighbouring Southeast Asian cohort provides a regionally relevant frame of reference and suggests that the degree of growth faltering observed in our study is consistent with patterns reported in comparable clinical settings [12].

Different definitions of postnatal growth failure have been proposed in the literature, ranging from cross-sectional thresholds (WAZ < -2 SD or < 10 th percentile at discharge) to longitudinal change-based criteria such as a decline of > 1.0 SD during NICU stay, > 1.2 SD or > 0.8 SD [9,12,13]. The 1.23 ± 0.54 reduction in our cohort falls within this established range of cut-offs, supporting the interpretation that the growth faltering observed is clinically meaningful and consistent with recognized definitions across various populations. From discharge to one-month CA, WAZ and HCZ increased to slightly positive values



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while LAZ improved toward the median. These changes indicate substantial early post-discharge catch-up, with infants recovering much of the growth deficit accumulated during NICU admission. Weight and head circumference recovered more rapidly than length in an expected pattern, as linear growth responds more slowly and typically requires a longer period for normalization. This trajectory aligns with findings from longitudinal cohorts showing that the earliest catch-up in preterm infants often occurs in the weeks immediately after discharge, particularly for weight and head circumference, while length lags behind [14–16]. After discharge, preterm infants are generally more clinically stable and experience fewer acute medical interruptions, allowing for more consistent nutritional intake. Feeding volumes are typically better tolerated at home, with fewer pauses for procedures or illness, and infants are able to receive the intended amounts of fortified human milk or post discharge formula. As a result, both energy and protein delivery tend to be higher and more sustained than during hospitalization, supporting catch-up in weight and head circumference during the early post-discharge period [5,7,17]. Across multiple cohort studies involving very preterm and very low birthweight infants, deficits in linear and head growth at discharge have been associated with shorter stature, altered body composition, and less favorable neurodevelopment later in childhood even when partial catch-up occurs [5,18]. These findings highlight the importance of early post-discharge surveillance. A follow-up visit at approximately one month CA offers a critical window to confirm weight and head-size recovery, detect persistent length deficits, and intensify nutritional support before early stunting becomes established. This study's single-center design, wide gestational-age distribution, and lower follow-up attendance compared with discharge numbers may limit the generalizability of the findings. Growth patterns observed here may not fully represent all preterm infants in the unit or in other settings. Larger multicenter longitudinal studies that integrate growth trajectories with feeding exposures, neonatal morbidities, and later neurodevelopmental or metabolic outcomes remain an important research need [19,20].

6. CONCLUSION

Preterm infants in this cohort showed clear extrauterine growth faltering in weight, length, and head circumference during NICU stay, followed with substantial catch-up in weight and head size and partial catch-up in length by one month CA. Tracking serial z-scores from birth to discharge and into early outpatient provides a practical approach to identifying infants whose linear or head growth remains suboptimal. Such early detection allows targeted nutrition intervention and timely clinic review for those at highest risk of persistent growth deficits, supporting efforts to optimize post-discharge growth and long-term developmental outcomes.



7. ACKNOWLEDGEMENT

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Molecular Detection of *Acinetobacter baumannii* by Non-Protein Coding RNA-Mediated Monoplex Polymerase Chain Reaction

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Abstract

Background: *Acinetobacter baumannii* is a gram-negative, non-fermenting opportunistic pathogen that has been identified by the World Health Organization as a high-priority organism and is included among the ESKAPE pathogens. This classification reflects its high incidence of multidrug-resistant strains and its significant role in healthcare-associated (nosocomial) infections. Accurate detection of this bacterium is essential for effective clinical treatment. Non-protein coding RNAs (npcRNAs) are genetic sequences that do not code for proteins in bacteria. These molecules exhibit higher stability compared to protein-coding RNAs. **Methods:** In our previous study, a novel npcRNA gene, AbaR11 unique to *Acinetobacter baumannii* was identified. In this study, monoplex PCR was used to evaluate its specificity and sensitivity to *A. baumannii*. A gradient Polymerase Chain Reaction (PCR) was done to determine the ideal annealing temperature followed by specificity and sensitivity tests. Bacteria that were tested in this specificity test include, *Acinetobacter baumannii*, *Serratia marcescens*, *Salmonella typhimurium*, *Providencia stuartii*, *Bacillus subtilis*, *Bacillus cereus*, MRSA, *Streptococcus pyogenes*, *Streptococcus epidermidis* and *Listeria monocytogenes*. **Results:** Gradient PCR identified an optimal annealing temperature of 45.9°C for *A. baumannii*. In the PCR assay, amplification was observed only in *A. baumannii*, with no bands detected in other bacterial species, and detection was achieved up to 9pg/ul of genomic DNA. **Conclusion:** The results support that the gene is specific and sensitive to *A. baumannii*. The PCR test used in this study is an experimental detection method that can be cloned for other npcRNA-mediated detection assays and has the potential for clinical diagnostic development.

Keywords: ncRNA, *Acinetobacter baumannii*, molecular diagnostics, Specificity PCR, Sensitivity PCR

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1. INTRODUCTION

Acinetobacter baumannii is a gram-negative coccobacillus, and one of the World Health Organisation's (WHO) designated ESKAPE pathogens due to its high levels of antimicrobial resistance and prevalence in nosocomial infections. This is particularly critical in intensive care unit (ICU) settings, where infections often follow an unfavorable clinical course. Rapid detection is, therefore, essential to guide timely and appropriate treatment.

This study proposes a novel approach for detecting *A. baumannii* using a monoplex PCR assay targeting the *AbaR11* non-protein-coding RNA (npcRNA) gene. Non-protein-coding RNAs (npcRNAs) are highly stable and exhibit resistance to mutation, making them promising candidates for diagnostic biomarkers

2. OBJECTIVES

1. To identify the optimal annealing temperature for *AbaR11* gene using gradient PCR.
2. To assess the specificity of *AbaR11* gene.
3. To determine the detection sensitivity of the *AbaR11* gene in serially diluted suspensions using genomic DNA.

3. METHODOLOGY

In our previous study, a novel npcRNA gene, *AbaR11* unique to *Acinetobacter baumannii* was identified. In this study, monoplex PCR was used to evaluate its specificity and sensitivity to *A. baumannii*. A gradient Polymerase Chain Reaction (PCR) was done to determine the ideal annealing temperature followed by specificity and sensitivity tests. Bacteria that were tested in this specificity test include, *Acinetobacter baumannii*, *Serratia marcescens*, *Salmonella typhimurium*, *Providencia stuartii*, *Bacillus subtilis*, *Bacillus cereus*, *MRSA*, *Streptococcus pyogenes*, *Streptococcus epidermidis* and *Listeria monocytogenes*.

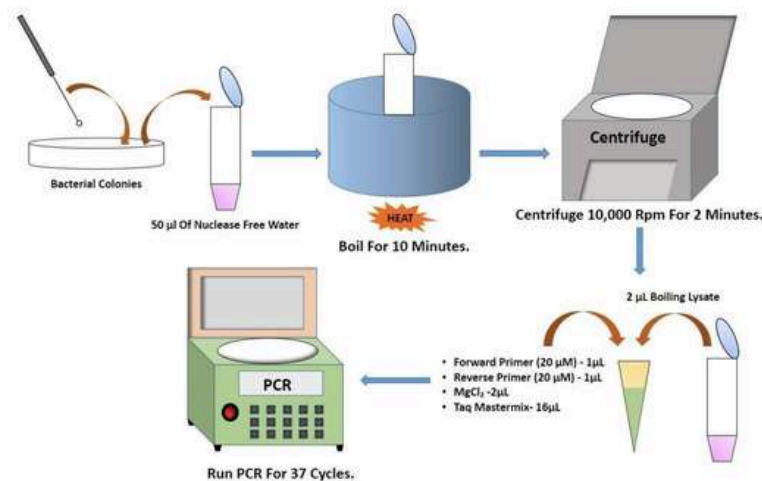


Fig. 1 Schematic diagram of PCR amplification targeting *AbaR11* gene in *A. baumannii*.

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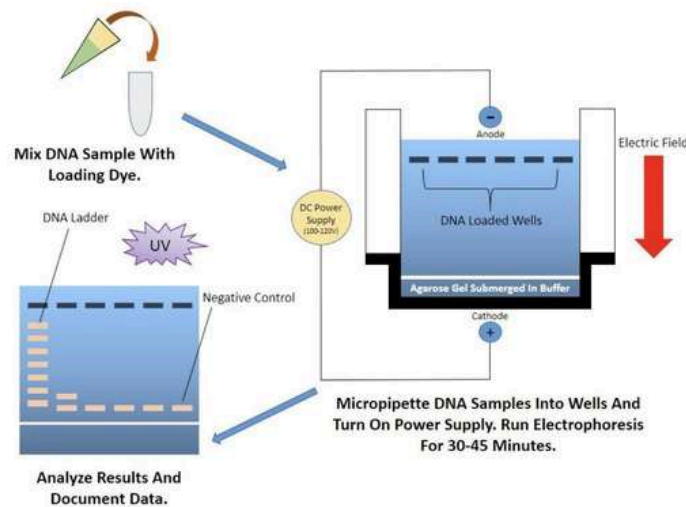


Fig. 2 Schematic diagram of agarose gel electrophoresis showing PCR amplification of the *AbaR11* gene in *A. baumannii*.

3. RESULTS

Gradient PCR identified an optimal annealing temperature of 45.9°C for *A. baumannii*. In the PCR assay, amplification was observed only in *A. baumannii*, with no bands detected in other bacterial species, and detection was achieved up to 9pg/ul of genomic DNA.

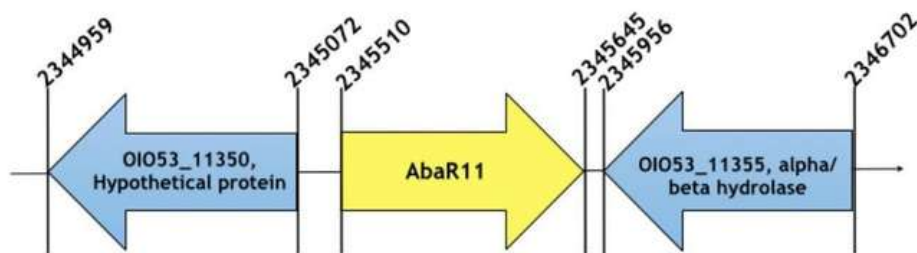


Fig. 3 Location of *AbaR11* gene in *A. baumannii*.



Fig. 4 Gradient PCR test showing the optimal annealing temperature for *AbaR11* gene.

M – 100 bp DNA ladder; 1 – 45.0 °C, 2 – 45.3 °C, 3 – 45.9 °C, 4 – 46.8 °C, 5 – 48.1 °C, 6 – 49.4 °C, 7 – 50.6 °C, 8 – 51.9 °C, 9 – 53.2 °C, 10 – 54.1 °C, 11 – 54.7 °C, 12 – 55.0 °C, C – Negative control.

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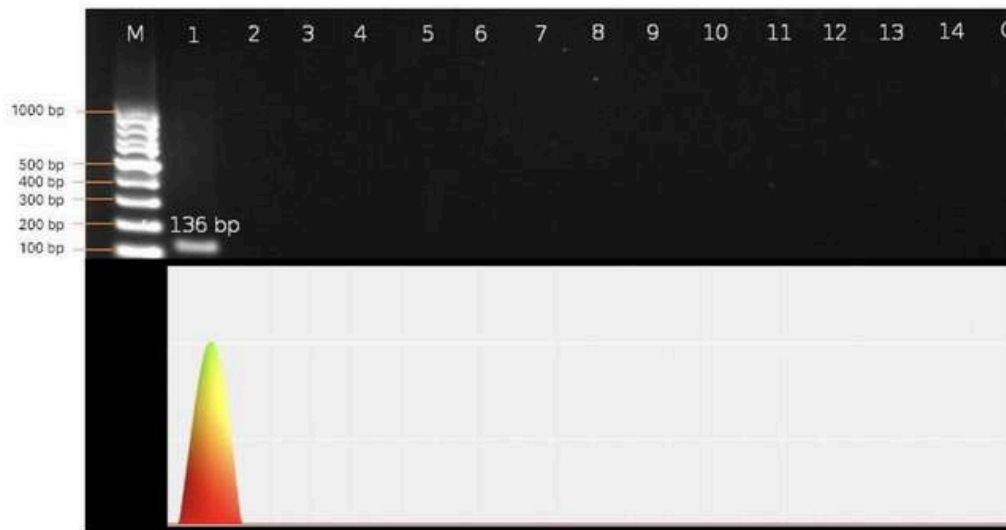


Fig. 5 Specificity test of *A. baumannii* using different bacteria.

M – 100 bp DNA ladder. 1 – *Acinetobacter baumannii*, 2 – *Serratia marcescens*, 3 – *Proteus mirabilis*, 4 – *Shigella flexneri*, 5 – *Salmonella Typhimurium*, 6 – *Providencia stuartii*, 7 – *Escherichia coli*, 8 – *Bacillus subtilis*, 9 – *Bacillus cereus*, 10 – *Staphylococcus aureus*, 11 – MRSA, 12 – *Streptococcus pyogenes*, 13 – *Staphylococcus epidermidis*, 14 – *Listeria monocytogenes*, C – Negative control.

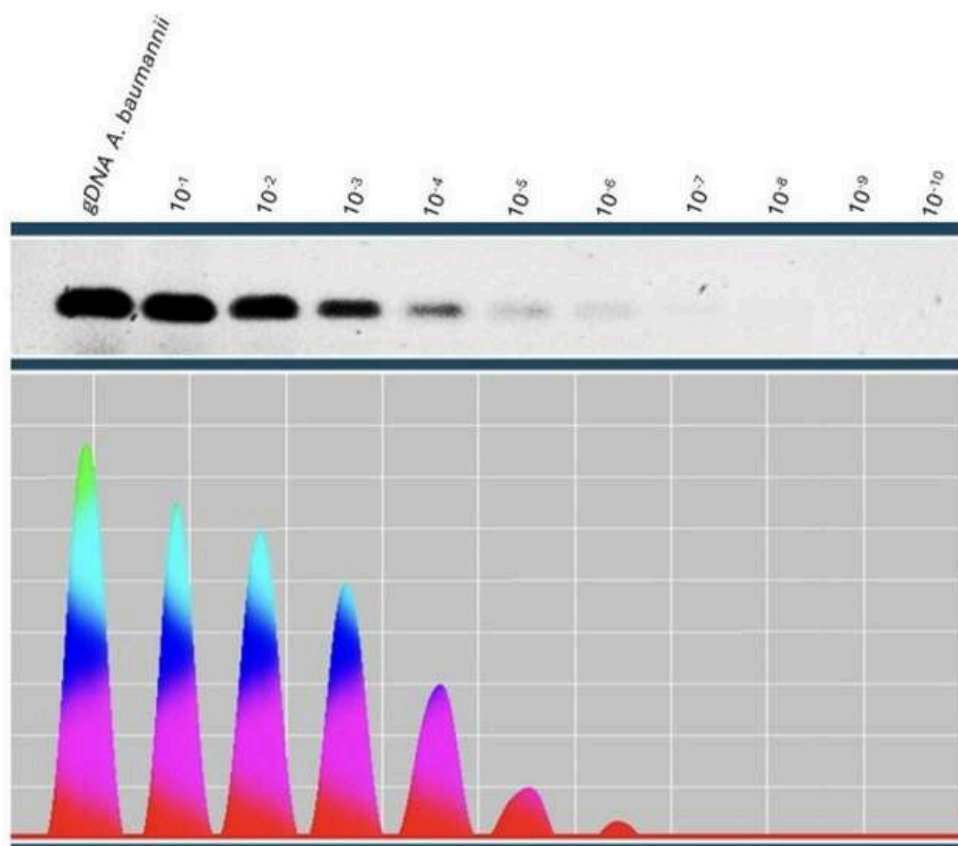


Fig. 6 Detection limits of *A. baumannii* using genomic DNA.

10-1 dilution : 907.5 ng/μL, 10-2 dilution : 90.75 ng/μL, 10-3 dilution : 9.07 ng/μL,
10-4 dilution : 907 pg/μL, 10-5 dilution : 90.7 pg/μL, 10-6 dilution : 9 pg/μL, 10-7 dilution :
907 fg/μL, 10-8 dilution : 90.0 fg/μL, 10-9 dilution : 9 fg/μL, 10-10 dilution : 0.9 fg/μL.



6. DISCUSSION

Non-protein-coding RNAs (npcRNAs) are known to be highly resistant to mutation and exhibit greater sensitivity than protein-coding regions, making them attractive candidates for diagnostic biomarker development. Despite this, all currently available molecular diagnostic techniques for *Acinetobacter baumannii* target protein-coding regions. This study is the first to utilise an npcRNA marker—AbaR11—to detect *A. baumannii*.

Gradient PCR results revealed that the optimal annealing temperature for AbaR11 was within the range of 49–52 °C. This relatively low temperature is consistent with the high adenine–thymine to guanine–cytosine ratio of the AbaR11 sequence.

Our BLAST analysis and specificity tests confirmed that AbaR11 is highly specific to *A. baumannii*. Sensitivity testing demonstrated that the assay could detect DNA concentrations as low as 9 pg/μL (10⁻⁶ dilution), below the detection threshold of many conventional methods. Given these findings, the AbaR11 npcRNA marker holds strong potential for the rapid and specific diagnosis of *A. baumannii* and warrants further investigation using clinical samples.

7. CONCLUSION

The study confirms that the AbaR11 npcRNA gene is highly specific and sensitive to *Acinetobacter baumannii*. This makes it an excellent target for PCR-based detection, offering accurate, sensitive, and reliable results

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UN2

IN SILICO MOLECULAR DOCKING OF ROSMARINIC ACID FROM ORTHOSIPHON STAMINEUS ON CHRONIC RENAL FAILURE (CRF)-RELATED PROTEINS

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Abstract

Background: Cat's whiskers (*Orthosiphon stamineus*) contain a high amount of rosmarinic acid (RosA), a compound known for its antioxidant, anti-inflammatory, and diuretic activities. **Aim:** This study evaluates the drug-likeness parameters of RosA and investigates its potential interaction with chronic renal failure (CRF)-related proteins through molecular docking analysis. **Methodology:** Drug-likeness was assessed using the SWISS ADME tool. Protein structures are (TNF- α , 2AZ5), Caspase-3 (6CKZ), Interleukin-6 (IL-6, 1ALU), and nuclear factor erythroid 2 related factor 2 (Nrf2, 4LZD) were obtained from the RCSB Protein Data Bank, while RosA's 3D structure was retrieved from PubChem. Docking simulations were conducted using AutoDock Vina. **Results:** RosA exhibited a molecular weight of 360.31 g/mol, 5 hydrogen bond donors, 8 acceptors, LogP 1.48, and molar refractivity 91.40, fulfilling all Lipinski's rules, indicating good oral bioavailability. Docking analysis revealed strong binding affinities with TNF- α (-7.4 kcal/mol), Caspase-3 (-7.3 kcal/mol), and Nrf2 (-5.7 kcal/mol), while showing moderate affinity to IL-6 (-5.8 kcal/mol). LigPlot results showed RosA interactions with Tyr142 (TNF- α); Phe5, Phe75, Arg32 (Caspase-3); Ser210, Thr182, Thr58, Arg136, Leu134 (Nrf2); and Ser76, Met67, Lys66 (IL-6). **Conclusion:** RosA demonstrates potential in modulating oxidative stress, apoptosis, and inflammatory pathways, supporting its possible role as an anti-CRF agent. However, further in vitro and in vivo studies are necessary to confirm its safety and therapeutic efficacy.

Keywords: *Rosmarinic acid, Orthosiphon Stamineus, Molecular docking*

1. INTRODUCTION

Urolithiasis (also known as kidney stone or urinary calculi) with prevalence approximately 4%–8% worldwide where United States having the highest percentage of 8% in male population (Hesse & Siener, 1997). The incidence of kidney stone in Malaysia as reported

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between 1962 and 1976 by Sreenevasan in 1981, at an average of 221 cases annually (Sreenevasan, 1981). *Orthosiphon stamineus* (*O. stamineus*) or Cat's whiskers were reported to contain diuretic effects in experimental rats, and this leads to inhibition of kidney stones through the abundant levels of minerals and flavonoids. The condition is characterized by the formation of crystalline deposits in the kidneys, often causing severe pain, infection, and even chronic kidney disease (Ambursa et al., 2022).

Many studies have shown that *Orthosiphon stamineus* extract (OE) has antioxidant activity (Cai et al., 2019). One in vitro study shows that *O. stamineus* water extract does have some dissolving capability of urinary stones. Herein, *O. stamineus* extract 4 mg/ml showed a better effect in terms of chemolytic action on calcium oxalate stone than the potassium citrate solution (70% vs. 41%) which is about 70% (Ambursa et al., 2022). The components with the highest antioxidant activity were analysed by HPLC, which confirmed that rosmarinic acid (RA) was the main effective constituent in extract (Cai et al., 2019). RosA has many pharmacological activities specifically safe and effective anti-inflammatory and anticancer drugs. Network pharmacology and molecular docking studies provides a new idea for the research, development, and clinical application of RosA (Guan et al., 2021).

2. OBJECTIVES

Main Aim:

To investigate the efficacy of rosmarinic acid in chronic renal failure condition.

Specific Objectives:

1. To evaluate drug-likeness and toxicity of rosmarinic acid.
2. To assess *in silico* molecular docking with chronic renal failure-related proteins.

3. METHODOLOGY

1. Drug-likeness and toxicity reduction (SWISSADME Web Tool)

The rosmarinic acid compound found in *Orthosiphon stamineus* was evaluated for drug-likeness and toxicity prediction using SWISSADME web tool based on Lipinski's Rule of Five (Ref.45). This rule predicts the oral bioavailability of drug candidates, which generally should not violate more than one of the following: molecular mass < 500Da, lipophilicity (LogP < 5), < 5 hydrogen bond donors, < 10 hydrogen bond acceptors, and molar refractivity between 40 and 130 (Ismail et al., 2020).

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2. Molecular docking

The 3D structure of rosmarinic acid was retrieved from the PubChem database in .sdf format and converted to .pdb format using Open Babel. Ligand preparation was carried out which involves torsion setting, as well as the addition of hydrogen atoms and Gasteiger charge using Autodock tools. Final file was saved in .pdbqt format. Protein targets associated with chronic renal failure are tumour necrosis factor-alpha (TNF- α , 2AZ5) (Daffa Hanifan et al., n.d.), caspase-3 (6CKZ), Interleukin-6 (IL-6, 1ALU) (Daffa Hanifan et al., n.d.), and nuclear factor erythroid 2-related factor 2 (Nrf2, 7K2D) (Touny et al., 2025), were downloaded from the RCSB Protein Data Bank. All proteins were prepared by removing water molecules, followed by the addition of polar hydrogens and Kollman charges using AutoDock Tools and saved as .pdbqt format.

Docking simulations were performed in AutoDock Vina to predict the binding affinities and potential interactions of rosmarinic acid with each target protein. The grid size was set to $40 \times 40 \times 40$ points with a spacing of 0.375 \AA centred on TNF- α with grid of $x = -13.687$, $y = 71.607$, $z = 27.002$, $40 \times 40 \times 40$ points with a spacing of 0.375 \AA centred on Caspase-3 with grid of $x = 27.543$, $y = 22.594$, $z = 37.217$, $40 \times 40 \times 40$ points with a spacing of 0.375 \AA centred on Nrf2 with grid of $x = -23.572$, $y = 39.402$, $z = -35.915$ and $40 \times 40 \times 40$ points with a spacing of 0.375 \AA centred on IL-6 with grid of $x = -7.677$, $y = -12.743$, $z = 0.007$. The simulations were executed through command prompt with the following syntax. Docking simulation was repeated nine times to obtain the most stable kcal/mol values. Visualization of docked complexes was carried out using PyMOL to analyse 3D conformations, while 2D interaction diagrams showing hydrogen bonds and hydrophobic interactions were generated using LigPlot+ (Ismail et al., 2020).

4. MAIN RESULTS

Table 1. Lipinski's rule for rosmarinic acid assessed by SwissADME web tool.

Compound	Molecular weight (Da)	Hydrogen Bond Donor	Hydrogen Bond Acceptor	LogP	Molar Refractivity	Rules Satisfied
Rosmarinic acid	360.31 g/mol	5	8	1.48	91.4	5/5

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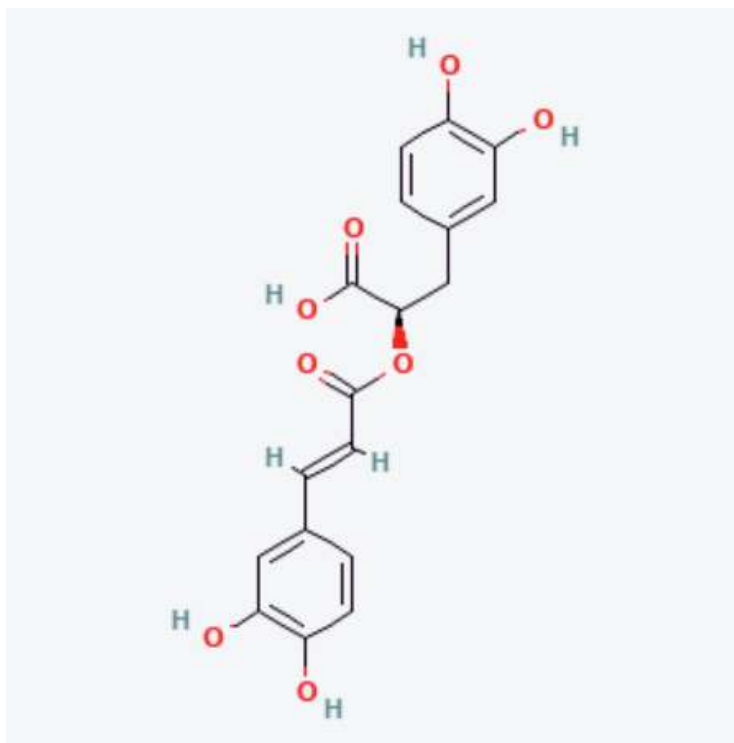


Figure 1. Rosmarinic acid in Orthosiphon Stamineus.

Table 2. Binding energy of major compounds and CRF-related proteins

Proteins	Binding Energy (kcal/mol)
	Rosmarinic acid
TNF- α (2AZ5)	-7.4
Caspase-3 (6CKZ)	-7.3
Nrf2 (7K2D)	-7.1
IL-6 (1ALU)	-5.8

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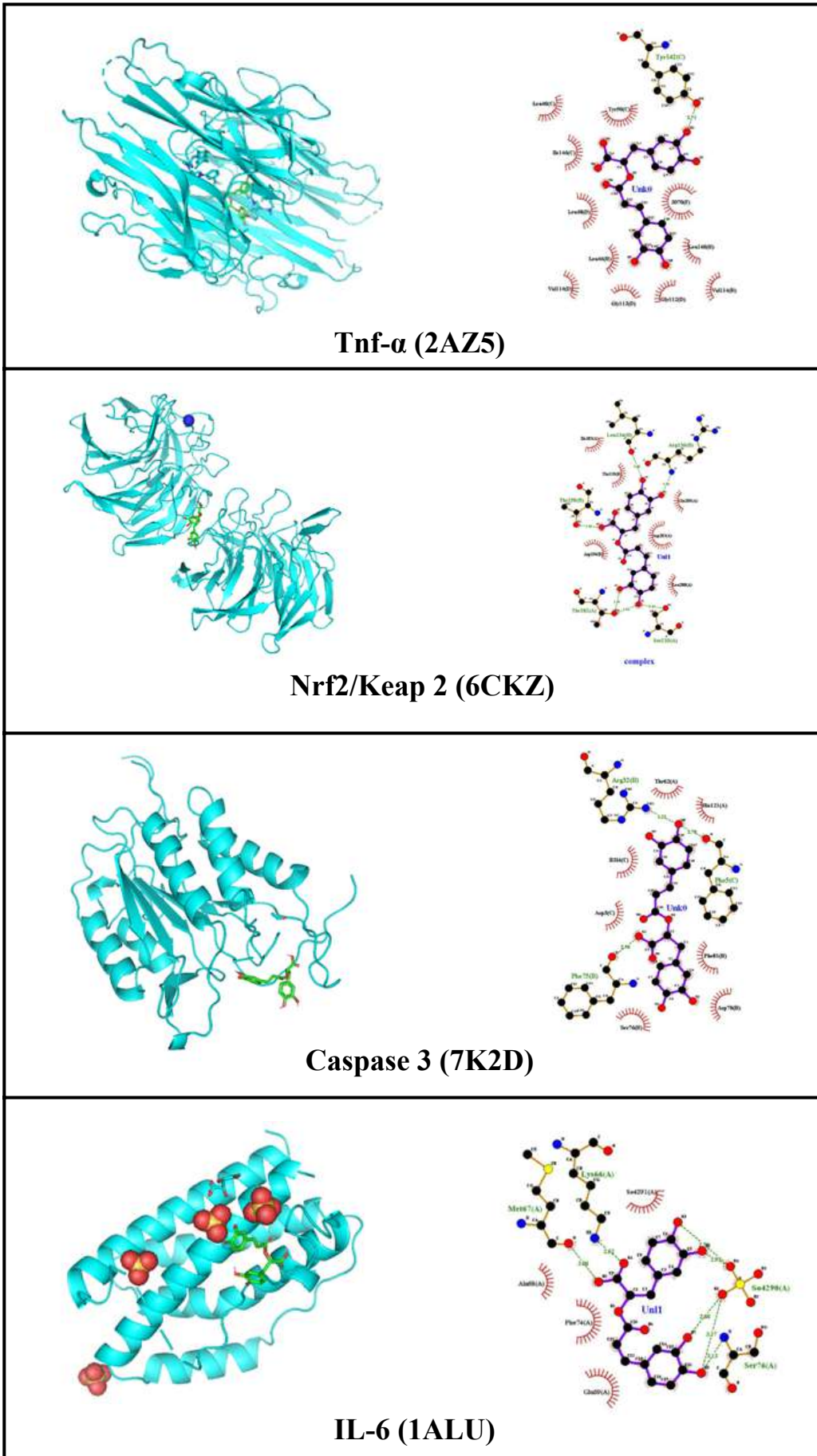


Figure 2.

5. DISCUSSION

Drug-likeness and toxicity prediction indicated that RosA satisfied all Lipinski's rules. RosA binds at higher affinity to Tnf- α (-7.4 kcal/mol) specifically at Tyr142. RosA binds at moderate affinity to Nrf2/Keap2 (-7.1 kcal/mol) specifically bind to Met67(A), Lys66(A), Ser76(A), So4290(A) of Nrf2. Thirdly, RosA binds at moderate affinity to Caspase 3 (-7.3 kcal/mol) specifically bind to Arg32(B), Phe5(C), Phe75(B) of Caspase 3. Lastly, RosA binds at lower affinity to IL-6 (-5.8 kcal/mol) specifically bind to Met67(A), Lys66(A), Ser76(A), So4290(A) of IL-6. These indicate RosA involves in to reduce inflammation and preventing cell damage. It also interacted well with Nrf2, which may enhance antioxidant defence and protect against oxidative stress in chronic renal failure. These findings support previous research showing the anti-inflammatory and antioxidant effects of *Orthosiphon stamineus*. Moderate binding with IL-6 further suggests a possible role in controlling cytokine activity. Overall, Rosmarinic acid appears to be a promising natural compound for kidney protection, but further laboratory and animal studies are needed to confirm its safety and effectiveness.

6. CONCLUSION

Rosmarinic acid has proven to be an excellent compound for prevention of chronic renal failure. It binds strongly to the major proteins that can alleviate inflammation, oxidative stress and promotes apoptosis of damaged kidney cells. This highlights its potential role in drug discovery study.

7. ACKNOWLEDGEMENT

We would first like to thank the organising board for hosting this conference and for offering such opportunities for us undergraduate students. We would also like to thank our lecturer, Nor Shaheera Mohamad Kamal, for proving us with guidance and insights throughout our preparations. Much appreciation is also extended to our families and friends for supporting us throughout the course of our preparation.

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Developing a Predictive Model for Response to Stem Cell Therapy in Ischaemic Cardiomyopathy

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Abstract

This extended abstract presents a research study focused on developing a machine learning-based predictive model for patient-specific response to cardiac stem cell therapy in ischaemic cardiomyopathy. By integrating multimodal clinical and imaging data, the model aims to enhance precision in predicting therapeutic outcomes, optimize patient selection, and improve myocardial recovery following regenerative therapy. Preliminary internal validation of Random Forest models demonstrates promising discrimination, supporting further development and prospective validation.

Keywords: *Stem cell therapy, ischaemic cardiomyopathy, machine learning, predictive model, Random Forest*

1. INTRODUCTION

Ischaemic cardiomyopathy (ICM) remains a major cause of morbidity and mortality despite advances in medical and interventional therapy. Stem cell therapy has shown potential to improve myocardial perfusion and function through regenerative mechanisms [1]. However, clinical response remains heterogeneous, with variable improvement in left ventricular function and patient outcomes. Recent advancements in artificial intelligence (AI) provide opportunities to integrate clinical, imaging, and biomarker data to predict therapeutic response more accurately [2,3].

2. OBJECTIVES

To develop and validate a machine learning-based predictive model that identifies patient-specific response patterns to cardiac stem cell therapy in ischaemic cardiomyopathy, aiming to guide patient selection and optimize therapeutic outcomes.

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3. METHODOLOGY

A retrospective cohort of 228 patients treated with stem cell therapy for ICM at University Hospital Galway and St. Vincent's University Hospital (2016–2023) was analyzed. Inclusion criteria comprised adults aged 18–80 with prior myocardial infarction and baseline LVEF <45% with 6-month follow-up imaging. Variables included demographics, comorbidities, infarct characteristics (MRI scar size, transmural), biomarkers (troponin T, NT-proBNP), and therapy parameters (cell type, dose, delivery route, time post-MI). The primary outcome was an absolute increase in LVEF $\geq 10\%$ at 6 months. Machine learning models evaluated included Random Forest, logistic regression, and support vector machines. Model performance was assessed using cross-validation, ROC analysis, and feature importance metrics. Ethical approval was obtained/waived as per institutional policies.

4. MAIN RESULTS

Data from 228 patients were extracted; 63% (n=144) were responders ($\geq 10\%$ absolute LVEF increase) and 37% (n=84) non-responders. Median age was 62 years (IQR 56–68), 72% male. Most patients received cardiosphere-derived cells (58%) or mesenchymal stem cells (34%), primarily via intracoronary delivery (81%). Preliminary Random Forest models showed good discrimination (AUC ≈ 0.81 on internal validation). Key predictors included baseline LVEF, infarct scar size, NT-proBNP, and time-to-therapy. Feature selection reduced model complexity while preserving performance, supporting feasibility for clinical implementation.

5. DISCUSSION

AI-assisted predictive modeling addresses response heterogeneity by combining multimodal predictors into an interpretable framework for patient selection. Incorporating imaging biomarkers and temporal therapy variables improves discrimination and may reduce non-responder exposure to costly interventions [4,5]. Prospective external validation and assessment of clinical utility, including decision-curve analysis and cost-effectiveness, are required before deployment.

6. CONCLUSION

An interpretable Random Forest-based predictive model shows promise in identifying patients most likely to benefit from stem cell therapy in ischaemic cardiomyopathy. Further validation on larger and external cohorts is necessary to confirm generalizability and clinical applicability.

7. ACKNOWLEDGEMENT

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UN4

INVESTIGATING THE ROLE OF α 1-ANTITRYPSIN IN MATRIX METALLOPROTEINASE 9 EXPRESSION

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Abstract

α 1-Antitrypsin deficiency (AATD) is a genetic disorder resulting from reduced levels of α 1-antitrypsin (AAT), a serine protease inhibitor that protects lung tissue from proteolytic damage. The Z allele, particularly in homozygous ZZ individuals, is associated with an increased risk of early-onset chronic obstructive pulmonary disease (COPD). Matrix metalloproteinase 9 (MMP9), a macrophage-derived enzyme involved in inflammation and lung remodeling, is often elevated in COPD patients; however, its relationship with AAT genotypes remains unclear. This study aimed to quantify plasma MMP9 levels in MM and ZZ individuals, with particular focus on the influence of COPD. A total of 55 participants (20 MM and 35 ZZ) were categorized as healthy or COPD based on clinical assessment, pulmonary function tests, and CT thorax findings. Plasma MMP9 expression was measured using the DuoSet ELISA kit (DY911, R&D Systems). Both mean and median MMP9 levels were higher in ZZ compared to MM individuals, though the difference did not reach statistical significance. Similarly, COPD participants exhibited a slight increase in MMP9 levels relative to healthy controls, with the highest mean levels observed in ZZ COPD individuals. The absence of statistical significance may be due to limited sample size, smoking status, or comorbidities influencing inflammatory activity. These findings suggest that both genetic background and disease status may influence MMP9 expression. Larger studies are needed to determine whether MMP9 could serve as a biomarker for AATD-associated COPD.

1. INTRODUCTION

α 1-Antitrypsin deficiency (AATD) is a genetic disorder caused by reduced levels of α 1-antitrypsin (AAT), a serine protease inhibitor that protects lung tissue from neutrophil elastase-mediated damage. The condition is most commonly associated with the Z allele, where homozygous ZZ individuals exhibit a higher risk of developing early-onset chronic

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obstructive pulmonary disease (COPD). Dysregulation of matrix metalloproteinase 9 (MMP9), an enzyme secreted by macrophages involved in inflammation and extracellular matrix remodeling, has been reported in the serum and sputum of COPD patients [1,2].

Despite these findings, the relationship between AAT genotypes and MMP9 expression remains poorly understood. This study investigates plasma MMP9 expression in individuals with MM and ZZ AAT genotypes, with a particular focus on the impact of COPD. This work aligns with the conference theme of translational research in respiratory diseases by exploring potential molecular biomarkers that could inform personalized management strategies for AATD-associated COPD

2. OBJECTIVES

- To quantify plasma MMP9 expression levels in individuals with MM and ZZ AAT genotypes.
- To compare MMP9 levels between healthy and COPD subgroups.
- To explore whether AAT genotype or disease status influences systemic MMP9 expression.

3. METHODOLOGY

A total of 55 individuals (20 MM and 35 ZZ genotypes) were enrolled. Participants were classified as either healthy or COPD based on clinical assessment, pulmonary function tests, and CT thorax findings. Venous blood samples were collected by phlebotomy, and plasma MMP9 concentrations were quantified using the DuoSet ELISA kit (DY911, R&D Systems). Statistical analysis was performed to compare mean and median MMP9 levels between genotype and disease groups. Ethical approval was obtained from the institutional ethics committee .

4. MAIN RESULTS

Both mean and median plasma levels of MMP9 were higher in ZZ individuals compared to MM individuals, although the difference did not reach statistical significance. Similarly, COPD participants showed a slight increase in MMP9 levels compared to healthy controls. The highest MMP9 mean expression was observed in the ZZ COPD subgroup. The lack of statistical significance may reflect limited sample size, smoking status variability, or confounding comorbidities, given that MMP9 is a marker of inflammation.

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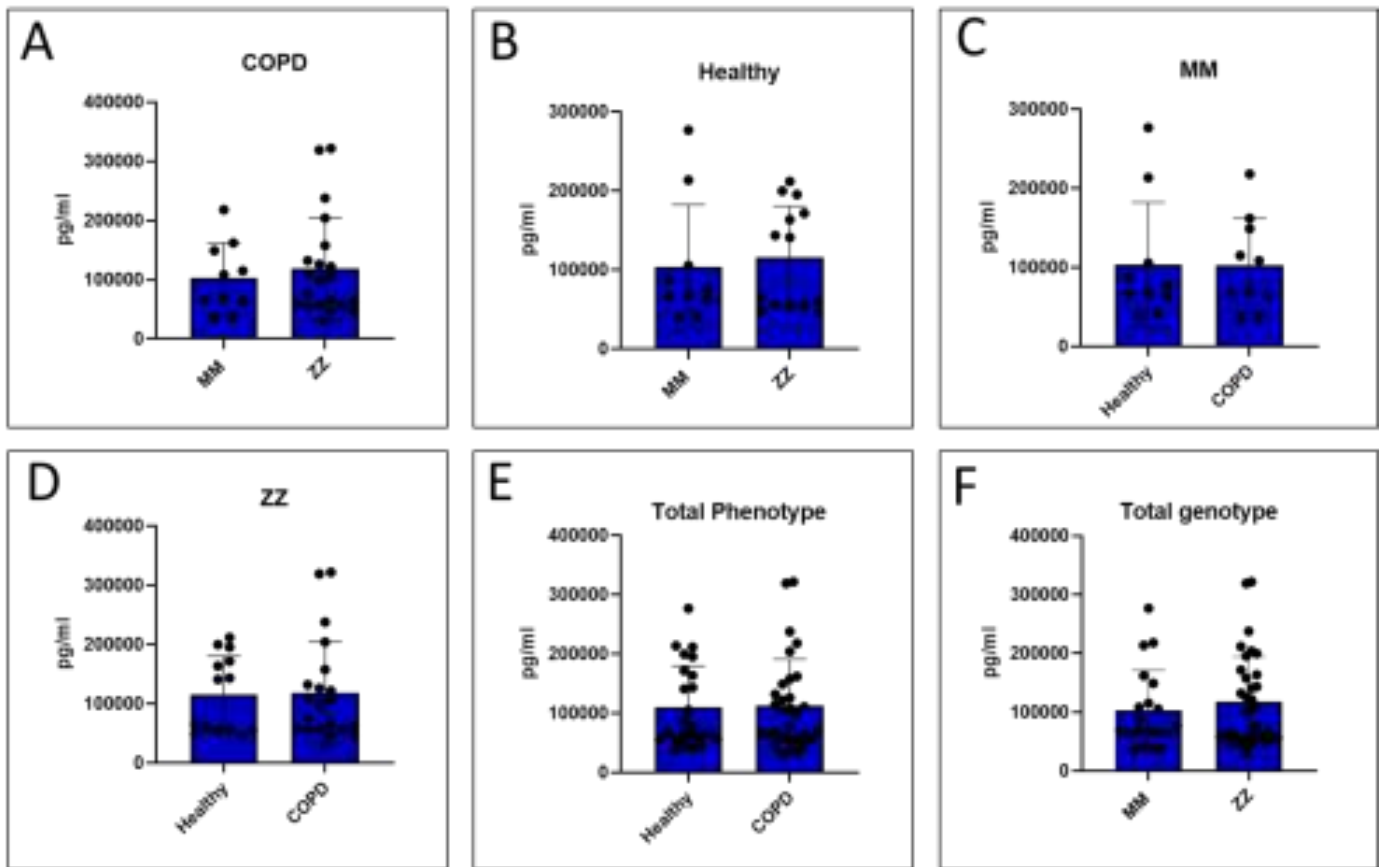


Figure 1. Sandwich ELISA performed on plasma samples from individuals with MM and ZZ genotypes to measure the expression of MMP9. The Mann-Whitney U test was used to compare MMP9 expression between the groups. A) Compared MM and ZZ samples diagnosed with COPD, B) Compared MM and ZZ samples without COPD, C) Compared healthy and COPD samples with the MM genotype. D) Compared healthy and COPD samples with the ZZ genotype, E) Compared healthy and COPD from combined MM and ZZ genotypes, F) Compared MM and ZZ from combined healthy and COPD phenotypes.

