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EDITORIAL

The role of microbiome and metabolomics in personalized ICU nutrition

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Abstract

Personalized nutrition in the intensive care unit (ICU) has evolved from traditional caloric replacement strategies toward a multidimensional, biology-driven model that incorporates microbiome ecology and metabolomic signatures. Critical illness induces profound alterations in gut microbial diversity, metabolite production, epithelial integrity, and systemic immune responses, all of which interact with nutritional therapies. Parallel advances in metabolomics offer real-time insight into mitochondrial function, substrate utilization, and catabolic stress, providing a framework for phase-specific nutritional targets. This review synthesizes current evidence on ICU nutrition guidelines, recent randomized trials, and emerging multi-omics science to propose an integrated approach to personalized feeding. Emphasis is placed on early enteral nutrition, avoidance of early overfeeding, moderated protein delivery, and the selective use of supplemental parenteral nutrition, contextualized within microbiome-host metabolic interactions. Preliminary studies suggest that microbiome-guided and metabolomics-informed nutrition could reduce infection risk, optimize metabolic tolerance, and support organ recovery, but clinical translation requires rigorous validation.

Keywords: critical illness, enteral feeding, metabolomics, personalized nutrition, short-chain fatty acids

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Introduction

During the past decade, critical care medicine has undergone a conceptual transformation in the way nutritional therapy is understood and delivered. Nutrition in the intensive care unit (ICU) is no longer perceived merely as the provision of calories and protein to prevent malnutrition. Instead, it has become a therapeutic tool deeply intertwined with immunologic function, metabolic resilience, mitochondrial performance, gut epithelial integrity, and the ecology of the intestinal microbiome. These elements shape a dynamic physiological landscape where nutrition is not simply a supportive measure but a modifiable determinant of outcomes. Critical illness induces rapid microbial disruption, leading to major consequences for infection risk, inflammatory balance, and nutrient processing. Evidence from metagenomic and metabolomic studies demonstrates that the gut and systemic metabolism shift dramatically in response to illness severity, therapeutic interventions, and nutritional status.[1-3]

This shift in perspective has been driven by converging scientific advances. On one hand, progress in microbiome research has demonstrated that critical illness induces rapid and profound disruption of the intestinal microbial community, with consequences for immune competence, susceptibility to infection, inflammatory tone, and nutrient processing.[1] Parallel advances in metabolomics allow clinicians to monitor mitochondrial stress, substrate utilization, and inflammatory metabolic signatures in real time.[4] Together, these developments suggest that a model of *personalized ICU nutrition*—guided by biological signatures rather than static formulas—may be achievable.

However, personalized nutrition in the ICU requires more than theoretical frameworks. It demands methodologies capable of capturing the status of the microbiome and metabolic phenotype in actionable ways. In this context, fecal diagnostics—including 16S rRNA sequencing, shotgun metagenomics, fecal metabolomics, short-chain fatty acid quantification (SCFA), and qPCR pathogen surveillance—have emerged as tools providing a detailed snapshot of microbial activity and mucosal health.[1-5] When interpreted alongside metabolomic profiles derived from blood, urine, or stool samples, these technologies open a path toward integrated, multi-omic nutritional decision-making.

This extended review examines the mechanistic basis of microbiome and metabolomic disturbances in critical illness; describes the major technologies available for fecal microbiome and metabolite analysis; evaluates evidence-based ICU nutrition strategies in light of these biological insights; and proposes a framework for integrating multi-omic data into a personalized ICU nutrition strategy. The central question addressed is how the gut microbiome and metabolomic phenotype can meaningfully inform nutritional decision-making at the bedside and whether these approaches can be translated into improved patient outcomes.

Methods

This review follows a narrative methodology aimed at synthesizing current knowledge from gastroenterology, critical care medicine, metabolomics, and microbial ecology as they relate to nutrition in critically ill adults. Literature published between 2014 and 2025 was analyzed.

A focused, non-systematic search was conducted in PubMed and Embase using combinations of the following terms: “critical illness,” “intensive care,” “ICU nutrition,” “enteral nutrition,” “parenteral nutrition,” “gut microbiome,” “dysbiosis,”

"metabolomics," "short-chain fatty acids," and "multi-omics." Reference lists of key articles and guidelines were also screened to identify additional relevant publications.

Inclusion criteria were adult critically ill patients (≥18 years); studies addressing nutritional therapy, gut microbiome, or metabolomics in the ICU context; randomized controlled trials, observational clinical studies, major guidelines, and mechanistic or translational work with clear relevance to ICU nutrition. Pediatric-only studies, non-ICU populations, and purely basic science work without a clear translational link to nutrition in critical illness were generally excluded, except when they provided essential mechanistic insight.

Priority was given to seminal works in the fields of critical care nutrition, intestinal microbiology, metabolomics, and critical illness physiology. Key references include the CALORIES trial comparing enteral and parenteral nutrition[6], early and late parenteral nutrition trials [7], ESPEN and ASPEN guidelines[8-9], microbiome studies in critical illness[1,5,10], and metabolomics studies addressing mitochondrial dysfunction.[4] Additional emphasis was placed on technologies for fecal analysis, including sequencing-based and metabolomic approaches.

Because this is a narrative and not a systematic review, formal risk-of-bias tools were not applied. However, randomized trials and guideline documents were considered higher-level evidence than observational or mechanistic studies, and this hierarchy is reflected in how recommendations are framed (established practice vs emerging or hypothesis-generating strategies).

The ICU microbiome and its nutritional implications

The rapid collapse of microbial diversity

Critical illness triggers abrupt dysbiosis, characterized by the loss of up to 90% of commensal anaerobes within the first hours of physiological insult [1]. Beneficial taxa such as *Ruminococcaceae* and *Lachnospiraceae* rapidly diminish, while opportunistic pathogens—including *Enterococcus*, *Enterobacteriaceae*, *Staphylococcus*, and *Pseudomonas*—expand aggressively.[1,10] This extreme microbial shift resembles ecological collapse observed in decomposition, reflecting the severity of physiologic stress.

The consequences extend beyond microbial composition. SCFA producers vanish, reducing production of butyrate—a critical energy source for colonocytes and a regulator of epithelial barrier integrity. Without these protective metabolites, epithelial tight junctions deteriorate, permeability increases, and microbial translocation becomes likely.[1,11]

The implications for nutrition are profound. Enteral feeding depends in part on an intact gut mucosa and a metabolically active microbial community capable of fermenting dietary components. When this ecosystem is disrupted, the gut becomes less tolerant of feeds, more susceptible to bacterial translocation, and less able to metabolize complex nutrients.

Drivers of dysbiosis during critical illness

A combination of direct and indirect insults accelerates dysbiosis in critically ill patients. A Multiple ICU-specific factors exacerbate dysbiosis (See **Table 1**)

Table 1. Multiple ICU-specific factors exacerbate dysbiosis:

ICU-specific factors	• **Broad-spectrum antibiotics** with anti-anaerobic activity, which correlate with mortality, infection, and microbial collapse [12]. • **Vasopressor therapy**, impairing mucosal perfusion. • **Sedatives and opioids**, slowing motility and promoting stasis [1]. • **Prolonged fasting**, removing fermentable substrates required for SCFA production [11]. • **Stress ulcer prophylaxis**, altering gastric pH and modifying microbial ecology [10].

Hemodynamic instability reduces mesenteric perfusion and impairs oxygen delivery to the mucosa. Sedation and opioids slow gastrointestinal motility, leading to stasis and promoting overgrowth of pathogenic bacteria. Stress ulcer prophylaxis modifies luminal pH and alters microbial composition[10] by creating an environment where acid-sensitive organisms can thrive. Broad-spectrum antibiotics—particularly those with anaerobic coverage—disproportionately eliminate beneficial commensals, allowing resistant organisms to dominate.[12]

Fasting itself is also a major contributor to dysbiosis. The absence of fermentable fiber deprives microbes of substrates needed for SCFA production, depriving colonocytes of their primary energy source and reducing mucous layer integrity. Because enteral nutrition stimulates bile acid flow, mucin secretion, and microbial fermentation, delayed feeding exacerbates the deleterious effects of dysbiosis.

Consequences for nutrient handling and feeding tolerance

The metabolic consequences of dysbiosis create a cycle of impaired nutrient utilization and feeding intolerance (See **Table 2**).

Table 2. Consequences for nutrient handling

Dysbiosis impairs:	• SCFA-mediated epithelial repair • Bile acid conversion • Lipid absorption • Carbohydrate fermentation • Gut motility

The absence of SCFAs weakens epithelial barrier function and disrupts metabolic signaling. Butyrate deficiency promotes goblet cell apoptosis, reduces mucus production, and increases epithelial permeability. Propionate and acetate—normally involved in gluconeogenesis and appetite regulation—become deficient, further altering energy homeostasis.

Loss of butyrate-producing organisms compromises the mucous barrier, increases permeability, and reduces tolerance to enteral feeding. Altered bile acid profiles further impair lipid digestion and mucosal immunity.[13]

Thus, fecal analysis of microbial diversity and SCFA production provides actionable information for predicting enteral nutrition tolerance.

For these reasons, understanding the microbial composition and metabolite environment of the gut may be instrumental in selecting nutritional strategies that restore homeostasis

Fecal diagnostic technologies and their role in ICU nutrition

16S rRNA gene sequencing

One of the most widely used and accessible fecal diagnostic techniques is 16S rRNA sequencing, which amplifies bacterial ribosomal genes to identify microbial taxa at the genus or family level. Although it provides limited functional information, it is useful for detecting major dysbiotic changes such as dominance of Enterococcus, depletion of butyrate-producing bacteria, or overgrowth of Proteobacteria. These patterns can guide clinicians in predicting enteral nutrition tolerance, assessing infection risk, and deciding whether fiber, probiotics, or microbial-targeted therapies may be beneficial.[1]

Shotgun metagenomics

Shotgun metagenomics offers higher resolution by sequencing the entire microbial DNA content rather than a single ribosomal region. This allows species-level identification and provides functional insights into metabolic pathways such as SCFA synthesis, mucin degradation, or bile acid transformation.[5] Shotgun metagenomics can determine whether the microbial community retains the capacity to produce butyrate or whether key functional genes have been lost. Such data influence decisions about whether to supplement fermentable fibers, introduce postbiotics (such as butyrate), or adjust lipid delivery.

Fecal metabolomics

Fecal metabolomics evaluates the biochemical output of the microbial ecosystem (**Table 3**).

Table 3. Fecal metabolomics

Fecal metabolomics quantifies:	• SCFAs (butyrate, acetate, propionate) • Primary and secondary bile acids • Amino acid derivatives • Polyamines such as putrescine and cadaverine (markers of protein fermentation)

SCFA levels, bile acid profiles, amino acid derivatives, polyamines, and microbial toxins provide direct evidence of metabolic capacities and deficiencies. Low fecal butyrate levels may signal a need for prebiotic fiber or cautious reintroduction of enteral feeding that suggests impaired epithelial support and poor tolerance of aggressive enteral feeding.[14] Elevated putrescine and cadaverine may indicate protein fermentation associated with catabolic stress or inadequate carbohydrate availability, suggesting review of protein dosing.

qPCR pathogen panels

Quantitative PCR panels offer rapid detection of pathogen overgrowth. High Enterococcus faecium burden, for instance, correlates with risk of bloodstream infection

and mortality[10], and may reflect inadequate microbial diversity. This information alone may alter nutrition; high carbohydrate loads, for example, can fuel Enterococcus expansion, suggesting the need to moderate glucose provision.

Fecal markers of epithelial integrity

Markers such as fecal calprotectin, zonulin, alpha-1 antitrypsin, and mucin fragments provide indirect information on epithelial damage and permeability. Elevated levels suggest a fragile mucosa that may poorly tolerate aggressive enteral feeding or hyperosmolar formulas.

Translating fecal analysis into nutritional decisions

Although fecal microbiome and metabolomic analyses offer rich biological information, their current use in routine ICU practice is limited by cost, turnaround time, and the need for specialized laboratory infrastructure and bioinformatic expertise. In most centers, rapid qPCR panels for key pathogens and a small set of fecal markers (such as calprotectin) are more feasible than full shotgun metagenomics or comprehensive fecal metabolomics.

For this reason, the decision examples provided in this section should be interpreted as conceptual pathways illustrating how future multi-omic data might inform nutrition, rather than as prescriptive protocols. At present, such strategies are best applied within research settings or as adjuncts to guideline-based care, rather than as stand-alone indications to change feeding practices. Interpretation of fecal data necessitates a structured decision-making approach (See **Table 4**).

Table 4. How fecal results guide nutrition

Examples:	• **Low butyrate** → cautious fiber introduction; consider postbiotics. • **High Enterococcus** → reduce simple carbohydrates; avoid overfeeding. • **Preserved SCFA pathways** (shotgun metagenomics) → safer progression to full enteral nutrition. • **Elevated bile acids** → adjust lipid delivery. • **High polyamines** → review protein load; risk of proteolytic fermentation

When butyrate-producing bacteria are depleted, introducing fermentable fibers may be beneficial, provided the patient's motility allows it. If fecal metabolomics indicates elevated secondary bile acids, reducing lipid infusion or modifying lipid composition may prevent further dysregulation. In cases of pathogen dominance, restricting simple carbohydrates and avoiding early high-caloric loads may reduce pathogenic expansion. Shotgun metagenomic evidence of preserved SCFA biosynthesis can support more ambitious enteral feeding strategies.
Thus, fecal analysis becomes not an academic exercise but a clinically actionable tool capable of informing feed type, macronutrient distribution, and progression of feeding.

Metabolomics in critical illness

Metabolomic signatures of metabolic stress

Metabolomics allows real-time characterization of metabolic pathways that are altered in critical illness. Elevated lactate, pyruvate, and acylcarnitine species signal mitochondrial

dysfunction and impaired oxidative phosphorylation [4]. Such patterns suggest caution in carbohydrate provision, as the patient may rely heavily on glycolysis and be unable to efficiently utilize glucose.

Altered branched-chain amino acids (BCAAs), and increased aromatic amino acids indicate skeletal muscle breakdown, highlighting the need to modulate protein provision based on catabolic status. The tryptophan–kynurenine ratio reflects immune activation[15] and predicts poor outcomes in sepsis, while lipidomic markers signal changes in fatty acid oxidation and phospholipid metabolism.

Metabolomics and substrate selection

These metabolic signatures can inform substrate allocation in nutritional prescriptions. For example, if fatty acid oxidation is impaired, clinicians may temporarily limit lipid administration to avoid lipid accumulation. Conversely, if glucose oxidation is suppressed, modestly increasing lipids and reducing carbohydrates may be preferable.

Protein requirements may be modulated based on amino acid turnover. Excessive early protein can impair autophagy and worsen outcomes, while insufficient protein during recovery phases may exacerbate muscle wasting.

Integration of metabolomics and microbiome data

Metabolomics and microbiome data are inherently complementary. Fecal SCFA levels reflect the metabolic activity of the microbiome, while plasma metabolomics represents whole-body metabolism. When combined, clinicians can differentiate between microbial-driven metabolic deficiencies (e.g., butyrate deficiency) and host-driven metabolic dysfunction (e.g., mitochondrial failure), guiding integrated nutritional interventions.

The integration of microbiome and metabolomic data is therefore attractive but remains largely investigational in critically ill adults. Most available studies are observational, with limited interventional data showing that altering nutrition based on specific metabolomic signatures improves hard clinical outcomes such as mortality, length of stay, or functional recovery.

Consequently, metabolomics-informed substrate selection should, at present, be viewed as a hypothesis-generating framework layered on top of established nutrition principles, rather than a replacement for guideline-based caloric and protein targets.

Evidence-based foundations of ICU nutrition

This section summarizes aspects of ICU nutrition that are currently supported by guidelines and large randomized trials and therefore can be considered standard of care, independent of microbiome or metabolomic testing.

Although biological signatures guide personalization, standard nutritional principles remain essential. Early enteral nutrition, if tolerated, supports microbial activity, prevents villus atrophy, and modulates inflammation. Clinical trials—including the CALORIES trial—demonstrate that the enteral route is not inferior to parenteral nutrition, provided caloric delivery is comparable.[6] Similarly, EPaNIC showed harm related to early supplemental PN, largely driven by overfeeding and impaired autophagy.[7]

Energy provision should be conservative during the acute phase, ESPEN recommends 70% of measured caloric requirements during early critical illness to prevent

overfeeding.[8] Indirect calorimetry is the gold standard for determining caloric requirements and prevents overfeeding. Predictive equations are unreliable during early critical illness.

Protein dosing remains controversial. High-dose early protein (>1.5 g/kg/day) may impair autophagy and worsen outcomes; moderate protein 1.0–1.3 g/kg/day is preferred until resolution of inflammation.[9] Higher doses may be introduced during recovery phases supporting anabolic rebuilding. ASPEN recommends delaying SPN until after day 7 in well-nourished patients.[9] Early SPN offers no mortality benefit and may worsen metabolic stress.

Taken together, early enteral nutrition (when hemodynamically feasible), avoidance of early overfeeding, moderate early protein delivery, and delayed initiation of supplemental parenteral nutrition in well-nourished patients represent core, guideline-supported pillars of ICU nutrition. Multi-omic data may refine these strategies in the future, but they should not currently displace these evidence-based foundations.

Integrating multi-omic data into personalized nutrition

The following framework is intentionally conceptual and reflects an emerging, biologically informed approach to ICU nutrition. It is built on associations between microbiome patterns, metabolomic signatures, and clinical outcomes, and extrapolates from existing physiological and mechanistic knowledge.

Personalizing ICU nutrition requires an integrated model that synthesizes microbiome analysis, fecal metabolomics, systemic metabolomics, clinical status, and organ function.

Fecal analysis guiding enteral feeding tolerance

When fecal SCFA levels are low, the gut may be poorly equipped to metabolize fiber-rich formulas. Introducing small volumes of fermentable fiber may stimulate microbial recovery, but large boluses may cause intolerance. If Enterococcus or Proteobacteria dominate, carbohydrate-rich feeds may promote pathogenic growth. Thus, fiber type, carbohydrate load, and formula osmolarity must be adapted based on microbial patterns.

Metabolomics guiding macronutrient allocation

If metabolomic evidence indicates mitochondrial dysfunction, clinicians should avoid aggressive carbohydrate infusion that may worsen lactate accumulation. Lactate elevation or mitochondrial stress markers merit reduction of carbohydrate load. Impaired β-oxidation suggests limiting lipid intake and adjusting lipid emulsions.

Multi-phase algorithmic feeding

Critical illness evolves through phases (**Table 5**).

Table 5. Phase-based algorithm

Phase-based algorithm	• **Early acute phase**: trophic EN; hypocaloric feeding; moderate protein; avoid early PN; avoid excessive carbs. • **Late acute phase**: gradual advance when SCFAs increase; adjust based on metabolomics. • **Recovery phase**: higher protein; increased energy; support anabolic rehabilitation.

During the early acute phase, permissive underfeeding, moderate protein dosing, reduced carbohydrate load, and microbiome-supportive strategies (such as cautious fiber introduction) may be optimal. As inflammation resolves, caloric intake is progressively increased to reach full requirement, guided by indirect calorimetry and metabolomics. In the recovery phase, anabolic support through increased protein provision becomes essential.

Importantly, these multi-phase, multi-omic algorithms have not yet been validated in randomized clinical trials. Their role at present is to guide hypothesis generation and protocol design for future studies, while day-to-day bedside practice should remain anchored in established guideline recommendations and individualized clinical judgment.

Clinical scenarios

The clinical scenarios presented illustrate how microbiome and metabolomic data might eventually refine nutrition strategies in specific ICU phenotypes such as sepsis, ARDS, and AKI. However, most of the microbiota-targeted interventions described (for example, specific prebiotics, postbiotics, strain-selected probiotics, and detailed substrate shifts based on omics) should currently be implemented, if at all, within clinical trials or structured quality-improvement programs with predefined safety and outcome monitoring.

Sepsis and septic shock

Sepsis produces profound dysbiosis, with diminished SCFA production and increased pathogenic expansion. Fecal metabolomics often shows low butyrate and altered bile acid profiles. Nutritional strategies should emphasize early trophic feeding, controlled carbohydrate delivery, and restoration of microbial fermentation capacity through fermentable fiber. Excess protein should be avoided during early shock, as metabolomic data reveal impaired amino acid oxidation.[14]

Acute respiratory distress syndrome (ARDS)

ARDS is characterized by systemic inflammation, increased catabolism, and impaired mitochondrial function. Metabolomics often shows elevated lactate and acylcarnitines, suggesting reduced tolerance to high carbohydrate loads. Moderate lipid-based calories may be beneficial, but total energy should remain conservative early on.[4]

Acute kidney injury (AKI)

Acute kidney injury alters nitrogen handling and amino acid clearance. Fecal metabolomics may reveal increased uremic toxins and changes in microbial fermentation patterns. Protein dosing should be carefully titrated, balancing the need to prevent catabolism with avoidance of nitrogen overload. Fiber that supports microbial nitrogen salvage may be beneficial.[15]

Challenges and future directions

Despite the promise of microbiome- and metabolomics-guided nutrition, substantial methodological, logistical, and economic challenges currently limit their widespread adoption. Fecal diagnostics and metabolomics platforms are not standardized across institutions, require specialized laboratory and bioinformatic capabilities, and often have turnaround times that are not yet compatible with real-time ICU decision-making in many settings. Moreover, while associations between microbiome patterns and outcomes are increasingly recognized, interventional evidence remains limited.

The cost and logistical complexity of sequencing and metabolomics limit widespread adoption, particularly in resource-limited settings. Moreover, while associations between microbiome patterns and outcomes are increasingly recognized, interventional evidence remains limited.

Future research priorities include pragmatic randomized trials comparing standard guideline-based nutrition with multi-omic–guided algorithms. These studies should evaluate not only biological endpoints (microbiome diversity, SCFA levels, metabolomic profiles) but also patient-centered outcomes such as infections, organ failure scores, ICU and hospital length of stay, mortality, and functional recovery. Decision-support tools, including artificial intelligence models, will need prospective validation to ensure that they provide clinically meaningful and safe recommendations that augment, rather than replace, clinician judgment.

Conclusion

Personalized ICU nutrition has entered a new era influenced by advances in microbiome science and metabolomics. Critical illness induces rapid dysbiosis and metabolic alterations that reshape nutrient handling and feeding tolerance. Fecal diagnostics and metabolomic profiling offer powerful tools to tailor nutrition to biological needs, supporting epithelial integrity, modulating immune responses, and optimizing substrate utilization.

The challenge now is to integrate these biological insights into routine clinical practice in a way that is methodologically rigorous and operationally feasible, particularly outside highly specialized centers. As multi-omic analysis becomes more accessible and is tested in well-designed clinical trials, nutrition therapy may evolve from a largely standardized intervention toward a more dynamic, biology-responsive strategy, while remaining grounded in established guideline-based principles of ICU nutrition.

Conflict of interest

The authors declared no conflict of interest regarding this article.

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CASE REPORT

The impact of nutritional therapy in malnourished patient with tongue squamous cell carcinoma undergoing chemoradiation: A case report

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Abstract

Background: Malnutrition affects 30%-50% of patients with head and neck carcinoma. It is associated with reduced survival, increased risk of complications, treatment interruption, and higher treatment-related toxicity.
Objective: This case aim to discuss about nutritional therapy in tongue carcinoma patient with malnourished and cachexia undergoing chemoradiotherapy.
Case: A 52-year-old man with squamous cell carcinoma of the tongue presented with clinically severe malnutrition and cachexia. Imaging revealed a solid mass involving the entire tongue and extending to the floor of the mouth, resulting in dysphagia. He undergo locoregional Intensity-Modulated Radiation Therapy (IMRT) 70/56 Gy in 35 fractions in concomitant with chemotherapy. Nutritional management involves enteral feeding with a gradual increase in energy intake from 40 kcal/kg body weight (BW) to 63 kcal/kg BW and protein from 2 to 3 g/kg BW. The patient received daily micronutrient supplementation consisting of 1 tablet of vitamin B complex three times daily, vitamin C 50 mg twice daily, zinc 20 mg twice daily, folic acid 500 mcg once daily. He also given 1 gram eicosapentaenoic acid (EPA). After one month, the patient demonstrated a weight gain of 1.8 kg (4.3%), increased handgrip strength, and functional capacity. Body composition analysis demonstrated increase in fat-free mass index (FFMI) from 15.2 to 15.8 kg/m^2, skeletal muscle index (SMI) from 5.6% to 5.9%, and fat mass from 5.3% to 5.6%.
Conclusion: Adequate energy and high protein intake along with micronutrients and EPA supplementation may help prevent deterioration of nutritional status, increase body weight, preserve muscle mass, and improve functional capacity in cancer patient undergoing chemoradiotherapy.

Keywords: tongue carcinoma, malnutrition, nutritional therapy, cachexia, chemoradiotherapy

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Introduction

Patients with head and neck cancer (HNC) undergoing chemoradiation are at risk for developing malnutrition due to reduced oral intake, treatment-related side effect, and tumor-induce hypermetabolism. Malnutrition adversely affects morbidity, quality of life, healing rate, treatment tolerance, and survival, highlighting the importance of early nutritional risk screening and comprehensive nutritional management.[1,2] Nutritional therapy constitutes an integral component of supportive care.[3]

Although malnutrition is highly prevalent in this population, reports detailing individualized nutritional strategies for patient with severe malnutrition complicated by cachexia undergoing chemoradiotherapy are scarce. This gap is clinically significant, as concurrent chemoradiotherapy can further compromise oral intake, amplifies systemic inflammation, and accelerate muscle loss. In this case, enteral nutritional therapy with a progressive increase in calorie and high protein target, combined with micronutrients and EPA supplementation was prescribed to prevent further weight loss, preserve muscle mass, and support functional capacity.

This case report aims to describe the implementation and clinical outcomes of an individualized nutritional therapy approach in a severely malnourished patient and cachexia with tongue carcinoma undergoing chemoradiotherapy, and to contribute practical insight into optimizing nutrition management in similar case.

Case Report

A 52-year-old man was diagnosed with squamous cell carcinoma of the tongue. The patient presented with dysphagia, jaw pain and trismus. Nutritional intake was provided by enteral nutrition through nasogastric tube (NGT), consisting of blenderized food and milk. The patient is neither nauseous nor vomiting. He passes stool once daily. Stool color is yellow with solid consistency. The patient experienced unintentional weight loss of 10.2 kg (19.6%) over the preceding six months. His body mass index (BMI) was 16.1 kg/m^2. However, the patient's nutritional status is classified as severely malnourished based on the Global Leadership Initiative on Malnutrition (GLIM) criteria for malnutrition dan cancer cachexia.

Computed tomography (CT) scan revealed a solid mass involving the entire tongue, predominantly on the right side. The lesion extended to the base of the tongue and infiltrated both intrinsic and extrinsic muscles, involving the masticator space (partially the medial pterygoid and masseter muscles) up to the right carotid space, involving the right palatine tonsil, right submandibular salivary gland, extending to the subcutaneous tissue of the right submandibular region with ulceration and intralesion air component. The mass reaches the base of the mouth and expands, narrowing the oropharyngeal cavity, especially on the right side. The mass measured approximately 7.4 x 7.2 x 9.5 cm with an estimated depth of invasion of 5 cm. No evidence of bone destruction or encasement of the internal carotid artery was identified. Multiple enlarged lymph nodes appear rounded in the neck region at levels Ia and Ib bilaterally and containing calcification components. The patient undergoing locoregional intensity-modulated radiotherapy with a total planned dose of 70/56 Gy in 35 fractions over five days per week, concomitant with cisplatin chemotherapy. At the first examination at clinical nutrition outpatient clinic, the patient had completed the third of 35 radiation fractions. Laboratory evaluation revealed anemia and leukocytosis while electrolyte levels, kidney function marker, and liver

function marker were within normal limits. The second visit occurred two weeks later, following hospitalization due to tounge bleeding. At that time, he had completed the 12th of 35 radiation fractions and third cycle of chemotherapy. The third visit took place one week later, at which point he had completed the 18th of 35 radiation fractions. At the fourth visit, one week after the third , he completed the 23th of 35 radiation fractions.

Enteral nutrition was intensified to meet requirement needs. Total caloric intake was increased from 40 to 63 kcal/kg body weight and protein intake was escalated from 2 to 3 g/kg. The protein formulation provided 16.8 - 28.1 g of branched-chain amino acids daily. The patient received daily micronutrients supplementation consisting of 1 tablet of vitamin B complex three times daily, vitamin C 50 mg twice daily, zinc 20 mg twice daily, folic acid 500 mcg. Additionally, the patient also prescribed 1 g of EPA supplementation daily.

Table 1. Nutritional prescription

Visit	Prescription	Description
I	Energy 1700 kcal (40 kcal/kgBW), protein 84 g (2 g/kgBW, 20%, N;NPC = 1:101), fat 50 g (27%), carbohydrates 183 g (53%)	The blenderized meal consisted of 2 servings of rice, 6 servings of low-fat animal protein, 4 servings of plant-based protein, 1 serving of vegetables, 3 servings of fruit, 4.5 servings of oil, 3 egg whites, and high-protein oral nutritional supplement (ONS) administered at 4 scoops once daily.
II	Energy 1900 kcal (44 kcal/kg body weight), protein 100 g (2.3 g/kg body weight, 21%, N:NPC = 1:91), fat 53 g (26%), carbohydrates 240 g (53%)	The blenderized meal consisted of 1.5 servings of rice, 4 servings of low-fat animal protein, 1 serving of plant-based protein, 1 serving of vegetables, 3 servings of oil, 2 servings of fruit, and high-protein ONS administered at 5 scoops three times daily.
III	Energy 2300 kcal (53 kcal/kg body weight), protein 114 g (2.7 g/kg body weight, 20%, N:NPC = 1:100), fat 79 g (31%), carbohydrates 267 g (49%)	The blenderized meal consisted of 2 servings of rice, 3 servings of low-fat animal protein, 2 servings of moderate-fat animal protein, 2 servings of plant-based protein, 1 serving of vegetables, 6 servings of oil, 2 servings of fruit, and high-protein ONS administered at 5 scoops three times daily.
IV	Energy 2700 kcal (63 kcal/kg body weight), protein 124 g (2.8 g/kg body weight, 18%, N:NPC = 1:112), fat 94 g (31%), carbohydrates 331 g (51%)	The blenderized meal consisted of 3 servings of potatoes, 4 servings of low-fat animal protein, 1 serving of medium-fat animal protein, 3 servings of plant-based protein, 2 servings of vegetables, 9 servings of olive oil, 3 servings of fruit, and high protein ONS administered at 5 scoops three times daily.

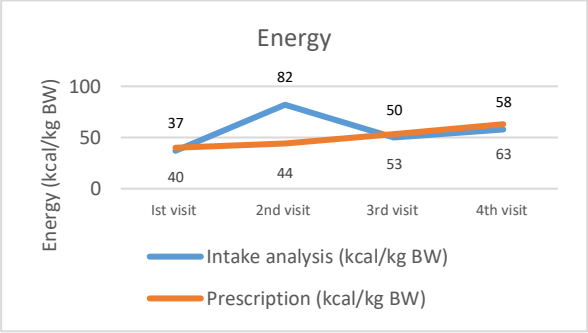

Figure 1. Energy intake

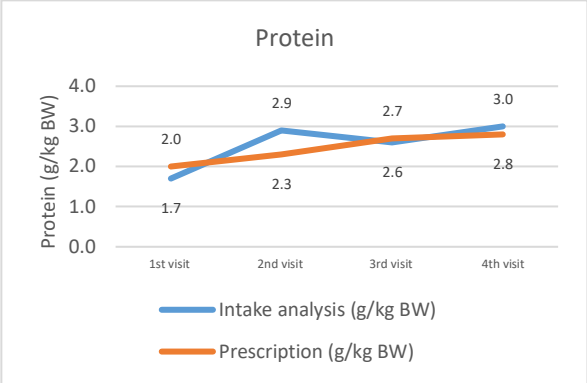

Figure 2. Protein intake

After one month of optimized nutritional management, the patient demonstrated clinical improvement, including a weight gain of 1.8 kg (4.3%), increased handgrip strength, and enhanced functional capacity. The Karnofsky Performance Scale score improved by 20 points, from 70 to 90. Body composition analysis using the Omron body composition monitor HBF-375® bioelectrical impedance analysis device showed an increase in FFMI (15.2 to 15.8 kg/m^2), SMI (5.6% to 5.87%), and fat mass (5.3% to 5.6%).

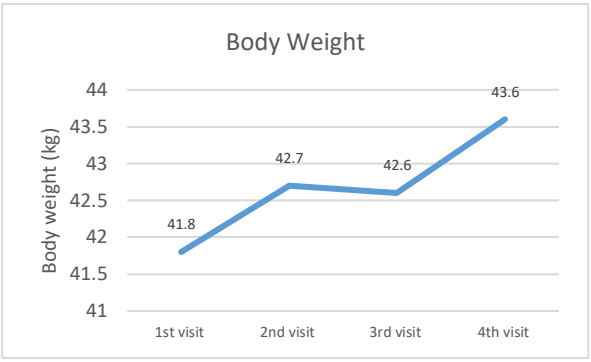

Figure 3. Body weight monitoring

Table 2. Body composition

Parameter	Baseline after 3rd radiation therapy (1st visit)		After 23rd radiation therapy, 3rd chemotherapy (4th visit)	
	Result	**Interpretation**	**Result**	**Interpretation**
Fat mass	5.3%	Low	5.6%	Low
Visceral fat	0.5%	Normal	1	Normal
Subcutaneous fat	N/A	N/A	N/A	N/A
Sceletal muscle mass	34.8%	Normal	34.9%	Normal
Free fat mass index (FFMI)	15.2	Low	15.8	Low
Skeletal mass index (SMI)	5.6	Low	5.87	Low

Table 3. Functional capacity

Visit	Karnofsky performance scale score	Handgrip strength	
		Right hand	Left hand
1st visit	70	20.6 (low)	20 (low)
2nd visit	70	18.8 (low)	18 (low)
3rd visit	90	21.4 (low)	19.3 (low)
4th visit	90	22.2 (low)	20.6 (low)

Discussion

This case highlights the importance of nutritional management in preventing deterioration of nutritional status in patient with tounge carcinoma patient undergoing chemoradiotherapy. One study reported that the risk of malnutrition in HNC patients increase from 11.9% before therapy to 49.4% following radiotherapy or chemoradiotherapy.[4] Several factors contribute to significant weight loss in this population, including tumor location, inflammation, metabolic alteration, and treatment-related adverse effects. Tumors in head and neck region can impair oral intake due to difficulty chewing, dysphagia, and pain. In addition, inflammatory responses and metabolic changes can further increase energy expenditure and promote catabolism, leading to energy deficit. Side effect of radiotherapy and chemotherapy such as mucositis, pain, nausea, vomiting, and fatigue further limit oral intake that exacerbate weight loss.[5] In this case, the patient experienced dysphagia due to squamous cell carcinoma of the tongue which infiltrated the entire glossus extended to the floor of the mouth, and narrowed the oropharyngeal cavity. The tumor location made adequate oral intake unattainable, while metabolic stress elevated energy requirement. Evaluation using the GLIM criteria indicated clinically severe malnutrition.

Since the tumor mass was unresectable, the patient undergo radiation therapy which uses ionizing radiation to induce DNA strand breaks. DNA damage lead to cell death or loss of proliferative capacity. The therapeutic target of radiation therapy is to reduce the number of cancer cells while preserving as many healthy cells as possible. However, normal tissues may also be damage depending on the dose and area of exposure.[6] Platinum-based chemotherapeutic agent, such as cisplatin, exert their effects by binding to purine bases and inducing DNA strand damage in cancer cells. This process inhibits cell division, ultimately leading to cell apoptosis. The adverse effects of chemotherapy include nausea, vomiting, loss of taste, anorexia, bone-marrow suppression, organ toxicity, and loss of muscle mass. Cisplatin may contribute to muscle mass reduction by promoting proteolysis, decreasing muscle protein synthesis, and inducing systemic inflammation.[7]

Alteration in protein metabolism, characterized by a net protein breakdown and increased oxidation of branched-chain amino acids (BCAAs), play a significant role in the development of cancer cachexia. The breakdown of host protein is partially driven by tumor-secreted factors and inflammatory cytokines produced by the host. Nutritional management in patients with cancer cachexia is intended to mitigate the negative energy balance and reduce net protein breakdown without stimulating tumor growth or adversely interfering with anticancer therapy. To promote anabolic processes, adequate caloric intake and appropriate nutrient composition are essential.[8]

Nutritional therapy is required to ensure adequate nutrient intake and optimize clinical outcomes in patients undergoing chemoradiotherapy, including improve treatment

tolerance, reduce treatment interruptions, decreased treatment-related toxicities, improved nutritional status, functional capacity, quality of life and overall survival.[9] The patient's basal energy expenditure (BEE) was estimated using the Harris-Benedict predictive equation, yielding a value of 1,100 kcal. Energy intake was targeted at twice the basal energy requirement to promote weight gain. Energy provision was gradually increased according to the patient's clinical condition. The European Society for Clinical Nutrition and Metabolism (ESPEN) recommends an energy target 25-30 kcal/kg/day and protein at >1 g/kg. When feasible, protein provision up to 1.5 g/kg/day is suggested for cancer patient.[10] In cases of cancer cachexia, protein intake of 1.2-2 g/kg body weight may be administered to overcome anabolic resistance.[11] Another guideline, the United Kingdom National Multidisciplinary Guideline, recommends aiming for energy and protein intakes of at least 30 kcal/kg/day and 1.2 g protein/kg/day in head and neck cancer patients receiving radiotherapy or chemoradiotherapy.[3]

A prospective observational study by Valle et al.,[12] evaluated the effect of higher energy consumption than recommended by ESPEN. A mean daily energy intake of 35±10 kcal/kg maintain stable body weight during and after chemoradiotherapy in patients with head and neck cancer.[12] Another case report indicated that prescribing a daily energy intake of 38-54 kcal/kgBW, protein 2.2-2.5 g/kg for breast cancer patient with severe malnutrition and cachexia also yielded positive outcome. In that case, energy target was calculated using the Harris–Benedict equation with the stress factor of 2.0, considering that the patient's severely malnourished status. After three weeks of monitoring, the patient demostrated improvements in body weight, muscle mass, and handgrip strength.[13] In the present case, energy provision was initiated at 40 kcal/kg BW, as the patient's dietary intake had already reached 37 kcal/kgBW but malnutrition persisted. Follow-up assessments during subsequent visits revealed no clinical symptoms of refeeding syndrome. The prescribed energy was gradually increased to promote weight gain and improve nutritional status. Protein was prescribed at 2-2.8 g/kg BW per day, but intake analysis showed patient consumption reached 3 g/kg BW per day. Follow-up laboratory evaluations demonstrated patient's serum urea and creatinine levels remained within normal limit, indicating preserved renal function and good tolerance to the high-protein regimen.

