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A Descriptive Study of Thesis Completion Challenges Among Medical Students

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Abstract

Background: The Final Project (FP) is a mandatory course for medical education students, typically undertaken in the sixth semester. It is divided into two stages: Final Project 1 (FP1) and Final Project 2 (FP2). In FP1, students develop, document, and present a research proposal, while in FP2, they execute the planned research, analyze the results, and present their findings. A decline in FP2 completion rates was observed in 2024, raising concerns about factors affecting student performance.

Methods: A descriptive analysis methods approach was used, combining quantitative surveys (n=91) and qualitative interviews. The survey, with 10 questions on a 4-point Likert scale, assessed factors affecting FP2 completion. Semi-structured interviews and written responses explored deeper insights, with thematic analysis identifying key barriers.

Results: Survey results revealed moderate motivation (mean=2.77) and high procrastination (mean=3.01). Time management (mean=2.86) and personal issues (mean=2.35) were significant challenges. The main delays were lack of motivation (36.26%) and time management issues (27.47%). Themes from interviews included motivation, time management, supervisor support, data access, and mental health.

Conclusions: Students face key challenges in completing the FP2 course, particularly low motivation, poor time management, and limited supervisor interaction. Addressing these issues through enhanced intrinsic motivation, effective feedback, and structured time management can foster more successful and high-effort student profiles.

Introduction

The Final Project (FP) is a mandatory course for medical education students, culminating in the production of an academic thesis and a first research endeavor that can be published. This project represents students' commitment and dedication to their chosen field of medicine, reflecting their motivation, interests, and perspectives on specific issues. Each student is assigned a faculty advisor who provides guidance and feedback throughout the thesis-writing

process. Weekly meetings between students and advisors are encouraged to discuss each chapter of the thesis, which includes defining the problem, background, research objectives, significance, literature review, theoretical framework, methodology, results discussion, and conclusions.[1]

In addition to writing the thesis, students must fulfill administrative requirements to ensure the FP runs smoothly. Ideally, successful completion of FP requires collaboration and mutual commitment between students and advisors. However, delays in the FP2 process can have significant consequences, particularly for medical students whose progression to clinical training depends on timely FP2 completion. These delays can arise from various factors, warranting a closer examination of challenges impacting the FP process.

Material And Methods

This study employed a mixed-methods approach, combining quantitative descriptive and qualitative methods. The mixed-methods design was chosen to capture a comprehensive understanding of the challenges faced by medical students in completing their Final Project 2 (FP2). Quantitative data provided an overview of the difficulties, while qualitative data offered deeper insights into the underlying issues.[2]

The study population consisted of sixth-semester medical students enrolled in the FP2 course. A purposive sampling method was used to select participants. A total of 91 students completed the survey, which served as the primary instrument for quantitative data collection. The survey consisted of 10 questions designed to evaluate factors affecting FP2 completion, measured on a 4-point Likert scale (1 = strongly disagree, 4 = strongly agree). The survey underwent face validation to ensure clarity and relevance. Quantitative data were analyzed descriptively, with frequencies and percentages used to summarize the responses. The Likert-scale data were further analyzed by calculating the mean and standard deviation for each question to identify trends in student perceptions.[2,3]

For qualitative data collection, semi-structured interviews and written responses submitted via Google Forms were utilized. The interviews aimed to explore students' experiences and challenges in greater depth. The qualitative data were analyzed using thematic analysis. The researchers began by reading the raw data multiple times to identify recurring patterns and commonalities. Similar pieces of information were grouped into themes that addressed the research questions. These themes were then analyzed and interpreted in the context of existing literature to draw meaningful conclusions.

Result

The survey conducted among 91 sixth-semester medical students revealed key challenges and factors impacting the completion of Final Project 2 (FP2).

Quantitative data showed varying levels of student motivation and engagement (Table 1). The average motivation level for completing FP2 was moderate (mean = 2.77, SD = 0.73), with frequent procrastination reported (mean = 3.01, SD = 0.74). Time management difficulties were prevalent (mean = 2.86, SD = 0.71), while personal issues disrupting focus had a lower average score (mean = 2.35, SD = 1.03). Students expressed moderate confidence in their ability to complete FP2 in the near future (mean = 2.32, SD = 1.02).

Regarding advisor interaction, students generally felt supported (mean = 3.18, SD = 0.78) and received clear feedback (mean = 3.16, SD = 0.73). However, challenges with communication were reported by some students (mean = 2.13, SD = 1.02). The need for in-depth guidance was also moderately high (mean = 2.79, SD = 0.84).

Table 1. Final Project Evaluation (n=91)

Dimension	Question	Mean	SD	Min-Max
Motivation	How motivated are you to complete your final project?	2.77	0.73	1-4
Procrastination	How often do you procrastinate on working on your final project?	3.01	0.74	2-4
Time management	Do you have difficulties with time management?	2.86	0.71	1-4
Personal problem	Do your personal problems interfere with your focus on completing your final project?	2.35	1.03	1-4
Confidence	How confident are you in completing your final project in the near future?	2.32	1.02	1-4
Supervision frequency	How often do you meet with your supervisor?	2.68	0.74	1-4
Supervisor support	Do you feel supported by your supervisor?	3.18	0.78	1-4
Supervisor feedback	How clear is the feedback you receive from your supervisor?	3.16	0.73	1-4
Communication difficulty	Do you find it difficult to communicate with your supervisor?	2.13	1.02	1-4
Supervision need	Do you feel the need for more in-depth supervision?	2.79	0.84	1-4

The primary factors causing delays in FP2 completion as shown in Table 2, included a lack of motivation (36.26%), difficulties with time management (27.47%), and personal or health issues (12.09%). Fewer students reported delays due to inadequate advisor guidance (3.30%) or challenges in finding references (6.59%).

Table 2. Main Causes of Delay (n=91)

Statement	n	Percentage
Lack of motivation	33	36.26
Difficulty in time management	25	27.47
Lack of guidance from the supervisor	3	3.30
Personal and health issues	11	12.09
Difficulty in finding references	6	6.59

The majority of students identified intensive guidance (47.25%) and mental support or counseling (39.56%) as critical to completing FP2 (Table 3).

Table 3. Things That Can Help in Completing the Thesis (n=91)

Statement	n	Percentage
Intensive supervision	43	47.25
Mental support or counseling	36	39.56

The qualitative analysis of the barriers to thesis completion among medical students revealed several key themes, each of which highlighted the challenges students face in successfully completing their theses.

1. Motivation

Motivation emerged as a critical factor in the thesis completion process. Many students identified internal motivation, such as self-drive, as a significant influence on their ability to overcome procrastination. One student noted, *"Motivation and I am afraid to submit my thesis for defense because the lead examiner is strict."*

This fear, often driven by a desire to avoid failure, frequently interfered with their ability to engage with the thesis process. Additionally, students expressed anxiety and fear about interacting with their advisors or examiners. For instance, one participant shared, *"I'm afraid to contact my advisor because I haven't updated him about my thesis for a long time."* External motivation also played a significant role, with students highlighting the importance of support systems from family, friends, and mentors. *"Support from friends who always remind me and help explain things I don't understand"* was cited as an essential motivator.

2. Time Management

Time management was another major barrier. Procrastination, or the tendency to delay work, was a frequent challenge mentioned by participants. One student explained, *"Motivating myself and reducing the time spent procrastinating."* Balancing the demands of regular coursework alongside thesis revisions was another issue students faced. As one participant noted, *"Managing time between regular classes and revising my thesis"* proved to be a constant struggle. Additionally, students expressed a need for more structured deadlines to ensure progress. *"Set deadlines for choosing a title and completing each chapter to avoid delays"* was a recommendation from one

participant who felt that a lack of concrete timelines contributed to delays.

3. Supervisor Support

The role of the thesis supervisor was also highlighted as a critical factor in the completion process. Students frequently mentioned the need for supervisors who are accessible and responsive. One student remarked, *"A supervisor who is more active in replying to WhatsApp messages"* as a desired quality. Moreover, the quality of feedback was frequently cited as a challenge. As one participant stated, *"Clearer guidance from my supervisor"* would help in making their thesis revisions more manageable. Students also expressed a preference for more frequent and intensive interactions with their advisors, particularly when working through complex sections like data analysis. *"Intensive supervision for data analysis classes"* was a key request.

4. Data Availability

Access to data was a significant barrier for many students, particularly those working in specialized fields. One student explained, *"I need enough samples. Diabetic retinopathy cases and their severity are rare at S Hospital."* Institutional barriers, such as delays in obtaining ethical approval, were also mentioned as obstacles. One student suggested, *"Speed up the ethical approval process so that the data collection can proceed smoothly."* Students also indicated a need for additional academic support in data collection, with one participant stating, *"Help with sample collection"* as a vital aspect of overcoming this barrier.

5. Mental and Emotional Support

Mental and emotional support were critical factors in managing the stress and anxiety associated with thesis writing. Many students acknowledged the toll that the thesis process took on their mental and physical health. As one student described, *"Improving my mental and physical health first so I can focus on my thesis"* was a necessary step before tackling their academic work. Support from family and friends also played a significant role in helping students maintain emotional stability. One participant expressed, *"The prayers and support from my parents"* helped them cope with the stress and maintain their focus on completing their thesis.

Discussion

The majority of students reported experiencing a decline in motivation during the implementation of Final Project II (FP2). This was attributed to various factors, including internal challenges such as lack of self-confidence and dilemmas regarding the likelihood of success. Howard J.L. et al. highlighted that intrinsic motivation is closely associated with academic success and student perseverance.[4] External factors also contributed to the decline in motivation; however, according to Self-

Determination Theory, extrinsic motivation can still be regulated and, thus, does not necessarily correlate with performance and persistence.[5] The type of motivation possessed by students may be a key determinant in how well they adapt to their academic environment.

Another prevalent obstacle was students' tendency to procrastinate and their difficulty in balancing academic responsibilities with research obligations. Many students reported a lack of structured time management, which often led to neglect of their research projects or working on them only close to the deadlines. Valle et al demonstrated that poor time management significantly increases the time students spend on other academic assignments.[6] Students who struggle with time management often fall into the "difficulties profile" or "low effort profile," both of which are associated with reduced academic efficiency. Implementing appropriate strategies to support students in developing effective time management skills during their studies is therefore crucial for academic success. High academic performance is often linked to students who demonstrate effective time management.[6,7]

Students also expressed concerns about the limited interaction with their academic supervisors. Many found it difficult to schedule meetings or receive timely and constructive feedback, which led to stagnation in research progress and a decline in self-confidence. According to Kamphinda and Chilemba, supervisory support plays a critical role in fostering a social environment that enhances the effectiveness of clinical learning.[8] Several factors, including academic workload, environmental and social influences, and prior experiences, may contribute to the limited interaction between students and supervisors.[9] Mubukee A.G. et al, found that positive relationships between students and supervisors significantly influence the effectiveness of the supervisory process. Furthermore, a lack of feedback from supervisors on students' work can negatively impact research performance.[10] Kamphinda emphasized that effective feedback mechanisms can enhance student confidence and positively affect their academic practices. Praise from supervisors also contributes to increased self-confidence.[8] Moreover, ongoing interaction between students and their supervisors fosters motivation, indicating that regular supervisory presence is essential for identifying solutions to emerging challenges and for improving students' research performance.

Conclusion

Studies indicate that students face significant challenges in completing the Final Project II (FP2) course. Among these, lack of motivation, inadequate time management, and limited interaction with academic supervisors were found to be the most influential factors and, therefore, may

require greater attention from the faculty. Course coordinators need to recognize that fostering intrinsic motivation in students is a key factor in ensuring their success. Moreover, effective feedback from supervisors, combined with encouragement to develop structured time management skills, can help students shift toward more effective and high-effort academic profiles.
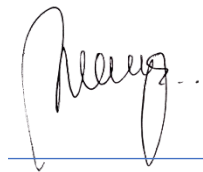
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(Neneng Suryadinata)

Dietary Intake and Physical Activity of Medical School Students at Universitas Pelita Harapan, Indonesia

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Abstract

Background: Medical students face high academic demands, which often lead to irregular eating patterns and a lack of physical activity, which can have a negative influence on their nutritional status and overall well-being. This study aimed to evaluate the dietary intake and physical activity levels among medical students at Universitas Pelita Harapan, Indonesia.

Methods: A cross-sectional study was conducted on 70 undergraduate medical students. Demographic data and physical activity levels (assessed using the International Physical Activity Questionnaire, IPAQ) were collected. Dietary intake was evaluated using a semi-quantitative food frequency questionnaire (SQ-FFQ), and nutrient intakes were analyzed and compared with the Indonesian Recommended Dietary Allowances (RDA) for women aged 19–29 years. Data analysis included descriptive statistics for continuous and categorical variables.

Results: There were 70 participants, with a mean age was 20.73 ± 0.81 years; the majority were female (n = 62). Physical activity levels were distributed as 35.7% low, 38.6% moderate, and 25.7% high. Mean daily energy intake (1677.58 kcal) was below the RDA, as were intakes of fat, carbohydrates, fiber, calcium, sodium, potassium, and vitamin A. Intakes of protein, phosphorus, iron, vitamin C, riboflavin, and niacin were above RDA recommendations.

Conclusions: Medical students at Universitas Pelita Harapan were found to have suboptimal dietary intake, particularly with regard to energy, fiber, and several micronutrients, as well as varying levels of physical activity. These findings emphasize the need for targeted interventions to promote balanced nutrition and regular physical activity in this population.

Introduction

It has become a concern that there is a high prevalence of unhealthy eating patterns and sedentary lifestyles among students worldwide, particularly among medical students who are expected to demonstrate health-promoting behaviors.[1,2] High academic pressure and irregular daily schedules are common in medical education. This can negatively impact eating habits and reduce time for physical activity, contributing to poor nutritional status and an increased risk of chronic disease later in life.[1,2]

Previous research has found that medical students often have inadequate consumption of fruits, vegetables, and dietary fiber, as well as excessive intake of processed foods, sodium, and saturated fat.[3–6] This condition is often accompanied by irregular meal times, skipping meals, and a reliance on convenient instant foods, while academic stress will make it worse.[2,7] In the Indonesian setting, similar challenges were also found, reflecting global and local trends in students' dietary behavior.[8]

Medical students also face challenges when it comes to physical activity, a key determinant of health. Previous research has found that most medical students are physically inactive and have a sedentary lifestyle, despite recognizing the benefits of regular exercise.[9–11] Unhealthy diet and lack of physical activity can have a negative impact on current health status as well as on academic performance and professional competence, especially as future healthcare providers who are expected to educate the public about healthy lifestyles.[12-14]

Currently, data on the dietary patterns and physical activity of Indonesian medical students is still scarce, particularly when compared with the Indonesian Recommended Dietary Allowance (RDA). Several previous studies have examined dietary intake or physical activity, but studies that address both in the context of medical education in Indonesia are still limited.[8,15]

Therefore, this study aims to fill this gap by assessing the dietary intake and physical activity levels of medical students at Universitas Pelita Harapan. Students from the School of Medicine, Universitas Pelita Harapan, were chosen because they represent the population of a private university in a large city in Indonesia who are prone to having an unhealthy diet and a sedentary lifestyle. The objectives of this research are: (1) to describe the sociodemographic of the samples; (2) to quantify dietary intake and compare it against the Indonesian RDA; (3) to evaluate physical activity levels using a validated instrument; and (4) to discuss the implications of these findings in the context of existing literature and medical education.

Material And Methods

This study used a quantitative, observational research design with a cross-sectional approach. The population included bachelor's degree students at the School of Medicine, Universitas Pelita Harapan, Tangerang, Indonesia, who fulfilled the study criteria. A purposive sampling method was used to select 70 respondents. The study was conducted from January to April 2025. Ethical approval was obtained from the Ethics Committee of the School of Medicine, Universitas Pelita Harapan, and all

respondents were required to read and complete an informed consent form at the beginning of the questionnaire.

Inclusion criteria included active medical bachelor program students who were willing to participate in this study. Exclusion criteria included those who were unable to complete the questionnaire. Data collection was carried out through an online survey using "KoboToolbox". Respondents completed a Semi-Quantitative Food Frequency Questionnaire (SQ-FFQ) to assess their daily dietary intake. The SQ-FFQ was adapted from the version developed by the Indonesian Ministry of Health for the 2010 Non-Communicable Disease Survey.[16] Physical activity was assessed using the International Physical Activity Questionnaire (IPAQ) short form, which has been validated for use in young adult populations.[17] The IPAQ categorizes activity levels as low, moderate, or high based on total weekly metabolic equivalent (MET)-minutes. Respondents were classified into one of these categories according to established scoring protocols.

Nutrient intakes were calculated using a standardized Indonesian food composition database. Daily intakes of energy, macronutrients (protein, fat, carbohydrates, fiber), selected minerals (calcium, phosphorus, iron, sodium, potassium, zinc), and vitamins (A, C, thiamin, riboflavin, niacin) were computed.

The calculated mean nutrient intakes were compared to the Indonesian RDA for females aged 19–29 years, as the majority of the sample were female. Intake adequacy was categorized as: below, adequate, or above the RDA for each nutrient.

Data were analysed using SPSS version 26 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to summarize continuous variables (mean, standard deviation, range) and categorical variables (frequency, percentage). Results are presented in tabular form. Nutrient intake status relative to RDA was interpreted descriptively.

Result
Sample Characteristics

The sociodemographic and physical activity characteristics of the study participants are summarized in Table 1.

Table 1. Sociodemographic and Physical Activity Characteristics of Participants (N = 70)

Variable	n	%	Mean ± SD / Range
Age (years)	-	-	
Sex			
- Female	62	88.6	
- Male	8	11.4	20.73 ± 0.81 (19–22)
Physical Activity (IPAQ)			
- Low	25	35.7	
- Moderate	27	38.6	
- High	18	25.7	

The mean age of participants was 20.73 years (SD ± 0.81; range 19–22). The majority of participants were female (88.6%). Physical activity classification indicated that 35.7% of students had low activity levels, 38.6% moderate, and 25.7% high.

Dietary Intake Patterns

The mean daily nutrient intakes, RDA values, and adequacy status are presented in Table 2.

Table 2. Mean Daily Nutrient Intakes of Medical Students Compared to Indonesian RDA (Female, 19–29 years, N = 70)

Nutrient	Mean Intake	RDA	Status vs RDA
Energy (kcal)	1677.58	2250	Below RDA
Protein (g)	65.49	59	Above RDA
Fat (g)	61.83	72	Below RDA
Carbohydrate (g)	214.07	309	Below RDA
Fiber (g)	12.11	30	Below RDA
Calcium (mg)	698.53	1100	Below RDA
Phosphorus (mg)	990.30	700	Above RDA
Iron (mg)	20.27	18	Above RDA
Sodium (mg)	738.96	1500	Below RDA
Potassium (mg)	1933.09	4700	Below RDA
Zinc (mg)	7.95	8	Adequate
Vitamin A (µg RE)	188.76	600	Below RDA
Vitamin C (mg)	113.25	75	Above RDA
Thiamin (mg)	0.84	1.1	Below RDA
Riboflavin (mg)	1.52	1.1	Above RDA
Niacin (mg)	18.21	14	Above RDA

*RDA = Recommended Dietary Allowance, Indonesia

Discussion

This study examines dietary intake and physical activity patterns among medical students at Pelita Harapan University in Indonesia. The results showed significant deficiencies in energy, fiber, and several micronutrients, with most students having low to moderate levels of physical activity. These findings are consistent with those reported in similar populations worldwide. [1,3,6]

Dietary Intake Patterns

Energy and Macronutrients

This study found that participants had a daily energy intake (1677.58 kcal) that was significantly lower than the RDA (2250 kcal). This is consistent with findings from studies in Pakistan, Saudi Arabia, and the United States, which also reported suboptimal energy intake among medical students, often associated with skipping meals and irregular eating habits.[1,2,6] Low energy intake can impair cognitive and physical performance, which is crucial for medical students facing busy academic schedules.

In contrast, protein intake exceeded the RDA (65.49 g vs. 59 g). Similar patterns have been found elsewhere, where protein-rich foods are often preferred for their satiety, but may not compensate for overall energy or micronutrient deficits.[3,5] Fat and carbohydrate intakes were both below recommended values, with carbohydrate

intake being particularly low (214.07 g vs. 309 g). This imbalance may reflect preferences or dietary constraints related to convenience and cost, as well as limited dietary variety.[4,18]

Fiber intake was very low compared to the RDA (12.11 g vs. 30 g), consistent with findings in medical students in the United States and Latin America.[3,9] Insufficient fiber intake has been associated with an increased risk of metabolic and gastrointestinal disorders, and may reflect low consumption of fruits, vegetables, and whole grains, as found in previous studies.[9]

Micronutrients

Calcium, sodium, potassium, and vitamin A intakes were all below RDA recommendations, echoing previous reports of micronutrient inadequacies among medical students.[3,6,10] Calcium deficiency is particularly concerning for young adults, given its importance for bone health and long-term prevention of osteoporosis. Low sodium and potassium intakes may indicate low consumption of mineral-rich foods and/or underreporting of processed food intake.[9] Vitamin A insufficiency, combined with low intake of fruits and vegetables, can have implications for immune and visual health.[10]

Phosphorus, iron, vitamin C, riboflavin, and niacin intakes exceeded recommendations. Elevated iron intake may be attributable to increased consumption of animal-sourced foods or iron-fortified products, which is beneficial for premenopausal women but may not fully mitigate other dietary insufficiencies.[8] High vitamin C intake may reflect consumption of specific fruits or beverages, though this does not appear to translate into adequate fiber or vitamin A intake, highlighting the complexity of dietary behaviors.[3]

Zinc intake was marginally adequate, consistent with findings from other student populations.[3,6] However, marginal deficiencies may still pose risks, particularly in the context of other micronutrient deficits.