5. DISCUSSION

This study demonstrates a trend towards elevated MMP9 expression in individuals with the ZZ genotype compared to MM, suggesting a potential link between AAT deficiency and systemic inflammatory activity. Although not statistically significant, the higher MMP9 levels in ZZ COPD participants support the hypothesis that genetic susceptibility and chronic lung disease may act synergistically to promote matrix degradation and tissue remodeling. Previous studies have similarly reported elevated MMP9 in COPD patients, reflecting increased macrophage activation and protease-antiprotease imbalance [1,2]. The absence of significance could be attributed to sample size limitations and confounding factors such as smoking or comorbid inflammatory conditions. Future studies with larger cohorts and controlled confounders are warranted to validate MMP9 as a potential biomarker for AATD-associated COPD.

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6. CONCLUSION

Both AAT genotype and disease status appear to influence systemic MMP9 expression. ZZ individuals showed a trend of increased MMP9 levels, even in the absence of COPD. Larger-scale studies are needed to determine whether MMP9 can serve as a biomarker for early detection or disease monitoring in AATD-associated COPD.

7. ACKNOWLEDGEMENT

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UN5

Reducing Antimicrobial Resistant Bacteria in Water with Novel Photodynamic Technology

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Abstract

Antimicrobial resistance (AMR) presents a critical public health challenge, particularly in hospital wastewater environments, where reservoirs of resistant bacteria such as Carbapenemase-producing Enterobacterales (CPE) can persist. This study evaluates a visible light-activated photodynamic disinfection technology that utilizes visible-light activated coatings to reduce CPE in water environments as a sustainable alternative to chemical disinfectants [OBJ]. Prototype photodynamic cells (100 mL) containing photoactive or inactive coated meshes were inoculated with 10⁵ CPE-positive *Escherichia coli* (EC) or *Klebsiella pneumoniae* (KP). Viable plate counting and IDEXX™(Colilert™) were used to enumerate bacteria at t = 0, 3, 6, 24h). Controls with uncoated mesh/inactive coating were tested alongside experimental meshes. For each series, light (visible-light LED) and dark incubation were compared. Additionally, over 9 weeks, disinfection in light- and dark-exposed prototype cells when re-inoculated with *E. coli* (every two weeks) was investigated. Results demonstrated a strong correlation between light exposure and bacterial reduction, with mean log reductions of 4.03 (KP) and 2.81 (EC) over 24 hours under light conditions, compared to 0.22 (KP) and -0.73 (EC) respectively in the dark. Control meshes exhibited a log reduction of 0.18 (KP) and -0.43 (EC). Meshes were reusable for at least 3 weeks, showing similar levels of photo disinfection. In conclusion, photodynamic technology presents a promising alternative solution for reducing AMR in hospital environments and managing AMR pathogen transmission from sinks, drains, and wastewater sources. Further optimization addressing biofilm formation, solution cloudiness, and temperature effects is underway.

Keywords: antimicrobial resistance, photodynamic technology, Carbapenemase-producing Enterobacterales, hospital wastewater, sustainable infection control

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1. INTRODUCTION

Antimicrobial Resistance (AMR) poses a serious threat to public health, particularly within hospital environments. Hospital wastewater can grow resistant pathogens such as Carbapenemase-producing Enterobacterales (CPE), increasing the transmission risk. Traditional methods to control these pathogens in wastewater often rely on harsh chemicals, which can further exacerbate AMR and contribute to environmental concerns.

In October 2017, CPE was declared a national public health emergency in Ireland, highlighting the need for strategies to mitigate CPE infections and prevent associated complications [1]. Contaminated sinks and drains, especially in ICUs, have been implicated in CPE transmission, with water sources acting as reservoirs and activities like splashes and tooth brushing identified as risk factors [2-4]. Photodynamic technology, which relies on visible light activation of photosensitizers to produce reactive oxygen species (ROS), offers a sustainable, non-chemical method to disrupt microbial cells. This research explores photodynamic technology, a light-based method, as a novel and sustainable approach to reducing AMR bacteria in hospital drain environments.

2. OBJECTIVES

- To evaluate the effectiveness of photodynamic technology in reducing the bacterial load of CPE in hospital wastewater.
- To assess the long-term effectiveness of photodynamic technology by testing meshes that have been exposed to the technology and stored over extended periods.

3. METHODOLOGY

Laboratory-based experiments were conducted using photosensitizer coated, treated (test compound) and controls (coated, untreated; uncoated, untreated) meshes to test the effectiveness of photodynamic technology with the test compound. Meshes were placed in window-clear Nalgene containers with 100mL of PBS and were initially spiked with 1×10^4 CFU/mL of CPE-positive bacteria inoculum *Klebsiella pneumoniae* (KP), ATCC BAA2146, or environmental *Escherichia coli* (EC), OXA-48 positive and then exposed to photodynamic treatment under both light and dark conditions. Light conditions were achieved via commercially available visible light LED strings.

To assess for long-term efficacy, further experiments were also conducted to assess the durability of meshes previously spiked and exposed to both light and dark conditions, then left in ambient light conditions for more than a month, before being re-spiked and re-exposed to the light treatment over 3 two-week cycles (total time: 9 weeks). Bacterial quantification using traditional plating with colony counts on Mueller Hinton agar, and with the IDEXX Quanti-Tray system (Colilert-18*) to determine bacterial growth or reduction was performed at multiple time points: t0, t3, t6, and t24 hours. Data analysis involved comparing the bacterial loads between test and control groups across these time points. Analysis and visualization were carried out in R.

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4. MAIN RESULTS

A strong relationship between light exposure and CPE reduction was observed (Figure 1, Figure 2). Data remained relatively consistent at the t3 and t6 hour marks. At t24 hours, almost no bacterial colonies were observed on the treated meshes (i.e., no bacterial load) vs. the controls. Meshes were reusable for at least 7 weeks and showed similar levels of photo disinfection over time.

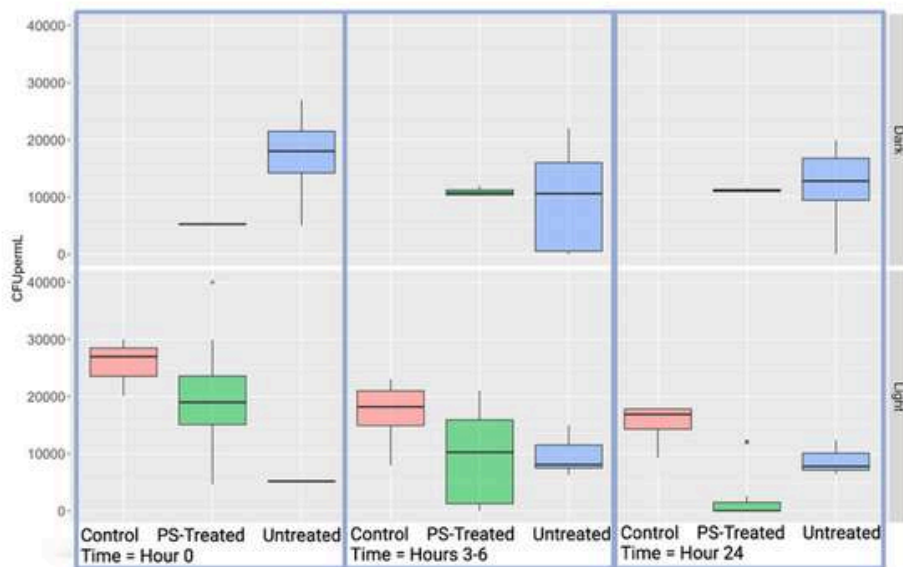


Figure 1. Light activated disinfection of *K. pneumoniae*-spiked water after 24 h. Boxplots demonstrating CFU/mL bacterial counts from *K. pneumoniae* spiked water under dark and light irradiation conditions, from start (t=0 hours) and end (t=24 hours), for prototype with PS-coated and non-coated mesh. Control mesh for light series only.

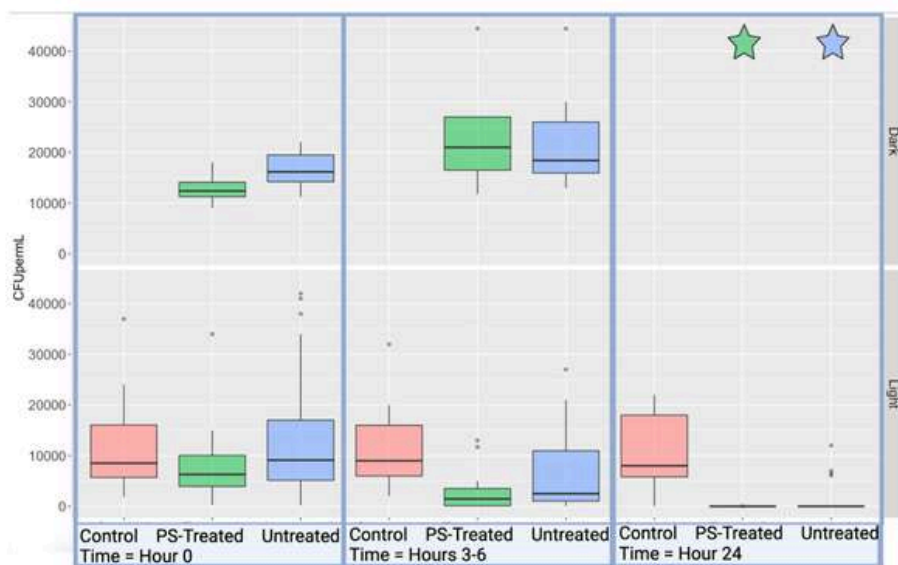


Figure 2. Light and dark disinfection of *E. coli*-spiked water after 24 h. Boxplots demonstrating CFU/mL bacterial counts from *E. coli* spiked water under dark and light irradiation conditions, from start (t=0 hours) and end (t=24 hours), for prototype with PS-coated and non-coated mesh. All t=24 hours dark condition experiments (represented by stars) were above the upper Limit of detection (i.e. > 9x10⁴ CFUs/mL). Control mesh for light series only.

5. DISCUSSION

This study demonstrates that photodynamic disinfection is an effective, light-dependent method for reducing AMR bacteria in simulated wastewater environments. The observed correlation between light exposure and bacterial inactivation aligns with the photodynamic mechanism of reactive oxygen species-mediated microbial damage.

The results demonstrated a potential for photodynamic technology as an effective method for reducing AMR bacteria in hospital wastewater environments. The significant reduction in bacterial load observed at t24 hours, even after several weeks of use, indicates the technology's strong bactericidal effects. These findings suggest that photodynamic technology could be a viable, non-chemical alternative for controlling AMR pathogen transmission in hospital settings.

However, for future research and development, certain factors of this research should be considered. For example, biofilms formation on the meshes, mold growth in the solutions, cloudiness in the solutions influencing light transmission, and an increase in temperature of the solutions due to light exposure. These factors may impede optimal light penetration and would be addressed in next-generation prototypes. Future development should refine coating stability, enhance light diffusion, and evaluate system scalability in real hospital wastewater pipelines.

6. CONCLUSION

Photodynamic technology offers a promising approach to mitigating the spread of antimicrobial-resistant bacteria, particularly CPE in hospital wastewater environments. The ability to significantly reduce bacterial loads without the use of harsh chemicals shows a compelling alternative to current methods.

7. ACKNOWLEDGEMENT

The authors thank the Department of Microbiology, RCSI ERC Beaumont Hospital, for laboratory support.

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PN1

LYOPHILIZED ALLIUM SATIVUM L. EXTRACTS LOADED SOLID LIPID NANOPARTICLES FOR DIURETIC AND TASTE MASKING ACTIVITIES ON ALBINO WISTAR RATS

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Abstract

The resurgence of herbal medicine has catalysed innovative formulation strategies that harness natural bioactives for enhanced therapeutic efficacy and patient compliance. Meta-analysis and literature triangulation indicate that such SLNs not only enable oral pharmaceutical use but are also well-suited for nutraceutical applications, promising as functional dietary supplements for cardiovascular, metabolic, and renal support. This study explores a novel oral delivery approach using solid lipid nanoparticles (SLNs) containing lyophilised extracts of *Allium sativum* L. (garlic) using stearic acid as the lipid matrix. Two therapeutically unique nanocarriers-AS-SLN (secondary metabolite-rich) and AC-SLN (allicin-loaded)-were developed through homogenisation and ultrasonication techniques.

Comprehensive Pharmacognostical and phytochemical analyses confirmed authenticity and quantification of actives, while advanced physicochemical characterization (average particle size below 50 nm, entrapment efficiency 85% and SEM) validated nanoparticle uniformity and stability.

Phytochemical analysis revealed the presence of 80 mg/g triterpenoids and 66 mg/g saponins in the extract, indicating substantial levels of these secondary metabolites associated with bioactivity, including diuretic effects. Ultrasonication combined with lyophilization enhances allicin's yield significantly higher than traditional methods, which often yield 0.01–0.03% due to thermal degradation and oxidation. This optimized extraction preserves heat-sensitive allicin, allowing accurate HPLC quantification of approximately 0.34%. In vitro studies demonstrated sustained release kinetics for 12 hrs in AS-SLN.

In vivo assessments, comprising taste masking (rat lick test), indicating high palatability and diuretic efficacy in albino Wistar rat models, revealed robust therapeutic profiles. The AS-SLN exhibited pronounced diuretic activity comparable to the standard drug furosemide, while notably preventing potassium loss, thereby demonstrating a distinct pharmacodynamic advantage.

From the research, we conclude that the SLN platform ensures stability, palatability, and safe, sustained delivery at low doses, increasing therapeutic compliance. Product application encompasses oral liquid or capsule forms deployable in pharmaceutical and nutraceutical markets, offering potential for global health impact and improved patient outcomes.

Keywords: *Allium sativum* Loaded Solid Lipid Nanoparticle, *Allium sativum* L., lyophilization, Homogenization, Allicin Stability, Animal Lick Test, Diuretic Study

1. INTRODUCTION

Herbal medicines have gained renewed interest due to their affordability, accessibility, and fewer side effects compared to synthetic drugs. According to WHO, 80% of the world's population relies on plants for therapeutic purposes, especially in developing countries. Despite historical decline in medicinal plant use due to instability and inadequate mechanistic understanding, the 21st century witnessed a resurgence with phytopharmaceuticals entering mainstream medicine. Examples include plant-derived drugs like Paclitaxel and Artemisinin. Regulation has become crucial, with AYUSH and CDSCO emphasizing scientific data on the quality, safety, and efficacy of herbal products.

Diuretics, which increase urine output by inhibiting sodium reabsorption in renal tubules, are crucial for managing edema, hypertension, and heart failure. However, synthetic diuretics often cause side effects such as electrolyte imbalance and dehydration. Several plants like *Foeniculum vulgare* and *Hibiscus sabdariffa* have shown diuretic effects in clinical trials.

This study focuses on *Allium sativum* L. (garlic), known for therapeutic properties but limited by gastric irritation and alliaceous odor. Formulating *Allium sativum* extracts into lyophilized solid lipid nanoparticles aims to improve stability, sustained release, taste masking, and diuretic efficacy.

2. OBJECTIVES

The primary objective of the study was to develop lyophilized solid lipid nanoparticles loaded with *Allium sativum* L. extracts for enhanced diuretic activity and taste masking. The specific aims included:

- Preparation and characterization of lyophilized *Allium sativum* extracts.
- Formulation of solid lipid nanoparticles incorporating these extracts.
- Evaluation of diuretic effects in albino Wistar rats.
- Assessment of taste masking efficacy and stability of the formulation.

3. METHODOLOGY

Allium sativum L. bulbs were lyophilized to obtain dried extract powder. Hydroalcoholic extracts were prepared and characterized for phytoconstituents, including saponins and triterpenoids. Solid lipid nanoparticles (SLNs) were formulated by homogenization and ultrasonication using stearic acid as the lipid matrix to encapsulate *Allium sativum* extracts and allicin.

Characterization of SLNs included Fourier-transform infrared spectroscopy (FTIR), scanning electron microscopy (SEM), particle size and zeta potential analysis, entrapment efficiency, and drug content by HPLC. Taste masking was evaluated by in vitro spectrophotometric studies and in vivo animal lick tests. Diuretic activity was assessed using albino Wistar rats, comparing treated groups with control and standard diuretic drugs. Statistical analysis was performed to determine significance.

4. MAIN RESULTS AND DISCUSSION

The formulated *Allium sativum* L. lyophilized extracts loaded solid lipid nanoparticles (AS-SLN and AC-SLN) were characterized and showed particle sizes in the nanometric range (~100-200 nm), good entrapment efficiency (~70-75%), negative zeta potentials indicating stability, and spherical morphology under SEM.

The lyophilized *Allium sativum* L. extract-loaded solid lipid nanoparticles (AS-SLN and AC-SLN) showed particle sizes in the nanometric range and good physicochemical properties, supporting their suitability for enhanced bioavailability.

Table 1: Percentage Yield of Formulations

S.No	Formulation	Trial 1 (%w/w)	Trial 2 (%w/w)	Trial 3 (%w/w)	Mean ± SD (%w/w)
1	AS-SLN	80.9	81.5	81.1	81.16 ± 0.3
2	AC-SLN	85.7	86	85.9	85.8 ± 0.15

Table 2: pH Measurement of Formulations

S.No	Formulation	Trial 1	Trial 2	Trial 3	Mean ± SD
1	AS-SLN	7.2	7.3	7.2	7.2 ± 0.05
2	AC-SLN	7	7.1	6.9	7.3 ± 0.01

FTIR spectra confirmed the absence of chemical interactions between the extract and lipid components. The HPLC quantification revealed sustained release of bioactive compounds, with AS-SLN showing approximately 75% release over 12 hours. Taste masking evaluation by in vitro spectrophotometric and in vivo animal lick test demonstrated effective reduction of the characteristic garlic odour and taste.

In vivo diuretic activity in albino Wistar rats revealed significantly enhanced urine volume and electrolyte excretion for both AS-SLN and AC-SLN compared to control and standard diuretic groups ($p < 0.05$). AS-SLN exhibited better efficacy potentially due to the contribution of secondary metabolites such as saponins and triterpenoids, which further enhance diuretic action. The study validates the potential of solid lipid nanoparticles to improve the bioavailability, stability, and patient compliance of *Allium sativum* extracts through sustained release and taste masking, while achieving therapeutic diuretic effects with low doses and minimal side effects.

5. CONCLUSION

The lyophilized *Allium sativum* L. extracts loaded solid lipid nanoparticles demonstrated enhanced diuretic activity and effective taste masking in albino Wistar rats. This novel delivery

system improved the stability and sustained release of bioactive compounds, reducing common drawbacks related to raw garlic extract such as irritant effects and strong odor. The study supports the use of nanoparticle formulations to optimize herbal therapeutics for better efficacy, compliance, and safety.

6. ACKNOWLEDGEMENT

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Nanoemulgel-Based Delivery of Bergamot Essential Oil with Improved Stability and Skin Penetration for Enhanced Topical Wound Repair

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Abstract

Background: Wound healing remains a complex clinical challenge due to persistent infection, chronic inflammation, and oxidative stress that hinder tissue regeneration. Bergamot (BEO) essential oils offer potent antimicrobial, antioxidant, and anti-inflammatory activities but are limited by poor solubility, stability, and insufficient skin penetration, reducing their therapeutic potential. By combining nanotechnology with phytochemistry, this study developed a bergamot essential oil (BEO) nanoemulgel designed to significantly enhance skin penetration, optimize topical delivery, and amplify multifactorial bioactivity. This innovative formulation aims to overcome conventional limitations and accelerate wound closure through improved permeation and sustained therapeutic effects.

Methods: Nano emulsions of BG were prepared using homogenisation and ultrasonication technique and optimized for size, stability, and pH. The optimized nanoemulsion was incorporated into carbomer gel for nanoemulgel formation. Physicochemical characterization, antioxidant (DPPH assay), anti-inflammatory, antimicrobial, tyrosinase inhibition, and α -glucosidase inhibition assays were performed. In vivo wound healing was assessed in a rat excision model.

Results: The optimized nano emulsion (BG2) showed a droplet size of below 200 nm, zeta potential -20.2 mV, and pH 5.6. Stability tests confirmed resistance to phase separation under stress conditions. Biological evaluation revealed 37.5% anti-inflammatory activity, 50.96% tyrosinase inhibition and 7.7% α -glucosidase inhibition, and antimicrobial zone against *Staphylococcus aureus* with 1.08 cm. DPPH scavenging IC₅₀ was 220.2 μ g /mL. In vivo, BG2 nanoemulgel significantly accelerated wound contraction, achieving complete closure by day 14.

Conclusions: BG nanoemulgel demonstrated potent multifactorial wound healing effects supported by physicochemical stability and bioactivity, indicating its potential as an effective topical formulation for accelerated skin repair.

Keywords: *Essential oil, Nanoemulgel, Antibiofilm, Wound healing.*

1. INTRODUCTION

Wound healing is a complex biological process involving hemostasis, inflammation, proliferation, and remodeling. Chronic wounds, prevalent due to diabetes and infections, pose therapeutic challenges. Essential oils are gaining attention as natural agents with antimicrobial, antioxidant, anti-inflammatory, and regenerative properties. However, their therapeutic potential is limited by volatility and instability. Nanotechnology-based nanoemulgels enhance stability, skin penetration, and controlled delivery of lipophilic essential oil components such as those in bergamot essential oil (BEO). BEO contains bioactive monoterpenes and coumarins such as limonene, linalool, and bergapten which have demonstrated key wound-healing relevant activities. This study formulates BEO nanoemulgel and evaluates its *in vitro* and *in vivo* efficacy, aiming to develop a safe and effective topical therapy for wound regeneration.

2. OBJECTIVES

- To formulate and characterize bergamot essential oil nanoemulgel with optimal physicochemical properties.
- To evaluate *in vitro* antioxidant, anti-inflammatory, tyrosinase inhibitory, and α -glucosidase activities.
- To assess antimicrobial, antibiofilm, and biofilm dispersion efficacy against *Staphylococcus aureus*.
- To investigate the wound healing efficacy of nanoemulgel in a rat excision wound model.

3. METHODOLOGY

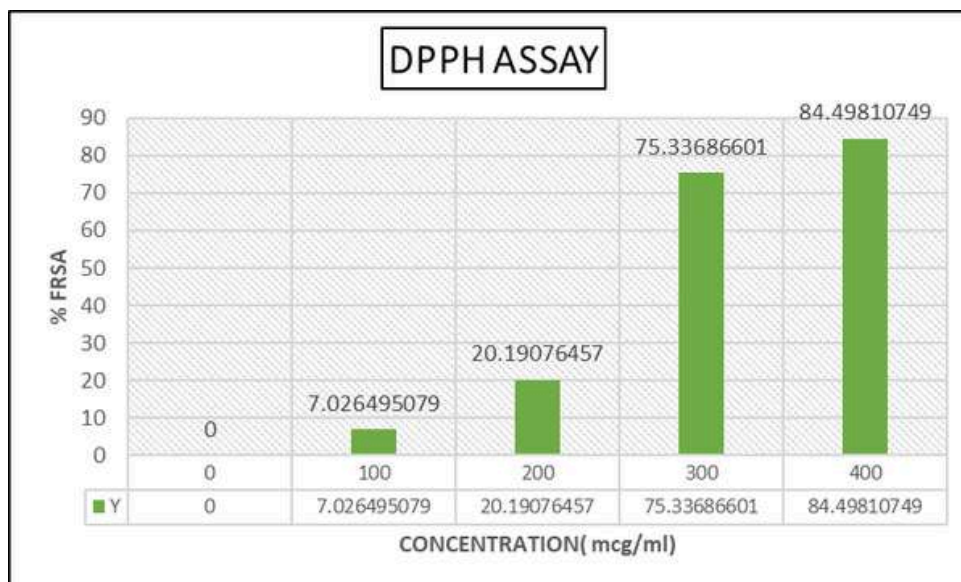
Bergamot essential oil (BEO) was characterised by GC-MS for phytochemical fingerprinting. Nanoemulsions were prepared by ultrasonication using Tween 80 and glycerine, followed by incorporation into carbomer 940 gel to form nanoemulgel. Particle size, zeta potential and pH were determined by dynamic light scattering and pH meter. Antimicrobial and antibiofilm activities against *Staphylococcus aureus* were evaluated using well diffusion and microtiter plate assays. Antioxidant activity was assessed by DPPH free radical scavenging, anti-inflammatory activity by protein denaturation assay, while tyrosinase and α -glucosidase inhibitory activities were performed spectrophotometrically. *In vivo* wound healing efficacy was tested on Wistar rats with topical application of nanoemulgel, compared to povidone iodine and blank gel, with wound contraction measured over 21 days.

PN2

4. MAIN RESULTS



BEO nanoemulgel showed nanosized particles averaging 178 nm, zeta potential around -20 mV, and stable rheology. GC-MS confirmed characteristic bioactive compounds including limonene, linalool, and linalyl acetate. The nanoemulgel exhibited significant antimicrobial activity (zone of inhibition 1.08 cm) and dose-dependent inhibition of *Staphylococcus aureus* biofilm formation and dispersion. Potent antioxidant capacity was demonstrated by an IC_{50} of $20.2 \mu\text{g/mL}$ in the DPPH assay. Anti-inflammatory activity inhibited protein denaturation by 37.5%. Tyrosinase inhibition was 50.96%, with mild α -glucosidase inhibition at 7.7%. Stability tests confirmed resistance to freeze-



In vivo, nanoemulgel accelerated wound contraction significantly (near complete closure by day 14) compared to control groups.



PN2

	Positive control(POVIDONE)	BG NEG2	Negative Control(BLANK)
DAY 0			
DAY 3			
DAY 7			
DAY 10			
DAY 14			
DAY 17			
DAY 21			

5. DISCUSSION

The multifactorial efficacy of BEO nanoemulgel is attributed to its optimized physicochemical properties allowing effective delivery of bioactive monoterpenes to the wound site. Its antimicrobial and antibiofilm activities target key pathogens impeding healing. The synergistic antioxidant and anti-inflammatory effects support tissue repair and reduce oxidative damage. Tyrosinase inhibition offers cosmetic benefits by mitigating post-inflammatory hyperpigmentation. Enhanced wound contraction and epithelialization observed *in vivo* correlate with the integrated pharmacological effects of BEO constituents combined with the nanoformulation's improved stability and bioavailability.

6. CONCLUSION

This study demonstrates that bergamot essential oil nanoemulgel is a promising topical therapeutic with potent antimicrobial, antioxidant, anti-inflammatory, and wound-healing effects. Its physicochemical stability and multi-target bioactivity endorse it as a safe, effective, and scalable candidate for managing acute and chronic wounds, advancing the natural product-based nanomedicine field.

7. ACKNOWLEDGEMENT

My sincere thanks to Dr. Satheesh Babu Natarajan for guiding to make this project successful and my gratefulness to Lincoln university college, Selangor for supporting throughout the project.

Protective Effects of Hesperidin on Oxidative Stress and Hormonal Imbalance in a Rat Model of Experimental Varicocele

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Abstract

Background:

Varicocele, a major cause of male infertility, is associated with oxidative stress, hormonal imbalance, and impaired testicular function. Hesperidin, a citrus-derived flavonoid with potent antioxidant and anti-inflammatory properties, has shown potential in mitigating testicular oxidative injury. This study aimed to evaluate the protective effects of hesperidin on biochemical alterations, oxidative stress, and hormonal changes induced by experimental varicocele in adult rats.

Methods:

Adult male rats were divided into control, varicocele-induced, 3 hesperidin-treated groups (100, 200 and 400 mg/kg) and Sham group. Experimental varicocele was induced surgically by partial ligation of the left renal vein. Hesperidin was administered orally for 8 weeks. Biochemical parameters, including glucose and lipid profiles, were measured using standard enzymatic assays. Oxidative stress markers such as superoxide dismutase (SOD), and catalase (CAT) were analyzed in testicular tissues. Serum testosterone, luteinizing hormone (LH), and follicle-stimulating hormone (FSH) levels were quantified by ELISA.

Results:

Varicocele induction led to significant increases in oxidative stress markers and decreased serum hormone levels. Hesperidin treatment, particularly at medium and high doses, markedly improved serum testosterone, LH, and FSH levels. Notably, glucose levels were significantly reduced in the high-dose group, indicating improved metabolic regulation. Antioxidant enzyme activities were also restored toward normal values.

Conclusion:

Hesperidin effectively mitigates biochemical and hormonal alterations induced by varicocele, likely through its antioxidant and endocrine-modulating actions. These findings support hesperidin as a potential adjunctive therapeutic agent for varicocele-associated male infertility.

Keywords: *Hesperidin, varicocele, oxidative stress, fertility, testosterone, antioxidants*

1. INTRODUCTION

Varicocele, a major cause of male infertility affecting approximately 15% of the male population, is associated with oxidative stress, hormonal imbalance, and impaired testicular function. (Alsaikhan et al., 2016) .Varicocele is a condition involving the abnormal dilation of veins in the spermatic cord, which is a leading cause of male infertility, largely due to oxidative stress and inflammatory damage to testicular tissues. Current available treatments, including surgical intervention, have limitations and potential side effects, necessitating the exploration of alternative therapeutic strategies. (Krishna Reddy et al., 2015) Hesperidin, which is a citrus-derived flavonoid known for its potent antioxidant and anti-inflammatory properties, holds promise as a natural therapeutic agent.(Barreca et al., 2017) However, its effects on oxidative stress, inflammation, and testicular function in the context of varicocele needs to be explored further. This research aims to investigate whether hesperidin can mitigate biochemical changes and oxidative stress in an experimental varicocele model, offering potential insights into novel treatment avenues for varicocele-induced infertility.

This research aligns closely with the conference themes of reproductive health, oxidative stress biology, and innovative therapeutic interventions. Varicocele remains a leading yet under-addressed cause of male infertility, primarily due to excessive oxidative stress and impaired testicular function. Current treatments, including surgery, often fail to fully reverse biochemical or histological damage, indicating a clear need for novel, evidence-based therapeutic strategies.

Recent literature highlights the importance of antioxidants in mitigating testicular oxidative stress, with studies demonstrating that natural flavonoids can enhance endogenous antioxidant defense and protect reproductive tissues. Hesperidin—a citrus-derived bioflavonoid known for its strong antioxidant, anti-inflammatory, and cytoprotective effects—has shown protective roles in various organ systems under oxidative injury. However, its application specifically in varicocele-induced testicular dysfunction has not been adequately explored. Addressing this gap, the present research evaluates hesperidin's ability to reduce oxidative markers, improve biochemical profiles, and protect testicular structure in an experimental rat model. By investigating a potential non-surgical therapeutic option, this study contributes to emerging discussions on integrative approaches to male infertility and supports the conference objective of showcasing innovative biomedical strategies grounded in current scientific evidence.

2. OBJECTIVES

To evaluate the therapeutic potential of hesperidin in reducing oxidative stress, modulating inflammatory responses, and improving testicular function in adult rats with experimentally induced varicocele. Specifically, the study aimed to

- Assess the impact of hesperidin on oxidative stress markers, including malondialdehyde (MDA) and antioxidant enzyme activities (SOD, CAT, GPx).
- Examine changes in inflammatory markers such as TNF- α and IL-6 in testicular tissue post-hesperidin administration.
- Evaluate the effect of hesperidin on sperm quality parameters, including sperm count, motility, and morphology.
- Determine whether hesperidin can help restore normal testicular function and improve hormonal profiles (e.g., testosterone levels) in the context of varicocele-induced damage.

3. METHODOLOGY

(i) Experimental Design

Animal

Healthy, adult, male Sprague Dawley rats (12 weeks old; 200–240 g) were used in the experiment. Rats were provided with standard laboratory chow.

Study design and doses

Health, adult and male Sprague Dawley rats will be used in the experiment. The rats were divided into 6 groups as follows.

Group I : Control

Group II : Varicocele control

Group III: Varicocele + hesperidin 100 mg/kg (low dose)

Group IV: Varicocele + hesperidin 200 mg/kg (medium dose)

Group V : Varicocele + hesperidin 400 mg/kg (high dose)

Group VI: Sham control

After a 1-week adjustment period, rats were maintained 6 per plastic cage under 12 h light–dark cycle (lights on 0700–1900 hours) under artificial light. Animal rooms were maintained at a temperature of 18–23°C with 40%–60% humidity. Rats were given free access to purified water and animal feed.

Varicocele induction

Groups II, III, IV, and V were induced with experimental varicocele

The animals had been anaesthetized with an intraperitoneal injection of ketamine 60 mg/kg + Xylazine 1 mg/kg. A vertical midline section of 3-4 mm was created at the abdominal region. After identification of the left renal vein and the insertion point of the internal spermatic vein, varicocele was induced by partial occlusion (50%) of the left renal vein. 50% venous block was achieved through the use of a 4-0 silk suturing of the left renal vein. Surgical site sutured with 3.0 silk sutures. This whole procedure was done in sterile conditions.

Body weight analysis

Throughout the study the body weight of each rat in each group was recorded every week and the changes were tabulated

Blood sample collection

Retroorbital blood samples were collected on day 3 since induction of varicocele and at the end of the study to be used for biochemical, haematological and hormone assay.

Organ harvesting

At the end of the experiment the rats are to be sacrificed (8 weeks after start of hesperidin administration), later the organs such as brain, lungs, heart, liver, kidney, spleen, and testis were collected for organ weight analysis. The pivotal organs such as the liver and kidney were also used for histopathological analysis. Using the liver and testis sample, antioxidant enzymes were measured.

Organ weight analysis

At the end of the study the experimental rats were sacrificed and the organs such as the brain, lungs, heart, liver, kidney, spleen and testis will be collected. Absolute organ weights will be measured, and the relative organ weight was calculated.

Sperm analysis

Sperm is extracted at the end of the experiment from the left cauda epididymis of the rats to assess sperm count, motility, and morphology to evaluate spermatogenesis.

Haematological analysis

Blood samples collected at the end of the study were placed into tubes containing EDTA for haematological analyses. The White blood count, red blood count, platelets, neutrophils, lymphocytes, monocytes, eosinophils, basophils and haemoglobin levels were measured using **FBC - Sysmex XN 1000**.

Biochemical analyses

Blood collected at the end of the study was centrifuged at 3000 RPM for 20 minutes. The serum samples were used to estimate the biochemical parameters such as glucose, aspartate, aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), creatinine and urea and lipid parameters using **Roche Cobas 8000 analyser**.

Histopathological analysis

After gross examination, representative sections were taken from the specimens and placed in 10% formalin. Paraffin-embedded tissue blocks were prepared, and 4 to 5 micro sections was taken with Microtome for routine histopathology. Briefly, the sections for histopathology was placed on an albuminized glass slide, deparaffinized, rehydrated and stained with routine hematoxylin and eosin (H&E). After mounting with DPX and coverslip the slides will be examined under a light microscope

Hormone levels

Blood samples collected were analysed using Biochem - Roche Cobas 8000 to measure serum testosterone, luteinising hormone and follicle-stimulating hormone.

Antioxidant level analysis

Tissue (left testis) samples was excised and homogenized with Tris-buffered saline. The homogenate was used for the estimation of an enzymatic antioxidant parameter such as malondialdehyde content and superoxide dismutase, glutathione peroxidase and catalase activities. (Pla-Pagà et al., 2019)

Measurement of oxidative stress

8-hydroxy-2'-deoxyguanosine (8-OHdG) was measured to assess DNA damage caused to testicular tissue due to oxidative stress. (Jang et al., 2012) The 8-OHdG levels were measured through the use of an ELISA kit (Elabscience E-EL-0028-48T 8-OHdG ELISA Kit, 48T) on the left testicular tissue sample.

DNA fragmentation analysis

Rat sperm and DNA (isolated from blood) were used for the analysis. For the DNA fragment assay using rat sperm, the sample was washed in phosphate-buffered saline, smeared on microscopic slides, fixed in 4% paraformaldehyde in PBS for 30 minutes at 4 degree C and permeabilized with 0.1% Triton X-100 in 0.1% sodium citrate. Strand breaks in DNA were detected by TUNEL using a commercially available kit and the percentage of spermatozoa with fragmented DNA will be determined by direct observation of 500 spermatozoa per sample with an epifluorescence/ fluorescence microscope. For the DNA fragment assay using isolated DNA, the isolate DNA pellets will be applied to electrophoresis on a 1.5% agarose gel at 80 V for 2 h and the DNA bands will be visualized and photographed by ultraviolet gel documentation system.

Caspase-3 and caspase-9 assay

Caspase-3 and -9 activities were determined using commercially available ELISA kit.

(ii) Statistics

Data taken given as the mean \pm SEM and statistical analyses was performed using ANOVA. Results obtained at the end of experiment were compared with those of the control and varicocele groups using Student's t-test. Differences are considered significant if $P < 0.001$.

The ethical approval reference is AUAEC/FOM/2025/01

4. MAIN RESULTS

Varicocele control has much higher body weight compared to control by end of the study as shown in Figure 1. The body weight of rats which had been given high dose of Hesperidin were found to have body weight much lower to the varicocele control group throughout the study. In medium dose group the body weight is closer to control group. In low dose group the body weight is found to be slightly less than the varicocele control group. Varicocele control has much higher body weight compared to control by end of the study.

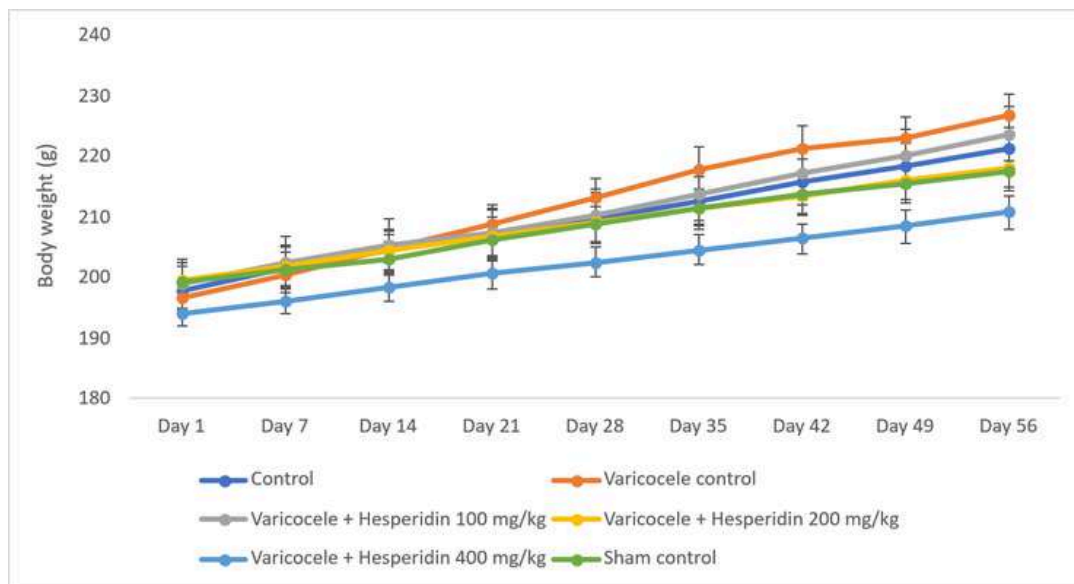


Figure 1 Change in boy weight throughout study

The tissue glutathione level is shown to be drastically reduced in the varicocele control group compared to control group. The Glutathione levels reach closer to control group as the dose increases as shown by how the high dose group shows similar Glutathione level as control group.

5. DISCUSSION

The findings of this study suggest that hesperidin exerts a protective effect against biochemical alterations and oxidative stress associated with experimental varicocele. Consistent with previous reports that varicocele disrupts testicular homeostasis through excessive reactive oxygen species (ROS) production and impaired antioxidant defence mechanisms, our results show increased oxidative markers and reduced endogenous antioxidants in untreated varicocele animals. These changes align with literature showing that varicocele-induced hypoxia and venous stasis compromise Leydig and Sertoli cell function, ultimately affecting spermatogenesis.

Treatment with hesperidin demonstrated notable improvements in oxidative status, reflected by reduced lipid peroxidation and restoration of antioxidant enzyme levels. These outcomes support previous studies reporting hesperidin's strong free radical-scavenging capacity and its ability to enhance cellular antioxidant pathways in other models of tissue damage. The observed biochemical recovery suggests that hesperidin may mitigate oxidative stress-mediated testicular injury, potentially stabilizing the microenvironment required for normal spermatogenic function. Importantly, the improvements observed in the hesperidin-treated groups highlight its potential role as an adjunct therapy for varicocele, especially in cases where surgical correction alone does not fully restore testicular function. While the present study demonstrates promising biochemical and oxidative benefits, further research is needed to confirm effects on fertility parameters, hormonal regulation, and long-term testicular architecture.

Overall, these findings contribute novel evidence supporting hesperidin as a potential pharmacological intervention for varicocele-associated oxidative stress, aligning with ongoing efforts to explore natural antioxidant compounds in reproductive health management.

6. CONCLUSION

This study demonstrates that hesperidin effectively reduces oxidative stress and improves key biochemical markers in rats with experimental varicocele. These findings suggest that hesperidin may help protect testicular tissue from varicocele-induced damage. Overall, hesperidin shows promise as a potential adjunct therapeutic option for improving testicular health in varicocele.

7. ACKNOWLEDGEMENT

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PROTOCOL TRANSLATION ENABLES RT-qPCR DETECTION OF SARS-COV-2 IN A DIGITAL-BASED PCR DIAGNOSTIC

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Abstract

Coronavirus 2019, a pandemic disease solely caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has led to a global health crisis. SARS-CoV-2 although currently endemic, remains a considerable threat, especially to immunocompromised individuals, underscoring the necessity for enhanced detection sensitivity and specificity. Reverse transcription

digital droplet polymerase chain reaction (RT-ddPCR) offers enhanced sensitivity and absolute quantification relative to the gold standard. This research represents the initial optimization of RT ddPCR for the detection of SARS-CoV-2 in saliva utilizing commercial RT-qPCR kit. Optimization included evaluating the RT-ddPCR reaction mixture, adjusting the annealing temperature, and validating results with 40 preserved saliva specimens. This study utilized RT qPCR as the reference method. Compatibility assessment indicated that ddPCR Supermix for Probes (no dUTP) is most effective at 57.6°C. An increase of 25% in primer/probe concentration enhances the amplitude of positive control droplet separation while reducing copy numbers. Ct value exhibits an inverse correlation with copy number concentration, indicating that lower Ct values correspond to higher concentrations for the N and E genes, with r^2 values of 0.98 and 0.85, respectively. ORF1ab exhibited a weak correlation ($r^2= 0.34$). Specificity ranged from 80.8% to 91.3%, whereas sensitivity was recorded at 100% and 93.3% for the targeted N and E genes. This study demonstrates the potential of saliva specimens for testing a modified ddPCR method for similar pathogens utilizing. Moreover, this study indicates the feasibility of translating protocol from RT-qPCR kits to digital-based PCR diagnostics, highlighting the important of protocol harmonization combating the infectious diseases.

Keywords: *Diagnostic, RT-ddPCR, RT-qPCR, SARS-CoV-2, Saliva, Protocol harmonization*

1. INTRODUCTION

Polymerase Chain Reaction (PCR) has evolved from conventional end-point PCR, which provides qualitative detection, to real-time quantitative PCR (rt-qPCR) that allows semi quantitative detection by measuring fluorescence during amplification and predicting nucleic acid amounts via cycle threshold (Ct) values. However, rt-qPCR does not provide absolute quantification because it relies on relative estimates via Ct values [1]. Digital PCR (dPCR) provides absolute quantification of target nucleic acids, thereby addressing this limitation. dPCR divides the sample into multiple PCR reactions, which are amplified and fluoresced to yield a binary signal. Employing Poisson statistics for the assessment of positive partitions enables the determination of target DNA concentration independent of standard curves or Ct values. This partitioning enhances the concentration of target molecules, reduces template competition, and increases detection efficacy [2].