One study showed higher protein intake, adequate energy intake and body weight stability were associated with an increased likelihood of maintaining skeletal muscle mass in cancer patient undergoig chemoradiotherapy or immunotherapy. In univariate analysis, protein intake demonstrated the strongest association with muscle mass preservation, followed by energy intake and percentage change in body weight.[12]

In the present case, the patient was prescribed high-protein diet. High protein diet promotes muscle anabolism in cancer patients by stimulating muscle protein synthesis and providing essential amino acids to support lean tissue accretion and overall energy intake. Protein intake should be derived from both animal and plant sources. Protein from animal sources has a higher biological value, but protein from plant sources is also important because it is not only a source of protein, but also includes essential amino acids and has other nutrients at the same time.[15,16] Branched-chain amino acids particularly leucine play a role in muscle protein synthesis. Foods rich in BCAAs consumed by patients included chicken eggs, chicken breast, and dairy products. The amount of leucine protein consumed by the patient was 4.8 g/day from ONS. Branched-chain amino acids may activate the mammalian target of rapamycin (mTOR) pathway and modulate inflammation, thereby decrease proteolysis and promoting protein synthesis

in skeletal muscle.[8] Low muscle mass is associated with decreased physical functional capacity, diminished quality of life, increased risk of treatment-related toxicity, and shorter survival.[17]

In the present case, the patient was prescribed EPA 1,240 mg/day, obtained from ONS and omega-3 fish oil capsules supplementation. The proposed anticancer effects of omega-3 polyunsaturated fatty acids (PUFAs) are attributed to changes in the fatty acid composition of cell membranes phospholipids of tumor cells, leading to alteration in membrane structure, fluidity and associated signaling pathways. Additionally, studies have demonstrated the immunomodulatory effects of omega-3 PUFAs. Limited evidence demonstrated reduction in polymorphonuclear concentration, C-reactive protein (CRP) and interleukin-6.[18] In this present case, follow-up laboratory examinations showed a reduction in leucocyte toward the normal reference range.

However, studies on EPA supplementation have reported inconsistent findings. A randomized controlled trial study in patients with head and neck squamous cell carcinoma found no benefit of EPA supplementation on body weight or muscle mass.[19] Conversely, a meta-analysis demonstrated that omega-3 supplementation significantly increased body weight in cancer patients with cachexia, particularly in spesific subgroup of patient with a baseline weight ≤60 kg and age ≥67 years.[20] Another systematic review reported high-protein, n-3 PUFA–enriched ONS supplementation in adult cancer patient receiving chemo(radio)therapy has been shown to significantly increase body weight compared with isocaloric controls (+1.89 kg; 95% CI 0.51–3.27; P = 0.02). In addition, these interventions were associated with attenuation of lean body mass loss and improvements in selected quality-of-life domains. These findings suggest that combining high protein intake with n-3 PUFA supplementation may help support muscle anabolism and mitigate the adverse effects of cancer-related malnutrition. While the underlying mechanisms are not directly assessed in these trials, the observed benefits are consistent with the proposed roles of protein in stimulating muscle protein synthesis and of n-3 PUFAs in modulating systemic inflammation.[21]

In line with this finding, the ESPEN guideline recommends the use of fish oil and omega-3 fatty acids in cancer patients undergoing chemotherapy who are at risk of weight loss or malnutrition, with a weak strength of recommendation, to improve appetite, lean body mass, and body weight.[10] Although omega-3 PUFAs demonstrate promising adjunctive potential in cancer therapy, further studies are warranted.

In the present case, patient was prescribed micronutrients including 1 tablet of vitamin B complex supplementation three times daily, folic acid 500 mcg daily, vitamin C 50 mg twice daily, and zinc 20 mg twice daily. The prescribed doses were in accordance with the Indonesian Recommended Dietary Allowances (RDA).[22] According to ESPEN recommendations, micronutrient supplementation should follow RDA and high-dose micronutrient supplementation is not advised in the absence of deficiency.[10]

B vitamins are essential for maintaining cellular functions and metabolic processes. The B complex supplement received by the patient consisted of vitamin B1 (2 mg), vitamin B2 (2 mg), nicotinamide (vitamin B3, 20 mg), calcium pantothenate (vitamin B5, 10 mg) and vitamin B6 (2 mg). Vitamin B1 is particularly significant for aerobic metabolism. Its active form, thiamine pyrophosphate (TPP), acts as a primary cofactor for pyruvate dehydrogenase that involve in gluconeogenesis. Thiamin also inhibite pyruvate dehydrogenase kinase (PDK). This inhibition maintains pyruvate dehydrogenase (PDH) activity and has been shown to decrease tumor cell proliferation

and glycolytic activity. Thiamine also directly contributes to ribose synthesis that require for DNA/RNA synthesis.[23]

Vitamin B2 or riboflavin plays a critical role in in antioxidant system as cofactor enzyme glutathione reductase. Study show riboflavin may mitigate cisplatin's toxic effects by reducing the inflammatory response and replenishing antioxidant enzymes and cellular reductants. Vitamin B3 is essential for generating coenzymes such as nicotinamide adenine dinucleotides (NAD) and NADPH which involved in several metabolic processes such as glycolysis, the Krebs Cycle, oxidative phosphorylation, and the hexose monophosphate shunt. NAD+ serves as a substrate for key enzymes like sirtuin 1 (SIRT1) and poly ADP-ribose polymerase 1 (PARP1). Poly ADP-ribose polilymerase 1 plays a role in DNA repair and apoptosis, while SIRT1 is associated with the regulation of gene expression, proliferation, differentiation, carcinogenesis and immune response.[23,24]

Pantothenate is a precursor to coenzyme A (CoA). CoA is then utilized as a fundamental coenzyme in numerous metabolic processes. Vitamin B6 plays a role in many biochemical reactions within the body, immune response, also modulates apoptosis by regulating oxidative stress, redox balance, and epigenetic alterations. Thus, pyridoxine deficiency could promote DNA damage and tumorigenesis.[23]

Folic acid (vitamin B9) play role in one-carbon metabolism which essential to DNA, RNA and protein methylation. Folate also have a role in converting deoxyuridine monophosphate (dUMP) to deoxythymidine monophosphate (dTMP), which is essential for DNA synthesis and repair. Folate deficiency can cause DNA strand breaks and an aberrant gene expression.[23]

Vitamin C has been suggested to confer radioprotective properties through the scavenging of reactive oxygen species (ROS) generated by ionizing radiation, thereby mitigating oxidatif DNA damage in normal tissue. Conversely, at high doses, vitamin C may potentiate radiation-induced cytotoxicity in tumor cells via pro-oxidant mechanism.[25]

Zinc involves in various cellular processes including act as enzyme cofactor, involve in cell proliferation and apoptosis, antioxidant activity. Zinc supplementation may decrease oxidative stress biomarkers and inflammatory cytokines. Regarding effect zinc to radiotherapy toxicities, some report documented zinc decreases mucosities but a systematic review also showed that supplementation of zinc did not significantly decrease adverse effect i.e weight loss, changes in taste, nausea, nor alleviate radiotoxicity.[26]

Limitation

This case has several limitations. This is a single-case study with a short follow-up period, lacks biochemical markers, and absence of control.

Conclusion

Adequate energy and high protein intake along with micronutrients and EPA supplementation may help prevent deterioration of nutritional status, increase body weight, preserve skeletal muscle mass, and improve functional capacity in cancer patient undergoing chemoradiotherapy.

Conflict of interest

The authors declared no conflict of interest regarding this article.

Ethic Statement

Written informed consent was obtained from the participant prior to data collection.

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Author Contributions

DR: Conceptualization, data acquisition, drafting the manuscript; DS and NRMM: Supervision, critical revision of the manuscript, interpretation of data, and final approval of the version to be published.

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ORIGINAL PAPER

Relationships between comorbidities and vitamin D intake with COVID-19 severity

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Abstract

Background: Vitamin D is a nutrient/hormone-like vitamin involved in immune regulation, which, in turn, affects morbidity and mortality rates, including in coronavirus disease 2019 (COVID-19). Vitamin D strengthens both specific and nonspecific immunity and modulates the body's response to infection.

Objective: This study aims to determine the association between comorbidities and vitamin D intake with the severity of COVID-19.

Methods: The study is a cross-sectional observational study with a sample comprised of 66 people, ages 19 to 58, receiving treatment for COVID-19 at Pasar Rebo District Hospital. The primary data were collected via a questionnaire administered via the WhatsApp application or through direct interviews, encompassing variables such as age, gender, comorbidity, and vitamin D intake. The Vitamin D Dietary Intake Questionnaire was conducted using the Food Frequency Questionnaire (FFQ). Vitamin D intake is categorized into two groups: low (<600 IU/day) and adequate (≥600-4,000 IU/day). Comorbidities are other illnesses that a person has, such as asthma, high blood pressure, diabetes, or heart disease. The severity of COVID-19 is an accordance with the criteria set by the Indonesian Society of Internal Medicine. Statistical analysis used SPSS version 22 to analyze univariate data and Fisher's exact test for bivariate analysis with a significance limit of $p < 0.05$.

Results: A total of 25.8% of the subjects had comorbidities, 62.1% experienced low vitamin D intake, and 53% experienced mild COVID-19 symptoms. The severity of COVID-19 cases does not correlate with age or gender. The severity of COVID-19 cases was significantly associated with comorbidities (p=0.001) and vitamin D intake (p=0.021).

Conclusion: An association was observed between vitamin D intake, comorbidities, and the severity of COVID-19.

Keywords: vitamin D, COVID-19, comorbidities

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Introduction

The World Health Organization has declared an international emergency due to the devastation caused by the COVID-19 epidemic.[1] An RNA virus, known as a coronavirus, carries small particles and can spread through droplets. The infection mainly occurs in animals, but currently, transmission is primarily human-to-human, and the spread is very aggressive.[2] Many factors, including the host, virus, and environment, can influence COVID-19 severity. Age can influence the severity of different cases.[3] Diet is another independent risk factor for developing serious infections. It is critical to consume healthy, fresh, and nutritious foods while avoiding diets high in saturated fats, sugar, and refined carbohydrates. Vitamin D deficiency may influence comorbidities and susceptibility to infectious disease.[3]

The immune system of the body greatly influences an individual's susceptibility, morbidity, and mortality from COVID-19, as with other viral diseases. One factor that can influence the body's immune response is vitamin D.[4] Vitamin D can reduce the risk of viral infection through a number of approaches, including strengthening both specific and nonspecific immunity and modulating the body's response to an infection. Vitamin D also plays a role in adaptive and innate immune responses, which are essential for inhibiting cytokine storms and reducing pro-inflammation responses.[4,5] Vitamin D deficiency has been hypothesized contributes to the occurrence of acute respiratory distress syndrome (ARDS) (SARS-CoV-2).[5] As previously explained, the objective of this study was to determine whether vitamin D intake and comorbidities were associated with COVID-19 severity.

Methods

This is an analytical observational study with a cross-sectional design. The research was conducted at Pasar Rebo District Hospital from November to December 2021. The research sample came from the medical records of 66 subjects inpatients aged 19-58 years diagnosed with COVID-19 who met the inclusion criteria. The inclusion criteria are as follows: patients diagnosed with COVID-19 by PCR test. The exclusion criteria are patients who are still under treatment in the hospital and patients who died during treatment. Primary data were collected through a questionnaire completed via the WhatsApp application, which included age, gender, and vitamin D intake, while comorbidities and COVID-19 severity were taken from medical records. Direct interviews are conducted when WhatsApp responses are unclear. Comorbidities are accompanying illnesses (asthma, hypertension, diabetes, heart disease) that describe the patient's condition apart from the primary illness, namely COVID-19, recorded in the medical record; "yes" indicates one or more comorbidities. The vitamin D dietary intake questionnaire was conducted using the Food Frequency Questionnaire (FFQ) past month. The vitamin D intake is categorized into two groups based on the Minister of Health Regulation Number 28 of 2019 concerning Nutritional Adequacy Rates; low (<600 IU/day) and adequate (≥600 - 4,000 IU/day). The severity of COVID-19 is an accordance with the criteria set by the Indonesian Society of Internal Medicine.[6] The severity of COVID-19 is determined by the patient's worst condition during hospital treatment.

To process and analyze the data, the Statistical Package for the Social Sciences (SPSS) 22.0 was used. Categorical variables were expressed as frequencies and percentages. Intergroup comparison was conducted using Fisher's exact test because the expected

count of less than 5 is more than 20%. To determine statistical significance, a p-value of less than 0.05 was used. Multivariate analysis was not considered due to insufficient data.

Results

The Research Ethics Commission of Universitas Trisakti, with number 104/KER-FK/IX/2021, declared this research to have passed the ethical test. After processing and counting the respondents, we analyzed 66 subjects, yielding a response rate of 100%. No data was missing or excluded from the analysis.

Table 1. Subject characteristics (N = 66)

Variables	Frequencies	
	N	(%)
Age		
19 – 48 years old	49	74.2
49 – 58 years old	17	25.8
Sex		
Men	36	54.5
Women	30	45.5
Comorbidities		
Yes	17	25.8
No	49	74.2
Vitamin D intakes		
Low	41	62.1
Adequate	25	37.9
Severity of COVID-19 cases		
Asymtomatic	10	15.2
Mild	35	53
Moderate	3	4.5
Severe	12	18.2
Critical	6	9.1

Table 1 displays the characteristics of the largest age group, the 19-48-year-olds, who account for 74.2% of the subjects. Most subjects were male (54.5%), and 74.2% of research subjects did not have comorbidities. The group with the highest vitamin D intake was the one with an insufficient intake, accounting for 62.1%. The most severe category of COVID-19 cases is the mild group, at 53%.

In **Table 2**, according to statistical tests, there was no significant association between age (p=0.064) and gender (p=0.791) and the severity of COVID-19 cases. Subjects with comorbidities had higher COVID-19 severity, this trend was evident in the statistical analysis, which showed a significant association (p=0.001). The group with the lowest vitamin D intake experienced the mildest symptoms of COVID-19, where the analysis showed a significant association between vitamin D intake and COVID-19 severity (p=0.021).

Table 2. Characteristics of subjects and vitamin D intake with severe COVID-19 cases

Variables	Severity of COVID-19										p-value
	Asymptomatic	%	Mild	%	Moderate	%	Severe	%	Critical	%	
Age											
19 – 48 y.o	9	18.4	26	53.1	0	0	9	18.4	5	10.2	0.064
49 – 58 y.o	1	5.9	9	52.9	3	17.6	3	17.6	1	5.9	
Sex											
Men	7	19.4	19	52.8	2	5.6	5	13.9	3	8.3	0.791
Women	3	10	16	53.3	1	3.3	7	23.3	3	10	
Comorbidities											
Yes	0	0	3	17.6	2	11.8	6	35.3	6	35.3	0.001*
No	10	20.4	32	65.3	1	2	6	12.2	0	0	
Vitamin D intakes											
Low	2	4.9	26	63.4	1	2.4	8	19.5	4	9.8	0.021*
Adequate	8	32	9	36	2	8	4	16	2	8	

Fisher's exact test; *p<0.05

Discussion

The largest group of subjects aged 19 – 48 years was 74.2%; this is also the same as the percentage of subjects with no cormobidities. Several factors can contribute to the high percentage of non-comorbidities in the 19-48-year-old group. Diabetes is typically diagnosed at age ≥40 years[7-9], as well as several reports, show that the presence of early-onset hypertension (onset at age ≤55 years) is lower[10].

Indonesia is a tropical country, yet many of its citizens have low vitamin D levels because they tend to avoid direct sunlight and don't eat enough vitamin D-rich foods. Fish oil, liver, and seafish like mackerel, salmon, sardines, and tuna are high sources of vitamin D.[11] In addition, vitamin D fortifies many foods, particularly dairy products and cereals.[11] However, in Indonesia, vitamin D intake is generally obtained from eggs and freshwater fish rather than seafish.[12] The FFQ used to analyze vitamin D intake included both dietary vitamin D and supplement use. Unfortunately, this questionnaire did not ask about sun exposure, leaving it unmeasured.

The body's immune system weakens with age, increasing the likelihood of infection and making it more challenging for individuals of that age to combat infections.[13] Based on statistical tests, there is no association between age and the severity of COVID-19 cases (p = 0.064), similar to Betsy Szeto et al.,[14] research. This also implies that individuals of all ages are susceptible to severe COVID-19. Younger children, who often have close contact with peers, can easily transmit the virus in school settings, while adults may spread it in workplaces or social gatherings. Older individuals, particularly in communal living environments, are at risk of rapid transmission due to shared spaces and activities. Even though it is risky, individuals can prevent it by following standard health protocols.[15]

Aging is linked to a variety of morbidities. As protective immunity deteriorates, older people become susceptible to infections and inflammatory diseases.[16] Older people are far more likely to make autoantibodies.[17] Essentially, immunological aging correlates with diminishing protective immunity alongside a rising prevalence of inflammatory

diseases. This, in turn, can lead to an increased risk of developing more serious illnesses. Therefore, it is important to take preventive measures to reduce the risk of age-related diseases. The absence of a correlation between age and COVID-19 severity may be due to the study participants' young age.

Different immunological responses to infection have at least partially contributed to the complexity of sex differences.[18] Males have more frequently experienced severe outcomes and deaths from COVID-19 than females, according to several studies.[19] Multivariate analysis, however, showed females experienced more severe systemic and total symptoms than males.[20] Numerous prior studies have assessed sex disparities in clinical outcomes among hospitalized or severely ill COVID-19 patients.[21] In contrast to previous research, this study found no association between gender and COVID-19 case severity ($p = 0.753$).

The study results showed a significant association between comorbidities (asthma, hypertension, DM, heart disease) and COVID-19 severity ($p = 0.001$). Felly Philipus Senewe et al.,[22] research revealed a significant relationship between comorbidities and COVID-19 cases (p-value = 0.001), indicating a correlation between the respondent's comorbidities and COVID-19 case severity. Comorbidities can influence COVID-19 progression and cause more severe organ damage. For example, individuals who experience low-grade inflammation due to hypertension, diabetes mellitus, and chronic kidney disease can influence the severity of COVID-19 cases due to a systemic inflammatory process with multiorgan involvement.[23]

The severity of COVID-19 cases was statistically significantly correlated with vitamin D intake ($p = 0.021$). The FFQ used in this study to analyze vitamin D intake includes data on intake from food and supplementation. Generally, the research discussed focuses on vitamin D intake from supplementation. Vitamin D supplementation helps lower the risk of death in Covid patients (OR: 0.48; 95% CI: 0.346–0.664; $p < 0.001$). Additionally, it was also observed that supplementation decreased the need for mechanical ventilation (OR: 0.54; 95% CI: 0.411–0.708; $p < 0.001$) and intensive care (OR: 0.35; 95% CI: 0.28–0.44; $p < 0.001$).[24]

Another meta-analysis of nine studies involving 870 participants revealed that vitamin D intake was linked to a decreased risk of death (RR: 0.76; 95% CI 0.60–0.97).[25] Additionally, other meta-analyses demonstrated a favorable impact of vitamin D3 supplementation on ICU admission (RR: 0.73; 95% CI: 0.57–0.95; $p = 0.02$) and COVID-19-related patient mortality (RR: 0.56; 95% CI: 0.34–0.91; $p = 0.02$).[26] In contrast to earlier research, a meta-analysis of eight randomized clinical trials (RCTs) revealed that giving vitamin D to COVID-19 patients did not significantly alter morbidity (OR: 0.50, 95% CI: 0.13–1.96).[27]

Vitamin D has different mechanisms for dealing with the risk of viral infections, such as COVID-19. COVID-19 has the hallmarks of a severe infection, namely a cytokine storm. Cytokine storms can trigger individual immune responses to inflammatory pathogens, leading to multiple organ failure and more severe cases of COVID-19.[28,29] Vitamin D has immunomodulatory properties and increases innate cellular immunity by reducing cytokine storms induced by the innate immune system, thereby affecting the body's defenses. The innate immune system produces pro-inflammatory and anti-inflammatory cytokines in response to bacterial and viral infections. The innate immune system supports innate immunity by producing several antimicrobial peptides (cathelicidins, defensins, and IL-37). Additionally, vitamin D modulates the production

and release of proinflammatory cytokines like IL-6, TNF-alpha, and interferon-gamma and controls responses mediated by Th lymphocytes.[30]

Vitamin D deficiency is linked with metabolic disorders, autoimmune diseases, and infections. Numerous research studies highlight the association between vitamin D deficiency and an elevated risk of respiratory tract infections. Furthermore, vitamin D deficiency is prevalent in critically ill patients and has been linked with more serious illnesses. The high number of severe COVID-19 patients with inadequate vitamin D levels suggests a link between low vitamin D levels and poor outcomes. Taking vitamin D might reduce the severity of the disease and increase the chances of recovery.[27]

Limitations of this study include the lack of control for potential confounding factors. Two potentially important confounding factors are subjects' cycle threshold (CT) values and sun exposure. Excluding patients who died during treatment and analyzing comorbidities as a single group may introduce bias. It must also be understood that dietary intake may not reflect serum vitamin D status. This study is a cross-sectional study, which means it cannot establish causality and primarily supports hypothesis formation.

Conclusion

Comorbidities and vitamin D intake are associated with the severity of COVID-19 infection. It is recommended that the initial assessment of COVID-19 patients include identification of comorbidities. Further research on the impact of vitamin D intake, adjusting for confounding variables, may be necessary to minimize the severity of COVID-19.

Conflict of interest

The authors declared no conflict of interest regarding this article.

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Author Contributions

MR: Conceptualization, data acquisition, formal analysis, interpretation of results, drafting the manuscript, and final approval of the version to be published; VS: Conceptualization, supervision, critical revision of the manuscript, interpretation of data, and final approval of the version to be published.

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ORIGINAL PAPER

Protein and branched-chain amino acid intake are associated with functional capacity in malnourished head and neck cancer patients undergoing chemoradiotherapy

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Abstract

Introduction: Head and neck cancer (HNC) patients are at high risk of malnutrition and functional decline. Protein and branched-chain amino acids (BCAA) are key nutrients for muscle protein synthesis and may influence functional capacity. This study examined the association between protein and BCAA intake and functional capacity in malnourished HNC patients receiving chemoradiotherapy.

Methods: A cross-sectional study was conducted at a radiotherapy outpatient clinic among malnourished HNC patients undergoing chemoradiotherapy (week 4–5). Energy and protein intake were assessed using three non-consecutive 24-hour food recalls, while BCAA intake was estimated using a semi-quantitative FFQ. Functional capacity was evaluated using the six-minute walk test (6MWT). Associations were analyzed using Spearman's correlation test.

Results: A total of 94 participants were included (mean age 46.9 ± 11.9 years; 61.7% male), with most diagnosed at stage IV disease. Median protein intake was 40.65 g/day (0.79 g/kg BW/day), with 74.5% classified as having inadequate protein intake. Median total BCAA intake was 9.08 g/day. The mean 6MWT distance was 332.9 ± 123.9 m. Significant moderate positive correlations were found between protein intake and 6MWT distance ($r = 0.444$; $p < 0.001$) and between BCAA intake and 6MWT distance ($r = 0.419$; $p < 0.001$).

Conclusion: Protein and BCAA intake showed a moderate association with functional capacity among malnourished HNC patients undergoing chemoradiotherapy. These findings support the importance of optimizing protein and BCAA intake to preserve functional status during active cancer treatment.

Keywords: branched-chain amino acids, functional capacity, head and neck cancer, protein intake, six-minute walk test

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Introduction

Head and neck cancer (HNC) represents a group of malignancies that ranks seventh globally in terms of incidence, with an estimated 900,000 new cases occurring annually.[1] According to data from Cipto Mangunkusumo Hospital, nasopharyngeal carcinoma, as the most frequent type of HNC, ranks fourth among all cancer cases, with a total of 1,338 cases.[2] Patients with HNC are at high risk for malnutrition, the prevalence of severe malnutrition in this population reaches 53% based on the criteria established by the European Society for Clinical Nutrition and Metabolism (ESPEN).[3] Approximately 60% of HNC patients are diagnosed at an advanced stage, where chemotherapy and radiotherapy serve as the primary therapeutic modalities. Both modalities contribute significantly to the deterioration of nutritional status, with the prevalence of malnutrition and sarcopenia increasing two- to three-fold following treatment compared to baseline.[4,5]

Metabolic alterations in cancer trigger a state of hypercatabolism, including accelerated muscle protein catabolism, particularly of branched-chain amino acids (BCAAs), which play a pivotal role in the depletion of muscle mass. Branched-chain amino acids are essential for stimulating muscle protein synthesis through the activation of the mTOR (mammalian target of rapamycin) pathway.[6,7] Side effects of oncological therapy, such as chemotherapy and radiotherapy, further exacerbate malnutrition.[8] Approximately 50–90% of patients experience chemoradiation-induced side effects, including mucositis, dysphagia, nausea, and vomiting, which result in diminished dietary intake.[8] Research indicates that the majority of cancer patients maintain protein intakes below the recommended levels, specifically less than 1 g/kg BW/day.[9]

Inadequate protein intake can lead to a decline in muscle mass and strength, subsequently reducing physical mobility, quality of life scores, and functional capacity.[10] Assessing functional capacity in cancer patients is critical for determining prognosis and treatment response, utilizing subjective methods such as the Karnofsky Scale as well as objective measures like the 6-minute walk test (6MWT) and the handgrip strength test.[11,12] Compared with other methods, the 6MWT provides a more comprehensive assessment of functional capacity by reflecting overall physical condition, including muscle strength, motor function, and cardiorespiratory fitness. As a submaximal exercise test, it is safe and well tolerated by patients with cancer.[11] Beyond being practical and cost-effective, this test serves as a prognostic indicator, a walking distance of $\geq$ 400 meters is associated with improved life expectancy.[11,12] Cancer patients with increased muscle strength and reduced fatigue tend to demonstrate better performance and greater distances in the 6MWT.[13] In HNC patients undergoing chemotherapy, a reduction in 6MWT distance has been observed starting from the end of the third week of therapy.[14]

The combination of adequate protein intake and sufficient physical activity facilitates muscle synthesis, thereby enhancing functional capacity.[14] A study on lung cancer patients found that protein intake correlates positively with improved functional capacity as measured by the Karnofsky Scale.[15] In advanced-stage cancer patients with malnutrition undergoing chemotherapy, whey protein supplementation at 1.5 g/kg BW/day for three months has been shown to improve handgrip strength as measured by digital hand dynamometry.[16]

The majority of previous studies regarding the role of protein and BCAAs in functional capacity have focused on supplementation-based interventions. This study, however, does not focus on supplementation; rather, it evaluates actual intake derived from daily dietary patterns. This approach potentially offers better adherence as it is more affordable and

accessible for patients. In addition, this study employs the 6MWT as a more objective measure of functional capacity, reflecting overall muscle function more comprehensively than commonly used methods such as the subjective Karnofsky score or the handgrip strength test that assesses only specific muscle groups. Therefore, this study is important to further clarify the relationship between protein and BCAA intake and the functional capacity of malnourished HNC patients undergoing chemoradiotherapy.

Methods

Study design and population

This cross-sectional study was conducted at the Radiotherapy Outpatient Clinic of Dr. Cipto Mangunkusumo National General Hospital, Jakarta, from August to November 2025. The samples of this study were 94 participats who met the inclusion and exclusion criteria and were recruited using consecutive sampling. Patients with HNC undergoing radiotherapy were identified from the daily clinic list. Eligible patients were approached during their clinic visits and invited to participate, and those who agreed provided written informed consent prior to enrollment.

Eligible participants were male and female patients aged 19–59 years who were diagnosed with HNC, had received chemotherapy, were undergoing radiotherapy in weeks 4–5, and were classified as malnourished based on The American Society for Parenteral and Enteral Nutrition (ASPEN) criteria. Exclusion criteria included inability to ambulate independently, high risk of falls, history of unstable angina or myocardial infarction within the past month, and chronic liver disease. This study has obtained research permit from Research Ethics Committee at the Faculty of Medicine, Universitas Indonesia with a research protocol KET-1083/UN2.F1/ETIK/PPM.00.02/2025.

Anthropometric measurements included body weight and height, measured twice and averaged. Nutritional status was determined using the ASPEN malnutrition criteria. Dietary data were collected by trained dietitians experienced in nutritional assessment, following standardized procedures to ensure consistency. Energy and protein intake were assessed using a 3×24-hour food recall conducted on nonconsecutive days. Protein intake reflected total consumption from both habitual dietary sources and any oral nutritional supplements consumed by the participants. Intake of BCAA was assessed using a semi-quantitative food frequency questionnaire adapted from a previously published study.[17,18] Participants were asked to report their usual dietary intake over the past month. To enhance the accuracy and consistency of dietary data collection, standardized portion size estimation tools (e.g., household measures and food models) were used, and probing techniques were applied by trained dietitians during interviews to minimize recall bias and reduce underreporting. All data were analyzed using Nutrisurvey 2007.

Physical activity was evaluated using the International Physical Activity Questionnaire–Short Form. Functional capacity was assessed using the 6-MWT following American Thoracic Society guidelines. Participants were instructed to walk as fast as possible, without running, back and forth along a flat, straight 30-m track for six minutes, and the total cumulative distance covered (meters) was recorded as the measure of functional capacity.

Statistical Analysis

Statistical analysis was performed using SPSS version 20. Data distribution was assessed using the Kolmogorov–Smirnov test. Normally distributed variables are presented as mean and standard deviation, while non-normally distributed variables are presented as median (minimum–maximum). Correlations between protein intake, BCAA intake, and functional capacity were analyzed using Pearson or Spearman correlation tests as appropriate.

Results

Among the 102 participants who consented to data collection, 8 were excluded (not meeting ASPEN malnutrition criteria, n = 4; inability to ambulate independently, n = 3; liver disease, n = 1), leaving 94 participants for analysis.

Table 1. Characteristics of patients

Characteristics	Results (n = 94)	Moderate malnutrition (n=37)	Severe malnutrition (n=57)	*p*-value
Age (years)	46.9 ±11.9	48.5 ±11.5	45.9 ±12.2	0.878
Sex, n (%)				
Men	58 (61.7)	22 (37.9)	36 (62.1)	0.719
Female	36 (38.3)	15 (41.7)	21(58.3)	
Cancer site, n (%)				
Nasopharynx	42 (44.7)	15 (35.7)	27 (64.3)	0.834
Sinonasal	14 (14.9)	6 (42.9)	8 (57.1)	
Tongue	12 (12.8)	5 (41.7)	7 (58.3)	
Larynx	16 (17)	8 (50)	8 (50)	
Others	10 (10.6)	3 (30)	7 (70)	
Cancer stage (n, %)				
II	2 (2.1)	1 (50)	1 (50)	0.025
III	22 (23.4)	14 (63.6)	8 (36.4)	
IV	70 (74.5)	22 (31.4)	48 (68.6)	
Radiation fraction	18.7 ±2.6	18.4 ±2.4	19 ±2.6	0.241
Body mass index (kg/m^2)	20.2 ±4.3	22.9 ±4.2	18.4 ±3.4	<0.001
Physical activity level (n,%)				
Low	79 (84)	32 (40.5)	47 (59.5)	0.789
Moderate	15 (16)	5 (33.3)	10 (66.7)	
High	0			
Energy intake (kcal/day)	1060 (308-2461)	1102 (308-2461)	1052 (496-2300)	0.425
Energy intake (kcal/kg BW/day)	21 (4-50)	20 (4-50)	22 (9-40)	0.276
Energy adequacy, (n,%)				
Low	75 (79.8)	32 (42.7)	43 (57.3)	0.193
Adequate	19 (20.2)	5 (26.3)	14 (73.7)	

Data are presented as mean ± SD, median (min–max), or n (%). Continuous variables were compared using independent samples t-test or Mann–Whitney U test according to distribution. Categorical variables were compared using chi-square or Fisher's exact test, as appropriate.

The mean age was 46.9 ± 11.9 years, and most participants were male (61.7%). The nasopharynx was the most common tumor site (44.7%), and most participants had stage IV disease (74.5%). Based on ASPEN malnutrition criteria, participants were categorized into moderate malnutrition (39.4%) and severe malnutrition (60.6%) groups. The mean body mass index was 20.2 ± 4.3 kg/m². Most participants had low physical activity (84.0%), and the median energy intake was 21.0 kcal/kg BW/day, with 79.8% showing low energy adequacy (<30 kcal/kg BW/day). Baseline characteristics were generally comparable between the moderate and severe malnutrition groups. However, participants with severe malnutrition had a significantly lower BMI than those with moderate malnutrition (18.5 ± 3.4 vs. 22.9 ± 4.3 kg/m², $p < 0.001$). Cancer stage distribution also differed significantly between groups ($p = 0.025$), with stage IV disease being more frequent in the severe malnutrition group. Participant characteristics are presented in **Table 1**.

Protein and BCAA Intake

The median protein intake was 40.65 g/day (range: 5.0–128.8 g/day), equivalent to 0.79 g/kg BW/day (range: 0.10–2.47 g/kg BW/day); 74.5% of participants did not meet the recommended intake of ≥1.2 g/kg BW/day. The median total BCAA intake was 9.08 g/day (range: 1.21–33.92 g/day), with median intakes of leucine, isoleucine, and valine of 4.20 g/day (0.80–15.13 g/day), 2.22 g/day (0.22–9.46 g/day), and 2.42 g/day (0.19–9.33 g/day), respectively (**Table 2**).

Table 2. Protein intake among study subjects

Characteristics	Results (n = 94)
Protein intake (g/day)	40.65 (5.0–128.8)
Protein intake (g/kg BW/day)	0.79 (0.10–2.47)
Protein adequacy (n, %)	
Low	70 (74.5)
Adequate	24 (25.5)
Total BCAA intake (g/day)	9.08 (1.21 – 33.92)
Leucine intake (g/day)	4.20 (0.80 – 15.13)
Isoleucine intake (g/day)	2.26 (0.22 – 9.46)
Valine intake (g/day)	2.42 (0.19 – 9.33)

Functional Capacity (6-Minute Walk Test)

The mean 6MWT distance was 332.9 ± 123.9 m. Male participants achieved significantly longer walking distances than female participants (354.7 ± 115.1 m vs 297.8 ± 131.0 m, $p = 0.030$) (**Table 3**).

Table 3. Six-minute walk test results among study subjects

Characteristics	Results (n = 94)	p value
6MWT (m)	332.9 ±123.9	
6MWT by sex (n, %)		
Men	354.7 ±115.1	0.030[a]
Female	297.8 ±131.0	

[a] Independent samples t-test.

Association between Protein Intake, BCAA Intake, and Functional Capacity

Protein intake was positively correlated with 6MWT distance (r = 0.444; p < 0.001). A similar positive association was observed between BCAA intake and functional capacity (r = 0.419; p < 0.001), indicating that higher protein and BCAA intakes were associated with better functional capacity, as shown in **Table 4**.

Tabel 4. Association of protein and BCAA intake with functional capacity among study subjects

Variable	6MWT	
	r value	p value
Protein intake	0.444[†]	<0.001[a]
BCAA intake	0.419[†]	<0.001[a]

Notes: BCAA, branched-chain amino acids; r, correlation coefficient; p, level of significance. [a] Spearman correlation test.

To account for potential confounding factors, multivariable linear regression analysis was performed adjusting for sex, body mass index, cancer stage and physical activity level. Protein and BCAA intake were analyzed in separate models.

Protein intake remained independently associated with 6MWT distance (B = 95.58, 95% CI: 46.41–144.75, p < 0.001). Similarly, BCAA intake was independently associated with functional capacity (B = 7.54, 95% CI: 3.22–11.86, p = 0.001).

Physical activity level was also significantly associated with 6MWT distance in both models (p = 0.019), while sex showed a borderline association. Cancer stage was not significantly associated with functional capacity.

Tabel 5. Multivariable linear regression analysis of protein and BCAA intake in relation to functional capacity

Variable	**Protein Model B (95% CI)**	**p-value**	**BCAA Model B (95% CI)**	**p-value**
Protein intake	95.58 (46.41–144.75)	<0.001	—	—
BCAA intake	—	—	7.54 (3.22–11.86)	0.001
Sex	-43.72 (-89.96–2.53)	0.064	-46.46 (-93.27–0.35)	0.052
Body mass index	-0.47 (-5.94–4.99)	0.864	-2.97 (-8.43–2.48)	0.281
Cancer stage	-21.66 (-68.67–25.36)	0.362	-24.28 (-72.02–23.46)	0.315
Physical activity	74.70 (12.58–136.81)	0.019	75.86 (12.77–138.94)	0.019

Notes: B, unstandardized regression coefficient; CI, confidence interval. Multivariable linear regression models were adjusted for sex, body mass index, physical activity level, and cancer stage. Cancer stage was categorized into stage II–III and stage IV. Protein and BCAA intake were analyzed in separate models to avoid collinearity.

Discussion

This study evaluated the association between protein and BCAA intake with functional capacity among malnourished patients with HNC undergoing concurrent chemoradiotherapy All participants were receiving active treatment and were characterized by advanced cancer stage, low physical activity levels, and poor nutritional status according to ASPEN criteria.

Protein and BCAA intakes in this study were generally inadequate, with most participants failing to achieve recommended intake levels. Although the relative contributions of leucine, isoleucine, and valine followed expected dietary patterns, absolute BCAA intake remained low. Similar findings have been reported among patients with HNC undergoing radiotherapy or chemoradiotherapy, indicating substantial nutritional challenges during active treatment. By comparison, Kristian et al.,[18] observed higher protein and BCAA intakes in patients who had not yet initiated active therapy, highlighting the adverse impact of treatment-related side effects on dietary intake. In addition to medical factors, social determinants such as education level, economic status, food access, and family support may further contribute to inadequate protein and BCAA intake during intensive cancer treatment.[19]

Functional capacity, assessed using the 6-MWT, was markedly reduced in this study compared with reference values in healthy individuals. This reduction aligns with findings reported by Mukhlisah et al.,[20] who demonstrated a significant decline in 6-MWT distance following chemotherapy. The impaired functional capacity observed in this population reflects the combined effects of systemic inflammation, cancer-related fatigue, reduced physical activity, and progressive loss of muscle mass during chemoradiotherapy.