Comparison with International Data

The present findings are consistent with studies from diverse settings, which report similar dietary inadequacies among medical students.[1-4,6,10] For example, González-Sosa et al. and Malinowska et al. documented inadequate adherence to healthy dietary patterns, including the Mediterranean diet, among medical students.[4,18] Carcoana et al. and Kesapragada et al. highlighted the gap between nutritional knowledge and practical dietary choices, suggesting that knowledge alone does not guarantee optimal intake.[3,5]

The prevalence of meal skipping, especially breakfast, was observed as a significant factor contributing to

inadequate energy and nutrient intake in several studies.[7,10] Saintila et al. reported that irregular breakfast consumption was associated with higher BMI and poorer dietary quality among medical students in Peru, paralleling trends in Indonesia.[10]

Physical Activity Patterns

The distribution of low (35.7%), moderate (38.6%), and high (25.7%) physical activity levels among participants is comparable to findings from other studies of medical students worldwide.[8,11,12] Kosendiak et al. reported that, during the COVID-19 pandemic, most medical students reduced their physical activity. This may be due to academic pressure, time constraints, and a lack of motivation to be active.[12]

The finding that over one-third of students had low physical activity is concerning, given the well-established benefits of regular exercise for physical, mental, and cognitive health. Szemik et al. and Yadav have emphasized the importance of integrating exercise into the daily routine of medical students to counteract stress and promote overall well-being.[13,14]

The International Physical Activity Questionnaire (IPAQ) provides a useful framework for interpreting activity levels across populations.[17]

Pengpid and Peltzer found that adherence to 24-hour movement guidelines varied widely among ASEAN university students and was closely associated with mental health and diet quality, supporting the regional relevance of our findings.[15]

Implications for Medical Education

The coexistence of suboptimal dietary intake and insufficient physical activity among medical students is particularly problematic, as these individuals are future healthcare providers and role models for healthy behavior. The discrepancy between nutrition knowledge and practice, as highlighted in several studies, suggests that interventions should go beyond didactic teaching to include experiential learning, behavior change strategies, and supportive environments.[3,5]

Medical schools should consider implementing targeted nutrition and lifestyle counseling services, peer support groups, and curricular integration of health promotion activities.[5,13] The use of digital tools and mobile applications, as explored by Marin, may facilitate self-monitoring and promote sustained behavior change.[19]

Limitations

This study has several limitations. The cross-sectional design precludes causal inference. The use of self-reported data for physical activity and dietary intake introduces potential for recall and social desirability bias. The sample was predominantly female, which may limit

generalizability to the broader student population. Future studies should consider larger, more diverse samples and longitudinal designs.

Conclusion

This study demonstrates that medical students at Universitas Pelita Harapan, Indonesia, exhibit suboptimal dietary intake, particularly with respect to energy, fiber, calcium, potassium, sodium, and vitamin A, alongside varied but frequently insufficient levels of physical activity. While protein, iron, phosphorus, vitamin C, riboflavin, and niacin intakes were above recommendations, these do not compensate for broader dietary inadequacies. The findings are consistent with international evidence documenting the vulnerability of medical students to poor nutritional behaviors, despite their health-related training.

Given the critical role of medical students as future healthcare providers, there is an urgent need for integrated interventions targeting both dietary and physical activity behaviors within medical curricula and campus environments. Such efforts are essential not only for the well-being of students themselves but also for their capacity to serve as effective advocates for health promotion in society.

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(Dwi Savitri Rivami)

Exploring the Association Between HIV Knowledge and Prevention Attitudes Among Health Science Students

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Abstract

Background: HIV continues to be a major public health concern worldwide, and comprehensive understanding has shown that HIV knowledge enhances effective prevention behaviors and helps prevent the transmission of the disease. Previous research conducted indicated that higher levels of knowledge were associated with more positive attitudes toward HIV prevention, specifically, 58.7% demonstrated good knowledge and 70.7% engaged in preventive actions. Health science students are a key group for HIV education, as they are future healthcare providers. However, limited research has been done among health science students.

Methods: A cross-sectional study was conducted with 295 health science students consisting of 193 medical and 102 non-medical students. Participants completed two questionnaires, i.e., HIV knowledge with 24 true/false items and HIV prevention attitudes with 23 items on a Likert scale. Descriptive and inferential statistics, including chi-square tests and multivariate logistic regression, were used to analyze the data.

Results: Of the respondents, 43.4% demonstrated good HIV knowledge, while 56.6% had poor knowledge. Regarding prevention attitudes, 59.7% exhibited favorable attitudes, while 40.3% had unfavorable attitudes. A significant positive association was found between HIV knowledge and prevention attitudes (p < 0.001, OR: 2.525, 95% CI: 1.546–4.123). Gender differences were noted, with females displaying more favorable attitudes (p < 0.001, OR: 2.551, 95% CI: 1.487–4.379). Medical students showed less favorable attitudes toward HIV prevention compared to non-medical students (p = 0.042, OR: 1.681, 95% CI: 1.017–2.778).

Conclusions: This study highlights the influence of HIV knowledge, gender, and faculty on HIV prevention attitudes among health science students, with females and non-medical students showing more engagement in prevention efforts. These findings underscore the need for comprehensive HIV education in university curricula to enhance both knowledge and preventive behaviors.

Introduction

The global health crisis posed by the Human Immunodeficiency Virus (HIV) and acquired immunodeficiency syndrome (AIDS) persists, prompting sustained efforts from both international and local initiatives to combat the pandemic.[1] HIV, a virus causing immune system deterioration culminating in Acquired Immunodeficiency Syndrome (AIDS), is a significant public health concern.[2] According to the Joint United Nations Program on HIV/AIDS (UNAIDS), an estimated 38.0 million individuals were infected with HIV

worldwide in 2019, with 36.2 million being adults. Additionally, approximately 7.1 million people are unaware of their HIV-positive status.[3.] The millennium development goals (MDGs) spurred a collective global response to address the escalating spread of HIV/AIDS.[4] Urgent action is needed to develop proactive programs emphasizing prevention education to curb the increasing incidence of HIV. In Indonesia, there were 640,000 cases of HIV/AIDS, with 46,000 being new cases, and the number of deaths increased by approximately 60% between 2010 and 2018.[5] The provinces with the highest number of HIV/AIDS cases include DKI Jakarta, West Java, Central Java, East Java, and Papua. The most affected age groups were 30-39 and 40-49 years old, with high school graduates being the largest educational group affected (54,5%).[6,7]

According to the provided data, Papua has one of the highest rates of HIV/AIDS among the provinces. The provincial government, especially in Merauke, is actively engaged in prevention and control efforts that have been made. These efforts include enhancing information and education, expanding the use of condoms, increasing efforts to prevent mother-to-child HIV transmission, and raising awareness about Regulation No. 3 of 2013 regarding STI, HIV, and AIDS prevention and control. The government's efforts in the field of prevention include the VCT

Program which aims to provide HIV counselling and testing services to the community.[8]

Adolescents and young adults, particularly university students, undergo significant social transitions such as completing education, transitioning to independent living, and experiencing their first sexual relationships.[2] This transitional phase, coupled with increased sexual activity, presents a substantial challenge in HIV prevention efforts targeting this demographic.[9] HIV prevention behaviour is influenced by personal beliefs and perceptions of the disease, as well as the availability of prevention strategies.[10] These personal perceptions are shaped by various intrapersonal factors affecting health behaviour. The lack of awareness or understanding of HIV is also a significant factor impeding changes in sexual behaviour among youth, placing them at a heightened risk of HIV infection.[11] Prevention of HIV/AIDS can be done by providing basic knowledge about infectious diseases to adolescents. Inappropriate forms of information can lead adolescents to promiscuity and other things that can lead to transmission of infectious diseases. Thus, so that adolescents understand and are aware of how dangerous HIV/AIDS is, it can be helped by providing basic knowledge about HIV/AIDS, so that they will have healthy attitudes and behaviours to avoid infectious diseases. In Indonesia,

socialisation efforts through education or counselling about HIV/AIDS among adolescents have not had a significant impact on increasing knowledge.[12]

A study by Khotibul et al. illustrates that a comprehensive understanding of HIV/AIDS significantly enhances prevention strategies and correlates with increased condom use among university students, thereby facilitating effective HIV/AIDS prevention behaviors.[13] This finding is supported by research conducted in Sumedang, which indicated that higher levels of knowledge were associated with more positive attitudes toward HIV/AIDS prevention; specifically, 58.7% of respondents demonstrated good knowledge, 50.0% exhibited moderate attitudes, and 70.7% engaged in preventive actions.[14] Furthermore, a comparative analysis in China revealed that students in education or minority-focused programs had the lowest levels of knowledge, intentions to use condoms, and self-efficacy, likely due to their rural backgrounds, which often lack adequate AIDS educational resources.[15] In addition, research among Indonesians across six major islands identified regional disparities in HIV/AIDS knowledge levels, with participants who had backgrounds in health education and prior involvement in HIV/AIDS programs scoring higher in knowledge, positively impacting their attitudes toward prevention.[16] However, medical students received the highest

average score for AIDS-related knowledge and had a medium level (tending towards good) in attitudes towards risk behaviour, intention, and self-efficacy of condom use. This may be attributed to the extensive AIDS-related education and possibly their conservative attitudes towards sexual behavior. Supporting this, a study among fourth-year nursing students in Indonesia found that 44 out of 88 respondents had good knowledge of HIV/AIDS, 43 had sufficient knowledge, and 1 had insufficient knowledge; additionally, 67 respondents held positive attitudes, 12 exhibited sufficient attitudes, and 9 showed poor attitudes. Overall, the research suggests that knowledge significantly influences attitudes, which in turn affect behavior, indicating that improved health knowledge can lead to proactive measures aimed at preventing the transmission of infectious diseases.[17] This research employed the HIV knowledge and HIV prevention attitudes questionnaires, based on the work of Ratyas Ekartika Puspita. The HIV knowledge questionnaire comprised 24 true-or-false statements, while the HIV prevention attitudes questionnaire included 23 items with response options of Strongly Disagree, Disagree, Agree, and Strongly Agree.[18]

However, previous research at Tribhuwana Tunggadewi University showed that 7 out of 10 students had good knowledge but poor preventive behaviour,

indicating no relationship between knowledge and HIV/AIDS preventive behaviour.[19] Two factors influencing attitudes towards HIV/AIDS knowledge and prevention attitude include education and residency (rural or urban). Parental education levels contribute to enhancing children's understanding of HIV and strategies for preventing its transmission. Higher parental education correlates with increased awareness among children about HIV prevention and protection, whereas lower education levels may elevate the risk of HIV/AIDS transmission.[20] A study showed that there is a significant relationship between place of residence and knowledge about HIV/AIDS and prevention attitude. The results showed that a person living in the countryside has a lower probability of having comprehensive knowledge about HIV/AIDS compared to those living in the city.[21] Based on the explanation above, there is limited research investigating the relationship between HIV/AIDS knowledge and HIV/AIDS preventive behaviors at the university level, particularly among medical students. Furthermore, similar studies have not been extensively conducted in other health-related faculties, such as nursing and health science students. Therefore, this study aims whether the knowledge of HIV/AIDS among health science students is related to their HIV prevention attitude that can be initiated by health science students.

Material And Methods

A cross-sectional study was conducted on health sciences students at Universitas Pelita Harapan, Indonesia. Data were collected through self-administered questionnaires.

The study targeted health science students from the Faculty of Medicine, Nursing, and Pharmacy. Inclusion criteria required participants to be in their third year or higher of study with no marital status. A convenience sampling technique was used to select participants from these faculties. The final sample included 295 students, consisting of 193 medical students and 102 non-medical students from faculty of nursing and pharmacy.

The independent variable was the HIV knowledge of health science students. The dependent variable was the HIV prevention attitudes of the students. Potential confounders considered in this study included gender, faculty, parental education, and the hometown of the students.

HIV Knowledge Questionnaire consisted of 24 items, each with a binary response option "correct" or "incorrect". HIV knowledge scores were categorized into two levels: "good" for scores within the range of 76% to 100%, and "poor" for scores below 75%. HIV Prevention Attitude Questionnaire consisted of 23 items, each rated on 4-point Likert scale, namely "strongly agree", "agree",

"disagree", and "strongly disagree". Scoring for favorable statements was assigned as follows: higher scores indicated more positive attitudes. For unfavorable statements, the scoring was reversed: higher scores indicated less favorable attitudes.

Data was processed and analyzed using SPSS version 26. Descriptive statistics were used to summarize the demographic characteristics of the participants, as well as their HIV knowledge and prevention attitudes. The Chi-square (χ^2) test was performed to assess the bivariate association between HIV knowledge and prevention attitudes. A multivariate analysis was conducted using logistic regression to adjust for potential confounders, including gender, faculty, and parental education. Odds ratios (OR) with 95% confidence intervals (CI) were calculated to determine the strength of these associations. A p-value of < 0.05 was considered statistically significant.

This study was reviewed and approved by the Research Ethics Committee of the Faculty of Medicine, Universitas Pelita Harapan with approval number: 237/K-LKJ/ETIK/VIII/2024. Participants were informed about the study's objectives and methods, and written informed consent was obtained from all participants. Participation was voluntary, and confidentiality was maintained throughout the study.

Result

A total of 336 respondents were initially included in the study, with 295 participants remaining who met the inclusion criteria. The sample was predominantly composed of 65.4% medical students, with the remaining 34.6% representing non-medical students. Most respondents were female, accounting for 75.3%, with only 24.7% male participants. Regarding hometown, 92.9% of respondents came from urban areas, and 7.1% were from rural areas. In terms of parental education, 22.7% of respondents had parents with a high school education or lower, 56.3% had parents with an undergraduate degree, and 21% had parents with a graduate degree.

The HIV knowledge questionnaire included 24 true-or-false questions. Based on the responses, 43.4% of the respondents demonstrated good HIV knowledge, while 56.6% exhibited poor knowledge. The HIV prevention attitudes questionnaire consisted of 23 items with responses on a four-point Likert scale. Overall, 59.7% of respondents exhibited favorable attitudes, while 40.3% demonstrated unfavorable attitudes.

Table 1. Characteristics and Distribution of HIV Knowledge and HIV Prevention Attitudes Among Health Science Students (n=295)

	Frequency (n)	Percentage (%)
Gender		
Male	73	24.7
Female	222	75.3
Hometown		
Rural	21	7.1
Urban	274	92.9
Parent Education		
Senior High School or Lower	67	22.7
Undergraduate Degree (D3/S1)	166	56.3
Graduate Degree (S2/S3)	62	21.0
Faculty		
Medical	193	65.42
Non-Medical (Nursing and Pharmacy)	102	34.57
Knowledge		
Good	128	43.38
Poor	167	56.62
Attitudes		
Favorable	176	59.66
Unfavorable	119	40.34

The relationship between HIV knowledge and HIV prevention attitudes was assessed using the Chi-Square test. Among those with good HIV knowledge, 71.9% had favorable HIV prevention attitudes, while 28.1% had unfavorable. In contrast, 50.3% of those with poor HIV knowledge showed favorable attitudes, and 49.7% exhibited unfavorable attitudes. The Chi-Square test revealed a statistically significant association between HIV knowledge and prevention attitudes (p-value = 0.000). The odds ratio (OR) of 2.525 (95% CI: 1.546–4.123) indicated that those with good HIV knowledge were 2.5 times more likely to have favorable attitudes toward HIV prevention compared to those with poor knowledge.

Regarding the association between faculty and HIV prevention attitudes, 67.6% of non-medical students demonstrated favorable attitudes, while 32.4% showed unfavorable attitudes. Among medical students, 55.4% exhibited favorable attitudes, and 44.6% had unfavorable attitudes. The Chi-Square test for faculty showed a p-value of 0.042, with an OR of 1.681 (95% CI: 1.017–2.778), indicating that non-medical students were 1.6 times more likely to have favorable HIV prevention attitudes than medical students.

Table 2. Association between HIV Knowledge, Other Variables, and HIV Prevention Attitudes (n=295)

Variable	Favorable Attitude	Unfavorable Attitude	Unadjusted OR (95% CI)	p-value
Knowledge				
Good	92 (71.9)	36 (28.1)	2.525 (1.546-4.123)	0.000*
Poor	84 (50.3)	83 (49.7)		
Gender				
Female	145 (65.3)	77 (34.7)	2.551 (1.487-4.379)	0.000*
Male	31 (42.5)	42 (57.5)		
Hometown				
Urban	164 (59.9)	110 (40.1)	1.118 (0.456-2.743)	0.821
Rural	12 (57.1)	9 (42.9)		
Parent Education				
Senior High School or Lower	40 (59.7)	27 (40.3)	1.481 (0.738-2.975)	0.269
Undergraduate Degree	105 (63.3)	61 (36.7)		
Graduate Degree	31 (50.0)	31 (50.0)	1.721 (0.955-3.103)	0.071
Faculty				
Non-medical	69 (67.6)	33 (32.4)	1.681 (1.017-2.778)	0.042*
Medical	107 (55.4)	86 (44.6)		

*Statistically significant at $p<0.05$, X^2 test

Between gender, HIV prevention attitudes showed significant differences. Of the female respondents, 65.3% demonstrated favorable attitudes, while 40.1% of females exhibited unfavorable attitudes. Among males, 42.5% had favorable attitudes, and 57.5% showed unfavorable attitudes. A Chi-Square test revealed a p-value of 0.000, with female students being 2.5 times more likely (OR: 2.551; 95% CI: 1.487–4.379) to have favorable attitudes compared to their male counterparts.

When examining the effect of hometown, 59.9% of respondents from urban areas exhibited favorable attitudes, while 57.1% of those from rural areas also had favorable attitudes. However, the Chi-Square test for hometown area showed a p-value of 0.821, suggesting that there was no significant association between hometown area (urban vs. rural) and attitudes toward HIV prevention.

Parental education levels were also explored in relation to HIV prevention attitudes. Among respondents with parents who had a high school education or lower, 59.7% demonstrated favorable attitudes, while 40.3% exhibited unfavorable attitudes. Among those with parents who had an undergraduate degree, 63.3% showed favorable attitudes, and 36.7% had unfavorable attitudes. Among respondents with graduate-educated parents, attitudes were split evenly, with 50% showing favorable

and 50% unfavorable attitudes. Chi-Square analysis revealed no significant association between parental education and HIV prevention attitudes, with p-values of 0.269 and 0.071 for the respective comparisons.

Multivariate analysis, which included variables such as knowledge, gender, faculty, and parental education, showed that HIV knowledge was the most significant predictor of favorable HIV prevention attitudes. The p-value for knowledge was 0.000, and the odds ratio of 2.841 indicated that students with good HIV knowledge were significantly more likely to have favorable attitudes toward HIV prevention than those with poor knowledge. Gender also had a significant impact on HIV prevention attitudes, whereas parental education and faculty showed no significant association.

Table 3. Association between HIV Knowledge and Prevention Attitudes Adjusted by Other Variables (n=295)

Variable	Adjusted OR (95% CI)	p-value
Knowledge	2.841 (1.698 – 4.752)	0.000*
Gender	2.386 (1.352 – 4.211)	0.003*
Parent education	1.095 (0.744 – 1.613)	0.645
Faculty	1.678 (0.960 – 2.934)	0.069

*Statistically significant at $p<0.05$

Discussion

This study included a total of 336 respondents, with 295 met the inclusion criteria, while the remaining 41 were excluded due to incomplete or unclear

questionnaire responses. Among the participants, 193 were medical students and 102 were non-medical students. The sample consisted of 75.3% female respondents, 92.9% of whom resided in rural areas. Around, 56.3% of respondents had parents with an undergraduate degree as their highest level of education. Additionally, 65.42% respondents were enrolled in medical faculties and 34.57% non-medical (Nursing and Pharmacy) faculty.

HIV knowledge among health science students revealed that 43.38% of respondents had good knowledge, while 56.62% had bad/fair knowledge. Among these students, good knowledge of clinical aspects of the disease may be attributed to classroom learning or participation in seminars and workshops. On the other hand, bad/fair HIV knowledge may result from lack of awareness regarding health information, health-related issues, and optimal health solutions. Additionally, insufficient understanding of the information received may lead to misconceptions and incorrect interpretations of certain health facts.[30]

The distribution of HIV prevention attitudes among health science students indicated that 59.66% exhibited favorable attitudes, while 40.34% had unfavorable attitudes. These findings align with research conducted by Pravitasari et al. (2024), which reported that 56% of respondents demonstrated a positive

attitude toward HIV prevention, whereas 44% exhibited a negative attitude.[31] This discrepancy may be attributed to respondents' reactions to their knowledge, awareness, and the attitudes they adopt, which contribute to the development of effective strategies for addressing the disease.[30]

The findings indicated that non-health students (Nursing and Pharmacy) had a higher mean score for attitudes toward HIV/AIDS prevention (76.63) compared to medical students (73.07). A statistically significant difference was observed, as reflected by a p-value of 0.004, suggesting a notable variation in prevention attitudes between nursing and pharmacy students and medical students. This aligns with previous studies showing that health students tend to actively seek out information on HIV/AIDS, contributing to a stronger understanding of prevention and management strategies. In contrast, while medical students possess more detailed knowledge about the medical aspects of HIV/AIDS, they may not be as involved in preventive activities outside of clinical practice.[32]

This study found no significant difference in HIV knowledge between medical students and non-medical students, regardless of gender. Among medical students, female students had a higher average HIV knowledge score of 74.22, while in non-medical students, male students scored higher with an average of

74.70. This finding is consistent with research by Haroun et al. (2015), which indicated that females had better HIV knowledge than males, although the difference was not statistically significant (61% vs. 59%; p = 0.06). The respondents' answers revealed that a significant proportion of males answered incorrectly to the question regarding whether HIV is incurable, with 38% of males responding incorrectly compared to 45% of females (p = 0.018). Additionally, males were more likely to incorrectly believe that "mosquito bites could be a mode of transmission," with 27% of males and 20% of females giving this incorrect response (p = 0.008). This suggests that male respondents had gaps in their understanding of crucial facts about HIV transmission and treatment.[33] In terms of HIV prevention attitudes, there was a significant difference between female and male medical students, with a p-value of 0.013 and a higher average score for females (74.41). In contrast, among non-medical students, there was no significant difference in HIV prevention attitudes between genders, although male students had a higher average score of 76.66. Overall, this study concludes that women tend to have a better HIV prevention attitude than men. These findings align with research by Lybella et al. (2015), which demonstrated that women generally exhibit more positive attitudes toward prevention efforts compared to men. Lybella et al. suggested that women are

more likely to avoid risky behaviors and are better at fostering a sense of self-protection than men.[34]