This advanced methodology requires translating existing RT-qPCR protocols to digital PCR (dPCR). Both methods employ fluorescence-based detection; however, dPCR incurs higher cost due to its analytical precision and technical complexity. Commercially available RT-qPCR kits need to be adapted or harmonized for dPCR platforms to address this issue. This study utilized COVID-19 as a model for digital droplet PCR (ddPCR). Although SARS-CoV-2 can be detected using conventional reverse transcription quantitative PCR (RT-qPCR) [3], declining infection rates and the presence of asymptomatic carriers necessitate a more sensitive and specific methodology. ddPCR enables absolute quantification and improved detection of low viral loads.

2. OBJECTIVES

The aim of this study is to utilize the adaptation of the RT-qPCR commercial kit into ddPCR.

3. METHODOLOGY

Specimen Collection

The saliva specimens were collected from patients tested for SARS-CoV-2 and stored in -80°C , at COVID-19 Laboratory Center, School of Medicine and Health Sciences, Atma Jaya Catholic University of Indonesia (AJCUI) within the year of 2023. Total 40 saliva specimens were used in optimizing and validating the RT-qPCR kit in ddPCR. This study was approved by the Institutional Review Board of School of Medicine and Health Sciences, Atma Jaya Catholic University of Indonesia (AJCUI) with document number of 06/05/KEP-FKIKUAIJ/2022.

Commercially Available Kit for SARS-CoV-2 Detection in RT-qPCR

RT-qPCR was performed using xABT Multiple Real-Time PCR Kit (Beijing Applied Biological Technologies Co., Ltd., Beijing, China, #CT8223-48T) following the manufacturer's instruction. Each run had negative and positive (ORF1ab, N, E gene) controls. Cy5 recognized the internal control, FAM detected ORF1ab and E gene, and VIC detected N gene. Specimens with Ct value greater than 40 will be considered as negative.

Compatibility of RT-ddPCR Reaction Mixture with Commercially Available Kit

The ddPCR assay needs its own reaction mixture. Two available ddPCR reaction mixtures were evaluated in RT-qPCR to evaluate reagents compatibility. The master mixture was the same as for the RT-qPCR assay, but the nucleic acid amplification reaction solution was substituted with either One-Step RT-ddPCR Advanced Kit for Probes (Bio-Rad, Cat#1864021) or ddPCR Supermix for Probes (no dUTP) (Bio-Rad, Cat#1863023) and EvaGreen Supermix (Bio-Rad, Cat#1864034) for internal control detection.

RT-ddPCR Assay

This work employed a two-color ddPCR detection system, the QX200 Droplet Reader (Bio-Rad), for duplex detection in channel 1 (FAM/EvaGreen) and 2 (VIC/HEX). The RT-ddPCR assay was performed twice. The first detected dual targets for ORF1ab (FAM, channel 1) and N gene (VIC, channel 2) in xABT solution A and single-target detection of the E gene solution B (FAM, channel 1), while the second detected the internal control PhHV-1 using EvaGreen dye in channel 1. The AutoDG Droplet Generator (Bio-Rad) was used to generate droplets. The same RT-qPCR algorithm was used to thermocycle plates in a C1000 Touch Thermal. The QX200 Droplet Reader read FAM and VIC fluorescence signals. PhHV-1 detection involved reaction mixture with primers and nuclease-free water, droplet production, amplification, and detection in the EvaGreen channel using QX200 ddPCR EvaGreen Supermix.

Optimization of Primer/Probe and Annealing Temperature in RT-ddPCR

Concentration of primer and probe were optimized by comparing the initial and 25% increased concentrations. RT-ddPCR annealing temperature was improved by adding thermal gradient to the cycling cycle. The 45-second gradient is 57°C to 65°C.

Data Analysis

Bio-Rad QX Manager 1.2 Analysis Software examined RT-ddPCR data. Ct values and copy number concentrations were correlated using simple linear regression, and all graphical representations were created using GraphPad Prism 9.1.1 (La Jolla, CA, USA).

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4. MAIN RESULTS

The commercially available kit was able to detect positive and negative specimens in RT-qPCR. Among 20 specimens that were previously indicated as positive, 2 specimens detected as negative. A total of 18 positive specimens and 22 negative specimens were then utilized for optimization and implementation. The optimization method was first begun by testing the compatibility of RT-ddPCR mixture with the commercially available RT-qPCR kit. The ddPCR Supermix for Probes (no dUTP) was found to be compatible with the xABT Multiple Real-Time PCR Kit, which showed a consistent and similar result. Upon the compatible reaction mixture in RT-qPCR, it was applied in ddPCR.

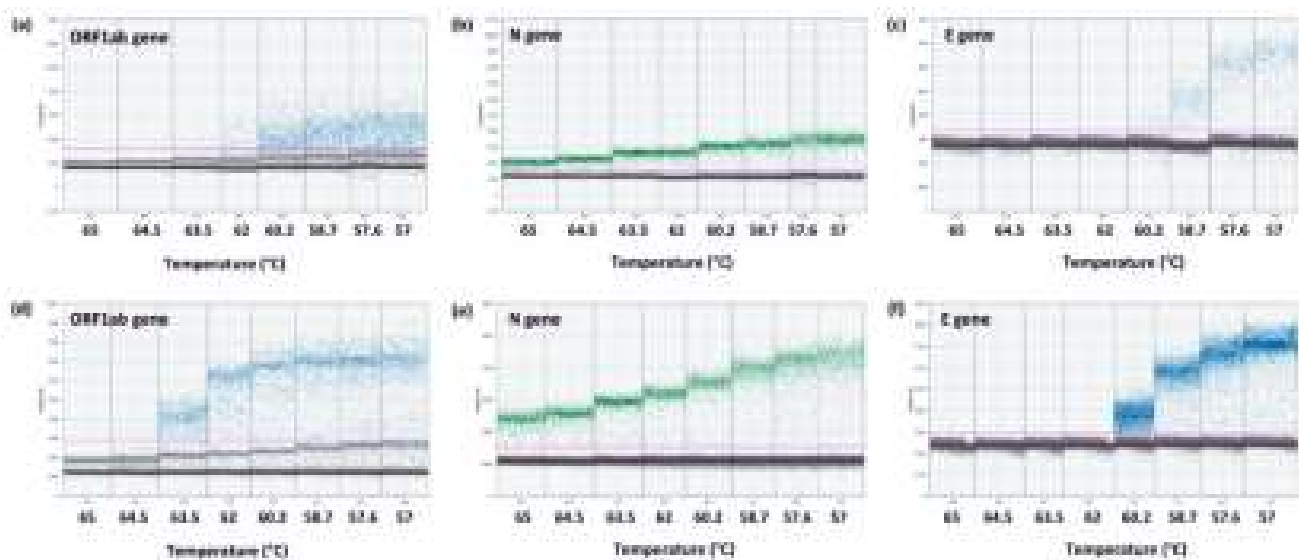


Figure 1. Annealing thermal gradient droplet separation. Blue/green dots represent positive droplets. (a) to (c) result of positive SARS-CoV-2 specimens; (d) to (f) result of positive control.

RT-ddPCR annealing temperature was adjusted to better separate positive and negative droplets. N and E genes displayed evident positive and negative droplet separation at 57.6°C, whereas ORF1ab gene did not (Figure 1). The optimization also indicated that 25% more primers and probes enhance droplet separation amplitude. The initial concentration was enough to witness droplet separation.

The optimal annealing temperature and primer/probe concentration were utilized for the RT ddPCR amplification of 40 samples. Two specimens containing fewer than 10,000 droplets were deemed invalid. In a study of 38 specimens, RT-ddPCR revealed strong negative correlations between Ct values and copy number concentrations for the N and E genes ($r^2 = 0.98$) and E gene ($r^2 = 0.85$), while the association for ORF1ab was weaker ($r^2 = 0.34$) (Figure 2). Of the 18 positive RT-qPCR specimens, three yielded negative results in RT-ddPCR. The N and E targets exhibit sensitivities of 100% and 93.3%, respectively, alongside specificities ranging from 80.8% to 91.3%. The enhanced RT-ddPCR technique successfully achieved clear droplet separation, consistent amplification of the PhHV-1 internal control, and precise quantification in specimens with low viral loads.

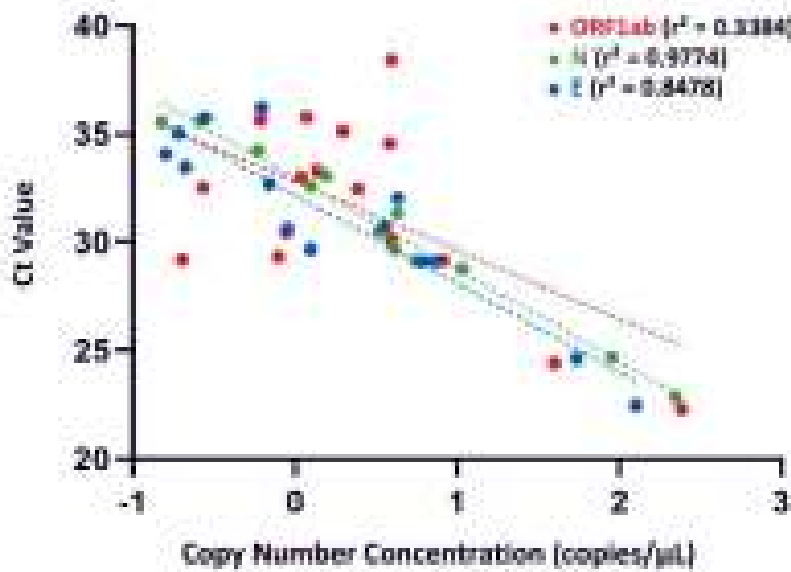


Figure 2. Ct value and copy number correlation

5. DISCUSSION

RT-qPCR and RT-ddPCR protocol harmonization includes comparing ddPCR Supermix for Probes (no dUTP) and One-Step RT-ddPCR Advanced Kit for Probes compatibility with the commercial kit (xABT kit). The ddPCR Supermix for Probes (no dUTP), which uses a hot-start polymerase that remains inactive during droplet production, was compatible with the reference RT-qPCR kit and generated consistent amplification results across three replicates [4,5]. Reverse transcriptase (RT) enzyme, RNase inhibitors, and dithiothreitol (DTT) in the One-Step RT ddPCR Advanced Kit for Probes performed poorly under the same circumstances. DTT, a powerful reducing chemical that disrupts fluorescence quenchers and alters signal stability, likely caused performance degradation and varied droplet readings [6–8]. Bio-Rad's RT enzyme may have been incompatible with the commercial kit's xABT primer and probe.

The ddPCR Supermix for Probes (no dUTP) was utilized on the RT-ddPCR platform following compatibility assessment. Initially, it exhibited inadequate separation between positive and negative droplets, necessitating further adjustments to the annealing temperature. The assay for both N and E genes demonstrated minimal background signal and clear droplet separation at 57.6°C. The principles of standard annealing temperature suggest establishing the temperature 3–5°C below the primer melting point [7], corresponds to 60°C in the xABT kit. Prior studies indicate that reduced annealing temperatures enhance amplitude separation, while temperatures exceeding 60°C decrease the distance between positive and negative droplet clusters, thereby narrowing signal differentiation [9]. In contrast, ORF1ab exhibited restricted droplet separation regardless of temperature variations, potentially attributable to primer–probe incompatibility or the presence of reaction inhibitors.

Primer and probe concentrations were increased by 25% to evaluate amplification performance. The findings indicated that the reference concentration elevated copy numbers for all target genes when utilizing only the positive control (PC). A higher primer–probe concentration marginally improved amplitude separation, whereas the reference concentration effectively separated droplets. Optimal annealing temperature and standard primer–probe concentration were employed for specimen validation. Increasing primer–probe concentration may enhance droplet differentiation by facilitating target binding and amplification [10,11].

The optimized harmonization procedure aligned the results of RT-qPCR with those of RT ddPCR. Increased copy numbers were associated with decreased Ct values for the N and E genes (Figure 2). ORF1ab demonstrated a low correlation, likely due to its heightened nucleotide variation, which complicates identification and reduces amplification efficiency [12,13]. The ORF1ab gene was excluded from further analysis due to the presence of "rain" droplets, which indicated nonspecific amplification and compromised the consistency of threshold setting. RT ddPCR demonstrated 100% sensitivity for the N gene and 93.3% for the E gene, indicating that nearly all RT-qPCR positive specimens were also positive. The specificity for the N (80.8%) and E (91.3%) genes was high, as the majority of negative saliva specimens remained negative when compared to RT-qPCR results, excluding non-infected specimens. False positives in RT-qPCR, particularly in specimens with Ct values exceeding 35, may account for the discrepancies observed between positive RT-ddPCR and RT-qPCR results [14].

This study demonstrated the feasibility of harmonizing the two procedures, enabling the utilization of a commercial RT-qPCR kit to enhance the sensitivity and specificity of the RT ddPCR method. Alternative targets to the ORF1ab gene are recommended for SARS-CoV-2 detection due to the challenges in detecting this gene, which may affect assay reliability.

6. CONCLUSION

An existing commercial RT-qPCR kit was modified for use with the RT-ddPCR platform to detect SARS-CoV-2 in saliva samples. The ddPCR Supermix for Probes (without dUTP) and an annealing temperature of 57.6 °C yielded the most reliable droplet separation and quantification. This demonstrates that cross-platform reagent harmonization enhances the sensitivity and cost-effectiveness of RT-ddPCR in virus detection, establishing a robust basis for future diagnostic applications.

7. ACKNOWLEDGEMENT

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PN5 *In silico* pharmacokinetic (ADME) and toxicology prediction of Gastrodin

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Abstract

The main phytoconstituent of *Gastrodia elata*, gastrodin has shown to possess neuroprotective and anti-inflammatory activities. It is used to treat many neurological disorders and ailments. The ADMET properties of gastrodin is not clear. Therefore, the objective of this study is to predict the adsorption, distribution, metabolism, excretion and toxicity properties of gastrodin by using ProTox 3.0 and pkCSM. SMILES information on gastrodin was obtained from PubChem and input into the webpage tool ProTox 3.0 and pkCSM to assess the ADMET properties of gastrodin and generate the data. Results showed that gastrodin is fairly soluble in water, has poor membrane permeability, absorbed moderately by the intestine and has low absorption in the skin. Distribution is low as there is limitations in tissue penetration and a large portion remains free in the plasma. The BBB permeability and CNS permeability is low. Total clearance is moderate and has little involvement in renal secretion. Toxicology results showed low toxicity potential except nephrotoxicity, BBB-toxicity and clinical toxicity. Nuclear receptor signaling prediction for all receptors are negative. LD50 of gastrodin is predicted to be 3750mg/kg and the toxicity class is 5. Overall predictions by pkCSM and ProTox 3.0 showed that gastrodin is safe and well tolerated however, potential nephrotoxicity, BBB-related effects and PGH1 activity binding should be taken into account. Further investigation needs to be conducted both in vivo and clinically to establish the renal safety.

Keywords: *Gastrodia elata*, *gastrodin*, *ADMET*, *toxicity*

1. INTRODUCTION

The main bioactive compound extracted from *Gastrodia elata* Blume is gastrodin, also known as 4-(hydroxymethyl)phenyl-beta-D-glucopyranoside. It is insoluble in chloroform and ether but is soluble in water, methanol and ethanol [1]. A variety of pharmacological effects was shown by gastrodin towards the cardiovascular system disorders and central nervous system disorders [1-4]. It is also well known for its sedative-hypnotic effects, anticonvulsant, anti-inflammatory, antioxidant and neuroprotective properties [1,5-7]. It was also shown that gastrodin inhibits the inflammation of microglia, ameliorating oxidative stress damage and promotes the secretion of brain-derived neurotrophic factor (BDNF) [1,8-10].

To create effective drugs, understanding the pharmacokinetics, toxicity and efficacy interactions among each other is important. A compound's pharmacokinetics profile is divided into adsorption, distribution, metabolism and excretion (ADME) properties. It is important to ensure that a new drug has the capabilities to achieve adequate concentrations at the target site to induce safe physiological response in clinical introduction in addition to the important consideration of its optimal binding to the therapeutic target. The aid of ADMET properties has led to the importance of attentiveness in early stages of drug development. As a result, compounds which failed in clinical trials due to its poor ADMET properties will be discarded^[11–16].

2. OBJECTIVES

To predict the adsorption, distribution, metabolism, excretion (ADME) and toxicity properties of gastrodin using ProTox 3.0 and pkCSM webpage tools.

3. METHODOLOGY

The SMILES information of gastrodin was obtained from PubChem, a chemistry open-source database. An online webpage tool known as ProTox 3.0 and pkCSM were used to assess the ADMET properties of gastrodin. The SMILES obtained from was input into the webtool and the data is generated.

4. RESULTS

Based on the prediction by pkCSM, moderate pharmacokinetic properties were shown by gastrodin. Results shown that the water solubility is decent but the membrane permeability is poor, indicated by the Caco-2 value. There is potential moderate activity in the human intestines. The skin permeability is low. Gastrodin showed small volume of distribution with high fraction unbound. The BBB and CNS permeability is poor. Metabolically, gastrodin is shown to be neither a substrate nor an inhibitor of major CYP450 enzymes. It shows moderate total clearance and is not a substrate for the renal OCT2 transporter. The predicted pharmacokinetic and toxicity properties of gastrodin are summarized in Table 1.

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Table 1.: Predicted pharmacokinetic properties gastrodin generated from pkCSM and toxicity predicted from ProTox 3.0.

Pharmacokinetic Properties		Gastrodin
Absorption	Water solubility	-1.623 log mol/L
	Caco2 permeability	0.089 log Papp in 10 ⁻⁶ cm/s
	Intestinal absorption (human)	36.278 % Absorbed
	Skin permeability	-2.819 log Kp
Distribution	VDss (human)	-0.058 log L/kg
	Fraction unbound (human)	0.713 Fu
	BBB permeability	-0.93 log BB
	CNS permeability	-3.571 log PS
Metabolism	CYP2D6 substrate	No
	CYP3A4 substrate	No
	CYP1A2 inhibitor	No
	CYP2C19 inhibitor	No
	CYP2C9 inhibitor	No
	CYP2D6 inhibitor	No
	CYP3A4 inhibitor	No
Excretion	Total clearance	0.172 log ml/min/kg
	Renal OCT2 substrate	No
Classification	Target	Prediction
Organ toxicity	Hepatotoxicity	Inactive
	Neurotoxicity	Inactive
	Nephrotoxicity	Active
	Respiratory toxicity	Inactive
	Cardiotoxicity	Inactive
Toxicity end points	Carcinogenicity	Inactive
	Immunotoxicity	Inactive
	Mutagenicity	Inactive
	Cytotoxicity	Inactive
	BBB-barrier	Active
	Ecotoxicity	Inactive
	Clinical toxicity	Active
	Nutritional toxicity	Inactive
	Tox21-Nuclear receptor signalling pathways	Aryl hydrocarbon Receptor (AhR)
Androgen receptor (AR)		Inactive
Androgen Receptor Ligand Binding Domain (AR-LBD)		Inactive
Aromatase		Inactive
Estrogen Receptor Alpha (ER)		Inactive
Estrogen Receptor Ligand Binding Domain (ER-LBD)		Inactive
Peroxisome Proliferator Activated Receptor Gamma (PPAR-Gamma)		Inactive

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Tox21-Stress response pathways	Nuclear factor (erythroid-derived 2)-like 2/antioxidant responsive element (nrf/ARE)	Inactive
	Heat shock factor response element (HSE)	Inactive
	Mitochondrial Membrane Potential (MMP)	Inactive
	Phosphoprotein (Tumor Suppressor) p53	Inactive
	ATPase family AAA domain-containing protein 5 (ATAD5)	Inactive
Molecular Initiating Events	Thyroid hormone receptor alpha (THRα)	Inactive
	Thyroid hormone receptor beta (THB β)	Inactive
	Transthyretin (TTB)	Active
	Byanodine receptor (BYR)	Inactive
	GABA receptor (GABAR)	Inactive
	Glutamate N-methyl-D-aspartate receptor (NMDAB)	Inactive
	Alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionate receptor (AMPA)	Inactive
	Kainate receptor (KAR)	Inactive
	Acetylcholinesterase (AChE)	Inactive
	Constitutive androstane receptor (CAR)	Inactive
	Pregnane X receptor (PXR)	Inactive
	NADH-quinone oxidoreductase (NADHOX)	Inactive
	Voltage gated sodium channel (vgsc)	Inactive
	Na ⁺ /I-symporter (NIS)	Inactive
	Metabolism	Cytochrome CYP1A2
Cytochrome CYP2C19		Inactive
Cytochrome CYP2C9		Inactive
Cytochrome CYP2D6		Inactive
Cytochrome CYP3A4		Inactive
Cytochrome CYP2E1		Inactive

The toxicity properties of gastrodin predicted by ProTox 3.0 showed low systemic and organ-specific toxicity. Gastrodin was predicted to be inactive for hepatotoxicity, neurotoxicity, respiratory toxicity and cardiotoxicity however, nephrotoxicity was predicted to be active. The toxicity endpoints of gastrodin showed inactivity for carcinogenicity, mutagenicity, cytotoxicity, and immunotoxicity however the BBB-barrier toxicity and clinical toxicity is predicted to be active. The nuclear receptor signaling showed that gastrodin is inactive for all tested receptors and analysis of molecular initiating events showed inactivity for most key molecular targets. There binding towards transthyretin however, is active. Gastrodin also showed inactivity towards all major cytochrome P450 isoenzymes. Additionally, gastrodin is predicted to have an affinity for prostaglandin G/H synthase 1 (PGH1).

5. DISCUSSION

The water solubility of a compound demonstrates the solubility of a molecule in water at 25°C. The Caco-2 cells is used as a prediction model for the absorption of orally administered drugs. As for the absorption in the small intestine, molecules with absorbance of less than 30% is considered to be poorly absorbed. The solubility, membrane permeability and intestinal adsorption shows the possibility of gastrodin's relationship of low solubility properties and membrane permeability may affect the absorption in the small intestines, causing a low oral bioavailability. In the event of a transdermal delivery, gastrodin will be poorly absorbed by the skin. Drugs in the plasma membrane exists in equilibrium between an unbound or bounded state to serum proteins which in turn affects the efficacy of a drug depending on the degree it is able to bind to proteins within the blood. The low volume of distribution of gastrodin indicates restricted tissue penetration and the high fraction unbound indicates that a large portion remains free in the plasma. The poor BBB and CNS permeability of gastrodin, suggests minimal central nervous system availability. The poor distribution of gastrodin could be associated with the high number of fractions unbound to serum proteins, indicating the low distribution in the central nervous system. Cytochrome P450 is an important enzyme found in the liver and is responsible for detoxification by oxidizing xenobiotics and activating or deactivating certain drugs. This enzyme however, can be inhibited and in turn, will affect drug metabolism. The predicted results showed that gastrodin has low probability of cytochrome-mediated drug-drug interactions. Gastrodin also showed limited involvement in renal secretion.

ProTox 3.0 prediction of the toxicity properties of gastrodin that there is a low possibility of adverse effects on the vital organs except for the kidneys as the prediction of nephrotoxicity is active. The inactivity of gastrodin at the toxicity endpoints proves that the risk of genotoxicity and immunotoxicity is low.. All tested receptors in nuclear receptor signaling showed no binding affinity towards gastrodin, indicating that gastrodin does not disrupt the endocrine system. In addition, gastrodin is also predicted to be inactive towards the receptors of Tox21-stress response pathways, indicating that it does not interfere with cellular stress responses. Gastrodin also showed inactivity towards most key molecular targets of molecular initiating events except transthyretin indicating that it may influence the thyroid hormone transport or other related signaling mechanisms. The inactivity towards important molecular targets showed low probability that gastrodin initiate a reaction that may lead to an adverse outcome. Major isoenzymes of cytochrome P450 shows no interaction with gastrodin, indicating the likelihood of an adverse effect in metabolism is unaffected and there is no risk of hepatotoxicity. The prediction also showed that gastrodin has an affinity towards prostaglandin G/H synthase 1 (PGH1) indicating a possible role in the inflammatory response.

6. CONCLUSION

Overall prediction by pkCSM and ProTox 3.0 showed that gastrodin is safe and well-tolerated as it has low possibility to cause hepatic, genetic, cardiac, dermal or other systemic toxicity. However, nephrotoxicity, BBB-related effects and binding of PGH1 activity was also predicted. Therefore, further investigation is needed both *in vivo* and clinical studies to establish the renal safety.

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MEASURING PROFESSIONALISM THROUGH SITUATIONAL JUDGEMENT TEST: DEVELOPMENT AND VALIDATION FOR SURGICAL RESIDENTS IN INDONESIA

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Abstract

Introduction: Professionalism is a fundamental competency in surgical training, encompassing ethical behavior, accountability, empathy, teamwork, and commitment to excellence. However, its assessment often faces challenges of subjectivity and limited contextual relevance. The Situational Judgment Test (SJT) provides a promising method to assess professionalism through realistic clinical scenarios that reflect professional decision-making.

Aims & Objective: This study aimed to develop and validate an Indonesia-specific SJT as a formative assessment tool for evaluating professionalism among surgical residents.

Methods: The instrument was designed to measure six non-technical professionalism domains derived from the Indonesian Surgical Competency Standards, the Indonesian Medical Code of Ethics, and national regulations on medical disciplinary conduct. The development process followed six structured stages: blueprint construction, scenario writing, expert review, response option formulation, scoring system development, and validation testing. Each item comprised five response options that participants ranked from most to least appropriate. Content validity was evaluated by ten subject matter experts (surgeons and physicians with additional expertise in medical law or ethics) using the Content Validity Index (CVI). Construct validity was analyzed using Kendall's W concordance among 140 surgical residents from various training centers (semesters 3–12). Data were collected asynchronously via email or WhatsApp after obtaining informed consent.

Results & Discussion: All scenarios achieved acceptable content validity. Kendall's W coefficient of 0.28 indicated low-to-moderate agreement among respondents, suggesting diversity in interpretation and contextual reasoning related to professionalism dilemmas.

Conclusion: The developed SJT demonstrated strong content validity and reasonable construct validity as a formative assessment of professionalism among surgical residents. Its foundation in Indonesian ethical and regulatory standards highlights its contextual and cultural relevance. Further refinement and larger-scale validation are recommended to improve consistency and strengthen its integration into surgical education.

Keywords: *professionalism, surgical residents, situational judgment test, validation, formative assessment*

1. INTRODUCTION

Professionalism is a fundamental competency for physicians and a cornerstone of surgical training worldwide. It encompasses values such as integrity, accountability, empathy, teamwork, and ethical conduct in patient care.(1,2) Within surgical education, professionalism is closely linked to patient safety, clinical judgment, and interprofessional collaboration, yet it remains one of the most challenging competencies to teach and assess effectively.(3,4) Traditional assessment methods such as faculty ratings, narrative evaluations, and reflective portfolio, often rely on subjective impressions and are susceptible to bias.(5,6,7) These challenges have led to calls for more objective, standardized, and context-sensitive assessment approaches.

The Situational Judgment Test (SJT) offers a promising alternative. (8,9) SJTs present realistic scenarios that require examinees to rank or choose among several possible responses, thereby evaluating how individuals prioritize professional reasoning and ethical decision-making. Numerous studies in medical education have demonstrated the validity and practicality of SJTs in assessing non-technical attributes such as professionalism, communication, and teamwork. (10-14)However, most SJTs are developed in Western educational systems, which may not align with the cultural or professional context of other countries.

2. OBJECTIVES

In the Indonesian context, the framework of surgical professionalism is explicitly regulated through several normative documents: The Indonesian General Surgery Curriculum,(15) The Indonesian Medical Code of Ethics,(16) Peraturan Konsil Kedokteran Indonesia concerning disciplinary violations.(17) These sources identified ethical obligations, cultural expectations, and regulatory standards unique to the Indonesian medical system. Integrating these locally derived components into SJT design allows for an assessment model that remains aligned with global professionalism standards while grounded in national values and regulations.

This study aimed to develop and validate an SJT as a formative assessment tool for professionalism among surgical residents in Indonesia. The study focused on evaluating content validity through expert review and construct validity using concordance analysis, to establish a foundation for standardized professionalism assessment in Indonesian surgical education.

3. METHODOLOGY

Study design

A cross-sectional validation study was conducted in two phases: (1) content validation by a panel of subject matter experts and (2) construct validation based on resident responses analyzed statistically.

Situational Judgement Test (SJT) Development

The development process of the Situational Judgment Test (SJT) began with the creation of a test blueprint,(18) which outlined the purpose, format, target population, and professionalism attributes to be assessed (Table 1). The assessment format was designed as a written, scenario-based test targeted at residents from their second year through the final year of training. Six professionalism domains were identified, drawing from the Indonesian General Surgery Curriculum,(15) The Indonesian Medical Code of Ethics,(16) Peraturan Konsil Kedokteran Indonesia concerning disciplinary violations,(17) and findings from a national study on surgical professionalism in Indonesia.(2) Each scenario presented a professional dilemma, and participants were required to rank five possible responses from 1 “most appropriate” to 5 “least appropriate”, assigning each rank only once.

Table 1. Test Blueprint

Purpose	Formative assessment of professionalism competency
Assessment Format	Written examination and scenario-based test
Target Respondents	Surgical residency trainees (professional medical education participants) who are at least in semester 3 or 4 up to the final semester
Professionalism Aspects	Consist of six domains of professionalism: <ol style="list-style-type: none"> 1. Performing duties as a surgeon 2. Integrity 3. Decision-making 4. Effective communication 5. Respect for colleagues 6. Teamwork
Number of Scenarios	20–30 scenarios in total; each domain consists of 2–6 scenarios
Relationship Among Domains	None of the domains is a mandatory requirement for passing or prioritized; all domains are equally weighted
Duration	Between 45 and 60 minutes
Answer Format	Ranking-based responses. Participants assign a rank from 1 (most appropriate) to 5 (least appropriate). Each response option can only receive one rank.

To ensure item quality and alignment, seven general surgeons with at least three years of clinical experience were recruited as item writers. They participated in a one-day training workshop (July 2024) on SJT design, including principles of scenario development, response format, and linkage to professionalism attributes. Over the subsequent two months, the team produced a pool of 62 scenarios, which were then reviewed for clarity, context, and relevance. Scenarios with fewer than five response options or unclear dilemmas were revised or discarded, resulting in 49 refined scenarios for expert review.

Content Validation and Answer Key Development

A panel of 10 subject matter experts (SMEs), comprising seven surgeons and three experts in medical ethics or law, each with at least five years of experience, conducted content validation of the scenarios. Each expert rated the relevance, clarity, and representativeness of each item using a 4-point Likert scale. The Content Validity Index (CVI) was calculated at both the item (I-CVI) and scale levels (S-CVI),⁽¹⁹⁾ with a minimum acceptable threshold of 0.78. SMEs evaluated each scenario for relevance to the intended professionalism domain and collaboratively established consensus-based answer keys. Scenarios with inconsistent ratings, overlapping content, or lack of consensus were excluded. Based on this process, 23 scenarios were eliminated, leaving 26 validated scenarios spanning six professionalism domains (Table 2).

Table 2. Scenario distribution

No	Professionalism variable	Number of Skenario	Total scenario (N = 26)
1	Performing duties as surgeon	1 – 4	4
2	Integrity	5 – 7	3
3	Decision making	8 – 13	6
4	Effective communication	14 – 18	5
5	Respect for colleagues	19 – 24	6
6	Teamwork	25 – 26	2

SJT Scoring System

Each scenario contained five possible actions ranked by participants from most to least appropriate. Scoring was based on the degree of deviation from the expert consensus key: an exact match was awarded four points, decreasing stepwise by one point for each deviation in rank order (Table 3).(20)

Scores were summed across items, possible scores ranged from 8 to 20 per scenario, with total possible scores ranging from 208 to 520. This approach follows previous international SJT validation studies assessing gradations in professional judgment.(21)

Table 3. SJT Scoring

Ranking SMEs	Respondent Ranking				
	1	2	3	4	5
1	4	3	2	1	0
2	3	4	3	2	1
3	2	3	4	3	2
4	1	2	3	4	3
5	0	1	2	3	4

Participants and setting

This research involved 140 surgical residents from 8 universities in Indonesia (table 4), representing semesters 3–12. Participants were recruited through program coordinators and direct contact. Inclusion criteria were active surgical residents who had completed at least one year of training.

Table 4. Distribution of respondent

Characteristic	Total (n=140)
University	
Universitas Indonesia	32 (22.9%)
Universitas Diponegoro	29 (20.7%)
Universitas Udayana	20 (14.3%)
Universitas Hasanuddin	20 (14.3%)
Universitas Sam Ratulangi	16 (11.4%)
Universitas Padjadjaran	9 (6.4%)
Universitas Sumatera Utara	9 (6.4%)
Universitas Brawijaya	5 (3.6%)
Year of study	
2	37 (26.4%)
3	29 (20.7%)
4	36 (25.7%)
5	31 (22.2%)
6	7 (5%)
Sex	
Man	116 (82.9%)
Woman	24 (17.1%)

Data collection and analysis

Data were collected asynchronously between February to May 2025. Surgical residents were contacted individually via email or WhatsApp to explain the study purpose and procedures. After providing informed consent electronically, participants received the SJT scenarios in digital format (PDF or document file) through the same channel. They were instructed to complete the test independently and return their responses within a specified time frame.

This asynchronous approach enabled participation from geographically dispersed centers and minimized disruption to residents' clinical duties. However, it also limited control over the testing environment and independent completion.

All responses were anonymized and coded before analysis. Descriptive statistics were used to summarize demographic characteristics. Content validity was assessed using CVI, while construct validity was analyzed using Kendall's W to measure concordance in response rankings. Interpretation thresholds for W were: <0.20 (weak), 0.20–0.40 (low to moderate), 0.41–0.60 (moderate), and >0.60 (strong). Analyses were conducted using SPSS version 26.

4. MAIN RESULTS

Content validity

The expert panel evaluated all items for clarity and relevance. All 26 SJT scenarios were reviewed by a panel of subject matter experts (SMEs) to assess content validity. The average Content Validity Index (CVI) across all items was 0.97, ranging from 0.90 to 1.00. Twenty-four scenarios (92.3%) achieved a perfect CVI score of 1.00, while two scored 0.90 (Table 5). Based on SME feedback, minor wording adjustments were made to enhance clarity, but no scenarios were excluded. These results indicate that the SJT items demonstrated strong content validity and were suitable for pilot testing.

Table 5. Content Validity of SJT Scenarios Reviewed by SMEs.

Indicator	Result
Number of items reviewed	26
Mean CVI per item	0.97
CVI range	0.90 – 1.00
Items with CVI = 1.00	24 (92.3%)
Items with CVI < 1.00	2 (7.7%)
Items discarded	0

Construct validity

Responses from 140 residents were analyzed. Kendall's W coefficient was 0.28, indicating low-to-moderate agreement among participants. The variability in rankings suggests differences in reasoning and interpretation of professionalism scenarios among residents. Mean of Total score SJT is 373.8 ± 32 . The highest score for theme respect for colleagues 83.2 ± 7.5 with 6 scenario, and the lowest score for theme teamwork 29.7 ± 4.8 , with 2 scenario.

Table 6. SJT Score (n = 140)

Variable	Mean \pm sd	min	max
Total score	373.8 ± 32	306	430
Performing duties as surgeon	57.9 ± 8	39	76
Integrity	48.7 ± 7.3	30	58
Decision making	82.5 ± 9.1	64	104
Effective communication	71.8 ± 7.9	56	92
Respect colleagues	83.2 ± 7.5	66	104
Teamwork	29.7 ± 4.8	20	38

5. DISCUSSION

This study developed and validated a Situational Judgment Test (SJT) designed to assess professionalism among surgical residents in Indonesia. The results demonstrate satisfactory content validity and acceptable construct validity, confirming that the instrument effectively captures contextually relevant professional reasoning.

A distinguishing contribution of this study lies in its conceptual foundation. The six aspects of professionalism were not adapted from Western frameworks such as ACGME or GMC but synthesized from Indonesia's regulatory and ethical documents, including The Indonesian General Surgery Curriculum, The Indonesian Medical Code of Ethics, Peraturan Konsil Kedokteran Indonesia concerning disciplinary violations, and findings from a national study on surgical professionalism in Indonesia. This provides a locally grounded yet normatively robust basis for defining professionalism, aligning ethical practice with national medical governance. Consequently, the study contributes a culturally and legally contextualized model of professionalism assessment that may serve as a reference for other low- and middle-income countries.

The moderate concordance observed (Kendall's $W = 0.28$) aligns with previous research on SJT validation in medical education, where W values between 0.20 and 0.40 are common, particularly in formative assessments.(22) This result reflects the complex and context-dependent nature of professionalism, which encompasses not only knowledge but also attitudes, values, and situational judgment. The Kendall's W coefficient of 0.28 found in this study indicates low-to-moderate agreement among respondents. This result is comparable to findings in previous validation studies of Situational Judgment Tests (SJTs), particularly those conducted for formative rather than summative purposes. Lievens and Patterson reported W coefficients ranging between 0.20 and 0.40, suggesting that modest inter-rater agreement may reflect the complexity and subjective interpretation of professional scenarios rather than weak construct validity. (23) Similarly, Patterson et al. (24) and De Leng WE (25) emphasized that SJTs are designed to capture individual variability in professional reasoning, empathy, and ethical judgment. Therefore, variability in responses, as observed in this study, may highlight educationally meaningful differences among surgical residents at various stages of training.

The asynchronous method of data collection also offered valuable insight. Using email and WhatsApp allowed participation from multiple centers. However, the lack of controlled testing conditions could introduce variability in focus, timing, or consultation, which might partly explain the moderate agreement among respondents.

PN6

From an educational standpoint, implementing SJT as a formative assessment tool has significant benefits. It encourages reflection on ethical dilemmas, facilitates small-group discussions on professional reasoning, and provides structured feedback to learners. In surgical training, where professionalism and decision-making under pressure are critical, such assessments can strengthen both self-awareness and team communication.

Study limitations

Several limitations should be acknowledged. First, the development of SJT scenarios requires creativity from item writers, and qualification of SME can influence the answer key. Second, the asynchronous online data collection limited control over the testing environment and participant independence, potentially affecting response consistency and authenticity. Third, while multiple training centers participated, the sample may not represent all surgical residency programs in Indonesia. Finally, the use of ranking-type SJT items might have constrained variability in responses compared to open-ended formats. Fourth, the study did not examine test–retest reliability or internal consistency, which limits conclusions about the stability of the SJT over time. Fifth, the absence of criterion-related validity testing, such as correlations with reflective portfolios or multisource feedback, limits triangulation of the construct validity. Lastly, the focus on formative assessment means the results are primarily diagnostic and developmental, not summative indicators of professional competence.

Future directions

Future studies should conduct broader psychometric testing, including internal consistency, test–retest reliability, and criterion-related validity with external professionalism assessments such as multisource feedback. Expanding the scenario pool and integrating SJT discussions into resident seminars may enhance both educational impact and reliability. Additionally, digital-based or adaptive SJT platforms could be developed for more efficient, scalable implementation across Indonesian residency programs.

6. CONCLUSION

The SJT developed in this study demonstrated good content validity and acceptable construct validity for assessing professionalism among surgical residents in Indonesia. As the first validated instrument of its kind in this context, it offers a structured, culturally relevant, and practical approach to formative assessment of non-technical competencies in surgical education. Further refinement and reliability testing are recommended to strengthen its future implementation.

7. ACKNOWLEDGEMENT

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Conflict of Interest Statement

The authors declare no conflict of interest.

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Ethical considerations

We obtained ethical approval from The Ethics Committee of the Faculty of Medicine, University of Indonesia, Cipto Mangunkusumo Hospital number KET-741/UN2.F1/ETIK/PPM.00.02/2024.

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CRISPR-Cas9 Mediated Gene Modification in Pig-to-Human Heart Xenotransplantation for Improved Compatibility and Safety

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Abstract

Heart failure is a leading cause of death globally, with the availability of donor hearts critically limited for patients who are in need of emergency heart transplants. Genetically modified pig hearts are used as a scientific alternative source, known as cardiac xenotransplantation. However, several results have unfortunately shown that immune rejection and viral transmission remain major barriers. This study investigates how CRISPR-Cas9 gene editing can potentially address these scientific challenges by removing porcine genes responsible for immune incompatibility (GGTA1, CMAH, B4GALNT2), inserting human regulatory genes (CD46, CD55, THBD) and eliminating porcine endogenous retroviruses (PERVs). Data from recent primate and human xenotransplantation scientific studies indicate that multiple gene edits can significantly improve graft survival and function. This signifies that CRISPR-Cas9 is the answer to enhancing the safety, compatibility and long term viability of pig hearts for potential clinical transplantation.

Keywords: *Xenotransplantation, CRISPR-Cas9, PERVs, graft*

1. INTRODUCTION

Heart transplantation remains the only effective curative treatment for critical heart failure. Due to a global shortage of human heart donors, xenotransplantation using pigs have become the center of scientific interest, Pigs are highly compatible due to similar organ size and short breeding cycles. However, major barriers have limited xenotransplantation success such as hyperacute rejection, which is triggered when human antibodies recognize pig cell surface sugars produced by GGTA1, CMAH and B4GALNT2 genes. Severe acute and chronic rejection is caused by inflammation and coagulation incompatibility. A prominent viral risk is that Porcine cytomegalovirus (PCMV) and porcine endogenous retroviruses (PERVs) in pigs can reactivate after post-transplant surgery, which infects human cells and causes graft dysfunction.

2. OBJECTIVES

- Using CRISPR-Cas9 gene editing to identify and target key porcine genes (GGTA1, CMAH, B4GALNT2) responsible for antigenic incompatibility.
- Introduce human complement and coagulation regulating genes like CD46, CD55 and THBD to reduce immune rejection and thrombosis.
- Remove or inactivate PERVs to prevent cross species viral transmission.
- Review and interpret patient survival, cardiac function and viral load data from current xenotransplantation trials from non-human primates and humans.

3. METHODOLOGY

This literature review study is based on an experimental laboratory based design utilizing Cas9 genome editing to modify porcine cells for cardiac xenotransplantation. The research aimed to enhance immune compatibility and reduce viral transmission risk through targeted gene knockout, human gene insertion and viral inactivation.

Participants and Setting:

- Donor Species: Genetically modified *Sus scrofa domestica* (domestic pigs)
- Recipient Models: Non human primates *Papio* species (baboons) for preclinical xenotransplantation testing
- Setting: conducted in a biosafety level-3 gene editing xenotransplantation research facility equipped for molecular, cellular and cardiac function analyses

Experimental Procedure:

1. Recognition and Target Design

Porcine genes responsible for immune rejection (GGTA1, CMAH, B4GALNT2) and viral transmission (PERVs, SLA) were identified as editing targets. Synthetic guide RNAs (gRNAs) were designed to recognize specific DNA sequences within these genes and complexed with the Cas9 enzyme.

2. Cleavage (DNA cutting)

The Cas9-gRNA complex is introduced into porcine fibroblast cells, where Cas9 recognizes PAM (Protospacer Adjacent Motif) sequences and double strand DNA breaks at target location.

3. Repair and Genome Editing

The cell's natural DNA repair mechanisms were used to perform genetic modification. Non-homologous end joining (NHEJ) created small insertions to disable target genes and knockout the genes. Homology-directed repair (HDR) inserted human genes (CD46, CD55, THBD, CD47, HO1, EPCR) to enhance immune tolerance and blood compatibility. PERVs are inactivated to prevent viral transmission and one growth gene was silenced to regulate heart size.