Cancer-related metabolic changes induce a hypercatabolic state characterized by increased muscle protein breakdown, particularly of BCAA, leading to loss of muscle mass.[6,7] In patients undergoing chemoradiotherapy, treatment-related side effects such as mucositis, dysphagia, nausea, and vomiting frequently reduce dietary intake, resulting in suboptimal protein consumption.[8] Consequently, suboptimal protein intake may attenuate its impact on functional performance, as reflected in measures such as the 6-MWT.[10,14]

A significant positive correlation was observed between protein intake and functional capacity in this study, supporting evidence that higher protein intake is associated with better physical performance in patients with cancer. Umaya et al.,[15] reported a positive association between dietary protein intake and functional status measured by the Karnofsky Performance Scale, while Ford et al.,[21] demonstrated improvements in physical performance among patients with colorectal cancer receiving higher protein intake during chemotherapy. These findings suggest that adequate protein intake may contribute to the preservation of functional capacity, even in the absence of measurable gains in muscle mass.

However, not all studies have demonstrated a functional benefit of higher protein intake. Uster et al.,[22] reported no improvement in functional capacity among patients with advanced gastrointestinal and lung cancer despite combined nutritional counseling targeting adequate protein intake and structured exercise. This lack of effect was attributed to refractory cachexia, advanced disease stage, older age, and reduced anabolic responsiveness. These findings indicate that the relationship between protein intake and functional capacity is likely context-dependent and may be attenuated in patients with severe metabolic impairment or those in late or palliative stages of disease.

In this study, BCAA intake was positively associated with functional capacity. Biologically, BCAAs, particularly leucine, stimulate muscle protein synthesis through activation of the mTOR signaling pathway and may attenuate muscle protein breakdown during catabolic stress.[23,24] Consistent with these mechanisms, studies in non-cancer populations by Park et al., [25] and Liao et al., [26] demonstrated positive associations between dietary BCAA intake and muscle strength, walking speed, and overall physical function. In oncology settings, Storck et al. similarly reported improvements in muscle strength among patients with advanced cancer receiving leucine-enriched amino acid supplementation combined with exercise, supporting the functional relevance of BCAA under catabolic conditions.

By comparison, Kusumawati et al., [27] and Fauzarianda et al., [28] reported no significant association between BCAA intake and functional outcomes in cancer patients, particularly among those with more stable nutritional status and not receiving radiotherapy. These findings indicate that the functional benefits of BCAA intake may be more evident under conditions of active treatment and malnutrition, as observed in the present study.

Multivariable analysis further confirmed the independent association between nutritional intake and functional capacity. After adjusting for sex, body mass index, physical activity level, and cancer stage, both protein and BCAA intake remained significantly associated with 6MWT distance. These findings suggest that the relationship between protein and BCAA intake and functional capacity is not solely explained by differences in baseline characteristics or disease severity.

Physical activity level also remained significantly associated with functional capacity, highlighting its important role alongside nutritional intake. In contrast, cancer stage was not significantly associated with 6MWT distance in the adjusted models, suggesting that nutritional factors may play a role in maintaining functional capacity regardless of disease stage.

Taken together, the findings of this study emphasize the importance of adequate protein and BCAA intake in maintaining functional capacity among malnourished patients with HNC undergoing chemoradiotherapy. Differences in findings across studies may be influenced by disease stage, treatment phase, age, and baseline nutritional status. These results support the integration of targeted nutritional strategies alongside physical activity interventions to mitigate functional decline during active cancer treatment.

This study has several strengths, including relatively homogeneous clinical characteristics and the use of an objective measure of functional capacity. However, the cross-sectional design limits causal inference, and dietary assessment is subject to recall bias. In addition, BCAA intake estimation relied on the USDA food composition database due to the lack of local data, which may limit the precision of BCAA intake assessment for Indonesian foods.

Conclusions

This study demonstrates that inadequate protein and BCAA intake is common among malnourished patients with HNC undergoing concurrent chemoradiotherapy and is associated with reduced functional capacity. Protein and BCAA intake were positively associated with better functional performance, suggesting a potential role in mitigating functional decline during active treatment. The findings highlight the importance of early and targeted nutritional strategies, particularly those emphasizing adequate protein and

BCAA intake, to support functional capacity in this vulnerable population. Future longitudinal and interventional studies are needed to clarify causal relationships and to determine optimal nutritional approaches across different stages of treatment and disease severity.

Conflict of interest

The authors declared no conflict of interest regarding this article.

Ethic Statement

Written informed consent was obtained from the participant prior to data collection.

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Author Contributions

TB: Conceptualization, data acquisition, formal analysis, interpretation of results, drafting of the manuscript, and final approval of the version to be published;
NRMM: Conceptualization, supervision, critical revision of the manuscript, interpretation of data, and final approval of the version to be published;
TZ. Tamin: Supervision, critical revision of the manuscript, interpretation of data, and final approval of the version to be published;
WL, KS, and IA: Supervision, critical revision of the manuscript for important intellectual content, and final approval of the version to be published.

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SYSTEMATIC REVIEW

Effect of vitamin D supplementation regimens on clinical outcomes in asthma: A systematic review

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Abstract

Background: Vitamin D has immunomodulatory properties that may improve asthma outcomes; however, randomized controlled trials (RCTs) have reported inconsistent findings. Variations in supplementation regimens, particularly bolus versus non-bolus dosing, may contribute to these discrepancies.
Objective: To systematically evaluate the effects of vitamin D supplementation on clinical outcomes in patients with asthma, with particular emphasis on dosing regimens.
Methods: A systematic review was conducted according to PRISMA guidelines and registered in PROSPERO (CRD420261378116). PubMed, Scopus, and the Cochrane Library were searched for RCTs investigating vitamin D supplementation in asthma. Studies were categorized into non-bolus (daily or weekly) and bolus (high-dose intermittent) regimens. Primary outcomes included asthma exacerbations, lung function, and asthma control. Risk of bias was assessed using the Cochrane Risk of Bias 2 tool.
Results: Six RCTs met the inclusion criteria. Non-bolus supplementation was more consistently associated with improved asthma control and modest improvements in lung function, whereas bolus regimens generally showed no significant clinical benefit. Limited benefits of bolus dosing were observed only among participants with severe vitamin D deficiency. Overall, the included studies demonstrated low risk of bias to some concerns.
Conclusions: Vitamin D supplementation may improve asthma outcomes, but its effectiveness appears to depend on the dosing regimen. Regular non-bolus supplementation may provide greater clinical benefits than intermittent bolus dosing, particularly in individuals with vitamin D deficiency. Further high-quality RCTs are needed to confirm regimen-specific effects.

Keywords: asthma, bolus, non-bolus, supplementation, systematic review, vitamin d

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Introduction

Asthma is a chronic inflammatory airway disease characterized by variable airflow limitation and recurrent episodes of wheezing, breathlessness, and coughing. Despite advances in pharmacological therapy, asthma control remains suboptimal in a significant proportion of patients, highlighting the need for adjunctive therapeutic strategies.[1-3]

Vitamin D has emerged as a potential modulator of asthma pathophysiology due to its effects on both innate and adaptive immune responses. It has been shown to enhance regulatory T-cell function, suppress pro-inflammatory cytokine production, and improve antimicrobial defense mechanisms. In addition, emerging evidence from nutritional intervention studies, including a recent systematic review and meta-analysis on astaxanthin supplementation in women with polycystic ovary syndrome (PCOS), has demonstrated that antioxidant supplementation may significantly reduce oxidative stress and improve inflammatory profiles. These findings further support the potential role of micronutrients, including vitamin D, in modulating inflammatory pathways relevant to asthma. Observational studies have consistently demonstrated an association between low serum vitamin D levels and increased asthma severity, reduced lung function, and higher risk of exacerbations.[4-9]

However, randomized controlled trials investigating vitamin D supplementation in asthma have yielded inconsistent results. While some studies report improvements in asthma control and lung function, others show no significant clinical benefit. Genetic and metabolic factors may also contribute to variability in disease susceptibility and treatment response. These discrepancies may be explained by differences in study populations, baseline vitamin D status, and importantly, the supplementation regimen.[5,10-14]
Emerging evidence suggests that the pattern of vitamin D administration particularly the distinction between bolus (high-dose intermittent) and non-bolus (daily or weekly) regimens may influence clinical outcomes. Large meta-analyses in respiratory diseases have demonstrated that regular daily dosing is associated with protective effects, whereas bolus dosing may not confer similar benefits.[6,15-17]

Given these considerations, it is important to systematically evaluate whether the efficacy of vitamin D supplementation in asthma is influenced by the dosing regimen. Therefore, this study aimed to systematically review the available evidence on vitamin D supplementation in asthma, with a particular focus on comparing bolus and non-bolus regimens in relation to clinical outcomes.

Methods

Study Design

This study was conducted as a systematic review following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) framework.[18] The review protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO) under the registration number CRD420261378116. The objective was to evaluate the effects of vitamin D supplementation on clinical outcomes in patients with asthma, with a specific focus on the role of different supplementation regimens.

Eligibility Criteria

Studies were considered eligible if they were randomized controlled trials involving patients with a clinical diagnosis of asthma and evaluated vitamin D supplementation in comparison with placebo or standard therapy. Only studies reporting clinically relevant outcomes, including asthma exacerbations, lung function parameters, or asthma control, were included in the analysis. Studies were excluded if they were observational in design, review articles, case reports, or conducted in animal models. In addition, studies that did not provide sufficient data on clinical outcomes were not included.

Literature Search

A comprehensive search of the literature was performed using electronic databases, including PubMed, Scopus, and the Cochrane Library. The search covered all available records up to the time of data collection. Keywords related to vitamin D and asthma were combined using Boolean operators to identify relevant studies. The search terms included variations of "vitamin D", "cholecalciferol", "asthma", "supplementation", and "randomized controlled trial". To ensure completeness, the reference lists of selected articles were also reviewed to identify additional studies that met the inclusion criteria.

Study Selection

All identified records were initially screened based on titles and abstracts to exclude studies that were clearly not relevant. Articles that appeared to meet the inclusion criteria were then assessed in full text. The selection process was conducted carefully to ensure that all included studies met the predefined criteria, and any discrepancies were resolved through discussion. The study selection process is illustrated in **Figure 1**.

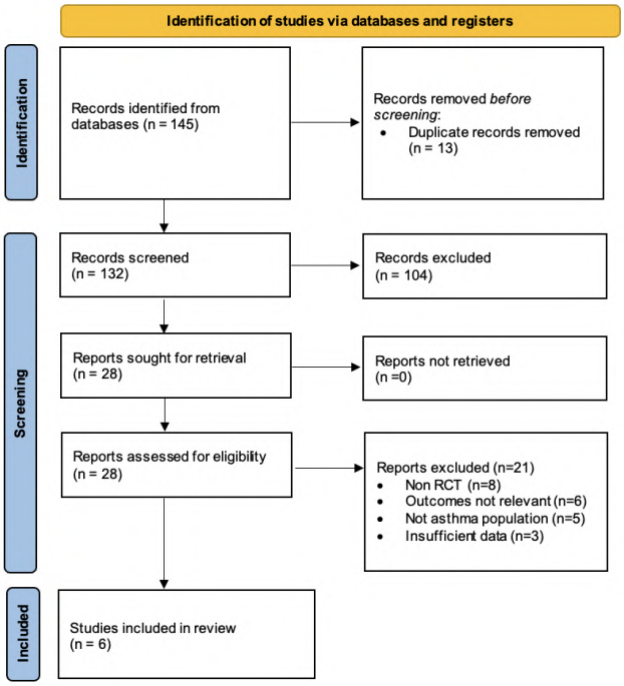

Figure 1. The study selection process by PRISMA flowchart

Data Extraction

Data from the included studies were extracted systematically using a predefined format. Extracted information included study characteristics, participant demographics, intervention details, and reported outcomes. Particular attention was given to the vitamin D supplementation protocol, including dosage, frequency, and duration, as these variables were essential for subsequent classification.

Classification of Supplementation Regimen

To evaluate the influence of dosing strategy, vitamin D supplementation protocols were classified according to the pattern of maintenance administration rather than the initial loading dose. Non-bolus regimens were defined as regular vitamin D supplementation administered daily or weekly to maintain relatively stable circulating 25-hydroxyvitamin D concentrations. Studies that included an initial loading dose followed by daily or weekly maintenance supplementation were also classified as non-bolus because sustained administration represented the principal therapeutic strategy.

Bolus regimens were defined as high-dose vitamin D administered intermittently at intervals of one month or longer without continuous daily or weekly maintenance dosing. This operational definition was adopted to distinguish intermittent pharmacological dosing from regular physiological replacement and to facilitate comparison between supplementation strategies across the included randomized controlled trials.

Outcomes of Interest

The main outcomes evaluated in this review included asthma exacerbations, lung function parameters such as forced expiratory volume in one second (FEV1) and the FEV1/FVC ratio, as well as measures of asthma control assessed using validated scoring systems. These outcomes were selected based on their clinical relevance and frequent reporting across studies.

Data Synthesis

A qualitative synthesis was conducted to summarize the findings of the included studies. Due to substantial heterogeneity in study design, population characteristics, intervention protocols, and outcome measures, a quantitative meta-analysis was not performed. The results were synthesized narratively, with a focus on differences between bolus and non-bolus supplementation regimens.

Results

Study Selection

A total of 132 records were identified through database searching. After removal of duplicates, 104 records were screened based on titles and abstracts. Of these, 28 articles were assessed for full-text eligibility, and 6 studies met the inclusion criteria.

Table 1. Characteristics of Included Studies on Vitamin D Supplementation Regimens and Clinical Outcomes in Asthma

Study	Design & Population	Regimen	Regimen Type	Outcomes	Main Findings
Watkins et al.,[16] 2024	RCT, adults with mild–moderate asthma (n=32)	125 µg/day (~5000 IU) for 12 weeks	Non-bolus (daily)	FEV1/FVC, ACT, inflammatory biomarkers	Small but significant improvement in FEV1/FVC; no significant effect on ACT or biomarkers
Denlinger et al.,[19] 2016	RCT, adults with asthma and vitamin D insufficiency (n=408)	Loading dose 100,000 IU + 4000 IU/day	Non-bolus (daily + loading)	Cold symptoms, exacerbations	No significant reduction in respiratory symptoms or clinical outcomes
Andújar-Espinosa et al.,[20] 2020	RCT, adults with asthma and vitamin D deficiency (n=112)	16,000 IU/week for 6 months (calcifediol)	Non-bolus (weekly)	ACT, quality of life, exacerbations	Significant improvement in asthma control and quality of life
Chiewchalermsri et al.,[21] 2023	RCT, HDM-allergic patients with/without asthma (n=34)	60,000 IU/week for 10 weeks	Non-bolus (weekly)	Symptom score, Treg function	Significant reduction in symptoms; improved regulatory T-cell function
Camargo et al.,[22] 2021	Post hoc RCT analysis, asthma/COPD subgroup (n=775)	100,000 IU/month	Bolus (monthly)	Exacerbations	No overall effect; benefit observed only in severe vitamin D deficiency
Sluyter et al.,[15] 2017	RCT, adults (n=442)	200,000 IU loading + 100,000 IU/month	Bolus (monthly)	FEV1 (lung function)	No significant overall improvement (benefit only in specific subgroups)

Abbreviations: ACT, Asthma Control Test; FEV1, forced expiratory volume in one second; FVC, forced vital capacity; ARI, acute respiratory infection. Non-bolus regimens refer to daily or weekly vitamin D supplementation, whereas bolus regimens refer to high-dose intermittent administration, typically given monthly or at longer intervals

Study Characteristics

The included studies were randomized controlled trials conducted in patients with asthma across different populations and settings. The sample sizes varied considerably, ranging from small-scale trials to larger multicenter studies. The duration of vitamin D supplementation also differed across studies, from short-term interventions to longer follow-up periods. There was notable variability in baseline characteristics, particularly in terms of vitamin D status, with several studies focusing specifically on patients with vitamin D deficiency or insufficiency. This variation in baseline status may have influenced the observed treatment effects.

In addition, substantial differences were observed in supplementation protocols. Some studies administered vitamin D on a daily or weekly basis, while others used high-dose intermittent regimens given monthly or at longer intervals. This variation in dosing strategy formed the basis for further subgroup classification.

Risk of Bias Assessment

The risk of bias of the included studies was assessed using the Cochrane Risk of Bias 2 (RoB 2) tool.[23] Overall, most studies demonstrated a low risk of bias across several domains, particularly in the randomization process, measurement of outcomes, and completeness of outcome data. These findings suggest that the majority of included trials were methodologically sound in terms of study design and outcome assessment.

However, some concerns were identified in specific domains. A number of studies showed potential bias related to deviations from intended interventions, which may reflect issues such as adherence to the intervention protocol or lack of blinding. In addition, some studies were judged to have concerns regarding selective reporting of outcomes, indicating that not all prespecified outcomes may have been fully reported.

The overall risk of bias across studies was therefore considered to range from low to some concerns. Larger, well-designed trials generally demonstrated a lower risk of bias, while smaller studies were more likely to present uncertainties in certain domains due to limited reporting. The detailed assessment of risk of bias for each included study is presented in **Figure 2A**, while the overall distribution of risk across domains is summarized in **Figure 2B**.

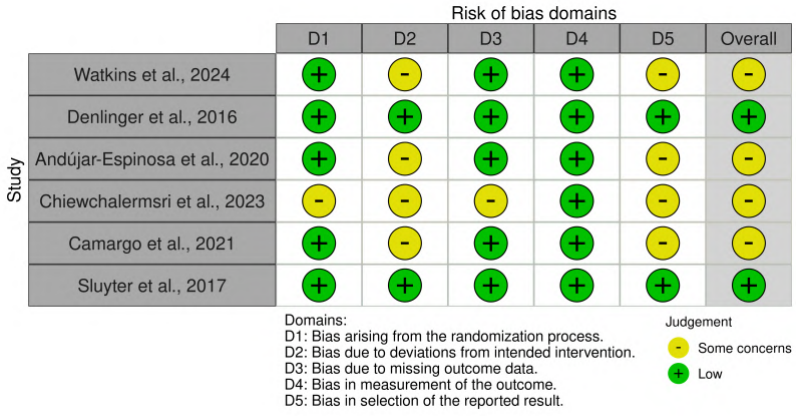

Figure 2A. Risk of bias assessment of included studies using the Cochrane Risk of Bias 2 (RoB 2) tool.

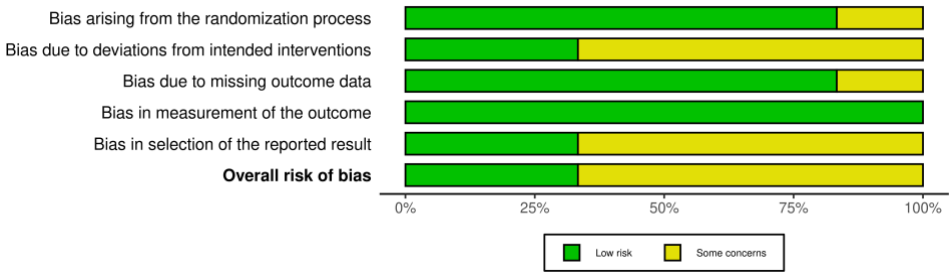

Figure 2B. Summary of risk of bias across included studies, presented as percentages for each domain.

Effects of Non-Bolus Supplementation

Studies that utilized non-bolus regimens, defined as daily or weekly administration of vitamin D, tended to demonstrate more consistent improvements in clinical outcomes. Several trials reported better asthma control, reflected by improvements in standardized assessment scores, along with modest gains in lung function parameters such as FEV1 and FEV1/FVC ratio.

The beneficial effects of supplementation appeared to be more evident in patients with lower baseline vitamin D levels. In these populations, regular supplementation was associated with a greater likelihood of improved clinical control. Although not all findings reached statistical significance, the overall trend suggested that consistent vitamin D intake may contribute to better disease management.

Effects of Bolus Supplementation

In contrast, studies employing bolus regimens, characterized by high-dose intermittent supplementation, generally reported less favorable outcomes. Most trials did not demonstrate significant improvements in asthma exacerbations, lung function, or symptom control when compared with placebo or standard treatment.

In some instances, potential benefits were observed in specific subgroups, particularly among individuals with marked vitamin D deficiency. However, these findings were not consistently replicated across studies. Overall, the results suggest that intermittent high-dose supplementation may not provide the same clinical advantages as more frequent dosing strategies.

Overall Synthesis of Evidence

To evaluate the influence of dosing strategy, vitamin D supplementation protocols were classified according to the pattern of maintenance administration rather than the initial loading dose. Non-bolus regimens were defined as regular vitamin D supplementation administered daily or weekly to maintain relatively stable circulating 25-hydroxyvitamin D concentrations. Studies that included an initial loading dose followed by daily or weekly maintenance supplementation were also classified as non-bolus because sustained administration represented the principal therapeutic strategy.

Bolus regimens were defined as high-dose vitamin D administered intermittently at intervals of one month or longer without continuous daily or weekly maintenance dosing. This operational definition was adopted to distinguish intermittent pharmacological dosing from regular physiological replacement and to facilitate comparison between supplementation strategies across the included randomized controlled trials. Overall, the available evidence suggests that regular non-bolus vitamin D supplementation is more consistently associated with improvements in asthma control than intermittent bolus administration. However, the magnitude of benefit appears to depend on baseline vitamin D status and study characteristics.

Discussion

The findings of this systematic review demonstrate that the effects of vitamin D supplementation on clinical outcomes in patients with asthma remain inconsistent across randomized controlled trials. While some studies reported improvements in asthma control and lung function, others did not observe significant benefits. This variability has been widely reported in the literature and suggests that additional factors may influence treatment response beyond supplementation alone.[3,13,24-26]

One of the most notable observations in the present review is the potential influence of supplementation regimen on clinical outcomes. Studies employing non-bolus regimens, characterized by daily or weekly administration, were more likely to report favorable effects, particularly in terms of asthma control. In contrast, studies using bolus regimens, involving high-dose intermittent supplementation, generally failed to demonstrate consistent clinical benefit. This pattern aligns with findings from several randomized trials in which regular dosing strategies were associated with improved clinical parameters, whereas intermittent high-dose regimens yielded neutral results.[16,20,27,28]

A plausible explanation for this difference lies in the pharmacokinetic profile of vitamin D. Regular supplementation is believed to maintain more stable circulating concentrations of 25-hydroxyvitamin D, which may be necessary for sustained immunomodulatory activity. In contrast, bolus dosing may induce transient increases in serum vitamin D levels followed by rapid declines, potentially limiting long-term biological effects.[29,30] This hypothesis is supported by evidence from meta-analyses in respiratory diseases, which have demonstrated that daily or weekly vitamin D supplementation is associated with protective effects, whereas intermittent bolus dosing does not confer similar benefits.[4,10,31-35]

In addition to dosing regimen, baseline vitamin D status appears to be an important determinant of response. Previous meta-analyses have shown that the protective effects of vitamin D supplementation on asthma exacerbations are more pronounced in individuals with marked vitamin D deficiency. Similarly, several trials included in this review reported greater clinical improvements among patients with lower baseline vitamin D levels. These findings suggest a potential interaction between baseline vitamin D status and treatment efficacy, which may partially explain the heterogeneity observed across studies. These observations are consistent with evidence from other nutritional interventions targeting oxidative stress, such as astaxanthin supplementation in women with PCOS, where significant reductions in oxidative stress markers have been reported. This suggests that modulation of oxidative stress may represent a common pathway through which micronutrients exert beneficial effects in inflammatory conditions.[7,10,36,37]

The variability in study outcomes may also be attributed to differences in study design and population characteristics. The included trials varied considerably in terms of sample size, duration of intervention, dosage of supplementation, and outcome measures. Some studies included participants with sufficient baseline vitamin D levels, which may have reduced the likelihood of detecting a clinically meaningful effect. These findings are consistent with previous studies demonstrating the importance of nutritional status and metabolic factors in determining clinical outcomes. Furthermore, the use of different endpoints, ranging from lung function parameters to symptom scores and exacerbation rates, limited the comparability of results across studies.[10,15,16,38-40]

An important consideration in interpreting the present findings is the limited number of randomized controlled trials specifically designed to compare vitamin D dosing strategies in patients with asthma. Considerable heterogeneity was observed across studies regarding participant characteristics, baseline vitamin D status, intervention protocols, treatment duration, and clinical outcome measures. These differences limited direct comparisons and precluded definitive conclusions regarding the superiority of one supplementation regimen over another. Nevertheless, the overall pattern consistently favored regular maintenance supplementation over intermittent high-dose administration.

This review has several limitations that should be considered. The number of included studies was relatively limited, and the heterogeneity in study design and outcome reporting restricted the feasibility of conducting a comprehensive meta-analysis. In addition, the classification of supplementation regimens was based primarily on dosing frequency, which may not fully capture differences in cumulative dose or duration of treatment. Nevertheless, the consistent pattern observed between regimen type and clinical outcomes provides important insight into the potential role of dosing strategy.

Overall, the findings suggest that vitamin D supplementation may have a role in asthma management; however, its effectiveness appears to depend on the supplementation regimen and baseline vitamin D status. Non-bolus regimens may offer greater clinical benefit compared to bolus dosing, particularly in individuals with deficiency. Future randomized controlled trials should be designed to specifically evaluate regimen-dependent effects and to identify patient subgroups most likely to benefit from supplementation.

Conclusions

This systematic review suggests that vitamin D supplementation may contribute to improved asthma outcomes, although its effectiveness appears to depend on the dosing regimen. Regular non-bolus supplementation showed a more consistent association with improved asthma control and modest improvements in lung function than intermittent bolus administration. However, given the limited number of eligible randomized controlled trials and the substantial heterogeneity among studies, these findings should be interpreted cautiously. Additional high-quality randomized controlled trials directly comparing dosing strategies are needed before definitive recommendations can be established.

Conflict of Interest

The authors declare no conflict of interest.

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Author Contributions

DP: Conceptualization, literature search, study selection, data acquisition, formal analysis, interpretation of results, drafting the manuscript, and final approval of the version to be published; NKS: Supervision, interpretation of results, critical revision of the manuscript for important intellectual content, and final approval of the version to be published; IWW: Conception and design of the study, interpretation of results, critical revision of the manuscript for important intellectual content, and final approval of the version to be published; AIWH: Supervision, interpretation of results, critical revision of the manuscript for important intellectual content, and final approval of the version to be published.

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CASE REPORT

The role of energy and protein adequacy in improving functional capacity in adult males with severe burn injury: A case series

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Abstract

Background: Burn injury represents a major global health problem with high mortality and disability rates, significantly affecting patients' quality of life, including in Indonesia. Patients with severe burns frequently experience a decline in functional capacity due to muscle weakness, which is exacerbated by the hypermetabolic response. Adequate daily caloric and protein intake is essential to preserve muscle mass and potentially improve patients' functional capacity.

Case report: The first case, a 39-year-old male with grade 2A–3 burn injury involving 35.5% of total body surface area (TBSA). Nutritional management was initiated at 10 kcal/kg body weight/day and protein 1 g/kg/day, then increased to 42 kcal/kg/day and 1.9 g/kg/day. The patient showed an improvement in the Functional Assessment for Burns–Critical Care (FAB-CC) score from 19 to 30. The second case, a 35-year-old male with grade 2A–3 burns involving 57.5% TBSA. Nutritional management was started at 10 kcal/kg/day and protein 0.4 g/kg/day, then gradually increased to 60 kcal/kg/day and protein 2.5 g/kg/day. The patient demonstrated improvement in the FAB-CC score from 3 to 20. Patients with burn injury experience hypermetabolism to support tissue repair and maintain vital organ function. Systemic inflammation and burn extent influence daily nutritional requirements. Adequate energy and protein intake play an important role in improving functional capacity in patients with burn injuries. All patients demonstrated increased daily energy and protein intake, which was associated with improved FAB-CC scores and functional capacity.

Conclusion: Both cases suggest that adequate energy and protein intake may support functional recovery in patients with burn injuries, as reflected by parallel improvements in FAB-CC scores during nutritional care. These findings underscore the importance of integrating optimal nutritional therapy within a multidisciplinary treatment strategy to maximize functional outcomes in burn patients.

Keywords: functional assessment for burns-critical care (FAB-CC), functional capacity, burn injury, nutrition

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Introduction

Burn injuries continue to represent an important public health burden in Indonesia, contributing substantially to both mortality and long-term morbidity. As a lower-middle-income country, Indonesia is affected by the broader global pattern in which burn-related deaths occur predominantly in low- and middle-income settings. The World Health Organization reports that more than 95% of fatal burn cases occur in these countries, while burns cause approximately 195,000 deaths worldwide each year, with almost two-thirds occurring in Africa and Southeast Asia. In the Indonesian context, flame burns and gas explosion-related injuries are frequently reported and are commonly associated with extensive total body surface area involvement.[1,2] Patients with severe burns often experience a decline in functional capacity due to muscle weakness during intensive care, which is exacerbated by the post-burn hypermetabolic response. This condition increases the need for medical care and is associated with mental health disturbances, reduced quality of life, and social isolation.[3,4]

Several instruments can be used to assess functional capacity, such as the Karnofsky Performance Scale (KPS) and the Chelsea Critical Care Physical Assessment Tool (CPAx). However, these instruments are less sensitive to changes in critically ill patients and are not specific to burn patients. The Functional Assessment for Burns–Critical Care (FAB-CC) was specifically developed for burn patients in intensive care settings, focusing on simple functional tasks and offering greater sensitivity to changes in functional capacity among critically ill burn patients.[5] Optimal nutritional support, with adequate energy and protein intake, can improve functional capacity by supporting wound healing, preventing muscle mass loss, and enhancing mobility and independence.[6]

Daily caloric and protein intake must be carefully monitored to preserve muscle mass and potentially improve functional capacity.[7,8] However, there are limited data describing early energy and protein provision and its impact on functional capacity assessed using FAB-CC in burn patients. Therefore, we present this case series to illustrate the role of energy and protein provision in improving functional capacity as assessed by FAB-CC.

Case report

Case 1

Clinical findings

A 39-year-old male was admitted with burns involving the face, chest, back, and both upper and lower extremities, which had occurred 2 days prior to hospitalization. The injury was caused by flame burns originating from cigarette ash sparks. The patient had no known comorbidities. On examination, he was found to have class II obesity with a body mass index (BMI) of 34.8 kg/m². Burn severity was classified as grade 2A–3, involving 35.5% of total body surface area (TBSA).

Before admission, the patient had received fluid resuscitation with 0.9% NaCl 2,000 mL/24 hours. During hospitalization, inflammatory parameters worsened, as shown by increases in C-reactive protein (CRP) and neutrophil-to-lymphocyte ratio (NLR). Electrolyte abnormalities were also noted, including hyponatremia (sodium 128.8 mmol/L) and hyperkalemia (potassium 5.2 mmol/L). The patient also developed hypoalbuminemia requiring correction

Nutritional assessment

At admission, nutritional screening using the Nutritional Risk Screening 2002 (NRS-2002) yielded a score of 3, indicating a risk of malnutrition. Despite pre-existing obesity, the patient remained at nutritional risk due to extensive burns and hypermetabolic stress. At admission, the patient's body weight was 85 kg based on anamnesis, whereas the initial bed-scale measurement was 91.2 kg. During follow-up, bed-scale body weight decreased to 84.5 kg on post-burn day 19 (hospital day 16) and 84.3 kg on post-burn day 20 (hospital day 17). This corresponded to a 1.7 kg (2.0%) reduction in body weight over the final 4 days of hospitalization. Functional capacity at baseline was poor, with an initial FAB-CC score of 3.

Intervention

Nutritional therapy was initiated at 10 kcal/kg/day with protein 1 g/kg/day, then gradually advanced according to clinical condition and tolerance, reaching energy total requirement by Xie equation around 42 kcal/kg/day and 1.99 g/kg/day of protein. Energy and protein intake decreased during the period of excisional debridement. Nutritional intervention was provided via the oral route using solid foods and hospital-based high-protein oral nutritional supplements in liquids form. Supportive correction for metabolic and electrolyte imbalance included NaCl capsules 1,000 mg, three times daily for hyponatremia, Kalitake® 5 g, three times daily for hyperkalemia, and 20% albumin IV 100 mL, administered three times for hypoalbuminemia.

Outcome

Functional capacity improved progressively during hospitalization, with the FAB-CC score increasing from 3 at admission to nearly 30 by day 17. Over the nutritional intervention, the patient demonstrated an improvement in functional capacity in parallel with increased energy and protein intake. When energy intake increased to 33 ± 0.8 kcal/kg body weight/day and protein intake to 1.5 ± 0.1 g/kg body weight/day, the patient's total FAB-CC score increased to 30—the highest score achieved during hospitalization—on nutrition days 14 to 17. At discharge, the patient had a FAB-CC score of 30, indicating the ability to stand, step, and perform activities independently.

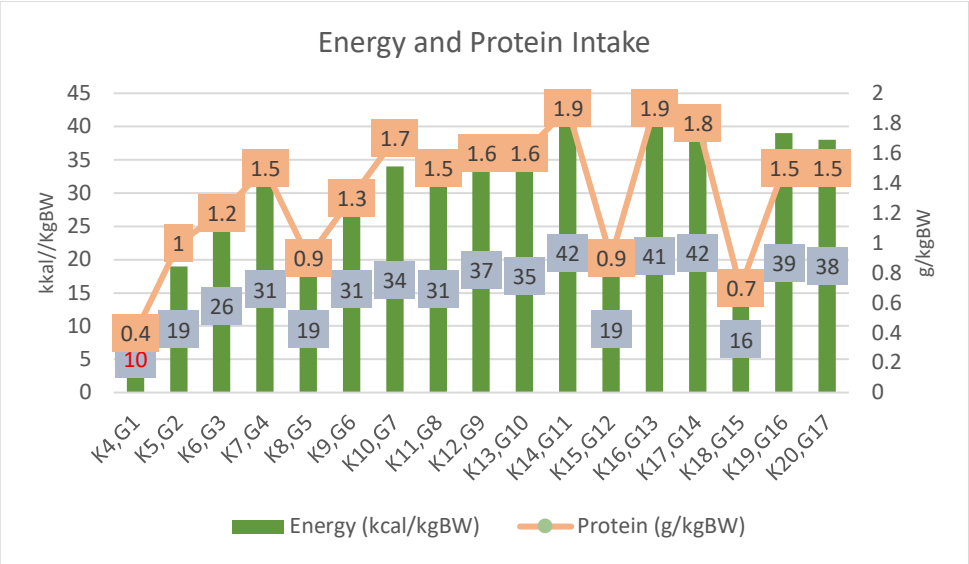

Figure 1. Energy and protein intake in case 1 during the observation period.
(K: post burn injury day; G: nutrition day)

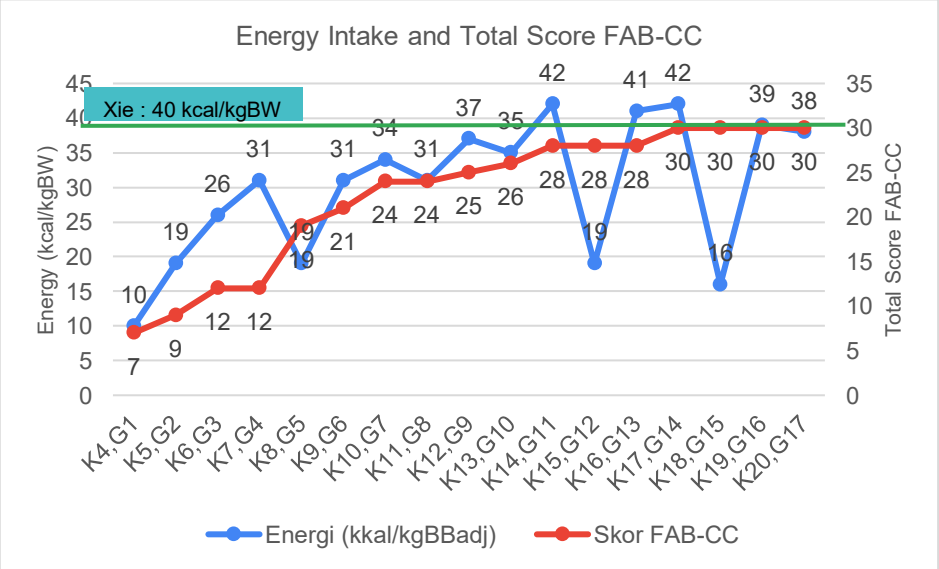

Figure 2. Energy intake pattern and total score FAB-CC during observation.
(K: post burn injury day; G: nutrition day)

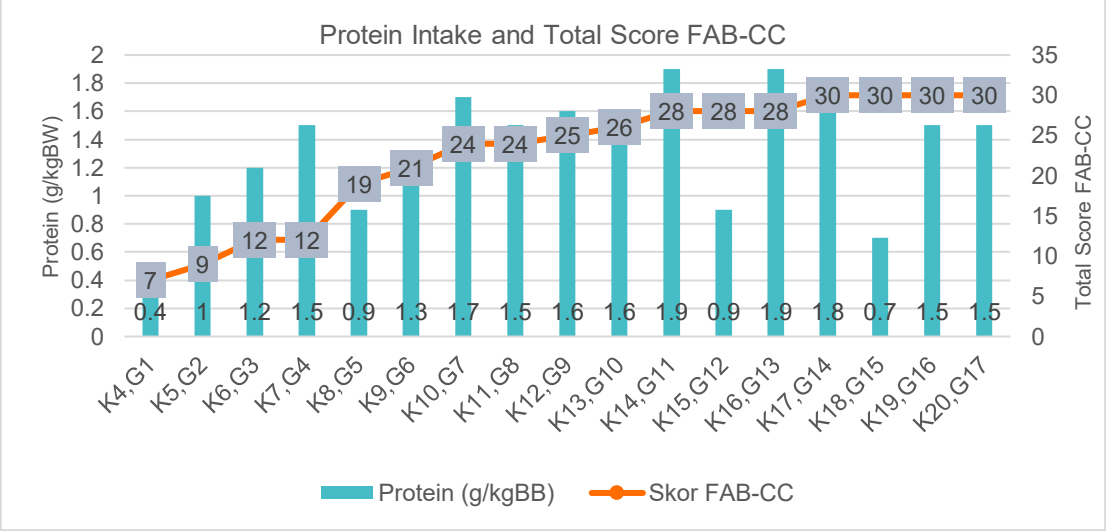

Figure 3. Protein intake pattern and total score FAB-CC during observation.
(K: post burn injury day; G: nutrition day)

Case 2

Clinical findings

A 35-year-old male was admitted with burns involving the face, back, genitalia, and both upper and lower extremities, which had occurred 3 days prior to admission. The injury was caused by hot water scalding while riding a motorcycle. On admission, the patient had no known comorbidities. Burn severity was classified as grade 2A–3, with a total burn area of 57.5% TBSA. Initial management included fluid resuscitation with Ringer's lactate. During hospitalization, inflammatory markers showed mixed trends: the neutrophil-to-lymphocyte ratio (NLR) decreased from 35.13 to 25.67, whereas procalcitonin increased from 1.3 ng/mL to 5.73 ng/mL. The clinical course was further complicated by septic shock and pan-drug-resistant infection, requiring admission to the intensive care unit for 3 days and mechanical ventilation for 2 days.