The study conducted a bivariate test to examine the relationship between HIV knowledge and HIV prevention attitudes in health science students. The results revealed a significant association with a p-value of 0.000, indicating a strong correlation. The odds ratio (OR) was calculated to be 2.525 (95% CI: 1.546-4.123), suggesting that individuals with bad or fair HIV/AIDS knowledge are at 2.5 times greater risk of having unfavorable HIV/AIDS prevention attitudes. This finding aligns with the findings by Permata et al (2024), which also demonstrated a significant relationship between HIV knowledge and prevention attitudes (p = 0.000).[35] Similarly, Pakpahan et al's study (2020) among NERS students confirmed a significant correlation (p = 0.000).[17] Priastana (2018) stated that there is a relationship between the level of HIV/AIDS knowledge and HIV/AIDS prevention, where adolescents with higher knowledge can determine HIV/AIDS prevention attitudes better.[36] A person's knowledge about something will affect their attitude. Proper knowledge significantly contributes to forming appropriate attitudes and allows for deeper consideration when making decisions. Therefore, knowledge about HIV/AIDS prevention can serve as the main pillar in HIV/AIDS prevention among adolescents, as good knowledge supports

efforts to combat the spread of HIV/AIDS.[37]

On the other hand, a study by Rajikan (2017) discovered that despite having low average HIV/AIDS knowledge scores, health science students exhibited a positive attitude towards HIV/AIDS. This could be attributed to the young age of the respondents (under 23 years old), which may limit their personal life experience. Additionally, Rajikan's study specifically focused on students in their first and second year of medical school, indicating that their level of knowledge might differ from that of students in their third year or higher.[38]

A P-value of 0.042 was obtained for the relationship between faculty and HIV/AIDS prevention attitudes, indicating a significant difference in attitudes toward HIV/AIDS prevention among health science students. The odds ratio (OR) was calculated as 1.681 with a 95% confidence interval (CI) of 1.017–2.778, suggesting that nursing and pharmacy students (non-medical) are 1.6 times more likely to have unsupportive attitudes toward HIV/AIDS prevention compared to medical students. These findings align with Ni Putu et al. (2018), who also observed a significant difference in prevention attitudes between medical students and those in Pharmacy and Nursing, with a p-value of 0.000. The discrepancy may be due to medical students receiving more credits for HIV-related topics in their curriculum compared

to Pharmacy and Nursing students.[32] Priastana suggested that knowledge acquired through education can shape a person's attitude towards taking preventive measures against HIV/AIDS.[36] Azizah (2016) also asserted that knowledge consistently has a significant impact on attitudes towards HIV/AIDS prevention.[39] This is further supported by Ni Putu's research, which found that medical students had the highest average level of knowledge related to HIV/AIDS.[32]

A significant association was found between gender and HIV/AIDS prevention attitudes among medicine, nursing, and pharmacy students, with a p-value of 0.000. This indicates a notable difference between male and female students in their attitudes toward HIV/AIDS prevention, with female respondents displaying more supportive attitudes than their male counterparts. The odds ratio suggests that females are 2.551 times more likely than males to have favorable attitudes toward HIV/AIDS prevention. These results are consistent with the study by Lybella et al. (2015), which showed that females tend to have more positive attitudes toward prevention efforts than males. Females generally tend to follow societal norms and act more cautiously compared to males. Psychologically, females are also more motivated and diligent in learning, which gives them a better understanding of how to behave in various situations, including those related to HIV/AIDS and its

prevention.[34] This theory is supported by data from KEMENKES in 2014, which indicates that the incidence of HIV/AIDS in Indonesia is higher among males than females.[40]

Analyses were also performed to evaluate the association between hometown (urban or rural) and parental education and toward HIV/AIDS prevention attitude among health science students. A p-value of 0.821 was obtained, indicating no statistically significant relationship between residential location and HIV/AIDS prevention attitudes. These findings are consistent with the study by Tiranda et al. (2018), which found that residence had no significant association with HIV/AIDS prevention attitudes (p-value = 1.000).[41] This suggests that although differences in prevention attitudes may exist between urban and rural university students, overall awareness and positive attitudes toward HIV/AIDS prevention remain consistently high across both groups.[42]

Additionally, the chi-square test results for combining the 'high school or lower' education category with the 'undergraduate degree' category yielded a p-value of 0.269, while the combination of the 'high school or lower' category with the 'graduate degree' category resulted in a p-value of 0.071. These p-values indicate that there is no significant association between parental education and HIV prevention attitudes. This suggests that

students' attitudes toward HIV/AIDS prevention are not strongly influenced by their parents' education levels, as they often acquire information from various other sources.[43] Research by Diyanah (2021) states that high parental education does not always guarantee that the parents will provide adequate education to their children about HIV.[43] As a result, many students develop awareness and prevention strategies for HIV/AIDS independently, without significant input from their parents.[43]

In multivariate analysis, it was discovered that knowledge of HIV was the most significant factor influencing HIV prevention attitudes among health science students, as indicated by the lowest p-value (0.000) and the highest odds ratio (OR) of 2.841 compared to the other three variables. According to Pakpahan et al. (2020), education level influences attitudes; more educated adolescents tend to have better attitudes. This is because education plays a crucial role in shaping and developing attitudes.[17] Additionally, Pravitasari et al. (2024) note that a person's attitude is shaped by their level of knowledge about a subject. Personal experiences, schooling, and emotions can also affect a person's attitude. Both positive and negative perspectives are linked to how much a person understands about HIV/AIDS. Therefore, the more knowledge an individual has about this issue, the more likely they are to have a

positive attitude toward HIV/AIDS prevention.[31]

Conclusion

This study highlights the critical role of HIV knowledge in shaping HIV prevention attitudes among health science students. Furthermore, attitudes toward HIV prevention were influenced by gender and faculty. Female students demonstrated more favorable prevention attitudes than males and non-medical students exhibited more engagement in prevention efforts than their medical counterparts. These findings underscore the importance of integrating comprehensive HIV education into university curricula, which should focus not only on knowledge but also on promoting preventive behaviors. The study's results also emphasize the need for further research to explore the long-term impact of such educational interventions and how they translate into real-world behaviors.

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(Shirley Moningkey)

Knowledge of coronary heart disease risk factors and associated dietary fat intake among medical students

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Abstract

Background: Coronary heart disease (CHD) prevalence has increased among young adults. The most common CHD risk factor among young adults was high daily fat intake. Knowledge regarding CHD risk factors was a crucial element in determining health behaviour, including healthy dietary patterns. However, the level of CHD knowledge and its association with dietary fat intake among medical students is still unclear.

Methods: The study was performed among preclinical medical students at the Pelita Harapan University, Indonesia. The CHD risk factor knowledge was assessed using the validated Heart Disease Fact Questionnaire (HDFQ), comprising of 25 items. The dietary fat intake was evaluated using the validated Block Dietary Fat Screener (BDFS) questionnaire.

Results: A total of 98 participants were included in this study. The median age of the participants was 19 years (IQR 18-20). Of the 98 participants, 71 (72%) participants had adequate knowledge of CHD risk factors. Older age, being female, and being in the third year of medical study were related to higher HDFQ scores. The daily fat intake was classified as high in 33 (34%) of participants and very high in 33 (34%) of participants. No significant difference in dietary fat intake level was observed between participants with and without adequate knowledge of CHD risk factors.

Conclusion: This study reveals that most medical students had adequate knowledge of CHD risk factors. However, the knowledge factor did not lead to healthy dietary pattern adoption among medical students, suggesting that the implementation of an education and training program to motivate lifestyle modification was required.

Introduction

Coronary heart disease (CHD) has emerged as a significant global health concern, increasingly affecting younger populations amid shifting lifestyle patterns.[1,2] The prevalence of CHD in young people ranges from 1% to 16% and is higher in South Asian population.[3-9] CHD in young adults was associated with high rates of major adverse cardiac event recurrences, worse long-term prognosis, and premature death.[10,11] Additionally, CHD in working-age individuals causes a reduction in workplace productivity.[12,13] Indonesia has been reported to have the second-worst disability-adjusted life years (DALYs) rates due to CHD.[12]

The CHD risk factors among young adults were commonly related to behavioural risk factors, such as smoking, unhealthy diet, and physical inactivity.[1,2] Knowledge regarding health risks was the

crucial element for individuals to adopt healthy behaviours.[14] Previous meta-analysis studies have demonstrated the low knowledge of CHD risk factors among young adults, resulting in poor attitudes towards CHD prevention.[15] The most prevalent CHD risk factors among young adults were high intake of dietary fat.[15,16] In young adults, due to the socio-cultural and environmental factors, the dietary pattern was generally shifted towards high consumption of fast foods, resulting in the increased serum saturated fatty acids (SFA), trans fats that eventually promote plaque formation in vascular.[17-19]

Given that adequate knowledge of CHD is an essential factor for fostering healthy behaviors, and it remains a persistent challenge among young individuals and underreported among medical students, in this study, we assess the level of CHD risk factor knowledge among medical students. In addition, we evaluate the dietary fat intake pattern among medical students and its relationship with the level of CHD knowledge to better understand the importance of the knowledge factor for motivating behavioral changes among medical students.

Material And Methods

Study design and participants

This cross-sectional study was conducted from March to June 2025 at the Medical Faculty of Pelita Harapan University, Banten, Indonesia. Participants were preclinical medical students enrolled through non-probability convenience sampling. Written informed consent was obtained from the participants. This study received ethical approval from the Pelita Harapan University research ethics committee (No: 181/K-LKJ/ETIK/IV/2025).

Data collection

Data was collected using the questionnaire disseminated through Google Forms or social media platforms, such as Line and WhatsApp. The socio-demographic variables, including age, gender, academic year, history of cardiovascular disease, and family history of cardiovascular disease, were collected. The knowledge of risk factors for the development of CHD was evaluated using a validated Heart Disease Fact Questionnaire (HDFQ) comprising 25 items.[20] The HDFQ demonstrated adequate internal consistency, with a Kuder-Richardson-20 reliability of 0.77, the corrected item-total correlations ranging from 0.18 to 0.41, and the test-retest reliability of 0.89.[20] Participants were asked to respond to each question with possible answers of true, false, or I do not know. The HDFQ scoring system consists of 1 point for each correct response and 0 for incorrect and "I do not know" responses. The final score was calculated by summing the points for all the items,

and a total score >20 indicated the good or optimal knowledge of participants, as described in a previous study.[21] Further, the different domains of cardiovascular disease knowledge were assessed through 25 items of HDFQ : (a) the role age, gender, genetics and family history was evaluated in items 1, 2, 3, and 25, (b) the CHD risk factors were measured in items 4, 6, 8, 12, 16, and 18, (c) the importance of exercise in cardiovascular disease prevention was assessed in items 13, 14, and 15, (d) the contribution of diet and cholesterol level in CHD was determined in items 9, 10, 11, 17, 20, and 22, and (e) the role of lifestyle intervention in CHD was assessed in item 5, 7, 19, 21, 23, 24.

The habitual fat intake was measured using the validated Block Dietary Fat Screener (BDFS) questionnaire.[22] This instrument consists of 17 items that evaluate the consumption frequency of 41 high-fat foods. The frequency of fat consumption was categorized as follows scales: 0 points = one time a month or less, 1 point = two to three times a month, 2 points = one to two times a week, 3 points = three to four times a week, and 4 points = from five to more times a week. The total score of 0 to 7 indicates very low-fat intake, 8 to 14 suggests the average fat intake, 15 to 22 equals high-fat intake, and ≥23 represents very high-fat intake individuals.

Statistical analysis

The numeric variables were described as median (interquartile range, IQR), and the nominal variables were shown as counts and percentages. JASP (version 0.19.3) was used for statistical analysis and graph drawing. In all analyses, a two-tailed p-value of less than 0.05 was considered statistically significant.

Result

Participants characteristics

A total of 98 participants were included in the present study. The median (IQR) age of participants was 19 (18-20) years, of which 38 (39%) were male and 60 (61%) were female. More than half of the participants (63%) were in their first year of preclinical medical studies. About 24 (25%) participants had a family history of cardiovascular disease. The general characteristics of participants are demonstrated in **Table 1**.

Table 1. The sociodemographic characteristics of participants

Variables	n = 98
Age, median (IQR)	19 (18-20)
Gender, n (%)	
Male	38 (39)
Female	60 (61)
Year of study, n (%)	
First year	63 (63)
Second year	19 (19)
Third year	16 (16)
Personal medical history of cardiovascular diseases, n (%)	
Yes	0 (0)
No	100 (100)

Family history of cardiovascular diseases, n (%)	
Yes	24 (25)
No	74 (75)

Assessment of CHD risk factor knowledge among participants

In this study, we observed that 27 (28%) participants had inadequate knowledge (HDFQ total score ≤20), whereas 71 (72%) participants showed adequate knowledge of CHD risk factors (HDFQ total score >20) (**Figure 1A**). The HDFQ total score was positively correlated with the age variable (p: 0.004, **Figure 1B**). A higher HDFQ score was found in females compared to males (mean: 22 vs. 21, p: 0.026, **Figure 1C**). In addition, the third-year medical students had greater HDFQ scores than the first-year medical students (mean: 23 vs. 21, p: 0.013, **Figure 1D**). There is no significant difference in the HDFQ score between participants with and without a family history of cardiovascular disease (**Figure 1E**).
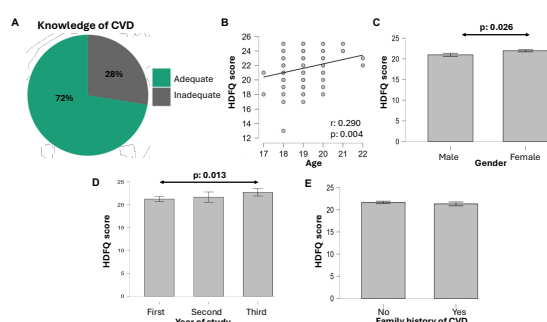
(A) A pie chart illustrates the percentage of participants with adequate and inadequate knowledge of cardiovascular disease. The level of knowledge was also evaluated based on the participant's age (B), gender (C), year of study in medical school (D), and family history (E). Statistical analysis was performed using the Spearman rank correlation test to evaluate correlations, the Mann-Whitney U test to compare two independent groups, and the Kruskal-Wallis test followed by Dunn's multiple comparison to compare more than two independent groups. Data was presented as mean ± standard error of the mean (SEM). Abbreviations in figure: CVD, cardiovascular disease; HDFQ, Heart Disease Fact Questionnaire.

From the HDFQ items analysis as shown in **Table 2**, we found that most participants recognized smoking, high blood pressure, high cholesterol, being overweight, diabetes, family history, and older age are risk factors for cardiovascular disease. However, only 43 (44%) participants knew the effect of gender on the risk of cardiovascular disease. In addition, we observed that most participants understand the cardiovascular disease prevention measures, for example, smoking cessation, regular physical activity, maintaining a healthy weight, and controlling high blood pressure, high blood sugar, and high cholesterol levels. Although a greater number of participants correctly answered the questions related to the role of diet and cholesterol in the risk of developing cardiovascular disease, we figured out that only 63 (64%) participants were aware of the tendency of low good cholesterol (high-density lipoprotein/HDL) in diabetes conditions.

Figure 1. Knowledge about the risk factors for the development of cardiovascular disease among medical students

Table 2. Response of Heart Disease Fact Questionnaire (HDFQ) among participants

No	Questions	Correct response	Frequency n (%)
1	A person always knows when they have heart disease	False	84 (86)
2	If someone has a family history of heart disease, the greater their risk of heart disease	True	91 (93)
3	The older a person is, the greater their risk of heart disease	True	91 (93)
4	Smoking is a risk factor for heart disease	True	94 (96)
5	A person who stops smoking will lower their risk of heart disease	True	83 (85)
6	High blood pressure is a risk factor for heart disease	True	96 (98)
7	Keeping blood pressure under control will reduce a person's risk for developing heart disease	True	94 (96)
8	High cholesterol is a risk factor for developing heart disease	True	96 (98)
9	Eating fatty foods does not affect blood cholesterol	False	80 (82)
10	If someone's good cholesterol (HDL) is high, he/she is at risk for heart disease	False	72 (73)
11	If someone's bad cholesterol (LDL) is high, he/she is at risk for heart disease	True	94 (96)
12	Being overweight increases a person's risk for heart disease	True	97 (99)
13	Regular physical activity will lower a person's chance of getting heart disease	True	93 (95)
14	Only exercising at a gym or in an exercise class will lower a person's chance of developing heart disease	False	69 (70)
15	Walking and gardening are considered exercise that will help lower a person's chance of developing heart disease	True	93 (95)
16	Diabetes is a risk factor for developing heart disease	True	91 (93)
17	High blood sugar puts strain on the heart	True	91 (93)
18	If someone's blood sugar is high over several months it can cause his/her cholesterol level to go up and increase his/her risk of heart disease	True	89 (91)
19	A person who has diabetes can reduce their risk of developing heart disease if they keep their blood sugar levels under control	True	82 (84)
20	People with diabetes rarely have high cholesterol	False	75 (77)
21	If a person has diabetes keeping their cholesterol under control will help to lower their chance of developing heart disease	True	85 (87)
22	People with diabetes tend to have low HDL cholesterol	True	63 (64)
23	Person who has diabetes can reduce their risk of developing heart disease if they keep their blood pressure under control	True	81 (83)
24	Person who has diabetes can reduce their risk of developing heart disease if they keep their weight under control	True	88 (90)
25	Men with diabetes have higher risk of heart disease than women with diabetes	False	43 (44)

Factors associated with the level of dietary fat consumption among participants

As shown in **Figure 2A**, most participants had dietary fat consumption in high (34%) to very high (34%) levels. There was no significant relationship between fat intake with age variable (**Figure 2B**), level of study of participants in medical school (**Figure 2D**), family history of cardiovascular disease (**Figure 2E**), and knowledge of cardiovascular disease (**Figure 2F**). A significantly higher BDFS score, indicating increased dietary fat consumption, was found in females than in males (mean: 21 vs. 17, p: 0.026, **Figure 2C**).
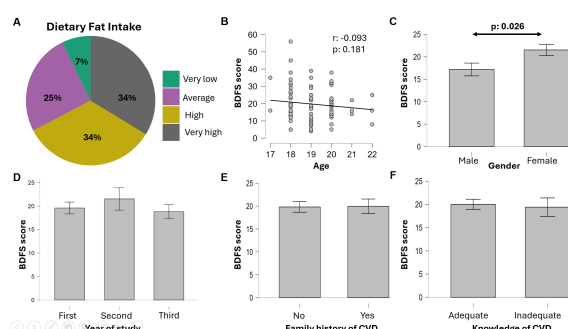
Figure 2. Level of dietary fat consumption among medical students

(A) A pie chart illustrates the percentage of participants with very low, average, high, and very high intake of fat. The level of dietary fat intake was also evaluated based on the participant's age (B), gender (C), year of study in medical school (D), family history (E), and knowledge of cardiovascular disease (F). Statistical analysis was performed using the Spearman rank correlation test to evaluate correlations, the Mann-Whitney U test to compare two independent groups, and the Kruskal-Wallis test followed by Dunn's multiple comparison to compare more than two independent groups. Data was presented as mean ± standard error of the mean (SEM). Abbreviations in figure: CVD, cardiovascular disease; BDFS, Block Dietary Fat Screener.

Discussion

Coronary heart disease (CHD) is the most common type of cardiovascular disease and the leading cause of mortality and morbidity globally, including in Indonesia.[12,23] Even though CHD is frequently found at older ages, several reports have shown an increase in CHD in young individuals, particularly in the Asian population.[4-9] The young CHD term is defined as CHD that occurred before the age of 45 years.[24] The consequence of young CHD is devastating, with a negative impact on productivity and an enhanced risk of cardiovascular event recurrence.[10,12]

The modifiable risk factors of CHD, such as smoking, sedentary lifestyle, hypertension, hyperlipidaemia, diabetes mellitus, obesity, and unhealthy dietary intake, were increased in prevalence among young adults.[1] The extent of atherosclerotic lesions in CHD was related to the CHD risk factors.[2,25,26] The most important primary prevention to prevent the cardiovascular events of CHD was promoting healthy lifestyle behaviour.[1,27] To achieve healthy lifestyle behaviours among individuals, adequate knowledge regarding CHD risk factors was a crucial factor.[28,29] Individual knowledge will influence the adoption and engagement towards healthy behaviour.

Medical students will eventually become professional healthcare workers involved in health promotion by encouraging people to adopt healthy lifestyles. Thus, they must have optimal knowledge of disease risk factors to prevent the development and progression of non-communicable diseases, such as CHD. In this study, we observed that 72% of participants demonstrated sufficient knowledge of CHD. This result is similar to previous studies in Saudi Arabia and Nigeria, showing the optimal CHD knowledge in healthcare students.[21,30] In terms of CHD risk factors, CHD management, and the role of physical activity in CHD risk reduction, more than 70% of respondents answered correctly

items in the HDFQ questionnaire, indicating good CHD knowledge in this area.[21,31] While respondents in this study recognised that high cholesterol was a risk factor for developing CHD and were able to identify the role of good cholesterol (HDL) and bad cholesterol (LDL) in CHD risk, they did not recognise that individuals with diabetes tend to have lower HDL cholesterol. In addition, the knowledge deficit regarding gender factors as CHD risk factors was observed in this study. Overall, these findings may suggest the lack of a comprehensive understanding of the role of diabetes, cholesterol, and hormones in CVD pathogenesis.

In the present study, significantly higher HDFQ scores were observed in females than in males. Previous studies have shown the differences in health literacy and the engagement activity of health-seeking information between females and males.[32-34] The differences are possibly related to the traditional role of females as family caregivers and children, and the greater concern about appearance and aesthetics in females. Moreover, we observed that third-year medical students had greater HDFQ scores than first-year students. This result may be due to more exposure to health information, clinical training, and critical thinking skills in third-year medical students than in first-year medical students. Furthermore, a positive

correlation was found between HDFQ scores and age, which may be explained by the fact that the age of participants is associated with their study level.

The daily intake of a high-fat diet was reported as the most common CHD risk factor among young adults.[2,16,35] The impact of dietary fat on artery disease was related to the types of fatty acids and cholesterol.[36] High levels of saturated fatty acids (SFA), trans fats, and cholesterol, particularly LDL cholesterol, can build up the lipids in the artery wall, leading to plaque formation and blood vessel narrowing. In the present study, the frequency of participants with high and very high daily fat consumption was 34% and 34%, respectively. This result is in line with existing findings that demonstrate unhealthy eating behaviours among medical students.[37,38] Previous studies have shown that stress levels among medical students may induce the release of the cortisol hormone to control stress, resulting in high fat intake.[39] In addition, the increased workload demands and study duration among medical students determine their food preferences, in which they tend to consume fast food, high in SFA and trans fats, for convenience reasons.[40,41] Further, gender differences in dietary patterns have been shown in prior studies.[42,43] Our study showed that females had higher daily fat consumption than males, which is similar to previous

studies.[44,45] This result is likely explained by the predominant disordered or impulsive eating behaviour and higher stress levels among females.[42,46-48]

Although in this study, we observed a large proportion of participants with adequate CHD knowledge, the high dietary fat intake, as one of the CHD risks, was prevalent among respondents. Besides the optimal CHD knowledge, the individual's perception towards CHD risk is also an important determinant in adherence and implementation of healthy lifestyle behaviours according to the Health Belief Model.[14] Our study consists of preclinical medical students who still lack experience and exposure to clinical settings, which may negatively impact their perception of CHD susceptibility, severity and threat, resulting in difficulty in translating the knowledge into healthy behaviour practices.