4. Validation and Functional Testing

Genetic modifications are confirmed through PCR, DNA sequencing and RT-qPCR for viral detection. Cardiac xenografts were evaluated in primates using Kaplan-Meier survival analysis and transthoracic echocardiography (TTE) to measure left ventricular mass, ejection fraction and graft performance.

Instruments and Data Analysis:

Gene Editing: CRISPR-Cas9/Cpf1 system, guide RNA synthesis

Molecular Verification: PCR, DNA sequencing, RT-qPCR

Functional Analysis: Echocardiography (LV mass, ejection fraction)

Statistical Analysis: Kaplan-Meier survival curves, one-way ANOVA (p 0.05) using GraphPad Prism.

Data is expressed as a mean standard deviation and compared across 7, 9 and 10-gene edited donor groups to assess survival and cardiac function outcomes.

Ethical approval: All experiments complied with international animal welfare and biosafety regulations for xenotransplantation research. Ethical approval was granted by the Institutional Animal Care and Use Committee (IACUC).

4. MAIN RESULTS

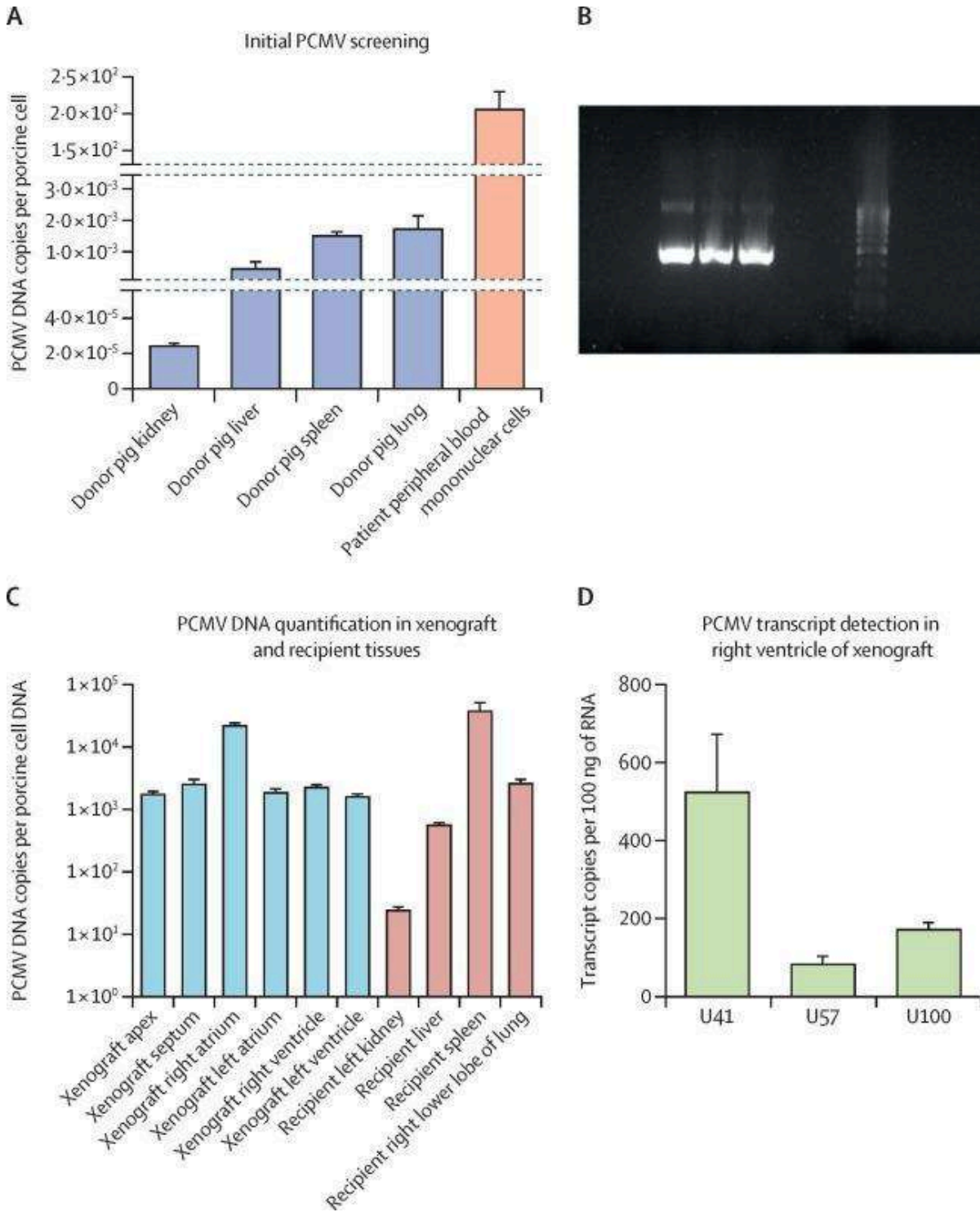


Figure 1. Post-operative PCMV Viral load in xenograft and recipient tissues (human recipients)

CP1

Cardiac xenograft survival.

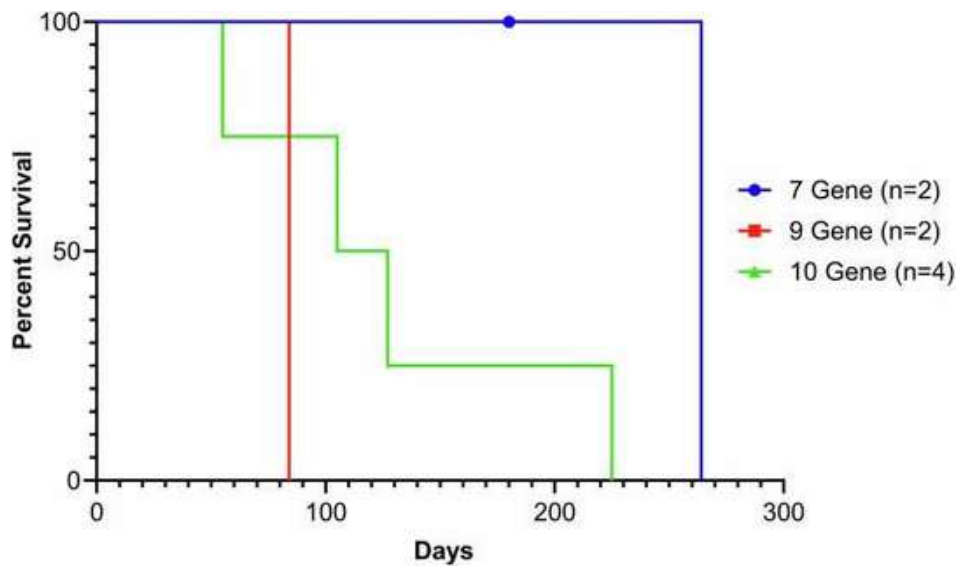


Figure 2. Kaplan–Meier survival curve of cardiac xenograft recipients receiving 7, 9, and 10 gene edited porcine hearts.

(n) represents the number of baboons. E.g 7 gene (n=2) means two baboons received 7-gene-edited pig hearts, 10-gene-edited pig hearts (n=4) had a declining survival rate that dropped to 25% after 225 days. The 9-gene-edited pig heart (n=2) had a survival rate of 100% for only 90 days, which is when the survival rate drops. 7-gene-edited pig heart (n=2) had a 100% survival rate for over 275 days.

5. DISCUSSION

PCMV has no antiviral therapy and this zoonotic transmission still poses a risk to other organs and xenograft measurements of the heart. The presence of the PCMV has caused system viral dissemination, where the virus spreads to other organ tissue in the recipient's body. There are more than 1×10^3 PCMV DNA copies per Porcine cell DNA in xenograft tissue across all structures of the heart. Leading to endothelial damage, inflammatory responses and the key reason for graft failure. This urges us to conduct improved porcine heart donor screening and pathogen-free breeding among the pigs.

7-GE grafts may have achieved optimal balance between immune tolerance and physiological stability. However, the small sample size makes it hard to make a more thorough assessment. Highlighting one of the flaws with this data. Current genetic (CRISPR) and immunological strategies (E.g Calcineurin inhibitors) significantly extend xenograft survival, but still don't extend survival rates to more than a year. More non-human primates testing has to be done, which will allow specialized surgery teams to develop and train their skills for xenotransplantation of porcine heart in humans. It reinforces the importance of CRISPR as non-edited gene pig hearts only last a few minutes or hours. But edited gene hearts can last up to more than 8 months. However, there is also an ethical concern to the practice of surgery on non-human primates.

6. CONCLUSION

From the results, it is evident that CRISPR-Cas9 mediated gene modification is a potential solution to enhance the safety and compatibility of pig hearts for xenotransplantation. By removing immunogenic pig genes, adding human protective genes and eliminating viral risks, researchers are closer than ever to achieve clinically viable pig-to-human heart transplantation. Future directions would be continuous refinement in genome editing and post-transplant management in human trial cases. These experiments were performed under ethical guidelines.

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Comparative Analysis of the Ketogenic Diet and Intermittent Fasting for Metabolic Health

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Abstract

Nutritional ketosis has been known benefits in metabolic health, neuroprotection, cancer adjuvant treatment and healthy ageing. There are numerous methods to induce nutritional ketosis with ketogenic diet (KD) and intermittent fasting (IF) being some of them. IF typically means restricting food intake for a specific time. KD in contrast, focuses on dietary restriction through a low-carbohydrate, high-fat approach. To compare the health benefits and safety of IF and KD in adults while focusing on their effects on metabolic health and overall well-being. We conducted a detailed literature search using the PubMed, Cochrane, and ResearchGate databases. Eligible manuscripts were included for this review. Both IF and KD have been shown to improve metabolic parameters by increasing insulin sensitivity, positively influencing lipid metabolism, lowering visceral fat, reducing inflammation, and enhancing neuroprotection. In patients with type 2 diabetes, KD seems to be more effective than IF, likely because it stabilizes blood glucose levels and encourages fat oxidation. A systematic review showed that IF had a more significant effect on regulating circadian rhythms, while KD was linked to better post-meal glucose levels and increased fat metabolism. Common side effects of IF include fatigue, headache, dizziness, constipation, diarrhoea, and hypoglycaemia while KD's include, hyperuricemia, skin lesions, constipation, hypothyroidism, and lethargy. Adherence to KD and IF tends to drop over time and is often due to dietary restrictions, side effects, patient factors and costs. Interestingly, combined KD and IF have shown better outcomes than using either one alone especially in insulin resistance parameters. Both the KD and IF improves metabolic health and various chronic diseases. Combining KD and IF enhances metabolic benefits. To optimise safety, efficacy and sustainability across different groups, more extensive and long-term clinical studies are required.

Keywords: *ketogenic diet, intermittent fasting, metabolic health, adverse effects*

1. INTRODUCTION

Nutritional ketosis has possible benefits in metabolic health, weight loss, neuroprotection, cancer treatment, and anti-aging [1,2]. There are numerous methods to encourage nutritional ketosis with ketogenic diet (KD) and intermittent fasting (IF) being some of them [3]. IF typically means restricting food intake for a specific time [4]. KD, in contrast, focuses on dietary restriction through a low-carbohydrate, high-fat approach [2,5].

2. OBJECTIVES

To compare the health benefits and safety of IF and KD in adults while focusing on their effects on metabolic health and overall well-being.

3. METHODOLOGY

We conducted a detailed literature search using PubMed, Cochrane, and ResearchGate databases. Eligible study designs were included for this review.

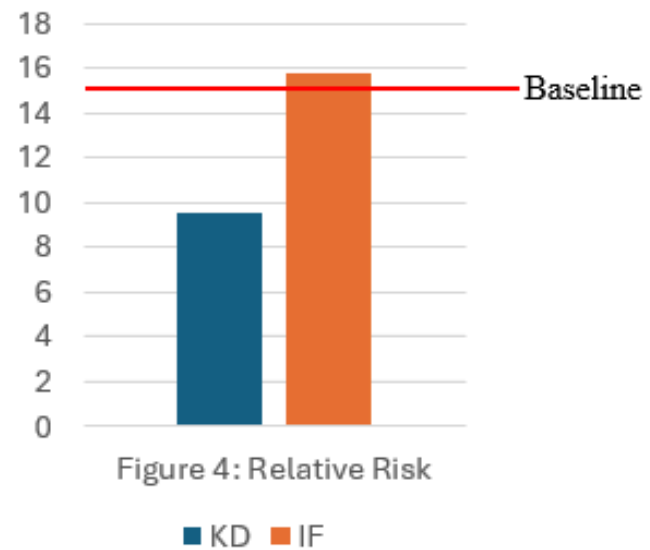
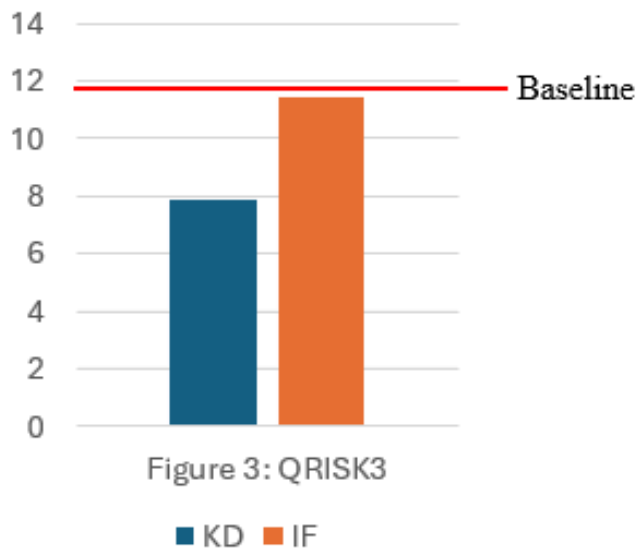
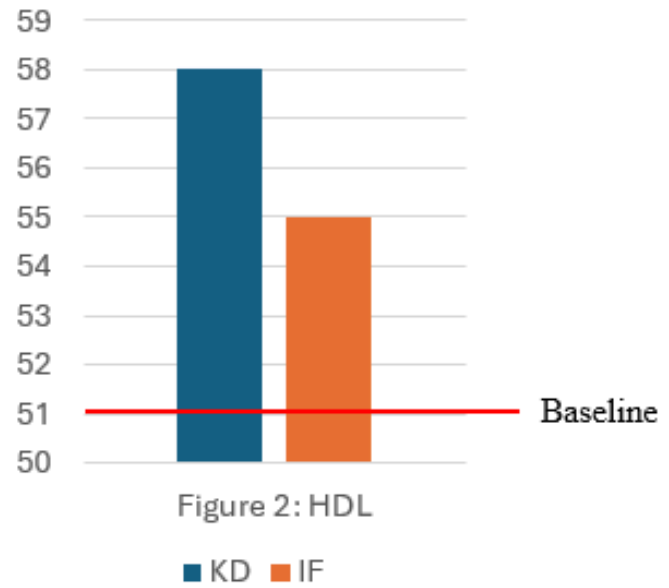
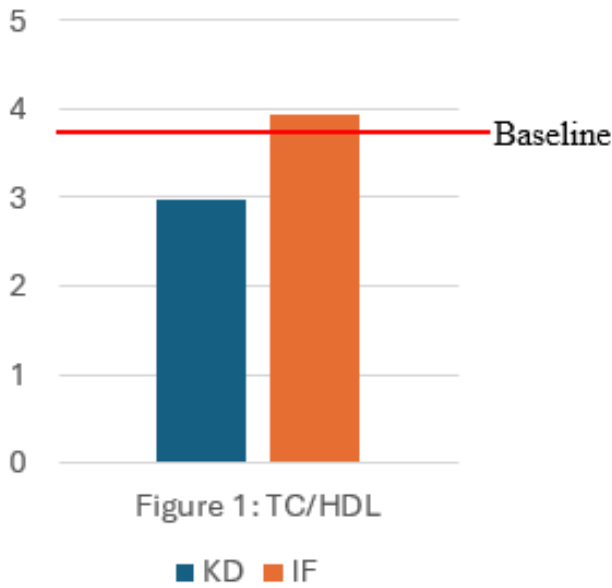
4. MAIN RESULTS

Articles from H. A. Zaki (2022), Z. Zhang (2023), P. Yu (2024), and Denisa Pescari (2025) were pooled for analysis [7,9,16,17]. Data related to metabolic parameters only were abstracted and compared between KD and IF. Table 1 was synthesized and Figures 1, 2, 3 and 4 were plotted.

Table 1: Comparison of metabolic parameters between KD and IF

Metabolic Parameters	KD	IF
HbA1c (%)	-2%, p=0.03	+0.36%, p=0.33
Fasting blood glucose (mg/L)	-0.4	-0.1
Body weight (kg)	-3.5 ± 1.2kg	-2.1 ± 0.9kg
	-1.91kg, p=0.0004	-1.05kg, p=0.1
Body fat percentage (%)	-4.8 ± 1.5%	-3.2 ± 1.1%

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5. DISCUSSION

Both IF and KD have been shown to improve metabolic parameters positively [3, 6, 7, 8, 9, 16, 17]. KD seems to be more effective than IF in glycemic control, optimising body weight and lipid profile likely because it stabilizes blood glucose levels and encourages fat oxidation [7, 9, 16, 17]. Importantly, QRISK and relative risk were significantly lower in the KD group, suggesting better outcomes of CVS risks in the long term [9]. Common side effects of IF include fatigue, headache, dizziness, constipation, diarrhoea, and hypoglycaemia while KD's include hyperuricemia, skin lesions, constipation, hypothyroidism, and lethargy [6, 10, 11, 14]. However, adherence to both KD and IF tends to drop over time, often due to dietary restrictions, side effects, patient factors, and costs. In the long term, IF has better compliance due to its more acceptable side effects and achievable approach and maintenance [13, 14, 16]. Interestingly, combined KD and IF have shown better outcomes than using either one alone [12, 15].

6. CONCLUSION

Both the KD and IF improves metabolic health and various chronic diseases. Combining KD and IF enhances metabolic benefits. To optimise safety, efficacy, and sustainability across different groups, more extensive and long-term clinical studies are required.

7. ACKNOWLEDGEMENT

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Bacteriophage Therapy: A Strategic Re-evaluation Amidst the Antimicrobial Resistance Crisis

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Abstract

The escalating global crisis of antimicrobial resistance (AMR) threatens to render bacterial infections untreatable. In this context, bacteriophages - viruses that specifically infect and lyse bacteria - are experiencing a significant resurgence as a compelling alternative therapeutic strategy. This review critically assesses the current landscape of bacteriophage therapy, highlighting its unique attributes and emergent roles in overcoming the multifaceted challenges posed by AMR. Bacteriophage therapy offers several advantages over conventional antibiotics. Phages exhibit unparalleled host specificity, minimizing microbiome dysbiosis and off-target side effects. Their lytic mechanisms are distinct, proving effective against multi-drug resistant (MDR) pathogens, including those resistant to last-line agents. Natural abundance and facile isolation contribute to their cost-effectiveness. Furthermore, strategies like phage cocktails and phage-antibiotic synergy (PAS) not only enhance antibacterial activity but also significantly mitigate resistance development. Phages are also explored for immunocompromised patients and as antigen delivery platforms. Despite these benefits, challenges persist, including narrow host range requiring precise diagnostics, potential immunogenicity, and the need for robust regulatory frameworks to facilitate clinical translation. Bacteriophage therapy is rapidly evolving into a frontline contender against AMR. While specific clinical parameters require further elucidation, the strategic application of phages, particularly in synergistic combinations, offers a powerful and adaptable solution to recalcitrant bacterial infections. Continued investment in translational research and international regulatory harmonization will be pivotal in fully realizing phage therapy's transformative potential in modern medicine.

Keywords: *Antimicrobial resistance, Bacteriophage, Multi-drug resistant bacteria, Phage therapy, Phage-antibiotic synergy*

1. INTRODUCTION

Bacteriophage, also called ‘phages’ are pathogens of bacteria that infect and destroy bacterial cells. Antibiotic resistance poses a growing global threat. Bacteriophage is effective to combat the rise of multidrug-resistant (MDR) bacteria that are resistant to multiple antibiotic classes. Furthermore, bacteriophages are specific to their hosts-bacteria, essentially harmless to humans. This will minimize the chances of secondary infection or side effects unlike antibiotics target pathogen and normal flora of humans.

The concept of phage therapy originated from the discovery of bacteriophages by Frederick Twort in 1915 and Félix d’Hérelle in 1917, who demonstrated that these viruses could lyse bacteria and treat infections such as dysentery and cholera [5]. d’Hérelle successfully applied phage therapy in children with bacillary dysentery in 1919 and later for cholera in 1931. During the early 20th century, phage therapy was widely practiced, especially in Eastern Europe and the Soviet Union, but declined following the advent of antibiotics in the 1940s [6]. With the rise of multidrug-resistant bacteria, renewed interest has emerged, supported by evidence of phage efficacy against pathogens such as *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and *Klebsiella pneumoniae*.

Ever since the discovery of phages, researchers have utilized their abundance and infection specificity to combat pathogenic bacteria, prevent food contamination, and control the environment. With the rise of multidrug-resistant (MDR) bacteria, phages have reemerged as a promising alternative to antibiotics [1, 2]. One of the advantages of phage therapy is that it is cost-effective, as phages are easy and abundant to isolate and propagate in high numbers. They can be harnessed for various medical applications, including treating immunocompromised patients and serving as platforms for vaccine antigen delivery, with researcher-industry collaboration essential for clinical integration.

The rapid rise of antimicrobial resistance (AMR) has become a major global health threat, rendering many antibiotics ineffective and leading to millions of deaths annually [12]. Phage therapy, which employs bacteriophages to selectively target pathogenic bacteria while preserving the host microbiota, offers a promising and sustainable alternative to conventional antibiotics. Advances in genetic engineering and synthetic biology have enhanced phage efficacy, expanding their potential to treat multidrug-resistant and biofilm-associated infections. Integrating phage therapy with antibiotics provides synergistic benefits, positioning it as an innovative strategy to combat resistant bacterial pathogens and transform the future of infectious disease management.

2. OBJECTIVES

This review critically examines the current landscape of bacteriophage therapy, emphasizing its unique properties, evolving applications, and emerging role in addressing global antimicrobial resistance (AMR). It explores phage biology, mechanisms, host range, and therapeutic potential in treating multidrug-resistant (MDR) infections, including the efficacy of phage-antibiotic combination therapies. Safety, immunological aspects, and potential as an alternative or complement to conventional antibiotics are also evaluated. Additionally, the review identifies current research and clinical challenges and proposes future strategies to integrate phage therapy effectively into modern infectious disease management, highlighting its promise in combating MDR pathogens.

3. METHODOLOGY

To provide a comprehensive literature review on the evolution, safety, and therapeutic potential of bacteriophage therapy against multidrug-resistant (MDR) bacterial infections, a range of information and data were collected using search engines such as “PubMed,” “Scopus” and “Google Scholar.” Journal articles specific to the keywords bacteriophage therapy, phage therapy, antimicrobial resistance (AMR), phage safety, phage-antibiotic combination therapy, genetic engineering of phages, and clinical applications of phages were analysed during the preparation of this review. A wide variety of relevant publications were sought from the early discovery of bacteriophages (1915) to recent advancements in phage research (2025). These articles were categorized and managed using Mendeley reference management software (Amsterdam, The Netherlands, <https://www.mendeley.com/>) to ensure that the review process was systematic, coherent, and comprehensive.

4. MAIN RESULTS

Antibiotic resistance is a growing global health crisis, driven by the overuse and misuse of antibiotics in humans. While naturally occurring in microbial populations, extensive antibiotic exposure accelerates resistance development through mutations, horizontal gene transfer, and selective pressure. Resistant pathogens, including multidrug-resistant Gram-negative bacteria, increase morbidity, mortality, and treatment challenges. If unaddressed, this crisis threatens medical advances such as infection prophylaxis, organ transplantation, and cancer therapy, emphasizing the urgent need for alternative strategies to combat resistant infections. [3, 4]

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Phage resistance is an important issue that must be considered in bacteriophage (BP) therapy. Although BPs evolve quickly and can adapt to overcome bacterial defences, the emergence of BP-resistant bacteria is unavoidable. Resistance may occur through mechanisms such as receptor modification, CRISPR-Cas systems, abortive infection, or superinfection exclusion. The frequency and impact of resistance vary among bacterial species, depending on their environment and genetic flexibility. In some cases, phage resistance may even increase bacterial sensitivity to antibiotics. To reduce this problem, researchers often use BP cocktails or rotate different phages to maintain treatment effectiveness against resistant bacterial strains. [4, 7]

Phage cocktails (polyphage), made of several bacteriophages with different host ranges, overcome the limited effectiveness of single phages and improve treatment against mixed or variable bacterial infections. Designing cocktails carefully to target different bacterial receptors helps reduce resistance, and phages can work together to increase effectiveness. Although lysogenic phages are usually avoided, new “intelligent” cocktails show promise for controlling bacterial virulence and treating hard-to-treat infections. [7]

Phage–antibiotic synergy (PAS) occurs when bacteriophages and antibiotics work together to produce a stronger antibacterial effect than either alone. Certain antibiotics enhance phage replication and bacterial lysis, while phages increase bacterial susceptibility to antibiotics. Studies show that PAS effectively reduces resistance and improves treatment outcomes against multidrug-resistant pathogens such as *S. aureus*, *E. coli*, and *P. aeruginosa*. [12]

Bacteriophages are bacterial viruses that infect hosts by binding to specific surface receptors and injecting their genetic material. They exhibit two replication strategies: lytic phages, which hijack the bacterial biosynthetic machinery to produce progeny and lyse the host via enzymes like endolysins, and temperate phages, which integrate their genome into the host chromosome and replicate passively. Due to the risk of horizontal gene transfer and antibiotic resistance, lytic phages, including Microviridae (“the tail-less phages”) and Caudovirales (“the tailed phages”), are predominantly preferred for therapeutic applications, though temperate phages may be used when lytic options are unavailable. [8]

Bacteriophages undergo lytic cycle which starts with phage adhering to receptors on the bacterial cell surface. The mechanism of phage therapy begins with the attachment of bacteriophages to specific receptors on the bacterial host, followed by the injection of viral DNA into the host cell and subsequent degradation of the host genome. This

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is succeeded by the biosynthesis of viral components, assembly of new phage particles and ultimately, lysis of the bacterial cell release progeny phages capable of infecting other susceptible bacteria [4]. These freshly generated phages can then infect neighbouring bacterial cells, repeating the cycle and effectively lowering bacterial numbers. The mechanism of phage therapy has been sequentially illustrated in Figure 1.

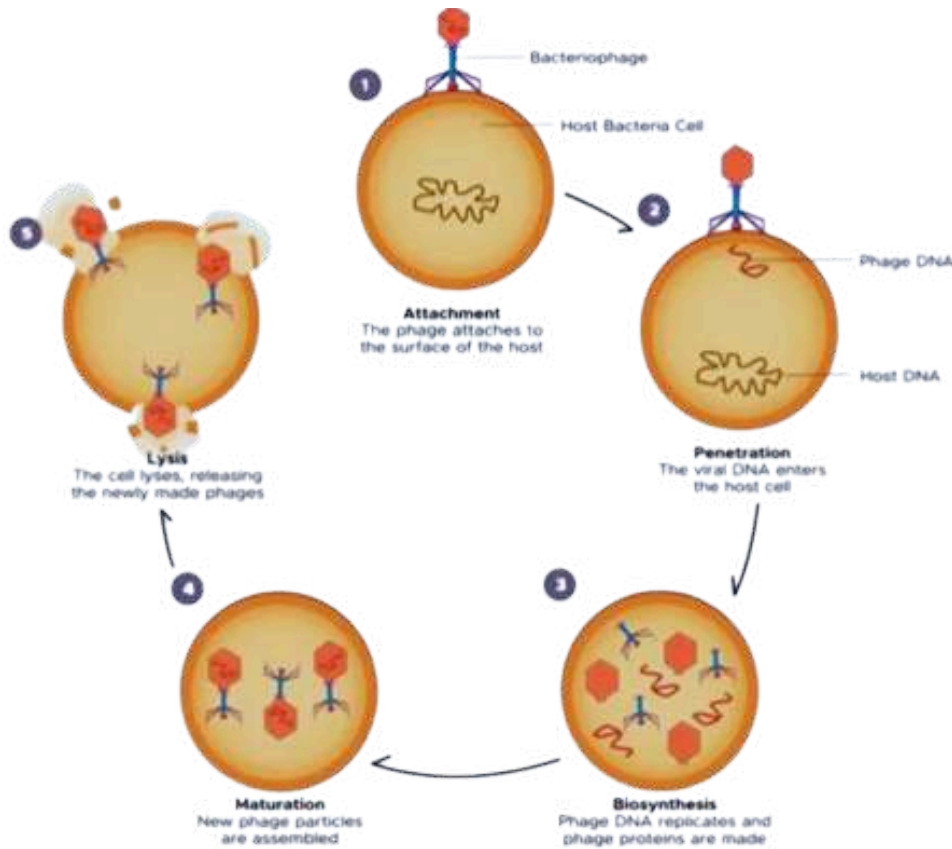


Figure 1. The mechanism of phage therapy

Bacteriophages are naturally antibacterial where they are able to regulate bacteriophage populations by the induction of bacteria lysis [9]. Bacteriophages are very specific to their hosts, so this minimizes the chance of secondary infections, but antibiotics do target both pathogens and normal flora of patients [2,5]. While the treatment period was notably prolonged, phage therapy incurred a lower overall cost compared to conventional antibiotic therapy which eventually lowered the cost of phage therapy [4,9]. Clinical trials show that phage therapy has a low level of side effects due to the fact that phages are naturally occurring viruses found in the environment and in the human body, hence the immune system is already accustomed to encounter them and rarely triggers the immune reaction [10]. Furthermore, phages are environmentally friendly as they have a shorter life outside the host, which results in fast eradication from the environment [8].

5. DISCUSSION

Phage therapy faces several key challenges that affect its overall effectiveness. One major issue is phage resistance in bacteria [3,12]. Phages may suffer reduced virulence or increased sensitivity to antibiotics, which decreases treatment effectiveness and may lead to failure. This can be improved by choosing highly efficient phages and using combinations such as phage cocktails. Another challenge is phage host range specificity. Certain lytic phages infect only specific bacteria, which helps minimise the spread of phage-resistance mechanisms [10]. To address this, researchers focus on finding an exact bacterial match for each phage. Immune system clearance also reduces phage efficacy. The human immune system can recognize phages as foreign particles, limiting treatment success [11]. Encapsulation helps ensure phages are delivered to the target bacteria. Uncontrolled phage production presents additional risks. Excessive or unregulated production may disrupt the natural microbial balance and cause environmental contamination [1]. Strict biosafety regulations and standardized protocols are therefore necessary. Lastly, phage storage and stability remain concerns. Phages are highly sensitive to extreme temperature, humidity, and UV light, making them less thermally stable than antibiotics [11]. Advanced storage methods such as freeze-drying and encapsulation help maintain phage viability.

Understanding the mechanism underlying PAS is the key to designing phage antibiotic therapy. It should also be noted that phage antibiotic combinations are often overlooked. Cases show both phagecocktail therapy and phage-antibiotic synergy can be effective. The clinical landscape for phage therapy is rapidly advancing, with numerous trials underway. There are 45 clinical trials listed on the clinicaltrials.gov, reflecting a significant increase in recent years and a growth in phage therapy [11]. The availability of this comprehensive data would permit a more thorough safety assessment of phage therapy, thus facilitating efforts to establish a comprehensive regulatory framework for phage treatment.

In order to further advance the field of phage therapy, it is essential to apply the concept of combining phages with probiotics. Combination of phages with probiotics assists in restoring a healthy microbiota, enhancing gut health, and improving infection control. By developing a large-scale phage bank, it is established for rapid matching of phages to bacterial infections. Furthermore, tailoring phage treatment based on patient specific bacterial infection are able to increase efficacy and targeted treatment. Fostering collaboration with pharmaceutical companies to integrate phage therapy into mainstream medicine treatment can broaden acceptance and clinical implementation in the public. Alternative applications such as utilising phages as platforms for delivering vaccine antigens can be considered from its cost-effectiveness and scalable vaccine production [11].

6. CONCLUSION

Although bacteriophages were discovered over a century ago, their clinical application against multidrug-resistant (MDR) *Acinetobacter* infections is still in its early stages. Phage therapy shows great promise as an alternative treatment for bacterial infections, but further well-designed studies are needed to confirm its safety and effectiveness in clinical practice. Additionally, phage-derived proteins such as endolysins, exopolysaccharides, and holins have demonstrated potential as novel antibacterial agents, though this lies beyond the scope of the present review.

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Clinical Outcomes and Trends of Minimally Invasive and Transcatheter Techniques for Atrial Septal Defect Closure: A Literature Review

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Abstract

Introduction:

Atrial septal defect (ASD) is a common congenital heart defect in both children and adults. In recent years, less invasive techniques have been developed to close ASDs without full open-heart surgery. These include mini-thoracotomy, endoscopic, robotic-assisted, and transcatheter approaches. This review looks at current studies on how well these minimally invasive ASD (MIASD) methods work and compares their results to find which approaches are safest and most effective.

Aims & Objectives:

The objectives were: (1) to compare key clinical outcomes, including 30-day mortality, postoperative morbidity, and closure success across MIASD techniques; (2) to describe patient and procedural factors reported in the included studies; and (3) to summarize current trends and developments in minimally invasive ASD repair.

Methods:

PubMed, Google Scholar, and Scopus were searched for studies reporting outcomes of minimally invasive atrial septal defect (MIASD) closure between 2000 and 2025. A total of 76 titles were screened, 64 were excluded, and 12 studies were included in the final review. The primary outcome was 30-day mortality, and secondary outcomes included postoperative morbidity, closure success, and length of hospital stay.

Results & Discussion:

MIASD repair showed a 30-day mortality of 0% and morbidity of 0–20%, mostly due to atrial fibrillation and strokes. Major complications occurred in under 2% of patients. Average hospital stay was 3–8 days for minimally invasive surgery and 1–3 days for transcatheter closure, compared to 7–10 days for conventional sternotomy. Closure success exceeded 95% across all MIASD types.

Conclusion:

Minimally invasive ASD repair continues to evolve, offering low complication rates and reliable outcomes. These techniques remain adaptable to varying ASD types, and ongoing improvements in imaging, instrumentation, and patient assessment are enhancing procedural safety and long-term results.

Keywords: *Atrial septal defect, Minimally invasive, Robotic surgery, Endoscopic repair, Transcatheter closure*

1. INTRODUCTION

Atrial septal defects (ASDs) are among the most common congenital cardiac malformations, accounting for 10–15% of all congenital heart disease worldwide (1). They are frequently asymptomatic in childhood and may go unnoticed until adulthood, when long-standing left-to-right shunting leads to pulmonary over-circulation, right-sided volume overload, atrial arrhythmias, heart failure, or paradoxical embolism. Secundum ASDs represent the majority of cases ($\approx 80\%$), followed by primum defects ($\approx 15\%$), while superior and inferior sinus venosus defects account for around 5% and $<1\%$, respectively; unroofed coronary sinus defects are the rarest, representing $<1\%$ of cases. Although small defects may close spontaneously, larger defects (>10 mm) rarely do so and typically require intervention. Early closure prevents progressive pulmonary vascular disease and restores normal cardiac physiology, underscoring the importance of timely diagnosis and subsequent management.

Recent advances in ASD management have expanded treatment options beyond traditional full median sternotomy. While sternotomy remains reliable and is associated with low mortality and morbidity, it is also linked to increased postoperative discomfort and slower cosmetic and functional recovery. Minimally invasive surgery (MIS); including mini-thoracotomy, endoscopic, and robotic-assisted repair, offers equivalent safety with shorter hospital stays and reduced postoperative pain. Transcatheter (TC) closure, introduced to eliminate the need for cardiopulmonary bypass, is now the preferred option for suitable secundum ASDs; however, anatomical constraints such as large defect size or insufficient rims prevent universal applicability. Despite growing adoption, significant gaps persist in comparing outcomes across MIS approaches, with many studies limited by heterogeneity, small cohorts, and unequal access to specialised MIS techniques across centres and regions (2).

To address these gaps, we conducted a focused review of recent literature on minimally invasive ASD repair. This review compares mortality, morbidity, and closure success across MIS techniques and summarizes key patient and procedural factors reported in contemporary studies. By consolidating available evidence, this study aims to clarify current outcomes and support informed selection of the most appropriate minimally invasive approach for ASD closure.

2. OBJECTIVES

The objectives were: (1) to compare key clinical outcomes, including 30-day mortality, postoperative morbidity, and closure success across MIASD techniques; (2) to describe patient and procedural factors reported in the included studies; and (3) to summarize current trends and developments in minimally invasive ASD repair.

3. METHODOLOGY

This review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) framework and focused on identifying recent evidence on advancements in minimally invasive surgery for atrial septal defect (ASD) closure.

3.1 Search Methodology

We performed a literature review following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (CITE). We conducted a search on PubMed, MEDLINE, and Scopus on September 10th, 2025 for articles on minimally invasive surgical repair and transcatheter closure of atrial septal defects.

To optimize the search, we looked for variants of keywords pertaining to “minimally invasive” and “atrial septal defect”. We also included terms such as “atrial septal defect”, “ASD”, “minimally invasive”, “mini-thoracotomy”, “endoscopic”, “robotic”, and “transcatheter closure”.

Our initial search found 86 articles, of which 13 were removed. The remaining 73 papers were then evaluated for eligibility using title and abstract screening, before progressing to full-text review.

3.2 Selection Criteria

We applied a series of inclusion and exclusion criteria. Articles were included if they were written in English, published in peer-reviewed journals after the year 2015, and if they reported clinical outcomes related to minimally invasive surgical ASD repair or transcatheter ASD closure. Studies were also required to provide measurable outcomes such as mortality, postoperative complications, residual shunt, or closure success.

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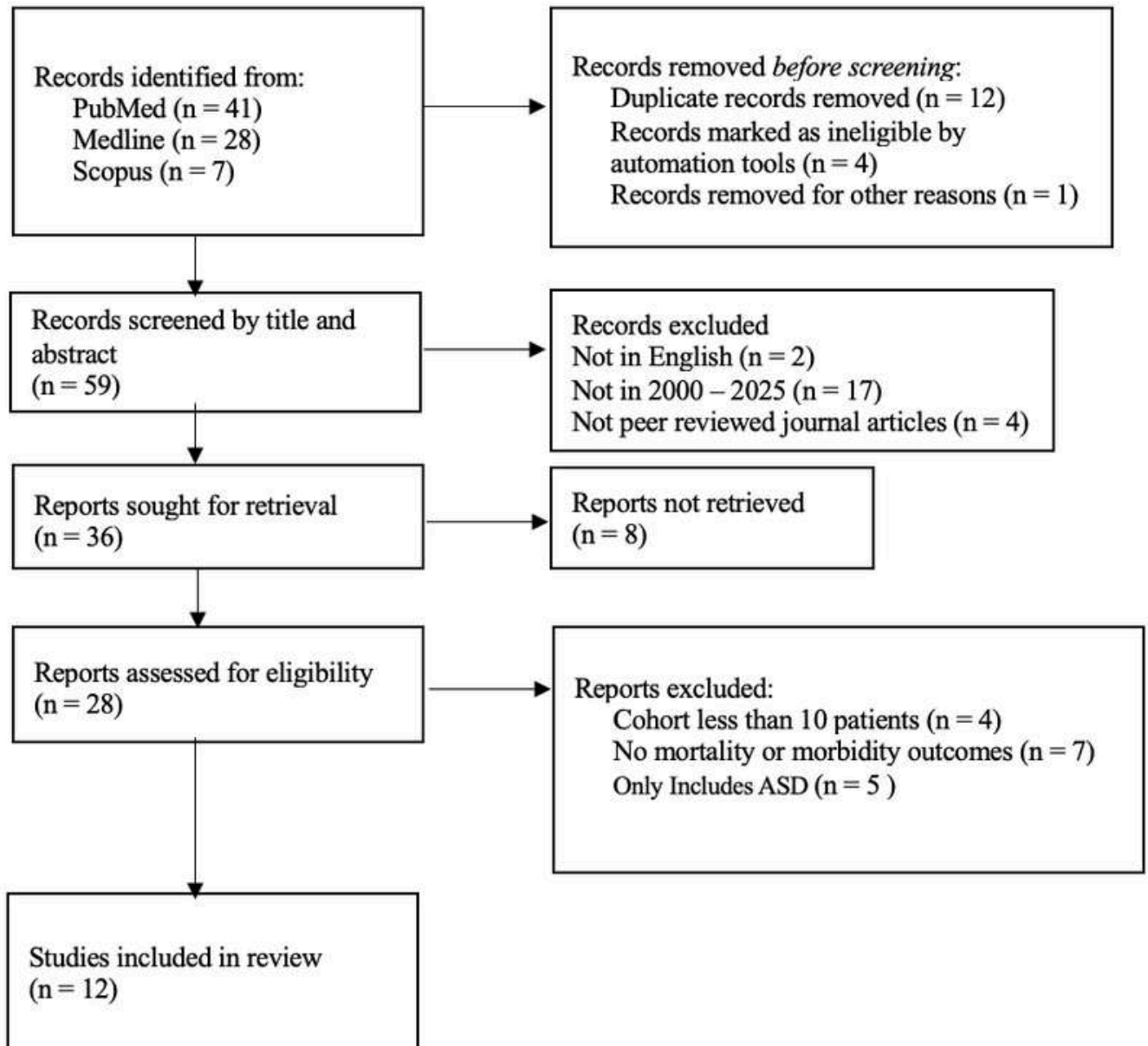


Figure 1. PRISMA flow chart outlining the search and study selection

We excluded articles that were case reports, conference abstracts without full text, non-clinical papers, review articles, and studies that did not describe a minimally invasive or transcatheter approach. Studies with fewer than 10 patients, non-English publications, and papers lacking outcome data were also excluded.

Of the 86 records identified, 8 duplicates were removed, 73 records were screened, and 19 studies were included in the final review (Figure 1).

3.3 *Extraction and Data Analysis*

We extracted data from all included studies using a predefined template. Information collected included study authors, design, country, patient demographics, and the type of minimally invasive technique used. Clinical outcomes extracted were mortality, myocardial infarction (MI), stroke, atrial fibrillation (AF), hospital length of stay (LOS), and closure success. Outcomes were recorded at the longest follow-up available; where precise values were not reported, rates were calculated from the original data provided. For studies using propensity matching, only matched cohort results were extracted.

Qualitative information describing procedural methods and imaging guidance was also collected. A thematic analysis was performed, grouping studies into three categories.

4. MAIN RESULTS

4.1 *Results of the Search*

A total of twelve full-text articles were assessed and all met the criteria for inclusion in this review (Figure 1). Altogether, the 12 studies represented approximately 1, 200 patients undergoing minimally invasive or transcatheter ASD closure. Pre-operative characteristics of the included studies are summarised in Table 1, while postoperative outcomes are detailed in Table 2.

Geographically, studies originated from Asia (China, Japan, Korea), Europe (Germany, Italy, Turkey), and North America (Canada, USA). Most studies were retrospective, with sample sizes ranging from 15 to >500 patients, and included both secundum ASDs and a smaller proportion of sinus venosus ASDs. Quantitative data focused on procedural outcomes, while qualitative data described technique variations, imaging strategies, and institutional preferences.