Nutritional assessment

At baseline, the patient was nutritionally normal, with a body mass index (BMI) of 21.7 kg/m². However, nutritional risk screening using NRS-2002 yielded a score of 3, indicating risk of malnutrition. During the 28-day monitoring period, body weight decreased from 55.7 kg to 51.5 kg. There was a 4.2 kg (8%) weight loss over 28 days, accompanied by energy intake below 75% of total estimated requirements during the last 3 weeks. Weight loss in Case 2 was greater than in Case 1, likely due to septic shock and pan-drug-resistant infection, which were associated with fever and reduced oral intake. Functional capacity on admission was poor, with an initial FAB-CC score of 3.

Intervention

Nutritional therapy was initiated conservatively at 10 kcal/kg/day with protein provision of 0.4 g/kg/day. Intake was then gradually advanced according to clinical tolerance and metabolic demands, reaching 60 kcal/kg/day and 2.5 g/kg/day of protein, as shown in

Figure 1. In parallel with medical and critical care management, the patient also underwent intensive monitoring of nutritional intake, body weight, and functional capacity throughout hospitalization.

Outcome

Nutritional intake increased progressively from 10–30 kcal/kg/day and 0.4–1.4 g/kg/day of protein in the early phase to 51–60 kcal/kg/day and 2.4–2.5 g/kg/day of protein at peak intake. This improvement in nutritional adequacy was accompanied by a parallel improvement in functional capacity, with the FAB-CC score increasing from 3 at admission to 23, reflecting better bed mobility, independent sitting, standing with minimal assistance, and self-care ability. However, this improvement was interrupted by septic shock, which led to a decline in functional status and necessitated ICU care. After recovery from the critical episode, the patient's functional capacity improved again, reaching a FAB-CC score of 20 by the end of hospitalization. The association between the patient's energy and protein intake profile and the improvement in functional capacity, as measured by the FAB-CC, is presented in **Figure 2** and **Figure 3**. Compared with Case 1, Case 2 demonstrated greater weight loss and lower FAB-CC scores, likely related to septic shock and pan-drug-resistant infection. The patient was discharged after 31 days of hospitalization with a final FAB-CC score of 20.

Discussion

Burn injuries are conditions that can lead to a significant decline in functional capacity among survivors.[9,10] Extensive tissue damage triggers both local and systemic inflammatory responses. Burns induce a hypermetabolic state in which the body's metabolic rate markedly increases to support tissue repair processes and to maintain vital organ function.[3,4,11]

Hypermetabolism in burn patients is characterized by increased energy requirements and alterations in carbohydrate, protein, and fat metabolism. The body increases gluconeogenesis and lipolysis to meet heightened energy demands, while insulin resistance may result in hyperglycemia. A major consequence of this hypermetabolic state is excessive protein catabolism, whereby skeletal muscle proteins are broken down to provide amino acids as substrates for gluconeogenesis and for the synthesis of acute-phase proteins, such as C-reactive protein (CRP). This hypermetabolic and hypercatabolic response may persist for months to years after the burn injury, with severity influenced by factors such as burn size, patient age, and pre-burn nutritional status. Consequently, burn patients may experience substantial loss of muscle mass, ultimately impairing functional capacity.[3,12,13] Therefore, comprehensive patient assessment, including evaluation of functional capacity, is essential because it is closely related to management strategies and prognosis.[4,14] Burn size is directly associated with the severity of hypermetabolism; energy requirements may increase up to 1.5–2 times the basal energy expenditure due to activation of the sympathetic nervous system, stress hormones, and systemic inflammatory responses. This condition is accompanied by massive nitrogen losses, increased protein turnover, and reductions in muscle mass of up to 15–20% within the first week if not managed adequately.[7,14]

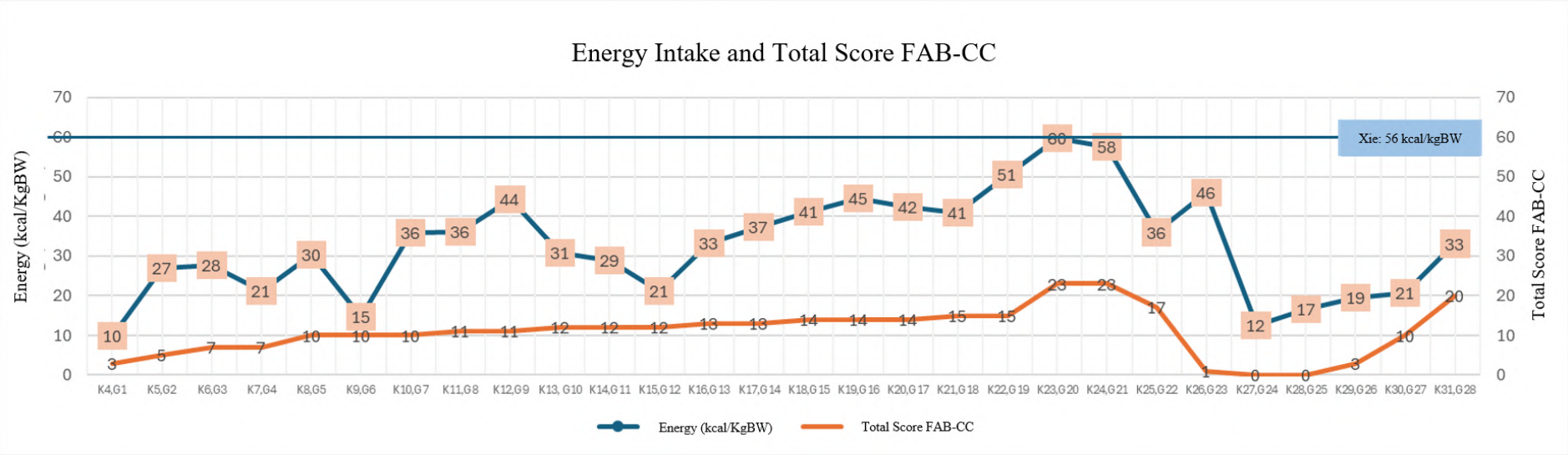

Figure 4. Energy intake and Total Score FAB-CC. (K: post burn injury day; G: nutrition day)

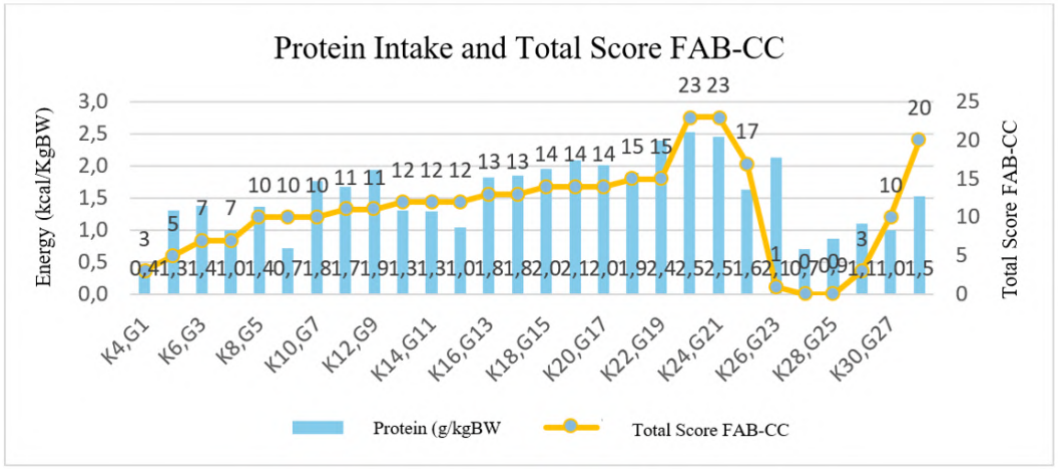

Figure 5. Protein intake and total score FAB-CC. (K: post burn injury day; G: nutrition day)

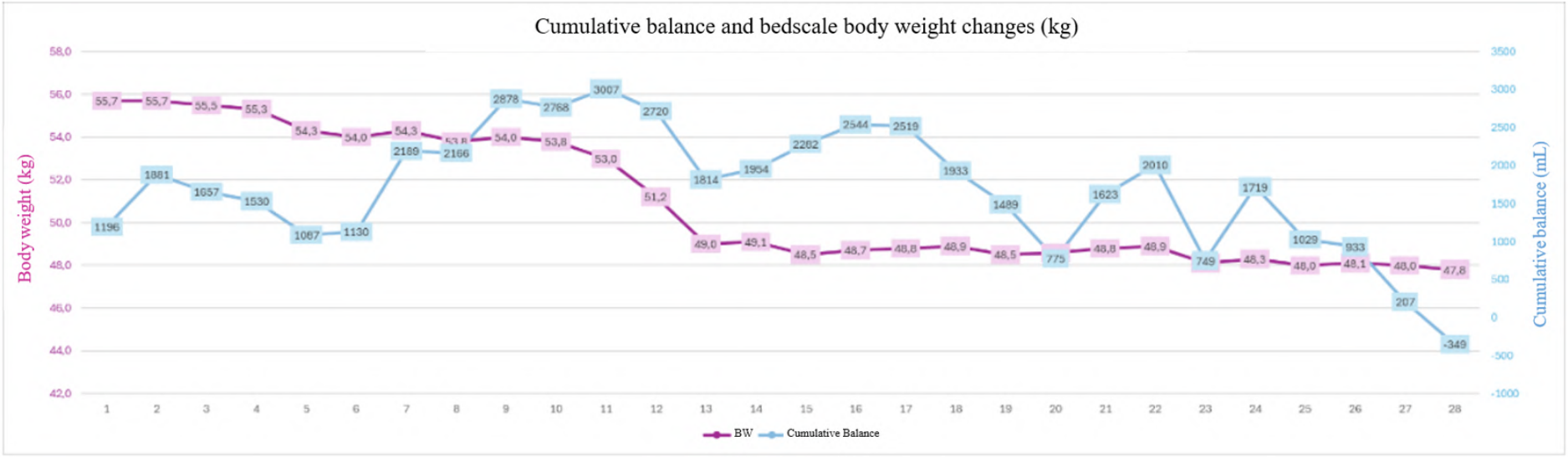

Figure 6. Bedscale body weight changes and cumulative balance observation. (K: post burn injury day; G: nutrition day)

The clinical characteristics and laboratory findings of each case are comprehensively summarized in Tables 1 and 2

Table 1. Characteristic of the case

Charateristic	Case 1	Case 2
Gender	Male	Male
Age	39 year old	35 year old
Etiology	Flame	Hot Water
Total Body Surface Area	35,5%	57,5%
Burnt depth	2A–3	2A–3
Time of Event	4 days prior to admission	3 days prior to admission
History of resuscitation	Achieved within 24 hours	Achieved within 24 hours
Urine output	0,8 mL/kgBW/hour	1,4 mL/kgBW/hour
Nutritional screening (NRS 2002)	Score 3 (At risk of malnutrition)	Score 3 (At risk of malnutrition)
Nutritional Status		
Body weight by history	86 kg	52 kg
Height	157 cm	160 cm
BMI	34.8 kg/m²	21.7 kg/m²
Interpretation	Class II obesity	Normal body weight
Final nutritional status at discharge	Class II obesity	Moderate malnutrition
Energy requirement based on Xie	2565 kkal (40 kcal/kg adjusted body weight)	2958 kkal (56 kcal/kg body weight)
Average intake during monitoring		
Energy (kcal)	1924	1644
Energy (kcal/kg body weight)	30	33
Protein (g/kg body weight)	1.3	1.5
Average bed-scale body weight during monitoring (kg)	88.5	51.1
Average total FAB-CC score	23	11
Excisional debridement to STSG procedures	3 times	3 times
Length of stay	18 days	29 days
Complications	None	Pan drug resistant infection, septic shock, step-up to ICU, bilateral plantar flexion contractures

Table 2. Laboratorium findings

	Case 1	Case 2
Hemoglobin (g/dL)	11,1 (9,6-18,6)[a]	10,5 (9,2-15,7) [a]
NLR	3,88 (1,17-3,97)[a]	18,6 (7,3-46,14) [a]
PCT (ng/mL)	13,5	3,9 (0,2-1,7) [a]
Albumin (g/dL)	2,39 (2,28-2,67)[a]	2,2 (1,75-2,6) [a]
Laktat (mmol/L)	4	3,5 (1,8-20,3) [a]

NLR: *Neutrophil to Lymphocyte Ratio*; PCT: Prokalsitonin, [a]median (minimum–maximum)

The Functional Assessment for Burns–Critical Care (FAB-CC) is an instrument used to assess functional capacity with good diagnostic performance.[12,15] In addition to hypermetabolism, systemic inflammatory responses in burn injuries also contribute to muscle breakdown through increased levels of cortisol and glucagon.[11,16] In both cases presented, inflammatory responses were evident, as indicated by elevated laboratory

parameters such as the neutrophil-to-lymphocyte ratio (NLR), procalcitonin, and C-reactive protein (CRP).

All patients demonstrated increases in daily energy and protein intake, which were associated with improvements in FAB-CC scores and functional capacity. For example, in Case 1, energy intake increased from 10 kcal/kg adjusted body weight to 42 kcal/kg adjusted body weight, and protein intake increased from 0.9 g/kg adjusted body weight to 1.9 g/kg adjusted body weight, concomitant with an improvement in the total FAB-CC score from 7 to 30 (full independence). In Case 2, progressive increases in energy intake (from 10 kcal/kg body weight to a peak of 60 kcal/kg body weight) and protein intake (from 0.4 g/kg body weight to 2.5 g/kg body weight) were accompanied by an increase in the total FAB-CC score from 3 to a maximum of 23. A total FAB-CC score of 23 indicates that the patient was not yet fully independent but had achieved relatively good physical function and was above the threshold for high risk of dependency (≥10).

All patients showed improvement in total FAB-CC scores in parallel with increasing daily nutritional intake, despite worsening inflammation, indicating the important role of adequate daily energy and protein intake in maintaining and improving functional capacity in burn injury patients. Nevertheless, factors beyond nutritional intake also influence recovery. Improvement in functional capacity in burn injury patients is determined by the interaction of patient-related factors (advanced age, sex, comorbidities, baseline nutritional status), burn injury severity and distribution, the clinical course in the intensive care unit, adequacy of energy and protein intake to prevent muscle loss, and the intensity and timing of physical rehabilitation programs. In addition, psychological factors and social support, including access to rehabilitation services, play a major role in the successful recovery of function and independence.[17,18]

The administration of high-protein formulas in burn patients is a crucial component of care to optimize healing and improve clinical outcomes. Burns cause significant metabolic stress, leading to increased protein catabolism, loss of muscle mass, and impaired immune function. High-protein formulas supply essential amino acids required for protein synthesis, support tissue repair, preserve muscle mass, and enhance immune function. Adequate protein intake has been shown to accelerate wound healing, reduce infectious complications, and shorten hospital length of stay in burn patients. Therefore, high-protein nutritional support represents an important nutritional intervention that contributes to recovery and rehabilitation in burn patients.[19,20]

A systematic review by Hampton et al. demonstrated that energy intake of 30–35 kcal/kg body weight combined with protein intake of 1.3–1.5 g/kg body weight significantly improved functional capacity, particularly muscle strength, in patients with severe burns. These findings have important practical implications for clinical practice, especially in the nutritional management of burn patients.[20,21] Energy provision of 25–48 kcal/kg body weight and protein intake of 1.2–2.2 g/kg body weight, as applied in both cases, may be considered as part of a care strategy to enhance functional capacity. Appropriate nutritional support can facilitate wound healing, prevent muscle mass loss, and improve patients' quality of life. Further studies are required to confirm these findings.

Study limitations

This study is limited by the absence of a control group and the lack of statistical analysis examining the association between energy and protein intake and functional recovery.

Interpretation of the findings is further constrained by important confounders, including sepsis, repeated debridement, and duration of ICU stay, all of which may affect both nutritional intake and functional outcomes. Further prospective studies with more rigorous methodology are needed to define the independent contribution of nutritional adequacy to functional improvement in patients with burn injury.

Conclusion

In conclusion, observations from both cases suggest that adequate energy and protein intake during nutritional care may contribute to improved functional capacity in patients with burn injuries. Across the observation period, mean energy intake of 30–33 kcal/kg/day and protein intake of 1.3–1.5 g/kg/day were accompanied by progressive improvement in functional status, as reflected by increases in FAB-CC scores from 0 to 23–30. However, this improvement in functional capacity cannot be attributed solely to increased energy and protein intake. It was also likely influenced by multidisciplinary management, including debridement performed by the plastic surgery team, infection control by the plastic surgery and infectious and tropical disease teams, adequate and regular rehabilitation provided by the rehabilitation medicine team, and supportive care from nursing staff and psychiatry in assisting the patient with daily activities. Although these findings should be interpreted cautiously given the descriptive nature of the report and the presence of clinical confounders, they support the potential importance of nutritional adequacy as part of a comprehensive multidisciplinary approach to promote functional recovery in burn patients.

Conflict of interest

The authors declared no conflict of interest regarding this article.

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Author Contributions

MK, WS, ANF: Conceptualization, data acquisition, formal analysis, interpretation of results, drafting the manuscript, and final approval of the version to be published; WS, AW, ANF: Supervision, critical revision of the manuscript, interpretation of data, and final approval of the version to be published; MK,WS: Conception and design of the study, critical revision of the manuscript for important intellectual content, and final approval of the version to be published.

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ORIGINAL PAPER

The association between sedentary behaviour and the risk of type 2 diabetes mellitus among medical students at Syiah Kuala University

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Abstract

Background: Sedentary behaviour is any waking behaviour characterized by an energy expenditure ≤1.5 METs while sitting or reclining posture. Medical students represent a young adult population that is prone to sedentary behaviour. Excessive sedentary behaviour may increase the risk of metabolic diseases, including type 2 diabetes mellitus (T2DM).

Objective: This study aimed to examine the association between sedentary behaviour and the risk of T2DM among medical students at Universitas Syiah Kuala.

Methods: This cross-sectional study involved 260 medical students at Universitas Syiah Kuala, selected using stratified random sampling, and was conducted from September 22 to October 17, 2025, at the Faculty of Medicine, Universitas Syiah Kuala. Sedentary behaviour was assessed using the Sedentary Behaviour Questionnaire (SBQ), while the risk of T2DM was evaluated using the Finnish Diabetes Risk Score (FINDRISC) which incorporates anthropometric measures including body mass index (BMI) and waist circumference.. Statistical analysis was performed using the Spearman rank correlation test with a significance level of $p < 0.05$.

Results: The majority of respondents had a high level of sedentary behaviour (44.6%). Most participants were classified as having a low risk of T2DM (48.5%), BMI < 25 kg/m² (53.5%), normal waist circumference (60.4%), and no family history of diabetes mellitus (45.4%). There was a statistically significant association between sedentary behaviour and the risk of T2DM ($p = 0.046$), with a very weak correlation strength ($r = 0.124$).

Conclusion: A statistically significant but very weak association between sedentary behaviour and the risk of T2DM among medical students at Syiah Kuala University.

Keywords: sedentary behaviour, type 2 diabetes mellitus risk, FINDRISC, medical students, sedentary behaviour questionnaires

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Introduction

Diabetes mellitus (DM) is a metabolic disorder characterized by elevated blood glucose levels resulting from impaired insulin secretion, reduced insulin effectiveness, or a combination of both.[1] Type 2 diabetes mellitus (T2DM) accounts for more than 90% of diabetes cases globally and is associated with high morbidity and mortality due to complications such as cardiovascular disease, nephropathy, retinopathy, neuropathy, and amputations.[2] This condition also imposes a substantial economic burden on individuals and healthcare systems.[3]

According to the IDF Diabetes Atlas (11th edition), an estimated 589 million adults aged 20–79 years live with diabetes, projected to reach 853 million by 2050. Indonesia ranks fifth worldwide, with 20.4 million individuals affected by diabetes, and this number is projected to rise to 28.6 million by 2050.[2] Nationally, the prevalence of DM increased from 10.9% based on the 2018 Basic Health Research (RISKESDAS) to 11.7% according to the 2023 Indonesian Health Survey (SKI). Type 2 diabetes mellitus represents the most common type of diabetes in Indonesia, accounting for 50.2% of all diagnosed diabetes mellitus cases nationwide. In Aceh Province, the proportion of T2DM reaches 54.8%, exceeding the national average.[4] Furthermore, the prevalence of DM in Banda Aceh has increased compared with the provincial average, from 1.7% and 2.4% to 2.28% across all age groups and 2.98% among individuals aged ≥15 years, emphasizing the urgent need for risk factor control in productive age populations.[5]

Type 2 Diabetes Mellitus (T2DM) is a multifactorial disease influenced by various risk factors, including genetic predisposition, obesity, unhealthy dietary patterns, physical inactivity, and sedentary behaviour. One of the major modifiable risk factors is lifestyle, particularly prolonged sedentary behaviour, which has been associated with metabolic dysregulation and increased risk of T2DM.[6] Sedentary behaviour is defined as any waking activity characterized by an energy expenditure ≤1.5 METs while in a sitting or reclining posture such as working at a computer, watching television, or using electronic devices. In this study, sedentary behaviour was measured using the Sedentary Behaviour Questionnaire (SBQ), a standardized and validated instrument that provides detailed information on daily sitting duration across various activities, and total sedentary time was calculated as hours per week based on the accumulation of reported sitting duration.[7] WHO recognises physical inactivity as a major risk factor for noncommunicable diseases and recommends reducing sedentary time and increasing physical activity.[8] In Indonesia, the prevalence of sedentary behaviour among individuals aged ≥10 years increased from 26.1% in 2013 to 33.5% in 2018.[9] Physiologically, prolonged sitting reduces skeletal muscle activity and glucose utilization, increases visceral adiposity, and promotes insulin resistance, ultimately leading to impaired glucose tolerance.[10–12]

Medical students represent a young adult population that is particularly vulnerable to sedentary behaviour despite having adequate health knowledge. High academic workload, prolonged sitting during lectures, and the use of leisure time for passive activities such as watching videos and using electronic devices contribute to extended daily sitting duration.[13–15] In addition to prolonged sitting duration, several studies have reported that sedentary behaviour is often accompanied by unhealthy dietary habits. University students who spend more time in sedentary activities tend to consume snacks and energy-dense foods and exhibit irregular eating patterns, which may further increase the risk of metabolic disturbances. Nevertheless, although dietary factors may contribute to metabolic alterations and an increased risk of type 2 diabetes mellitus, the present study

specifically focuses on sedentary duration as the primary variable of interest.[16–18] Several studies have reported that medical students spend approximately 7–10 hours per day in sedentary activities, with more than 50% classified as having high sedentary levels.[19–22] This population is therefore important to study, as medical students are expected to serve as role models in promoting healthy lifestyles and, in the future, act as agents of change within the community.[23] This issue is further underscored by the increasing trend of T2DM among productive age populations, whereas the disease was previously more common among individuals aged over 45 years.[24,25]

Along with the increasing exposure to sedentary behaviour at a young age, early detection of T2DM risk has become increasingly important, particularly among productive and undiagnosed populations. Indonesia currently ranks third globally in the number of undiagnosed diabetes cases, with approximately 15 million affected adults.[2] In this study, the risk of T2DM was assessed using the Finnish Diabetes Risk Score (FINDRISC), a non-invasive, easy-to-administer, and validated questionnaire designed to predict the risk of developing T2DM within the next ten years in the general population.[26]

The association between sedentary behaviour and the risk of T2DM has been demonstrated in numerous previous studies. Several investigations have reported a significant relationship between sedentary behaviour and increased T2DM risk, with p-values <0.05.[9,27,28] Prolonged sitting habits since adolescence, such as watching television for more than four hours per day, have also been shown to increase the risk of developing T2DM in adulthood.[29] However, most studies have focused on populations already diagnosed with diabetes or older age groups. Research examining the risk of T2DM among productive-age populations, particularly medical students, remains limited, highlighting the need for further investigation in this group.

Based on these considerations, this study aimed to analyze the association between sedentary behaviour and the risk of type 2 diabetes mellitus among medical students at Universitas Syiah Kuala. This study contributes to the existing literature by providing evidence on lifestyle-related determinants of T2DM risk in a young, undiagnosed population and may serve as a scientific basis for promotive and preventive interventions within the academic environment. The findings are expected to benefit educational institutions, healthcare professionals, and policymakers in developing strategies to reduce sedentary behaviour as an early preventive measure against T2DM.

Methods

This study employed a cross-sectional design to analyze the association between sedentary behaviour and the risk of type 2 diabetes mellitus (T2DM) among medical students of the Medical Education Program at Universitas Syiah Kuala. Data collection was conducted from September 22 to October 17, 2025 after obtaining ethical approval from the Ethics Committee of the Faculty of Medicine, Universitas Syiah Kuala (Ethical approval number: 200/EA/FK/2025).

The study population consisted of all active medical students at Universitas Syiah Kuala. The sample was selected using stratified random sampling with cohorts defined by students' year of entry (2022, 2023, and 2024). The population was first divided into strata according to cohort, and the number of participants from each stratum was determined proportionally to its size. Within each stratum, respondents were selected using simple random sampling through a computer-generated randomization process. The

required sample size was calculated using the Slovin formula, resulting in a total of 260 respondents. The inclusion criteria were active medical students from the 2022, 2023, and 2024 cohorts, willingness to participate in the study, and no history of diabetes diagnosed by medical professionals. The exclusion criteria included respondents with severe illnesses that significantly limited daily physical activity, such as cardiovascular disease, stroke, chronic pulmonary disorders, or severe musculoskeletal diseases diagnosed by medical professionals, and those with incomplete questionnaire responses.

Data were collected using the Sedentary Behaviour Questionnaire (SBQ) to assess sedentary behaviour across various daily activities and the Finnish Diabetes Risk Score (FINDRISC) to evaluate the risk of T2DM. Both instruments are standardized, validated, and non-invasive measurement tools. For the SBQ, participants reported the duration of sitting time separately for weekdays and weekend days across multiple sedentary activities. Total sedentary time per week was calculated by multiplying weekday sitting time by five and weekend sitting time by two, then summing the values to obtain total hours per week. Sedentary Behaviour was subsequently categorized into low (<60 hours/week), moderate (≥60 to <81.5 hours/week), and high (≥81.5 hours/week) based on previously established cut-off points.[30] In this study, T2DM risk was classified into five categories according to standard FINDRISC criteria: low (<7), slightly elevated (7–11), moderate (12–14), high (15–20), and very high (>20).[31–33] Univariate analysis was conducted to describe the distribution of respondent characteristics and the categories of each variable. Bivariate analysis was performed using the Spearman rank correlation test with a significance level of $p < 0.05$.

Results

A total of 260 respondents participated in this study. The general characteristics of the respondents are presented in **Table 1**.

Table 1. General characteristics of respondents (n = 260)

Characteristics	Frequency n(%)
Sex	
Male	78(30)
Female	182(70)
Age (years)	
17	2(0.8)
18	15(5.8)
19	81(31.2)
20	85(32.7)
21	56(21.5)
22	17(6.5)
23	2(0.8)
24	2(0.8)
Cohort	
2022	70(26.9)
2023	86(33.1)
2024	104(40)
Body mass index (BMI)	
< 25 kg/m2	139(53.5)
25-27 kg/m2	30(11.5)
> 27 kg/m2	91(35)

Characteristics	Frequency n(%)
Waist circumference	
Female < 80 cm, Male < 90 cm	157(60.4)
Female ≥ 80 cm, Male ≥ 90 cm	103(39.6)
Family history of diabetes mellitus	
No	118(45.4)
Yes : Parents or Siblings	84(32.3)
Yes : Non biological relatives	51(19.6)
Yes : Both (parents/siblings and non biological relatives)	7(2.7)
Sedentary behaviour	
Low	75(28.8)
Moderate	69(26.5)
High	116(44.6)
Risk of type 2 diabetes mellitus	
Low	126(48.5)
Slightly low	91(35)
Moderate	35(13.5)
High	8(3.1)
Very High	0(0)

Table 1 shows that the majority of respondents were female (182 participants, 70%). The most common age group was 20 years (85 participants, 32.7%). Most respondents were from the 2024 cohort (104 participants, 40%). More than half of the respondents had a body mass index (BMI) < 25 kg/m² (139 participants, 53.5%) and normal waist circumference (157 participants, 60.4%). Most respondents had no family history of diabetes mellitus (118 participants, 45.4%). A high level of sedentary behaviour was observed in 116 respondents (44.6%). Regarding the risk of T2DM, nearly half of the respondents were classified as having a low risk (126 participants, 48.5%).

Table 2. Sedentary behaviour levels among medical students at Syiah Kuala University by gender

	Sedentary behaviour			
Sex	**Low n(%)**	**Moderate n(%)**	**High n(%)**	**Total n(%)**
Female	49(26.9)	49(26.9)	84(46.2)	182(100)
Male	26(33.3)	20(25.6)	32(41)	78(100)

The distribution of sedentary behaviour levels according to gender is presented in **Table 2.** Female students had a higher proportion of high sedentary behaviour (84 participants, 46.2%) compared to male students (32 participants, 41%). Overall, female students tended to exhibit higher sedentary behaviour levels than male students.

Table 3. Types of sedentary activities among medical students at Syiah Kuala University

Sedentary Activities	Weekdays (hours/day) Mean (SD)	Weekend (hours/day) Mean (SD)
Watching television/videos	2.95(1.87)	3.61(2.00)
Playing computer/laptop/video games	1.42(1.64)	1.81(1.88)
Sitting while listening to music/radio	1.59(1.66)	1.77(1.76)
Sedentary Activities	**Weekdays (hours/day) Mean (SD)**	**Weekend (hours/day) Mean (SD)**
Sitting while calling/texting/using gadgets	2.17(1.89)	2.13(1.85)
Desk work/computer-based activities	1.74(1.71)	1.38(1.52)
Sitting while reading books/magazines	0.92(1.20)	0.75(1.12)
Playing musical instruments	0.10(0.39)	0.12(0.43)
Arts, crafts, or handicraft activities	0.17(0.49)	0.23(0.65)
Driving/transportation	1.24(1.34)	1.01(1.10)
Total sedentary duration (hours/week)	61.58(34.07)	25.63(13.01)
Total sedentary duration weekdays and weekend(hours/week)	87.22(45.15)	

The types of sedentary activities performed by the respondents on weekdays and weekends are summarized in **Table 3**. The most common sedentary activities on both weekdays and weekends were watching television or videos and using mobile phones for communication or recreational purposes, with an average duration of more than 2 hours/day. Activities with the lowest duration included playing musical instruments and engaging in arts or handicraft activities. These findings indicate that most sedentary time among medical students was spent on screen-based activities.

Table 4. Risk of type 2 diabetes mellitus among medical students at Syiah Kuala University by gender

	Risk of T2DM				
Sex	**Low n(%)**	**Slightly low n(%)**	**Moderate n(%)**	**High n(%)**	**Total n(%)**
Female	96(52.7)	59(32.4)	21(11.5)	6(3.3)	182(100)
Male	30(38.5)	32(41)	14(17.9)	2(2.6)	78(100)

Table 4 presents the distribution of T2DM risk according to gender. Most respondents of both sexes were classified as having a low risk of T2DM. Male students showed a higher proportion in the moderate-risk category (17.9% vs 11.5%), whereas female students showed a slightly higher proportion in the high-risk category (3.3% vs 2.6%).

Table 5 shows Spearman rank correlation analysis revealed a statistically significant association between sedentary behaviour level and the risk of T2DM ($r = 0.124$; 95% CI: 0.017–0.235; $p = 0.046$). Although statistically significant, the strength of the correlation was very weak, indicating minimal clinical or practical relevance in this population. low prevalence of family history of diabetes.

Table 5. Association between Sedentary Behaviour and Risk of Type 2 Diabetes Mellitus

Sedentary Behaviour	*Risk of T2DM*				*r (CI 95%)*	*p-value*
	Low n(%)	Slightly low n(%)	Moderate n(%)	High n(%)		
Low	43(57.3)	21(28)	9(12)	2(2.7)		
Moderate	36(52.2)	21(30.4)	9(13)	3(4.3)	0.124 (0.017-0.235)	0.046
High	47(40.5)	49(42.2)	17(14.7)	3(2.6)		

Discussion

The majority of medical students at Universitas Syiah Kuala were classified as having a high sedentary behaviour (44.6%). This finding indicates that prolonged sitting behaviour is a dominant habit within this population.[14] A study by Annisa et al.,[34] similarly reported that most medical students at Universitas Mulawarman exhibited moderate (88%) and high (6.6%) sedentary behaviours. Lateef et al.,[35] also observed a comparable pattern among medical students in India, where a substantial proportion of students were categorized as having a high sedentary behaviour (22.4%), making them the group with the lowest physical activity levels compared to students from other academic disciplines. These findings are further supported by Deolalikar et al.,[36] who reported that medical students in North India spent more than 7 hours per day sitting. Janampa-Apaza et al.,[13] found that medical students in Peru spent more than 8 hours per day in sedentary activities. Leisure time dominated by passive behaviours, such as screen use and television viewing, further contributes to the accumulation of sedentary behavior. The high sedentary behaviour among medical students is largely attributable to heavy academic workloads, prolonged sitting during lectures, extended study durations, and passive leisure activities such as watching videos or using electronic devices, all of which increase total sitting time and promote sedentary behavior.[13,14]

Based on gender differences, female students tended to have higher sedentary behaviour levels in both moderate and high categories compared to male students. Herreros-Irarrázabal et al.,[19] reported that female medical students in Latin America spent more sedentary time (420 minutes/day) than males (360 minutes/day).[19] Lateef et al.,[27] also found that sedentary behaviour was slightly more prevalent among female students (30.6%) than males (29.7%). Janampa-Apaza et al.,[13] documented that 50.9% of female medical students in Peru spent more than 8 hours per day in sedentary activities. Lower physical activity levels among female students are often associated with motivational and psychosocial factors, including lower self-confidence in performing certain physical activities, safety concerns related to outdoor exercise, and limited access to or comfort with available sports facilities. The accumulation of these barriers contributes to prolonged sedentary behaviour among female students.[37]

This study also provides an overview of the predominant types of sedentary activities. Based on the analysis of 16 items from the Sedentary Behaviour Questionnaire (SBQ), the average total sedentary duration among students reached 87.22 hours per week. Total weekly sedentary time was calculated by multiplying the reported weekday duration by five and weekend duration by two, and then summing both values. Higher durations were observed on weekdays compared to weekends. On weekdays, the most frequently

reported sedentary activities included watching television or videos (2.95 hours/day), sitting while using electronic devices (2.17 hours/day), and documentary activities or computer use (1.74 hours/day), indicating that most sedentary time was associated with screen-based activities and academic demands. A similar pattern was observed on weekends, with sedentary activities dominated by watching television or videos (3.61 hours/day), device use (2.13 hours/day), and playing computer or video games (1.81 hours/day), with a tendency toward increased viewing duration compared to weekdays. Overall, screen-based activities were the most common sedentary behaviors on both weekdays and weekends, with average durations exceeding 2 hours per day. These findings are consistent with those of Vella and Nelson,[38] who reported that university students spent approximately 2 hours per day on screen time (2.0 ± 1.6 hours/day) as part of a total sedentary duration of 8.4–8.7 hours per day. Santoso et al.,[21] also reported similar patterns among medical students at Universitas Udayana, where smartphone use or chatting averaged 238–252 minutes per day (approximately 4 hours/day), along with other screen-based activities such as completing assignments using laptops or computers (136–206 minutes/day), watching DVD or playing video games (82–129 minutes/day), and computer or laptop use (106–118 minutes/day).[21] These patterns indicate that although sedentary behavior is multidimensional, screen-based activities are the primary contributors to high sedentary behaviour among medical students.

The majority of students were classified as having low to moderately low risk of type 2 diabetes mellitus (T2DM) based on FINDRISC scores. Algadheeb et al. similarly reported that most medical students in Riyadh had a low risk of T2DM (98.8%).[39] Sintawati et al.,[31] found that 64.1% of students were in the low-risk category, with only a small proportion classified as high risk (4%). Chamba et al.,[41] reported that 62.5% of medical students at Universidad de Guayaquil were at low risk for T2DM, with no participants categorized as having high or very high risk.

Factors such as young age, lower obesity prevalence, and relatively healthier lifestyles contribute to low T2DM risk scores. The pathological process of T2DM develops progressively and often remains subclinical at younger ages, particularly among individuals under 25–30 years.[42] Additionally, obesity prevalence is generally lower among students, limiting the presence of major T2DM risk factors.[43]

Nevertheless, this study identified a subgroup at risk, with 16.6% of respondents categorized as having moderate to high T2DM risk. This finding indicates variability in metabolic risk among medical students and suggests the accumulation of risk factors such as central obesity, family history of diabetes, and early metabolic changes detected through FINDRISC scores.