Several limitations in this study should be acknowledged. First, the study was conducted among undergraduate medical students from a single institution, restricting the generalizability of the results. Second, this study uses a non-probability convenience sampling that may cause an imbalance proportion of participants' characteristics and affect the statistical analysis result. Third, the self-reported questionnaire used to evaluate the knowledge of CHD risk and dietary fat intake may be subject to recall and social desirability bias.

Conclusion

This study highlighted the adequate knowledge of CHD risks among preclinical medical students. Levels of education, age, and gender were factors that related to knowledge of CHD risk factors. Considering the optimal knowledge of CHD risk factors was not aligned with the actual health lifestyle behaviour, in which we observed the overconsumption of fat in the majority of respondents, indicating that the implementation of education and training programs to enhance awareness and assist medical students in adopting positive lifestyle behaviour is needed.

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(Ratna Sari Wijaya)

Dapsone Induced Methemoglobinemia in Pediatric Patient: A Case Report

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Abstract

Background: Acquired methemoglobinemia is significantly more common than the congenital form, though it remains a rare condition. Most cases arise from accidental chemical exposure or the use of topical and local anesthetics.

Case Description: We present a case of 14-year-old male presented with complaints of dark grayish discoloration of the skin on the face and hands, persisting for the past two months prior to admission. He was later diagnosed with dapsone induced methemoglobinemia. Patient was then discharged with oral therapy consisting of agents with antioxidant properties and instructed to discontinue dapsone consumption.

Conclusions: In pediatric patients undergoing dapsone therapy, the risk of dapsone induced methemoglobinemia should be carefully considered to ensure early identification and prompt management, thus minimizing the potential for severe complications.

Introduction

Acquired methemoglobinemia is much more frequently encountered than the congenital form; although, remains an unommon occurrence. Most cases are due to inadvertent exposure to a chemical or through the use of topical or local anesthetics.[1] Methemoglobin levels below 10% typically cause skin discoloration but are often asymptomatic.

As methemoglobin levels rise, clinical manifestations such as dyspnea, syncope, chest pain, and palpitations may progress to tachypnea, arrhythmias, seizures, delirium, altered consciousness, severe hypoxemia, and potentially coma.[2] Therefore, Accurate diagnosis of methemoglobinemia and timely administration of appropriate treatment are essential. Here we described a case of dapsone induced methemoglobinemia in pediatric patient

Case Description

A 14-year-old male presented at our hospital with dark grayish discoloration of the skin on the face and hands persisting for the past two months prior to admission. The patient had a medical history of leprosy diagnosed seven months prior to admission. The treatment regimen consisted of multi-drug therapy for multibacillary leprosy, including 600 mg of rifampicin once a month, 100 mg of dapsone once daily, 300 mg of clofazimine once a month, and 50 mg of clofazimine

once daily. The patient has consistently taken the medication daily and continues to attend monthly check-ups at the community health center.

Upon physical examination, consciousness and examination of the lungs and heart were within normal limits; however, peripheral arterial oxygen saturation showed mild hypoxia, measuring 88% on room air. On dermatological examination, dark grayish discoloration was observed in the facial region and on both the right and left hands. Blood evaluation revealed hemolytic anemia due to drug induced hemoglobinopathy and fully compensated metabolic acidosis. Investigations including chest X-ray, electrocardiogram, echocardiography were carried out, and the results were within normal limits.

Figure 1. Blood work evaluation

Hematology	8/8/2024	14/8/2024	15/8/2024	Reference value
Hemoglobin	11.0 g/dl	10.9 g/dl	-	13.20-17.30
Hematocrit	33.1 %	33.6 %	-	40.00-52.00
Red blood cell	3.5 10^6/uL	3.5 10^6/uL	-	4.40-5.90
Leucocyte	4.7 10^3/uL	4.3 10^3/uL	-	3.80-10.60
Platelet	202 10^3/uL	177 10^3/uL	-	150-440
MCV	94.8 fL	95.5 fl	-	80.0-100.0
MCH	31.5 pg	31.0 pg	-	26.0-34.0
MCHC	33.2 g/dL	32.4 g/dL	-	32.0-36.0
LED	-	3 mm/ hour	-	0-10
Differential count				
Basophil	1 %	1 %	-	0-1
Eosinophil	6 %	2 %	-	2-4
Band neutrophil	2 %	3 %	-	0-6
Segmented neutrophil	48 %	52 %	-	50-70
Lymphocyte	36 %	36 %	-	20-40
Monocyte	7 %	6 %	-	2-8
Bleeding time	1.00 minute	-	-	1-3
PT-INR				
Control	11.3 Seconds	-	-	
PT (Prothrombin time)	12.6 seconds	-	-	9.4-11.3
PT-INR	1.2 seconds	-	-	
APTT				
Control	24.7 seconds	-	-	
APTT	34.3 Seconds	-	-	23.4-31.5
Liver function tests				
SGOT	34 U/L	-	-	0-40
SGPT	18 U/L	-	-	0-41
De Ritis Ratio (SGOT/SGPT)	1.9	-	-	
Ureum	35 mg/dL	-	-	<50
Creatinine				
Creatinine	0.64 mg/dL	-	-	0.46-0.77
eGFR	90 mm/minute/1.73 m2	-	-	eGFR : > 90 Normal
Random blood glucose	130 mg/dL	-	-	60-100

Creatinine				
Creatinine	0.64 mg/dL	-	-	0.46-0.77
eGFR	90 mm/minute/1.73 m2	-	-	eGFR : > 90 Normal
Random blood glucose	130 mg/dL	-	-	60-100
Electrolytes				
Natrium	134 mmol/L	-	-	136-145
Kalium	4.0 mmol/L	-	-	3.5-5.1
Chloride	102 mmol/L	-	-	98-107
Chemistry				
LDH	-	-	451 U/L	135.0-225.0
Immunology/serology				
SARS-CoV-2 Antigen	-	-	Negative	Negative
Hematology				
D-dimer	-	-	0.24 ug/mL	< 0.5
G6PD	-	-	19.3 U/gr Hb	10-14.2
Blood gas analysis				
Temperature	-	37.3 Celsius	-	
PH	-	7.360	-	7.35-7.45
pO2	-	180 mmHg	-	83.0-108.0
pCO2	-	30.1 mmHg	-	35.0-48.0
HCO3 (-)	-	16.6 mmol/L	-	21.0-28.0
CO2 Total	-	17.5 mmol/L	-	24.0-30.0
Base excess	-	-7.4 mmol/L	-	-2.4-2.3
SaO2	-	H 99.6 %	-	
Natrium (Na)	-	144 mmol/L	-	
Kalium (K)	-	3.6 mmol/L	-	
Chloride (Cl)	-	104 mmol/L	-	
Calcium (Ca)	-	0.5 mg/dL	-	
Hematocrit	-	28 %	-	

Table 2. Peripheral blood smear examination

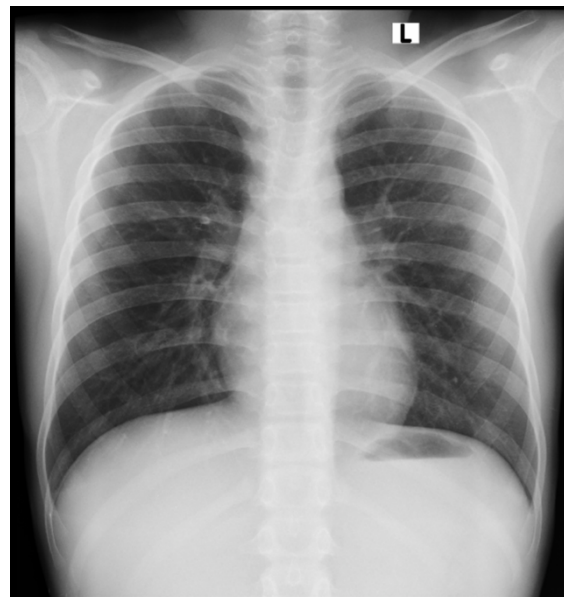|	Results
Peripheral blood smear	Normocytic normochromic anaemia with signs of haemolysis, suspected glucose-6-phosphate-dehydrogenase deficiency or drug-induced haemolytic anaemia, accompanied by relative eosinophilia, suggestive of an allergic response

Figure 1. Chest X-ray posterioanterior view revealed no opacities or consolidation observed in both lungs, heart size and structure are within normal limits.

Intravenous therapy with 1 gram of vitamin C was administered once daily, alongside oral therapy with 600 mg of N-acetylcysteine, given twice daily. Initial peripheral arterial oxygen saturation measurement was 88% on room air, which

improved to 92% with the application of a simple mask at 7 L/min. Patient was instructed to discontinue dapsone consumption. By the second day of treatment, peripheral arterial oxygen saturation improved to 90% on room air and 93% with the application of a simple mask at 7 L/min.

On the third day, peripheral arterial oxygen saturation increased to 92% on room air and 94% with simple mask at 7 L/min, and by the fourth day, it further improved to 97% on room air. Therefore the patient was discharged and continues to be monitored at the outpatient clinic. Oral therapy of 500 mg vitamin C was given once daily, 600 mg of N-acetylcysteine given twice daily and the patient was instructed to discontinue dapsone.

Discussion

Dapsone is a common cause of acquired methemoglobinemia. Dapsone consumption results in its metabolism in the liver through the cytochrome P450 enzyme system, primarily via CYP2E1, while also acting as a substrate for CYP2C9 and CYP3A. The drug undergoes metabolism through N-acetylation and N-hydroxylation, processes that can lead to hematotoxicity associated with the formation of methemoglobin.[4] Methemoglobin is a metalloprotein characterised by the oxidation of heme iron from its ferrous form (Fe^{2+}) to its ferric form (Fe^{3+}). Various chemicals can facilitate the oxidation of

Fe^{2+} to Fe^{3+}, a form that is incapable to carry oxygen.[3]

The clinical manifestations associated with methemoglobinemia include decreased oxygen saturation accompanied by changes in skin color, such as pallor, grayish hues, or cyanosis. These changes may occur asymptomatically with methemoglobin levels below 10% in the blood. Clinical manifestations of cyanosis and dark brown blood typically emerge in patients with methemoglobin levels ranging from 10% to 30%, often without accompanying symptoms. In patients with methemoglobin levels between 30% and 50%, clinical findings such as dyspnea, dizziness, syncope, confusion, chest pain, palpitations, headache, and fatigue are commonly observed. Patients with methemoglobin levels between 50% and 70% may exhibit symptoms including fatigue, chest pain, palpitations, headache, and confusion, along with clinical signs of tachypnea, metabolic acidosis, arrhythmias, seizures, delirium, and potential coma. In cases where methemoglobin levels exceed 70%, severe clinical manifestations, including severe hypoxemia and the risk of death are frequently noted. In our patient, mild hypoxemia was observed with a peripheral arterial oxygen saturation of 88% on room air. A dark grayish discoloration of the skin on the face and hands, had been present for two months prior to admission without any accompanying systemic symptoms.

This presentation suggests an estimated methemoglobin level below 10% in the blood.[2]

Methemoglobinemia is a clinical diagnosis based on history and presenting symptoms, including hypoxemia refractory to supplemental oxygen and the likely presence of chocolate-colored blood. "Refractory hypoxemia" is a significant diagnostic clue. The diagnosis is confirmed by arterial or venous blood gas with advanced pulse oximetry devices such as the Masimo Pulse CO-oximeter, which will speciate hemoglobin to determine the methemoglobin concentration and percentage.[1]

Another modality for evaluating methemoglobinemia is the "oxygen saturation gap". Oxygen saturation gap refers to the discrepancy between oxygen saturation calculated by a standard blood gas analyzer and the value obtained from a pulse oximeter. This phenomenon may indicate an underlying hemoglobinopathy. If the gap exceeds 5%, it may suggest the presence of an abnormal hemoglobin variant, such as in cases of carbon monoxide poisoning, methemoglobinemia, or sulfhemoglobinemia. Additionaly metabolic acidosis may be associated with elevated methemoglobin levels in critical cases.

In our patient, there was evidence of refractory hypoxemia, as indicated by a peripheral arterial oxygen saturation of 88% on room air and a maximum increase to 92% on a simple mask at 7 L/Min. Additionally, the oxygen saturation gap exceeded 5%, suggesting the presence of a hemoglobinopathy.[5] The arterial blood gas analysis also revealed fully compensated metabolic acidosis. Unfortunately, we do not have access to pulse oximetry devices such as the Masimo Pulse CO-oximeter.

Methemoglobinemia does not directly cause hemolysis; however, many oxidizing agents that induce methemoglobinemia can also lead to hemolysis. Assessing glucose-6-phosphate-dehydrogenase levels is critical in excluding the possibility of hemolysis mediated by oxidative stress, including the formation of Heinz bodies or damage to cellular membranes. This evaluation is particularly important for patients with impaired oxidative stress tolerance, as seen in individuals with glucose-6-phosphate-dehydrogenase deficiency.[2]

Screening for glucose-6-phosphate-dehydrogenase deficiency is recommended due to patients with glucose-6-phosphate-dehydrogenase deficiency are less tolerant of pharmacologic oxidative stress and are at risk for substantial hemolysis. It is essential to rule out glucose-6-phosphate-dehydrogenase deficiency before initiating dapsone therapy in all patients. Another reason for evaluating glucose-6-phosphate-dehydrogenase deficiency is to assess the suitability of methylene blue therapy.

Patients with hereditary methemoglobin reductase deficiency or glucose-6-phosphate-dehydrogenase deficiency may not respond to methylene blue, and its use can significantly worsen methemoglobinemia and induce hemolysis.[6,7]

In our patient, glucose-6-phosphate-dehydrogenase deficiency was not found; however, the peripheral blood smear examination revealed hemolytic anemia due to drug-induced causes. To Minimize differential diagnosis, additional laboratory investigations such as electrolyte and glucose levels can be performed. If hemolysis is suspected, further testing should include a complete blood count, total and direct bilirubin levels, a peripheral blood smear, and a urinalysis dipstick to detect occult blood.

Therapeutic modalities ranged from Emergency and supportive measures, specific drugs and antidotes, decontamination, and enhanced elimination. Emergency and supportive measure include Maintaining an open air way, providing ventilatory support if necessary, and administering supplemental oxygen. Usually, mild methemoglobinemia (<15–20%) will resolve spontaneously and requires no intervention. In cases of dapsone-induced methemoglobinemia, supplemental oxygen is critical due to methemoglobin's reduced ability to transport oxygen, causing hypoxia despite normal respiratory function.

Although oxygen alone cannot lower methemoglobin levels, it supports tissue oxygenation until definitive treatment, such as methylene blue, can be provided. This interim oxygen therapy is essential for managing hypoxic symptoms and avoiding complications from inadequate oxygen delivery.[11]

Specific drugs and antidotes, Methylene blue is indicated in symptomatic patients with methemoglobin levels higher than 20% or for those in whom even minimal compromise of oxygencarrying capacity is potentially harmful (eg, pre-existing anemia, congestive heart failure, lung disease, acute coronary syndrome). Administer methylene blue, 1–2 mg/kg (0.1–0.2 mL/kg of 1% solution), over several minutes. The dose may be repeated once in 15–20 minutes if necessary.[8]

Decontamination, consider activated charcoal Administer 60–100 g orally or via gastric tube, mixed in aqueous slurry for ingestions within 1 hour.[7] Enhanced elimination, If methylene blue is contraindicated (eg, glucose-6-phosphate-dehydrogenase deficiency) or has not been effective, red blood cell transfusion or exchange transfusion may be necessary in patients with severe methemoglobinemia. Hyperbaric oxygen is theoretically capable of supplying sufficient oxygen independently of hemoglobin and may be useful in extremely serious cases that do not respond rapidly to antidotal treatment.[2]

Ascorbic acid or Vitamin C is a natural water-soluble vitamin which reduces excessive oxidative stress. Ascorbic acid can directly reduce methemoglobinemia. Ascorbic acid is the treatment of choice when methylene blue is not available and in cases of methemoglobinemia and glucose-6-phosphate-dehydrogenase deficiency.[9] However, ascorbic acid has limited utility in acute settings due to its slow onset of acion, despite its ability to reverse methemoglobin via an alternative metabolic pathway.[8]

N-acetylcysteine has three main mechanisms of action: as a free radical scavenger; a precursor for glutathione biosynthesis; and a reducer of disulfide bonds[14]. A combination of both N-acetylcysteine's anti-oxidant properties and replenishment of glutathione is hypothesised to subdue the methemoglobinemia accumulation seen.[10] In our patient, methylene blue was not administered as the first-line antidote for methemoglobinemia due to its unavailability. we opted to initiate intravenous therapy with 1 gram of vitamin C once daily, in conjunction with oral therapy of 600 mg of N-acetylcysteine administered twice daily.

Conclusion

In pediatric patients undergoing dapsone therapy, the risk of dapsone-induced methemoglobinemia should be carefully considered to ensure early identification and prompt management, thus minimizing the potential for severe complications.

Acknowledgment

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(Leni Lukman)

Isolated Abducens Nerve Palsy: A Case Report of Cerebral Pseudocyst of Dorello's Canal

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Abstract

Background:
Abducens nerve is the second longest intracranial path out of all of the cranial nerves. Abducens nerve pasly had a prevalence 11.3/100.000 and mostly seen in adults. Isolated abducens nerve palsy due to neoplastic lesion are rare and mostly related to skull base tumor.

Case Description:
We present a case of 57 years old woman with complaints of red right eye and worsening headache associates with diplopia on the right lateral gaze for three days prior admission. She was later diagnosed with isolated abducens nerve palsy associated to neoplasm cause in Dorello's canal. Patient was then discharged with symptomatic therapy and educated for head posturing and avoid triggers.

Conclusions:
Abducens nerve palsy is the most common isolated ocular nerve palsy. The incidence of mass formation such as neoplastic lesion or cyst are rare.

Introduction

Of all the cranial nerves, the abducens nerve has the second longest intracranial path. This nerve may be impacted at the petrous apex, cavernous sinus, superior orbital fissure, or eye orbit. Anything that compresses or stretches the nerve can damage the abducens nerve. Therefore, it is critical to pinpoint the lesion of abducens nerve palsy for proper diagnosis and therapy. Isolated abducens nerve palsy due to neoplastic lesion[1,2,3] are rare and mostly related to skull base tumor. Kim et al, found that only 14.3% of the 807 confirmed cases of solitary abducens nerve palsy were connected to neoplasm.[4] Here we described a case of isolated abducens nerve palsy associated with neoplasm lesion in Dorello's canal (petroclival venous confluence).

Case Summary

A 57 years old woman presented at our hospital with a red right eye and worsening headache associated with diplopia on the right lateral gaze for three days prior to admission. The patient claimed that she had experienced these complaints for one year. Upon neurological assessment, there

was binocular horizontal diplopia associated with total right abducens nerve palsy. Other physical and blood examinations are normal. There were no signs of elevated intracranial pressure. Investigations including perimetry and optical coherence tomography were carried out, and the results were within normal limits. Magnetic resonance imaging (MRI) with contrast revealed a dilated right dorello's canal with a non-enhanced cystic lesion on the right side of the superoposterior cavernous sinus (0.8 x 0.5 x 0.5 cm), raising the possibility of a pseudocyst. There is no evidence of either aneurysm or thrombosis of the cavernous sinus. When compared to previous MRI (one year prior), it was comparable.
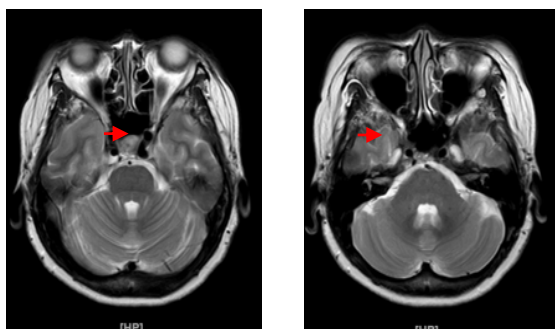

Figure 1. Magnetic Resonance Imaging (MRI) with contrast in T2 sequences revealed a dilated right dorello's canal with a non-enhanced cystic lesion on the right side of the superoposterior cavernous sinus (0,8x0,5x0,5 cm).

Although we were unable to make a definitive diagnosis, we assumed the lesion was benign. Therefore the patient was discharged and continues to be monitored at the outpatient clinic without any operation. Symptomatic therapy was administered, and the patient was educated for head posturing and on how to avoid potential triggers.