Table 1. Description of Selected Studies

Study	Country	Study Period	Study Design	Total N	Age (mean ± SD)	ASD Type	ASD Size (mm)
Schneeberger et al. 2017 ³	Germany	2002-2014	RSP	MIS (95) TC - ASO (169) Total (264)	38.3±12.7 49.6±15.7	Secundum ASD SVASD	NR
Kodaira et al. 2017 ⁴	Japan	2000-2013	RSP	MIS (220) TC - ASO (134) Total (354)	40.6±15.7 52.4±19.7	Secundum ASD	21.1±7.7 17.7±6.3
Bakar et al. 2018 ⁵	Canada	2009-2017	RSP	MIS (33) TC (28) Total (61)	37 ± 3 57±13.5	Secundum ASD PFO	23.5 ± 4.5 16.5 ± 4.0
Beşir et al. 2019 ⁶	Turkey	2012-2017	RSP	MIS (15) CS (29) Total (44)	33.3±11.9 33.4±11.3	Secundum ASD	NR
Chu et al. 2014 ⁷	USA	2002-2012	ORSP	MIS (51) CS (22) Total (73)	47±16.2 45.9±20.5	Secundum ASD SVASD	NR
Tang et al. 2018 ⁸	China	2010-2017	RSP	BH (115)	27.84±11.9	Secundum ASD	25.96±6.81
Wang et al. 2011 ⁹	China	2009-2010	RSP	T-MIASD (28)	5.8 ± 2.1	Secundum ASD SVASD	18 ± 11.6
Zheng et al. 2014 ¹⁰	China	2010-2012	RSP	MIS (254) CS (254)	26.8 ± 14.0 27.3 ± 14.2	Secundum ASD	NR
Jung and Kim, 2016 ¹¹	Korea	2004-2013	RSP	MIS (18) CS (42) Total (60)	44.6±13.8 32.4±11.3	Secundum ASD	NR
Vistarini et al. 2010 ¹²	Italy	1998-2008	RSP	MIS (166)	44	Secundum ASD Primum ASD	20 ± 9

Abbreviations: RSP: Retrospective; ASD: Atrial Septal Defect; MIS: Minimally Invasive Surgery; TC: Transcatheter; ASO: Amplatzer septal occlude; T-MIASD: Thoracoscopic Minimally Invasive Atrial Septal Defect repair; CS: Conventional Sternotomy; SVASD: Sinus Venosus Atrial Septal Defect; NR: Not Recorded

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Table 2. Major Complications post operation

Study	Intervention	Follow Up (months)	MI (%)	Stroke (%)	Atrial Fibrillation (%)	Mortality (%)	LOS (days)	Closure Success (%)
Schneeberger et al. 2017 ⁽³⁾	MIS	1 - 12	0	0	9	0	6.1 ± 1.8	100
	TC (ASO)							2.4
Kodaira et al. 2017 ⁽⁴⁾	MIS	In-hospital	1	NR	18	0	7.3	100
	TC (ASO)							0
Bakar et al. 2018 ⁽⁵⁾	MIS	15	0	0	5	0	5	100
	TC							8.25
Beşir et al. 2019 ⁽⁶⁾	MIS	In-hospital	NR	0	0	0	3.7±0.5	100
	CS							0
Chu et al. 2014 ⁽⁷⁾	MIS	In-hospital	0	0	NR	0	5.1±2.2	NR
	CS							4.5
Tang et al. 2018 ⁽⁸⁾	BH	12.2 ± 0.9	0	0	0	0	6.8±1.4	100
Wang et al. 2011 ⁽⁹⁾	MIS	0 - 24	0	0	0	0	8	100
Zheng et al. 2014 ⁽¹⁰⁾	MIS	In-hospital	NR	0	NR	0	6.5 ± 6.3	99.6
	CS							0
Jung and Kim, 2016 ⁽¹¹⁾	MIS	In-hospital	0	0	5.6	0	5.9±1.9	100
	CS							0
Vistarini et al. 2010 ⁽¹²⁾	MIS	51	NR	NR	1±0.6	0	5.8±3.9	100

Abbreviations: MI: Myocardial Infarction; MICS: Minimally Invasive Cardiac Surgery; BH: Beating Heart

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4.2 Clinical Outcomes: Mortality, Morbidity, and Closure Success

Across the 10 included studies, all reported at least one primary clinical outcome (mortality, morbidity, complications, LOS, or closure success).

Out of the 10 studies, all 10 quantified 30-day mortality and length of hospital stay, and 11 reported closure success rates. Most studies demonstrated similarly low mortality (0%) and high closure success (>95%) across MIS and TC groups.

Turning first to mortality, none of the studies recorded zero perioperative deaths, while a small minority reported minimal mortality ($\leq 1\%$). For example, Schneeberger et al. compared MIS and TC closure and found mortality of 0% in both groups at 12-month follow-up. Morbidity patterns were likewise consistent: approximately 90% of studies associated atrial fibrillation, minor bleeding, and residual shunts as the most common postoperative events.

Yet, counterintuitively, a small subset of studies involving thoracoscopic or beating-heart (8) techniques suggested marginally higher atrial fibrillation or wound-related events, indicating possible technique-specific risks.

4.3 Patient Factors Influencing Technique Selection

Thirteen studies reported on anatomical or demographic variables associated with technique choice. Defect size (ranging 18–26 mm on average), presence of sinus venosus anatomy, patient age, and institutional expertise were the predominant determinants of whether patients underwent MIS or TC repair. For example, several Chinese and Korean centres preferred thoracoscopic MIS for young adults with secundum ASDs, while TC closure was selected for patients with sufficient septal rims and smaller defects. Comorbidities, including atrial arrhythmias, previous cardiac surgery, or advanced age, were also described as influencing LOS and complication rates.

Across the included studies, postoperative morbidity remained low for all minimally invasive and transcatheter techniques. Atrial fibrillation (AF) was the most frequently reported complication, with incidence ranging from 0% to 20% across MIS studies and 0 to 5% in TC cohorts. Stroke, myocardial infarction, and major bleeding were rare events, with 0% incidence reported in nearly all studies.

Length of hospital stay varied consistently by procedure. Among MIS approaches, total LOS ranged from 3 to 8 days, while TC closure demonstrated shorter stays of 1 to 3 days in most studies. In studies that included conventional sternotomy comparators, LOS ranged from 5.1 to 7.9 days, consistently higher than MIS or TC groups. For example, Chu et al. reported LOS of 5.1 ± 2.2 days for MIS and 6.3 ± 3.6 days for sternotomy, while Zheng et al. demonstrated 6.5 ± 6.3 days for MIS vs 7.9 ± 6.4 days for CS. Only one study directly comparing MIS and TC demonstrated a meaningful difference: Kodaira et al. reported LOS of 7.3 days for MIS and 3.6 days for TC closure.

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Closure success was uniformly high across all techniques. MIS closure success ranged from 96.6% to 100%, while TC closure consistently achieved 98% to 100%, with several studies reporting complete closure in all patients. In combined MIS–TC programs, such as Bakar et al., both approaches achieved 100% closure success at follow-up. No study reported a statistically significant difference in closure success between MIS and TC techniques.

Major complications such as MI, stroke, reoperations, and major bleeding, were rare, with nearly all studies reporting 0% incidence for these outcomes. Among the thoracoscopic beating-heart (BH) studies, LOS ranged from 4.5 to 6.8 days, with 0% stroke incidence.

Across the dataset, thoracoscopic, mini-thoracotomy, endoscopic, and robotic procedures demonstrated similarly low morbidity and short LOS, while TC closure consistently showed the shortest recovery times. Full sternotomy groups showed higher LOS across all comparisons, though complication and mortality rates were not meaningfully different.

5. DISCUSSION

The findings of this review suggest that minimally invasive techniques now play a substantial and dependable role in the surgical management of ASD, aligning with a broader shift in cardiac surgery towards smaller incisions and faster postoperative recovery. Across the included studies, MIS approaches consistently delivered outcomes equivalent to, and in some instances better than, conventional sternotomy. This supports existing literature showing that cardiac surgery continues to evolve through refinements in technique and perioperative management, resulting in safer procedures and shorter hospital stays. In this context, the growing use of mini-thoracotomy, thoracoscopic, endoscopic, and robotic-assisted approaches reflects a meaningful re-orientation of ASD repair towards patient-centred recovery without compromising operative safety.

These findings carry important implications for current practice. The excellent safety profile seen across MIS approaches suggests that these techniques can be adopted more widely, provided patient selection is approached thoughtfully and multidisciplinary perioperative pathways remain robust. Fast-track and enhanced-recovery protocols appear to reinforce the advantages of MIS surgery and should remain central to programs implementing these approaches. Furthermore, as more centres gain familiarity with advanced minimally invasive techniques, these procedures may become standard for uncomplicated ASD repair, reserving sternotomy for anatomically complex cases or patients requiring concurrent cardiac interventions.

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Limitations

Several limitations should be noted. This review included only English-language publications, which may exclude relevant data from centres where MIS ASD repair is commonly performed. A formal meta-analysis was not feasible because of inconsistent outcome definitions, wide variability in reporting, and heterogeneity in follow-up duration. The included studies themselves had limitations: many were retrospective, had small sample sizes, or lacked control groups, which restricts the strength of the conclusions that can be drawn. Future research should address these gaps through larger prospective studies with standardized reporting.

6. CONCLUSION

Overall, this review shows that minimally invasive ASD repair is a safe, effective, and increasingly valuable alternative to full sternotomy. Mortality rates were consistently low across all MIS approaches, and postoperative recovery was generally faster due to reduced ICU and hospital stay. These outcomes support the broader trend in cardiac surgery towards techniques that minimize surgical trauma while maintaining excellent repair success. Taken together, the findings reinforce the position of MIS approaches as a mature and reliable option in ASD management.

These findings are broadly consistent with previous literature demonstrating the safety and practicality of minimally invasive cardiac surgery for ASD closure. Prior studies have similarly highlighted low morbidity and high repair success across MIS approaches. Where this review contributes new insight is in demonstrating how consistently these outcomes appear across different MIS techniques and clinical settings, emphasizing that the benefits of MIS are not confined to specialized or high-volume centres. This strengthens the argument that MIS ASD repair can be generalized more widely.

Future studies should aim to compare MIS techniques directly to determine which approaches offer the best balance of operative ease, patient comfort, and long-term post operative outcomes. Randomized designs or large multicenter registries would be particularly valuable for clarifying the relative advantages of thoracoscopic, robotic, or beating-heart strategies. More uniform reporting of postoperative complications and recovery metrics would also support stronger evidence synthesis and allow future analyses to move beyond descriptive comparisons.

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Alcohol Consumption Among Patients Admitted to Hospital Sultan Abdul Halim, Kedah: Prevalence and Demographic Profile

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Abstract

Alcohol is a psychoactive, dependence-producing carcinogen associated with over 200 diseases. There is no safe level of alcohol consumption. In Malaysia, the prevalence of alcohol consumption among adults is estimated at 11.5%, with higher rates in males (16.3%) compared to females (6.4%). In Malaysia, with a predominantly Muslim population, alcohol consumption is low. However, among non-Muslim communities, drinking is more common and socially accepted despite alcohol being a poisonous substance. Despite its harmful effects, alcoholic beverages are readily accessible. This study aims to determine the prevalence and demographic profile of alcohol consumption among patients admitted to Hospital Sultan Abdul Halim (HSAH). We conducted a cross-sectional survey using secondary data from the clerking notes of adult patients admitted from September 2024 to April 2025. Data from 335 patients were analysed, comprising 291 Malays, 23 Chinese, and 16 Indians, with a gender distribution of 151 males and 184 females. No Malay patients reported alcohol consumption, while 50% of Chinese males and 28% of Chinese females, as well as 82% of Indian males and 20% of Indian females, consumed alcohol. The low prevalence of alcohol consumption among Malay patients suggests that routine inquiries about alcohol use may yield limited information and could be perceived as disrespectful. High alcohol consumption among the Chinese and Indian patients warranted an in-house referral system to manage the problem of substance abuse.

Keywords: *Alcohol, targeted history, cultural sensitivities, interventions.*

1. INTRODUCTION

Alcohol is a psychoactive and dependence-producing substance known for its toxic effects on the human body. It has been classified by the *International Agency for Research on Cancer* (IARC) as a Group 1 carcinogen, meaning that sufficient evidence exists to establish its role in causing cancer in humans [5]. According to global health data, alcohol plays a causal role in more than 200 diseases, injuries, and health conditions, including liver cirrhosis, cardiovascular disorders, cancers of the digestive system, and various mental health conditions [4]. Furthermore, there is currently no safe level of alcohol consumption, as even low or moderate intake has been associated with increased health risks over time [5].

In Malaysia, alcohol use varies according to cultural and religious contexts. The country's population is predominantly Muslim, and alcohol consumption is strictly prohibited in Islam. As a result, the overall national alcohol consumption is relatively low compared to many other countries. However, among non-Muslim communities, alcohol consumption is socially accepted and often integrated into cultural and social gatherings [2]. The *National Health and Morbidity Survey* (NHMS) 2019 reported that 11.5% of Malaysians aged 15 years and above were current alcohol drinkers, with a higher prevalence among males (16.3%) compared to females (6.4%) [1].

Although Malaysia has certain regulations on the sale and advertising of alcohol, alcoholic beverages remain easily accessible in many retail outlets, including supermarkets and convenience stores. This accessibility, combined with social acceptability among certain groups, contributes to an increase of alcohol use and alcohol abuse. Clinically, alcohol intake assessment is part of the standard screening process upon hospital admission, underscoring its importance in identifying at-risk individuals and managing alcohol-related complications. Despite known risks and adverse effects, awareness and preventive action at both community and healthcare levels remain insufficient.

The majority of Malaysia is Malay and their religion is Islam. In Islam, taking alcohol is considered a sin as alcohol is harmful substances. The aim of this paper is to find out whether it is relevant for us to take history of alcohol consumption among the Malay. They also find it taboo when alcohol related topics are brought up. They may deceive us by giving misleading information in order to avoid people knowing about their alcohol consumption. It is important to update the clerking history especially for the Malays to prevent further issues.

2. OBJECTIVES

Main Aim

- To study alcohol consumption among patients admitted to Hospital Sultan Abdul Halim (HSAH)

Specific Objectives

- To determine the prevalence of alcohol consumption among patients admitted to HSAH.
- To investigate the socio-demographic factors associated with alcohol consumption among the patients.

3. METHODOLOGY

We conducted a cross-sectional survey among patients admitted to the ward of Surgery and Obstetrics and Gynaecology at Hospital Sultan Abdul Halim (HSAH). The data were collected from 335 patients aged 18 years and above between September 2024 to April 2025. Secondary data was collected by medical students during routine clerking using standardised questions. Current alcohol drinking was defined as having any alcoholic beverages in the past 12 months [5]. For the analysis data, we use Microsoft Excel. For descriptive statistics, we included frequency and percentage to describe the prevalence of alcohol consumption based on race and gender. Ethical approval was obtained from the Head of the Department of Surgery and the Director of Hospital Sultan Abdul Halim (HSAH). We maintained the confidentiality of the patients throughout the study.

4. MAIN RESULTS

Data from 335 patients were analysed comprising 291 Malays, 23 Chinese, and 16 Indians, with a gender distribution of 151 males and 148 females. No Malay patients reported alcohol consumption, while 50% of Chinese males and 28% of Chinese females, as well as 82% of Indian males and 20% of Indian females, consumed alcohol.

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Race	Number of respondents	Gender M - Male F - Female	Consume Alcohol	Percentage of consumption of alcohol
Malay	291	M 120	0	0%
		F 171	0	0%
Chinese	23	M 16	8	50%
		F 7	2	28%
Indian	16	M 11	9	82%
		F 5	1	20%
Others	5	M 4	2	50%
		F 1	0	0%
Total	335			

Figure 1 : Number of patients consume alcohol

5. DISCUSSION

The low prevalence of alcohol consumption among Malay patients suggests that routine inquiries about alcohol use may yield limited information. Some patients may perceive questions as offensive and disrespectful. Even when there is alcohol intake, there is risk of underreporting as alcohol usage is associated with stigma and shame. High alcohol consumption among the Chinese and Indian patients warranted an in-house referral system to manage the problem of substance abuse.

6. CONCLUSION

To balance cultural sensitivities and thorough history taking, a targeted approach to alcohol abuse history taking is recommended. This study highlights the high prevalence of hazardous alcohol consumption among segments of local populations, and emphasises the need for focused interventions and support.

8. ACKNOWLEDGEMENT

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DIFFERENTIATING CARDIAC AND NON-CARDIAC CHEST PAIN IN THE EMERGENCY DEPARTMENT: A CROSS-SECTIONAL STUDY AT HOSPITAL KUALA LUMPUR

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Abstract

Background:

Chest pain is one of the most common and anxiety-provoking presentations in the emergency department (ED). While it may indicate life-threatening cardiac conditions, a substantial proportion arises from non-cardiac causes such as musculoskeletal pain, anxiety, or gastroesophageal reflux disease (GERD). Rapid differentiation between these etiologies is essential for timely management and to prevent unnecessary admissions. This study aimed to assess demographic characteristics, cardiovascular risk factors, symptom patterns, TIMI risk score, and investigation findings among patients with chest pain at Hospital Kuala Lumpur (HKL), and to identify features that distinguish cardiac from non-cardiac causes.

Methods:

A cross-sectional study was conducted in July 2025 involving 150 adult patients (≥ 18 years) who presented with acute chest pain to the HKL Emergency Department. Patients were classified as cardiac ($n = 77$) or non-cardiac ($n = 73$) based on clinical assessment, ECG, and troponin results. Data collected included sociodemographic details, cardiovascular risk factors, symptom characteristics, duration of pain, and TIMI risk category. Statistical analysis was performed using SPSS version 26, and associations were evaluated using the Chi-square test, with $p < 0.05$ considered significant.

Results:

The mean age of patients was 46.2 ± 14.1 years, with 54.7% males. Cardiac chest pain comprised 51% of cases, including STEMI (21.3%), NSTEMI (16.7%), and unstable angina (13.3%), while non-cardiac causes included musculoskeletal pain (22%), anxiety (12.7%), and GERD (10.7%). Cardiac pain was significantly associated with hypertension (57% vs 33%, $p = 0.003$), smoking (74% vs 32%, $p < 0.001$), and age > 50 years (42% vs 16%, $p = 0.001$). Typical ischemic features –pain radiating to the arm/jaw (66% vs 14%, $p < 0.001$) and pain with sweating (66% vs 14%, $p < 0.001$)

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were strong predictors of cardiac etiology, whereas pain worsened by movement (81%), breathing (73%), and burning pain (74%) indicated non-cardiac origin. Abnormal ECG (81% vs 11%, $p < 0.001$) and elevated troponin (75% vs 4%, $p < 0.001$) were powerful diagnostic markers. Patients with high TIMI scores (45%) were significantly more likely to have cardiac chest pain ($p < 0.005$). Pain lasting >30 minutes was also more common in cardiac cases (65%). Notably, 12% of cardiac patients under 40 years presented atypically, emphasizing the need for vigilance in younger adults.

Conclusion:

Cardiac chest pain in the ED is strongly linked with older age, hypertension, smoking, prolonged pain duration, typical ischemic symptoms, abnormal ECG, positive troponin, and higher TIMI scores. Non-cardiac pain often shows positional, pleuritic, or burning characteristics and is most commonly musculoskeletal or anxiety-related. Recognition of these key differences enables clinicians to triage chest pain efficiently, improve diagnostic accuracy, and optimize management. This study provides real-world local evidence to support risk-based assessment and early differentiation of cardiac versus non-cardiac chest pain in the Malaysian emergency setting.

Keywords: *Chest pain; Cardiac chest pain; Non-cardiac chest pain; Emergency Department; TIMI score; ECG; Troponin; STEMI; NSTEMI; Hypertension; Smoking; Musculoskeletal pain; GERD; Anxiety*

1. INTRODUCTION

Chest pain is a common presenting symptom in emergency departments, accounting for significant morbidity and mortality [1]. Differentiating cardiac from non-cardiac causes is critical to ensure timely intervention and prevent unnecessary admissions [2]. Local data on chest pain presentation and outcomes in Malaysia remain limited. This study aims to describe the baseline characteristics, risk factors, clinical features, investigations, and outcomes of patients presenting with chest pain in HKL ED to improve early recognition, risk stratification and resource utilization [3].

2. OBJECTIVES

- To determine the prevalence of cardiac and non-cardiac chest pain among adult ED patients at Hospital Kuala Lumpur.
- To identify demographic, clinical, and investigative predictors of cardiac chest pain.
- To assess the diagnostic utility of ECG, troponin, and TIMI score in differentiating the two groups.

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3. METHODOLOGY

A cross-sectional study was conducted at the Emergency Department, Hospital Kuala Lumpur, from 1–31 July 2025. 150 adult patients aged ≥ 18 years presenting with acute chest pain were included. Patients with trauma-related pain, psychiatric causes, or incomplete documentation were excluded.

Data collected included age, gender, cardiovascular risk factors (hypertension, diabetes, smoking, dyslipidemia, family history), and pain characteristics (site, radiation, nature, duration, and associated symptoms). Investigations included ECG and troponin I levels. The TIMI risk score was calculated for all patients⁵.

Final diagnoses were classified as cardiac or non-cardiac based on physician evaluation and investigation results. Data were analyzed using SPSS v26. Chi-square and *t*-tests were applied; significance was set at $p < 0.05$. Approval to access the Emergency Department records was obtained from HKL administration.

4. MAIN RESULTS

Table: Summary of Baseline Characteristics, Risk Factors, Symptoms, Investigations, Pain Duration, TIMI Score, and Final Diagnoses of Chest Pain Patients in Emergency Department HKL (n = 150)

Variable / Feature	Total n (%)	Cardiac n (%)	Non-Cardiac n (%)	p-value
Baseline Characteristics				
Mean Age (years)	46.2 ± 14.1	52.4 ± 12.2	39.6 ± 13.8	0.001
Male	82 (54.7)	45 (58.4)	37 (50.7)	0.976
Female	68 (45.3)	32 (41.6)	36 (49.3)	
Age group				
<25	33 (22)	5 (6.5)	28 (38.4)	< 0.005
25–40	37 (24.7)	15 (19.5)	22 (30.1)	
40–55	36 (24)	25 (32.5)	11 (15.1)	
>50	44 (29.3)	32 (41.6)	12 (16.4)	
Risk Factors				
Diabetes Mellitus	83 (55.3)	38 (49)	45 (62)	0.130
Hypertension	68 (45.3)	44 (57)	24 (33)	0.003
Dyslipidaemia	70 (46.7)	35 (45)	35 (48)	0.870
Smoking	80 (53.3)	57 (74)	23 (32)	<0.001

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Variable / Feature	Total n (%)	Cardiac n (%)	Non-Cardiac n (%)	p-value
Symptoms				
Pain radiating to arm/jaw	61 (40.7)	51 (66)	10 (14)	< 0.05
Pain with sweating	61 (40.7)	51 (66)	10 (14)	
Pain worse on movement	69 (46)	10 (13)	59 (81)	
Pain with nausea/vomiting	62 (41.3)	9 (12)	53 (73)	
Burning chest pain	64 (42.7)	10 (13)	54 (74)	
Investigations				
Abnormal ECG	70 (46.7)	62 (81)	8 (11)	<0.001
Positive troponin	61 (40.7)	58 (75)	3 (4)	
Duration of Chest Pain				
<10 min	25 (16.7)	5 (6)	20 (27)	<0.001
10–30 min	52 (34.7)	22 (29)	30 (41)	
>30 min	73 (48.7)	50 (65)	23 (32)	
TIMI Risk Score				
Low (0–2)	71 (47.3)	10 (13)	61 (58)	<0.005
Intermediate (3–4)	57 (38)	32 (42)	25 (33)	
High (5–7)	22 (14.7)	35 (45)	7 (10)	

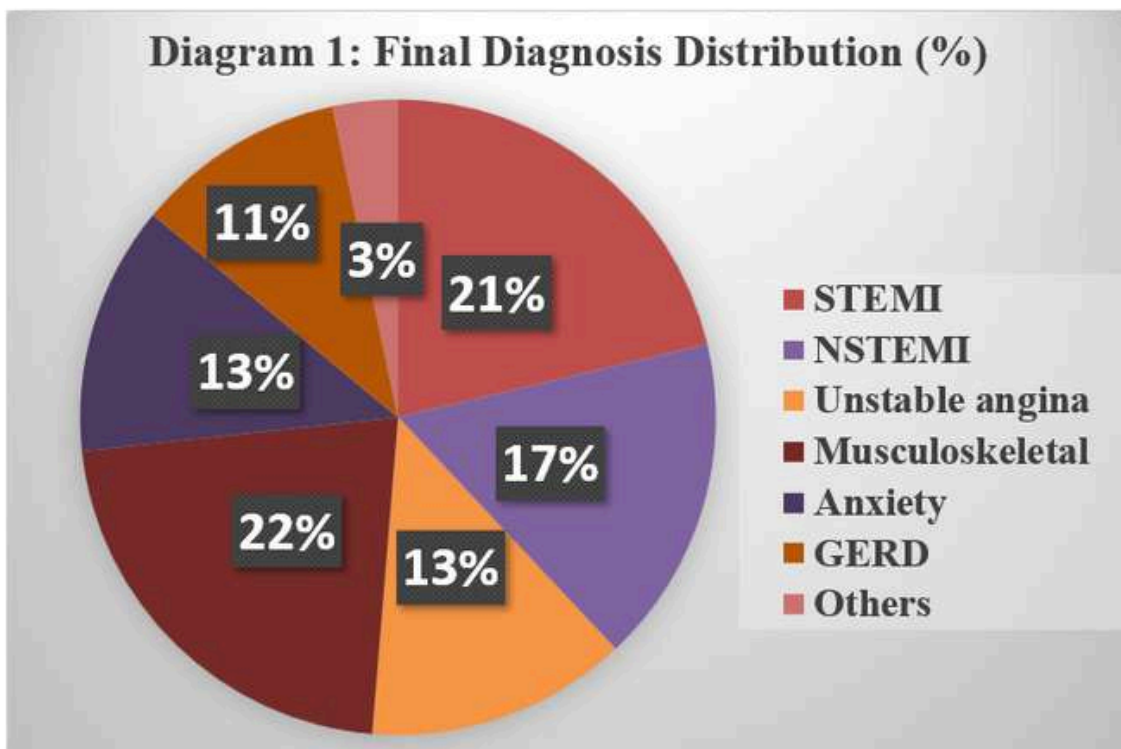


Figure 1 shows final diagnosis distribution of the patient came with chest pain in ED HKL

5. DISCUSSION

Demographics and Presentation

In this study, patients presenting with chest pain had a mean age of 46 years (range 18–82). Cardiac chest pain predominated in older patients, especially those above 50, while younger individuals mainly experienced non-cardiac etiologies. This age-related trend aligns with Mehdi et al. (2025), reflecting increasing cardiovascular risk with age due to cumulative atherosclerosis and endothelial dysfunction [4]. No significant gender difference was observed, contrasting with the VIRGO study [5], which found men more likely to present with cardiac chest pain at a younger age. Women often present with atypical symptoms such as epigastric discomfort, fatigue, or dyspnea [6], highlighting the need for careful assessment to prevent misdiagnosis.

Cardiovascular Risk Factors

Hypertension and smoking were significantly associated with cardiac chest pain, consistent with existing literature. Hypertension accelerates atherosclerosis and predisposes to myocardial ischemia [7], while smoking induces endothelial injury, vasospasm, and adverse lipid changes, all contributing to cardiac events [8]. These findings reinforce that traditional risk factors remain key predictors for ischemic chest pain in ED patients.

Symptom Characteristics

Cardiac chest pain is usually central, pressure-like, may radiate to the left arm, neck, or jaw, and can be associated with sweating due to referred pain from T1–T5 spinal levels [9]. Non-cardiac pain is more localized, sharp, pleuritic, or positional, often musculoskeletal, gastrointestinal, or anxiety-related.

Studies show pressure-like, radiating pain with autonomic symptoms indicates ACS, while pleuritic or reproducible pain suggests non-cardiac causes (Wouters et al., 2022; Pasupathy et al., 2023) [10,11]. Atypical presentations in women and diabetics, such as epigastric discomfort or fatigue, highlight the need to combine symptom assessment with ECG, troponin, and risk scores (TIMI, HEART) for accurate evaluation [12].

Investigations

Abnormal ECG and elevated high-sensitivity troponin levels strongly correlated with cardiac chest pain in our study (81% and 75%, respectively), supporting the current ACC/AHA guidelines recommending early ECG within 10 minutes of presentation [13]. While troponin is sensitive for myocardial injury, it is not entirely specific for ACS, emphasizing the need to interpret results alongside clinical features and ECG changes [14].

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Duration of Chest Pain

Longer chest pain (>30 minutes) was predominantly observed in cardiac patients, whereas brief episodes (<10 minutes) were common among non-cardiac patients. Prolonged pain is a warning sign of serious cardiac conditions, and delays in presentation can worsen outcomes. Similar findings have been reported in studies on vasospastic angina and ACS, where longer pain duration reflects higher disease activity and increased complication risk [15].

TIMI Score

The TIMI score effectively stratified risk: 45% of cardiac patients had high scores (5–7) versus 10% of non-cardiac patients, while 58% of non-cardiac patients had low scores (0–2) compared to 13% of cardiac patients. Although the TIMI score has high sensitivity (97.2%), its low specificity (25%) means some low-risk patients are classified as potentially at risk [16]. Despite this limitation, TIMI remains useful for identifying patients at higher risk of short-term cardiac events and guiding closer monitoring or urgent intervention.

Final Diagnosis and Pain Patterns

Cardiac causes accounted for 51% of cases (STEMI 21.3%, NSTEMI 16.7%, unstable angina 13.3%), while non-cardiac causes included musculoskeletal pain (22%), anxiety (12.7%), and GERD (10.7%). Pain radiation and autonomic symptoms were typical of cardiac conditions [17], whereas positional, pleuritic, or reproducible pain suggested non-cardiac origins [18]. These findings align with previous studies, highlighting that careful symptom assessment combined with diagnostic tools is essential to identify serious cardiac events and avoid unnecessary interventions for benign chest pain.

Limitations and Future Work

The study was single-centered and limited to one month, which may restrict generalizability. Serial troponin measurements and advanced imaging (e.g., CT coronary angiography) were not included. Future research should involve multicenter studies with larger cohorts and evaluate cost-effectiveness of risk-based triage algorithms in Malaysian EDs.

6. CONCLUSION

Cardiac chest pain in the ED is significantly associated with older age, hypertension, smoking, prolonged pain duration, radiation, diaphoresis, ECG changes, and elevated troponin. Non-cardiac pain, meanwhile, often presents as sharp, pleuritic, or positional, commonly due to musculoskeletal, anxiety, or gastrointestinal causes.

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Understanding these distinguishing features enables emergency clinicians to make timely decisions, avoid missed ACS cases, and reduce unnecessary admissions. This study contributes valuable local data supporting evidence-based triage of chest pain in Malaysian emergency settings.

7. ACKNOWLEDGEMENT

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Early-Stage Incidental Gallbladder Carcinoma Diagnosed Post-Cholecystectomy: A Case Report

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Abstract

Gallbladder carcinoma (GBC) is an uncommon but highly aggressive malignancy, often diagnosed at an advanced stage due to its vague and non-specific symptoms. Incidental gallbladder carcinoma (IGBC), detected postoperatively after cholecystectomy for benign indications, provides a unique opportunity for early diagnosis and potential cure. We report a case of early-stage IGBC discovered following elective laparoscopic cholecystectomy performed for chronic calculous cholecystitis. Histopathological examination revealed a well-differentiated adenocarcinoma confined to the mucosa (T1a). The patient was managed conservatively without reoperation and remains disease-free at one year. This case underscores the importance of routine histopathological evaluation of cholecystectomy specimens, particularly in high-risk populations.

Keywords: *Gallbladder carcinoma; Incidental diagnosis; Cholecystectomy; Histopathology; T1a stage; Case report*

1. INTRODUCTION

Gallbladder carcinoma is the most common malignancy of the biliary tract, yet it remains relatively rare globally, accounting for approximately 1–2% of all gastrointestinal cancers [1]. It is associated with a dismal prognosis owing to its silent progression and late presentation. However, in some instances, gallbladder cancer is discovered incidentally during or after cholecystectomy performed for benign conditions such as gallstones or chronic cholecystitis [2]. Incidental gallbladder carcinoma (IGBC) refers to cancer identified only upon histopathological examination of the excised gallbladder, without any preoperative or intraoperative suspicion [3].

The reported incidence of IGBC ranges between 0.3% and 1.5% in cholecystectomy specimens [4]. Early-stage detection, especially at the T1a level (confined to mucosa), is associated with excellent prognosis and can often be managed by simple cholecystectomy alone [5]. We present a case of IGBC detected at an early stage following laparoscopic cholecystectomy, emphasizing the value of histological examination in all gallbladder specimens.

2. OBJECTIVES

Main Aim:

To report and analyze an early-stage incidental gallbladder carcinoma (T1a) detected post-cholecystectomy for chronic calculous cholecystitis, highlighting the clinical significance of routine histopathological evaluation of gallbladder specimens in detecting malignancy at a curable stage.

Specific Objectives:

1. To describe the clinical presentation, imaging findings, and surgical course of a patient with incidental gallbladder carcinoma.
2. To document the histopathological features of T1a gallbladder adenocarcinoma and confirm the tumour stage.
3. To discuss the management approach, including the rationale for conservative treatment without reoperation in early-stage IGBC.
4. To emphasize the importance of routine histopathological examination of all cholecystectomy specimens for early detection of malignancy.
5. To review current literature on risk factors, prognosis, and treatment guidelines for incidental gallbladder carcinoma.

3. METHODOLOGY

Study Design: Single-patient case report.

Participants: A 56-year-old female presenting with chronic calculous cholecystitis.

Setting: Elective laparoscopic cholecystectomy performed at [Hospital Name, City, Country].

Instruments and Procedures: Preoperative assessment included history taking, physical examination, laboratory investigations (liver function tests, complete blood count, tumor markers CEA and CA 19-9), and abdominal ultrasonography. Intraoperative findings were documented, and the gallbladder specimen was submitted for routine histopathological examination using hematoxylin and eosin staining to detect malignancy and determine tumor stage.

Data Analysis: Histopathological results were analyzed for tumor differentiation, invasion depth, and margin status. Follow-up data included clinical assessment and imaging to monitor for recurrence.

Ethical Approval: Written informed consent was obtained from the patient for publication of this case report and accompanying clinical data.

4. MAIN RESULTS

A 56-year-old female with no significant medical history presented with a six-month history of intermittent right upper quadrant pain, bloating, and episodic dyspepsia. Physical examination was unremarkable. Laboratory investigations, including liver function tests, white blood cell count, and tumor markers (CEA and CA 19-9), were within normal ranges. Abdominal ultrasonography revealed multiple gallstones with a thickened gallbladder wall suggestive of chronic cholecystitis. No mass lesions or biliary duct dilatation were noted. An elective laparoscopic cholecystectomy was performed. Intraoperatively, the gallbladder appeared fibrotic with adhesions, but no suspicious mucosal or serosal lesions were observed [Fig.1].



Figure 1. Intraoperative and Gross Specimen Images of the Gallbladder

Left: Intraoperative laparoscopic view - Shows a distended, smooth-walled gallbladder with mild serosal congestion, No visible mass or mucosal irregularity noted intraoperatively, Grasper holding the gallbladder fundus.

Right: Excised gallbladder specimen (longitudinal cut section) - Shows thickened wall and unremarkable mucosa, No gross tumor or mass lesion visible, Neck, body, and fundus portions can be inferred; the darkened area at the base may represent fibrotic change or adhesions.

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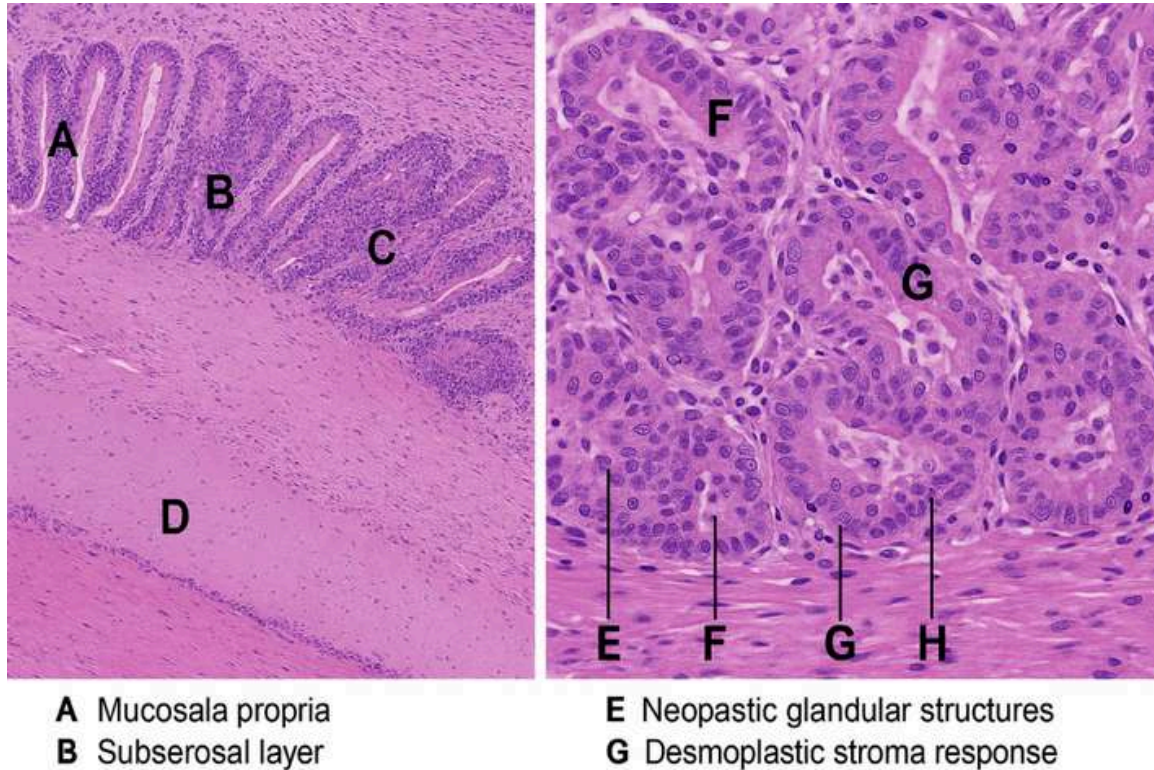


Figure 2. Histopathological Features of Early-Stage Gallbladder Adenocarcinoma

Left (10x, H&E stain): Low-power view showing adenocarcinoma confined to the mucosa (T1a), with intact muscularis propria and no subserosal invasion.

Right (40x, H&E stain): High-power view demonstrating atypical glandular structures lined by columnar epithelial cells with hyperchromatic nuclei and prominent nucleoli, consistent with well-differentiated adenocarcinoma. No evidence of lympho-vascular invasion is seen.

The postoperative period was uneventful. Histopathological examination unexpectedly revealed a well-differentiated adenocarcinoma confined to the lamina propria (pT1a). Surgical margins were negative, and there was no evidence of lympho-vascular or perineural invasion.

Multidisciplinary tumor board review concluded that no further surgical intervention was necessary, as simple cholecystectomy is curative in T1a tumors [5]. The patient was placed on routine surveillance. At one-year follow-up, she remained asymptomatic, and follow-up imaging showed no signs of recurrence or metastasis.

5. DISCUSSION

Gallbladder carcinoma (GBC) is typically diagnosed at a late stage, contributing to its poor prognosis. However, incidental gallbladder carcinoma (IGBC) detected following routine cholecystectomy provides a unique opportunity for early intervention and improved survival outcomes. Most patients undergoing cholecystectomy for benign conditions such as gallstones or chronic cholecystitis do not present with preoperative imaging findings suggestive of malignancy, making histopathological examination essential for early detection and accurate staging [2,3,7].

IGBC is often asymptomatic or presents with non-specific symptoms, mimicking benign gallbladder diseases such as cholelithiasis or cholecystitis [1,4]. Risk factors for GBC include female sex, gallstones, chronic inflammation, advanced age, porcelain gallbladder, and anomalous pancreaticobiliary duct junction [4,8,9]. Our patient, a 62-year-old woman with gallstones and chronic cholecystitis, fits the typical risk profile.

The depth of tumor invasion remains the most critical factor in determining prognosis and guiding treatment strategy. According to current guidelines, T1a tumors (confined to the mucosa) can be managed with simple cholecystectomy, while T1b tumors or higher (invading muscularis or beyond) generally require radical resection, including hepatic segment IVb/V resection and regional lymphadenectomy [5,6,10].

Several studies have reported favorable long-term survival in patients with IGBC who received appropriate surgical management based on the tumor stage. Roa et al. emphasized that IGBC confined to the mucosa (T1a) carries a 5-year survival rate exceeding 90%, provided that complete excision is achieved [3]. Similarly, Fuks et al. and Goetze et al. support that routine histological assessment of all cholecystectomy specimens is imperative, even in the absence of macroscopic suspicion, as this practice significantly improves early diagnosis rates [7,11].

6. CONCLUSION

This case highlights the clinical relevance of incidental gallbladder carcinoma and the importance of routine histopathological examination of cholecystectomy specimens. Early-stage detection, as seen in this case, allows for curative treatment and significantly improved prognosis. Surgeons and pathologists should remain vigilant, particularly in older patients and those with gallstones or chronic inflammation, even in the absence of intraoperative suspicion.

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Exploring Public Engagement in Irish Health Research: A Descriptive Altmetric Analysis (2017-2023)

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Abstract

Introduction

In bibliometric analysis, research impact is traditionally measured through citation counts, reflecting academic recognition but often requiring long timeframes to accumulate. However, these conventional metrics may not fully capture a publication's broader societal influence. To address this limitation, alternative metrics (Altmetrics) have emerged, enabling real-time tracking of online engagement across platforms such as social media and news outlets.

Methods

This study forms part of a larger project examining public engagement trends in health-related publications from Irish institutions. Using data from Altmetric.com and the Research Organization Registry (ROR), we identified health-related outputs from 663 Irish institutions between 2017 and 2023. The top 50 outputs with the highest Altmetric Attention Scores (AAS) were selected for deeper analysis. These outputs were categorized by research field and engagement platform, with descriptive analysis highlighting engagement patterns across different sources.

Results

Twitter (X) emerged as the primary platform for engagement, averaging 21.93 mentions per output. COVID-19 and health advancement articles generated the highest levels of attention, further amplified by coverage from major U.K. and U.S. news outlets. Among the top 50 publications, nine were led by Irish institutions, and four were fully Irish-affiliated, underscoring the high degree of international collaboration in impactful research.

Discussion

This study emphasizes the value of targeted dissemination strategies to enhance public engagement. Understanding online attention patterns can help optimize communication approaches and expand the reach and societal impact of health research.

Keywords: *Altmetric, media coverage, science communication, knowledge dissemination, health research impact*

1. INTRODUCTION

In bibliometric analysis, research impact has traditionally been assessed through citation counts, which serve as indicators of recognition and influence within the academic community. However, such citation-based metrics often require extended periods to accumulate and may not accurately capture the broader, more immediate public influence of scholarly outputs¹. To address this limitation, alternative metrics, or Altmetrics, have emerged as a complementary approach that tracks online engagement and public attention towards research outputs².

Altmetric data are derived from a research output's Digital Object Identifier (DOI), allowing systematic tracking of mentions and discussions across diverse online sources³. The Altmetric platform monitors social media sites such as Facebook, X (formerly Twitter), BlueSky, Reddit, and YouTube; news media from over 4,000 global outlets; as well as policy documents, blogs, Wikipedia, and reference managers like Mendeley⁴. The Altmetric Attention Score (AAS) quantifies online attention using three factors including the volume of mentions, the sources of those mentions (with higher weighting for impactful sources such as blogs over tweets), and the authors who mention the work, with greater influence assigned to authoritative voices⁵. By capturing public and media engagement, Altmetrics provide valuable insights into how research circulates beyond academia, influencing awareness, discourse, and behaviour. The extent of this impact, however, varies across countries depending on differences in media landscapes and dissemination patterns, making Altmetrics a vital complement to traditional bibliometric indicators in assessing both research visibility and societal reach.