Based on gender differences, T2DM risk was slightly higher among female students (3.3%) compared to male students (2.6%). Ajaykumar et al.,[44] reported that most female students were in the low-risk category (44.4%), with a small proportion at moderately increased risk (16.6%) and 1.4% at moderate risk. In contrast, among male students, 34.3% were classified as low risk and 2.5% as moderately increased risk. Mahajan et al. further reported that 69% of female participants were categorized as having moderate risk, substantially higher than males (41%). Higher T2DM risk among females is primarily associated with lower physical activity levels and higher prevalence of central obesity. Approximately 51% of female students reported no physical activity, a markedly higher proportion than males (29%).[43,44] Reduced physical activity negatively affects insulin sensitivity, thereby increasing diabetes risk among female students.[44]

This study demonstrated a statistically significant association between sedentary behaviour and T2DM risk ($p = 0.046$), although the strength of the association was very weak ($r = 0.124$). This indicates that while increased sedentary behavior contributes to higher T2DM risk, its impact remains minimal among medical students. This is reflected in the distribution of results, where most respondents remained in the low-risk category despite having moderate to high sedentary behaviour. These findings are consistent with those of Julliyana et al.,[27] who also reported a significant but weak association between sedentary behaviour and diabetes risk among high school students in Sumedang.[27] Scandiffio and Janssen reported that certain types of sedentary behavior, such as watching television for more than 4 hours per day, have a stronger impact on future T2DM risk, suggesting that not all sedentary behaviors exert equal metabolic effects.[10] Physiologically, prolonged sitting reduces skeletal muscle contractions, leading to decreased glucose utilization. Skeletal muscle is the primary site of glucose uptake, therefore, reduced muscle activity diminishes glucose clearance from circulation. This condition also decreases lipoprotein lipase activity and inhibits GLUT-4 translocation to the muscle cell membrane, both of which play critical roles in glucose metabolism. The accumulation of these mechanisms may induce insulin resistance and increase the risk of T2DM later in life.[10]

Cohort findings by Bennett et al.,[45] demonstrated a 13% increase in diabetes risk for each additional hour of sedentary time however, this effect was attenuated after adjusting for body mass index (BMI), highlighting adiposity as an important mediator. Sedentary behaviour promotes visceral fat accumulation and low-grade inflammation, which reduce insulin sensitivity and disrupt metabolic regulation.[11] Stronger associations between sedentary behaviour and diabetes have been reported in older or metabolically high-risk populations, such as in studies by Ambarita et al.,[9] among patients diagnosed with diabetes and Bialangi et al.[28] among individuals at high risk for prediabetes ($p < 0.001$).

Conversely, studies such as those conducted in Hisayama, Nurdina, and Meisinger cohorts reported no association between sedentary behaviour and T2DM incidence among healthy adult populations. These findings suggest that the metabolic impact of sedentary behavior is highly dependent on baseline metabolic status, particularly BMI and insulin sensitivity. When confounding factors such as obesity, dietary patterns, and family history are controlled, the association between sedentary behaviour and diabetes risk often becomes weak or non-significant.[46–48]

The literature supports that sedentary behaviour contributes to T2DM risk. however, its effect is strongly influenced by BMI, genetic predisposition, and baseline metabolic health. Among young and generally healthy populations, the association tends to be weak or absent, whereas in older or metabolically high-risk populations, the relationship becomes more pronounced.

In this study, the weak association observed may be explained by the characteristics of the respondents, most of whom had normal BMI, were of young age, had low prevalence of family history of diabetes, and still engaged in at least 30 minutes of physical activity. Physical activity has been shown to reduce diabetes risk by nearly 50% in certain populations and may offset much of the negative impact of sedentary behavior.[45] The majority of respondents were aged 19–21 years, an age group that typically maintains good insulin sensitivity and optimal metabolic reserve. In young adults, diabetes risk remains low despite relatively high sedentary behavior due to preserved pancreatic β-cell function and insulin responsiveness. However, persistent sedentary behavior over time may gradually impair insulin sensitivity and β-cell

function.[49] Additionally, most respondents had normal BMI, which serves as a protective factor. BMI is a key mediator in the relationship between sedentary time and diabetes risk, as individuals with normal BMI tend to maintain more stable glucose regulation, reducing the immediate impact of sedentary behavior.[49,50] Studies suggest that approximately 60–67% of the association between sedentary behavior and diabetes risk is mediated by BMI.[45]

This study reinforces the understanding that sedentary behaviour is associated with increased T2DM risk. However, among young populations with generally good metabolic health, the effect appears to be relatively minimal due to protective factors such as younger age, normal BMI and waist circumference, adequate physical activity, and a low prevalence of family history of diabetes. Nevertheless, sedentary behaviour should still be considered a long-term risk factor, as its impact may become more pronounced with advancing age and declining insulin sensitivity. These findings emphasize the importance of intermediary variables such as BMI, waist circumference, physical activity level, and genetic factors in strengthening or attenuating the relationship between sedentary behaviour and T2DM risk. Medical students represent a transitional population that already shows early risk indicators yet still has substantial opportunities for prevention through reducing sedentary behavior and increasing physical activity. If sedentary habits persist into adulthood, the risk of metabolic disorders may increase in parallel with declining insulin sensitivity and the accumulation of additional risk factors.

Conclusion

The majority of medical students at Universitas Syiah Kuala were classified as having a high sedentary behaviour (44.6%). Most respondents were categorized as having a low risk of type 2 diabetes mellitus (T2DM) (48.5%), while 16.6% were classified as having moderate to high T2DM risk. Female students showed a slightly higher proportion in the high-risk category compared to male students (3.3% vs 2.6%). The average daily sedentary duration among respondents was 87.22 hours per week.

A statistically significant but very weak correlation was observed between sedentary behaviour and T2DM risk among medical students at Universitas Syiah Kuala ($r = 0.124$; $p = 0.046$), indicating minimal practical significance in this population.

Conflict of interest

The authors declared no conflict of interest regarding this article.

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Author Contributions

JHM: Conceptualization, data acquisition, formal analysis, interpretation of results, drafting the manuscript, and project administration; TM: Conception and design of the study, supervision, interpretation of data, critical revision of the manuscript for important intellectual content, and final approval of the version to be published; HM: Conception and design of the study, supervision, interpretation of data, critical revision of the manuscript for important intellectual content, and final approval of the version to be published; DS: supervision, interpretation of data, conception and design of the study, critical revision of the manuscript for important intellectual content, and final approval of the version to be published; H: supervision, interpretation of data, conception and design of the study, critical revision of the manuscript for important intellectual content, and final approval of the version to be published.

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ORIGINAL PAPER

Complementary feeding practices and stunting among children aged 6-24 months in Banda Aceh, Indonesia

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Abstract

Background: Stunting is a significant nutritional issue in Indonesia, reflecting chronic malnutrition. Key factors influencing stunting incidence include inaccuracies in complementary feeding, such as timing, texture, portion size, frequency, and variety of food.

Objective: This study aims to examine complementary feeding practices and stunting among children aged 6-24 Months in Banda Aceh, Indonesia.

Methods: This cross-sectional study was conducted in 4 public health centers with the highest stunting prevalence. A total of 105 respondents were selected using proportional random sampling. Data were collected through interviews using a questionnaire on complementary feeding practices and the Individual Dietary Diversity Score (IDDS) and anthropometric measurements from maternal and child health (KIA) books. Data were analysed using the Spearman-Rank test.

Results: The results showed that most children were aged 12–24 months (64.8%) and male (50.5%). The majority of mothers provided complementary foods at the appropriate age (91.4%), with appropriate texture (96.2%), appropriate frequency (55.2%), appropriate portion (66.7%), and moderate food diversity (47.6%). Spearman correlation analysis showed significant associations between stunting and texture (p=0.029; r=−0.213), portion (p=0.000; r=−0.499), frequency (p=0.000; r=−0.420), and food variety (p=0.000; r=−0.715). In this study, the time of first complementary feeding was the only factor that was not significantly related to stunting (p=0.580; r=−0.055).

Conclusion: In conclusion, texture, portion size, feeding frequency, and, especially, dietary variety are significantly associated with stunting. Education on correct complementary feeding practices is needed to prevent stunting.

Keywords: children 6-24 months, complementary feeding, individual dietary diversity score (IDDS), stunting

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Introduction

Child nutrition remains a major issue in the population structure. Stunting is a nutritional problem that arises when children receive insufficient nutrition. Stunting is a nutritional status assessed by height or length relative to age, indicated by a Z-Score below -2 standard deviations (SD).[1,2,3] Based on the results of the 2022 Indonesian Nutritional Status Survey (SSGI), the stunting rate in Indonesia remains quite high at 21.6%.[4] Factors directly related to stunting include food intake and infectious diseases. Indirect factors include family food security, parenting patterns, health services, and environmental sanitation.[5,6]

The golden period, namely, the first 1000 days of life, from the fetal period to the child's second birthday, is characterized by rapid growth and development.[7,8] The prevalence of stunting based on the age group of the 2022 SSGI results, namely the risk of stunting increased by 1.6 times from the age group of 6-11 months, namely 13.7%, to the age group of 12-23 months, namely 22.4%.[4] At this age, child growth is supported by the provision of complementary foods. This shows involvement in providing complementary foods from the age of 6 months, including age suitability, frequency, quantity, texture, and variety of foods.[1,5]

Complementary foods are highly nutritious foods and drinks, other than breast milk, given to babies to meet their nutritional needs.[1] Research by Resti et al.[9] states that children who are given appropriate complementary foods have a 91.7% lower chance of experiencing stunting compared to children who do not receive appropriate complementary foods. In research by Virginia et al.[10], it is stated that there is a relationship between the frequency, texture, amount, and age of first giving complementary foods with the incidence of stunting in children aged 6-24 months in Leyangan Village, East Ungaran District, Semarang Regency.

According to the Indonesian Health Survey (SKI) in Aceh province, the prevalence of stunting in 2023 was 29.8%.[11] The prevalence of stunting in Banda Aceh City in 2023 was 21.7%,[12] and the Community Health Centers with the highest prevalence of stunting were Jeulingke Community Health Center at 13.1%, Baiturrahman Community Health Center at 9.9%, Lampaseh City Community Health Center at 8.8%, and Meuraxa Community Health Center at 8.7%.[13] Based on the description above, the researcher is interested in examining the relationship between complementary feeding practices and the incidence of stunting among children aged 6-24 months at the Banda Aceh City Community Health Center.

Methods

This study used a cross-sectional approach. It was conducted at four community health centers with the highest stunting prevalence in Banda Aceh: Jeulingke Community Health Center, Baiturrahman Community Health Center, Lampaseh Kota Community Health Center, and Meuraxa Community Health Center. The study was conducted from August to September 2025. The population consisted of 1,269 mothers with children aged 6-24 months. The sampling technique used was proportional random sampling, with 105 respondents. All research procedures received ethical clearance (No. 100/EA/FK/2025) from the Ethics Committee of the Faculty of Medicine, Syiah Kuala University, and adhered to the principles of confidentiality, informed consent, and the protection of research participants.

Inclusion criteria were mothers/caregivers who were willing to participate, resided at the four community health centers, and brought their KIA (Child Health Information) booklets. Exclusion criteria included children with congenital abnormalities, chronic illnesses, a history of recurrent infections, premature birth, and low birth weight. The instruments used were a questionnaire containing respondent identity data and a questionnaire on complementary feeding practices compiled based on the WHO (2005) Guiding Principles for Feeding Non-Breastfed Children 6–24 Months of Age.[14] This questionnaire included questions about the age at which complementary feeding was first introduced, as well as texture, portion, and frequency, which were completed by the mother/guardian by selecting the answer that best matched the child's condition. To measure the diversity of complementary feeding and the Individual Dietary Diversity Score (IDDS) questionnaire was used, developed by the Food and Nutrition Technical Assistance Project (FANTA, 2006).[15] This instrument uses a food consumption recall method for the last 24 hours to identify the types of food consumed and assess the level of diversity of respondents' food intake. The assessment covers 7 food categories, namely cereals, nuts, animal products, eggs, dairy products and their derivatives, vegetables, and fruits that are sources of vitamin A, and other fruits and vegetables. Meanwhile, the instrument for measuring stunting incidence in children was body length-for-age (PB/U), obtained through child growth and development examinations conducted at the Community Health Center or Integrated Health Post, as shown in the KIA book. Univariate analysis used a frequency distribution table, and bivariate analysis used the Spearman rank correlation test to determine the strength of the relationship.

Results

Based on the study conducted among 105 respondents, the results are presented in **Table 1**. Based on **Table 1**, most of the subjects were in the 12-24 months age group (68 respondents, 64.7%), and 53 respondents (50.5%) were male. For maternal characteristics, the majority of mothers were aged 20-35 years, as many as 84 respondents (80%), with the majority of respondents working as housewives as many as 88 (83.8%), and the mother's last education was mostly senior high school as many as 49 respondents (46.7%).

Table 1. General characteristics of respondents

Characteristics	Frequency (n) = 105	Percentage (%)
Child's age (Months)		
6-8	11	10.5
9-11	26	24.8
12-24	68	64.8
Sex		
Male	53	50.5
Female	52	49.5
Mother's age		
<20 years	0	0
20-35 years	84	80
>35 years	21	20
Mother's occupation		
Housewife	88	83.8

Characteristics	Frequency (n) = 105	Percentage (%)
Employee	10	9.5
Self-employed	7	6.7
Mother's Education		
Elementary school	0	0
Junior high school	11	10.5
Senior high school	49	46.7
Diploma/Bachelor's degree or higher	45	42.9

Table 2. Stunting incidents and complementary feeding practices

Category	Frequency (n) = 105	Percentage (%)
Stunting status		
Length-for-Age (LAZ)		
Severely stunted	6	5.7
Stunted	43	41
Normal	55	52.3
Tall	1	1
Stunting classification		
Not stunted	56	53.3
Stunted	49	46.7
Complementary feeding practices		
Age at first introduction		
< 6 months	9	8.6
≥ 6 months	96	91.4
Texture		
Inappropriate	4	3.8
Appropriate	101	96.2
Feeding frequency		
Inappropriate	58	55.2
Appropriate	47	44.8
Portion size		
Inappropriate	70	66.7
Appropriate	35	33.3
Dietary diversity		
Low (≤ 3)	17	16.2
Moderate (4-5)	50	47.6
High (≥ 6-7)	38	36.2

Based on **Table 2** above, among the PB/U, 55 respondents (52.4%) are in the normal group, and, based on stunting incidence, 49 respondents (46.7%) are categorized as stunting. In the practice of providing complementary feeding to children aged 6-24 months based on the age of the first time providing complementary feeding as many as 96 respondents (91.4%) were given at the age of ≥6 months, the texture of providing complementary feeding as many as 101 respondents (96.2%) received food textures appropriate to their age, the frequency of providing complementary feeding that is not appropriate for their age is 58 respondents (55.2%), the portion of providing complementary feeding that is not appropriate for their age is 70 respondents (66.7%). Based on the diversity of complementary feeding, the moderate group has the largest number, namely 50 respondents (47.6%).

Table 3. Association between complementary feeding practices and stunting

	Stunting Classification				Total		p-value	r
	Not Stunted		Stunted					
	n	%	n	%	n	%		
Age at first introduction of complementary feeding								
Inappropriate	4	44,4	5	55,6	9	100		
Appropriate	52	54,2	44	45,8	96	100	0,580	-0,055
Texture of complementary feeding								
Inappropriate	0	0,0	4	100	4	100		
Appropriate	56	55,5	45	44,5	101	100	0.029	-0.213
Portion size of complementary feeding								
Inappropriate	25	35,7	45	64,3	70	100		
Appropriate	31	88,6	4	11,4	35	100	0.000	-0.499
Feeding frequency of complementary feeding								
Inappropriate	20	34,5	38	65,5	58	100		
Appropriate	36	76,6	11	23,4	47	100	0.000	-0.420
Dietary diversity of complementary feeding								
Low	0	0	17	100	17	100		
Moderate	19	38	31	62	50	100	0.000	-0.715
High	37	97,4	1	2,6	38	100		

Based on **Table 3**, 5 respondents (55.6%) experienced stunting when complementary feeding was not provided at the appropriate time (<6 months). After statistical analysis using the Spearman rank test, a p-value of 0.580 (p>0.05) and a correlation coefficient of r = -0.055 were obtained. These results indicate no relationship between the age at which complementary feeding was first given and the incidence of stunting.

Four respondents (100%) experienced stunting when the texture of complementary feeding was inappropriate for their age. After analysis using the Spearman test, a p-value of 0.029 (p<0.05) and a correlation coefficient of r = -0.213 were obtained. These results indicate a significant relationship between the texture of complementary feeding and the incidence of stunting. A negative relationship means that when one variable increases, the other variable tends to decrease. This means that the more appropriate the texture of complementary feeding given to the child's age stage, the lower the incidence of stunting tends to be.

Forty-five respondents (64.3%) reported stunting in children whose complementary feeding portions were not age-appropriate. After analysis using the Spearman test, a p-value of 0.000 (p<0.05) and a correlation coefficient of r = -0.499 were obtained. These results indicate a significant relationship between the portion of complementary feeding provided and the incidence of stunting. The correlation is moderate, meaning that the more appropriate or sufficient the complementary feeding, the lower the incidence of stunting.

Thirty-eight respondents (65.5%) reported stunting in children whose complementary feeding frequency was not age-appropriate. After analysis using the Spearman test, a significance value of p = 0.000 (p <0.05) and a correlation coefficient of r = -0.420 were obtained. These results indicate a significant relationship between the frequency of complementary feeding and the incidence of stunting. The correlation value for the

negative relationship is moderate, indicating that the more appropriate or frequent the provision of complementary feeding is to the child's age needs, the lower the incidence of stunting tends to be.

Lastly, 17 respondents (100%) in the low group experienced stunting and used a variety of complementary feeding supplements. After analysis using the Spearman test, a p-value of 0.000 ($p<0.05$) and a correlation coefficient of $r = -0.715$ were obtained. These results indicate a significant relationship between the diversity of complementary feeding and the incidence of stunting. The correlation value of the negative relationship is very strong. The direction of the negative correlation indicates that the higher the level of food diversity consumed by children, the lower the incidence of stunting tends to be.

Discussion

Stunting

Table 2 shows that 56 children aged 6-24 months (the majority) did not experience stunting. However, stunting among children aged 6-24 months was quite high, with 49 respondents (46.7%). This finding aligns with research by Ayuningtyas[16] (2022), which found that 81.9% of children did not experience stunting, while the remaining 18.1% did. Stunting is a form of chronic malnutrition influenced by various factors and can persist across generations. Stunting is caused by two factors: direct and indirect.[17,18] Direct factors that influence stunting include nutritional intake and infectious diseases such as worms, acute respiratory infections (ARI), and diarrhea. Indirect factors include family food availability, parenting patterns, environmental sanitation, and health services.[19,20] These indirect factors impact nutritional intake and the health status of mothers and children. Interventions aimed at addressing these indirect factors are expected to prevent nutritional problems.[21]

Stunting, also known as chronic malnutrition, occurs when a child experiences stunted growth, resulting in a height that is not appropriate for their age. Stunting not only affects physical development but also has long-term impacts on cognitive function, learning ability, and productivity levels in adulthood.[22,23] In Indonesia, short stature in children is often considered hereditary. This misperception is one of the obstacles to efforts to reduce stunting rates.[24]

Association between complementary feeding practices and stunting

This study aimed to analyze the relationship between complementary feeding practices and stunting in children aged 6-24 months in Banda Aceh, Indonesia. The results showed a correlation between complementary feeding texture, portion size, frequency, and variety, and stunting. However, the age at which complementary feeding was first introduced was not significantly associated with age at weaning.

The statistical test results showed a p-value of 0.580 ($p>0.05$) and an r-value of -0.055, indicating no relationship between the age of first introduction of complementary foods and the incidence of stunting in children aged 6-24 months. This indicates that providing complementary foods early (<6 months) or on time (≥6 months) does not significantly affect the incidence of stunting in the respondents of this study. However, children who received complementary foods too early had a higher stunting rate (55.6%) than those

given complementary foods according to age (45.8%). This indicates a tendency that providing complementary foods too early can increase the risk of stunting.

Physiologically, children who are given complementary foods before 6 months of age tend to have immature digestive systems, which can make them unable to digest foods other than breast milk properly. This is due to immature digestive enzymes, increased intestinal permeability, and suboptimal immune function of the gastrointestinal mucosa. Introducing complementary foods too early can impair nutrient absorption, increase the risk of diarrhea and gastrointestinal infections, and reduce immunity, all of which can affect a child's growth and development.[25,26,27]

This finding is consistent with Wangiyana's[28] (2020) research, which found that the age at which complementary foods were introduced was unrelated to stunting (p=0.854). However, this result differs from research by Himawati et al.[29] (2022), which showed that the time of first introduction of complementary foods was related to the incidence of stunting (p=0.012). These differences in results may be due to several factors. First, the difference in sample size: this study included 105 respondents, while Himawati's included 52. This study's larger sample size allows for more representative results. Second, differences in statistical analysis methods: this study used the Spearman rank test to assess the strength of the relationship, while Himawati's study used the chi-square test, which only assesses the presence or absence of a relationship. Third, differences in research locations: this study was conducted in an urban area that provides more adequate access to health and education services than rural areas.

Furthermore, the results showed that food texture, portion, frequency, and diversity were more strongly related than the age at which complementary feeding was first introduced. This suggests that the adequacy and quality of nutrient intake after the introduction of complementary feeding are more important in determining a child's growth and development. Research by Hasanah et al.[30] (2020) explains that the incidence of stunting is a multifactorial condition; apart from the age of giving complementary feeding, other factors such as the quality and diversity of food, frequency of giving, maternal nutritional status, and the family's socio-economic conditions also play a role in increasing the risk of stunting.

This study found a significant correlation between the texture of complementary foods and stunting (p=0.029 and r=-0.213). The negative correlation indicates that the more inappropriate the texture of the food given to the child's age, the higher the risk of stunting. A child's digestive abilities develop along with their age. Children who are frequently given complementary foods with a texture that is too runny have a higher risk of experiencing energy and protein deficiencies due to the low nutrient density in each serving. Providing complementary foods with an appropriate texture not only ensures that nutritional needs are met but also plays a role in stimulating the development of a child's eating skills, such as oral motor coordination, chewing ability, and the gradual swallowing process.[25,31]

Furthermore, this study showed a significant relationship between complementary feeding portions and stunting (p=0.000, r=-0.499). The negative correlation value indicates that the more inappropriate the portion of food given to a child, the greater the risk of stunting. Inappropriate or insufficient food portions can lead to chronic energy and protein deficiencies, which hinder a child's growth. Conversely, portions appropriate to a child's age and needs will help ensure adequate intake of macronutrients (carbohydrates, protein, fat) and micronutrients (Fe, Zinc, vitamin A, and other minerals), thereby supporting optimal growth and physical development.[32,33] These results align with

Wahyuni's[34] (2023) study, which found a relationship between adequate complementary feeding and stunting status, with a p-value of 0.037.

This study also found that the frequency of complementary feeding was significantly associated with stunting (p=0.000, r=-0.420). The negative correlation value indicates that the more irregular the frequency of complementary feeding, the higher the risk of stunting. Children who receive complementary feeding less frequently than recommended are at risk of experiencing a chronic energy deficit that can inhibit child growth, which can lead to chronic malnutrition, which is at high risk of stunting.[35] These results also align with Wangiyana's[28] (2020) research, which found a significant relationship between the frequency of complementary feeding and the incidence of stunting, with a p-value of 0.047.

The frequency of giving complementary food should be adjusted to the growth and development stages of children aged 6-24 months, namely, 6-8 months receive complementary food 2-3 times a day, 9-11 months and 12-24 months receive complementary food 3-4 times a day, each age group is given additional snacks or nutritious snacks 1-2 times a day.[31] The frequency of complementary food for children should be as often as possible because children can only consume food little by little, while their energy and nutritional needs must still be met. A sufficient, or even optimal, frequency of providing complementary foods will help ensure adequate energy, protein, and important micronutrient intake, in line with the physiological needs of children at each stage of their development.[35,36]

The variable with the strongest relationship with stunting in this study was complementary foods diversity (p=0.000, r=-0.715). The strong negative correlation indicates that the greater the diversity of the food provided, the lower the risk of stunting in children. Children who receive only monotonous or carbohydrate-rich foods are at increased risk of micronutrient deficiencies, which can inhibit growth hormone synthesis and tissue formation, thereby increasing the risk of stunting.[37] According to the WHO, complementary feeding diversity is defined as the variety of foods provided to children aged 6-24 months, consisting of staple foods, side dishes, vegetables, and fruits. This variety of foods is measured by the number of food groups consumed by children over 24 hours.[25,33] World health organization (WHO) recommends that children consume at least 4 types of foods from 7 food categories: cereals, nuts, animal products, eggs, dairy products and their derivatives, vegetables, and other fruits and vegetables, which are sources of vitamin A. Providing a variety of foods is highly effective in overcoming malnutrition in children.[33,38]

These results align with research by Prasetyo et al.[39] (2023) in Batur Village, which found a significant relationship between dietary diversity and nutritional status (height/age), with a p-value of <0.001 and a correlation coefficient of r=0.618. This finding aligns with research in Indonesia (based on data from the 2014-2015 Indonesia Family Life Survey), which showed that dietary diversity is significantly associated with stunting. The types of food significantly associated with stunting are meat, eggs, milk, and dairy products, as well as vegetables and fruit as sources of vitamin A.[40]

The diversity of food as a dominant factor in preventing stunting in this study is also relevant to local conditions in Banda Aceh, a coastal area with abundant availability of animal food sources, especially sea fish such as tuna, mackerel, and tuna, which contain high protein sources and important micronutrients such as iron, zinc, and omega-3. In addition, the community has access to other foods, such as eggs, chicken, beef, nuts, vegetables, and local fruits, that support children's nutritional needs. The availability of

diverse food sources theoretically provides families with a high opportunity to prepare balanced, nutritious meals for children.[41,42]

However, the results of this study indicate that although local food sources are available, the diversity of food provided to children is not optimal. This indicates that the problem of stunting in this region is not caused by limited access to food but is influenced by factors such as mothers' levels of education and knowledge, maternal occupation, economic conditions, and socio-cultural values. Mothers with higher education and adequate nutritional knowledge tend to understand the importance of food variety and can adjust their macro- and micronutrient intake to meet their needs properly.[43,44] Economic limitations and low levels of education often lead to monotonous, unvaried complementary feeding, which can lead to deficiencies in essential nutrients and increase the risk of stunting. In addition, maternal occupation can affect the time and attention devoted to preparing food. At the same time, cultural habits and family traditions passed down from generation to generation can limit the variety of food ingredients provided.[45,46] This condition shows that the availability of food sources alone is not enough to prevent stunting without the practice of providing a diverse, nutritionally balanced diet.

Thus, the results of this study indicate that stunting prevention efforts in Banda Aceh need to focus on increasing the diversity of food provided to children by utilizing available local food sources and educating mothers and families about the importance of providing a diverse and nutritionally balanced diet to support child growth and prevent the risk of stunting.

This study has limitations because dietary diversity was assessed using the IDDS score, which relies on interviews with mothers/guardians and may be subject to recall bias. Furthermore, the questionnaire counted only the number of food groups consumed, without considering portion sizes. Therefore, it is possible that subjects consumed a diverse diet, but not in sufficient quantities.

Conclusion

Based on the research results, it can be concluded that there is a relationship between the texture, portion, frequency, and diversity of complementary feeding and the incidence of stunting among children aged 6-24 months in Banda Aceh, Indonesia. However, the age at which complementary feeding was first introduced was not associated with stunting. Future studies are recommended to include socioeconomic factors and maternal characteristics, and to analyse energy intake, to provide a more comprehensive understanding of stunting determinants.

Conflict of interest

The authors declared no conflict of interest regarding this article.

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Author Contributions

NM: contributed to conceptualization, study design, data collection, formal analysis, interpretation of the findings, and drafting of the manuscript. MS: contributed to supervision, and methodological guidance. HN: contributed to validation of the data, interpretation of the findings, and critical revision of the manuscript for important intellectual content. BT: contributed to academic supervision and substantial revision of the manuscript. DA: contributed to methodological support, critical review, and final approval of the manuscript for publication. All authors have read and approved the final version of the manuscript.

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ORIGINAL ARTICLE

Paradoxical rise in interleukin-6 following brown rice intake: A postprandial study in sedentary workers

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Abstract

Background: Brown rice is thought to have anti-inflammatory effects due to its high dietary fiber and phenolic content; however, evidence in sedentary populations is limited. IL-6 is a key pleiotropic cytokine responsive to postprandial inflammation.

Objective: This study compared postprandial IL-6 levels after brown vs. white rice consumption in sedentary workers.

Methods: In this open-label, parallel-group trial, 28 normoweight participants (22 women, 6 men) consumed 150 g of rice, 60 g of fried eggs, and 70 g of tofu stew. Nutritional composition was determined from available sources, with fat content of brown rice (2.4 g/100 g) obtained from the manufacturer's laboratory report and that of white rice (0.5 g/100 g) from published data. Participants were randomized by gender into brown rice (n=13, age 30.15 ± 6.71) and a white rice groups (n=15, age 27 [23-48]). IL-6 levels were measured at baseline (10-hour fast) and 4 hours post-meal. Previous-day intake (24-hour food recall) and physical activity (IPAQ-SF) were recorded. Non-parametric tests were applied.

Results: Participants averaged 321.5 ± 181.2 METs. Despite higher fat content in brown rice, intake did not differ significantly between groups. IL-6 changes were not statistically significant (p=0.069). However, the brown rice group showed a numerically higher postprandial IL-6 level, while the control group remained relatively stable.

Conclusions: No significant IL-6 differences were observed, however the paradoxical elevation following brown rice consumption is probably due to subtle influences of nutrient composition or participant characteristics. Further studies with stricter dietary control and biomarkers are warranted.

Keywords: inflammation, interleukin-6, sedentary behavior, whole grains

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Introduction

Rice is a staple food that dominates the global caloric supply, contributing to over 50% of daily energy intake in many populations, including Indonesia.[1,2] Its consumption level in Indonesia reaches 13 – 46 times higher than that of other carbohydrate sources, with an average of 6.7 kg per capita per month in 2021. However, the majority of rice consumed is refined grain, specifically white rice.[3] The milling and polishing processes remove the bran and germ layers, which are rich in fiber and bioactive compounds, resulting in lower fiber content and a higher glycemic index (GI).[4] These characteristics have been associated with increased inflammatory responses.

Several studies have reported that high GI-foods are associated with adverse metabolic and inflammatory responses.[4–6] Such foods can increase postprandial glucose excursions, promote oxidative stress and activate inflammatory signaling. Experimental evidence further suggests that high-GI meals may enhance pro-inflammatory signaling, including NF-kB signaling in mononuclear cells.[5] In this context, white rice, particularly high-GI varieties such as IR-64 (GI = 79)[7], may contribute to an increased risk of inflammation due to its combination of high GI and low fiber content.

Therefore, this situation opens up opportunity for exploring alternative carbohydrate sources that are more beneficial from a health perspective. Brown rice emerges as a promising functional food commodity because it its a whole grain rich in fiber and phenolic compounds.[8] This content contributes to a lower glycemic index and has the potential to reduce the risk of inflammation.[4] As research on brown rice continues to grow, its popularity in society is also steadily increasing, prompting the government to strive to enhance its availability.[3,9]

Despite its huge potential, research on the effects of brown rice consumption in population with sedentary lifestyle remains very limited. Yet, this population is increasingly growing in the modernized era. Based on WHO report, approximately 27.5% of adults over 18 years old globally have sedentary behavior and low physical activity.[10] This phenomenon is becoming more prominent due to the lack of public open spaces, the penetration of television, mobile devices, video players, and the increase in occupational sedentary behaviors, such as office work.[11] This condition is highly relevant in Indonesia, considering 36.3% of the population aged fifteen and over, equivalent to nearly 50 million of people, work as office employees or staff, a group highly vulnerable to a sedentary lifestyle.[12]

This study was conducted to examine the effect of brown rice intake on differences in postprandial inflammatory responses compared to white rice in those population. The postprandial inflammatory response is of particular concern as it is a factor that can underlie the development of insulin resistance and atherosclerosis.[12,13] This response is assessed using the inflammatory marker IL-6, whose levels can increase by 30 - 40% starting from 3 hours after a meal and peak at 6 hours after a meal.[12,14] Abnormal, persistent activation of this response – which can last for more than 16 hours per day – can lead to persistent activation of the immune system and result in chronic low-grade inflammation, thereby increasing the risk of metabolic and cardiovascular diseases.[12,13] Specifically, this study aims to measure the effect of consuming 150 g of rice – either whole grains (brown rice) or refine grains (white rice) - on changes in IL-6 levels among sedentary workers. This portion size was selected to reflect a commonly consumed daily serving.

Methods

Study design and settings

This experimental study employed a parallel, randomized, open-label design. It was conducted from August 2024 to May 2025 in the administrative work environment of the Faculty of Medicine, Universitas Indonesia. Interleukin-6 (IL-6) levels were measured at the Biochemistry Laboratory of the Faculty of Medicine, Universitas Indonesia, Jakarta. Ethical approval was obtained from the Health Research Ethics Committee of the Faculty of Medicine, Universitas Indonesia (No: KET-1779/UN2.F1/ETIK/PPM.00.02/2024).

Participants

The subjects were sedentary administrative staff aged 21–59 years with normal body mass index (BMI: 18.5–22.9 kg/m²) and low physical activity (≤600 MET-min/week) who provided written informed consent. A total of 30 subjects were recruited and randomly allocated into two parallel groups: 15 in the intervention group (brown rice) and 15 in the control group (white rice). Exclusion criteria included pregnancy, breastfeeding, menopause, smoking, alcohol consumption, vegetarian diet, food allergies, chronic diseases (diabetes, cardiovascular disease, cancer), immunosuppressant use, and antioxidant supplement intake within 24 hours.

Procedures

Subjects received meals containing carbohydrates, fats, and proteins. Each meal consisted of 150 g of rice (white or brown), 60 g of omelette, 70 g of tofu stew, and 250 ml of water. The nutritional composition of the meals was calculated using NutriSurvey 2007 software based on the predefined meal design. The nutritional values of the rice used in the analysis were inputted into the software based on available compositional data sources as shown in Table. 1, the control group meal provided 515.2 kcal, 128.8 g carbohydrates, 27.1 g protein, and 12.8 g fat, while the intervention meal provided 473.6 kcal, 118.4 g carbohydrates, 33.2 g protein, and 15.6 g fat.

The nutritional composition of rice was determined from available data sources. The fat content of brown rice (2.4 g/100 g) was obtained from the manufacturer's laboratory analysis report, while that of white rice (0.5 g/100 g) was derived from previously published compositional data.[15]

The white rice used was IR-64 variety, and the brown rice was Aek Sibundong variety, known for its high nutritional and antioxidant/anti-inflammatory properties.

Pre-intervention

After detailed explanations, subjects were randomized into groups. They fasted for 10 hours (21:30–07:30) before intervention, consuming only water. Strenuous exercise was prohibited 48–60 hours prior, and caffeine intake was restricted 24 hours before. Subjects maintained their usual sedentary activities (e.g., sitting, watching TV, computer use) and were provided with an instruction sheet outlining what to do and what to avoid prior to the intervention.

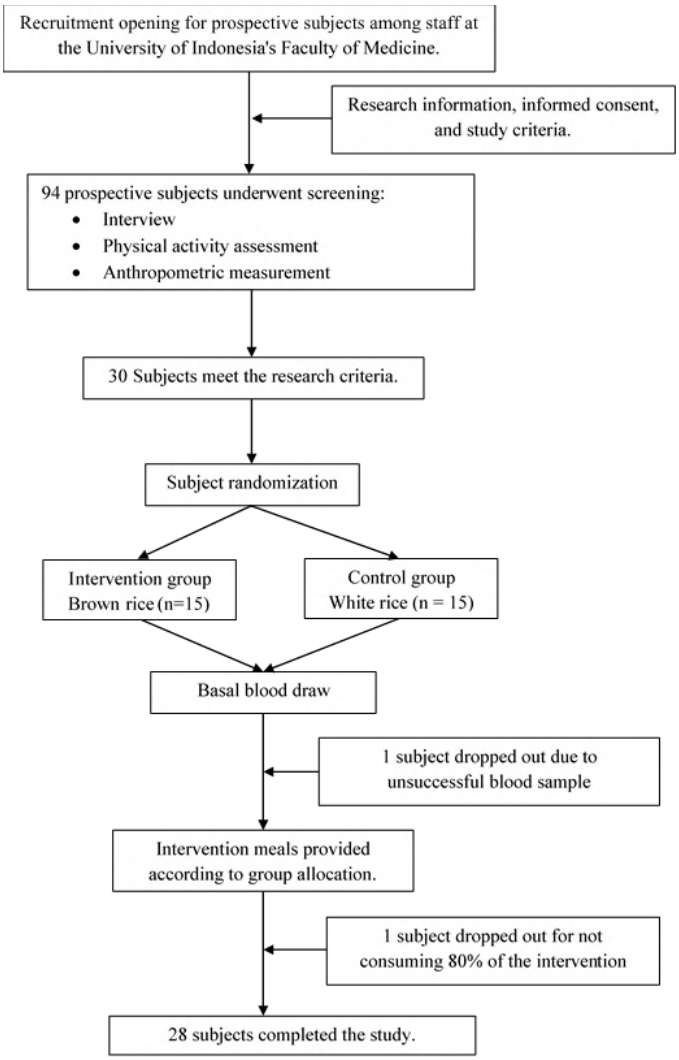

Figure 1. Research flow

Table 1. Macronutrient composition in intervention and control group food

	Carbohydrate (g)	**Protein (g)**	**Fat (g)**	**Fiber (g)**
Intervention group				
Brown rice (150 g)	110.3	16.7	3.6	6.4
Fried egg (60 g)	0.7	6.9	8.8	-
Tofu stew (70 g)	7.4	9.6	3.2	0.3
Total (g)	118.4	33.2	15.6	6.7
Energy (kcal)	473.6	132.8	140.4	
Percentage (%)	63.4	17.7	18.8	

	Carbohydrate (g)	Protein (g)	Fat (g)	Fiber (g)
Control group				
White rice (150 g)	120.7	10.6	0.8	0.6
Omelette (60 g)	0.7	6.9	8.8	-
Tofu stew (70 g)	7.4	9.6	3.2	0.3
Total (g)	128.8	27.1	12.8	0.9
energy (kcal)	515.2	108.4	115.2	
Percentage (%)	69.7	14.7	15.6	

Nutritional values were calculated by the authors using NutriSurvey 2007.

During Intervention

On the study day, fasting blood was drawn at 07:30–08:00 for baseline IL-6 measurement. Subjects then consumed their allocated meal within 15–20 minutes. They remained sedentary (≤1.5 METs) until the 4-hour postprandial blood draw at 12:00, permitted only water intake during this period.

Post-intervention

Postprandial blood samples were collected at 12:00 (4 hours after intervention). Subject observation forms and complaint logs were collected for documentation.

Sociodemographic Data

Subject characteristics (age, sex, BMI, physical activity, calorie and fiber intake) were collected via interviews and questionnaires. BMI was calculated as weight/height² (kg/m²). Physical activity was assessed using the validated International Physical Activity Questionnaire-Short Form (IPAQ-SF), which consists of seven items evaluating vigorous, moderate, and light activities, including walking and sitting time over the past 7 days; results were converted into metabolic equivalents (METs) based on the IPAQ scoring protocol. Dietary intake was assessed using a 24-hour food recall conducted on a weekday and analyzed using NutriSurvey 2007. Pre-study briefings covered research objectives, procedures, and questionnaire completion.