Discussion

According to reports, abducens nerve palsy are the most typical isolated ocular motor cranial neuropathy.[3,5] The yearly prevalence of abducens palsy is 11.3/100,000 and mostly seen in adults.[6] The abducens nerve's neuroanatomy is separated into four unique sections: the nucleus, the cisternal part, the cavernous region, and the orbital portion. The abducens nucleus originates from the caudal dorsal pons, below the fourth ventricle. These nerve fibers emerge and leave the nucleus superiorly to form the abducens fascicle in the brainstem, then exits the brainstem at the pontomedullary junction to reach the subarachnoid region. The nerve then turns sharply and rises steeply over the tip of the petrous part of temporal bone towards the clivus within a fibrous sheath called Dorello's canal and enters the inferior dura mater to the posterior clinoid process. Dorello's canal is the gap between the petrous apex and the superolateral section of the clivus, which is superiorly restricted by the petrosphenoidal ligament of Gruber (Gruber's ligament). The components included in this canal are bound together and significantly limit their mobility. The inner meningeal tube that surrounds the nerve severely

limits the movement of the abducens nerve within Dorello's canal. Because the abducens nerve is anchored in Dorello's canal, it is vulnerable to straining when intracranial pressure rises for a variety of reasons such as venous congestion, edematous pressure or cancerous infiltrates.[7,8] This nerve then enters the cavernous sinus along with the oculomotor nerve, trochlear nerve, and the first branch of trigeminal nerve. Before following the sphenoidal fissure, it laterally follows the internal carotid artery and medially to the sinus lateral wall. The nerve then enters the orbit via the superior orbital fissure within the tendinous ring, eventually reaching the lateral rectus muscle.[5,7]
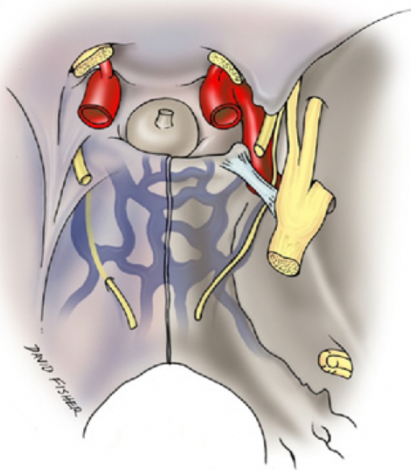

Figure 2. The abducens nerve are illustrated schematically as they proceed through the Dorello canal. The nerve enters the dura near the beginning of the canal on the left side and goes anteriorly into the cavernous sinus through the opening inferior to the Gruber ligament, as seen on the right side of the picture.[9]

The isolated sixth nerve palsy has different kinds of etiology. The most common underlying pathology is microvascular causes, about 56% cases are caused by vascular disease especially in advanced age. Isolated abducens paralysis is associated with a vascular risk factor such as diabetes (44.4%), hypertension (33.3%), coronary artery disease (13.9%), smoking (13.9%), and hyperlipidemia (8.3%). The other most common etiology are idiopathic (27.2%), inflammatory diseases (8.3%), infections (8.3%) such as Lyme disease, syphilis, tuberculosis and cryptococcus, increased intracranial pressure (8.3%), demyelinating (2.5%), cerebral aneurysm (1.9%) and procedure-related injury (1%). Neoplasm (5.6%) and trauma (4.9%) may also affect the abducens nerve at any point along its course and resulting in sixth nerve palsy.[10]

A summary of six retrospective studies on patients with sixth nerve paresis showed 6% to 30% attributed to a miscellaneous group that includes migraine, pseudotumor cerebri, multiple sclerosis. Furthermore 6% to 29% etiology are undetermined, indicating vulnerability of the nerve to conditions which are transient, benign, and unrecognizable.[11] Our case described a female patient with no comorbidities or vascular risk factors, presented with an episode of diplopia and right sided headache. Ischemic, autoimmune, inflammatory, and traumatic causes were ruled out since the history and laboratory

tests were inconclusive. However, neuroimaging using contrast MRI was done and showed pseudocyst on the right superoposterior cavernous sinus of the dorello's canal.

MRI is an efficient and safe tool for determining the underlying cause of isolated abducens nerve palsy in patients without identifiable vasculopathic risk factors. It is useful for identifying brain demyelination, infarction, infections, neoplasm, and other mass lesions that are related to nerve palsy.[12,13] In our case, it is suspected that the pseudocyst is likely to cause abducens nerve palsy in our patient by increasing pressure in the dorello's canal and compressing the abducens nerve. This is a rare occurrence of isolated abducens nerve palsy caused by benign neoplastic lesion.[12,13,14]

Patients who develop sixth nerve palsy will often present with binocular horizontal diplopia and notable weakness of ipsilateral lateral rectus muscle leading to a deficit eye abduction of the affected side.[3] In our patients, we saw two common symptoms: diplopia and ipsilateral weakness. The two typical symptoms might lead to side effects that develop in later stages such as headache, vomiting and conjunctival injection that cause eye soreness. Patients also present with a head turn and/or strabismus to maintain binocularity and binocular fusion as coping mechanisms to diplopia in long term findings as seen in our patient.

Therapeutic modalities ranged from conservative treatment, botulinum toxin injections, and surgical treatment in cases of abducens nerve palsy. Due to the size of the pseudocyst that is relatively the same as the previous imaging one year ago, it is concluded that the pseudocyst is not progressive. Treatment that was suggested to the patients are conservative treatment such as patching, and prism therapy could be used to prevent amblyopia in the affected eye. Patching consists of closing each alternating eye for hours using eye patch. Another conservative treatment suggested is prism therapy which requires the placement of a temporary press-on prism on the lens of the affected eye. Other modalities such as botulism injection could also be given to this kind of cases with residual function of the lateral rectus muscle. Surgical treatment of the lateral rectus muscle called strabismus surgery was also suggested in this case. This surgery consists of resection, recession, or transposition of the eye muscles.[15,16,17]

Conclusion

The abducens nerve palsy is the most common isolated ocular nerve palsy due to its neuroanatomy and the long intracranial course. Multiple etiologies are recognized based on the location of an abnormality, however the incidence of mass formation such as neoplastic lesion or cyst are rare. In the absence of risk factors or positive laboratory and clinical results,

neuroimaging such as MRI scan can be a valuable diagnostic technique in determining the specific origin of sixth nerve palsy.

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(Vivien Puspitasari)

A Rare Manifestation of 'Complex' Post Streptococcus Infection Movement Disorder in Paediatric Patient a Case Report

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Abstract

Background: Post Streptococcal Movement Disorder (PSMD) is a rare disease. One of the PSMD diagnosis is Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infection (PANDAS).

Case Description: 10 year old female with involuntary movement including myoclonic jerks, chorea and stereotype. Movement duration is 5 minutes, repetitive and sensitive to loud noise. Patient has history of respiratory infection 2 weeks ago with Positive ASTO test. Patients showed improvement after treatment with antibiotics, corticosteroids and antipsychotics.

Conclusion: The pathophysiology of PANDAS begins with Group A beta-hemolytic infection that causes cross reaction in cortical structures and basal ganglia due to molecular mimicry. Currently there is no definitive test for PANDAS,where diagnosis is primarily confirmed by identifying signs, symptoms and physical neurological examination.

Introduction

Post streptococcal movement disorder (PSMD) is a rare movement disorder following streptococcus infection. PSMD includes Sydenham's chorea, tics, dystonia, tremor, and stereotypy. One of the diagnoses included in the PSMD category is Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infection (PANDAS).

The main symptoms experienced by PANDAS patients are obsessive-compulsive disorder and/or tic disorder and may be accompanied by attention deficit disorder, oppositional behaviour, emotional lability, and impulsivity after the patient experiences a streptococcus infection. Overall, the symptoms experienced by PANDAS patients are nonspecific, ranging from hyperactivity, chorea movements, loss of fine motor skills, and motor disorders resembling seizures. These symptoms also have a temporal relationship with the presence of infection, where more severe symptoms are found in patients with a longer duration of GHABS infection.

Comorbidities that can be caused by PANDAS are ADHD, Oppositional Defiant Disorder, and depression.[1,2]

Group A B-Hemolytic Streptococcus (GAHBS) is the main cause of bacterial pharyngitis. According to previous research, the incidence of PANDAS is 1 in 200 children. The age of the PANDAS patient population is 1-13 years with a sex ratio of 2:1, with a higher incidence in males. A previous study also found that the average age of PANDAS incidence is 6.3 years. The incidence at this age correlates with the frequency of GHABS infections occurring in the prepubertal age group.[1,2]

Pathogenesis of PANDAS has the same mechanism as Sydenham's chorea. When infection with streptococcus bacteria (Group A beta-hemolytic) occurs, an antibody response occurs that cross-reacts with cortical structures due to molecular mimicry. This cross-reaction causes the neurological symptoms found in PANDAS patients. Previous studies have found two immunological components that play a role in the pathophysiology of PANDAS, namely Lysoanglisodie GM1 and Calcium Modulin Kinase II. Lysoanglisoside GM1 is an antigen that causes a cross-reaction in monoclonal antibodies. Another pathophysiological mechanism of Lysoanglisode GM1 is to stop the reaction of autoantibodies in the putamen caudate nucleus, causing movement disorders and cognitive impairment. Another immune component that plays a role in the

pathophysiology is CaMKII. The binding of tyrosine kinase is carried out by CaMKII, resulting in the conversion of tyrosine to dopamine, which affects patient movement. GHABS has the ability to activate CaMKII.[3]

The cortical structure affected by this autoimmune process is the basal ganglia. This structure plays a role in motor learning, motor control, behaviour, and executive function. When the physiological function of the basal ganglia is disrupted, symptoms such as movement disorders (tic disorder, chorea) and behavioural disorders such as OCD, impulsivity, and hyperactivity.[3]
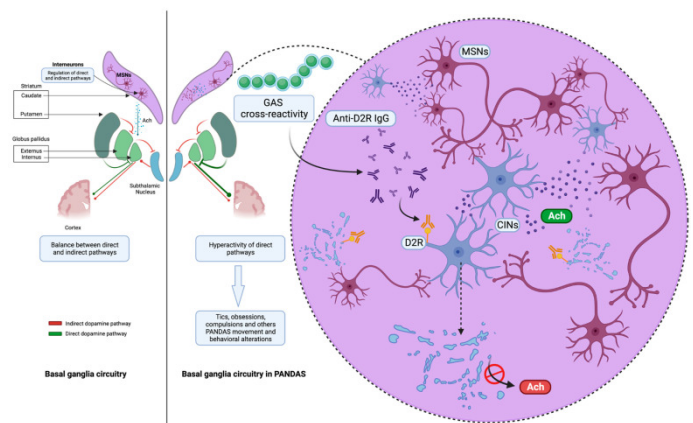

Figure 1. PANDAS Patophysiology[2]

Other types of PSMD that can be found are Pediatric Acute-onset Neuropsychiatric Syndrome (PANS), Childhood Acute Neuropsychiatric Symptoms (CANS), and Pediatric Infection-Triggered Autoimmune Neuropsychiatric Disorders(PITAND).[2,3]

Table 1. Diagnostic Criteria in PSMD

PANDAS	PANS
- OCD dan/atau Tic Disorder(DSM-IV) - Prepubertal onset of symptoms - Episodic Symptoms - Hubungan dengan infeksi GHABS(hasil kultur positif/ peningkatan titer antibodi GABHS) - Ditemukan Gejala Neurologis seperti hiperaktivitas motorik, tics atau chorea	- OCD present on onset or sudden food intake disorder - ≥ 2 Neurological symptoms: 1. Anxiety 2. Emotional lability and/or depression 3. Irritability, aggression or oppositional behavior 4. Behavioral Regression 5. Performance issues at school 6. Motoric or sensoric disturbance 7. Somatic symptoms such as sleep disturbance or enueresis 8. Symptoms are not caused by other diseases

CANS	PITAND
Acute onset of Symptoms Main Diagnostic Criteria: OCD Secondary Diagnostic Criteria : - Tics - Dysfagia - Hyperactivity - Anxiety - Psychosis - Emotional Lability - Growth Regression - Sensitivity towards sensory stimulus - Monophasic or polyphasic disease course	Pediatric Onset, lifelong OCD or tic disorder. Sudden onset with recurrent relapsing/remitting disease pattern - Symptom exacerbations that may last up to 4 weeks. - Neurological findings when patient during exacerbation of OCD and Tic disorder. - History of infection prior to symptoms - Patient did/did not experience significant symptoms between exacerbations of OCD/ tic disorder

The treatment of PANDAS consists of three main pillars: antibiotics, psychotherapy, and immunomodulatory drugs. Antibiotics are given to treat GHABS infection. The types of antibiotics used are beta-lactams such as azithromycin and clindamycin. Previous studies have shown that patients have excellent symptom resolution after antibiotic therapy. The use of antibiotics as prophylaxis can also be considered because reinfection with GHABS can re-trigger PANDAS symptoms in patients who are already asymptomatic. Other modalities that can be used to prevent infection besides antibiotics are tonsillectomy and/or adenoidectomy.[2,4]

Immunomodulatory therapy is given to reduce the severity of the patient's symptoms. The most commonly used immunomodulatory modality is corticosteroids, but other modalities can also be used such as IVIG and plasmapheresis. Previous research has found IVIG effectiveness of 45% and IVIG effectiveness of 56% in terms of symptom reduction. Other pharmacogenomic immunomodulatory therapies that can be used are rituximab and mycophenolate mofetil.[2,4]

Psychotherapeutic management of PSMD is cognitive behavioral therapy (CBT) used to treat tic disorders and OCD in patients. Selective Serotonin Reuptake Inhibitors are the first-line drugs used for OCD therapy in PANDAS patients. Both psychotherapeutic modalities need to be tailored and adjusted according to the patient's needs.[4]

Case Report

We report a 10-year-old female patient with the main complaint of involuntary movements in the trunk and upper and lower extremities in the past 2 months before the examination. The movement manifestations were complex and unusual tics: tonic-clonic movements in both upper and lower extremities, accompanied by back flexion such as opisthotonus, tongue fasciculation, and oculogyric tic. The duration of the movement was 5 minutes with 1-minute intervals without movement. During the movement, the patient could be questioned, was relevant, and remained oriented. The patient had a history of respiratory tract infection 2 weeks before the onset of the movement disorder. The patient also had a history of verruca vulgaris therapy surgery before the onset of symptoms.

On physical examination, the patient's weight was 27 kg, blood pressure 110/70 mmHg, pulse 72 x/min, respiratory rate 19 x/min, and temperature 36.4'C. The patient's consciousness was E4M6V5. The results of the patient's general status examination were within normal limits. In the supporting examination, the results of MRI and EEG were within normal limits. The ASTO examination showed positive results.

Therapy given to the patient:

- Methylprednisolone 1x800 mg -> taper off 4x125mg per day
- Ranitidine 3x30 mg
- Clonazepam 2x0.5 mg -> 1x0.5 mg
- Haloperidol 1mg - 0 - 0.5mg
- Valproic Acid 2x5 cc
- Ampicillin 4 x 750 mg -> switched to phenoxymethyl penicillin 3 x 500 mg after discharge.

Figure 2. Patient experiencing tonic clonic tic in both upper and lower extremities

Figure 3. Patient experiencing opisthotonus like tic

Figure 4. Patient experience tic in the for of tongue fasciculation.

Discussion

The diagnosis of PANDAS is established through the patient's clinical symptoms. There are five diagnostic criteria for PANDAS[5,6]:

- Presence of OCD and/or tic disorder
- Pediatric onset (age 3 years - puberty)
- Episodic severity of symptoms, acute onset with high severity
- Symptoms have a temporal relationship with group A beta-hemolytic streptococcus infection
- There are neurological symptoms such as motor hyperactivity, tics, or chorea.

The severity level in PANDAS patients has 3 levels[6]:

1. Mild Case
   o Symptoms are significant and interfere with activities at school/home.
   o Patients experience symptoms for a few hours a day.
2. Moderate Case
   o Symptoms are difficult and inhibit daily activities.
   o Patients experience symptoms 50-70% of their waking hours.
3. Severe Case
   o Symptoms are very difficult and life-threatening.
   o Patients experience symptoms 50-70% of their waking hours.

This patient has clinical signs that meet the diagnostic criteria for PANDAS. The main symptom in this patient is a movement disorder in the form of complex and unusual tics such as tonic-clonic movements of the upper and lower extremities, back flexion like opisthotonus, tongue fasciculation, and oculogyric tics. The patient's age (10 years) is also a population that fits the diagnostic criteria for PANDAS, which is 3 years to puberty. The characteristics of the symptoms experienced by the patient, where there is a duration of movement for 5 minutes with periods without movement, and the onset of symptoms, are included in the diagnostic criteria for an acute and episodic onset of the disease course. The patient's symptoms also have a temporal relationship where the onset of symptoms occurs after streptococcus bacterial infection. This temporal relationship is also a diagnostic criterion. This patient also has neurological symptoms, namely involuntary

movements in the form of tic disorder. The severity level experienced by this patient is moderate because the patient's movement disorder interferes with daily activities and is experienced approximately 50-70% of the waking hours. Currently, there are no supporting examinations that can be used to establish the diagnosis of PANDAS.[5,6]

The treatment given to this patient was antibiotics (ampicillin and phenoxy methyl penicillin), corticosteroids (methylprednisolone), and antipsychotic medication (clonazepam and haloperidol). The therapy given to this patient is in accordance with the three main modalities of PANDAS therapy that have been established in previous studies, namely antimicrobial therapy, immunomodulatory therapy, and psychotherapeutic therapy. The patient showed improvement after undergoing treatment until symptom-free. Patients can have a good prognosis with immediate therapy and prevention of recurrent GHABS infection. Although PANDAS is a rare disease, this diagnosis still needs to be considered in paediatric patients diagnosed with GHABS infection.[3]

Conclusion

PSMD is a spectrum of movement disorders that occur following streptococcus bacterial infection. A type of PSMD that is commonly found is PANDAS. Due to the high prevalence of GAHBS infection this can be the underlying etiology of OCD and tic disorders in the pediatric population. Currently there are no specific tests to confirm the diagnosis of PANDAS, where diagnosis can only be given through clinical examination and history of infection. Therefore

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Efficacy and Safety of Stem Cell Therapy for Spinal Cord Injury in Adults: A Systematic Review and Meta-Analysis

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Abstract

Background: Despite encouraging early results, clinical outcomes remain inconsistent across trials. This study aimed to systematically evaluate the efficacy and safety of stem cell therapy in adults with spinal cord injury (SCI).

Methods: A systematic review and meta-analysis were conducted following PRISMA 2020 guidelines. PubMed, EMBASE, and Scopus were searched until 18 October 2025. Eligible studies included adult SCI patients receiving stem cell therapy with measurable neurological outcomes. Data synthesis was performed using Review Manager 5.4 under a random-effects model, reporting pooled risk ratios (RR) with 95% confidence intervals (CIs). Risk of bias was assessed using ROBINS-I, and evidence certainty was graded via GRADE.

Result: Thirteen studies involving 470 participants (286 intervention, 184 control) were included. Stem cell therapy significantly improved neurological recovery compared with controls (RR = 2.64; 95% CI 1.70–4.10; p < 0.0001; I² = 0%). Subgroup analyses showed consistent benefits across baseline AIS classifications (RR = 2.61; 95% CI 1.71–3.98) and cell doses (RR = 2.75; 95% CI 1.63–4.64). No major safety signals were identified. GRADE assessment rated the certainty of efficacy evidence as moderate.

Conclusions: Stem cell therapy yields significant neurological improvement in adult SCI with a favorable safety profile. The findings support its regenerative potential through neuroprotective and remyelinating mechanisms. However, larger randomized controlled trials are required to validate efficacy, optimize protocols, and assess long-term safety.

Introduction

Stem cell therapy has emerged as a promising regenerative approach for spinal cord injury (SCI), a condition that results in irreversible neurological deficits due to the limited intrinsic repair capacity of the central nervous system.[1] The rationale for using stem cells lies in their ability to differentiate into neural lineages, secrete neurotrophic factors, and modulate the

hostile post-injury microenvironment that inhibits axonal regrowth.[1,2] Unlike pharmacologic or surgical interventions that primarily aim to limit secondary damage, stem cells offer a biological means to restore neural circuitry, promote remyelination, and enhance functional recovery. Such potential has driven extensive experimental and clinical interest in translating stem cell–based therapies into viable treatments for SCI.[3]

Over the past two decades, multiple clinical trials have evaluated various stem cell types—most notably mesenchymal stem cells (MSCs), neural stem/progenitor cells (NSPCs), and induced pluripotent stem cells (iPSCs)—for their safety and regenerative efficacy.[4] While some studies have reported improvements in sensory and motor scores, outcomes remain heterogeneous, with inconsistent methodologies, variable injury levels, and differing routes and timing of cell administration.[5–7] Moreover, long-term safety concerns such as immune reactions, ectopic tissue formation, and tumorigenicity continue to limit widespread clinical application. The lack of standardized protocols and robust evidence synthesis has created uncertainty regarding the true clinical benefit of stem cell therapy in adults with SCI.[8]

The physiological complexity of SCI involves both primary mechanical insult and secondary injury mechanisms, including ischemia, excitotoxicity, inflammation, and glial scar formation, all of which impede endogenous regeneration.[9] Stem cell therapy aims to counteract these processes by replacing lost neurons and oligodendrocytes, secreting anti-inflammatory cytokines, and promoting neuroplasticity within spared neural networks.[10] Given the growing but fragmented body of evidence, a systematic and quantitative assessment is crucial to clarify clinical outcomes and safety profiles. This study therefore aims to conduct a systematic review and meta-analysis to evaluate the efficacy and safety of stem cell therapy for spinal cord injury in adults.

Material And Methods

This systematic review included studies that assessed the efficacy and safety of stem cell therapy in adult patients aged 18 years or older with spinal cord injury (SCI), regardless of the injury's level or severity. Eligible study designs comprised randomized controlled trials (RCTs), non-randomized controlled studies, and prospective cohort studies that reported at least one measurable functional, neurological, or safety outcome. Excluded studies included case reports, animal studies, reviews, and conference abstracts lacking sufficient data.

A comprehensive literature search was performed across PubMed, EMBASE,

and Scopus from their inception until 18 October 2025. To ensure thoroughness, the reference lists of included studies and relevant reviews were manually screened to identify additional eligible publications. The search strategy employed both Medical Subject Headings (MeSH) and free-text terms associated with "spinal cord injury," "stem cell therapy," "transplantation," and "regeneration," with Boolean operators and database-specific filters applied to optimize retrieval.

The study selection process involved independent screening of titles and abstracts by all reviewers, followed by full-text assessments to confirm eligibility. Any disagreements were resolved through discussion and consensus, ensuring methodological consistency. This process adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines.[11] Data extraction was conducted independently by two reviewers using a standardized form, which captured key study characteristics such as authorship, publication year, design, sample size, participant demographics, stem cell type and source, route and timing of administration, follow-up duration, and outcome measures.

Primary outcomes of interest included functional and neurological improvements, commonly evaluated through the American Spinal Injury Association (ASIA) Impairment Scale (AIS) or equivalent motor and sensory scores. Secondary outcomes encompassed adverse events, complication rates, and mortality. Additional data regarding intervention characteristics, such as cell type, dosage, delivery method, and study funding sources were also systematically recorded.

The risk of bias in each study was evaluated using the ROBINS-I (Risk of Bias in Non-Randomized Studies of Interventions) tool across seven domains. Independent assessments by all reviewers were reconciled through discussion to ensure reliability. For effect measures, all outcomes were treated as dichotomous data and expressed as Risk Ratios (RRs) with corresponding 95% confidence intervals (CIs), facilitating standardized comparisons across studies.

Data synthesis was performed through meta-analysis using Review Manager (RevMan) version 5.4. A random-effects model (DerSimonian–Laird method) with the Mantel–Haenszel approach was applied for dichotomous outcomes, while the Restricted Maximum Likelihood (REML) method was used for continuous data. Statistical heterogeneity was quantified using the I^2 statistic, and significance was set at $p < 0.05$. Forest plots were generated to illustrate pooled effect estimates, and funnel plots were used to assess publication bias. Sensitivity analyses tested the robustness of results.