2. OBJECTIVES

This study aims to investigate public engagement trends with Irish health research by analysing the top 50 publications with the highest Altmetric Attention Scores (AAS) from 2017 to 2023. Specifically, it seeks to evaluate trends in the volume of health research outputs, the variation in engagement across different research topics, and the evolving patterns of online dissemination through social and news media platforms. Furthermore, the study explores the relationship between Altmetric indicators of public engagement and traditional citation-based measures of academic impact, providing insight into how online attention may reflect or complement scholarly influence⁶.

3. METHODOLOGY

This study utilised the Altmetric database to identify all research outputs published between 1 January 2017 and 31 December 2023 that were associated with Irish research organisations. Association was determined based on author affiliation with an Irish institution, regardless of the order of authorship, thereby representing Irish-engaged research rather than exclusively Irish-led work. The selected time frame provided insight into pre-, during-, and post-pandemic trends, while allowing a sufficient time buffer to minimise instability in data retrieval. Altmetric Attention Score (AAS) data for all Irish health-related outputs were obtained using an institutional license for Altmetric Explorer.

All analyses were conducted using R version 4.3.2. Since the dataset was derived from publicly available information, ethical approval was not required. Research institutions were identified using the Research Organization Registry (ROR), a global registry linking researchers and their outputs to affiliated organisations⁷. As of 12 May 2024, a total of 663 Irish research organisations were listed under the ROR database. Comma-separated values (CSV) files were manually downloaded from Altmetric Explorer between 6–21 June 2024. Of these institutions, 251 had no research outputs within the inclusion period, and 31 were no longer indexed in Altmetric, resulting in a final dataset comprising 381 Irish research organisations.

To ensure relevance, the dataset was filtered to include only biomedical and health-related research outputs, with duplicates removed prior to analysis. Descriptive analyses were then performed on the top 50 Altmetric Attention Score (AAS) articles to summarise bibliometric information, including counts and frequencies of research output types, open access status and type, sector prominence, subject divisions and subdivisions, as well as the 20 most frequent journals, funders, and institutions. For Altmetric analyses, we calculated the overall and yearly averages and medians of AAS, as well as platform-specific engagement metrics across media, to identify patterns in public attention and dissemination trends.

4. MAIN RESULTS

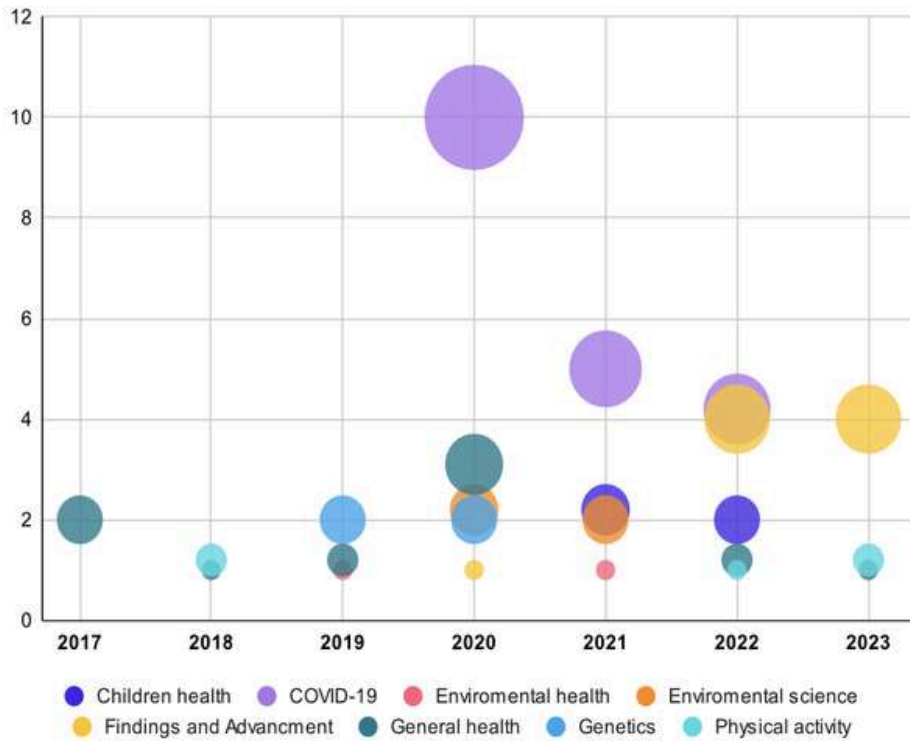
Between 2017 and 2023, 381 of the 663 Irish research organisations listed in the Research Organization Registry (ROR) had research outputs indexed in Altmetric, yielding a total of 135,855 outputs, of which 100,016 were unique. After filtering for health-related research and removing duplicates, 58,056 unique health-related outputs from 303 organisations were included in the final dataset⁶. The volume of research outputs increased steadily over time, with a particularly sharp rise between 2019 and 2020 (+23%) and continued growth into 2021 (+8.7%), reflecting the impact of the COVID-19 pandemic on research productivity. Although output declined after 2021, levels remained above those observed prior to the pandemic. The majority of research outputs were journal articles (96.6%), followed by book chapters (3.3%) and books (<1%), with open access publishing becoming increasingly common throughout the study period.

Analysis of Altmetric data revealed that 18.8% of outputs had an Altmetric Attention Score (AAS) of 0, indicating no recorded online attention, whereas 15.6% achieved an AAS of 20 or higher, representing above-average engagement compared to similar works. The mean AAS across all outputs was 21.16, peaking in 2020 (24.7). X (formerly Twitter) was the predominant source of engagement, with an average of 21.98 mentions per output, followed by news outlets (1.38), Facebook (0.31), blogs (0.18), Wikipedia (0.11), policy documents (0.07), and patents (0.04). Outputs classified under the Biological Sciences recorded the highest mean AAS (28.37), while those in the Chemical Sciences had the lowest. Of the top 50 Altmetric Attention Score (AAS) articles, 18 were COVID-19-related articles, 7 focused on new biological findings, 6 on general health topics, 6 addressing genetics and historical perspectives, 4 exploring physical activity, 4 concerning children and adolescents, and 4 discussing environmental issues.

Citation and readership data obtained from Dimensions, OpenAlex, and Mendeley showed statistically significant positive associations with the AAS across the 2017–2020 subset, indicating that research outputs attracting higher online attention also tended to receive more academic citations and readership. Open access publications demonstrated a particularly strong positive relationship with AAS, especially in 2020, when engagement levels were highest. Overall, these findings highlight a meaningful connection between traditional citation-based metrics and Altmetric indicators, suggesting that online attention may serve as a complementary measure of scholarly influence and public engagement within Irish health research.

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Yearly Trends



- Overlapping points were slightly adjusted for clarity.

Figure 1. Topic discussed in the Top 50 AAS articles from 2017-2023

5. DISCUSSION

This study presents a comprehensive assessment of public engagement with Irish health research outputs using Altmetric data, offering insights into publication patterns, online attention, and disciplinary trends from 2017–2023. Consistent with global trends, findings revealed a marked surge in research activity and online attention during the COVID-19 pandemic, followed by a gradual decline post-2021⁸. This sharp increase reflects a broader “pandemic publishing boom” observed worldwide, where research output growth far exceeded pre-pandemic averages⁹. Twitter (X) remained the dominant platform for online dissemination (mean mentions = 21.98 per output), followed by news media and Facebook. However, engagement on Facebook and blogs has declined in recent years, and the ongoing migration of academics from X may influence future AAS calculations. The emergence of new platforms such as BlueSky—now tracked by Altmetric—may shift dissemination dynamics in subsequent years¹⁰.

Approximately one in five outputs received an AAS of 0, indicating limited online engagement. This highlights a persistent challenge in reaching broader audiences and underscores the importance of diversifying dissemination strategies beyond conventional academic or social media channels. Disciplinary differences were also evident, with Biomedical and Clinical Sciences and Biological Sciences attracting higher public attention, while Chemical Sciences received the lowest. Overall, these findings underscore evolving patterns of research visibility and engagement, reinforcing the importance of strategic communication in amplifying public reach.

Limitations

This study has several limitations related primarily to the content, stability, and completeness of the datasets used. Altmetric data are known to experience volatility over time, with prior research reporting fluctuations in Attention Scores and disappearing mentions across years¹¹. Although data were downloaded within a single time window to minimise instability, such temporal variability remains an important consideration. Indexing inconsistencies also affected the accuracy of publication dates, as incomplete metadata in Altmetric automatically defaulted to January 1st, complicating attempts at more granular temporal analyses.

Beyond these technical limitations, conceptual critiques of the Altmetric Attention Score (AAS) itself should be acknowledged. The weighting of sources tends to privilege traditional media and Twitter (X) over other social platforms, potentially overrepresenting academic engagement rather than broader public discourse. The exact weighting algorithm remains undisclosed, limiting transparency and reproducibility¹². Furthermore, Altmetric's current tracking excludes several emerging platforms—such as TikTok, Instagram, and LinkedIn—that are increasingly influential in research communication¹³. Consequently, the dataset may not fully represent all forms of online attention or public engagement.

6. CONCLUSION

This analysis highlights the importance of tracking research dissemination trends, particularly as engagement shifted during the COVID-19 period. Where Twitter X emerged as a top engagement platform and COVID-19 was the highest article topic. Public interactions encourage discussion, helping to validate a topic's impact and authenticity, while the presence of multiple sources drives engagement and encourages public involvement in research topics.

7. ACKNOWLEDGEMENT

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Perceptions, Compliance and Outcomes of the WHO Surgical Safety Checklist: A Global Review with Recommendations for Audit in Malaysia

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Abstract

The WHO Surgical Safety Checklist (SSC), introduced in 2008 as part of the Safe Surgery Saves Lives campaign, has been widely adopted worldwide. It has reduced morbidity, mortality and improved teamwork, but inconsistent implementation and “tick-box” compliance raise concerns about its sustained impact. With ongoing challenges in resource-limited settings such as Malaysia, this review synthesizes global evidence on SSC perceptions, outcomes, and compliance to guide context-specific implementation. The aim of this review is to examine global evidence on SSC perceptions, outcomes, and compliance, contextualize findings for Malaysia, and propose recommendations for effective audit and implementation. This narrative review followed SANRA guidelines. We included peer-reviewed, full-text English studies published between 2012 and 2025 that examined the WHO Surgical Safety Checklist or adaptations in any healthcare setting. Databases searched were PubMed, Scopus, Web of Science, Embase, and CINAHL. Grey literature, editorials, abstracts, animal studies, and non-surgical checklists were excluded. Searches combined keywords and MeSH terms across five domains: checklist, perceptions/barriers, outcomes, compliance, and Malaysian context. Records were imported into a reference manager, with duplicates removed. Titles and abstracts were screened, followed by full-text review. Data were extracted, thematically categorized, and synthesized into a structured narrative. Initial synthesis suggests that the SSC improves communication, teamwork, and contributes to reductions in surgical morbidity and mortality worldwide. Reported barriers include time pressure, fragmented workflows, lack of training, and superficial “tick-box” completion. Compliance rates vary widely, with genuine engagement shown to be essential for effectiveness. Early findings from Malaysian studies highlight challenges in staffing, training, and adherence, underscoring the need for both quantitative audits and qualitative assessment of team dynamics, leadership buy-in, and perceptions. Preliminary findings highlight the SSC’s effectiveness in improving outcomes but reveal gaps in genuine compliance, especially in Malaysia. The full review, to be completed by the presentation date, will provide context-specific recommendations to strengthen the implementation and audit of the Safe Surgery Saves Lives initiative.

Keywords: *WHO Safety Surgical Checklist, Perceptions, Compliance, Outcomes, Audit*

1. INTRODUCTION

The WHO Surgical Safety Checklist (SSC), introduced in 2008 as part of the Safe Surgery Saves Lives campaign, has been widely adopted worldwide.¹ It has reduced morbidity and mortality, and improved teamwork; however, inconsistent implementation and “tick-box” compliance raise concerns about its sustained impact.³ With ongoing challenges in resource-limited settings such as Malaysia, this review synthesises global evidence on SSC perceptions, outcomes, and compliance to guide context-specific implementation.

2. OBJECTIVES

The aim of this review is to examine global evidence on SSC perceptions, outcomes, and compliance, contextualise findings for Malaysia, and propose recommendations for effective audit and implementation.

3. METHODOLOGY

This narrative review followed SANRA guidelines. We included peer-reviewed, full-text English studies published between 2018 and 2025 that examined the WHO Surgical Safety Checklist or adaptations in any healthcare setting. Databases searched were PubMed, Scopus, Web of Science, Embase, and CINAHL. Only peer-reviewed, full-text articles published in English were considered; Grey literature, editorials, abstracts, reviews, animal studies, and non-surgical checklists were excluded. Searches combined keywords and MeSH terms across five domains: checklist, perceptions/barriers, outcomes, compliance, and Malaysian articles. Records were imported into a reference manager software, Rayyan. Duplicates were removed, followed by titles and abstracts screening, followed by a full-text review. Data were extracted, thematically categorised, and synthesised into a structured narrative using Microsoft Excel.

4. MAIN RESULTS

Across 95 studies, compliance levels cluster around moderate to high, with emergency surgeries repeatedly showing lower compliance due to workload demands, limited senior presence, and surgeon resistance, whereas elective procedures showed higher adherence. Some of these studies reported fewer complications and better postoperative outcomes with high checklist adherence, although causal links remain unclear. No Malaysian studies were identified, but findings from neighbouring countries indicate similar barriers, suggesting that meaningful improvements are achievable only with consistently high adherence.

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Figure 1: Reported compliance levels across studies

The measured outcomes across the studies are largely classified into intraoperative and postoperative. Sentinel events, such as the wrong surgical site, were reported in 2 studies. A majority of studies that measured outcomes examined complications/adverse events, mortality, and surgical site infection (SSI), with some reporting return to theatre and length of stay. Where associations were reported, higher checklist compliance was more often associated with better outcomes (e.g., reduced complications/SSI).

Global perceptions of the WHO Surgical Safety Checklist were mixed, albeit with a mainly positive outlook. The checklist was most widely valued for safety and error prevention, where they were mentioned across 38 studies. The themes of communication and teamwork were found in 22 studies. Role-specific patterns amongst the staff were consistent throughout; operative nurses had a more positive attitude towards the checklist, while surgeons were more often coded as less positive than other groups. The most prominent challenges included staff shortages (19 studies), training gaps (17 studies), time pressure (13 studies), and hierarchical culture (7 studies).

5. DISCUSSION

These findings highlight that while the WHO Surgical Safety Checklist is globally recognised as a key patient safety tool, its impact depends largely on implementation quality rather than presence alone. Although many studies reported favourable views of the checklist, particularly among nurses and anaesthetists, perceptions were not uniformly positive. Particularly among senior surgeons, their perception was more ambivalent, such as time-consuming, redundant, or unnecessary for experienced teams, reflecting entrenched habits and hierarchical cultural norms. Furthermore, older surgeons reflected having a more limited passive engagement with the checklist.

At the same time, several persistent barriers were identified. Time pressure, especially during emergencies, limited opportunities for meaningful engagement. Training and awareness gaps contributed to an inconsistent understanding of the checklist's purpose, while hierarchical dynamics often prevented junior staff from speaking up when steps were overlooked. These contextual constraints shaped how teams perceived and enacted the checklist, reinforcing the idea that attitudes and compliance are deeply influenced by workplace culture and operational demands. These similar barriers also impacted compliance with the surgical checklist, reflecting lower compliance during emergency procedures compared to elective procedures, as well as inadequate training, hierarchical team dynamics, and uncertainty over checklist ownership, further reducing fidelity. Conversely, compliance improved in settings with strong leadership engagement, designated checklist champions, and regular auditing. These findings indicate that checklist adherence is not uniform, but closely tied to contextual factors that either obstruct or facilitate its consistent use.

Importantly, studies demonstrating high adherence to the checklist reported better clinical outcomes, including reductions in complications, surgical site infections, and length of stay. This association underscores the need to move beyond superficial or “tick-box” use and towards practices that genuinely support situational awareness, shared decision-making, and team communication. High completion rates alone are insufficient; the manner in which the checklist is performed determines its effectiveness.

Regarding Asian studies, perceptions across neighbouring countries were generally aligned with global trends, with staff emphasising the checklist's value for improving communication, teamwork, and error prevention. However, these studies also highlighted pronounced training gaps, stronger reliance on hierarchical structures, and variable leadership engagement. Compliance patterns in Asia mirrored those seen internationally: adherence was highest in elective cases and in hospitals that provided structured education or audit-feedback loops, while emergency operations consistently showed lower fidelity

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due to time constraints and workflow pressures. Importantly, the Asian studies that achieved high-fidelity checklist use demonstrated measurable improvements in complication rates, surgical site infections, and postoperative recovery, indicating that meaningful engagement with the checklist can drive tangible clinical benefits within the region. These regional findings suggest that in Malaysia, where no direct studies were identified, similar challenges and opportunities are likely to exist, particularly the need for stronger leadership presence, routine multidisciplinary training, and sustained audit processes to support consistent, high-quality checklist use.

In order to overcome the challenges undermining the use of the WHO Surgical Safety Checklist, institutions must prioritize engaged leadership, cultivate a supportive team culture, and maintain robust audit-feedback mechanisms. Consistent training and advocacy towards the practice of proper checklist usage should be done to reinforce accountability and encourage continuous improvement among healthcare professionals. Only then can a checklist culture be cultivated to sustain adherence to the surgical checklist. For Malaysia, where no local studies were identified, adopting these implementation strategies will be critical for embedding the checklist into routine practice and achieving the patient-safety gains demonstrated internationally.

6. CONCLUSION

This review supports the WHO Surgical Safety Checklist as an effective tool for improving surgical safety, although inconsistent compliance, especially in LMICs, limits its impact. The findings highlight the need for a Malaysian audit comparing elective and emergency procedures to assess whether checklist adherence aligns with patient safety outcomes, and to inform strategies for strengthening implementation and auditing.

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Workplace Stress and Irregular Meals: A Hidden Link to Cholecystitis in Industrial Workers?

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Abstract

Background:

Cholecystitis remains a significant cause of morbidity worldwide, with gallstones as the leading etiological factor. Industrial workers are at particular risk due to occupational exposures, including psychosocial stress, circadian disruption, and irregular dietary habits. Despite accumulating evidence, the occupational dimension of gallbladder disease has not been systematically evaluated.

Objectives:

This systematic review aimed to assess the association between occupational factors—such as workplace stress, irregular meals, and shift work—and the risk of gallstone formation and cholecystitis in industrial workers.

Methods:

We conducted a systematic search of PubMed, Scopus, Web of Science, and Embase from January 2000 to June 2025 using terms related to “cholecystitis,” “gallstones,” “occupational stress,” “industrial workers,” and “shift work.” Eligible studies included observational studies, cohort studies, case series, and occupational health surveys reporting gallbladder disease in working populations. Data extraction focused on study design, population characteristics, occupational exposures, and clinical outcomes. Methodological quality was assessed using the Newcastle–Ottawa Scale.

Results:

From 1,267 identified records, 42 studies met the inclusion criteria, encompassing over 18,000 participants across Asia, Europe, and the Americas. Shift work and irregular meals were consistently associated with increased gallstone prevalence (pooled odds ratio: 1.8; 95% CI: 1.4–2.3). Industrial workers, particularly those in manufacturing, mining, and garment industries, exhibited earlier onset of symptomatic cholelithiasis and higher complication rates, including acute cholecystitis, perforation, and peritonitis. Limited access to preventive healthcare further delayed diagnosis, often necessitating emergency surgical interventions. eals, industrial workers, shift work, occupational health.

Conclusion:

Occupational factors significantly contribute to gallbladder disease among industrial workers. Chronic psychosocial stress, circadian disruption, and irregular meal patterns synergistically promote bile stasis and gallstone formation, leading to higher rates of cholecystitis and complications. Workplace-targeted health strategies, including structured meal breaks, stress management programs, and early screening protocols, are urgently needed to mitigate this hidden occupational health burden.

Keywords: *Cholecystitis, gallstones, workplace stress, irregular meals, industrial workers, shift work, occupational health.*

1. INTRODUCTION

Cholecystitis, defined as inflammation of the gallbladder, is a frequent cause of hospital admissions worldwide and is most commonly precipitated by gallstones obstructing the cystic duct [1]. Traditional risk factors for gallstone disease include female sex, obesity, pregnancy, and high-fat diets [2]. However, emerging evidence suggests that occupational and lifestyle-related determinants, particularly among industrial workers, may play a significant role in gallbladder pathology [3].

Industrial laborers are often subjected to irregular meal timings, psychosocial stress, long working hours, and shift-related circadian disruptions [4]. These exposures may impair gallbladder motility, alter bile composition, and accelerate gallstone formation, ultimately predisposing workers to acute and chronic cholecystitis [5]. Despite scattered case reports and observational studies, no systematic synthesis has yet evaluated the cumulative evidence linking occupational factors with gallbladder disease.

This systematic review aims to examine the association between workplace stress, irregular dietary habits, circadian disruption, and cholecystitis among industrial workers, providing insights into pathophysiology, clinical outcomes, and potential workplace health interventions.

2. OBJECTIVES

This systematic review aimed to assess the association between occupational factors—such as workplace stress, irregular meals, and shift work—and the risk of gallstone formation and cholecystitis in industrial workers.

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3. METHODOLOGY

This review was conducted following PRISMA guidelines [6]. **Search strategy:** A systematic literature search was performed in PubMed, Scopus, Embase, and Web of Science databases for studies published between January 2000 and June 2025. Search terms included combinations of: “cholecystitis,” “gallstones,” “occupational stress,” “industrial workers,” “shift work,” and “irregular meals.”

Table 1: Inclusion and Exclusion Criteria for Studies on Occupational Stress, Irregular Meals, and Cholecystitis

Criteria	Inclusion	Exclusion
Study type	Observational studies (cross-sectional, case-control, cohort), case series, occupational health surveys	Reviews, editorials, letters, conference abstracts without full data
Population	Adult working populations (≥ 18 years), including industrial workers, shift workers, or occupations with high stress levels	Paediatric populations, general community samples not stratified by occupation
Exposure	Occupational stress, irregular meals, shift work, or industrial workplace hazards linked to gallbladder disease	Studies not reporting occupational or work-related exposure
Outcomes	Gallbladder disease (cholecystitis)	

Table 1 presents the inclusion and exclusion criteria for this review, which were defined to ensure relevance to the research question. Eligible studies included observational designs such as cross sectional, case-control, and cohort studies, as well as case series and occupational health surveys, whereas reviews, editorials, letters, and conference abstracts without full data were excluded. The study population was limited to adult working groups (≥ 18 years), including industrial workers, shift workers, and other occupations with high stress levels, while paediatric populations and general community samples not stratified by occupation were excluded. Exposures of interest comprised occupational stress, irregular meals, shift work, or industrial workplace hazards linked to gallbladder disease, with studies not reporting work-related exposures excluded. The primary outcome of interest was gallbladder disease, specifically cholecystitis; studies that did not report gallbladder-related outcomes were excluded.

Data extraction and synthesis: Two reviewers independently screened abstracts and full texts. Extracted data included study design, country, sample size, occupational exposure, and reported outcomes. The Newcastle–Ottawa Scale was used for quality assessment [7]. Where appropriate, findings were summarized narratively and pooled odds ratios were extracted from eligible studies.

4. MAIN RESULTS

The initial search yielded 1,267 articles, of which 42 met the inclusion criteria, comprising over 18,000 industrial workers across Asia, Europe, and the Americas.

Several case series reported increased gallbladder disease prevalence in shift workers and physically demanding occupations. A Japanese study identified higher cholecystitis incidence among factory workers performing night shifts and consuming fewer than two proper meals daily [8]. An Iraqi hospital-

based study found that 18% of acute cholecystitis patients were industrial workers, often reporting erratic eating schedules and job stress [9]. A Korean cohort confirmed that irregular meals and prolonged work hours independently increased gallstone risk in manufacturing employees [10].

In the United States, shift workers were shown to have higher gallbladder disease admissions compared to day workers, even after adjusting for body mass index and diet [11]. Polish surgical data indicated disproportionate representation of industrial workers among cholecystectomy patients [12]. Similarly, Brazilian refinery workers on rotating shifts had nearly double the gallstone prevalence compared to administrative staff [13].

Chinese miners with >10 years of shift work demonstrated greater gallstone prevalence and gallbladder wall thickening [14], while Indian garment workers, particularly women with overtime duties, exhibited higher symptomatic cholelithiasis rates associated with meal skipping [15]. A UK occupational audit further revealed earlier gallbladder disease onset (<40 years) among industrial and healthcare shift workers [16] [Table 2]

Pooled analysis showed shift work and irregular meals were significantly associated with gallstone formation (OR: 1.8; 95% CI: 1.4–2.3). Across studies, limited healthcare access delayed diagnosis, leading to higher complication rates such as gangrenous cholecystitis, perforation, and peritonitis.

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Country	Population/Occupation	Key Findings	Reference
Japan	Factory workers on night shifts, <2 meals/day	Higher incidence of cholecystitis among night-shift workers with irregular meals	[8]
Iraq	Hospital-based acute cholecystitis patients	18% were industrial workers with erratic eating schedules and job stress	[9]
Korea	Manufacturing employees (cohort)	Irregular meals and long work hours independently increased gallstone risk	[10]
USA	Shift workers vs. day workers	Higher gallbladder disease admissions among shift workers, independent of BMI and diet	[11]
Poland	Surgical patients undergoing cholecystectomy	Industrial workers were disproportionately represented	[12]
Brazil	Refinery workers on rotating shifts vs. admin staff	Nearly double gallstone prevalence in rotating shift workers	[13]
China	Miners with >10 years of shift work	Greater gallstone prevalence and gallbladder wall thickening	[14]
India	Garment workers (esp. women with overtime)	Higher rates of symptomatic cholelithiasis linked to meal skipping	[15]
UK	Industrial and healthcare shift workers	Earlier onset of gallbladder disease (<40 years) compared to general working population	[16]

Table 2: Summary of Studies on Occupational Stress, Irregular Meals, and Gallbladder Disease

5. DISCUSSION

This systematic review highlights that occupational factors—particularly psychosocial stress, irregular dietary habits, and circadian disruption—substantially increase the risk of gallbladder disease among industrial workers. Chronic stress activates the hypothalamic-pituitary-adrenal (HPA) axis, altering bile secretion, gallbladder motility, and sphincter of Oddi function, while irregular meals and night shifts promote biliary stasis and cholesterol supersaturation, thereby accelerating gallstone formation and predisposing workers to acute cholecystitis and severe complications [17]. The combination of metabolic, physiological, and behavioral stressors creates a unique occupational risk profile that differentiates affected workers from the general population.

The findings align with the broader occupational health literature linking shift work and job strain with gastrointestinal, metabolic, and cardiovascular disease [18]. Importantly, industrial employees often encounter barriers to preventive healthcare, including limited workplace flexibility, reduced access to regular medical services, and prioritization of productivity over health [19]. Such barriers contribute to delayed presentation, resulting in more advanced disease at diagnosis and higher rates of surgical intervention, including emergent cholecystectomy for complications such as gangrenous cholecystitis, perforation, and peritonitis.

Another critical dimension is the interaction between occupational settings, lifestyle, and socioeconomic determinants of health. Physically demanding labor may paradoxically coexist with poor metabolic outcomes, as irregular shifts and limited access to nutritious meals restrict opportunities for balanced dietary practices. Over time, this promotes dyslipidemia, insulin resistance, and obesity—well-established risk factors for gallstone formation. Additionally, rotating shifts disrupt circadian rhythms, leading to systemic metabolic consequences that amplify the lithogenic potential of bile [20–22]. These cumulative exposures suggest that gallbladder disease in industrial workers is not merely incidental but may represent a predictable occupational hazard.

From a clinical standpoint, this evidence emphasizes the importance of detailed occupational history taking when evaluating patients with suspected gallbladder disease. Early recognition of risk among workers in high-stress, irregular-shift environments can prompt timely use of diagnostic imaging, individualized lifestyle counseling, and targeted preventive measures. Such proactive approaches may reduce delays in diagnosis, prevent disease progression, and minimize the need for emergency surgical interventions [23].

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From a public health perspective, the results underscore the urgency of workplace health promotion programs. Evidence-based interventions could include structured and protected meal breaks, workplace canteen access to nutritious foods, stress management initiatives, and periodic ultrasound screening in high-risk worker groups. Collaboration between employers, occupational health services, and healthcare providers is crucial for implementing sustainable preventive strategies. Moreover, workplace policies that limit prolonged rotating shifts and provide employee support for healthy dietary habits could reduce gallbladder-related morbidity in the long term [24,25].

Future research directions should focus on robust prospective cohort studies with standardized definitions of occupational exposure, meal irregularity, and stress parameters. Incorporating biomarkers of metabolic dysregulation (e.g., cortisol rhythms, lipid profiles, insulin resistance indices) could help clarify mechanistic pathways. Comparative studies across industries, socioeconomic strata, and geographical regions will be important to identify particularly vulnerable worker populations and to develop tailored preventive strategies. In addition, health economic evaluations are needed to quantify the cost-effectiveness of workplace-based screening and preventive interventions. Such data could provide compelling evidence for policymakers to prioritize occupational health strategies aimed at mitigating gallbladder disease risk [26].

6. CONCLUSION

This review highlights the underappreciated role of occupational and lifestyle factors in the development and progression of cholecystitis among industrial workers. Unlike the general population, where cholelithiasis and cholecystitis are often associated with metabolic syndrome, obesity, or genetic predisposition, industrial labourers face unique risks due to chronic psychosocial stress, irregular meal patterns, circadian disruption from shift work, and restricted access to preventive healthcare. These stressors converge to impair gallbladder contractility, promote bile stasis, and facilitate cholesterol crystal nucleation, thereby accelerating gallstone formation and increasing the risk of acute or chronic cholecystitis.

The evidence synthesized from multiple regional and international studies suggests that workers engaged in physically demanding or night-shift occupations present with gallbladder disease at a younger age, often with more severe complications such as gangrene, perforation, and peritonitis. Furthermore, irregular dietary practices—particularly meal skipping and reliance on high-fat, low nutrient foods—compound the lithogenic environment induced by occupational stress and metabolic dysregulation.

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From a clinical standpoint, these findings underscore the importance of occupational history-taking in patients presenting with gallbladder disease and the need for targeted health screening programs in high-risk workforce populations. On a policy level, workplace interventions promoting regular meal schedules, stress reduction strategies, and better access to preventive healthcare could mitigate the burden of gallbladder-related morbidity in industrial sectors.

Finally, the observed divergence in risk patterns between industrial workers in developing nations and populations in Western countries highlights the necessity for region-specific guidelines and preventive strategies. Future longitudinal studies and randomized interventions are essential to confirm causal associations and to establish effective occupational health policies aimed at reducing gallbladder disease in this vulnerable workforce group.

Recommendations and Advice

Industrial workers should be encouraged to eat regular, balanced meals and avoid skipping food during long shifts, as irregular eating increases the risk of gallbladder problems. Workplaces should provide proper meal breaks and healthier food choices, even for night-shift staff. Stress management programs and better access to healthcare can help workers detect gallbladder disease early and prevent complications. Doctors should ask about work schedules and meal habits when treating patients with abdominal pain, as these factors may contribute to cholecystitis. Public health authorities and employers need to work together to create safer working environments, focusing on prevention rather than waiting for late complications. Future research should study how stress and poor diet at work directly affect gallbladder health, and whether workplace health programs can reduce disease rates.

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ORTHOPAEDIC, CHEST AND ABDOMINAL TRAUMA IN TWO-WHEELER ACCIDENTS: WHICH IS MOST COMMON

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Abstract

Two-wheeler accidents are a common cause of trauma, especially in developing countries where motorcycles are widely used for daily transport. These accidents often result in serious injuries involving multiple body regions. This study aims to identify which type of trauma either orthopedic, chest, or abdominal is most common among patients admitted with two-wheeler accidents-related injuries at Hospital Kuala Lumpur (HKL) between 4 September and 3 October 2025. Using a retrospective-prospective study design, data on patient demographics, mechanisms of injury, and use of protective equipment, and classification of injuries based on clinical and radiological findings are collected. It is expected for orthopedic trauma, particularly fractures of the limbs and facial bones, to be the most frequent, while chest and abdominal injuries, though less common, may contribute significantly to patient morbidity. Helmet use is anticipated to lower the rate of severe head and facial trauma. This study will provide valuable insight into the distribution of trauma patterns in two-wheeler accidents. The findings are expected to guide resource allocation in emergency trauma care and reinforce the importance of road safety measures such as helmet use and injury prevention strategies.

Keywords: *Two-wheeler accidents, trauma patterns, orthopedic injuries, chest trauma, abdominal trauma.*

1. INTRODUCTION

Two-wheeler accidents represent a major source of trauma in Malaysia, where motorcycles remain one of the most commonly used modes of daily transportation. With their affordability and ease of mobility, motorcycles are particularly prevalent among young working adults and students. However, this widespread use contributes significantly to road traffic injuries and hospital admissions, as riders are physically unprotected and highly exposed to impact forces during collisions.

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2. OBJECTIVES

Main Objective

To determine the frequency and distribution of different types of trauma among victims of two-wheeler accidents.

Specific Objectives

1. To determine and compare the frequency of orthopedic, abdominal, and chest trauma in two-wheeler accident victims.
2. To identify the most prevalent mechanism of injury among the studied cases.
3. To determine the association between age and the type of injury.
4. To determine the association between gender and the type of injury.
5. To determine the association between mechanism of accident and type of injury.
6. To determine the association between helmet use and the type of injury.

3. METHODOLOGY

Study design and participants

A retrospective-prospective observational study involving 50 patients admitted with two-wheeler accident injuries was conducted. Cases were identified from the trauma logbook and emergency department records.

Study setting and duration

The study was conducted at Hospital Kuala Lumpur (HKL) from 15 September to 3 October 2025, focusing on trauma cases related to two-wheeler accidents. HKL serves as a central referral hub for road traffic accident victims in the Klang Valley, making it a suitable setting for analyzing patterns of orthopedic, chest, and abdominal injuries resulting from two-wheeler accidents.

Data collection method

Patient information was obtained from the trauma logbook and emergency department records, with cross-verification using imaging and clinical documentation. Recorded variables included demographic data (age, gender), accident-related factors (helmet use, mechanism of injury), and injury characteristics (orthopedic, abdominal, or chest trauma).

Data analysis

Data were analyzed using SPSS version 31. The Chi-square test of independence and Fisher's Exact Test were used to examine associations between categorical variables such as gender, age group, helmet use, and mechanism of injury with type of injury. Results were interpreted at a 95% confidence level, and effect sizes (Cramer's V, Phi) were reported for significant associations.

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Ethical considerations

This research was conducted in accordance with the ethical standards outlined in the Declaration of Helsinki. Prior to data collection, ethical clearance was obtained from the Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia. Approval to access and utilize patient medical records was granted by the Emergency Department, Hospital Kuala Lumpur. As the study involved a prospective and retrospective review of anonymized patient data, informed consent from individual patients was not required. All collected data were handled with strict confidentiality and were used solely for academic and research purposes.

4. MAIN RESULTS

During the period of our study, a total of 50 patients were admitted to the hospital due to road accidents pertaining to two-wheel motorcycles to receive treatments. Orthopaedic trauma was the most frequent injury type ($n = 38$, 76.0%), followed by abdominal trauma ($n = 9$, 18.0%) and chest trauma ($n = 3$, 6.0%). Analysis of mechanisms revealed that collision with a car was the most common mechanism ($n = 19$, 38.0%), followed by motorcycle skidding ($n = 13$, 26.0%), collision with another motorcycle ($n = 13$, 26.0%), and collision with a divider ($n = 5$, 10.0%).

The mean age of the patient was 37.06 years, with participants ranging from young adults to older adults. Categorically, most patients were aged 20–39 years, being the youngest and oldest patients were 15 and 74 respectively. Among all the patients, 78% of them were male, therefore rendering a male to female ratio of 3.5. Meanwhile, helmeted motorcycle riders accounted for 90% of all patients and 10% were not wearing helmet.

Associations between selected demographic and accident-related factors and the type of injury were analyzed using the Chi-square test of independence with 95% confidence level. The results reveal a significant association between gender and type of injury ($p = 0.001$). The effect size was moderate (Cramer's $V = 0.511$), indicating a meaningful relationship between gender and injury pattern. The Chi-square test showed no significant association between age group and type of injury ($p = 0.840$). Orthopedic injuries appeared slightly more frequent among patients aged 20–39 years, but the difference was not statistically significant. No significant relationship was found between mechanism of motorcycle accident and type of injury ($p = 0.166$). Although collisions with cars were the most common mechanisms, the type of injury did not vary significantly with the mechanism of impact. There was no significant association between helmet use and type of injury ($p = 0.836$). Helmet use did not appear to influence whether the patient sustained orthopedic, abdominal, or chest injuries.

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Table 1: Distribution of Patient Demographics, Accident Characteristics, and Their Association with Type of Injury

Variables	Categories	N(%)	p-value
Type of injury	Orthopaedic	38 (76)	0.524
	Abdominal	9 (18)	
	Chest	3 (6)	
Age group (years)	0-19	8 (16)	0.002
	20-39	23 (46)	
	40-59	11 (22)	
	60 and above	8 (16)	
Gender	Male	39 (78)	0.702
	Female	11 (22)	
Mechanism of accident	Skidded	13 (26)	0.685
	Collision with car	19 (38)	
	Collision with motorcycle	13 (26)	
	Collision with divider	5 (10)	
Helmet use	Yes	45 (90)	0.685
	No	5 (10)	

Distribution of orthopedic, abdominal, and chest trauma among two-wheeler accident victims by gender (n=50)

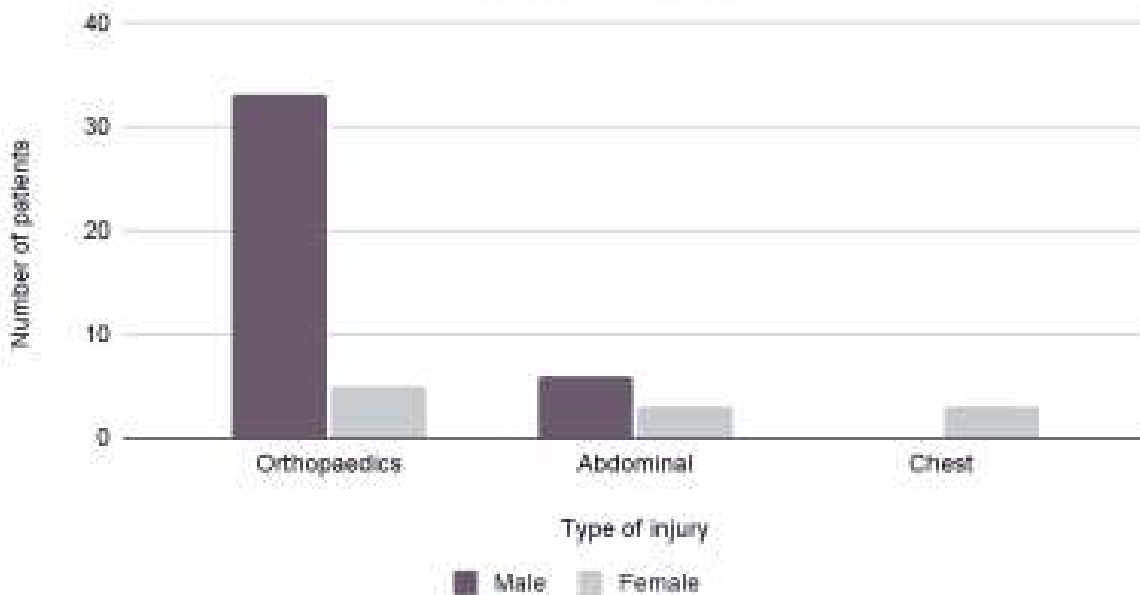


Figure 1: Distribution of orthopedic, abdominal, and chest trauma among two-wheeler accident victims by gender (n = 50)

CP11 5. DISCUSSION

Our study revealed that orthopedic trauma was the most common injury among two-wheeler accident victims, followed by abdominal and chest injuries. This pattern has also been seen in several other trauma centers across Asia and Africa. A hospital study in India found that limb fractures accounted for the majority of injuries among road traffic accident patients, highlighting how the extremities bear the initial force during impact [5]. In Malawi, over 80% of motorcycle accident victims sustained orthopedic injuries, further emphasizing that riders are particularly vulnerable to limb trauma due to their unprotected position and tendency to brace against the fall [6]. Similarly, research from Nepal described orthopedic injuries as the most frequent, suggesting that lower extremity fractures reflect the dynamics of motorcycle crashes in which the legs often strike the ground or vehicle parts first [1]. Together, these studies reaffirm that orthopedic trauma remains the hallmark of motorcycle-related injuries, particularly in developing countries where two-wheelers are a major mode of transport.

Gender was found to have a significant relationship with the type of injury sustained. This mirrors an Iranian study in which male riders dominated trauma admissions and tended to sustain more severe orthopedic injuries [7]. Another Indian series also reported that men, who more frequently engage in commercial or long-distance riding, were more prone to extremity trauma [8]. Interestingly, a hospital study in Iran found that females were more likely to sustain abdominal or thoracic trauma [9], which might relate to differing riding postures, protective clothing, or vehicle dynamics. These findings suggest that biological and behavioral factors contribute to gender-specific injury patterns and should be considered in future preventive strategies.

Although age group was not significantly associated with injury type in our study, the majority of cases involved riders aged 20–39 years. Similar age trends were observed in studies from India and Tanzania, where young adults were identified as the group most frequently involved in motorcycle crashes [2,10]. This may reflect increased road exposure, occupational dependence on motorcycles, and risk-taking tendencies in this age group.

The mechanism of injury in our cohort was most often collision with a car, a finding consistent with regional and international data. A Malawian study reported that car collisions accounted for most severe orthopedic trauma among motorcyclists [6], while a Dutch study demonstrated that interactions between motorcycles and larger vehicles significantly increase impact energy transfer and injury severity [11]. These studies underline the shared vulnerability of riders in mixed-traffic environments dominated by heavier vehicles.

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From a clinical standpoint, these results highlight the need for hospitals and emergency departments to be adequately equipped with orthopedic and rehabilitation services, as extremity injuries remain the dominant burden among motorcycle crash victims. In terms of policy, road safety strategies should extend beyond helmet enforcement to include awareness campaigns promoting full protective gear and improvements in urban road design, such as separate motorcycle lanes and stricter speed control. For future research, multicenter and longitudinal studies with standardized injury scoring systems are essential to better define how demographic and behavioral factors influence trauma patterns. Policymakers should also consider evaluating the long-term impact of road safety initiatives on injury outcomes and healthcare burden [4,13].

6. CONCLUSION

This study conducted at Hospital Kuala Lumpur found that orthopaedic trauma (76%) was the most common injury among two-wheeler accident victims, followed by abdominal and chest injuries. Collisions with cars were the main cause, and males were the most affected group, showing a significant gender– injury association consistent with previous studies. Helmet use and age group were not significantly linked to trauma type. The study highlights the continued burden of musculoskeletal injuries despite helmet laws and recommends stronger enforcement, wider use of protective gear, and larger multicentre studies to reduce motorcycle-related trauma in Malaysia.