Analysis of IL-6 level

Venous blood (5 mL) was drawn from the cubital fossa at baseline and 4 hours post-intervention. Samples were centrifuged at 3000 rpm for 10 minutes to separate plasma, which was then aliquoted and stored at -20°C until analysis. IL-6 levels were quantified using sandwich ELISA (FineTest® Human IL-6 Kit) at the Biochemistry Laboratory. The assay involved incubation, washing, enzymatic reactions, and optical density

measurement at 450 nm. The change (Δ) in IL-6 levels were calculated by subtracting baseline IL-6 levels from postprandial levels measured 4 hours after meal consumption.

Statistical analysis

Data were analyzed using SPSS v27. Univariable analysis included baseline IL-6 levels and sociodemographic data. Normality was assessed with Shapiro-Wilk test. Within-group differences were analyzed with non parametric test Wilcoxon, and between-group differences with Mann-Whitney. A p-value <0.05 was considered significant.

Results

Baseline characteristics

Data were analyzed per protocol, including all 28 subjects who completed the study. Baseline characteristics are shown in **Table 2**. The overall median age was 27 years (range: 23-48). The mean age was higher in the intervention group (30.1 ± 6.7 years) than the control group (28.6 years). The cohort consisted of 6 males and 24 females, with a balanced sex distribution (20% male, 80% female) across both groups.

The mean body mass index (BMI) for all subjects was 20.9 ± 1.2 kg/m², with similar values in each group. The mean physical activity level, measured in metabolic equivalent minutes/week (IPAQ-SF), was 321.5 ± 181.2. The median baseline IL-6 concentration was 0.82 pg/dL (range: 0.06–17.73). As indicated by p-values in **Table 2**, all baseline characteristics were homogeneous between the control and intervention groups.

Table 2. Baseline Characteristics of Subjects

Characteristics[1]	Both groups (N = 28)	Control group[2] (n = 15)	Intervention group[3] (n = 13)	p value
Age (year)	27 (23 – 48)*	27 (23 – 48)*	30.1 ± 6.7	0.711
Gender[4]				
Male (20%)	6	3	3	0.843
Female (80%)	24	12	10	
BMI (kg/m²)	20.9 ± 1.2	20.9 ± 1.2	21.0 ± 1.3	0.873
METs[5] (minutes/week)	321.5 ± 181.2	327.6 ± 179.5	314.5 ± 190.1	0.853
Baseline IL-6 level (pg/dL)	0.82 (0.06-17.73)	0.9 (0.06-4.60)	0.82 (0.24-17.73)	0.950

[1] All data are presented as mean ± standard deviation, except * median (min – max)
[2] The control group is the group that received white rice
[3] The intervention group is the group that received brown rice
[4] Data are presented as n (number)
BMI: Body Mass Index; METs: Metabolic Equivalent of Task; IL-6: Interleukin-6

Energy, macronutrients, and fiber intake

Dietary intake was assessed via a 24-hour food recall from the day before the intervention. Complete data were available for 23 subjects. The mean energy intake was 1482.6 kcal/day. The control group had a slightly higher mean intake (1369.8 kcal/day for intervention vs. control). Mean carbohydrate intake was lower in the intervention group (152.2 g/day) compared to the control. Protein intake was higher in the control group (59.6 g vs. 50.9 g), as was fat intake (40.9% of energy). Mean fiber intake was similar between groups (control: 7.5 g/day; intervention: 8.1 g/day; overall: 7.8 g/day).

Table 3. Characteristics of subjects' intake with 1x24-h food recall prior to the study day

Intake	Both groups (N = 23)	Control group (n = 12)	Intervention group (n = 11)	p value
Energy (kcal/day)	1482.6 ± 435.3	1586.0 ± 398.8	1369.8 ± 463.9	0.242
Carbohydrate (g/day)	161.9 ± 56.7	170.9 ± 62.2	152.2 ± 51.2	0.442
Protein (g/day)	55.4 ±16.2	59.6 ± 12.9	50.9 ± 18.8	0.206
Fat (%)	39.8 ± 8.3	40.9 ± 8.2	38.6 ± 8.6	0.518
Fiber (g/day)	7.8 ± 4.0	7.5 ± 3.7	8.1 ± 4.4	0.726

IL-6 levels

IL-6 levels were analyzed per protocol (**Table 4**). In the brown rice group, post-intervention IL-6 was non-significantly higher than baseline (p=0.087). The white rice group showed a non-significant decrease (p=0.910). The between-group difference in IL-6 change was not statistically significant (p=0.069), although the intervention group had a numerically higher postprandial median IL-6 level (**Table 5**).

Table 4. Changes in IL-6 levels in each group pre- and post-intervention

	Pre-intervention IL-6 Level (pg/mL)	Post-intervention IL-6 Level (pg/mL)	p value*
Control group[1] (n=15)	0.94 (0.06 – 4.60)	0.90 (0.05 – 4.30)	0.910
Intervention group[2] (n=13)	0.82 (0.24 – 17.73)	1.34 (0.29 – 13.50)	0.087

*Wilcoxon

Table 5. Changes in IL-6 levels in the control and intervention groups

	Control group[1] (n= 15)	Intervention group[2] (n= 13)	p value*
Changes in IL-6 levels (pg/mL)	0.02 (-2.69 – 1.14)	0.52 (-6.14 – 11.46)	0.069

*Mann-Whitney

A boxplot illustrates the distribution of IL-6 changes. Visually, the change appears larger in the intervention group, but statistical tests confirmed this difference was not significant (p>0.05, 95% CI), indicating no meaningful difference between groups.

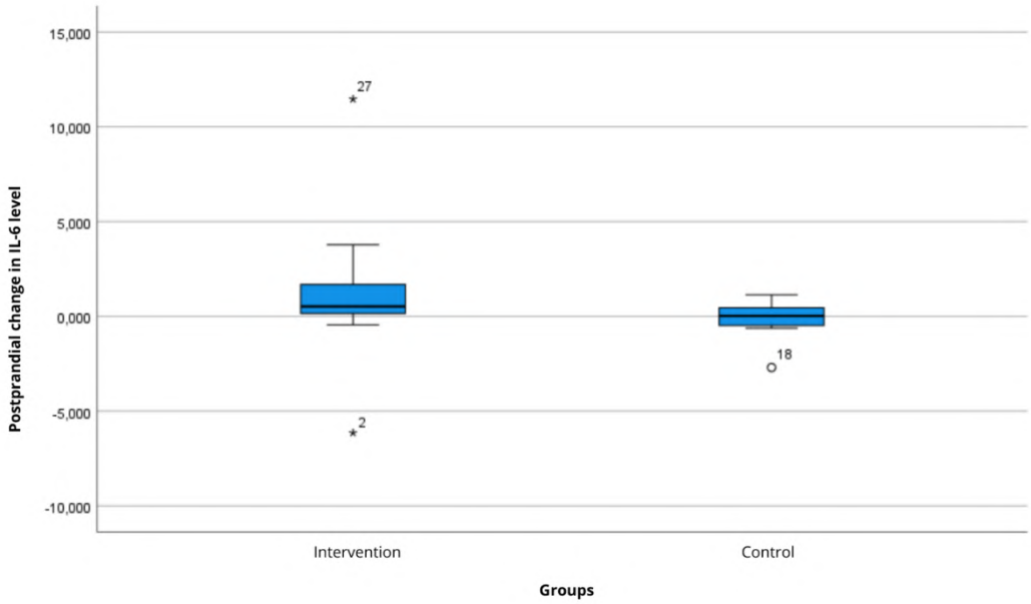

Figure 2. Boxplot of the difference in interleukin-6 level changes between the control and intervention groups.

Discussion

Based on author's knowledge, this study is the first postprandial study in healthy sedentary individuals comparing the effects of brown and white rice on inflammatory marker interleukin-6. This study involved healthy adults (21 – 59 years old, median of age is 27 years old) with low physical activity (IPAQ ≤600 METs/minutes/week). Subjects were given test meals consisting of 150 g of rice (white rice for the control group and brown rice for the intervention group), 70 g of tofu stew, and 60 g of an omelette. IL-6 level were measured at baseline (after a 10 hours fast) and 4 hours after eating.

Subjects were recruited from both sexes, but the proportion of female (80%) was more dominant than male due to a larger number of female prospective subjects meeting the inclusion criteria, primarily because active male smokers were excluded. Active smokers were excluded because smoking significantly increases inflammatory status and IL-6 levels, which could interfere with the study results.[16–18] Subjects were selected from office workers, who are known to be at risk of having low physical activity patterns. In this

study, subjects had an average MET of 321.58/week. Although sedentary behavior is associated with the risk of future increases in BMI[19], all subjects in this study had a BMI within the normal range.

The subjects' calorie and macronutrient intake before the intervention did not differ significantly, with an average intake of 1482.65 kcal per day. Sedentary dietary patterns are often associated with unhealthy diet preferences[20–22], but efforts were made to minimize intake variation before the intervention by instructing subjects not to change their diet and to discontinue supplements. The macronutrient composition of rice is influenced by the degree of milling. Unsorted brown rice (Aek Sibundong variety) has higher fat, protein, and fiber content, but was found to have lower carbohydrates compared to white rice (IR-64).[23–25] The test meal in the control group had a composition of 69.7% carbohydrates, 14.7% protein, and 15.6% fat (12.8g). Meanwhile, the intervention group's meal consisted of 63.4% carbohydrates, 17.7% protein, and 18.8% fat (15.6g). The energy content of both groups was approximately 700 kcal. The percentage of fat in the intervention meal was relatively lower compared to previous studies which reached 60-70% fat.[6,14,26]

IL-6 is a pleiotropic cytokine with a dual role: it acts as a pro-inflammatory adipokine from adipose tissue and as an anti-inflammatory myokine secreted by muscles during physical activity.[27,28] IL-6 is also involved in the regulation of energy metabolism, particularly by promoting lipolysis and fatty acid mobilization from adipose tissue and enhancing fatty acid uptake in skeletal muscle under basal conditions.[29] In addition, IL-6 has been proposed to act as an energy allocator that facilitates glucose uptake in metabolically active tissues, although its effects on glucose metabolism vary depending on physiological conditions.[30] In the postprandial state, IL-6 concentration typically peaks around 6 hours after a meal, increasing up to two-fold from the baseline value.[31–33] Therefore, the measurement taken at the 4th hour in this study may not have captured the peak concentration, but rather reflects the early phase of postprandial inflammatory dynamics.

The results showed no statistically significant difference ($p>0.05$) in the change of IL-6 levels between the brown rice and white rice groups.Although IL-6 levels were numerically higher in the intervention group, this difference did not reach statistical significance. This observation may be related to differences in meal composition, such as fat content; however, this interpretation remains speculative and should be interpreted with caution. Previous evidence suggests that dietary fat may influence postprandial IL-6 responses through several interconnected mechanisms, including the translocation of lipopolysaccharides (LPS) via chylomicrons, stimulation of adipose tissue-derived cytokine release, and the induction of oxidative stress through lipoprotein oxidation.[26,34–37] Nevertheless, these mechanisms are proposed based on prior studies and cannot be directly inferred from the present findings.

This finding aligns with several previous studies which also found no postprandial increase in IL-6 when the fat content in the test meal was not excessively high (around 10-40g)[34] or in subjects with a healthy metabolic status.[26,35,36] A systematic review indicated that out of 45 studies, 10 studies found no significant changes in IL-6 following the consumption of high-fat meals.[37] The study by Callcott et al.,[38,39] on pigmented rice showed a significant decrease in IL-6 at 1 and 2 hours after consumption in healthy subjects, indicating that the measurement at the 4th hour might have missed the initial decrease dynamics influenced by the antioxidants in brown rice. Other studies show that the type of fatty acid (saturated vs. unsaturated) or the type of carbohydrate (high vs. low

glycemic index) does not always consistently produce different IL-6 responses, highlighting the complexity of the postprandial inflammatory response.[40] Food matrix, nutrient bioaccessibility, and interactions with metabolic factors such as insulin and triglycerides play important roles.[41]

From a clinical perspective, these finding suggest that substituting white rice with brown rice in a single meal may not produce immediate differences in postprandial IL-6 levels in healthy sedentary individuals. Therefore, dietary recommendations aimed at reducing inflammation should consider overall dietary patterns, total fat intake, and metabolic status rather than focusing solely on the type of staple carbohydrate. Brown rice may still offer long-term health benefits due to its higher fiber and bioactive compound, but its acute anti-inflammatory effect may be limited.

This study has several limitations, such as the use of a 1x24 hour food recall and the IPAQ questionnaire, which carry a risk of recall bias; an open-label design that potentially introduces a placebo effect; and the estimation of the test meals' nutritional composition from secondary data rather than direct analysis.

For future research, it is recommended that similar studies be conducted by combining brown rice with other anti-inflammatory foods and measuring additional parameters such as blood glucose levels, triglycerides, and body composition (body fat percentage, muscle mass) to understand their relationship with the inflammatory response. Furthermore, serial blood sampling should be performed until at least 6 hours postprandial to capture the peak IL-6 concentration.

Conclusions

In conclusion, the acute consumption of either brown rice or white rice within the context of a daily meal with low total fat content did not significantly affect IL-6 levels at the 4-hour after eating in healthy, sedentary individuals. The postprandial IL-6 response is a complex process influenced by the interaction of various factors beyond the type of rice, including the total fat amount, food matrix, and the individual's metabolic status.

Conflict of interest

There is no conflict of interest

Acknowledgement

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Ethic Statement

This study was approved by the Health Research Ethics Committee of the Faculty of Medicine, Universitas Indonesia (Approval No: KET-1779/UN2.F1/ETIK/PPM.00.02/2024). The study was conducted in accordance with the

principles of the Declaration of Helsinki. Written informed consent was obtained from the participant prior to data collection.

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Author Contributions

RFP: Conceptualization, data acquisition, formal analysis, interpretation of results, drafting the manuscript, and final approval of the version to be published.
SWJ: Supervision, interpretation of the data, critical revision of the manuscript for important intellectual content, and final approval of the version to be published.
WL: Conceptualization, study design supervision and consultation, critical revision of the manuscript for important intellectual content, and final approval of the version to be published.

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ORIGINAL ARTICLE

Relationship between caffeine consumption and physical activity with arterial elasticity in medical students

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Abstract

Background: Medical students often consume high amounts of caffeine due to heavy academic demands and tend to be less physically active.

Objective: This study aimed to investigate the relationship between caffeine consumption and physical activity with arterial elasticity in medical students at the Faculty of Medicine, Universitas Pembangunan Nasional Veteran Jakarta in 2025.

Methods: This cross-sectional study included 80 undergraduate medical students aged 18–23 years, recruited through consecutive sampling. Data on physical activity, caffeine consumption, and demographics were collected using validated questionnaires. Stress, sleep quality, and eating habits were assessed using the PSS-10, PSQI, and AFHC, respectively. Only healthy participants with low to moderate stress, good sleep quality, and healthy eating habits were included in this study. The SA-3000P Accelerated Photoplethysmography (APG) analyzer was used to assess arterial elasticity, and the results were categorized as suboptimal, normal, or optimal.

Results: Suboptimal arterial elasticity was observed in 51.3% of participants. Caffeine consumption was moderate in most participants (61.3%), while physical activity levels were moderate in 57.5% of the participants. The Chi-square test showed a significant association between caffeine consumption and arterial elasticity ($p = 0.012$), whereas physical activity showed no significant association ($p = 0.093$).

Conclusions: High caffeine consumption was associated with reduced arterial elasticity in medical students, whereas physical activity was not significantly associated. These findings suggest a potential association between caffeine intake and vascular health in young adults.

Keywords: arterial elasticity, caffeine consumption, medical students, physical activity

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Introduction

The World Health Organization (WHO) states that cardiovascular disease is responsible for 17.9 million deaths each year worldwide. In Indonesia, this disease is the leading cause of death.[1] The considerable burden highlights that this condition remains a major health concern and emphasizes the urgent need for stronger preventive strategies.

One important biomarker that reflects vascular health is arterial elasticity.[2] Arterial elasticity is the ability of blood vessels to stretch and then return to their original shape (recoil) during the cardiac cycle. Reduced arterial elasticity results from an imbalance between elastin and collagen fibers in the vascular wall, contributing to elevated blood pressure, hemodynamic disturbances, and an increased risk of cardiovascular disease.[3] Arterial elasticity can be assessed non-invasively using Accelerated Photoplethysmography (APG), a simple and rapid method suitable for vascular evaluation.[2]

Despite various prevention and therapeutic efforts, the incidence of cardiovascular disease remains high. This indicates the need for a deeper understanding of the risk factors leading to vascular dysfunction. Young individuals, especially medical students, tend to have two risk factors for reduced arterial elasticity, namely high consumption of caffeine and lack of physical activity.[4] More than 80% of the world's population is caffeine consumers, with total consumption reaching around 120,000 tons per year. Caffeine consumption is also very common among students, especially medical students, with a reported prevalence of consumption reaching 94%.[5] The caffeine is found in various products, such as coffee, tea, soda, and chocolate.[6] In Indonesia, coffee consumption as the primary source of caffeine shows an increasing trend in the general population, from 8.2% in 2019 to 24% in 2021.[4] Besides its stimulant effects on the central nervous system, caffeine is known to have effects on the cardiovascular system, including through mechanisms of vasoconstriction, increased blood pressure, and decreased arterial elasticity.[7]

On the other hand, physical activity plays an important role in maintaining arterial elasticity. Research shows lower arterial elasticity in individuals with low physical activity levels compared to those with high physical activity levels.[8] However, WHO data from the 2022 Physical Activity Country Profile indicates that 33.5% of the adult population in Indonesia does not meet the minimum physical activity recommendation of 150 minutes of moderate-intensity activity or 75 minutes of vigorous-intensity activity per week.[1]

The high mortality rate due to cardiovascular disease in Indonesia emphasizes the importance of prevention strategies that focus on modifiable risk factors from a young age. In the context of student life, high caffeine consumption and low physical activity are two potential risk factors for decreased vascular function. Medical students tend to adopt a sedentary lifestyle due to high academic demands.[9] In addition, high caffeine consumption, particularly from coffee, is common among medical students to maintain alertness and stamina during academic activities.[10] Although several studies have examined the relationship between caffeine consumption and physical activity on vascular health, studies evaluating both factors, especially in medical students, are still limited. Therefore, this study aims to investigate the relationship between caffeine consumption and physical activity with arterial elasticity in medical students at the Faculty of Medicine, Universitas Pembangunan Nasional Veteran Jakarta. The results of this study are expected to serve as a basis for developing promotive and preventive

strategies as well as early detection of cardiovascular disease risk in the young adult population.

Methods

The study used a cross-sectional design and was conducted from July to December 2025 at the Physiology and Nutrition Laboratory Unit, Medical Education and Research Center, Universitas Pembangunan Nasional Veteran Jakarta (UPNVJ). The study population consisted of students from the Faculty of Medicine UPNVJ.

The research participants were UPNVJ Faculty of Medicine students in the 2024/2025 academic year, aged 18-23 years, with mild or moderate stress levels, good sleep quality, good eating habits, non-smokers, no history of diabetes mellitus or cardiovascular disease, and no consumption of alcohol or medications that could affect vascular function. Eligibility screening was carried out using structured self-administered questionnaires and validated assessment instruments. All information was obtained directly from participants through self-report to ensure they met the inclusion criteria before enrollment.

The sample size was calculated using the difference of two proportions formula with $\alpha = 5\%$, $\beta = 80\%$, $P_1 = 0.565$ (proportion of participants with reduced arterial elasticity in the high caffeine group of the general population)[11], and $P_2 = 0.258$ (proportion of participants with reduced arterial elasticity in the healthy participants group of the general population).[12] The calculation resulted in 74 participants. The sample size was increased by 10% to 81 participants to account for possible non-response. Participants were selected using consecutive sampling. Arterial elasticity was measured using the Accelerate Photoplethysmography (APG) Analyzer SA-3000P with a sensitivity of 71.4% and specificity of 90%. Arterial elasticity was categorized as suboptimal (<30), normal (30-70), and optimal (>70).[13] The APG examination was performed by inserting the index finger into a finger probe for 2-3 minutes. Participants were asked to remove all metal accessories and then sit comfortably, and were instructed not to talk, move, or fall asleep during the measurement process. Before the examination, participants were asked not to consume caffeine for at least 4-6 hours or engage in strenuous exercise beforehand. The examination was conducted in a comfortable room with adequate temperature and lighting.

Caffeine consumption was assessed using the Caffeine Consumption Questionnaire-Revised (CCQ-R). The average accuracy of CCQ-R reporting reached 83.5%, and more than 60% of participants achieved an accuracy level of ≥ 85%, meeting the standards for inter-rater agreement. The reliability test results for this questionnaire yielded a Cronbach's alpha > 0.70.[14] Construct validity was reinforced by the absence of demographic factors influencing reporting accuracy. These results make the CCQ-R suitable for use in research and clinical practice.[15] The Modified Caffeine Consumption Questionnaire-Revised (mCCQ-R) is a modification of the Indonesian version of the CCQ-R, tailored to foods and beverages containing caffeine in Indonesia. The validity test results in the research population showed an average accuracy of 89%, with 73% of participants having a score >85%. Furthermore, caffeine consumption was categorized as low <100 mg, moderate 100-300 mg, and high >300 mg.[16]

Physical activity was measured using the Global Physical Activity Questionnaire (GPAQ) in Metabolic Equivalent of Task (MET) units for a week. This questionnaire has moderate to good reliability with Spearman's rho values of 0.67-0.73. Physical activity

levels were categorized as high (MET > 3000), moderate (600≤MET≤3000), and low (MET < 600).[17]

Stress levels were measured using the Perceived Stress Scale (PSS)-10 questionnaire. Stress scores were categorized as low (0-13), moderate (14-26), and high (27-40).[18] The Indonesian version of the PSS-10 is known to be valid and reliable, with a Cronbach's alpha of 0.83.[19]

Sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI) with a Cronbach's alpha of 0.79.[20] A total PSQI score > 7 indicates poor sleep quality.[21] Eating habits were assessed using the Adolescent Food Habits Checklist (AFHC), which includes measurement of fat intake, high-energy foods, fruit and vegetable consumption, snack consumption, and nutritional knowledge. Scores of AFHC were categorized as good eating habits (score ≥12) and poor eating habits (score < 12). This questionnaire has been translated into Indonesian and demonstrated good reliability, with a Cronbach's alpha of 0.86.[22]

Univariate analysis was performed to describe the characteristics of the participants, physical activity, caffeine consumption habits, and arterial elasticity. Categorical variables were presented as frequencies and percentages. Continuous variables were first tested for normality using the Shapiro-Wilk test and then presented as mean ± standard deviation (SD) if normally distributed or median and interquartile range (IQR) if non-normally distributed. The Chi-square test was used to determine the relationship between caffeine consumption and physical activity with arterial elasticity. If the assumptions of the Chi-square test were not met, an alternative method, including cell merging, was applied. A p-value less than 0.05 was considered statistically significant. All data were analyzed using SPSS software version 24.

This study obtained ethical approval from the Health Research Ethics Committee of Universitas Pembangunan Nasional Veteran Jakarta, with number 317/XII/2025/KEP.

Results

One of the 81 study participants was excluded for being 17 years old, which did not meet the eligibility criteria (18-23 years). Therefore, a total of 80 participants were included in the final analysis. The number of male and female participants was equal, with a median age of 21 years. Most participants had a normal body mass index (BMI) (43.8%) and low stress levels (68.8%). As shown in **Table 1**, there were no significant differences in age (p = 0.598), sex (p = 0.371), BMI (p = 0.915), or stress level (p = 0.264) across arterial elasticity groups.

Table 1. Participants' characteristics according to arterial status

Characteristics	Arterial Elasticity		p-value
	Suboptimal n = 41	Normal+Optimal n = 39	
Age, median (IQR)	20 (2)	21 (2)	0.598[a]
Sex, n (%)			
Male	23 (57.5)	17 (42.5)	0.371[b]
Female	18 (45.0)	22 (55.0)	
BMI, n (%)			
Underweight	1 (33.3)	2 (66.7)	0.915[b]
Normoweight	18 (51.4)	17 (48.6)	
Overweight	11 (50.0)	11 (50.0)	

Obese	11 (55.0)	9 (45.0)	
Stress level, n (%)			
Low	31 (56.4)	24 (43.6)	0.264[b]
Moderate	10 (40.0)	15 (60.0)	

Notes: [a]Kruskal-Wallis test, [b]Chi-square test, Arterial elasticity: suboptimal (<30), normal (30–70), optimal (>70).

As presented in **Table 2**, most participants reported moderate caffeine consumption (61.3%) and moderate levels of physical activity (57.5%).

Table 2. Distribution of caffeine consumption and physical activity among the participants

Characteristics	Arterial Elasticity	
	Suboptimal n = 41	Normal+Optimal n = 39
Caffeine consumption, n (%)		
High	7 (100)	0 (0,0)
Moderate	23 (46.9)	26 (53.1)
Low	11 (45.8)	13 (54.2)
Physical Activity, n (%)		
High	14 (70.0)	6 (30.0)
Moderate	21 (45.7)	25 (54.3)
Low	6 (42.9)	8 (57.1)

Notes: Caffeine consumption: low (<100 mg/day), moderate (100–300 mg/day), high (>300 mg/day). Physical activity: high (MET > 3000), moderate (600–3000), low (<600). Arterial elasticity: suboptimal (<30), normal (30–70), optimal (>70).

The mean daily caffeine consumption was 166.79 mg, ranging from 0 to 619.91 mg/day. Based on caffeine sources, participants primarily consume caffeine from coffee (65%) and tea (63.8%) (**Figure 1**).

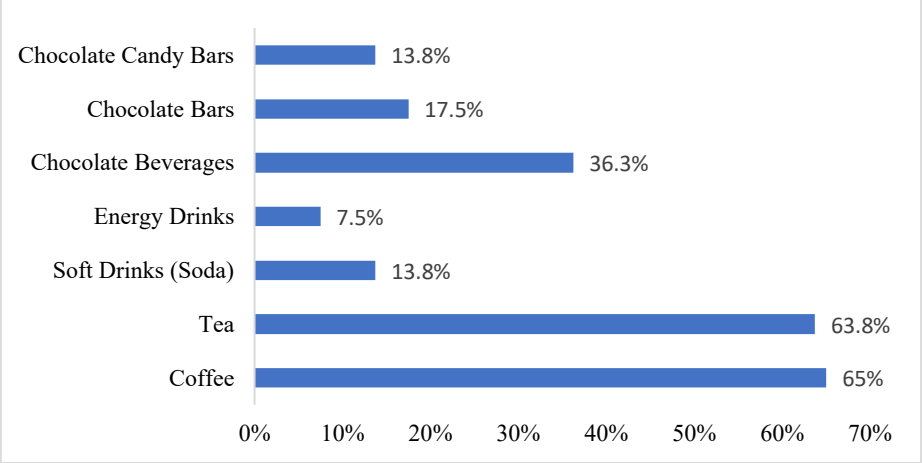

Figure 1. Distribution of caffeine consumption sources

In this study, 41 participants (51.2%) were classified as having suboptimal arterial elasticity (**Figure 2**).

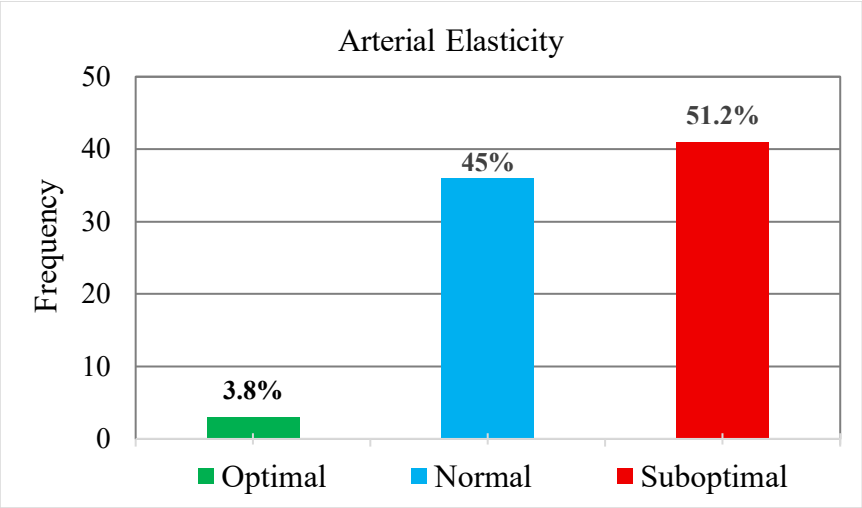

Figure 2. Distribution of arterial elasticity

Chi-square analysis demonstrated a significant association between caffeine consumption and arterial elasticity (p = 0.012) (**Table 3**).

Table 3. Association between caffeine consumption and arterial elasticity

Caffeine Consumption	Arterial Elasticity				Total		p-value
	Suboptimal		Optimal + Normal				
	N	%	N	%	N	%	
High	7	100	0	0	7	100	0.012
Low + Moderate	34	46.6	39	53.4	73	100	

In contrast, physical activity was not significantly associated with arterial elasticity (p = 0.093) (**Table 4**).

Table 4. Association between physical activity and arterial elasticity

Physical Activity	Arterial Elasticity				Total		p-value
	Suboptimal		Optimal + Normal				
	N	%	N	%	N	%	
Low + Moderate	27	45.0	33	55.0	60	100	0.093
High	14	70.0	6	30.0	20	100	

Discussion

The distribution of participant characteristics was comparable between the suboptimal and normal+optimal arterial elasticity groups. No significant differences were observed in age, sex, BMI, or stress level between the two groups (p > 0.05) (**Table 1**). These findings indicate that the participants were relatively homogeneous across arterial elasticity categories.

The study results found that 41 (51.2%) participants had suboptimal arterial elasticity. Vascular aging can occur at a young age, a condition known as early vascular aging (EVA), caused by the accumulation of risk factors.[23] The results of studies in the 20-30

age group show that metabolite levels, such as histidine and beta-alanine, are positively associated with arterial elasticity as measured by carotid-femoral Pulse Wave Velocity (cfPWV). This indicates that metabolic changes can contribute to EVA and confirms that arterial elasticity can decrease subclinically from a young age.[24]

The majority of caffeine consumption among participants was in the moderate category, with an average of 166.79 mg/day, ranging from 0 to 619.91 mg/day. This finding is in line with a study of 103 first-year medical students in Perak, Malaysia, which showed that 86% of participants consumed caffeine to stay alert during lectures or when they had to study at night.[25] Similarly, a study among college undergraduates reported an average caffeine intake of approximately 159 mg/day, with most students consuming caffeine to enhance mood and cognitive performance. In that study, coffee and tea were identified as the primary sources of caffeine, while energy drink consumption was less common. In the present study, coffee was the primary source of caffeine consumption. This data is in line with data from the Indonesian Ministry of Agriculture, which shows a 15.8% increase in coffee consumption in Indonesia from 2019 to 2021.[4]

This study shows that the majority of participants engaged in moderate-intensity physical activity. These results are in line with the Indonesian Health Survey (SKI), which recorded that the prevalence of physical activity among individuals aged 15-24 in Indonesia was 54.8% in the moderate intensity category.[26]

Participants with high caffeine consumption had a significantly higher proportion of suboptimal arterial elasticity than those with low or moderate caffeine consumption ($p = 0.012$). This finding indicates an association between high caffeine intake and arterial elasticity status. One possible explanation is that irregular consumption of high doses of caffeine may be associated with vasoconstriction, increased blood pressure, and sympathetic nervous system activation, thereby increasing hemodynamic stress on arterial walls. These physiological responses have been suggested to be associated with reduced arterial elasticity.[27]

In contrast, several previous studies have reported that long-term regular caffeine consumption may be associated with improved endothelial function and reduced inflammation markers, such as lower CRP and E-Selectin.[28] Other studies have shown that regular consumption of 400-600 mg/day of caffeine for one week or 400 mg/day for two weeks can increase adenosine A2A receptor activity and cAMP accumulation, which contributes to improved vascular function and increased arterial elasticity.[29] Additionally, regular moderate caffeine consumption (>3 cups/day) has been reported to be associated with higher arterial elasticity compared with lower consumption (≤3 cups/day) in individuals aged 17 years.[27] These findings suggest that long-term regular (habitual) caffeine consumption, whether low, moderate, or high dose, has a positive effect on arterial elasticity by preventing inflammation and increasing adenosine A2A and cAMP activity.

However, those findings differ from the results of the present study, which showed that higher caffeine consumption was associated with a greater proportion of suboptimal arterial elasticity. This discrepancy may be explained by differences in consumption patterns. Participants with irregular caffeine consumption patterns may experience less physiological adaptation to caffeine exposure. In this condition, caffeine may act as an acute trigger through increased sympathetic nerve activity, blood pressure, and vascular response, likely because the endothelium has not yet adapted to caffeine exposure.[30] Long-term, irregular consumption of high-dose caffeine has the potential to cause persistent increases in blood pressure, oxidative stress, and endothelial dysfunction. The

combination of these factors can worsen the quality of the arterial walls and reduce arterial elasticity.[27,30] These mechanisms may contribute to reduced arterial elasticity, although causal relationships cannot be confirmed due to the observational nature of this present study.

Short-term caffeine consumption appears to produce vascular responses that differ from habitual long-term regular consumption, but may resemble the effects observed in individuals without physiological adaptation to caffeine. Research by Kadek et al.,[31] shows that short-term consumption of moderate doses of caffeine (2-3 cups) can increase heart rate and blood pressure for 2 to 5 hours afterward due to caffeine's direct stimulation of the adrenal medulla to release the hormone epinephrine and block adenosine receptors. Other analyses have demonstrated an increase in systolic blood pressure of 10-20 mmHg after 60 minutes of consuming a moderate dose of caffeine (150 mg) due to the inhibitory mechanism on phosphodiesterase.[7] This exposure to high blood pressure can put mechanical stress on the vascular wall, which can cause endothelial dysfunction. This condition can further trigger the vascular remodeling process and lead to a decrease in arterial elasticity.[32] These findings suggest that short-term caffeine consumption can cause a decrease in arterial elasticity.

In this study, participants with high caffeine consumption (>300 mg/day) had a higher proportion of suboptimal arterial elasticity than those with low or moderate caffeine consumption. These results are consistent with similar studies showing that irregular exposure to high doses of caffeine can trigger a sympathetic response, increased blood pressure, and changes in vascular function that contribute to decreased arterial elasticity.[33] However, due to the cross-sectional design, these findings reflect an association rather than a causal relationship. Therefore, moderating caffeine consumption may be considered as a potential strategy to support arterial elasticity in young adults. In this study, participants with lower caffeine intake (≤ 300 mg/day) tended to exhibit normal or optimal arterial elasticity. This finding aligns with existing literature suggesting that caffeine intake up to approximately 400 mg/day is generally considered safe in healthy adults (19 years or older).[34] This restriction is important to prevent a decrease in arterial elasticity that can occur due to excessive caffeine consumption, as well as to help maintain endothelial function and overall cardiovascular health.

The results of this study show that there is no relationship between physical activity and arterial elasticity ($p = 0.093$). The lack of a significant association in this study may be explained by the cross-sectional design, which does not capture long-term exposure to physical activity. Regular physical activity is known to improve endothelial function and enhance arterial elasticity by reducing inflammatory and oxidative stress pathways in vascular tissue, as well as increasing antioxidant enzyme levels and nitric oxide bioavailability.[35] Evidence from the literature suggests that the vascular effects of physical activity are dependent on the intensity and duration of the activity. A meta-analysis demonstrated that acute exercise does not immediately increase arterial elasticity but may produce transient improvements within 30 minutes, which return to baseline after 24 hours. The studies also show that only moderate-to-vigorous physical activity of sufficient duration (30-59 minutes) produces measurable improvements in arterial elasticity.[36] These findings indicate that short-term or sporadic physical activity may not lead to sustained vascular changes, particularly when measured outside the acute response window. Consistently, short-duration physical activity does not produce significant changes in arterial elasticity.[37] Acutely, physical activity can decrease smooth muscle tone and increase arterial compliance and arterial elasticity, as measured by PWV. These

effects are temporary because they do not alter the structure of the arterial wall. However, in the long term, repeated hemodynamic exposure from regular exercise induces endothelial adaptation, increased vasodilation capacity, and increased vascular density, which permanently improves arterial elasticity.[36] This concept is supported by a longitudinal study involving male firefighters aged 20–49 years, in which participants were classified into light-, moderate-, and vigorous-intensity physical activity groups and followed over one year. Body composition, arterial elasticity, VO_2 max, and handgrip strength were assessed at baseline and follow-up. Physical activity was evaluated using the International Physical Activity Questionnaire (IPAQ). All participants were guided by the same trained examiner using standardized instructions to minimize self-reported bias. The study demonstrated improvements in arterial elasticity across all groups, with the greatest enhancement observed among those engaging in the vigorous-intensity group. Additionally, arterial elasticity was inversely associated with age, BMI, and relative fat mass, and positively associated with VO_2 max and muscle mass.[38]

Further supporting evidence comes from a study in young adults in Brazil, which found that waist circumference partially mediated the relationship between moderate-to-vigorous physical activity and arterial elasticity. This suggests that the beneficial vascular effects of physical activity may be partly driven by its role in reducing body weight and visceral fat, both of which are closely linked to reduced arterial elasticity.[39] In line with this, a study among medical students found that those with the lowest muscle mass-to-visceral fat (MVF) ratio had a 6.54-fold higher risk of suboptimal arterial elasticity than those with low or high MVF ratios.[40]

Another important consideration is the method used to assess physical activity. In this study, physical activity was measured using self-reported questionnaires, which are prone to recall bias and may not accurately capture the intensity and duration of the activity. This limitation may have contributed to the non-significant findings. In contrast, studies employing objective measurements provide stronger evidence of an association. Accelerometer-based assessments have shown a significant relationship between physical activity and arterial elasticity.[39]

Additionally, the relatively homogenous characteristics of the study population may have contributed to the lack of a significant association between physical activity and arterial elasticity. Variables such as age and BMI did not differ significantly between arterial elasticity groups, indicating limited variability in key vascular determinants.