Publication bias was visually examined via funnel plots and statistically assessed using Egger's regression test for outcomes with at least ten studies. Finally, the overall quality and certainty of evidence were appraised using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework. Evidence was categorized as high, moderate, low, or very low depending on risk of bias, inconsistency, indirectness, imprecision, and potential publication bias.

Result

Work should be reported in SI units. Undue repetition in text and tables should be avoided. Comment on validity and significance of results is appropriate but broader discussion of their implication is restricted to the next section. Subheadings that aid clarity of presentation within this and the previous section are encouraged.

The purpose of the Results is to state your findings and make interpretations and/or opinions, explain the implications of your findings, and make suggestions for future research. The main function is to answer the questions posed in the introduction, explain how the results support the answers and, how the answers fit in with existing knowledge on the topic. The Discussion is considered the heart of the paper and usually requires several writing attempts.
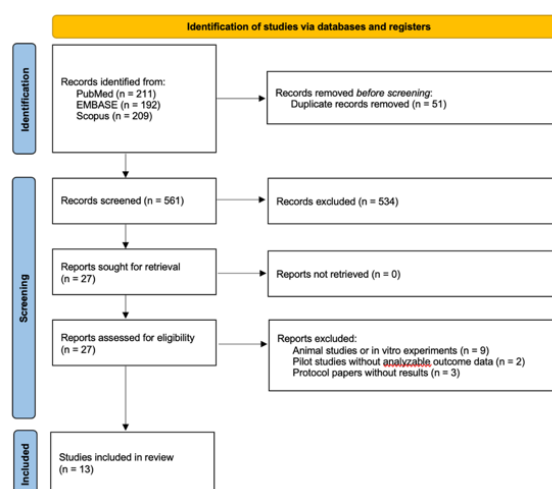

Figure 1. PRISMA diagram of the study selection process

A total of 612 records were initially identified from the databases, including PubMed (n = 211), EMBASE (n = 192), and Scopus (n = 209). After the removal of 51 duplicate records, 561 unique studies were screened by title and abstract. Of these, 534 records were excluded for not meeting the eligibility criteria. Twenty-seven full-text articles were assessed for eligibility, and none were excluded due to retrieval issues. Following full-text review, nine studies were excluded for being animal or in vitro experiments, two were excluded as pilot studies without analyzable outcome data, and three were protocol papers without results. Ultimately, 13 studies met the inclusion criteria and were included in the final systematic review and meta-analysis (Figure 1).[5,7,12–22]

The risk of bias assessment using the ROBINS-I tool demonstrated that most included studies exhibited a low risk of

bias across the seven evaluated domains, particularly regarding confounding factors and participant selection (Figure 2). A few studies presented moderate risk primarily due to missing data, classification of interventions, or incomplete outcome reporting.
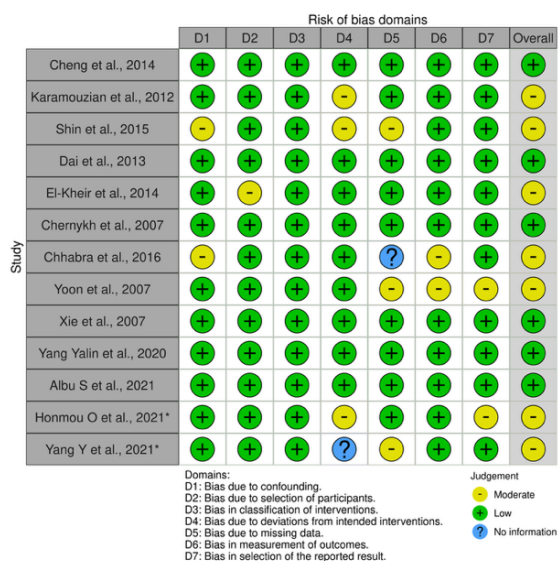

Figure 2. Risk of bias of eligible studies using ROBINS-I

Table 1. Demographic characteristics of included studies.

Study (Author, Year)	Country	Participants (SCT / Control)	Mean or Range of Age (yrs)	Injury Level (SCT / Control)	Preinjury Grade (AIS)	Stem Cell Source	Cell Quantity	Delivery Technique
Cheng et al., 2014	China	10 / 14	35.25	Thoracolumbar / –	AIS A	Umbilical cord MSCs	$4×10^7$	Local lesion injection
Karamouzian et al., 2012	Iran	11 / 20	33.4	Thoracic / Thoracic	AIS A	Bone marrow MSCs	$7×10^5$ – $1.2×10^6$	Lumbar puncture
Shin et al., 2015	Korea	19 / 15	37.2	Cervical / Cervical	AIS A–B	Human neural stem/progenitor cells	10^8	Direct lesion injection
Dai et al., 2013	China	20 / 20	34.9	Cervical / Cervical	AIS A	Bone marrow MSCs	$2×10^7$	Lesion site injection
El-Kheir et al., 2014	Egypt	50 / 20	16–45	10 cervical & 40thoracic / 7 crvical & 13 thoracic	AIS A or B	Bone marrow MSCs	$2×10^6$ per kg	Lumbar puncture
Chernykh et al., 2007	Russia	18 / 18	32.4	Cervical, thoracic, lumbar (varied)	AIS A	Bone marrow mononuclear cells	NR	Injection into cystic cavity & IV
Chhabra et al., 2016	India	14 / 7	24.9	Thoracic / Thoracic	AIS A	Bone marrow MSCs	$7×10^8$ – 10^9	Lumbar puncture or lesion injection
Yoon et al., 2007	Korea	35 / 13	41.3	23 cervical, 12 thoracic / 7 cervical, 6 thoracic	AIS A	Bone marrow MSCs	$1.98×10^8$	Injection into lesion
Xie et al., 2007	China	11 / 13	18–49 (SCT), 21–53 (Ctrl)	Cervical, thoracic, lumbar / similar	AIS A–D	Bone marrow MSCs	$2–5×10^9$	Lumbar puncture
Yang Yalin et al., 2020	China	34 / 34	27–43	44 Cervical/24 Thoracic	AIS A–D	Autologous bone marrow		Intrathecal
Albu S et al., 2021	Spain	10 / 10	25–47	Thoracic	AIS A–D	Allogeneic umbilical cord cells		Intrathecal
Honmou O et al., 2021*	Japan	13 / –	21–66	Cervical	AIS A–D	Autologous bone marrow		Intravenous
Yang Y et al., 2021*	China	41 / –	18–65	24 Cervical/ 7 Thoracic/10 Dorsal-lumbar	AIS A–D	Allogeneic umbilical cord cells		Intrathecal

*Single arm clinical trial
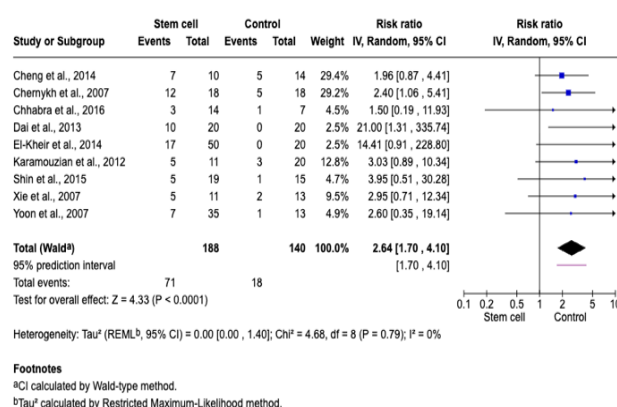
Table 2. GRADE summary of findings.

Outcome (follow-up)	Participants (studies)	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Overall certainty (GRADE)	Relative effect	Absolute effect (per 100 pts)*
AIS grade improvement (overall) (longest available)	532 (13)	Mostly non-randomized comparative studies	Not serious†	Not serious (I²=0%)	Not serious (adults with SCI)	Not serious (95% CI excludes no effect)	MODERATE ⊕⊕⊕◯	RR 2.64 (95% CI 1.70–4.10) (Figure 3)	+21 more/100 improved (from +9 to +40 more) — assuming a 13/100 control risk from Figure 3
AIS grade improvement by baseline AIS (A vs B/C)	532 (13)	Mostly non-randomized	Not serious†	Not serious (I²=0% within subgroups)	Not serious	Not serious	MODERATE ⊕⊕⊕◯	RR 2.61 (1.71–3.98) (Figure 4)	From a 13/100 control risk: +21 more/100 (from +9 to +38 more)
AIS grade improvement by cell dose (10⁶, 10⁷, 10⁸ cells)	492 (11)	Mostly non-randomized	Not serious†	Not serious (I²=0%; no subgroup diffs)	Not serious	Not serious	MODERATE ⊕⊕⊕◯	RR 2.75 (1.63–4.64) (Figure 5)	From a 13/100 control risk: +23 more/100 (from +8 to +47 more)

A total of 286 participants received stem cell therapy (SCT) and 184 participants served as controls across the 13 included studies. The studies were conducted in Asia (China, Korea, Japan, India), Europe (Spain), Russia, and Egypt, reflecting a diverse geographic representation. The mean or range of participant ages varied between 16 and 66 years, indicating that most studies focused on adult populations with both acute and chronic spinal cord injuries. The majority of participants had cervical or thoracic injuries, with baseline preinjury AIS grades ranging from A to D, although most were complete injuries (AIS A).

The predominant stem cell sources were bone marrow–derived MSCs (used in 8 studies), followed by umbilical cord–derived MSCs (2 studies), allogeneic umbilical cord cells (2 studies), and neural stem/progenitor cells (1 study). The delivery methods varied across studies: lumbar puncture/intrathecal injection was the most common route (7 studies), while others used direct lesion site injections, intravenous infusion, or combined approaches (e.g., intralesional and intravenous). Reported cell quantities ranged widely from 7×10^5 to 5×10^9 cells, with some studies expressing dosage relative to body weight (e.g., 2×10^6 cells/kg).

Meta-analysis

The overall pooled meta-analysis demonstrated a statistically significant improvement in AIS grading following stem cell therapy compared with control treatment (RR = 2.64, 95% CI: 1.70–4.10, $p < 0.0001$; $I^2 = 0\%$) (Figure 3). Subgroup analysis according to baseline AIS classification also showed a significant overall effect (RR = 2.61, 95% CI: 1.71–3.98, $p < 0.0001$; $I^2 = 0\%$) across both AIS A and AIS B/C groups (Figure 4). When stratified by administered cell quantity, the pooled estimate remained significant (RR = 2.75, 95% CI: 1.63–4.64, $p = 0.0002$; $I^2 = 0\%$) (Figure 5). Across all analyses, no significant heterogeneity was observed ($\tau^2 = 0.00$; $\chi^2 = 4.68$, df = 8, $p = 0.79$ for the main model), and the funnel plots demonstrated symmetry, indicating a low likelihood of publication bias.
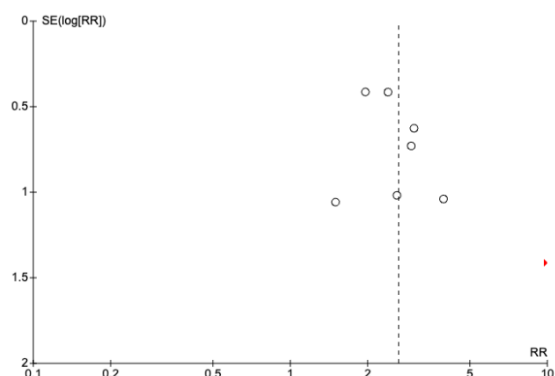

Study or Subgroup	Stem cell Events	Total	Control Events	Total	Weight	Risk ratio IV, Random, 95% CI
Cheng et al., 2014	7	10	5	14	29.4%	1.96 [0.87 , 4.41]
Chernykh et al., 2007	12	18	5	18	29.2%	2.40 [1.06 , 5.41]
Chhabra et al., 2016	3	14	1	7	4.5%	1.50 [0.19 , 11.93]
Dai et al., 2013	10	20	0	20	2.5%	21.00 [1.31 , 335.74]
El-Kheir et al., 2014	17	50	0	20	2.5%	14.41 [0.91 , 228.80]
Karamouzian et al., 2012	5	11	3	20	12.8%	3.03 [0.89 , 10.34]
Shin et al., 2015	5	19	1	15	4.7%	3.95 [0.51 , 30.28]
Xie et al., 2007	5	11	2	13	9.5%	2.95 [0.71 , 12.34]
Yoon et al., 2007	7	35	1	13	4.9%	2.60 [0.35 , 19.14]
Total (Wald[a])		188		140	100.0%	2.64 [1.70 , 4.10]
95% prediction interval						[1.70 , 4.10]
Total events:	71		18			

Test for overall effect: Z = 4.33 (P < 0.0001)

Heterogeneity: Tau² (REML[b], 95% CI) = 0.00 [0.00 , 1.40]; Chi² = 4.68, df = 8 (P = 0.79); I² = 0%

Footnotes
[a]CI calculated by Wald-type method.
[b]Tau² calculated by Restricted Maximum-Likelihood method.

Figure 3. Pooled meta-analysis of improvement rates in AIS grading following stem cell therapy.
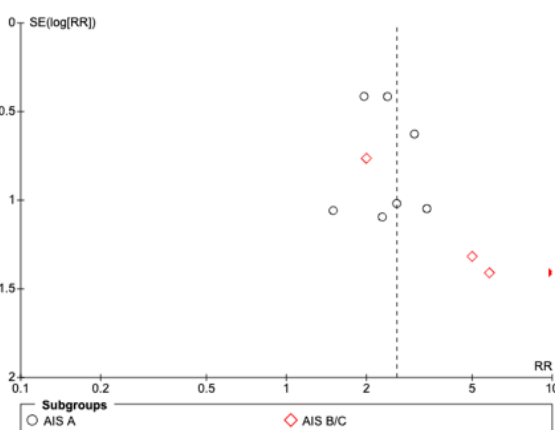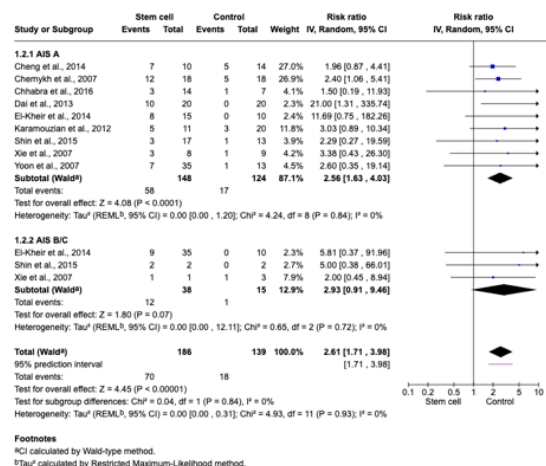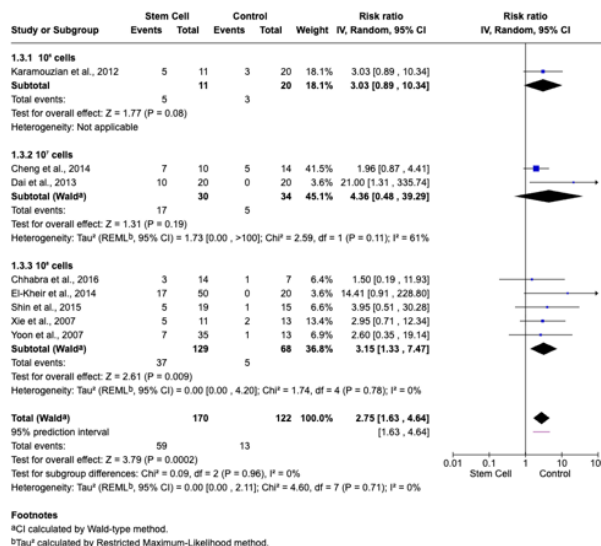

Figure 4. Subgroup meta-analysis comparing AIS grade improvement between stem cell therapy and control groups across different baseline AIS classifications.

Figure 5. Subgroup meta-analysis comparing AIS grade improvement between stem cell therapy and control groups according to varying administered cell doses.

GRADE Certainty Assessment

The GRADE assessment (table 2) indicated moderate certainty of evidence for the efficacy of stem cell therapy in improving neurological outcomes among adults with spinal cord injury. Evidence consistency and low heterogeneity supported upgrading from low to moderate certainty, despite the predominance of non-randomized studies. In contrast, the certainty of evidence for safety outcomes was rated very low because of limited

data, inconsistent reporting, and potential bias in adverse event documentation.

Discussion

The nature and findings of the study are placed in context of other relevant published data. The present meta-analysis demonstrated a significant improvement in neurological recovery among adult patients with SCI who received stem cell therapy compared with controls (RR = 2.64, 95% CI: 1.70–4.10, p < 0.0001). Subgroup analyses revealed consistent effects across different baseline AIS classifications (RR = 2.61) and cell dose groups (RR = 2.75), with minimal heterogeneity (I² = 0%) across studies. These findings suggest a robust and reproducible therapeutic effect of stem cell transplantation for promoting functional improvement following SCI. The consistency of effect sizes across subgroups implies that stem cell therapy benefits may be relatively independent of baseline severity or administered cell quantity, underscoring its potential as a broadly applicable regenerative intervention.

Several studies in related neurological conditions support the efficacy of stem cell therapy in enhancing neural recovery, lending further weight to the current findings.[23,24] For instance, meta-analyses in ischemic stroke and traumatic brain injury have similarly demonstrated significant improvements in functional outcomes following MSCs administration, with effect estimates comparable to those observed in SCI populations.[25,26] However, conflicting evidence exists; some trials in chronic SCI reported limited or transient functional recovery, likely due to the extensive gliosis and scar tissue that restrict cellular integration. These mixed outcomes across diseases and time points highlight that while stem cells possess regenerative potential, their efficacy may be modulated by injury chronicity, host immune responses, and local microenvironmental factors.

The beneficial effects of stem cell therapy can be attributed to several mechanisms. Following SCI, primary mechanical insult initiates a cascade of secondary injury processes, including ischemia, excitotoxicity, inflammation, and glial scar formation, which collectively impair axonal conduction and neuronal survival.[27] Transplanted stem cells—particularly MSCs and neural progenitors—can mitigate these effects by secreting neurotrophic factors such as brain-derived neurotrophic factor (BDNF) and glial cell line–derived neurotrophic factor (GDNF), promoting angiogenesis, and modulating the immune response toward a reparative phenotype.[28–30] Moreover, some stem cells may differentiate into oligodendrocytes or neurons, contributing to remyelination and restoration of neural circuitry.[29] This neuroprotective and neuroregenerative

synergy underlies the physiological plausibility of the observed clinical improvements.[30]

Despite encouraging results, several limitations and translational challenges remain. The included studies displayed variability in stem cell sources, delivery routes, and dosing protocols, which may influence therapeutic efficacy and safety. The long-term survival, differentiation, and integration of transplanted cells within the spinal cord remain uncertain, raising theoretical concerns regarding tumorigenicity and ectopic tissue formation. Furthermore, the pharmacological microenvironment of the injured spinal cord—characterized by persistent inflammation, oxidative stress, and inhibitory extracellular matrix molecules—can hinder stem cell viability and function. Future research should therefore focus on optimizing cell type selection, timing of administration, and combination therapies (e.g., growth factors or biomaterial scaffolds) to enhance cell survival, integration, and functional outcomes.

Study Limitations

Several limitations should be acknowledged when interpreting the findings of this meta-analysis. First, most included studies were non-randomized clinical trials with small sample sizes, introducing potential selection and performance biases despite overall low risk scores under the ROBINS-I tool. Second, there was heterogeneity in study protocols, including differences in stem cell sources, doses, delivery routes, and follow-up durations, which may influence treatment outcomes and complicate direct comparison. Third, most trials lacked long-term follow-up data, limiting assessment of the durability and safety of neurological improvements. Fourth, despite the use of random-effects modeling, publication bias cannot be fully excluded, as negative or null studies are less likely to be reported. Lastly, variability in outcome assessment tools, such as differences in AIS scoring criteria or assessor blinding, may have introduced subjective bias in evaluating neurological improvement.

Conclusion

This systematic review and meta-analysis demonstrated that stem cell therapy significantly improves neurological recovery in adults with spinal cord injury, with consistent benefits observed across injury severity and cell dose subgroups. The pooled evidence supports the potential of stem cell–based interventions as an effective regenerative approach for spinal cord repair, likely mediated by neuroprotective, anti-inflammatory, and remyelinating mechanisms. However, the certainty of evidence remains moderate, primarily due to methodological limitations and heterogeneous study designs. Further large-scale, randomized controlled trials

with standardized protocols and long-term follow-up are warranted to confirm therapeutic efficacy, establish optimal treatment parameters, and ensure safety before widespread clinical adoption.

Acknowledgment

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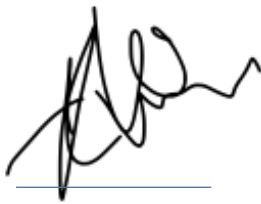
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(Anadya Rhadika)

Investigating the Prognostic Value of Serum Albumin Levels in Patients Undergoing Hemodialysis: A Systematic Review and Meta-analysis

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Abstract

Background: Hypoalbuminemia, characterized by low serum albumin levels, is frequently observed in patients undergoing hemodialysis and has been identified as a potential predictor of increased mortality risk. This systematic review aims to evaluate the relationship between hypoalbuminemia and mortality in hemodialysis patients, assessing the prognostic value of serum albumin levels as an indicator for patient outcomes.

Methods: A comprehensive search was conducted in databases including PubMed, Europe PMC, and Scopus to identify relevant studies. Studies were included if they investigated the association between serum albumin levels and mortality outcomes in adult patients undergoing hemodialysis. Data extraction was performed independently by two reviewers, focusing on study characteristics, patient demographics, albumin levels, and mortality outcomes. Quality assessment of studies was conducted using the Newcastle-Ottawa Scale (NOS).

Result: A total of eight studies, encompassing 45,178 hemodialysis patients with a mean age in the 50s, met the inclusion criteria. The studies had a combined male cohort of 22,501 individuals. The definition of hypoalbuminemia varied across studies, with cutoff values ranging from 3.0 to 3.9 g/dL. Follow-up durations spanned from as early as 3 months to a maximum of 6.1 years. The meta-analysis revealed a pooled hazard ratio (HR) of 1.08 (95% CI: 0.94–1.25), suggesting a non-significant association between hypoalbuminemia and increased mortality risk (P = 0.28). However, substantial heterogeneity was present (I² = 79%), indicating variability across studies.