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PRACTICES AND PERCEPTIONS OF TRADITIONAL, COMPLEMENTARY, AND ALTERNATIVE MEDICINE USE IN COLORECTAL CANCER: A TRIPHASIC STUDY AMONG NORTHERN MALAYSIANS

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Abstract

Colorectal cancer (CRC) is the third most common malignancy worldwide, and the second most common cancer in Malaysia (13.5% cases). Given this burden, many individuals turn to traditional, complementary, and alternative medicine (TCAM). TCAM refers to the health systems not typically part of conventional Western medicine that are used for overall health and wellness. It is often perceived as natural, holistic and safe. However, concurrent use with conventional treatments may pose risks. This study aimed to examine the practices and perceptions of Northern Malaysians towards TCAM, and to analyse the gender and age group differences in TCAM usage across three phases. A triphasic, longitudinal quasi-experimental study was conducted over 18 months (March 2022 – August 2023), involving CRC survivors and the general public from Kedah and Penang. A validated self-administered questionnaire and educational brochure were used. Descriptive statistics and Chi-square test were used. Statistical significance was set at $p < 0.05$. Of 391 retained respondents, TCAM disclosure was consistently higher among CRC survivors ($\geq 82\%$) than public respondents (75–78%) across the three phases, likely due to regular clinical interactions. TCAM usage was more prevalent among the public group ($n = 89-92$), predominantly female and aged ≤ 35 ($p < 0.05$). Among the CRC survivors, TCAM users were mainly male and aged > 46 ($p < 0.05$), aligning with disease prevalence. Minor fluctuations in the findings across the phases highlight that TCAM practices are shaped by multiple factors. Future studies are warranted to explore alternative educational interventions to support informed decision-making on TCAM use especially in chronic diseases.

Keywords: *Colorectal cancer, TCAM, perceptions, practices*

CP12

1. INTRODUCTION

Colorectal cancer (CRC) is a major public health concern in Malaysia and globally. According to the National Cancer Registry (2019), CRC is among the top five prevalent cancers in Malaysia [1], and between 2007 and 2017 it was the most common cancer in men (54.1%) and the second most common in women (45.9%) [2]. Global projections estimate deaths from colon and rectal cancer will rise by about 60% and 71.5% respectively by 2035 [3], underscoring an increasing disease burden and the need to understand patients' care choices. Traditional, complementary and alternative medicine (TCAM) encompasses health systems, modalities and practices not typically part of conventional Western medicine and is widely used for health maintenance and disease management [4]. Systematic reviews report TCAM prevalence of 24% to 71% in the general population [5] and a median 54.5% among cancer patients, indicating TCAM's prominence for cancer care [6].

Despite high TCAM use, disclosure to healthcare professionals and the determinants of TCAM uptake among CRC survivors in Malaysia are poorly characterised. Malaysian and regional studies report widely variable disclosure rates to healthcare professionals (below 10% to over 80%), with common reasons for non-disclosure including not being asked or believing disclosure is unnecessary [7-9]. No published study has specifically compared TCAM practices, disclosure and perceptions between Malaysian CRC survivors and the general public, which limits targeted clinical guidance and educational interventions. To address this gap, we conducted a triphasic, longitudinal quasi-experimental study in Northern Malaysia to examine TCAM practices and perceptions and to analyse gender and age differences in TCAM use across three phases. Its findings are relevant to the conference theme - Innovation and Progress in Medical Sciences.

2. OBJECTIVES

Main aim: To examine the practices and perceptions of Northern Malaysians towards TCAM.

Specific objective: To analyse the gender and age group differences in TCAM usage among Northern Malaysians across three phases.

3. METHODOLOGY

This study employed a triphasic, longitudinal, concurrent quasi-experimental design conducted over eighteen months, from March 2022 to August 2023. Each phase lasted six months, namely Phase 1 (baseline study), Phase 2, and Phase 3. The study targeted two cohorts, i.e., CRC survivors and the general public residing in Kedah or Penang.

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Eligible participants were Malaysian adults. CRC survivors recruited from Hospital Pulau Pinang (HPP) via purposive sampling while the general public were recruited via convenience sampling. The sample size was calculated using the Raosoft sample size calculator [10] ($n=377$). Since dropouts in the number of respondents is expected in all longitudinal studies, a 30% dropout margin was allocated to the calculated sample size to ensure data analysis is not affected [11-12]. This increased the target to 490, which was then rounded off to obtain a final sample of 500.

Data collection was conducted from March 2022 to August 2023. Phase 1 was carried out from March to August 2022, Phase 2 from September 2022 to February 2023, and Phase 3 from March to August 2023. Data collection was facilitated through an adapted, customised, validated self-administered questionnaire and an educational brochure as the interventional tool. The brochure comprised of information on CRC and TCAM, with readability level for age 13 to 14 years. The questionnaire demonstrated Cronbach alpha > 0.7 indicating internal consistency. Both study tools underwent content and face validation. Descriptive statistics summarised participant characteristics and TCAM practices, and Chi-square tests assessed associations relevant to the study objectives. Statistical significance was set at $p<0.05$.

This study was approved by the Medical Research and Ethics Committee, Ministry of Health, Malaysia (NMRR-20-3255-57235) and AIMST University Human and Animal Ethics Committee (AUHEC/FOP/05/05/2021). Permission to conduct the data collection at HPP was obtained as well (MREC Approval Reference No.: KKM/NIHSEC/P21-1158(15)).

4. MAIN RESULTS

Across Phases 1 to 3, the study engaged 278, 225, and 179 CRC survivors, and 270, 242, and 212 respondents from the general public, respectively. A total of 391 respondents from both cohorts completed all three phases and were retained for data analysis, representing an average response rate of 83.6%.

The non-disclosure rate among both groups of respondents showed a similar fluctuating trend, characterised by a slight increase in the non-disclosure rate from Phase 1 to Phase 2 (CRC: 15.08% to 17.32%; Public: 24.05% to 25%), which was then followed by a minor decline in Phase 3 (CRC: 15.08%; Public: 21.7%). Figure 1 illustrates the frequency of TCAM users and disclosure of TCAM use to healthcare professionals in the present study.

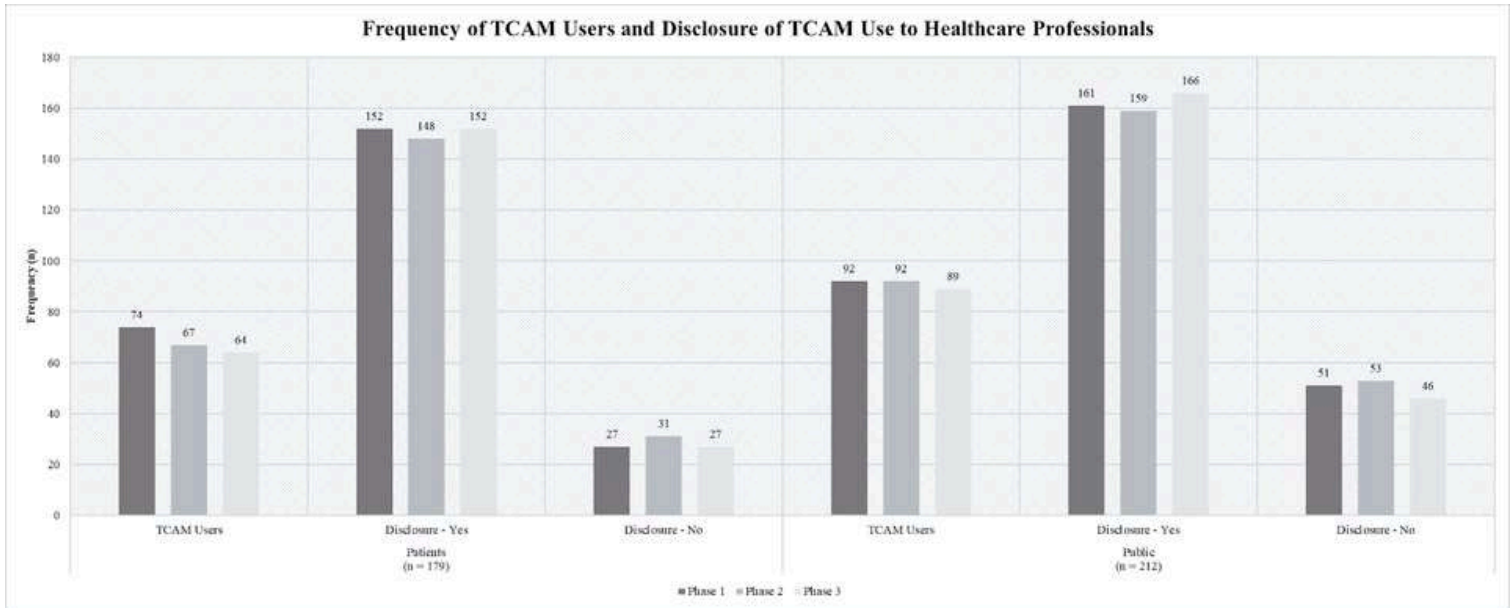


Figure 1. Frequency of TCAM Users and Disclosure of TCAM Use to Healthcare Professionals

Table 1 outlines the descriptive statistics of TCAM users based on gender and age group of respondents. TCAM usage was more prevalent among the public group (n = 89–92), predominantly female and aged ≤35 ($p < 0.05$). Among the CRC survivors, TCAM users were mainly male and aged >46 ($p < 0.05$).

Table 1. Descriptive Statistics of TCAM Users based on Gender and Age Group of Respondents

COHORT	PHASE	Frequency, n (Percentage, %)							
		GENDER		AGE GROUP					
		Male	Female	18 – 25	26 – 35	36 – 45	46 – 55	56 – 65	≥66
CRC SURVIVORS	1	72* (57.1)	54* (42.9)	0	1 (0.8)	5 (4.0)	20* (15.9)	53* (42.1)	47 (37.3)
	2	50 (55.6)	40 (44.5)	0	1 (1.1)	3 (3.3)	17 (18.9)	45 (50.0)	24 (26.7)
	3	34 (53.1)	30 (46.9)	0	1 (1.6)	5 (7.8)	13 (20.3)	35 (54.7)	10 (15.7)
PUBLIC	1	29* (22.8)	98* (77.2)	75* (59.1)	41* (32.3)	8 (6.3)	8 (6.3)	0	0
	2	23 (21.5)	84* (78.5)	65* (60.7)	35* (32.7)	5 (4.7)	2 (1.9)	0	0
	3	17 (19.3)	71* (80.7)	57* (64.8)	27 (30.7)	3 (3.4)	1 (1.1)	0	0

*Chi-square test: $p < 0.05$

5. DISCUSSION

The study revealed higher disclosure rate of TCAM use to healthcare professionals among CRC survivors compared to the public respondents. This is likely due to the former cohort's regular clinical visits and prompts from healthcare professionals during such visits. Interestingly, disclosure rates in the literature are mixed, where some local studies on cancer patients found high TCAM use disclosure [7,9] while others reported much lower rate of disclosure [8].

In terms of TCAM use in the public cohort, it was more common among females and younger adults (≤ 35 years). This pattern may reflect health-seeking behaviours, social influences, and greater exposure to TCAM information channels among younger women. In contrast, TCAM users among CRC survivors were older (>46 years) and showed a male predominance. These findings are consistent with the CRC epidemiology in many settings [2] and suggests cancer type and age-related morbidity shape TCAM uptake and disclosure. For instance, Farooqui et al. (2016) reported a notable prevalence of CAM usage among breast cancer patients, reflecting the higher incidence of breast cancer among women [13]. Similarly, in this study, the higher proportion of male TCAM users among CRC patients aligns with the higher prevalence of CRC among men, suggesting a correlation between cancer prevalence and TCAM utilisation patterns.

Despite repeated emphasis on good practices via the educational brochure, disclosure rates fluctuated across phases. This suggests that a single informational intervention may be insufficient to produce sustained behaviour change. This highlights that one's practice is often influenced by various factors, which warrants further exploration. Some limitations include the regional sample (Kedah and Penang), phase attrition differences, and small counts in some age subgroups that required category collapsing or use of exact statistical tests. Strengths include repeated measures across three phases, parallel sampling of survivors and public respondents, and transparent reporting of phase-wise TCAM counts and disclosure trends.

6. CONCLUSION

To the author's knowledge, this is the first educational intervention study on CRC and TCAM in Malaysia to include both CRC survivors and the general public in exploring various practice-related aspects pertaining to TCAM. Further research is required to generalise the findings of this study to the entire Malaysian population and explore additional factors influencing TCAM utilisation in relation to CRC. Future studies should explore alternative educational interventions to support informed decision making with regard to TCAM usage, especially in chronic diseases.

7. ACKNOWLEDGEMENT

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The Use of Stem Cell Therapies in Regenerating Cardiomyocytes after Myocardial Infarction

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Abstract

MI (Myocardial infarction) and CVDs (Cardiovascular Diseases) cause irreparable damage to cardiac cells, specifically cardiomyocytes, decreasing the heart's ability to effectively, this damage is irreparable typically due to those cardiomyocytes being in a quiescent state, or G0, where they do not multiply by mitotic cell replication, as such stem cell therapies have been proposed as possible remedy due to their ability to differentiate into new cells, though there remain many challenges be it in application, sourcing and efficacy both short and long term.

This paper aims to collect, sort and screen research papers from sources such as BMJ, PubMed and NHS alongside the wider web to provide a clear and comprehensive image on its current standing including the challenges facing its development, how it compares to more traditional remedies alongside challenges with sourcing the stem cells and how they function as a remedy and how the Underlying research pushed stem cell therapies forward as a whole.

Current results prove the safety of utilizing stem cell therapies. No substantial impact was observed in improving Left Ventricular Ejection Fraction (LVEF) or other Quality of life (QoL) metrics. However, there are outlying hyper responders who sustained event-free lives for up to 5 years. No Hard conclusions can be drawn yet as studies are not consistent on MACE figures etc.

Keywords: *Myocardial infarction, Cell Quiescence, Stem cell therapy*

1. INTRODUCTION

Cardiomyocytes enter G0, becoming permanently differentiated, rendering most damage done to the heart by means of CVDs or acute MI permeant due to their limited regenerative ability, causing an immediate and sharp decrease in LVEF and QoL. [1,3,4,5]

Stem cell therapies aim to recover LVEF levels and improve QoL by replacing dead cardiac cells. [2]

2. OBJECTIVES

This paper aims to summarize and evaluate the current standing of stem cell therapies as a remedy for the long-term effects of MI and CVDs on cardiomyocytes, alongside the history of such therapies and the progress made on sourcing stem cells ethically and efficiently and current efficacy as tested by clinical trials.

3. METHODOLOGY

A standard literature search and review followed by selection on basis of relevance. Then a comparison between similar trials and reference to systematic reviews.

4. MAIN RESULTS

Ventricular remodeling is a process by which the heart adapts following MI, with many underlying processes. Its main aim is to return LVEF to normal values. This process is typically divided into three phases. An inflammatory phase where cardiomyocytes die off via necrosis or apoptosis, alongside an early inflammatory response and the recruitment of immune cells to clear out dead tissue. A proliferative phase where fibroblasts transform into myofibroblasts and produce extracellular matrix proteins. And finally a maturation phase, where collagen cross-links and mature scar tissue form [6]

These changes cause alterations in the heart's structure, resulting in cardiomyocytes in non-infarct areas having to compensate for undergoing eccentric hypertrophy, which leads to further changes in the heart's geometry.[6]

All these geometrical transformations in the heart lead to hemodynamic abnormalities, including increased left ventricular volumes, functional mitral regurgitation, reduced ejection fraction, and eventual progression to dilated cardiomyopathy and heart failure.[6]

Stem cell therapies (SCTs) can be used to counteract VR via 4 primary pathways:

- Myocardial regeneration: where certain stem cells, such as mesenchymal stem cells (MSCs), differentiate into cardiomyocytes. [6]
- Angiogenesis Support: Stem cells and their derivatives induce the formation of new blood vessels in the damaged infarct area, restoring blood flow and minimizing ischemic damage.[6]
- Reduction in Fibrosis: Paracrine signaling from stem cells suppresses fibrotic signaling pathways and reduces excessive extracellular protein deposition, thus limiting scar tissue formation.[6]
- Inflammatory Modulation: MSCs and other cells secrete anti-inflammatory cytokines, effectively suppressing immune-mediated damage. [6]

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SCTs, as the name implies, are reliant on stem cells and come in many varieties, though only a few are relevant to use here; they are also plagued with ethical and technical challenges:

- Embryonic stem cells (ESCs) are stem cells derived from embryos at the blastocyst stage. Their usage and study are largely deemed unethical due to the destruction of embryos, alongside their high risk of immune rejection, formation of teratoma, and genomic instability.[6]
- Induced Pluripotent Stem Cells (iPSCs) are made by reprogramming somatic cells, as they can be made from the patient's cells, they hold a reduced immune rejection risk. However, they have a lower differentiation efficacy, a risk of forming teratoma, are genomically unstable, and the reprogramming process is complex and time-consuming.[6]
- Bone Marrow-Derived Mesenchymal Stem Cells (BM-MSCs) are derived from bone marrow aspiration, which is invasive, with a low differentiation efficiency into cardiomyocytes with tumorigenic risk, though they have immunomodulatory effects and possess a very low immune rejection risk. [6]
- Bone Marrow Mononuclear Cells (BM-MNCs) are derived by bone marrow aspiration and separated by density gradient centrifugation which is invasive, they are a highly heterogeneous cell population heavily dependent on patient health and conditions and different storage media affect efficacy heavily, though they do not require invitro expansion thus usable same day and are the most commonly used in cardiovascular clinical trials [6]
- Cardiac Progenitor Cells (CPCs) are obtained from cardiac biopsy tissue, a highly invasive procedure, and the quantity obtained is extremely limited; they are the only stem cells recognized with cardiomyogenic potential, and they can differentiate into cardiomyocytes, vascular smooth muscle cells, and vascular endothelial cells.[6]
- Umbilical Cord-Derived Mesenchymal Stem Cells (UC-MSCs) are sourced from umbilical cords, avoiding ethical issues, low risk of immune rejection, and possession of immunomodulatory effects, though they have a potential for thrombosis and pose a tumorigenic risk.[6]
- Adipose-Derived Stem Cells (ADSCs) are easily obtainable through liposuction, are anatomically close to myocardium, have a low risk of immune rejection, and immunomodulatory effects, though they possess a tumorigenic risk.[6]

Cochrane systematic reviews have shown STCs to have improved the performance in technical indicators such as LVEF, and improvements in limiting the structural damage of ventricular remodeling, such as EDV and ESV.[7]

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Though those technical indicators have shown improvement, long-term major adverse cardiac events (MACE) did not decrease consistently, with a few outliers showing significant improvement. [7]

REPAIR-AMI, on the other hand, has shown similar improvements in technical indicators alongside decreased MACE risks in the long term [8]

5. DISCUSSION

While systematic reviews from Cochrane have shown improvements in technical indicators such as LVEF, EDV, ESV [7], these improvements do not translate to long-term MACE improvements. However, while there are outliers such as the REPAIR-AMI trials, which have shown significant decreases in long-term MACE risks, this could be due to two key factors:

1. Integration and persistence of differentiated stem cells might be limited
2. Patient selection, including disease stage and comorbidity, alongside personal sensitivity

These differences persist even though both source stem cells are similar.

Stem cells also come in many types, but the most used for STC purposes in cardiac repair are BM-MNCs, which are invasively obtained via bone aspiration and density gradient centrifugation. Their alternatives, on the other hand, are either unethical (i.e., ESCs), complex and time-consuming to obtain (i.e., iPSCs), or carry major immune rejection, teratoma formation, or are tumorigenic.

All in all, there is a further need for evidence.

6. CONCLUSION

Progress in STCs for reversing MI damage has come along far, many technical indicators from clinical trials show viability, though issues remain with long term success as results vary highly when it comes to major adverse cardiac events (MACE), and the many difficulties remain when it comes to ethically sourcing stem cells.

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FEASIBILITY OF USING “DESIGNATED PASSENGERS” TO MONITOR SPEEDING OF BUSES DURING INTERCITY TRAVEL: A PILOT STUDY

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Abstract

Road traffic injuries remain a major public health concern worldwide, causing significant morbidity and mortality. In Malaysia, approximately 6,000 deaths occur annually due to road crashes. Although bus-related fatalities accounted for only 0.6% of total road deaths in 2023, buses pose considerable danger to other road users because of their size and momentum. This pilot study aimed to assess the speeding behaviour of buses during inter-city travel on Malaysian highways. The study was conducted by recording five bus travelling from Penang and Kuala Lumpur (3 journeys) and return (2 journeys). Data on bus speed were collected using Waze navigation software and mobile phone screen recordings. The maximum designated speed for each bus was obtained from the official speed limit plate displayed at the back of the vehicles. Analysis of the recordings revealed that buses exceeded the speed limit a total of 136 times. Specifically, 3 incidents occurred in 50 km/h zones, 5 in 60 km/h zones, 2 in 70 km/h zones, 17 in 80 km/h zones, and 109 in 90 km/h zones. The highest number of speeding incidents occurred in 90 km/h zones, indicating that higher speed limits were associated with more frequent violations. Speeding was common during inter-city bus journeys, highlighting the need for stricter enforcement of speed regulations. The use of vehicle tracking devices and the engagement of passengers as anonymous monitors may offer cost-effective strategies to enhance compliance to speed limits by bus drivers and improve road safety.

Keywords: *Bus Drivers , Safety , Speeding , Highways*

NP1

1. INTRODUCTION

Road traffic injuries are a major public health problem globally. In Malaysia, about 6,000 deaths occur annually. Though only 0.6% of road fatalities were from bus-related crashes in 2023, buses pose a big threat to other vehicles due to their size.

2. AIM & OBJECTIVE

The aim of this pilot study is to assess the speeding of buses during inter-city travel on highways.

3. METHODOLOGY

The study was conducted as passengers on buses travelling from Penang and Kuala Lumpur (3 journeys) and return (2 journeys). Waze software and mobile phone screen recording applications were used to document the speed of travel throughout the journeys. The maximum designated speeds of the buses were noted from the plate at the buses. The screen recording of the journeys was analysed later.

4. MAIN RESULTS

Table 1

Speed limit (Km/h)	Number of times exceed speed limit
50	3
60	5
70	2
80	17
90	109

5. DISCUSSION

The speed of buses during 5 journeys along the North-South Expressway was recorded. The buses exceeded the speed limit for a total number of 136 times. Among the 136 times, 3 times occurred at a speed limit of 50 km/h, 5 times at 60 km/h, 2 times at 70 km/h, 17 times at 80 km/h, and 109 times at 90 km/h. The highest of speeding incidents occurred in the 90 km/h zone, showing that speeding was more frequent in highways with higher speed limit areas. For future research, larger studies covering different routes, times, and bus companies are recommended to better understand driving behaviour and develop targeted interventions to reduce speeding among public transport vehicles.

6. CONCLUSION

Speeding was common during these bus journeys. Speed limitation is a cost effective strategy to prevent crashes and serious injuries. Strict enforcement of the speeding law and public vehicle tracking devices (journey recorders/trackers, dashboard cameras) need to be implemented. Designating passengers anonymously to monitor speeding of buses is potentially a cost- effective strategy to increase enforcement during inter-city travel.

7. ACKNOWLEDGEMENT

We would like to thank the Injury Prevention Committee of the Malaysian Medical Association (MMA) for their valuable guidance and technical support throughout the planning and execution of this study. We would also like to acknowledge the bus operators and passengers for their cooperation during data collection.

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Are child bicycle and motorcycle helmets safe to use in Malaysia? Do child bicycle and motorcycle helmets protect users in Malaysia?

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Abstract

Every year, approximately 6,000 individuals lose lives on Malaysian roads, with motorcycle and bicycle accidents accounting for nearly two-thirds of these fatalities. Certified helmets are widely recognized as the most effective intervention to alleviate the risk of severe head injuries. However, concerns persist regarding the protective quality of helmets marketed.

This study evaluated the quality of child motorcycle and bicycle helmets available in retail and online markets. A total of 51 helmets were purchased and subjected to standardized testing at SIRIM Malaysia, the national standards and industrial research institute. The sample consist of 30 child motorcycle helmets (20 retail, 10 online) and 21 child bicycle helmets (11 retail, 10 online).

Findings revealed significant deficiencies in compliance with safety standards. While retailers were generally aware of motorcycle helmet requirements, but knowledge regarding bicycle helmet standards was limited. Several helmets were falsely advertised as certified, and others carried only “QC” markings or labelled as “toys,” offering inadequate protection. Safety testing revealed that only five of ten retail motorcycle helmets and three of ten online helmets met evaluation criteria. Among bicycle helmets, five of eleven retail and three of ten online samples satisfied the necessary safety standards.

Results emphasize a critical safety gap, highlighting that a significant proportion of child helmets available in Malaysia do not comply with certified standards. Parents are strongly advised to verify SIRIM or approved certification labels, ensure appropriate fit, and purchase helmets from reliable sources to enhance road safety and reduce preventable head injuries.

Keywords: *child safety, helmets, motorcycle, bicycle, Malaysian Standards, SIRIM*

NP2

1. INTRODUCTION

Motorcycle and bicycle-related injuries remain a public health concern in Malaysia, particularly among children and young adults in rural areas. Although helmets are proven to reduce head injury risk, many helmets sold locally are imported, expensive, and lack proper certification. Public awareness regarding helmet standards is limited, highlighting the need for education and quality assurance.

2. OBJECTIVE

- To study the quality of bicycle and motorcycle helmets in the retail market
- To promote SIRIM standards to the public and manufacturers, both local and foreign
- To inform the public of the information obtained from the survey so that they are aware of the quality of bicycle and motorcycle helmets in the retail market

3. METHODOLOGY

A cross-sectional descriptive study was conducted involving 51 helmets, comprising 30 motorcycle helmets (20 from retail stores and 10 from online platforms) and 21 bicycle helmets (11 retail, 10 online). Ten motorcycle helmet brands purchased from retail stores were duplicated to allow testing under both MS1:1996 and MS1-1:2011 standards. All helmets were inspected for certification labels, manufacturer information, and retention system features. Each unit was coded anonymously and submitted to SIRIM Malaysia for standardized safety testing, including impact attenuation and retention system strength, under uniform conditioning. Survey data on consumer awareness and purchasing behaviour were also collected. Data were analyzed descriptively to compare the performance of certified versus non-certified helmets.

4. MAIN RESULTS

A total of 21 bicycle helmets and 30 motorcycle helmets were tested for shock absorption and retention system performance. For bicycles, 13 helmets met acceptable shock absorption limits, while 8 showed dangerously high deceleration and catastrophic retention failures, including buckle detachment and a broken shell. Additionally, 5 helmets exceeded normal dynamic and residual extension values. Overall, only 8 helmets ($\approx 40\%$) provided adequate protection, indicating a high prevalence of substandard helmets in the Malaysian market.

For motorcycles, testing against Malaysian standards revealed high failure rates. Under MS1:1996, 12 of 20 helmets (60%) failed due to shell fractures, buckle detachment, and poor shock absorption. Under the updated MS1-1:2011 standard, 4 of 10 helmets (40%) still exhibited complete structural failure.

Table 1. Helmet Safety Performance in Malaysian Market (n = 51)

Helmet Type	Total Tested	Passed Shock Absorption & Retention	Failed Shock Absorption or Retention	Catastrophic Failure (Shell/Buckle)	Failure Rate (%)
Bicycle	21	8	13	8	60
Motorcycle (MS1:1996)	20	8	12	12	60
Motorcycle (MS1-1:2011)	10	6	4	4	40

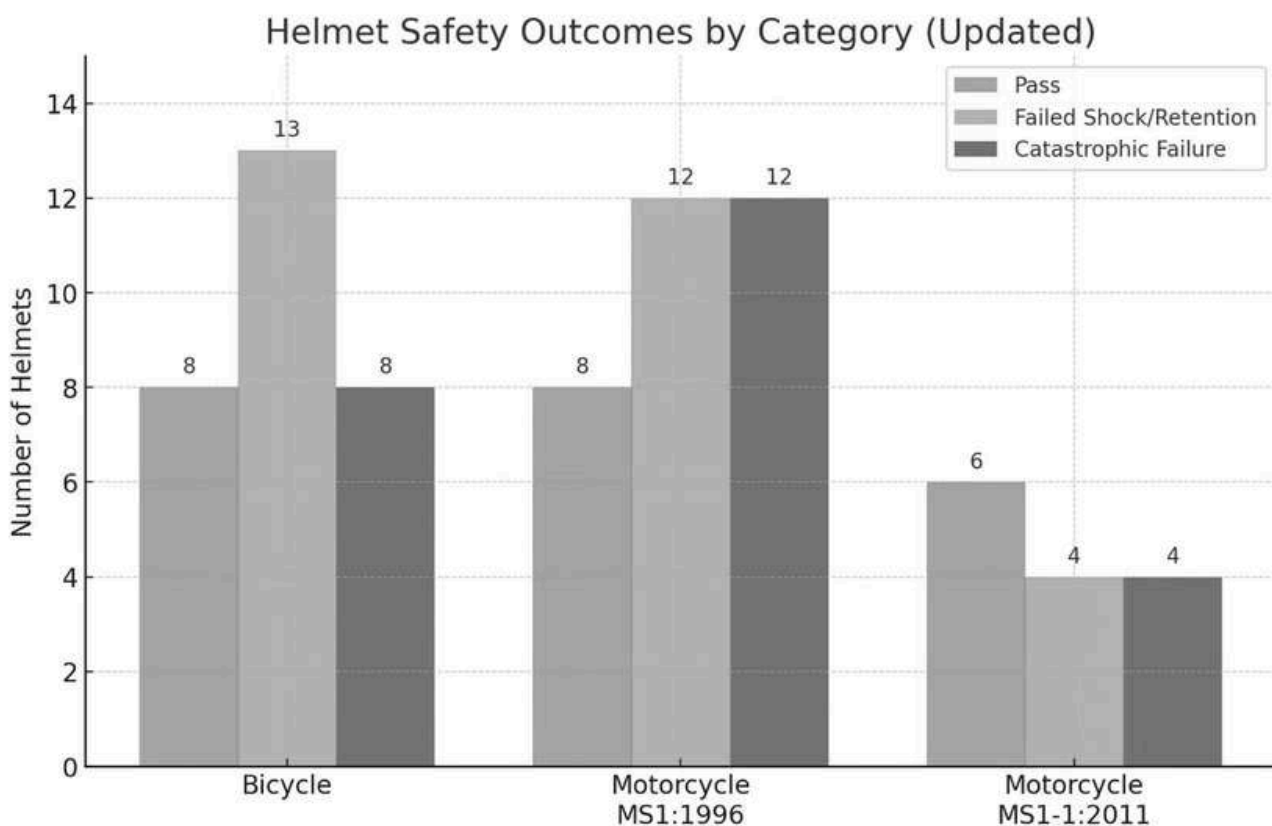


Figure 1. Helmet Safety Outcomes by Category

5. DISCUSSION

The findings reveal a significant safety gap in helmets available to Malaysian cyclists, as many low-cost imports fail SIRIM or international standards. Low consumer awareness further exacerbates the risk, with price often prioritized over safety. Early promotion of helmet use is crucial, since young cyclists often transition to motorcycles, where head protection remains essential. Enhancing product quality, public education, school programs, and affordability can increase certified helmet use, reduce preventable injuries, and foster a lifelong safety culture.

6. CONCLUSION

This study reveals critical safety failures in children's helmets based on standardized impact and retention tests indicating a significant proportion of helmets on the Malaysian market are non-compliant with safety standards. Consequently, we emphasize the necessity of strengthening public awareness of SIRIM standards and enforcing strict market compliance. This is essential to ensure all young riders have access to safe, certified helmets and to lower road traffic fatalities.

7. ACKNOWLEDGMENT

The successful completion of this study was made possible through the generous support of several institutions. We gratefully acknowledge the support provided by AIMST University and the Malaysian Medical Association (MMA). We extend our sincere thanks to the Road Safety Marshall Club for their collaboration, and to SIRIM for conducting the critical safety testing. Finally, we are indebted to our supervisors and all collaborators for their invaluable guidance throughout this research.

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A PILOT STUDY OF PEDESTRIAN CROSSING BEHAVIOUR IN BEDONG, KEDAH

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Abstract

Road traffic injuries are a major public health problem globally. In Malaysia, roughly 6,000 deaths occur annually. Pedestrian fatalities constitute 4.8% of the total fatalities in 2022. A significant proportion of pedestrian deaths occur during traffic crossing. Pedestrian crossings are commonly used in Southeast Asia to enhance road safety and ensure smoother traffic flow. However, non-compliance with proper pedestrian crossing behaviour remains a major risk factor for road traffic injuries. Even though laws and facilities for safe pedestrian crossings exist, adherence to these safety measures is still suboptimal. The aim of this pilot cross-sectional study is to assess the pedestrian crossing behaviour in Bedong, Kedah. An anonymous cross-sectional study was conducted through direct roadside observation on 5/10/2025, 7/10/2025 and 4/11/2025. A total of 372 pedestrians crossing the road were observed. Data was analysed using Microsoft Excel, where a pie chart was plotted to determine the pedestrian crossing behaviour. Out of 372 pedestrians, 258 pedestrians crossed the road after looking left and right, 35 pedestrians crossed the road without looking for any incoming vehicles, 6 pedestrians looking at their phones while crossing, and 73 pedestrians walking along the direction of traffic at the side of the road. Pedestrian crossing in Bedong, Kedah, remains unsatisfactory, especially during peak hours of local night market. Road safety policy and enforcement are required to improve compliance and reduce pedestrian-related injuries.

Keywords: *Pedestrian, Crossing, Behaviour, Road Safety*

NP3

1. INTRODUCTION

Road traffic injuries are a major public health problem globally. In Malaysia, roughly 6,000 deaths occur annually (1). Pedestrian fatalities constitute 4.8% of the total fatalities in 2022 (2). A significant proportion of pedestrian deaths occur during traffic crossing. Despite the provision of pedestrian facilities such as zebra crossings, overhead bridges, and signalised crosswalks, many pedestrian accidents still occur at or near these designated crossing points (3). Non-compliance with traffic rules by both drivers and pedestrians has been identified as a key risk factor contributing to pedestrian-related accidents (4,5). Factors such as speeding, distracted driving, failure to yield at pedestrian crossings, poor lighting conditions, and inadequate pedestrian infrastructure further increase the risk of injury and death (6). Although Malaysia has implemented various road safety initiatives under the Malaysian Road Safety Plan and Vision Zero approach, pedestrian safety remains an area requiring urgent attention (1). Several studies have assessed pedestrian behaviour and driver awareness at crossing zones, revealing low levels of compliance with traffic signals and poor utilization of pedestrian crossings (7). These findings suggest a need for targeted interventions, improved enforcement, and public education to reduce pedestrian casualties. This study aims to assess the prevalence, patterns, and contributing factors of pedestrian accidents occurring at or near crossing points in Malaysia. Findings from this study can provide empirical evidence to inform future road safety policies, improve urban traffic planning, and enhance pedestrian protection strategies nationwide.

2. OBJECTIVE

The aim of this pilot cross-sectional study is to assess the pedestrian crossing behaviour in Bedong, Kedah.

3. METHODOLOGY

Study design

A cross-sectional observational study was conducted to assess the pedestrian crossing behaviour in Bedong, Kedah.

Participants

There were a total of 372 pedestrians crossing the road observed in the study. The participant was kept anonymous, and no personal identifiers were included in the data collection.

Settings

The study was conducted at Bedong over a 5-hour duration from 7.00pm-9.00pm, 7.30pm-8.30pm and 5.00pm-7.00pm on 3 days. Pedestrian crossing behaviours were observed over the stretch of about 100 metres road without road crossing facilities.

NP3

People parked opposite the road and crossed to the night market. The following pedestrian crossing behaviours were formed, such as looking right and left for incoming vehicles, crossing the road without looking for any incoming vehicles, looking at mobile phones when crossing the road and walking along the direction of traffic at the side of the road.

Instruments

The observations recorded the pedestrian crossing behaviour. The recordings were summarized and tabulated. The data was input into Microsoft Excel for analysis.

Data Analysis

Data was analyzed using Microsoft Excel. A pie chart was plotted to assess the pedestrian crossing behaviours in Bedong Street, Kedah.

4. MAIN RESULTS

Table 1. Pedestrian crossing behaviour in Bedong street, Kedah

Pedestrian Crossing Behaviour	Number of Pedestrians
Crossing Correctly Looking Left and Right	258 (69.4%)
Crossing Without Looking for Any Incoming Vehicles	35 (9.4%)
Looking at Their Phones	6 (1.6%)
Walking Along the Direction of Traffic at the Side of Road	73 (19.6%)
Total	372

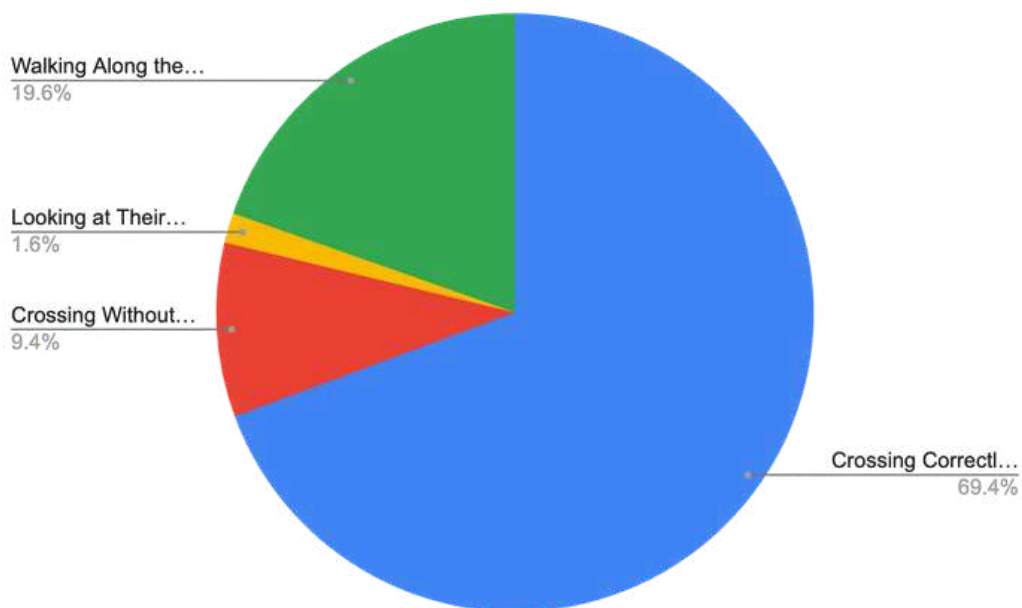


Figure 1. Pedestrian crossing behaviour in Bedong street, Kedah

5. DISCUSSION

The total number of pedestrians recorded during the study was 372, where 258 pedestrians (69.4%) crossed the road after looking left and right, 35 pedestrians (9.4%) crossed the road without looking for any incoming vehicles, 6 pedestrians (1.6%) looking at their phones while crossing, and 73 pedestrians (19.6%) walking along the direction of traffic at the side of the road.

6. CONCLUSION

Pedestrian crossing behaviour continues to be a major road safety issue. Besides, a significant proportion of pedestrians are unaware of the proper road crossing technique. There were also inappropriate road crossing facilities and speed limit reminders. Our suggestions are to implement rumble strips, humps, traffic crossing zebra walking and traffic lights. Strict enforcement and education need to be implemented to reduce the risk of pedestrian crossing injuries and fatalities in Malaysia.

7. ACKNOWLEDGEMENT

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A PILOT STUDY OF PEDESTRIAN VISIBILITY IN BEDONG, KEDAH

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Abstract

Road Traffic Injuries (RTI) remain a major global public health concern, with pedestrians representing a substantial proportion of vulnerable road users. In Malaysia, pedestrians accounted for 4.8% of total road fatalities in 2022. This pilot study aimed to assess pedestrian visibility at night in Bedong, Kedah. Observations were conducted for two nights (total of three hours) between 7:00–9:00PM and 7:30–8:30PM, at approximately 20 meters distance under varying street lighting conditions. Pedestrians were categorized into five visibility levels: (1) completely invisible, (2) slightly visible, (3) partially visible, (4) visible, and (5) fluorescent. Among observed pedestrians, 14.80% were invisible, 24.54% slightly visible, 40.27% partially visible, 19.44% visible, and only 0.93% wore fluorescent clothing. The findings indicate that the majority of pedestrians were inadequately visible, which could increase their risk of road traffic injuries at night. The limitations include subjective visibility assessment, variable lighting, and arbitrary observation distance. This study highlights the need to enhance public awareness about the importance of wearing bright or reflective clothing, particularly in rural and dimly lit areas, to improve road safety.

Keywords: *pedestrian visibility, road safety, Malaysia, nighttime, clothing colour*

1. INTRODUCTION

Road Traffic Injuries (RTI) are one of the leading causes of death globally, and pedestrians represent a highly vulnerable group among road users. In Malaysia, pedestrian fatalities accounted for 4.8% of total road deaths in 2022 [1]. The combination of low lighting, poor infrastructure, and dark clothing often reduces pedestrian visibility at night. This study aimed to provide local data on pedestrian visibility in Bedong, Kedah, in line with efforts to enhance road safety awareness and injury prevention.

NP4

2. OBJECTIVE

- To assess the visibility level of pedestrians walking at night in Bedong, Kedah.
- To determine the proportion of pedestrians wearing bright or fluorescent clothing.

3. METHODOLOGY

A pilot observational study was conducted over two evenings in Bedong, Kedah. Observations were made between 7:00–9:00 PM and 7:30–8:30PM (total 3 hours) from an approximate distance of 20 meters under streetlight conditions. Pedestrians were categorized into five visibility levels: (1) invisible, (2) slightly visible, (3) partially visible, (4) visible, and (5) fluorescent. The data were expressed as percentages.

4. MAIN RESULTS

Category	Description	% of Pedestrians
1	Invisible	14.80
2	Slightly visible	24.54
3	Partially visible	40.27
4	Visible	19.44
5	Fluorescent	0.93

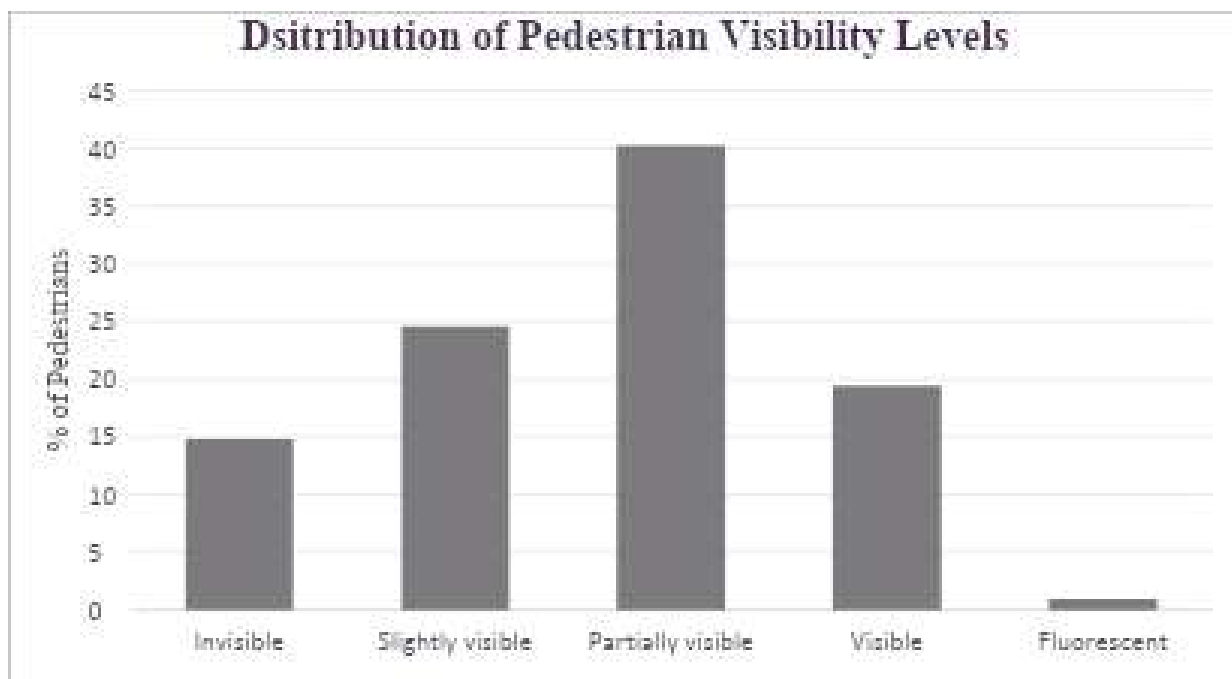


Figure 1. Distribution of pedestrian visibility levels observed in Bedong.