This study has several strengths. First, restricting caffeine consumption before the measurement helped minimize its acute effects, allowing the result to better reflect participants' baseline vascular condition. Second, the relatively homogeneous characteristics of the participants reduced the influence of potential confounding factors such as age, sex, BMI, and stress level. Furthermore, focusing on young adults provides valuable insight into early vascular changes and highlights the role of modifiable lifestyle factors in vascular health.

This study also has several limitations that should be considered when interpreting the results. Physical activity was measured using a questionnaire, so the data obtained are subjective and potentially to reporting bias. This study also did not include lipid profile testing, so the possible influence of dyslipidemia on arterial elasticity could not be evaluated.

Conclusions

There is a significant relationship between caffeine consumption and arterial elasticity. Participants with high caffeine consumption had a significantly higher proportion of suboptimal arterial elasticity than those with low or moderate caffeine consumption ($p = 0.012$).

These findings suggest that excessive caffeine consumption may be associated with reduced arterial elasticity. Therefore, limitation of caffeine consumption to no more than 300 mg per day is recommended to maintain arterial elasticity and cardiovascular function. In contrast, physical activity did not show a significant relationship ($p = 0.093$). Further research is recommended involving a larger population and using more objective physical activity measurement tools, such as accelerometers or pedometers.

Conflict of Interest

The authors declare no conflicts of interest related to this article.

Ethic Statement

Written informed consent was obtained from the participant prior to data collection.

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Author Contributions

CKA: design of the study, data acquisition, interpretation of data, drafting the manuscript; NB: conceptualization, design of the study, interpretation of data, critical revision of the manuscript for important intellectual content, and final approval of the version to be published; IM: design of the study, interpretation of data; MC: design of the study, interpretation of data

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ORIGINAL PAPER

Knowledge, attitudes, and practices towards sustainable diets and food choice motives among IPB university students with overweight and obesity: A cross-sectional study

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Abstract

Background: The prevalence of overweight and obesity among university students Indonesia has been rising, with food choices playing a central role in both nutritional and environmental outcomes. However, evidence on knowledge, attitudes, and practices (KAP) toward sustainable diets and their relationship with food choice motives among students with overweight and obesity remains absent in the Indonesian context. This study aimed to determine the association between KAP of sustainable diets and food choice motives among overweight and obese students at IPB University (*Institut Pertanian Bogor*).

Methods: A cross-sectional study was conducted at IPB University Dramaga Campus, Bogor. A total of 97 subjects from undergraduate and postgraduate students from non-nutrition majors were recruited with a purposive sampling technique. Bivariate analysis was performed using the Spearman rank correlation test, and multivariate analysis was performed using binary logistic regression.

Results: Most of the subjects (86.6%) had a poor knowledge. Similarly, attitude and practice were also predominantly poor (76.3% and 92.8%, respectively). Spearman correlation analysis revealed significant associations between knowledge and attitude, knowledge and practice, and attitude and practice ($p<0.05$). The multivariate analysis demonstrated that a good attitude towards a sustainable diet was significantly associated with food choice motives among IPB University Students with overweight and obesity (OR=5.280; 95%CI=1.768-15.769; p=0.003).

Conclusion: Attitude of sustainable diet was significantly associated with food choice motives among IPB University students with overweight and obesity. University health programs should integrate sustainable diet education targeting attitudinal change, particularly among students with excess body weight.

Keywords: attitude, food choice motives, knowledge, sustainable diet

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Introduction

Overweight and obesity have become major public health issues globally, particularly among young adults, including among university students in Indonesia.[1] Recent data (*Survei Kesehatan Indonesia* or SKI) indicates that the prevalence of adult obesity (aged >18 years old) in Indonesia has increased to approximately 23.4% in 2023, making a persistent upward trajectory over the past decade.[2] According to the *Riset Kesehatan Dasar* report, the prevalence of overweight and obesity among adults has steadily risen from 10.5% in 2007 to more than 21.8% by 2018, with the most recent SKI data reinforcing this trend.[3,4] Emerging evidence indicates that university students in Indonesia are also affected by rising rates of overweight and obesity. Many cross-sectional studies reported that the prevalence of overweight and/or obesity among Indonesian students ranged from 20.7% to 73.6%.[5,6,7,8] Based on previous research from Sakai[23], it was found that around 23% of the Institut Pertanian Bogor (IPB) student population is overweight.

The increasing prevalence of overweight and obesity among both the general adult population and university students reflects broader dynamics of nutrition transition occurring in Indonesia. The nutritional status patterns highlight a significant nutritional transition in Indonesia, where increased consumption of energy-dense and highly processed foods, coupled with sedentary lifestyles, contributes to increasing rates of overweight and obesity.[2,9,10,11]

Fundamental to addressing these nutritional issues is understanding the role of dietary behaviors and food choices[12]. Nutritional knowledge, which reflects an individual's understanding of dietary guidelines, nutritional content, and the health implications of different foods, has been consistently linked to dietary intake.[13,14,15] However, nutritional knowledge alone may not fully explain dietary choices among young adults. Behavioral and environmental factors, including availability of unhealthy food options, food label literacy, cultural eating norms, and personal attitudes toward foods, also influence food choices.[16,17]

In addition, food choices also have broader implications for environmental sustainability[18]. The concept of sustainable diets introduces nutritional adequacy with ecological impact, emphasizing food consumption patterns that support human health while minimizing environmental degradation, conserving biodiversity, and ensuring equitable access to nutritious foods.[19] A cross-sectional study, exploring sustainable nutrition behaviors among university students in Ankara, Turkey, indicates that food literacy and sustainable eating practices are associated with reduced consumption of ultra-processed foods and more environmentally responsible dietary patterns.[20] Growing interest in sustainable diets has highlighted a persistent knowledge gap. Although university students often recognize the importance of healthy and sustainable eating, limited skills, motivation, and supportive environments constrain the translation of knowledge into consistent practice.[21,22]

Understanding these dynamics is essential not only for improving individual health but also for advancing the United Nations Sustainable Development Goals (SDGs), particularly SDG 2 (Zero Hunger) and SDG 12 (Responsible Consumption and Production). Examining how nutrition knowledge, sustainability-related attitudes, and dietary practices interact to shape food choices among overweight or obese university students can inform targeted interventions that address both obesity prevention and sustainable consumption.[23] Therefore, the study aims to determine the correlation

between knowledge level, attitude, and practice of sustainable diet practices, and food choices among overweight/obese IPB students.

Methods

The study used an observational cross-sectional design. The study was conducted from November 2025 until January 2026 at IPB University Dramaga Campus, Bogor. The population was college students who were overweight or obese. The sample criteria were taken using a purposive sampling technique. The inclusion criteria were as follows: (1) Active undergraduate or graduate (master's) students at IPB University from non-nutrition science major; (2) Subjects aged 18-30 years (3) Nutritional status for aged 18 years included over nutrition based on BMI-for age (IMT/U) with Z-scores ranged from 1.0<*Z-Score*≤2.0 (Ministry of Health 2020) or for aged ≥19 years based on IMT with classified into overweight (Body Mass Index 23.0-24.9 kg/m^2) and obese (Body Mass Index≥ 25.0 kg/ m^2)[24]; (4) Willing to participate in the research; and (5) In good health (both physically and mentally). The exclusion criteria included: (1) Subject not giving the information or data completely; (2) Students with an acute or chronic illness history; and (3) Currently following a specific diet or restriction on specific food types. The study protocol received ethical approval from the Health Research Commission, Faculty of Dental Medicine, Universitas Airlangga, No. 1136/HRECC.FODM/XI/2025 dated Nov 10, 2025. Informed consent was obtained from all subjects prior to participation.

The calculation of the sample based on the estimation proportion formula with precision absolute from Lwanga and Lemeshow[25], determines the proportion of food choices. According to a survey from the Iris Global Eating, Drinking & Sustainability Survey[26], 58% of the Indonesian population chooses food based on sustainability or environmentally friendly considerations.[27] Based on this, the minimum sample obtained was 95 subjects. A total of 97 subjects were initially obtained from this study. The minimum sample of this study is 95 subjects based on the estimation proportion formula with precision absolute from Lwanga and Lemeshow.[25] The subjects were selected using purposive sampling with inclusion and exclusion criteria.

The independent variables in this study are the Knowledge Level, Attitude, and Practice (KAP) regarding sustainable diet, while the dependent variable is food choice motives. The data were collected through questionnaires administered during interviews. Individual and socioeconomic characteristics were collected, including age, gender, educational status, residential status, pocket money, place of origin and nutritional status. Information on sustainable diets was obtained to determine the extent to which subjects were exposed to them.

The KAP of a sustainable diet was adopted from the Sustainable Healthy Eating Diet Index (SHED) and Sustainable Diet Questionnaire (SUSDQ) and translated into Indonesian. The SHED questionnaire has previously been validated by Canyolu[28], in the adult population in Turkey, and the SUSDQ questionnaire has also been validated by Joshi[29], in the adult population in India. The food choice motives of subjects in this study were obtained using the Food Choice Questionnaire (FCQ) from Steptoe[30], which was later adapted and modified by Tanziha[31], to incorporate additional dimensions related to religion and dietary taboos. For the specific food choice question prior to a sustainable diet, the environment dimension was added from the SUSDQ questionnaire item. All subjects were selected using a Likert scale from 1 (not at all important) to 5 (extremely important). The dimension of food choice in this questionnaire consists of 11 dimensions,

such as health, mood, convenience, sensory appeal, natural content, price, environment, familiarity, ethical concern, weight control, and religion and taboo.

Before the research was carried out, we conducted a validity and reliability test of the questionnaire. The trial questionnaire was administered to subjects with the same characteristics as the research subjects. The sample consisted of 30 students from non-nutrition majors at Bogor Ibn Khaldun University. The validity test used the corrected item-total correlation and was run in SPSS Version 26. An item for a questionnaire is considered valid if the r value> 0.30. Meanwhile, the reliability of the KAP questionnaires on sustainable diet and food choice was assessed using Cronbach's alpha. For internal consistency testing, the item is considered reliable if the Cronbach's alpha coefficient is >0.70.[32]

The KAP of sustainable diet consists of 60 questions. The knowledge item has been tested for validity (0.377-0.769) and reliability (0.877), and the attitude item was divided into two items. The good attitude was obtained for validity (0.376-0.730) and reliability (0.70). At the same time, the poor attitude was obtained for validity (0.382-0.643). The practice of a sustainable diet has been tested for validity (0.495-0.817) and reliability (0.920). The food choice questionnaire was obtained for validity (0.393-0.809) and reliability (0.966). The result shows that the questionnaires used were valid and reliable. After the pilot test of the questionnaire, the final questionnaire for all variables related to the knowledge, attitude, and practice of the sustainable diet domain comprised 52 questions, with each domain containing 14 questions. The level of knowledge of a sustainable diet is measured using a Likert scale with three options: yes (1), no (2), and do not know (3). Each subject who answered yes was given 1 point if appropriate, and 0 if not. Scores for the knowledge level of sustainable diet were obtained by dividing the number of correct answers by the total number of questions and multiplying by 100. The list of KAP questionnaires on sustainable diets is shown in **Table 1**.

Table 1. Knowledge level, attitude, and practice (KAP) of sustainable diet questions

Number	Topic	Description
1-3	Knowledge, attitude, practice, and concepts of a sustainable diet	Definition, principles, and impacts of sustainable diet (knowledge domain), attitude, and practice of sustainable diet
4-6	The environmental impacts of animal and plant-based consumption	The impact of red-meat consumption and options for choosing plant-based protein options
7-8	Food waste	The utilization of food waste into compost and the impact of food waste on the environment
9-11	Local, organic, and seasonal food	The impact of local and imported food on the environment, and the consumption of seasonal fruits and vegetables
12-14	Nutrition and health dimension	The effect of ultra-processed food consumption. dietary diversity. and intake of sugar. salt. and saturated fat in a sustainable diet

For the attitude and practice of a sustainable diet. Scores were calculated as the number of correct answers divided by the maximum possible score for the number of questions answered. multiplied by 100. The classification of knowledge level was divided into two scales: (1) subjects were considered to have good knowledge if they obtained a score >80% of the total questions. (2) Subjects where poor knowledge is obtained as a score <80% of the total questions.

Data analysis was performed using Statistical Package for the Social Sciences (SPSS) 26.0. The Kolmogorov-Smirnov test was used to assess the normality of the data. Descriptive statistics for categorical variables are presented as frequencies and percentages. In contrast, numerical variables are presented as the means and standard deviations (for normally distributed data) and as medians and interquartile ranges (IQRs) for non-normally distributed data. The KAP data on sustainable diet are not normally distributed, so Spearman's rank test is used. Spearman's correlations were used to examine the relationship between each dimension of food choice motives and the KAP variable for a sustainable diet. All variables are considered significant if the p-value <0.05. A binary logistic regression analysis was used to determine the correlation between knowledge level, attitude, sustainable diet practices, and food choice motives among overweight/obesity IPB students. The dependent variables were food choice motives. According to research from Marty[33], some of the dimensions, such as health, natural content, and ethical concern, represent the "health and sustainability" dimension and have an influence and are proven consistently positively associated with indicators of a sustainable diet. In this study, the food choice motives are combined from several dimensions, such as health, natural content, and ethical concern, into a composite score to represent food choices in relation to a sustainable diet indicator. Moreover, the dependent variables are categorized as 0=not important and 1=important with a cut-off point from the median score.

Results

There were 97 subjects in total, with their characteristics including gender, age, educational level, residential status, pocket money, place of origin, exposure to information, sources of a sustainable diet, and nutritional status. Most subjects were women (53.6%) and men (45%), were between 18 and 21 years of age, while 18% were above 21 years. Regarding the educational levels, 87.6% were undergraduate students and 12.4% were postgraduate students at a university. More than half of the subjects (51.5%) live in boarding houses, while 27.8% live in houses and 20.6% live in dormitories.

The median pocket money for the subject ranges from Rp 1,500,000. Most of the subjects with a percentage of 81.4% come from Java, Bali, and Nusa Tenggara Island. In the population (age <19 years), more than half of the subjects (71.4%) had an overweight nutritional status. In contrast, 28.6% were categorized as obese in the population (age ≥19 years), most subjects (55.3%) were categorized as obese 1. Besides, 63.9% of subjects still answered "No" to receiving information about a sustainable diet, whereas 36.1% answered "Yes" to having been exposed to or received such information. In the major, 3.1% of subjects answered "Yes" to participating in a seminar/workshop related to a sustainable diet, while 96.9% answered "No". Characteristics of subjects are shown in **Table 2**.

Table 2. Demographic and socioeconomic characteristics of the subjects

Variable	Frequency (n=97)	%
Gender		
Female	52	53.6
Male	45	46.4
Age range (Years)		
18-21	79	81.4
22-30	18	18.6
Median (min; max)		20 (18;27)
Educational level		
Undergraduate	85	87.6
Postgraduate	12	12.4
Residential status		
Boarding house	50	51.5
House	27	27.8
Dormitory	20	20.6
Pocket money		
Low (Rp <1,000,000)	7	7.2
Moderate (Rp 1,000,000-1,500,000)	37	38.1
High (Rp >1,500,000)	53	54.6
Median (min; max)	Rp >1.500.000 (Rp <1.000.000; Rp >1.500.000)	
Place of origin		
Sumatra	14	14.4
Java. Bali. and Nusa Tenggara	79	81.4
Kalimantan	1	1.0
Sulawesi	1	1.0
Maluku and Papua	2	2.1
BMI-z-score category (<19 years)		
Overweight	15	71.4
Obese	6	28.6
Body mass index (BMI) (≥19 years)		
Overweight (At Risk)	23	30.3
Obese I	42	55.3
Obese II	11	14.5
Received information about a sustainable diet		
Yes	35	36.1
No	62	63.9
Sources of information on a sustainable diet are obtained through:		
Lecturer	2	3.7
Internet	35	64.8
Book	4	7.4
Friends	7	12.9
Parents	4	7.4
Television	2	3.7
Have participated in a seminar/workshop related to a sustainable diet:		
Yes	3	3.1
No	94	96.9

Most of the subjects (68%) knew the definition and concept of a sustainable diet, while just 29.0% gave the responses "not know" and "no" (2.1%). However, more than half (56.7%) of subjects answered "not know" about the impacts of a sustainable diet on greenhouse gas emissions. Also, a few subjects (31%) answered "know" that reducing meat consumption can reduce greenhouse gas emissions. Apart from that, 88.7% of subjects chose "yes" to the statement that tempeh and tofu are local plant-based proteins that are more environmentally friendly. However, in terms of the efficiency of resource or land use between plant-based and animal-based proteins, few subjects answered "yes" to the total amount (46.4%).

On the other hand, based on health considerations, more than 50% of the subjects knew that reducing ultra-processed foods is part of the principles of a sustainable diet, as well as the recommendations to limit sugar, salt, and saturated fat. However, subjects tended to still "not know" (49%) that food diversity is part of a sustainable diet. Regarding food waste reduction, the subjects answered "yes" (62%) that food waste harms the environment. The distribution of the subject's knowledge on sustainable diet is shown in **Figure 1**.

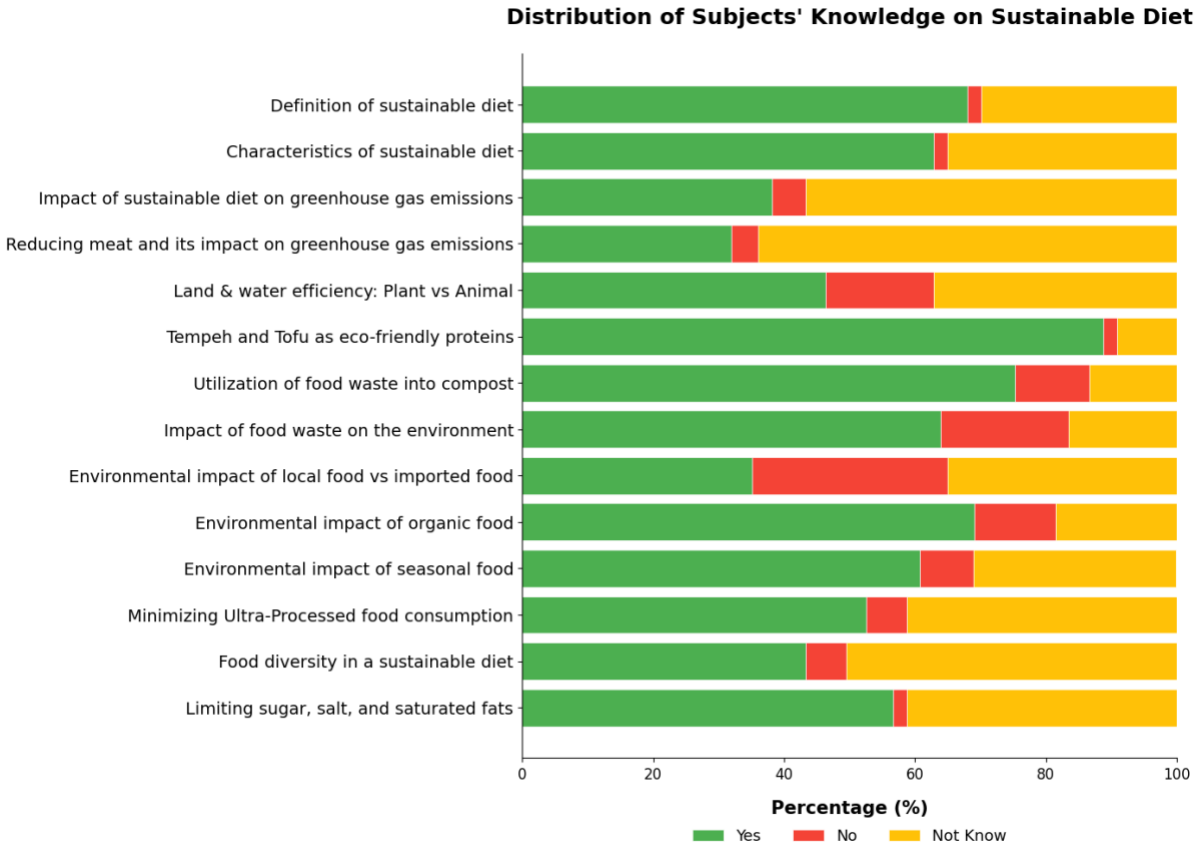

Figure 1. Distribution of subjects' knowledge on sustainable diet

The attitude towards awareness of the impact of food waste on the environment **(Figure 2)** was the most positive reported by subjects in the sustainable diet context. Regarding the attitude of the sustainable diet concept, subjects answered "agree" (53%) that it is important for health and environmental sustainability. More than 50% of subjects answered "neutral" regarding their attitude toward reducing meat consumption to reduce greenhouse gas emissions. 49% of subjects "agree" that tempeh and tofu are the local plant-based protein sources, which are more environmentally friendly. Therefore, inconsistencies were found in attitudes regarding minimizing ultra-processed food consumption. At the same time, the subjects felt "agree" with the total 42% of subjects if it did not correlate with sustainable diet principles.

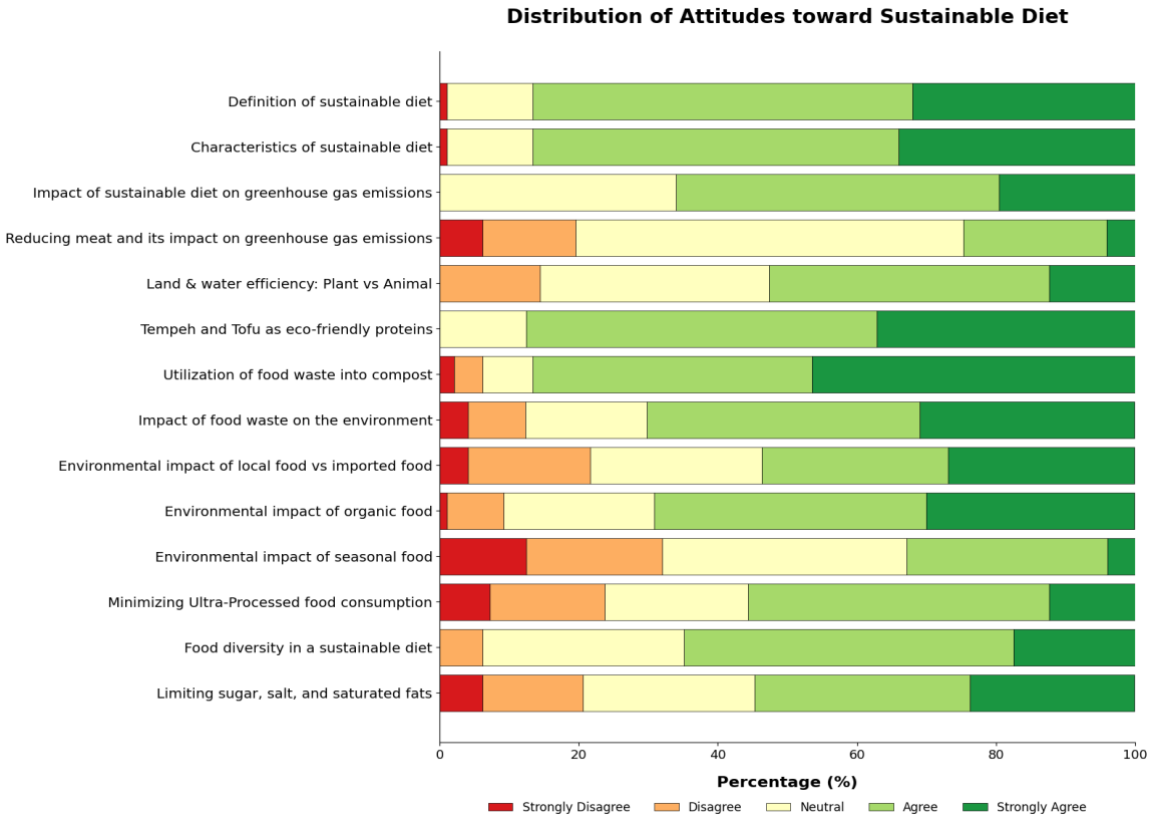

Figure 2. Distribution of attitudes toward a sustainable diet

In terms of practical aspects (**Figure 3**) below, the most practiced were consuming tempeh and tofu as sources of local vegetable protein, as they are more environmentally friendly. This practice is consistent with the subjects' knowledge level and attitude. Unlike the aspects of utilizing food waste in compost, there was a knowledge, attitude, and practice gap. Where, in the practical aspects, subjects (40.2%) reported "never" processing food waste into compost. Regarding local food, most subjects choose "often" as the frequency, with 39% consuming local food rather than imported food because it has a lower negative impact on the environment. Conceptually, the practice of choosing eco-friendly food was characterized by a high frequency of "sometimes" responses, suggesting some obstacles to implementing a sustainable diet.

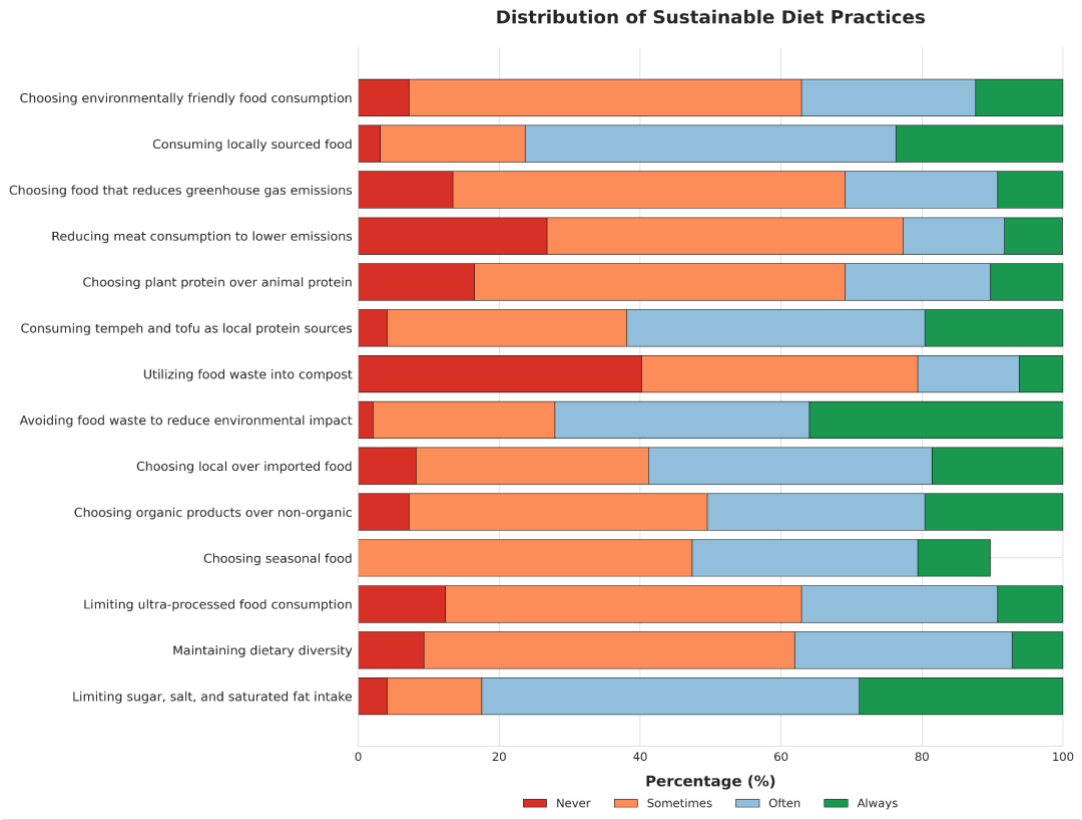

Figure 3. Distribution of sustainable diet practices

As illustrated in **Figure 4**, most of the subjects had poor knowledge (86.6%), whereas only 13.4% were categorized as good. Similarly, attitude (76.3%) and practice (92.8%) of a sustainable diet were most often classified as poor, respectively. Overall, the findings indicate that the knowledge level, attitude, and practice regarding sustainable diet remain low in this population.

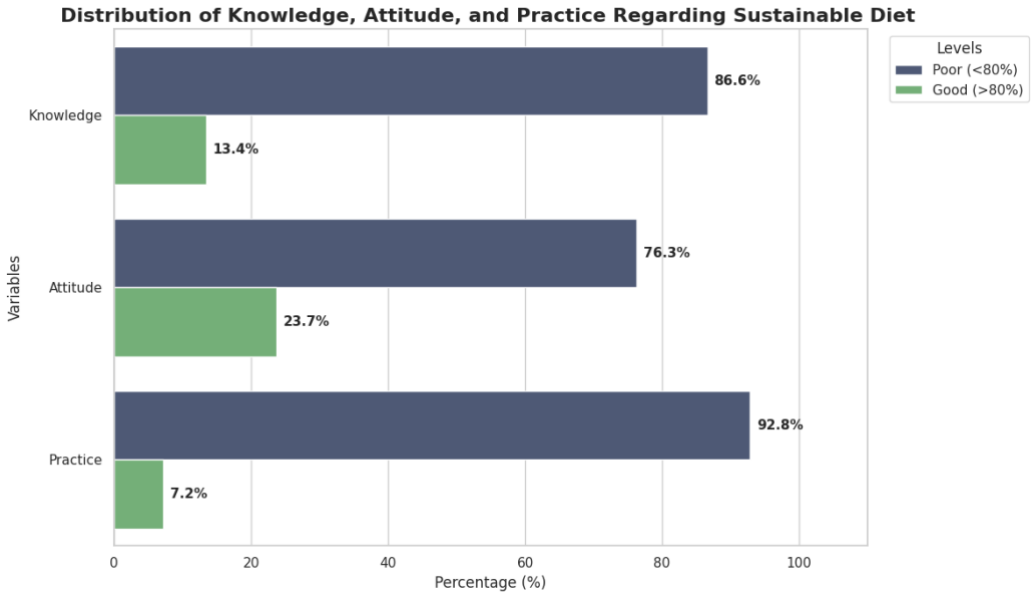

Figure 4. Distribution of knowledge. attitude. and practice regarding a sustainable diet

The mean scores for all subjects are presented in **Table 3**. Based on statistical analysis of food choice motives, the most commonly ranked motives among respondents were health (mean score = 4.53), followed by price (mean score = 4.45), and religion and taboo (mean score = 4.20). In contrast, familiarity (mean score = 3.76), and ethical concern (mean score = 4,01) were the lowest ranked of food choice motives in this population.

Table 3. Analysis for food choice motives

Food Choice Motives	Mean ± SD	Median (Min−Max)
Health	4.53 ± 0.45	4.60 (3.00−5.00)
Mood	4.30 ± 0.67	4.33 (2.00−5.00)
Convenience	4.27 ± 0.60	4.27 (2.50−5.00)
Sensory appeal	4.13 ± 0.64	4.00 (2.00−5.00)
Natural content	4.24 ± 0.67	4.33 (2.00−5.00)
Price	4.45 ± 0.67	4.67 (1.00−5.00)
Environment	4.16 ± 0.71	4.00 (2.33−5.00)
Weight control	4.07 ± 0.72	4.00 (2.00−5.00)
Familiarity	3.76 ± 0.84	3.67 (1.00−5.00)
Ethical concern	4.01 ± 0.86	4.00 (1.00−5.00)
Religion and taboo	4.25 ± 0.60	4.20 (2.60−5.00)

The correlation analysis in **Table 4** demonstrated a significant weak positive correlation between knowledge level and attitudes (r=0.279, p=0.006) and between knowledge level and practices of sustainable diet (r=0.241, p=0.017). On the other hand, there was a significant moderate positive correlation between attitudes and practices of sustainable diet (r=0.407. p<0.001), tested using Spearman's correlation (p-value <0.05). Determining the strength of the correlation, Spearman's rho test results, and the direction of the relationship is based on the cut-off from Schober.[34]

Table 4. Correlation between the variables of KAP on sustainable diet

Variables	p-values	Correlation coefficient (r)
Knowledge level – attitudes	0.006*	0.279
Knowledge level – practices	0.017*	0.241
Attitudes – practices	<0.001*	0.407

*p-value < 0.05 (correlation analysis using Spearman's rho test)

The correlation between the KAP of sustainable diet and food choice motives is shown in **Table 5**. Binary logistic regression was used to analyze each independent variable against the dependent variable (bivariate analysis) to determine candidate variables for multivariate analysis. and the selected variables were those with a p-value <0.25. Variables with a p-value <0.25 in bivariate analysis were included as candidates for multivariable logistic regression, in accordance with the criterion recommended by Hosmer and Lemeshow () to retain variables of potential explanatory relevance prior to model building. This threshold is intentionally more liberal than the conventional p<0.05 to minimize the risk of omitting important confounders or effect modifiers at the screening stage.The multivariate analysis demonstrated the adjusted odds ratio (AOR) for gender. The last analysis obtained that the strongest predictor of food choice motives was attitude regarding a sustainable diet. Subjects with a good attitude have a 5.280 times

greater chance of considering food choice motives important compared to subjects with poor attitudes ($p<0.05$, OR=5.280).

Table 5. Result of the binary logistic regression analysis of KAP associated with food choice motives

Variables	Univariate analysis OR (95% CI)	p-value	Multivariate analysis OR (95% CI)	p-value
Gender				
Female (reference)				
Male	0.580 (0.259 – 1.297)	0.185	0.638 (0.266 – 1.530)	0.314
Age				
Late adolescence (18-21 years) (reference)				
Early adulthood (21-30 years)	0.590 (0.207 – 1.678)	0.322		
Pocket money				
Low (reference)				
Medium	0.882 (0.173 – 4.506)	0.880		
High	0.621 (0.126 – 3.049)	0.557		
Education level				
Undergraduate (reference)				
Postgraduate	1.024 (0.306 – 3.429)	0.970		
Residential status				
Boarding house (reference)				
House	1.371 (0.536 – 3.505)	0.510		
Dormitory	1.909 (0.665 – 5.480)	0.229		
Place of origin				
Outside Java island (reference)				
Java island	1.447 (0.525 – 3.987)	0.474		
Knowledge				
Poor (reference)				
Good	2.596 (0.741 − 9.092)	0.136	1.340 (0.325 – 5.533)	0.685

Variables	Univariate analysis OR (95% CI)	p-value	Multivariate analysis OR (95% CI)	p-value
Attitude				
Poor (reference)				
Good	5.280 (1.768 – 15.769)	0.003	5.280 (1.768 – 15.769)	**0.003***

*p-value < 0.05, significant correlation using binary logistic regression analysis; reference category used as the baseline for comparison in the logistic regression analysis, with OR fixed at 1

Discussion

Based on our study, most of the subjects were not yet aware of a sustainable diet. The percentage of good knowledge scores is similar to attitude and practices, which were categorized as poor. According to knowledge levels, most subjects were unaware of greenhouse gas emissions and of how meat consumption impacts the environment. In line with the study from Keisyafa,[35] on students in Universitas Pendidikan Indonesia (UPI), only 41.30% of students believe that sustainable eating patterns can reduce the carbon footprint to support the SDGs 2030. Another study revealed that most subjects (>70%) did not understand ecological and carbon footprints.[36]

Research on students at universities in Istanbul, Turkey, found that students' practical scores are lower than their knowledge scores.[37] This lack of understanding among students stems from the belief that sustainable nutrition or a sustainable diet is expensive, even though students perceive it as healthy.[36] There is a strong correlation between knowledge and attitude toward sustainable diets and purchasing power.[37]

Statistically, there was a significant correlation (p<0.05) between each of the KAP of sustainable diet as an independent variable, and this result is in line with the research hypothesis of this study. Align with previous studies from Marchi,[38] who declared that nutritional and environmental attitudes were found to affect nutritional and environmental practices significantly. Other studies reveal a significant correlation between knowledge about sustainable diets and sustainable eating practices, and that motivation serves as a mediating role in this relationship.[39] In this study, a moderate but positive correlation was found between attitude and the practice of a sustainable diet ($r = 0.407$, $p < 0.001$). These findings are consistent with previous studies showing that pro-environmental attitudes and behaviors were not strongly associated ($r=0.29$, $p<0.001$).[40]

Based on our findings, the main food choice motives of most subjects were health, followed by price, religion and taboo. These findings align with a study from Maulida,[41] in the population of adolescents in East Jakarta, while "health" aspects were the most important when choosing food. In Malaysia, findings from Azmi & Sharkawi,[42] indicate that "religion" is one of the top three important aspects of food choices. Also, research from Yugharyanti,[43] showed that price was second-highest score of food choice motives among the student population of the faculty of public health at Diponegoro University. Meanwhile, familiarity motivates the lowest of food choices in this population. Consistent with research in population at the United Arab Emirates University, familiarity and eco-ethics were ranked as the least important of food choice motives.[44]

The binomial logistic regression models in this study showed that attitude was the most significant predictor of sustainable diet, along with food choice motives, among

overweight/obesity IPB students. No significant correlation was found between socioeconomics and sociodemographics of subjects, knowledge level, and subjects' food choice motives (p>0.05). Based on the systematic review from Glenisson,[45] attitude was the most frequently appearing as a key element to foster sustainable intention and behaviors. Individual beliefs play a key role in the final choice of food. Behavior-based attitudes are an effective predictor of green behavior.[38] Other systematic reviews have shown that in the theory of planned behavior, attitudes had the strongest correlation with intention, with norms and perceived behavioral control affecting dietary patterns.[46]

This study has several limitations. First, the small sample size and underrepresentation of university populations in IPB students, along with the use of purposive sampling criteria, may have led to participation bias. Furthermore, the selection of food choice dimensions for the binary logistic regression was based solely on the literature, as there is no gold standard for categorizing food choice variables in the context of sustainable diet research, especially in Indonesia. The advantage of this study is that it is the first to examine the correlation between KAP of sustainable diet and food choice motives among overweight or obese students in Indonesia. Further research should be conducted not only on students, but also on the young adult population in Indonesia, to ensure the results are representative of the population. Also, the sampling technique used is stratified random sampling in the population of young adults. Furthermore, the food choice motives variable is directly selected based on the sustainable diet context.

Conclusion

The current research emphasizes the correlation between KAP of sustainable diet and food choice motives among overweight/obesity IPB students. These results showed that attitudes towards a sustainable diet were significantly associated with food choice motives. In contrast, no significant association was found between knowledge level and the practice of a sustainable diet and food choice motives. Attitude toward a sustainable diet was the strongest correlate of of food choice motives among overweight/obese IPB students. Based on these findings, university health programs should integrate sustainable diet education into campus health promotion initiatives. Such modules ought to address knowledge, attitudes, and behavioral practices, particularly among students with overweight and obesity. Future intervention studies using longitudinal or experimental designs are warranted to evaluate the effectiveness of such programs and to establish the causal directionality of the observed associations.

Conflict of interest

The authors declared no conflict of interest regarding this article.