Conclusions: Hypoalbuminemia showed a non-significant association with mortality in hemodialysis patients, though variability across studies suggests further research is needed for clarity.

Introduction

Patients with end-stage renal disease (ESRD) undergoing maintenance hemodialysis face a markedly increased risk of morbidity and mortality, primarily due to cardiovascular complications, malnutrition, and inflammation.[1,2] Among various biochemical markers, serum albumin has emerged as a key indicator of nutritional and inflammatory status. Low serum albumin levels, or hypoalbuminemia, are frequently encountered in hemodialysis populations and have been consistently associated with adverse clinical outcomes, including hospitalization, infection, and mortality.[3,4]

From a clinical perspective, serum albumin measurement is routinely performed in dialysis units due to its simplicity, cost-effectiveness, and availability, making it a practical biomarker for risk assessment.[5–7] However, while hypoalbuminemia is recognized as a marker of poor prognosis, its precise prognostic value remains incompletely defined.[8,9] Understanding this relationship is crucial for guiding interventions aimed at improving survival in hemodialysis patients.

Given the high burden of mortality in this patient group and the widespread use of serum albumin as a monitoring tool, a systematic evaluation of existing evidence is warranted to clarify its prognostic significance. Therefore, this study aims to investigate the prognostic value of serum albumin levels in patients undergoing hemodialysis through a systematic review and meta-analysis.

Material And Methods

Please state the study design and its methodology. Details relevant to the conduct of the study

This systematic review and meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines.[10]

A comprehensive electronic search was performed across PubMed, Europe PMC, and Scopus databases from inception until October 18, 2025, to identify studies investigating the association between serum albumin levels and mortality among adult patients undergoing maintenance hemodialysis. Search terms combined Medical Subject Headings (MeSH) and free-text words related to "albumin," "hemodialysis," and "mortality." Detailed search terms is presented in table 1. Reference lists of eligible studies and relevant reviews were also screened to ensure completeness of the evidence base.

Table 1. Search strategy used in each database

Database	Search queries used
PubMed	("hypoalbuminaemia"[All Fields] OR "hypoalbuminemia"[MeSH Terms] OR "hypoalbuminemia"[All Fields]) AND ("renal replacement therapy"[MeSH Terms] OR

	("renal"[All Fields] AND "replacement"[All Fields] AND "therapy"[All Fields]) OR "renal replacement therapy"[All Fields] OR ("haemodialysis"[All Fields] OR "renal dialysis"[MeSH Terms] OR ("renal"[All Fields] AND "dialysis"[All Fields]) OR "renal dialysis"[All Fields] OR "hemodialysis"[All Fields])) AND ("mortality"[MeSH Terms] OR "mortality"[All Fields] OR "mortalities"[All Fields] OR "mortality"[MeSH Subheading])
Scopus	hypoalbuminemia AND renal AND replacement AND therapy OR hemodialysis AND mortality
Europe PMC	hypoalbuminemia AND renal replacement therapy OR hemodialysis AND mortality

Studies were eligible for inclusion if they were original observational investigations, either prospective or retrospective in design, that evaluated the relationship between serum albumin levels and mortality in adult patients (≥18 years) undergoing regular hemodialysis. Studies were excluded if they involved pediatric populations, patients treated with peritoneal dialysis, case reports, reviews, conference abstracts, or editorials lacking primary data. Articles were also excluded if mortality outcomes were not reported or if data were insufficient to compute risk estimates.

The primary outcome of interest was all-cause mortality among adults undergoing maintenance hemodialysis. Mortality was defined as death from any cause during the follow-up period, as reported in each study. When available, cause-specific mortality and both adjusted and unadjusted risk estimates were extracted for descriptive and comparative analyses. Studies reporting survival outcomes without explicitly defining mortality were included if sufficient data could be extracted to compute relative risk estimates.

All retrieved titles and abstracts were independently screened by two reviewers who were blinded to each other's decisions, and full texts of potentially eligible studies were then assessed for final inclusion. Disagreements regarding study eligibility were resolved through discussion and consensus. Following data saturation of included studies, a manual hand-search of their reference lists was performed to identify additional relevant records.

Data extraction was conducted independently by the same two reviewers using a pre-designed data collection form. Extracted information included study characteristics (author, year, country, and design), sample size, demographic and clinical data of participants, serum albumin measurement methods and thresholds, follow-up duration, and reported mortality outcomes. Extracted effect measures were recorded as hazard ratio (HR) or equivalent estimates with their corresponding 95% confidence intervals (CIs). Any discrepancies in data extraction were

reviewed jointly until consensus was achieved.

Methodological quality was assessed for all included studies using the Newcastle–Ottawa Scale (NOS), which evaluates three domains: selection of participants, comparability of study groups, and ascertainment of outcomes. Both reviewers performed this assessment independently and were blinded to each other's ratings; disagreements were resolved by discussion. The same independent, blinded, and consensus-based approach was used for both study selection and quality appraisal to minimize reviewer bias.

The certainty of evidence for each pooled outcome was assessed in accordance with the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework. This evaluation considered the risk of bias, inconsistency, indirectness, imprecision, and potential publication bias across the included studies. Evidence certainty was subsequently categorized as high, moderate, low, or very low, reflecting the overall confidence in the pooled estimates.

Statistical analyses were conducted using Review Manager (RevMan) version 5.4. A random-effects model was applied using the Restricted Maximum Likelihood (REML) estimation method, with Wald-type confidence intervals to account for inter-

study variability. Pooled HR with corresponding 95% confidence intervals (CIs) were calculated, and statistical significance was set at $p < 0.05$. The random-effects model was applied regardless of the level of heterogeneity to ensure conservative and generalizable pooled estimates. Statistical heterogeneity was quantified using the I² statistic and assessed through Cochran's Q test. Forest plots were generated to visualize pooled effect estimates, and funnel plots, together with Egger's and Begg's tests, were used to explore potential publication bias.

Result

Work should be reported in SI units. Undue repetition in text and tables should be avoided. Comment on validity and significance of results is appropriate but broader discussion of their implication is
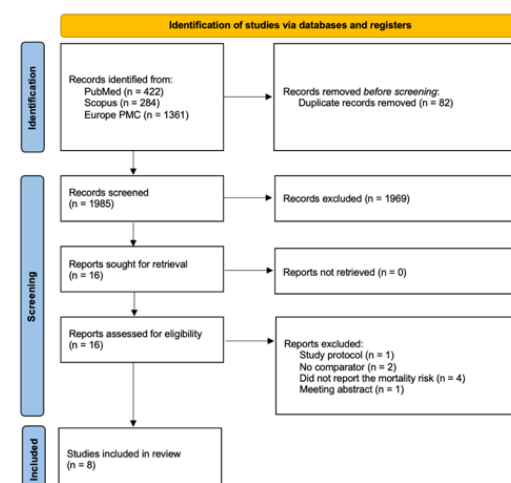

Figure 1. PRISMA flow diagram

A total of 1,985 records were identified through database searches, including PubMed (n = 422), Scopus (n =

284), and Europe PMC (n = 1,361). After removing 82 duplicate records prior to screening, 1,985 unique studies were screened for eligibility. Of these, 1,969 were excluded based on title and abstract review, leaving 16 reports sought for full-text retrieval, all of which were successfully obtained. Upon full-text assessment, six studies were excluded for reasons including being a study protocol (n = 1), lacking a comparator (n = 2), not reporting mortality risk (n = 4), or being a meeting abstract (n = 1). Ultimately, eight studies met all inclusion criteria and were included in the final systematic review (Figure 1).[3,4,11–16]

Across the eight included studies summarized in Table 2, sample sizes ranged widely from small single-center cohorts (Cooper et al., 2003; n = 109) to large national registries (Chertow et al., 2005; n = 40,538). Male representation was generally higher across studies, varying from approximately 52 % to 63 %. Mean or median patient ages spanned from the early 50s to the mid-60s, reflecting predominantly older adult and elderly dialysis populations. Study populations included diverse geographic and clinical settings: end-stage renal disease (ESRD) or chronic hemodialysis patients in Pakistan, Japan, China, Australia, and Brazil, as well as critically ill or acute kidney injury (AKI) cohorts on continuous renal replacement therapy (CRRT) in South Korea and the United States. Study periods ranged from the early 1990s to 2016, with most being retrospective cohort designs or follow-up observational analyses. The definitions of hypoalbuminemia varied slightly across studies, most often using thresholds between ≤ 3.5 g/dL and < 4.0 g/dL, though some studies stratified by albumin tertiles or broader categories.

Frequent comorbidities typical of dialysis populations, including diabetes (ranging from 17 % to 68 %), anemia (Hb < 11 g/dL), and chronic inflammation. Hemodialysis vintage and modality were noted in several studies, with median dialysis durations between 2 and 7 years in chronic HD populations and ≤ 3 months in incident ESRD cases. Average body mass indices were mostly in the normal-to-overweight range, while serum albumin levels averaged ~3.5 to 4.0 g/dL. Many cohorts were predominantly of one ethnicity (e.g., 86 % Caucasian in Thongprayoon et al., 2021), while others reflected local regional populations.

Table 2. Demographic characteristics of included studies

Study (Author, Year)	Sample Size (n)	Sex Distribution	Mean/Range of Age	Population / Setting	Albumin Cutoff for Hypoalbuminemia	Study Duration / Data Collection Period	Key Clinical Characteristics
Anees & Ibrahim (2006)	185	52.8% male, 47.2% female	Not reported	ESRD patients at Shalamar Hospital, Lahore, Pakistan	< 4.0 g/dL	June 2003 – October 2006	67.6% diabetes, 16.8% glomerulonephritis, 9.7% hypertension; 91.1% anemic (Hb <11 g/dL); 67% hypoalbuminemic
Moon et al. (2019)	1,581	60.5% male	63.2 ± 15.2 years	AKI patients on CRRT (South Korea)	Tertiles: ≤ 2.4 g/dL / 2.5–2.9 g/dL / ≥ 3.0 g/dL (lowest tertile ≤ 2.4 g/dL = hypoalbuminemic)	2010 – 2016	Differences across tertiles in AKI cause, dialysis dose, malignancy, hemoglobin, potassium, and APACHE II score; overall mortality 65.8%
Thongprayoon et al. (2021)	911	57 % male (520/911)	59.2 ± 14.9	Critically ill CRRT patients (USA)	≤ 2.4 / 2.5–2.9 / 3.0–3.4 / ≥ 3.5 g/dL	Dec 2006 – Nov 2015	86 % Caucasian; BMI 32.0 ± 15.8; no age or sex difference across albumin groups (p > 0.05); Caucasian proportion rose with higher albumin (p = 0.002). Severe hypoalbuminemia (≤ 2.4 g/dL) linked to highest mortality.
Tang et al. (2021)	447 total (Low ABL n = 151, Moderate n = 147, High n = 149)	62.3 % M (low), 61.2 % M (moderate), 62.4 % M (high)	63.9 ± 14.6 (low), 58.2 ± 15.3 (moderate), 52.0 ± 14.6 (high)	Chronic hemodialysis patients, China	Low ≤ 35.7 g/L (3.57 g/dL); Moderate 35.7 < ALB ≤ 38.9 g/L; High > 38.9 g/L	Retrospective; period not stated	Hemoglobin: 90 (73–106) g/L (low), 104 (90–116) g/L (moderate), 107 (95–119) g/L (high); RBC (×10¹²/L): 3.33 (low), 3.6 (moderate), 3.68 (high); significant differences in age, Hb, and RBC (p < 0.001).
Iseki et al. (1997)	1,186 total (Died n = 342; Survived n = 844)	58.1 % male (55.3 % died; 59.2 % survived)	52.4 ± 0.4 (overall); 62.9 ± 0.7 (died); 48.8 ± 0.5 (survived)	Chronic HD patients, Okinawa, Japan	< 3.9 g/dL (mean albumin: 3.7 ± 0.03 died vs 4.0 ± 0.02 survived)	Baseline: January 1991; Follow-up through 1995	Mean serum albumin 3.9 ± 0.01 g/dL; diastolic BP 80.8 ± 0.4 mmHg (77.1 died vs 82.3 survived); diabetes 17.6 % overall (35.4 % died); BMI 21.6 ± 0.1 kg/m²; total protein 6.5 ± 0.02 g/dL; study linked low albumin and low DBP with increased mortality (p < 0.0001).

Study (Author, Year)	Sample Size (n)	Sex Distribution	Mean/Range of Age	Population / Setting	Albumin Cutoff for Hypoalbuminemia	Study Duration / Data Collection Period	Key Clinical Characteristics
Cooper et al. (2003)	109 total (PD = 52; HD = 57)	PD: 25F / 27M; HD: 22F / 35M	PD: 63.9 ± 1.8; HD: 57.7 ± 2.1	ESRD patients initiating dialysis (Australia)	Hypoalbuminemia defined as < 3.6 g/dL for HD and < 2.0 g/dL for PD	Not specified	Time on dialysis: PD 1.6 ± 0.2 months; HD 2.9 ± 0.3 months (p = 0.0003); no sex difference (p = 0.3); PD group older (p = 0.03). Study concluded hypoalbuminemia and protein malnutrition at dialysis initiation predicted increased morbidity and mortality.
Chertow et al. (2005)	40,538 total; Prealbumin group: 7,815 (19.3%)	51.0 % female (with prealbumin); 51.3 % (without)	61.5 ± 15.1 (with prealbumin); 60.3 ± 15.1 (without)	Chronic hemodialysis patients on thrice-weekly HD, USA	Prealbumin categorized a priori into 7 groups: <15, 15–20, 20–25, 25–30, 30–35, 35–40, ≥40 mg/dL	Labs averaged from final 3 months of 1997; cohort as of Jan 1, 1998	46.3 % Caucasian in prealbumin group vs 35.2 % in non-prealbumin; mean difference in age significant (p < 0.0001); used averaged lab values for exposure; lower prealbumin strongly associated with increased mortality and hospitalization risk.
Antunes et al. (2016)	221 (from 275 invited)	59 % male (130/221)	Median 50 (IQR 38–63)	Adult HD patients, two dialysis centers in Maceió, Brazil (INRV-SCMM & CDR-Sanatorium)	< 3.8 g/dL (hypoalbuminemia)	13-month prospective follow-up	Median HD vintage 7 years (IQR 4–9); diabetes 29 %; mean Hb 10.6 ± 1.9 g/dL; CRP 1.0 (0.19–1.29) mg/dL; ferritin 424.8 ng/mL; transferrin saturation 29.8 ± 10.6 %; hypoalbuminemia and high CRP predicted hospitalization; 4.9 % had temporary catheter at baseline.

The pooled overall effect estimate demonstrated no significant association between hypoalbuminemia and mortality among patients undergoing hemodialysis, with a combined hazard ratio (HR) of 1.08 (95% CI: 0.94–1.25, p = 0.28). Considerable heterogeneity was observed across studies (I^2 = 79%), indicating substantial variability in study outcomes (Figure 2).
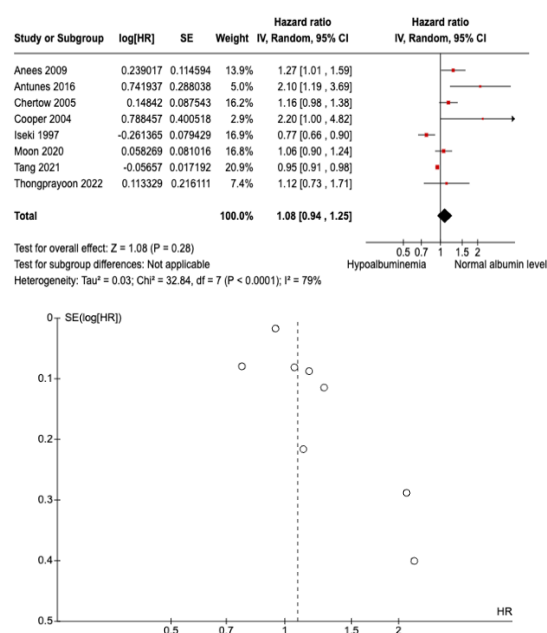

Figure 2. Meta-analysis showing an insignificant results of hypoalbuminemia to predict mortality in patients undergoing hemodialysis.

The methodological quality of the included studies was evaluated using the NOS, as summarized in Table 3. Most studies demonstrated moderate to high quality, with total scores ranging from 6 to 9 out of 9 possible points. Overall, five studies were rated as low risk of bias, while three showed moderate risk, indicating generally reliable study designs across the

included literature. GRADE analysis for certainty assessment was also to appear moderate – low risk of bias.

Table 3. Newcastle–Ottawa Scale (NOS) assessment for risk of bias

Study (Author, Year)	Selection	Comparability	Outcome / Exposure	Total Score	Risk of Bias
Anees & Ibrahim (2006)	★★★	★	★★	6 / 9	Moderate
Moon et al. (2019)	★★★★	★★	★★★	9 / 9	Low
Thongprayoon et al. (2021)	★★★★	★★	★★	8 / 9	Low
Tang et al. (2021)	★★★	★★	★★	7 / 9	Moderate
Iseki et al. (1997)	★★★★	★★	★★★	9 / 9	Low
Cooper et al. (2003)	★★★	★	★★	6 / 9	Moderate
Chertow et al. (2005)	★★★★	★★	★★★	9 / 9	Low
Antunes et al. (2016)	★★★	★★	★★	7 / 9	Moderate

Table 4. GRADE Summary of Findings Framework

Outcome	No. of Studies	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Overall Certainty of Evidence	Summary of Findings
Demographic characteristics of dialysis patients	8	⊕⊕○○	⊕⊕⊕○	⊕⊕⊕⊕	⊕⊕⊕⊕	⊕⊕⊕⊕	Moderate (⊕⊕⊕○)	Populations were predominantly male, middle to older age, with high prevalence of diabetes and hypertension.
Prevalence of hypoalbuminemia	8	⊕⊕○○	⊕⊕○○	⊕⊕⊕○	⊕⊕⊕○	⊕⊕○○	Moderate (⊕⊕⊕○)	Hypoalbuminemia prevalence ranged from 60–75%, depending on albumin cutoff (≤2.4–4.0 g/dL).
Association between hypoalbuminemia and mortality	8	⊕⊕○○	⊕○○○	⊕⊕⊕○	⊕⊕○○	⊕⊕○○	Low (⊕⊕○○)	Pooled analysis showed no significant association (HR 1.08, 95% CI: 0.94–1.25, p = 0.28).
Overall quality of evidence	—	—	—	—	—	—	Moderate to Low (⊕⊕– ⊕⊕⊕○)	Evidence limited by observational design and heterogeneity; demographic and prevalence data consistent, but mortality findings uncertain.

Discussion

The demographic characteristics summarized in this review reflect considerable variability across populations, geographic regions, and dialysis modalities. Participants' ages ranged from middle-aged to elderly, with male predominance observed in most cohorts, consistent with the known higher prevalence of CKD and ESRD in men. Studies conducted across diverse regions, including South Asia, East Asia, Australia, North America, and South America, highlighted differences in comorbidities, such as diabetes, hypertension, and cardiovascular disease, which are known contributors to both CKD progression and adverse outcomes. These findings align with previous epidemiological data indicating that CKD prevalence increases with age and comorbidity burden, and that metabolic and vascular alterations contribute to disease progression.[17–19] CKD and dialysis profoundly affect homeostatic regulation, particularly in cardiovascular and metabolic systems, which may explain demographic patterns of risk and survival observed among the included cohorts.[20]

Regarding hypoalbuminemia, the present systematic review and meta-analysis found wide variation in the definitions and thresholds used across studies, ranging from ≤2.4 g/dL in critically ill patients to <4.0 g/dL in stable hemodialysis cohorts. The prevalence of hypoalbuminemia was consistently high, reinforcing its role as a marker of poor nutritional and inflammatory status. Supporting evidence from prior studies indicates that serum albumin reflects not only protein-energy malnutrition but also systemic inflammation and capillary leak, both of which are prevalent in dialysis patients.[21–23] However, some conflicting data exist, particularly in acute kidney injury populations where transient hypoalbuminemia may not carry the same prognostic weight as in chronic dialysis patients.[24,25] Albumin serves multiple physiological functions, it maintains oncotic pressure, binds endogenous and exogenous molecules, and possesses antioxidant properties.[24] Thus, explaining why reduced levels reflect both disease severity and impaired homeostasis.

The pooled results of this meta-analysis revealed that hypoalbuminemia was not significantly associated with increased mortality among dialysis patients, with a combined HR of 1.08 (95% CI 0.94–1.25, $p = 0.28$). This finding contrasts with earlier literature where low albumin was a strong independent predictor of mortality, possibly reflecting variations in patient selection, dialysis adequacy, and advances in supportive care over time.[26,27] Some supporting studies, such as those by Iseki et al. (1997) and Tang et al. (2021), did demonstrate associations between lower albumin and adverse outcomes, while others, including

Moon et al. (2019) and Thongprayoon et al. (2021), reported no significant relationship after adjustment for confounders.[4,12,14,14] From a physiological and pathophysiological perspective, mortality in dialysis patients is multifactorial, where albumin may act more as a surrogate marker than a direct cause. Hence, while hypoalbuminemia remains an important indicator of clinical frailty and systemic illness, its predictive value for mortality may be attenuated in contemporary dialysis populations.[28]

Study Limitations

This review has several limitations that should be considered when interpreting the findings. First, there was significant heterogeneity among the included studies in terms of population characteristics, albumin cutoff definitions, dialysis modalities, and study designs, which may have influenced the pooled estimates. Second, most included studies were observational and retrospective, making them subject to selection bias, confounding, and incomplete data reporting. Additionally, several studies lacked standardized methods for assessing nutritional or inflammatory status, limiting comparability across cohorts. Publication bias cannot be excluded, as studies reporting null associations between albumin and mortality may have been underrepresented.[29,30] Finally, the meta-analysis included studies spanning multiple

decades, during which dialysis techniques and patient management strategies have evolved, potentially affecting mortality outcomes and albumin levels.

Conclusion

This systematic review and meta-analysis demonstrated that while hypoalbuminemia remains a frequent finding among patients undergoing hemodialysis, its association with mortality was not statistically significant when data were pooled across studies. Despite this, albumin continues to serve as a critical marker of nutritional and inflammatory status in dialysis populations and should be interpreted within the broader context of patient comorbidities and treatment adequacy. These findings underscore the multifactorial nature of mortality in renal replacement therapy, suggesting that albumin alone may not be a sufficient predictor of survival. Future prospective studies with standardized definitions, adjustment for confounders, and longitudinal assessment of nutritional and inflammatory parameters are warranted to clarify the prognostic value of serum albumin in contemporary dialysis care.