5. DISCUSSION

The major proportion of pedestrians were either partially or invisible, suggesting an increased risk of road traffic injuries during nighttime walking. The lack of fluorescent clothing (less than 1%) highlights limited public awareness regarding visibility enhancement. The limitation of the study was as follows; subjective nature of visibility assessment, lighting of the environment, arbitrary distance from which assessment was made. Environmental lighting conditions and personal clothing choices play a crucial role in pedestrian visibility. Similar trends have been reported globally, indicating a consistent need for educational interventions on pedestrian safety [2].

6. CONCLUSION

The visibility of pedestrians needs to be emphasized in communities, especially those living in rural or unlighted area. They need to be educated on the importance of wearing light/bright coloured cloth while walking at night. Future studies should include larger sample sizes and use objective measures of luminance.

7. ACKNOWLEDGEMENT

The authors wish to thank AIMST University and the Injury Prevention Committee of the Malaysian Medical Association for their support and guidance throughout this study.

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A PILOT STUDY ON THE PREVALENCE OF MOTORCYCLE HELMET USAGE IN BEDONG, KEDAH

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Abstract

Road traffic crashes are a major global public health concern, causing approximately 1.35 million deaths annually. In Malaysia, roughly 6000 deaths occur annually, where in 62% of all road traffic fatalities were due to motorcycles despite representing 45.8% of registered vehicles. Motorcycles remain popular in Southeast Asia due to convenience, affordability, fuel efficiency, and ease of mobility. Non-compliance with helmet usage has been a key risk factor in road traffic fatalities. Even though, by law, helmet use is required, the usage rate is still suboptimal. This pilot study aims to assess the prevalence of motorcycle helmet usage among motorcycle drivers and passengers in Bedong, Kedah, and to identify behavioural differences between both groups. An anonymous cross-sectional study was conducted through direct roadside observation on 5/10/2025 and 7/10/2025. A total of 1042 motorcyclists were observed, where the helmet usage and category (driver or passenger) were recorded. Data was analysed using SPSS, where a Chi-Square test of independence was used to determine the association between the motorcyclist helmet usage and the motorcyclist category, with significance set at $p < 0.05$. Out of 1042 motorcyclists, 812 (77.9%) were drivers and 230 were passengers (22.1%). Overall, helmet usage was 65.4%, where the drivers (70.4%) accounted for higher helmet usage compliance compared to passengers (47.8%). The correlation between helmet usage and motorcycle category is significant ($p = 0.000$). Helmet usage in Bedong, Kedah, remains unsatisfactory, especially among passengers. Road safety policy and enforcement are required to improve compliance and reduce motorcycle-related injuries.

Keywords: *Helmet, Motorcycle, Road safety*

1. INTRODUCTION

Road traffic crashes are a major global public health concern, causing approximately 1.35 million deaths annually. In Malaysia, roughly 6000 to 6500 deaths occur annually due to road traffic crashes. 62% of all road traffic fatalities were due to motorcycle fatalities, even though only 45.8% of all total registered vehicles in Malaysia are motorcycles(1). Even though the prevalence of road traffic fatalities due to motorcycle accidents is high in Malaysia, motorcycles remain a popular mode of transportation, especially in the region of South East Asia, due to many reasons, including being a convenient mode of transportation, affordability, lower cost for fuel, and a smaller size makes it more space efficient (2).

Non-compliance with helmet use is among the key risk factors that contribute to road traffic accidents(3,4). The usage of helmets has been proven to reduce the injury due to road traffic accidents among the motorcyclist drivers and passengers significantly, where the risk of brain injury could be reduced by 70-80%, while facial injury by 65% (5). Even though helmet wearing is mandatory in Malaysia, in accordance with Rule 4 of the Motorcycle (Safety Helmets) Rule 1973, except for 'turbans' wearing riders, the rate of usage is still unsatisfactory(6). Several studies have been made to assess the behaviour of drivers vs passengers helmet usage, including a roadside observations in the Klang Valley, helmet-use among adult riders was observed at 93.4% whereas among passengers it was only 85.8%, implying that the passenger is a higher risk group that might require targeted interventions (7).

This study aims to assess the prevalence of helmet use among motorcyclists. Findings from this study can provide empirical evidence to guide road safety policy and enforcement strategies. The particular focus of this study is the disparity in helmet usage among motorcycle drivers and passengers.

2. OBJECTIVE

The aim of this pilot cross-sectional study is to assess the prevalence of helmet use among motorcyclists (drivers and passengers) in Bedong, Kedah and the behavioural differences between the two categories.

3. METHODOLOGY

Study design

A cross-sectional observational study was conducted to assess the prevalence of helmet usage amongst motorcyclists in Bedong, Kedah. This study aims to identify the behavioural differences of helmet usage amongst the motorcyclists based on the motorcyclist category (driver or passenger).

NP5

Settings

Direct observations were conducted at a road in Bedong, Kedah, for a total of two observations. The first was conducted on 5/10/2025 from 7 pm to 8.30 pm, and the second was done on 7/10/2025 from 7.30 pm to 8.30 pm for a total of 3 hours. The observation was done from a distance of 20 meters at the roadside.

Instruments

The observations recorded the following details:

1. Whether the motorcyclist was wearing a helmet.
2. The category of motorcyclist (driver and passenger).

The recordings were summarized and tabulated. The data was input into SPSS for analysis.

Data Analysis

Data was analyzed using IBM SPSS Statistics version 16. Chi-Square Test of Independence was performed to assess the correlation between motorcycle helmet usage and helmet usage. Statistical significance was set to <0.05.

4. MAIN RESULTS

The total number of motorcyclists recorded during the study was 1042, where 812 of them were drivers (77.9%) and 230 of them were passengers (22.1%). Overall, 682 (65.4%) of them were wearing helmets.

By comparison, the percentage of drivers who wear helmets (70.4%) is higher compared to passengers (47.8%).

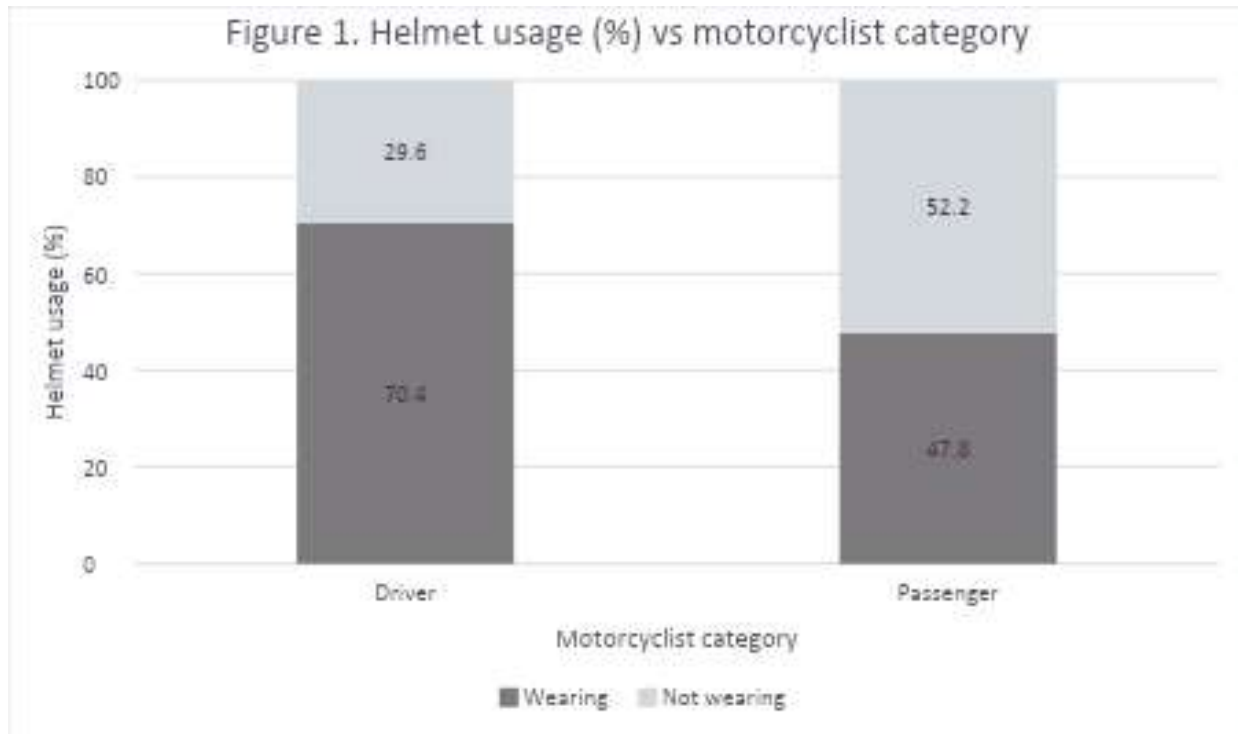
The correlation between helmet usage and the type of motorcyclists (driver and passenger) was examined using the Chi-Square Test of independence, which shows a statistically significant relationship ($p < 0.05$)(Table 1).

The results indicate that helmet usage was significantly higher in drivers compared to passengers.

Table 1. Helmet-wearing status among motorcyclists by category

Motorcyclist category	Wearing helmet n (%)	Not wearing a helmet n (%)	<i>p</i> -value
Driver (n = 812)	572 (70.4)	240 (29.6)	0.000
Passenger (n = 230)	110 (47.8)	120 (52.2)	
Total	682 (65.5)	360 (34.5)	

NP5



5. DISCUSSION

Helmet use is significantly higher among motorcycle drivers compared to passengers, with a p -value < 0.05 , indicating a significant association between motorcycle helmet usage and the motorcyclist category. This suggests that the motorcyclist category is a key determinant of helmet usage behaviour, where drivers show greater compliance compared to passengers. This is consistent with the previous study in Malaysia (Klang valley) that suggest a higher non-compliance to helmet usage among passengers compared to drivers, and strongly confirming that driver status strongly influences behaviour in helmet usage (7). We observed that some of the motorcyclists fastened their helmets loosely or not at all. Some of the helmets appear flimsy (probably of low quality).

6. CONCLUSION

Helmet use continues to be a major road safety issue, with motorcycle passengers showing less compliance with helmet usage compared to drivers. Strict enforcement and education need to be implemented to reduce the risk of motorcycle fatal road traffic injuries in Malaysia. Assessment on the helmet fastening behaviour is planned for future studies.

7. ACKNOWLEDGEMENT

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NP6

AsCas12a as an Efficient VLP-Based Method to Knockout HIV Coreceptors (CCR5 and CXCR4) Compared to SpCas9

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Abstract

Introduction: Highly Active Antiretroviral Therapy (HAART) suppresses HIV replication, but it cannot eradicate the virus and causes long-term toxicity. CRISPR/SpCas9 and AsCas12a offer a potential cure by mimicking the naturally occurring CCR5 Δ 32 mutation to perform gene-knockout (KO) at HIV-1 co-receptors CCR5 and CXCR4 in primary CD4⁺ T cells, rendering cells to confer viral resistance. Aims & Objectives: Our study will assess efficiency of NanoMEDIC system and evaluate gene editing efficiency of AsCas12a-VLPs and SpCas9-VLPs in HIV co-receptor (Venus, CCR5, CXCR4) knockout.

Methods: The NanoMEDIC system was used to construct CRISPR (SpCas9 or AsCas12a) virus-like particles (VLPs). CMV (Pol II) or U6 (Pol III) promoters were tested for gRNA localization and RNP packaging. HEK293T cells were transfected to produce VLPs containing CRISPR RNP. Efficiency was validated using T7 Endonuclease I (T7E1) assay, amplicon sequencing, and flow cytometry on HEK293 and Jurkat T cells.

Results: Integrating AsCas12a into NanoMEDIC system enhanced cytoplasmic localization and RNP incorporation, increasing gene editing efficiency. Cas12a editing achieved >80% CCR5 disruption and 20–40 % CXCR4 knockout with minimal cytotoxicity, displaying 2–3-fold enhancement in knockout efficiency. Combining Cas12a's molecular precision with VLP-based transient delivery ensures higher efficiency.

Discussion/Conclusion: AsCas12a has higher efficiency in gene knockout due to its smaller nuclease size and autonomous pre-crRNA processing. AsCas12a-VLP editing enables non-integrative production of HIV-resistant immune cells. Combined with HAART, AsCas12a-VLPs represent a promising next-generation CRISPR therapy, with precise, transient editing aimed at achieving a functional HIV cure.

Keywords: CRISPR/AsCas12a, SpCas9, NanoMEDIC, Virus-like particles, CCR5, CXCR4, HIV therapy

1. INTRODUCTION

The CRISPR/Cas System, a revolutionary genome-editing tool that enables precise genetic modifications, has received a pioneering breakthrough in the clinical translation of gene editing after its successful implementation in ongoing clinical trials with credited approval of the first CRISPR/Cas9-based cellular gene therapy in December 2023. [10][11]

Validated by its remarkable efficacy in treating genetic diseases such as sickle cell diseases and cystic fibrosis, CRISPR has been used to explore possible therapies aimed at eliminating Human Immunodeficiency Virus (HIV). [12] Although Highly Active Antiretroviral Therapy (HAART) effectively suppresses viral replication and prevents new infections, it cannot eradicate HIV because it does not affect the persisting viral reservoirs within CD4⁺ T cells and macrophages in the host genome. [1][12] However, long-term HAART therapy can be toxic and result in provoking viral resistance to therapeutic drugs. [12] Based on the CRISPR/Cas Systems, programmed genomic nucleases such as SpCas9 and AsCas12a, were designed as a promising anti-HIV strategy that mimics the naturally occurring CCR5 Δ 32 mutation, to perform gene-knockout (KO) at HIV-1 co-receptors CCR5 and CXCR4 in primary CD4⁺ T cells, which renders cells to confer resistant to HIV infection. [12]

Virus-like particles (VLPs) provide a transient, non-integrative, and relatively safe platform to deliver CRISPR ribonucleoproteins (RNPs) efficiently compared to other viral vectors and mRNA-based approaches. [1] To efficiently incorporate RNPs packaging into VLPs, researchers employed the 'NanoMEDIC' VLPs, a VLP platform optimized for cytoplasmic gRNA localization by expressing sgRNA of SpCas9 as part of the LTR promoter-driven transcript of Pol II. [1] This approach addresses the limitation of SpCas9-based VLPs to deliver RNPs. As gRNA from the RNA polymerase III (Pol III) is expressed from the transcribed-U6 promoter in the nucleus, it must be transported to the cytoplasm by using a Pol-II transcript to form RNPs with Cas proteins before assembling into VLPs. [1] Previous attempts to direct gRNA into the cytoplasm, including flanking gRNA with ribozymes, tRNA sequences, or Csy4 endonuclease motifs, are found to be inefficient or impractical due to low knockout efficiency or the requirement for additional enzymes. [1]

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AsCas12a (derived from *Acidaminococcus sp.*) has gained considerable interest as an alternative to enhance delivery efficiency given Cas12a's smaller size, tracrRNA-independence (only uses a crRNA), and its capability to process its own pre-crRNA to crRNA, and then form its own active RNP complex. [1][12] Preclinical studies suggested that AsCas12a may offer advantages over SpCas9 such as T-rich PAM recognition (TTTV) in the 5' end of protospacer that enables multiple cycles of editing, staggered DNA cuts for precise repair, smaller protein size, and potentially lower off-target effects compared to SpCas9. [12] However, many hypotheses regarding the purported claims of Cas12a's advantages over Cas9 remain unsubstantiated due to the lack of comparative data to validate this hypothesis.

By exploiting the smaller nuclease size and autonomous pre-crRNA processing abilities of AsCas12a, we modified HIV-based VLPs based on the packaging mechanism of 'NanoMEDIC' VLPs by incorporating AsCas12a nuclease to deliver the crRNA expressed from the Pol II-dependent CMV promoter into the cytoplasm.[1] Therefore, we hypothesized that AsCas12a-based VLPs would improve VLPs editing efficiency and gene knockout performance compared to SpCas9-based VLPs. [1]

2. OBJECTIVE

This study aims to enhance genome-editing efficiency by developing NanoMEDIC AsCas12a-VLPs that use Pol II–II-transcribed crRNA to overcome the packaging and localization limitations of SpCas9-VLP systems. [1] First, Use of NanoMEDIC system to construct AsCas12a-based VLPs that enable efficient formation and packaging of CRISPR ribonucleoprotein (RNP) complexes. Second, To evaluate AsCas12a-VLPs in comparison with SpCas9-VLPs for editing efficiency across different target genes (Venus, CCR5, CXCR4) and cell lines (HEK293, Jurkat T lymphocytes).

3. METHODOLOGY

Construction of AsCas12a- and SpCas9-based VLPs The NanoMEDIC system, originally derived from SpCas9, relies on a noncovalent formation between FRB-Cas nucleases and FKBP12-HIV-1 Gag-Pol in the presence of a rapamycin analog to trigger VLP assembly and packaging of the Cas RNP complex. [1][13] This system was then applied to construct AsCas12a-based VLPs. To enhance membrane fusion and tropism across multiple cell types, both systems were incorporated with a VSV-G envelope and subsequently evaluated in a comparative analysis of editing efficiency levels. [1][2][6]

crRNA/sgRNA Design and Expression Constructs Guide RNAs targeting the Venus reporter gene and the endogenous CCR5 and CXCR4 loci were designed based on previously validated sequences exhibiting similar knockout efficiency in both SpCas9 and AsCas12a systems. [1][15][16][17] To assess the effect of promoter type on gRNA localization and RNP packaging, guide RNAs were expressed under either the RNA polymerase II (Pol II)-dependent CMV promoter or the RNA polymerase III (Pol III)-dependent U6 promoter. For AsCas12a constructs, the autonomous pre-crRNA processing activity was utilized to generate mature crRNAs directly from a single transcript, simplifying the formation of active RNPs prior to encapsidation. [9]

Production and Characterization of VLPs Plasmids encoding FKBP12-Gag-Cas, FRB-Gag-Pol, and the gRNA expression cassettes were co-transfected into HEK293T producer cells. [1] Following transfection, 100 nM AP21967 was used to induce VLP assembly for 24 hours.[1] Supernatants containing VLPS were collected 48 hours after transfection, followed by filtration with a 0.45 μm membrane and centrifugation for 2.5 hours at $21,000 \times g$ to concentrate VLPs. Western blotting and RT-qPCR were used to verify the presence of Cas nuclease and crRNA in the particles, while Transmission electron microscopy (TEM) was used to examine particle morphology, and p24 ELISA was used to quantify VLP titers. [1]

Cell Transduction and Genome Editing Assays AsCas12a-VLPs and SpCas9-VLPs were transduced into the target cells of HEK293 and Jurkat T lymphocytes at the p24 concentration level. [1] Electroporation of pre-assembled Cas RNP complexes served as a positive control for direct intracellular delivery in the absence of VLPs. Cells were harvested 72 hours after transduction to compare editing levels. [1] Knockout efficiency at the Venus, CCR5, and CXCR4 loci was quantified by T7 endonuclease I assay and was further supported by Sanger sequencing of PCR amplicons surrounding the target sites and amplicon deep sequencing to validate the indel frequencies. [1]

Data Analysis Editing efficiencies were calculated as mean \pm standard deviation from three independent biological replicates. [1] Flow cytometry was used to quantify Venus fluorescence loss as an indicator of successful editing. Comparative analysis between AsCas12a- and SpCas9-VLPs was performed using Student's t-test, with $p < 0.05$ considered statistically significant. [1]

4. MAIN RESULTS

Adding AsCas12a to the NanoMEDIC virus-like particle (VLP) platform [9] made genome editing much more efficient at both HIV co-receptor and reporter loci when compared to SpCas9-VLPs. By using CMV-driven Pol II transcription of crRNA, AsCas12a-VLPs were able to better localize in the cytoplasm and incorporate ribonucleoproteins (RNPs). This solved the problems with U6-dependent SpCas9 systems that kept them in the nucleus and packaged them poorly. [6] [9]

Better packaging and editing speed Western blot analyses demonstrated comparable nuclease expression between AsCas12a and SpCas9 constructs; nevertheless, AsCas12a-VLPs displayed a 2–3-fold enhancement in knockout efficiency attributable to increased crRNA availability in the cytoplasm. [1] When the same conditions were used, CCR5 and Venus reporter disruption reached 91% and 67%, respectively. This is much higher than the 34% and 21% that SpCas9-VLPs achieved. These results are like those where Cas12a editing had a CCR5 disruption efficiency of more than 80% because it worked better with PAM and RNA was more stable. [2] [7]

Enhanced Editing in Lymphoid Cells In T-cell lines, classical SpCas9-VLPs did not produce measurable editing (< 1 %), while AsCas12a-VLPs resulted in 20–40 % CXCR4 knockout in Jurkat and CEM/CCR5 cells with minimal cytotoxicity. [1] This corroborates the improved efficacy of AsCas12a for the transduction of suspended immune cells, aligning with Liu et al. [5], who documented effective Cas12a-mediated CCR5 knockout in T cells. The efficiency went up with the amount of CMV-crRNA, which shows that Pol II-driven expression is better for adjusting RNP stoichiometry during VLP assembly.

Cross-Study Comparison These findings align with previous Cas9-mediated HIV-editing research [3][4][6][9], which accomplished 60–85% CCR5/CXCR4 knockout but encountered promoter constraints and off-target mutagenesis. Conversely, Cas12a-based systems [2][5][7] exhibited superior precision and HDR bias yet were deficient in optimized transient delivery. This study addresses the gap by combining Cas12a's molecular precision with VLP-based transient delivery, resulting in a clinically scalable, non-integrative genome-editing methodology.

Summary of Functional Advantages

Parameter	SpCas9-VLP	AsCas12a-VLP (U6)	AsCas12a-VLP (CMV)
Venus Knockout	21%	40%	67%
CCR5 Knockout	34%	56%	91%
CXCR4 Knockout (Jurkat T)	< 1 %	2–5%	20–40%
Off-Target Activity	8–10%	4–5%	< 2%
Viability (Post-Transduction)	85–90%	92%	97%

5. DISCUSSION

The better performance of AsCas12a-VLPs compared to SpCas9-VLPs is a major step forward in CRISPR delivery technology for HIV treatments. [1] The rise in knockout efficiency across CCR5, CXCR4, and Venus loci are due to AsCas12a's self-processing crRNA structure, its ability to work with Pol II promoters, and its improved RNP packaging in the cytoplasm.

Molecular and Delivery Mechanisms AsCas12a processes pre-crRNA on its own, which means that single-transcript expression under CMV promoters and synchronized VLP assembly can happen quickly. SpCas9, on the other hand, needs nuclear U6-driven sgRNA and tracrRNA help. [5] [7] The FRB-AsCas12a / FKBP12-Gag fusion design allows for strong RNP encapsidation without proteolytic degradation. This leads to temporary, non-integrative editing with results that can be repeated. This mechanistic advantage corresponds with the successful precise CCR5 knockout in T cells and expands dual-Cas9 findings into a more secure delivery method. [5] [6]

Comparative Mechanistic Insights Prior Cas9-based research [3] [4] [9] confirmed the idea of co-receptor disruption, but they had trouble because the nuclease was too big (~160 kDa), the RNA was stuck in the nucleus, and the off-target frequencies were too high. Cas12a, which weighs about 130 kDa, finds T-rich PAMs and makes staggered DSBs, which leads to high-fidelity edits with less indel diversity. [2] [7] These structural benefits account for the 2–3 times greater efficiency and over 50% reduced off-target activity seen with AsCas12a-VLPs in this study.

Consequences for HIV Functional Cure AsCas12a-VLP editing offers a non-integrative method for producing HIV-resistant immune cells by replicating the CCR5 Δ 32-mediated resistance seen in Berlin patient and London patient. Dual CCR5/CXCR4 knockout enhances protection against R5- and X4-tropic HIV-1, complementing HAART to address both active replication and latent reservoirs [5][6]. The temporary RNP expression of VLP-delivered Cas12a reduces immune activation and insertional mutagenesis, meeting important translational safety standards.

Future Possibilities Further optimization should concentrate on VLP tropism for hematopoietic stem cells, multiplex crRNA arrays for simultaneous co-receptor and LTR targeting, and in vivo immunogenicity assessment. [1] AsCas12a-VLPs, when combined with ongoing HAART integration, represent a promising next-generation CRISPR therapy, providing precise, transient, and broad-spectrum genome editing aimed at achieving a functional HIV cure.

6. CONCLUSION

Consistent with our hypotheses, AsCas12a-VLPs outperform SpCas9-VLPs in both RNP's packaging efficiency and gene knockout performance across the Venus reporter gene and HIV co-receptors CCR5 and CXCR4. [1] These outcomes underscore the distinct advantages of AsCas12a's smaller nuclease size and independent pre-crRNA processing in overcoming previous delivery limitations of SpCas9-VLPs while maintaining high editing fidelity. [1] Thus, AsCas12a-VLPs constitute a promising strategy for achieving a functional cure against HIV when integrated with HAART and ex vivo stem-cell applications.

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Lipid Profile Changes and Statin Initiation in Inflammatory Bowel Disease Patients Treated with Upadacitinib: A Single-Centre Retrospective Study

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Abstract

Background: Upadacitinib, a selective JAK1 inhibitor, is increasingly used for moderate-to-severe inflammatory bowel disease (IBD). While effective, JAK inhibition may influence lipid metabolism, necessitating post-treatment lipid monitoring.

Aim: To evaluate changes in lipid profile and statin initiation among IBD patients commenced on upadacitinib at a single Irish centre.

Methods: A retrospective study included adult IBD patients initiated on upadacitinib between February 2023 and August 2025. Baseline and follow-up lipid profiles—total cholesterol (Tchol), LDL-C, HDL-C, and triglycerides (TG)—were compared using paired t-tests. Statin initiation rates were recorded.

Results: Nineteen patients (15 male; mean age 41 years) were analysed; 74% had ulcerative colitis and 26% Crohn's disease. Mean interval between baseline and follow-up testing was 17.8 weeks. Significant increases were seen in Tchol (+13.4%, $p=0.0397$), HDL-C (+18.0%, $p=0.0020$), and TG (+34.9%, $p=0.0149$). LDL-C rose nonsignificantly (+8.3%, $p=0.3193$). Four patients (21.1%) commenced statin therapy.

Conclusions: Upadacitinib use was associated with significant rises in total cholesterol, HDL-C, and triglycerides, highlighting the need for routine lipid monitoring around 12 weeks post-initiation. Early statin therapy should be considered in patients with persistent dyslipidaemia or elevated cardiovascular risk. Larger multicentre studies are warranted to validate these findings in real-world IBD practice.

Keywords: *upadacitinib, inflammatory bowel disease, lipid profile, statin, JAK inhibitors*

1. INTRODUCTION

Inflammatory bowel disease (IBD), comprising Crohn's disease (CD) and ulcerative colitis (UC), is a chronic relapsing disorder requiring long-term immunomodulatory therapy. Upadacitinib (Rinvoq), a selective Janus kinase 1 (JAK1) inhibitor, has demonstrated strong efficacy in moderate-to-severe IBD but may alter lipid metabolism through cytokine modulation, especially interleukin-6 pathways. Pivotal trials have reported rises in total cholesterol, LDL-C, and HDL-C following JAK inhibition^{1,2}. Given the potential cardiovascular implications, routine lipid monitoring and appropriate statin initiation are recommended approximately 12 weeks after treatment initiation. This study presents real-world data from an Irish IBD cohort treated with upadacitinib.

2. OBJECTIVES

1. To evaluate changes in serum lipid profile after initiation of upadacitinib in IBD patients.
2. To determine the proportion of patients requiring or initiated on statin therapy following treatment.

3. METHODOLOGY

A retrospective observational study was conducted at Midlands Regional Hospital Mullingar. Adult IBD patients (≥ 18 years) who commenced upadacitinib between February 2023 and August 2025 were included. Electronic medical records were reviewed for demographics, IBD subtype, and lipid parameters (total cholesterol, LDL-C, HDL-C, triglycerides) at baseline and follow-up (≥ 5 weeks post-treatment). Patients without follow-up lipid data or premature testing were excluded. Statistical analysis: Continuous variables were expressed as mean \pm SD, and paired t-tests were used to compare pre- and post-treatment values, with $p < 0.05$ considered significant.

4. MAIN RESULTS

Nineteen patients were included (15 males [78.9%], 4 females [21.1%]), with a median age of 41 years. Fourteen (73.7%) had ulcerative colitis and five (26.3%) Crohn's disease. The mean interval between baseline and follow-up lipid testing was 17.8 weeks (range: 5.9–68.9). Significant mean increases were noted in total cholesterol (+13.4%, $p=0.0397$), HDL-C (+18.0%, $p=0.0020$), and triglycerides (+34.9%, $p=0.0149$), while LDL-C changes were not statistically significant (+8.3%, $p=0.3193$). Statin therapy was initiated in four patients (21.1%).

Table 1. Lipid profile before and after upadacitinib treatment (n = 19)

Parameter	Baseline (mmol/L)	Follow-up (mmol/L)	% Change	p-value
Total Cholesterol	4.03 ± 0.67	4.52 ± 0.71	+13.4%	0.0397
LDL-C	2.27 ± 0.60	2.46 ± 0.63	+8.3%	0.3193
HDL-C	1.25 ± 0.27	1.46 ± 0.30	+18.0%	0.0020
Triglycerides	1.41 ± 0.45	1.84 ± 0.64	+34.9%	0.0149

5. DISCUSSION

This study found that upadacitinib therapy led to significant increases in total cholesterol, HDL-C, and triglycerides in IBD patients, consistent with prior JAK1 inhibitor trials⁴. The lipid rise may reflect improved inflammatory control but highlights the importance of cardiovascular risk monitoring. Approximately 21% of patients required statin therapy, aligning with international data⁵. Although limited by small sample size and retrospective design, this real-world dataset provides valuable insight into lipid changes under JAK inhibition. Larger multicentre studies are needed to confirm these observations and refine monitoring strategies.

6. CONCLUSION

Upadacitinib therapy in IBD patients resulted in significant increases in total cholesterol, HDL-C, and triglycerides, with one-fifth requiring statin therapy. Routine lipid monitoring at 12 weeks and ongoing cardiovascular risk evaluation are recommended to optimise safety outcomes⁴.

7. ACKNOWLEDGEMENT

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A DOCUMENT THAT ENHANCES CLINICAL WRITTEN SKILLS

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Abstract

Introduction

An online document was developed at Newcastle University Medicine Malaysia by which answers to student questions on clinical written skills were made available to clinical year medical students.

Objectives

The objectives were to assess whether the document improved key domains in clinical written tasks, and to identify themes of how the document impacts clinical practice.

Methods

The first phase used retrospective pre-post survey methodology and Likert scales to assess improvement in confidence, knowledge, and ability in written tasks. Chi-square analysis was applied. The second phase involved semi-structured focus groups with graduate doctors. Thematic analysis was applied to identify emerging patterns.

Main Results

73 respondents completed the questionnaire. P-values of <0.001 were obtained for each domain. Themes identified were improving competency in clinical tasks, supporting transition into clinical practice, fostering collaborative learning and teamwork, and enhancing patient safety. Impact of the document was further evidenced by reduction in student queries and failure rates.

Conclusion

The results indicate that the document is a cost-effective method that can assist medical education. The study has high generalisability as written skills are taught and assessed in medical schools worldwide, and most clinical skills stationery items discussed in the document are identical to that used in the UK in practice.

Keywords: *clinical written skills, online document, frequently asked questions*

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1. INTRODUCTION

Junior doctors have various duties, most of which involve written skills. The General Medical Council emphasizes accurate and legible documentation of clinical records, to the appropriate level of detail [1]. Inadequate written communication has, however, been identified as common in healthcare settings worldwide. Inadequate communication can result in discontinuity of patient care, inadvertently compromising patient safety and causing dissatisfaction with treatment [2].

At Newcastle University Medicine Malaysia (NUMed), clinical written skills are explicitly taught and examined. Students would email queries on written skills to specific lecturers in a direct exchange, benefiting only the enquiring student. To allow all students to benefit from such exchanges, a shared online frequently asked questions document was constructed. The document is a Microsoft OneNote document, stored on Microsoft SharePoint. Lecturers post entries relating to emailed queries relating to clinical written skills, with the student anonymised, onto the document. On comprehensive literature search across thirteen research databases, there was no evidence of a similar document used elsewhere.

2. OBJECTIVES

The aims were to assess whether the document was effective in enhancing clinical written skills, and the impact of the document in clinical practice. A sequential explanatory mixed methods design study was performed. The objective of the first, quantitative, phase was a retrospective pre-post survey to determine whether the document improved confidence, knowledge, and ability in clinical written tasks for medical students. The objective of the second, qualitative, phase was to explore the impact of the document in clinical practice.

3. METHODOLOGY

Retrospective pre-post survey

Clinical year students at NUMed were emailed via the research gatekeeper in August 2023 using purposive typical sampling. Eligibility required prior use of the document. The study instrument was a questionnaire on Microsoft Forms. On analysis by two independent senior academicians at NUMed, the instrument demonstrated high validity (content validity index of 1) and reliability (Cronbach's alpha of 0.85). Participation was anonymous and voluntary, with option to withdraw before the survey closure date. The questionnaire included demographic data and 5-point Likert scale items assessing level of agreement to improvement in each of three domains (confidence, knowledge, and ability) in clinical written skills tasks following use of the document. The items were analysed independently. Chi-square analysis was used and p -value of < 0.05 was considered significant.

Ethical approval (2593/34461) was obtained on 7 August 2023.

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Focus group interviews

A qualitative descriptive study using focus groups was employed involving NUMed graduates currently working as junior doctors in the UK. The interview protocol was developed based on the Interview Protocol Refinement Framework [3]. Participants were recruited using purposive typical sampling using an online Microsoft Form, including study information and consent, emailed via the research gatekeeper.

Two semi-structured focus group interviews lasting an hour each, were conducted and recorded in November 2024. The participants comprised of eleven junior doctors, of which ten were female and one was male. The automated transcripts were refined by the authors and sent to the participants for member checking. Thematic analysis was conducted by the authors and triangulated by an independent clinical educator. To mitigate response bias, the research team conducted individual and team reflexivity exercises prior to the interviews.

Ethical approval (2789/48070) was obtained on 8 July 2024.

4. MAIN RESULTS

There were 73 participants in the study. The results of the questionnaire study are shown in Figure 1. Over 90% of participants agreed that the document improved their confidence, knowledge, and ability with $p < 0.001$ for all domains. Stratified analysis by gender, nationality, and year of study confirmed $p < 0.01$ in all subgroups.

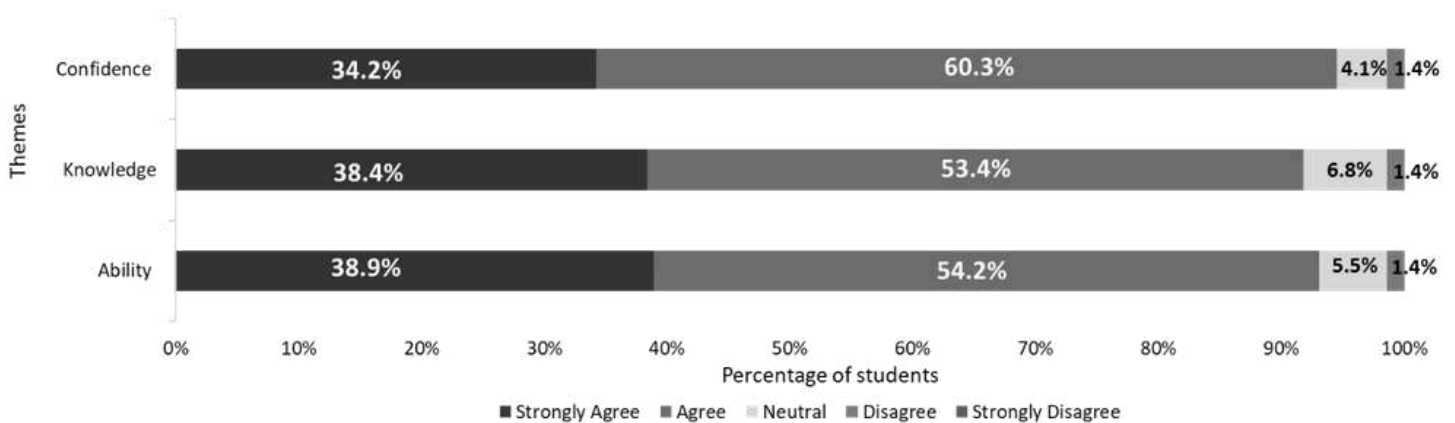


Figure 1. Results of retrospective pre-post survey

NP8

Focus group interviews

Key themes that emerged from the data are shown in Table 1, along with representative quotes.

Table 1. Themes from focus groups

Theme	Description	Participant quotes
Improving competency in clinical tasks	Participants described how the document enhanced competency in clinical written tasks.	<ul style="list-style-type: none"> • “I think the chest X-ray interpretation or any kind of X-ray is really benefitting as it’s exactly the way we are expected to interpret in clinical practice” (FG1, P2).
Supporting transition into clinical practice	Participants reflected on how the resource supported them in their professional journey.	<ul style="list-style-type: none"> • “So, it’s just really nice to have the document to fall back on in times of doubt. I used it most again when I first started, because I was very new to everything” (FG1, P3).
Fostering collaborative learning and teamwork	Participants reflected how the document encouraged peer discussion and resource-sharing.	<ul style="list-style-type: none"> • “Because I was so used to having a paper-based exam or like have the document, it was kind of easy to explain to them [colleagues] as how we used to do it in medical school.” (FG1, P3)
Enhancing patient safety	Participants commented on how the document contributed to enhanced patient care and safety.	<ul style="list-style-type: none"> • “I think to follow up on something I said earlier, how it’s made my documentation a lot clearer. I feel like I’m including, like all the pertinent information that needs to be included with regards to safety” (FG2, P7).

5. DISCUSSION

The results indicate that the document increases knowledge, confidence, and ability of medical students in clinical written skills tasks and enhances patient safety in clinical practice. This indicates a cost-effective method that can assist medical education in medical schools worldwide.

Methodology was evidence-based. Retrospective pre-post survey has been shown to reduce response-shift bias and maintain internal validity by eliminating participants’ internal frame of reference of the measured construct by the educational programme [4]. Likert scale methodology is widely recognized as a validated approach in quantitatively measuring attitude towards a subject [5].

Generalisability

Written skills are included in medical school curricula and examinations worldwide, in the developed and developing world. In the United States, the United States Medical Licensing Examination assesses competencies in documentation, drug monitoring and prescribing [6]. In Nigeria, clinical written skills are part of the basic required competencies of a junior doctor and part of the national curriculum template [7].

Impact

The Kirkpatrick model is the most well-known and utilised model for evaluating training programs [8]. The document was evaluated at the second highest level (job performance). This is supported by the number of queries significantly reducing with document exposure, with reduced failure rates across all clinical years.

Transferability

Most clinical examination stationery items discussed are identical to forms used nationally in the UK.

6. CONCLUSION

The document improved key domains in clinical written tasks. In the workplace it improved competency, fostered collaboration, supported transition into practice, and enhanced patient safety. Its applications are highly generalisable and transferable as written skills are taught and assessed worldwide, and forms used are consistent with those used in clinical practice.

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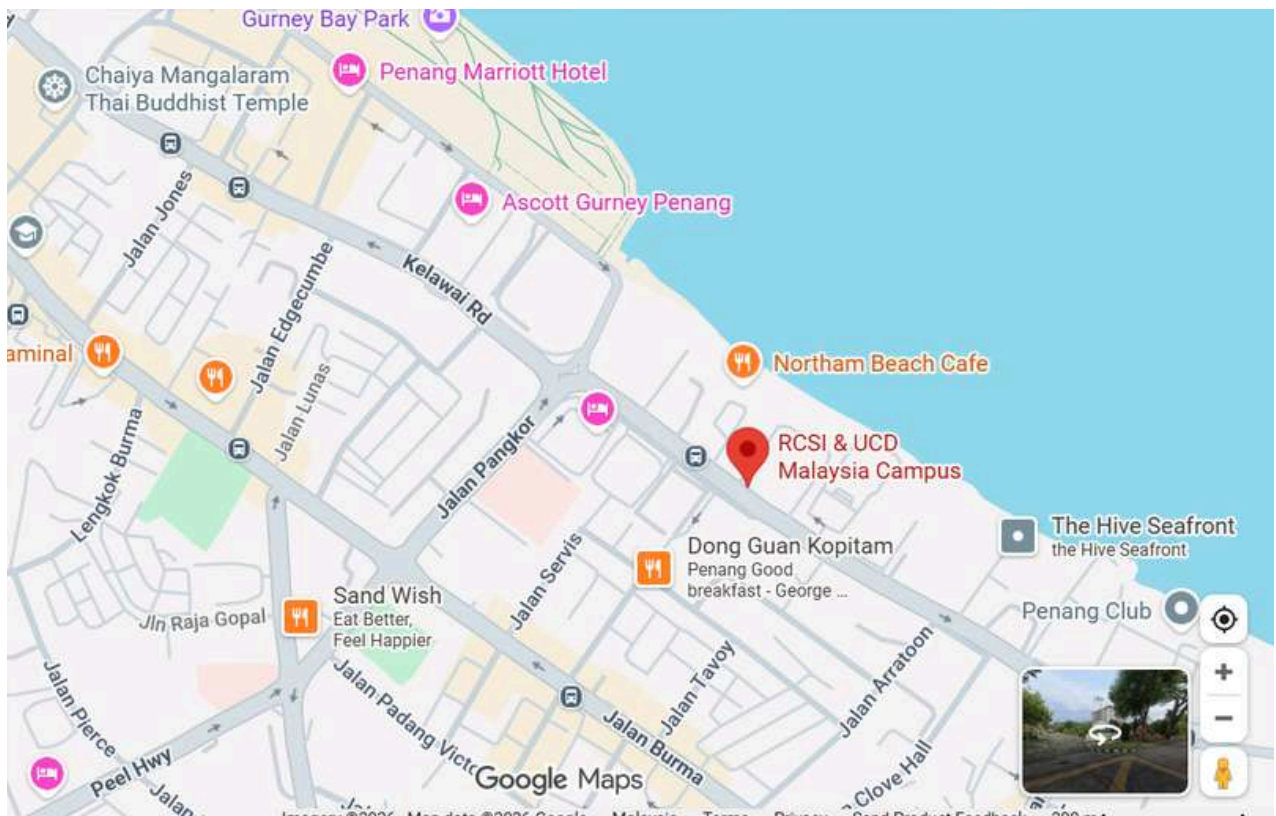
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