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(Jessica Adrya)

The Role of Glycemic Load, Dairy, and Fatty Acids in Acne Disorders: A Systematic Review and Meta-Analysis

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Abstract

Background: Modern dietary patterns characterized by high glycemic load, dairy consumption, and imbalanced fatty acid profiles may aggravate acne through insulin, IGF-1, and inflammatory pathways. However, findings across studies remain inconsistent. This systematic review and meta-analysis aimed to evaluate the associations between dietary glycemic load, glycemic index, dairy intake, and fatty acid composition with acne disorders.

Methods: Following PRISMA 2020 guidelines, PubMed, EMBASE, and Scopus were systematically searched to September 2025. Eligible human studies assessing quantitative relationships between these dietary exposures and acne risk or severity were included. Random-effects meta-analyses were performed using the Hartung–Knapp–Sidik–Jonkman method, with effect sizes expressed as standardized mean differences (SMD) or risk ratios (RR).

Result: Five studies encompassing 716 participants (426 acne, 290 controls) met the inclusion criteria. Pooled estimates indicated no significant associations for glycemic load (SMD = 0.09; 95% CI −0.30 to 0.49), glycemic index (SMD = 0.09; 95% CI −0.30 to 0.49), fatty acids/adiponectin (SMD = 0.11; 95% CI −0.74 to 0.97), or dairy consumption (RR = 1.04; 95% CI 0.25 to 4.25). Heterogeneity ranged from moderate to high (I^2 = 65–90%). Certainty of evidence was moderate for glycemic and dairy outcomes, and low for fatty acids.

Conclusions: No significant pooled associations were observed between dietary glycemic load, dairy intake, or fatty acids and acne risk. Despite biological plausibility linking diet to acne via hormonal and inflammatory mechanisms, evidence remains inconsistent. Larger, controlled trials are warranted to define the role of nutritional interventions in acne management.

Introduction

Acne vulgaris is one of the most prevalent dermatological disorders worldwide, affecting approximately 9.4% of the global population and ranking as the eighth most common disease burden.[1] Its pathogenesis is multifactorial, involving excess sebum production, follicular hyperkeratinization, inflammation, and colonization by *Cutibacterium acnes*.[2,3] While genetic predisposition plays a role, emerging evidence increasingly implicates dietary and metabolic factors in modulating acne severity and persistence.[3] In particular, modern dietary patterns characterized by high glycemic load, elevated intake of saturated fats, and widespread dairy consumption have been hypothesized to exacerbate acne through hormonal and inflammatory pathways.[4]

From a clinical perspective, the dietary–acne connection remains controversial. Dermatologists are frequently asked by patients whether modifying their diet can improve acne outcomes, yet existing recommendations remain inconsistent. Several studies suggest that high-glycemic-load diets stimulate insulin and insulin-like growth factor 1 (IGF-1) signaling, promoting androgen-mediated sebum production and keratinocyte proliferation.[5,6] Similarly, dairy intake has been linked to acne due to its bioactive hormones and ability to increase IGF-1 concentrations.[7] Moreover, fatty acid profiles, particularly a high omega-6

to omega-3 ratio, may drive inflammation via eicosanoid pathways, further contributing to lesion formation. Despite these proposed mechanisms, the evidence base is fragmented, with heterogeneity in study design, dietary assessment, and population demographics.[7]

Given these discrepancies and the growing patient demand for evidence-based dietary guidance, a comprehensive synthesis of available data is essential. To address this clinical and public health need, the present study aims to systematically review and quantitatively analyze the association between glycemic load, dairy consumption, and fatty acid intake with acne disorders. This systematic review and meta-analysis seeks to clarify the strength, direction, and consistency of these dietary relationships to inform dermatologic practice and guide future research in nutritional interventions for acne management.

Material And Methods

This systematic review and meta-analysis were conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines.[8] The study protocol was established a priori, and no external funding was received. A comprehensive search of the PubMed, EMBASE, and Scopus databases was conducted from inception until 29 September 2025, using

combinations of controlled vocabulary and free-text terms related to acne, glycemic index, glycemic load, dairy, and fatty acids. Boolean operators were used to optimize sensitivity and specificity. To ensure completeness, the reference lists of all included articles and relevant reviews were hand-searched for additional eligible studies.

Eligible studies were selected based on the Population, Intervention, Comparator, and Outcome (PICO) framework. The population of interest included individuals of any age or sex diagnosed with acne vulgaris or acneiform eruptions. The exposures comprised dietary factors such as glycemic index, glycemic load, dairy consumption (including milk, yogurt, and cheese), and fatty acid composition (saturated, monounsaturated, polyunsaturated, omega-3, and omega-6 fatty acids). Comparators included individuals or groups with lower dietary exposures or non-acne controls. The primary outcomes were metabolic and nutritional parameters associated with acne, specifically the glycemic index (GI), defined as the incremental area under the postprandial blood glucose response curve after consuming a test food containing 50 g of carbohydrates relative to glucose, as well as glycemic load (GL), calculated by multiplying the GI of a food by its carbohydrate content (g) and dividing by 100. Fat content was defined as the proportion of total fat, saturated fat, or specific fatty acid subclasses expressed relative to total energy intake. Secondary outcomes included acne severity, lesion count, and inflammatory biomarkers when available. Studies were included if they were original human research (cross-sectional, case-control, cohort, or interventional) reporting quantitative associations between these dietary exposures and acne-related outcomes. Reviews, editorials, animal studies, conference abstracts, and studies lacking a comparison group or quantitative dietary data were excluded.

All records retrieved from the databases were imported into a reference management software, and duplicates were removed. Titles and abstracts were screened independently by all reviewers, followed by full-text evaluation of potentially relevant articles. Any discrepancies were resolved through discussion and consensus. A pre-piloted data extraction sheet was developed in Microsoft Excel, capturing study characteristics (author, year, country, design, population demographics, sample size), details of dietary assessment methods, definitions of exposures, outcomes measured, and key findings. Data extraction was performed independently by all reviewers to ensure consistency and accuracy.

The risk of bias in the included studies was evaluated using the Quality

Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool, assessing four domains: patient selection, index test, reference standard, and flow and timing. Disagreements were resolved through consensus.[9] The certainty of evidence for each outcome was appraised using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach, considering study limitations, inconsistency, indirectness, imprecision, and potential publication bias.[10]

Statistical analyses were performed using Review Manager (RevMan) version 5.4. Effect estimates were expressed as relative risks (RRs) with corresponding 95% confidence intervals (CIs). Given the anticipated heterogeneity among studies, a random-effects model was applied throughout, regardless of the degree of statistical heterogeneity. The restricted maximum likelihood (REML) method was used to estimate between-study variance, and the Hartung–Knapp–Sidik–Jonkman (HKSJ) adjustment was applied to derive more robust confidence intervals, particularly in analyses with a limited number of studies. Statistical heterogeneity was quantified using the I^2 statistic, with values of 25%, 50%, and 75% representing low, moderate, and high heterogeneity, respectively. Statistical significance was set at $p < 0.05$. Forest plots were generated to illustrate pooled estimates, while funnel plots were used to evaluate potential publication bias. Subgroup and sensitivity analyses were conducted when sufficient data were available.
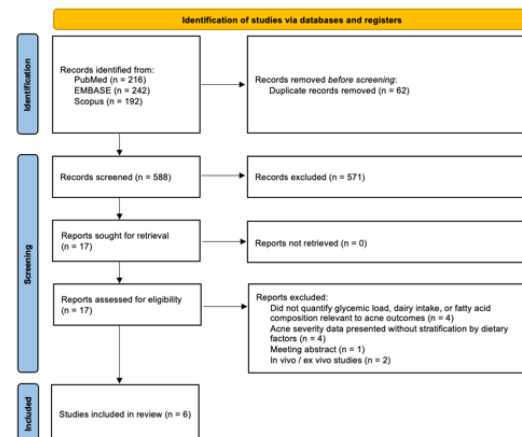
Result

Figure 1. PRISMA 2020 Flow Diagram for this Systematic Review and Meta-analysis

A total of 650 records were initially identified through database searches, including 216 from PubMed, 242 from EMBASE, and 192 from Scopus. After removing 62 duplicate records, 588 unique studies remained for title and abstract screening. Of these, 571 records were excluded based on irrelevance to the review topic, leaving 17 full-text articles for eligibility assessment. None of the reports were excluded due to retrieval issues. Following full-text review, 12 studies were excluded for specific reasons: four did not quantify glycemic load, dairy intake, or fatty acid composition relevant to acne outcomes; four presented acne severity data without stratification by dietary factors; one was a meeting abstract; and

two were in vivo or ex vivo experimental studies.

Consequently, a total of six eligible studies (figure 1) comprising 716 participants (426 with acne and 290 controls) were included, spanning populations from the United States, Turkey, and Malaysia.[11–16] Participants were predominantly young adults, with mean ages ranging from 16 to 25 years and a female predominance of approximately 55–65%. All studies evaluated dietary or metabolic factors influencing acne severity or risk, focusing primarily on glycemic load/index, dairy consumption, and lipid composition. Collectively, these studies were designed to explore how nutritional patterns influence metabolic and hormonal pathways implicated in acne pathogenesis, thereby guiding potential nutritional interventions for acne management.

Across the included studies, consistent trends emerged linking high-glycemic-load diets and greater dairy or fat intake with acne prevalence and severity. Acne cohorts demonstrated higher fasting insulin, IGF-1, and HOMA-IR levels compared to controls, even in the absence of BMI differences—suggesting diet-induced metabolic alterations rather than obesity as the key driver. In particular, participants with higher glycemic load and frequent milk consumption had significantly increased acne severity and

hormonal activity, supporting a metabolic–nutritional axis in acne development. Collectively, these findings highlight that dietary modification may offer clinically meaningful benefits as adjunctive strategies for acne management. Detailed demographic characteristics data is available in table 1.
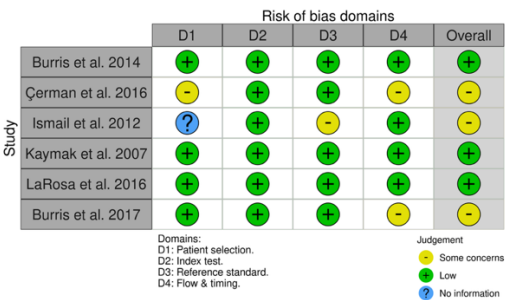
Risk of Bias Analysis

Figure 2. QUADAS-2 Risk of Bias Analysis for Glycemic Load, Dairy, and Fatty Acids in Patients with Acne Disorders

The overall quality of the included studies was moderate to high, as assessed using the QUADAS-2 tool (Figure 2). Most studies demonstrated a low risk of bias across key domains, particularly in patient selection, index testing, and flow and timing. Minor concerns were noted in reference standard reporting and participant recruitment methods in two studies, while one study provided insufficient information on participant selection.

**Table 1.** Demographic and study characteristics of eligible studies

Study ID	Year	Country / Region	Study Design	Total Sample Size (n)	Mean Age (years)	Gender (% female)	Exposure(s) Assessed	Primary Outcome
Burris et al.	2014	USA	Cross-sectional	248	21 ± 2 (18–25)	53.6	Milk intake; saturated & trans-fat intake; diet beliefs	Acne severity categories vs dietary intake (milk, fats)
Çerman et al.	2016	Turkey	Case–control	86 (50 acne/36 control)	19.0 (acne 18.8 ± 3.2; control 19.1 ± 3.5)	58.1	Dietary GI/GL; milk frequency	HOMA-IR, adiponectin, acne severity vs dietary glycemic factors
Ismail et al.	2012	Malaysia	Case–control	88 (44/44)	18–30 (range)	65.9	Dietary glycemic load; milk & ice-cream frequency; energy intake	Acne presence/severity (CASS) vs GL and dairy intake
Kaymak et al.	2007	Turkey	Case–control	91 (49/42)	20.4 ± 1.9 (19–34)	61.5	Dietary GI/GL; insulin, IGF-1, IGFBP-3, leptin	Hormonal/metabolic differences by acne status; diet–hormone links
LaRosa et al.	2016	USA	Cross-sectional (teens)	225 (120 acne/105 control)	16.8 ± 1.4 overall	53.3	Dairy consumption; saturated/trans-fat	Acne status & QoL vs dairy/fat intake
Burris et al.	2017	USA	Cross-sectional	64 (32 mod/severe acne; 32 no acne)	21.8 ± 3.5	73.0	Dietary glycemic load; metabolic hormones	Insulin, HOMA-IR, IGF-1 differences by acne status; GL comparison

*GI/GL = glycemic index/glycemic load; HOMA-IR = homeostasis model assessment of insulin resistance; IGF-1 = insulin-like growth factor-1; IGFBP-3 = insulin-like growth factor-binding protein-3; QoL = quality of life; CASS = Comprehensive Acne Severity Scale.

Meta-analysis

The pooled analysis of five eligible studies demonstrated no statistically significant association between glycemic load and acne risk, with a SMD of 0.09 (95% CI: −0.30 to 0.49; P = 0.54; I² = 67%) (Figure 3). Similarly, the meta-analysis of glycemic index showed an overall SMD of 0.09 (95% CI: −0.30 to 0.49; P = 0.54; I² = 67%) (Figure 4). For fatty acids and adiponectin, the pooled estimate was 0.11 (95% CI: −0.74 to 0.97; P = 0.70; I² = 90%) (Figure 5). Finally, dairy consumption showed a pooled RR of 1.04 (95% CI: 0.25 to 4.25; P = 0.92; I² = 65%) (Figure 6).

Sensitivity analyses were conducted to evaluate the robustness of pooled estimates across included studies. Excluding individual studies sequentially did not substantially alter the overall direction or magnitude of the effect for glycemic load, glycemic index, fatty acid/adiponectin, or dairy intake outcomes. The consistency of results across random-effects and Hartung–Knapp–Sidik–Jonkman models further confirmed the stability of the findings. Heterogeneity remained moderate to high (I² = 65–90%) but did not materially impact the pooled effect estimates.
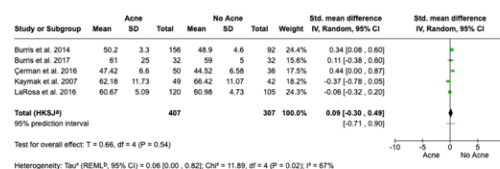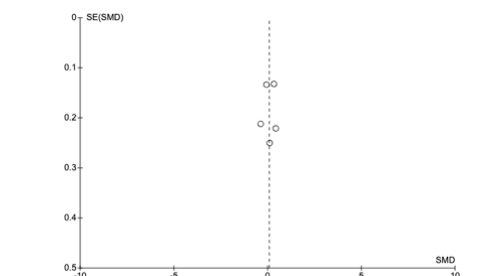
Figure 3. Pooled effect of dietary glycemic load on acne risk
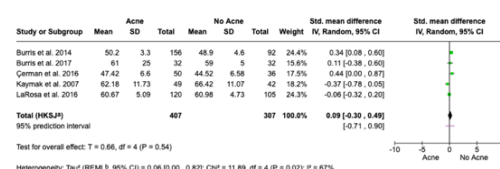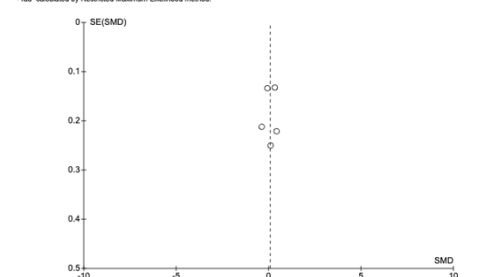
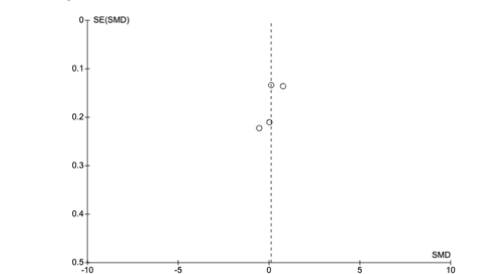**Figure 4.** Pooled effect of dietary glycemic index on acne risk
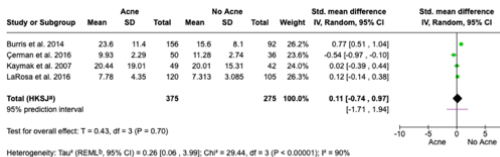
Figure 5. Pooled effect of dietary fatty acids and adiponectin levels on acne risk

Figure 6. Pooled effect of dairy consumption on acne risk

GRADE Certainty Assessment

The certainty of evidence, as assessed using the GRADE approach (Table 2), ranged from low to moderate across nutritional interventions. Glycemic load, glycemic index, and dairy intake outcomes demonstrated moderate certainty of evidence, while fatty acid/adiponectin studies were rated low certainty due to high heterogeneity and wide confidence intervals.

Table 2. GRADE Summary of Findings for Nutritional Interventions in Acne Management

Outcome	No. of Studies	Risk of Bias	Inconsistency	Indirectness	Imprecision	Overall Certainty
Glycemic Load and Acne Risk	5	Moderate	Moderate ($I^2 = 67\%$)	Not serious	Serious (wide CI)	⊕⊕⊕○ Moderate
Glycemic Index and Acne Risk	4	Low	Moderate ($I^2 = 67\%$)	Not serious	Serious (CI crosses null)	⊕⊕⊕○ Moderate
Fatty Acids / Adiponectin and Acne Risk	4	Moderate	High ($I^2 = 90\%$)	Not serious	Serious	⊕⊕○○ Low
Dairy Consumption and Acne Risk	3	Low	Moderate ($I^2 = 65\%$)	Not serious	Serious	⊕⊕⊕○ Moderate

Discussion

Across all included studies, dietary interventions demonstrated modest and inconsistent associations with acne outcomes, likely due to heterogeneity in design, exposure quantification, and population characteristics. The collective evidence supports the nutritional–endocrine–inflammatory axis as a unifying model, where diet influences insulin and IGF-1 signaling, mTORC1 pathway activation, and lipid metabolism within sebaceous glands.[17] However, the varying cultural dietary patterns and self-reported measures complicate cross-study comparisons. It is plausible that genetic polymorphisms, hormonal sensitivity, and gut microbiome composition modulate the dietary influence on acne, suggesting a multifactorial interaction rather than a single causal pathway.[18]

The pooled analysis revealed no significant association between dietary glycemic load and acne risk (SMD = 0.09; 95% CI: −0.30 to 0.49). This aligns with the findings of LaRosa et al. (2016), who reported no clear improvement in acne lesions after short-term low-glycemic dietary intervention, but contrasts with Smith et al. (2007), who demonstrated reduced lesion counts and improved insulin sensitivity in low-glycemic groups.[11,19] High-glycemic diets increase circulating insulin and IGF-1, stimulating keratinocyte proliferation and sebaceous gland activity.[20] However, the lack of significance in this analysis may reflect differences in dietary adherence, participant age, and baseline dietary habits, suggesting the glycemic pathway's contribution to acne may be modulated by individual metabolic variability rather than a uniform causal effect.[21]

The glycemic index also showed no significant overall association with acne risk. Supporting evidence from Burris et al. (2017) suggests only weak correlations between glycemic index and acne severity after adjusting for confounders, while Ismail et al. (2012) reported opposite findings, indicating a higher glycemic index correlated with greater acne prevalence among adolescents.[13,16] The glycemic index measures carbohydrate quality rather than total intake, which may inadequately capture the postprandial hormonal spikes responsible for acne pathogenesis. Insulin-mediated increases in IGF-1, mTORC1 activation, and suppression of FOXO1 transcription factor have been proposed as mechanistic links, yet dietary diversity and inter-study methodological variability may obscure these effects in pooled data.[22,23]

For fatty acids and adiponectin levels, the meta-analysis showed no significant pooled effect, though substantial heterogeneity (I² = 90%) was observed. These findings partly agree with Kaymak et al. (2007), who reported no consistent differences in serum fatty acid composition between acne and control groups, but contrast with studies suggesting low omega-3 and high saturated fat intake may aggravate acne inflammation.[12] It is known that omega-3 fatty acids exert anti-inflammatory actions by reducing pro-inflammatory cytokines (IL-1β, TNF-α) and altering sebum lipid composition.[24] Conversely, diets rich in saturated fats and trans fats promote lipogenesis and oxidative stress, potentially contributing to comedogenesis.[25] The observed variability may therefore stem from unaccounted dietary confounders and different definitions of "fatty acid exposure."

The pooled risk ratio indicated no significant relationship between dairy intake and acne risk. This is consistent with Çerman et al. (2016) but conflicts with

Adebamowo et al. (2005), who found a positive association between milk consumption and acne among adolescents in the Nurses' Health Study II.[14,26] The discrepancy may be explained by differences in milk processing, hormonal content, and consumption frequency. Dairy proteins stimulate insulin and IGF-1 secretion, which may exacerbate acne via androgen receptor activation and sebocyte proliferation.[27] Nonetheless, the null association in the present synthesis suggests that the influence of dairy on acne may depend on dose, type (skim vs. whole milk), and hormonal composition, emphasizing the complexity of dietary–endocrine interactions.

Study Limitation

This meta-analysis is limited by the small number of eligible studies and moderate-to-high heterogeneity in study design, population characteristics, and exposure assessment. Most included studies were observational, restricting causal inference. Variability in dietary reporting tools, acne grading systems, and adjustment for confounders may have introduced measurement bias. Publication bias could not be excluded due to limited study numbers, and the predominance of self-reported dietary data likely reduced internal validity. Future studies should adopt standardized dietary measures, objective biochemical endpoints, and randomized controlled designs.

Conclusion

This systematic review and meta-analysis found no significant pooled associations between glycemic load, glycemic index, fatty acid intake, or dairy consumption and acne risk. While the direction of effects aligns with proposed metabolic and hormonal mechanisms, current evidence remains inconsistent and of moderate certainty. Nutritional interventions may hold value as adjunctive strategies for acne management, but stronger evidence from well-controlled, longitudinal, and mechanistically informed studies is required to clarify causal links and guide clinical recommendations.
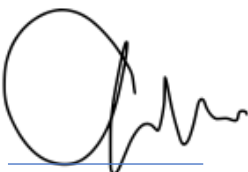
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(Claudia Felicia Limanda)