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Author Contributions

DFS: Conceptualization, methodology, data acquisition, formal analysis, interpretation of results, drafting the manuscript, and final approval of the version to be published; SAM: Supervision, writing, review and editing, critical revision of the manuscript, and final approval of the version to be published; IT: Supervision, writing, review and editing, and final approval of the version to be published.

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ORIGINAL PAPER

Spatial analysis and factors related to stunting prevalence in Lampung Province in 2024 (INSS Data in 2024)

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Abstract

Background: Stunting is a growth and developmental disorder caused by chronic malnutrition and recurrent infections and is defined as a Height-for-Age Z-score (HAZ) below −2 standard deviations. Despite ongoing interventions, stunting remains a major public health problem in Indonesia. Geographic Information Systems (GIS) can be used to identify the spatial distribution of stunting; however, spatial studies on stunting in Indonesia remain limited.

Objective: This study aimed to analyze spatial patterns and factors associated with stunting prevalence in Lampung Province in 2024.

Methods: A cross-sectional study was conducted using secondary data from the 2024 Indonesian Nutrition Status Survey (INSS). The study population consisted of 8,964 children under five years of age, with 2,778 children included after data cleaning. Data were analyzed using univariate, bivariate, and spatial analyses.

Results: The prevalence of stunting was 15.3%, while 84.7% of children were not stunted. Exclusive breastfeeding, birth weight, and maternal age were significantly associated with stunting prevalence ($p<0.05$). Spatial analysis showed significant associations of exclusive breastfeeding in several districts/cities, birth weight in West Coast, West Lampung, and East Lampung, and maternal age in Central Lampung.

Conclusion: Exclusive breastfeeding, birth weight, and maternal age were associated with stunting prevalence in Lampung Province in 2024.

Keywords: birth weight, exclusive breastfeeding, maternal age, spatial analysis, stunting

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Introduction

Stunting remains a major public health and nutritional problem among children worldwide.[1]According to the World Health Organization (WHO), stunting is defined as impaired growth and development resulting from chronic malnutrition and recurrent infections,[2-4] which are characterized by a z-score value of less than -2SD/standard deviation (stunted).[5] Stunting can adversely affect children's growth and development and may reduce their productivity in adulthood.[6]

On a global scale, in 2024 it is estimated that around 150 million children or 23.2% of children under five will experience stunting.[7,8] The results of the 2024 Indonesian Nutrition Status Survey (INSS) reported that the national stunting prevalence dropped to 19.8% [9]. However, this figure is still far from the long-term target and shows the need for focused and contextual interventions.[10] According to INSS, the percentage of stunting in Lampung Province has decreased from 15.2% in 2022 to 14.9% in 2023. However, the prevalence of stunting has increased slightly to 15.9% in 2024.[11]

The prevalence of stunting is influenced by various risk factors, factors that are often associated with the prevalence of stunting include the condition of the baby at birth and the condition of the mother.[12,13] Children's health practices such as exclusive breastfeeding play a role in ensuring nutritional adequacy[14] and preventing infectious diseases that can hinder children's growth.[15,16] Exclusive breastfeeding refers to feeding infants only breast milk during the first six months of life, without providing any additional food or liquids, including water.[17-19] Birth weight is an important indicator of fetal growth and development during pregnancy. Infants born with low birth weight are at greater risk of experiencing growth problems, including stunting during childhood,[20,21] Birth weight refers to the baby's body mass at birth, which is measured in grams.[22] Birth weight is generally categorized into low birth weight (LBW) and normal birth weight (NBW).[22, 23]

Low birth weight (LBW) is defined as a birth weight of less than 2.500 grams, whereas NBW is defined as a birth weight of 2.500 grams or more.[24,25] Maternal age reflects the biological readiness of a woman for pregnancy,[26] Maternal age at childbirth is defined as the mother's age at the time of delivery. Maternal age was categorized into two groups: risk age (<20 years or >35 years) and non-risk age (20–34 years). This categorization was based on reproductive health recommendations indicating that pregnancies occurring before the age of 20 years or after 35 years are associated with increased maternal and child health risks.[27,28] Based on research conducted by,[29] which was carried out on children under five aged 24-59 months, namely factors related to the prevalence of stunting include history of LBW, intake energy, carbohydrate, fat, history of diarrhea diseases, exclusive breastfeeding, complementary food, maternal nutritional status, history of anemia, and maternal age.

In this study, the use of Geographic Information System (GIS) is carried out which is a computing-based system designed to understand and manage geographic information.[30,31] Research based on spatial analysis related to stunting in Indonesia, both at the national and regional levels, is still rare. Thus, this study was conducted to analyze the spatial distribution pattern of stunting prevalence and factors related to stunting in Lampung Province in 2024 using INSS data and GIS approach as a basis for developing more targeted policy recommendations and interventions.[32] This study aims to analyze the spatial patterns of stunting prevalence and its association with exclusive breastfeeding, birth weight, and maternal age.

Methods

This study is quantitative research with a cross-sectional design. This study uses data from the 2024 INSS, which is a national survey organized by the Ministry of Health of the Republic of Indonesia. The survey was carried out in stages from January to December 2024. The follow-up analysis conducted by the researcher was carried out from March to April 2026. The population in this study is all children under five in Lampung Province and is recorded in INSS 2024, which is 8,964 children under five. Data cleaning was performed to identify records with missing or incomplete information on the study variables. The inclusion criteria were children under five years of age recorded in the INSS with complete data on stunting status, exclusive breastfeeding, birth weight, and maternal age. The exclusion criteria were records with missing, incomplete, or inconsistent data on one or more study variables. Records meeting the exclusion criteria were removed during the data cleaning process. As a result, 2,778 children met the inclusion criteria and were included in the final analysis.

Data were obtained from the INSS database, and then the process of cleaning, coding, and analysis is carried out. Data analysis was carried out in stages including univariate, bivariate, and spatial analysis. Univariate analysis was used to describe the distribution of respondent characteristics and research variables.[33] Bivariate analysis was performed using the chi-square test at a 5% significance level ($\alpha = 0.05$)[34] to assess the association between the independent variables and stunting prevalence. Spatial analysis was carried out to identify the distribution pattern of stunting prevalence geographically in Lampung Province using Quantum GIS software. This research received ethical approval from the Health Research Ethics Committee, Malahayati University (Approval No: 5190/EC/KEP UNMAL/II/2026).

Results

Respondent characteristics

Table 1 presents the characteristics of the 2,778 children under five included in this study. The proportion of children under five who were stunting at 15.3% and those who were not stunting at 84.7%. The majority of children under five received exclusive breastfeeding (92.6%), while a small percentage did not receive exclusive breastfeeding (7.4%). Based on birth weight, most children under five have a NBW (94.6%), while 5.4% are classified as LBW. In addition, the majority of mothers were in the non-risk age (68.4%), while 31.6% were in the risk age.

Table 1. Characteristics of respondents

Variable	Result
Stunting	
Not Stunting	2,354 (84.7%)
Stunting	424 (15.3%)
Exclusive Breastfeeding	
Exclusive Breastfeeding	2,573 (92.6%)
Not Exclusive Breastfeeding	205 (7.4%)
Birth Weight	
Normal Birth Weight	2,629 (94.6%)
Low Birth Weight	149 (5.4%)
Mother's Age	
Non Risk Age	1,899 (68.4%)
Risk Age	879 (31.6%)

Spatial distribution of stunting prevalence in Lampung province, 2024

Figure 1 presents the spatial distribution of stunting prevalence in Lampung Province in 2024. The classification of stunting prevalence was based on height-for-age anthropometric measurements according to the standards established by the Ministry of Health and the WHO. Based on the results of the analysis, it shows that the areas that experience the most stunting prevalence are in Metro City and the least are in Mesuji Regency.

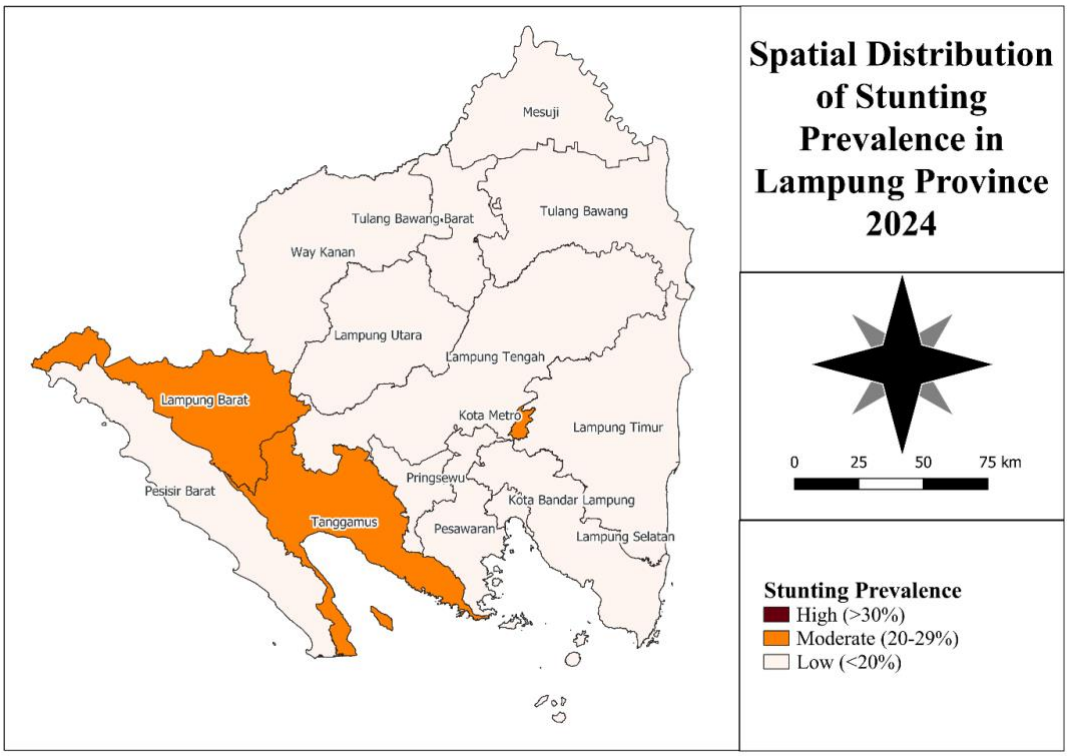

Figure 1. Spatial distribution of stunting prevalence in Lampung province 2024

The prevalence of stunting in districts/cities in Lampung Province, there are no areas that are included in the high category. Based on the classification of stunting prevalence according to the WHO, there are three areas that are included in the medium category (20-29%), namely Metro City with a stunting prevalence of 20.8%, Tanggamus Regency of 21.9% and West Lampung Regency of 22.2%. Most of the other districts/cities are in the low category (<20%). The results show spatial variation in stunting prevalence in Lampung Province. Metro City recorded the highest stunting prevalence (20.8%), while Mesuji Regency had the lowest prevalence. Based on the WHO classification, no regency/city was categorized as having a high prevalence of stunting. Three areas were classified as having a moderate prevalence (20–29%), namely West Lampung Regency (22.2%), Tanggamus Regency (21.9%), and Metro City (20.8%). The remaining regencies/cities were classified as having a low prevalence of stunting (<20%).

Spatial pattern of the relationship between exclusive breastfeeding and stunting prevalence in Lampung province in 2024

In **Figure 2**, the map shows that the areas of Bandar Lampung City, West Lampung Regency, East Lampung Regency, Mesuji Regency, Pesawaran Regency, West Tulang Bawang Regency, Way Kanan Regency, Central Lampung Regency, Pringsewu Regency, Tulang Bawang Regency, South Lampung and Metro City have a P <0.05, which means that the region has a relationship between the exclusive breastfeeding variable and stunting prevalence.

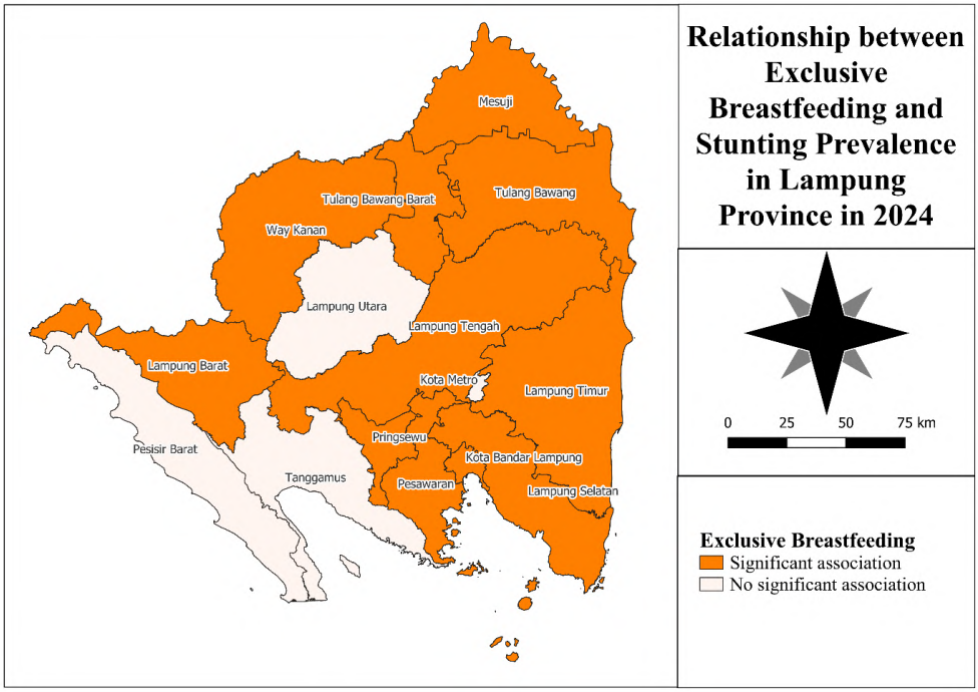

Figure 2. Spatial pattern of the relationship between exclusive breastfeeding and stunting prevalence in Lampung province in 2024

Spatial pattern of the relationship between birth weight and stunting prevalence in Lampung province in 2024

Figure 3 shows that the areas of West Coast Regency, West Lampung Regency, and East Lampung Regency have a P <0.05, which means that the area has a relationship between the birth weight variable and the prevalence of stunting.

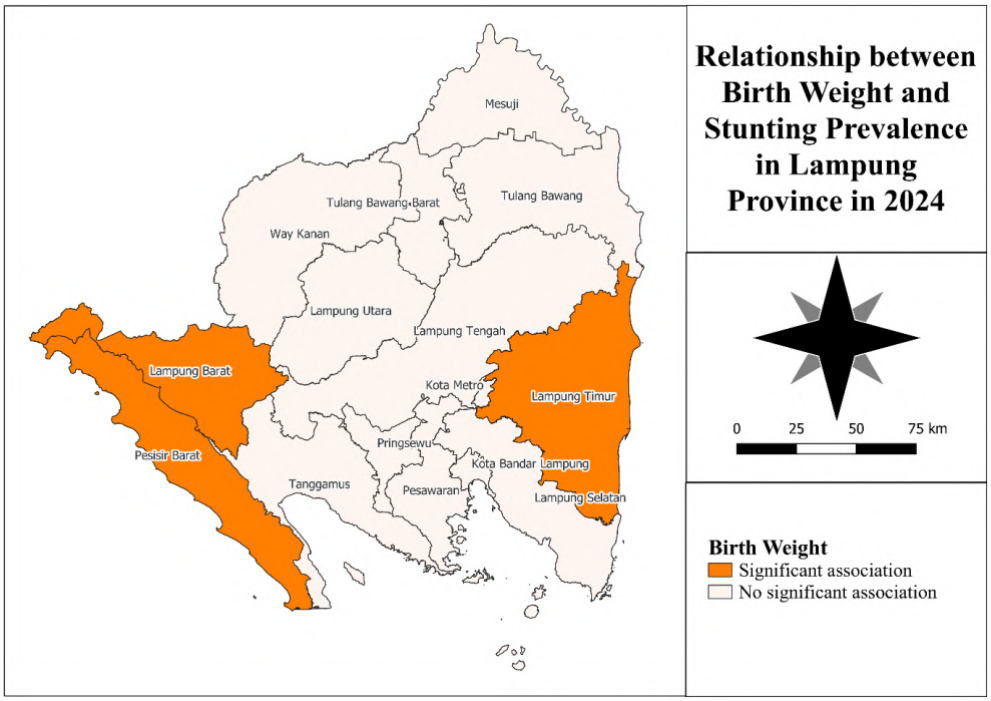

Figure 3. Spatial pattern of the relationship between birth weight and stunting prevalence in Lampung province in 2024

Spatial patterns of the relationship between maternal age and stunting prevalence in Lampung province in 2024

The map shows that the Central Lampung Regency area has a P <0.05, which means that the region has a relationship between the maternal age variable and the prevalence of stunting.

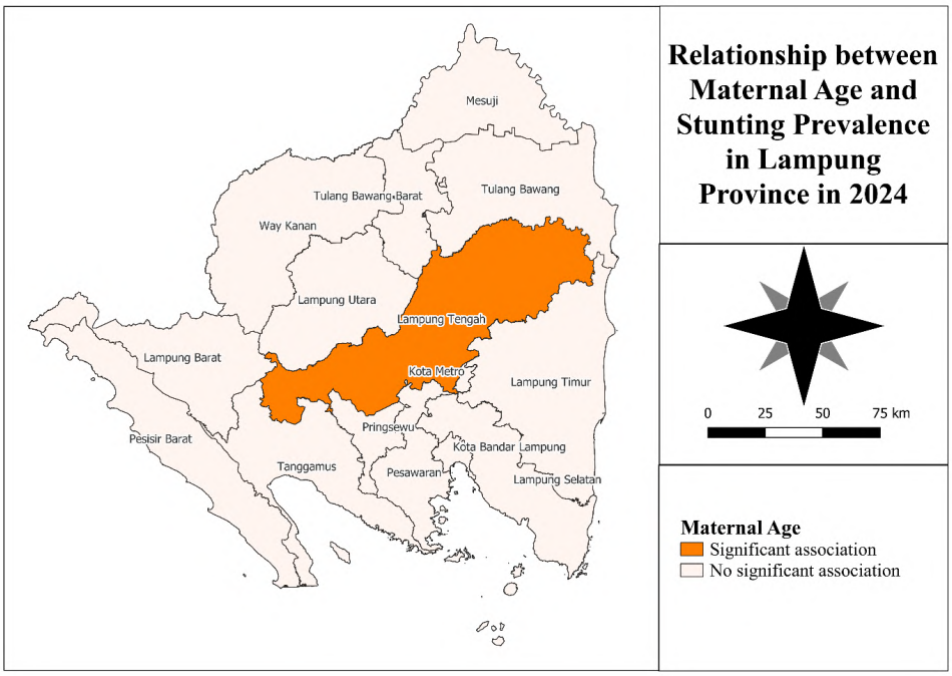

Figure 4. Spatial patterns of the relationship between maternal age and stunting prevalence in Lampung province in 2024

Discussion

This study shows that of the total 2,778 children under five studied, the majority are not stunted, namely 2354 children under five (84.7%). Meanwhile, there are 424 children under five (15.3%) who are stunted. Based on the stunting prevalence classification, there are three areas that are included in the medium category, namely Metro City with a stunting prevalence of 20.8%, Tanggamus Regency at 21.9% and West Lampung Regency at 22.2%. Most of the other districts/cities fall into the low category. The results of this study show that although most of the children under five are not stunted, although most children under five were not stunted, the stunting prevalence of 15.3% remains a public health concern because stunting can have long-term effects on human capital.[35] Children who experience stunting not only experience physical growth inhibitions, but are also at risk of cognitive development disorders, decreased learning ability, and lower productivity in adulthood.[36]

In this study, most children under five had received exclusive breastfeeding. Areas that have a significant relationship between exclusive breastfeeding and stunting prevalence are Bandar Lampung City, West Lampung Regency, East Lampung Regency, Mesuji Regency, Pesawaran Regency, West Tulang Bawang Regency, Way Kanan Regency, Central Lampung Regency, Pringsewu Regency, Tulang Bawang Regency, South Lampung and Metro City. Children under five who do not receive exclusive breastfeeding are more likely to experience inadequate nutrient intake during the critical first six months of life, a period characterized by rapid growth and development.[37] Breast milk provides essential nutrients, including high-quality proteins, fats, carbohydrates, vitamins, and minerals that support optimal physical growth.[38] Exclusive breastfeeding for the first six months is recommended because breast milk alone is sufficient to meet an infant's nutritional and physiological needs during this period. Frequent infections and inadequate nutrient intake during early life may impair linear growth and increase the risk of growth

faltering. Consequently, children who do not receive exclusive breastfeeding may be more susceptible to chronic undernutrition, which can contribute to the development of stunting.[39] The results of this study are in accordance with research conducted by Fesliria which shows that there is a significant relationship between exclusive breastfeeding and the occurrence of stunting.[40] Children under five who do not receive exclusive breastfeeding have a 2.28 times higher risk of experiencing stunting compared to children under five who receive exclusive breastfeeding.

In the birth weight variable, it was found that most of the children under five had normal birth weight. Areas that have a significant relationship between the birth weight and the prevalence of stunting are West Coast Regency, West Lampung Regency, and East Lampung Regency. Children born with LBW are at greater risk of developing stunting because LBW reflects suboptimal fetal growth and inadequate nutritional conditions during pregnancy.[41] Although stunting is assessed after birth and is influenced by postnatal factors, growth restriction that occurs during the intrauterine period may have long-term consequences for a child's growth trajectory. Infants with LBW often have reduced nutrient reserves, impaired organ development, and a lower capacity for catch-up growth compared with infants born at normal weight.[42] If adequate nutrition and health care are not provided during infancy and early childhood, these initial growth deficits may persist and contribute to impaired linear growth. Therefore, low birth weight can be considered an early indicator of vulnerability to stunting, linking adverse intrauterine conditions with subsequent growth failure during childhood. The results of this study are in accordance with research conducted by Kinaya Pranindita dan Hary Cahyati, which showed that a history of low birth weight has a significant relationship with the prevalence of stunting.[29]

Mothers who become pregnant during adolescence (<20 years) are still undergoing their own physical growth and development, resulting in competition for nutrients between the mother and the fetus. This condition may increase the risk of inadequate fetal growth, low birth weight, and poor nutritional status at birth, which are recognized risk factors for stunting. Conversely, pregnancies at advanced maternal age (>35 years) are associated with a higher risk of pregnancy complications, such as hypertension and placental insufficiency, which may impair fetal growth and development.[43] Therefore, maternal age can affect child nutritional outcomes through its influence on fetal growth, birth outcomes, and the quality of postnatal care, ultimately increasing the risk of stunting.[44] The area that has a significant association between maternal age and stunting prevalence is Central Lampung Regency. The results of this study are in accordance with research conducted by Nuridah Hasrun[45] which shows that there is a significant relationship between maternal age and the emergence of stunting in children under five. The study showed that 35-year-old mothers were more likely to have children who were stunted than mothers between the ages of 20 and 35, as evidenced by a *P* 0.015.Click or tap here to enter text.

One limitation of this study was the substantial amount of missing data, which reduced the final sample size after data cleaning and may have introduced selection bias. Furthermore, although the INSS dataset contains numerous variables that may be associated with stunting prevalence, this study focused on exclusive breastfeeding, birth weight, and maternal age because these variables had relatively complete data and were considered relevant to the study objectives.

Conclusion

This study shows that most of the children under five in Lampung Province do not experience stunting, with the highest prevalence in Metro City and the lowest in Mesuji Regency. Most of the children under five have received exclusive breastfeeding, and there is a significant relationship between exclusive breastfeeding and stunting prevalence, with a significant regional distribution in several districts/cities in Lampung Province. In addition, the majority of children under five have normal birth weight, and the weight birth is significantly related to the prevalence of stunting, especially in West Coast Regency, West Lampung, and East Lampung. Maternal age also shows a significant relationship with stunting prevalence, with significant areas in Central Lampung Regency. Overall, exclusive breastfeeding factors, birth weight, and maternal age play a role in stunting prevalence in Lampung Province in 2024.

Conflict of interest

The authors declared no conflict of interest regarding this article.

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Author Contributions

FES: Conceptualization, data acquisition, formal analysis, interpretation of results, drafting the manuscript, and final approval of the version to be published; RY: Supervision, critical revision of the manuscript, interpretation of data, and final approval of the version to be published; AMS: Conception and design of the study, critical revision of the manuscript for important intellectual content, and final approval of the version to be published.

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ORIGINAL ARTICLE

Comparison of WHO global and Asia-Pacific body mass index classifications for screening low birth weight risk among pregnant women in urban Indonesia

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Abstract

Background: Low birth weight (LBW) remains a major contributor to neonatal morbidity and mortality. Maternal body mass index (BMI) is widely used to identify pregnancies at risk of adverse birth outcomes; however, the optimal BMI classification for Asian populations remains uncertain. This study compared the WHO Global and WHO Asia-Pacific BMI classifications in identifying pregnant women at risk of delivering LBW infants.
Methods: An unmatched case-control study was conducted among 729 pregnant women attending 10 primary healthcare centers in Jakarta, Indonesia. Cases comprised 368 women who delivered LBW infants (2,500 g), while 361 women with normal birth weight infants served as controls. Logistic regression models were developed using both BMI classifications and compared using the area under the receiver operating characteristic curve (AUC), Akaike Information Criterion (AIC), and Nagelkerke R^2. Screening performance was assessed using sensitivity, specificity, positive predictive value, and negative predictive value.
Results: After adjustment for maternal age, preterm delivery, and pregnancy-induced hypertension, both BMI classifications showed comparable predictive performance (WHO Global: AUC=0.646; Asia-Pacific: AUC=0.634). BMI category was not independently associated with LBW in either model. However, using obesity as the screening threshold, the WHO Asia-Pacific classification demonstrated substantially higher sensitivity than the WHO Global classification (49.5% vs. 16.3%), although specificity was lower.
Conclusions: Although both BMI classifications showed similar predictive performance, the WHO Asia-Pacific classification identified a substantially greater proportion of women at risk of delivering LBW infants. These findings support the use of population-specific BMI 2 thresholds to strengthen antenatal nutritional screening in Indonesian and other Asian populations.

Keywords: body mass index, low birth weight, maternal obesity, screening, sensitivity, urban Indonesia, WHO Asia-Pacific, WHO Global

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Introduction

Low birth weight (LBW), defined as birth weight below 2,500 grams at delivery regardless of gestational age, is a critical global public health concern and one of the strongest predictors of neonatal mortality, short-term morbidities, and long-term developmental and cardiometabolic sequelae.[1,2] One in ten livebirths (13.4 million) were preterm (known as born too soon) and one in five (23.4 million) were small for gestational age (SGA; known as born too small) in 2020. Of 135 million livebirths in 2020, 35.3 million (26.2%) were small vulnerable newborns (SVNs), defined as any baby born preterm, or SGA or both preterm and SGA. Together, these three vulnerable newborn types account for 99.5% of the world's 20 million LBW babies. Nearly two thirds (63.0%) of the world's term SGA newborns are in southern Asia (14.8 million, 40.9% of livebirths). Preterm birth rates have less regional variation but are also highest in southern Asia (13.2%).[3,4] In Indonesia, the national proportion of LBW was 6.5% according to the Survei Status Gizi Indonesia (SSGI) 2024. However, facility-based surveillance from urban primary health centers (Puskesmas) populations consistently documents higher rates, reflecting the high-risk clinical profile of primary care antenatal attendees.[5,6]

Maternal pre-pregnancy BMI is a key modifiable determinant of LBW, acting through pathways including pregnancy-induced hypertension (PIH), placental vascular insufficiency, and medically indicated preterm delivery.[7,8] Furthermore, Indonesia is experiencing a rapid and continuing nutritional transition, national obesity prevalence among adult women rose from 14.8% in 2013 to 29.3% in the 2018 Riskesdas, more than double the prevalence among men (14.5%), signaling rising obesity-related pregnancy risk.[9,10] Moreover, Asian individuals face higher risks for type 2 diabetes, cardiovascular disease, and metabolic syndrome at BMI levels classified as 'normal' by WHO Global criteria.[11,12] However, BMI's screening utility depends on the classification system used to define overweight and obesity.

This raises a foundational question regarding which BMI classification system is most appropriate for Asian populations, including Indonesia. The WHO Global classification defines overweight as BMI ≥25.0 kg/m² and obesity as ≥30.0 kg/m², thresholds derived largely from Western populations.[13] Asian populations have higher body fat and cardiometabolic risk at lower BMI than Western populations, providing the rationale for lower thresholds.[14,15] In recognition of this, the WHO Expert Consultation proposed Asia-Pacific-specific thresholds: overweight at BMI ≥23.0 kg/m² and obesity at BMI ≥25.0 kg/m².[13]

Consequently, the 5 kg/m² difference in the obesity threshold between these two systems directly affects screening sensitivity, as a lower threshold captures more at-risk women. Studies in Chinese pregnant populations found that women with BMI 25.0–28.0 kg/m², 'overweight' by WHO Global but 'obese' by Asia-Pacific criteria, experienced adverse perinatal outcomes comparable to women with higher BMI, and that the Asia-Pacific threshold offered superior discriminative validity.[16] Studies in Asian women in Hawaii found that applying Asia-Pacific cut-offs reclassified at least 40% of women into higher BMI categories.[15] Predictive modelling and screening nonetheless serve different purposes: models estimate independent risk contributions, whereas screening tools prioritize early identification of at-risk individuals.[17,18]

Yet, to our knowledge limited Indonesian study has directly compared the screening performance of both systems for LBW detection. This gap is not merely geographic: Indonesia's ethnic diversity, dietary patterns, and distinct nutritional-transition trajectory may limit generalizability of BMI–risk associations from Chinese, Korean, or Hawaiian

cohorts. Jakarta, an advanced site of this transition with rising obesity and persistent adverse birth outcomes which offers a particularly relevant setting, especially as the only prior Indonesian study using Asia-specific BMI criteria examined gestational weight gain rather than LBW screening. This study therefore compared WHO Global and Asia-Pacific BMI classifications for identifying LBW risk among pregnant women attending Puskesmas in urban Indonesia.

Methods

Study design and participants

An unmatched case-control study was conducted using data from antenatal care and birth records of pregnant women. Participants were recruited from 10 primary healthcare centers (Puskesmas), including eight in Central Jakarta and two in East Jakarta, Indonesia, between January 2023 and December 2024. Cases consisted of women delivering LBW infants, while controls were women delivering infants with normal birth weight recruited from the same primary healthcare centers. The study was conducted in accordance with the Declaration of Helsinki Cases were defined as women with singleton pregnancies who delivered LBW infants (birth weight <2,500 grams) at participating Puskesmas and controls as women with singleton pregnancies who delivered infants with normal birth weight (≥2,500 g) at the same Puskesmas network; all identified LBW deliveries across the 10 facilities were included as cases (n=368), alongside 361 eligible controls.

Sample size was calculated a priori using an unmatched case-control formula (α=0.05, 80% power, 1:1 ratio), based on an independent estimate of obesity prevalence among Indonesian pregnant women under Asia-Pacific criteria (14.4%; Battung et al.)[19] and a minimum clinically meaningful odds ratio of 2.0. This yielded a minimum required sample of 428 (214 cases, 214 controls). For both cases and controls, complete records were required for: birth weight at delivery, BMI at first antenatal visit (first trimester), gestational age at delivery, maternal age, and PIH status. Women with multiple gestations or missing data on any primary study variable were excluded. A total of 729 participants (368 cases, 361 controls) met all inclusion criteria and were included in the final analysis.

Primary Outcome

The primary outcome was LBW, defined as birth weight <2,500 grams at delivery regardless of gestational age, classified as binary (LBW=1; Normal birth weight ≥2,500 g=0) per WHO definition.[1]

Exposure: BMI Classification Systems

BMI (kg/m²) was calculated from weight and height measured at the first antenatal visit (first trimester). Weight and height were measured by trained Puskesmas midwives following the standardized anthropometric procedures specified in the Indonesian Ministry of Health's Integrated Antenatal Care Guidelines (Pedoman Pelayanan Antenatal Terpadu), which mandate calibrated digital or beam scales (precision ±0.1 kg) and stadiometers (precision ±0.1 cm) at all Puskesmas nationwide. As this was a retrospective analysis of routinely collected records, facility-specific equipment models and calibration logs were once in a year based on every puskesmas; while national guidelines standardize

the measurement protocol, minor between-facility variation in equipment cannot be entirely excluded (see Limitations). Two parallel three-category classification systems were applied: WHO Global BMI classification: Normal weight (BMI <25.0 kg/m², reference), Overweight (BMI 25.0–29.9 kg/m²), Obese (BMI ≥30.0 kg/m²). WHO Asia-Pacific BMI classification: Normal weight (BMI <23.0 kg/m², reference), Overweight (BMI 23.0–24.9 kg/m²), Obese (BMI ≥25.0 kg/m²).

Both systems were operationalized as three-category variables to enable direct structural comparability. Where the dataset contained more granular sub-categories (e.g., Obese I, Obese II, Morbidly Obese), these were merged into a single Obese category for each system. One participant with underweight BMI under WHO Global criteria (BMI <18.5 kg/m²; n=1) was excluded from WHO Global model analysis.

Covariates

Covariates were selected a priori based on established clinical evidence: (1) maternal age as a continuous variable (years); (2) gestational age at delivery, dichotomized as term (≥37 weeks, reference) versus preterm (<37 weeks); and (3) PIH, as binary (yes/no). Data on anemia and gestational diabetes mellitus were not available for access.

Statistical analysis

All statistical analyses were performed using JASP version 0.18 (University of Amsterdam, Netherlands). Descriptive statistics were calculated for all variables. Between-group differences were assessed using Pearson chi-square tests. Two binary logistic regression models were constructed: Model A (WHO Global BMI + covariates) and Model B (WHO Asia-Pacific BMI + covariates). Crude (unadjusted) and adjusted odds ratios (aOR) with 95% confidence intervals (CI) and Wald p-values are reported for all predictors. Multicollinearity was assessed using Variance Inflation Factor (VIF); VIF <10 was considered acceptable.

Model performance was compared using: AIC (lower = better fit); Nagelkerke R^2 (pseudo-explained variance); and AUC from the ROC curve. Both crude and adjusted models were compared. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) from the logistic regression model were assessed at the default classification threshold (p=0.50). Separately, crude screening diagnostic performance was computed using the 'obese' category in each system as the screen-positive threshold, directly reflecting the clinical scenario where women classified as obese receive enhanced surveillance.[20] Reclassification analysis quantified women reclassified from WHO Global 'normal weight' to Asia-Pacific 'overweight' or 'obese' and their LBW rate. Statistical significance: α=0.05 (two-tailed).

Ethical approval

This study received ethical approval from the Health Research Ethics Committee, Faculty of Medicine, Universitas Indonesia (Approval No: 1698/UN2.F1/ETIK/PPM.00.02/2024). The study used anonymized secondary medical record data, and all procedures complied with the ethical principles of the Declaration of Helsinki.

Results

Participant characteristics

A total of 729 participants were included: 368 cases (women who delivered LBW infants) and 361 controls (women who delivered normal birth weight infants), recruited from 10 Puskesmas across Central and East Jakarta. Baseline characteristics are presented in **Table 1**. Preterm delivery was documented in 211 women (28.9%) overall and was strongly associated with LBW case status (70.1% of cases vs. 29.9% of controls delivered preterm; p<0.001). PIH was present in 26 women (3.6%) and was significantly associated with case status (80.8% of PIH-positive women were cases; p=0.003). Maternal age distribution did not differ significantly between cases and controls (p=0.897).

Under WHO Global criteria, 381 participants (52.3%) were normal weight, 242 (33.2%) overweight, and 106 (14.5%) obese; the proportion of LBW cases was 48.8%, 50.4%, and 56.6% respectively across these categories (p=0.366). Under Asia-Pacific criteria, 257 (35.3%) were normal, 127 (17.4%) overweight, and 345 (47.3%) obese; LBW case proportions were 47.9%, 49.6%, and 52.8% respectively (p=0.482). Neither classification achieved statistical significance in bivariate analysis. The key structural difference was the proportion classified as obese: 14.5% (WHO Global) versus 47.3% (Asia-Pacific) a 3.3-fold difference directly attributable to the 5 kg/m² lower obesity threshold of the Asia-Pacific system. Overall, maternal age and pregnancy-induced hypertension (PIH) differed between mothers delivering LBW and normal birth weight infants. Women who delivered LBW infants also had a higher proportion of preterm births than those delivering normal birth weight infants. The distribution of maternal BMI varied depending on the BMI classification system used, with the WHO Asia-Pacific classification categorizing a larger proportion of women as overweight or obese than the WHO Global classification.

Table 1. Baseline characteristics of study participants by birth weight outcome (N=729)

Characteristic	Total (N=729)	Low Birth Weight (n=368)	Normal Birth Weight (n=361)	p-value
Maternal Age, n (%)				
<20 years	46 (6.3%)	22 (47.8%)	24 (52.2%)	0.897[a]
20–35 years (ref.)	579 (79.4%)	292 (50.4%)	287 (49.6%)	
>35 years	104 (14.3%)	54 (51.9%)	50 (48.1%)	
Gestational Age at Delivery, n (%)				
Term (≥37 weeks, ref.)	518 (71.1%)	220 (42.5%)	298 (57.5%)	<0.001[a]
Preterm (<37 weeks)	211 (28.9%)	148 (70.1%)	63 (29.9%)	
Pregnancy-Induced Hypertension (PIH), n (%)				
Yes	26 (3.6%)	21 (80.8%)	5 (19.2%)	0.003[a]
No	703 (96.4%)	347 (49.4%)	356 (50.6%)	
WHO Global BMI Classification, n (%)				
Normal weight (BMI <25.0 kg/m²)	381 (52.3%)	186 (48.8%)	195 (51.2%)	0.366[a]
Overweight (BMI 25.0–29.9 kg/m²)	242 (33.2%)	122 (50.4%)	120 (49.6%)	
Obese (BMI ≥30.0 kg/m²)	106 (14.5%)	60 (56.6%)	46 (43.4%)	
WHO Asia-Pacific BMI Classification, n (%)				
Normal weight (BMI <23.0 kg/m²)	257 (35.3%)	123 (47.9%)	134 (52.1%)	0.482[a]

Overweight (BMI 23.0–24.9 kg/m²)	127 (17.4%)	63 (49.6%)	64 (50.4%)
Obese (BMI ≥25.0 kg/m²)	345 (47.3%)	182 (52.8%)	163 (47.2%)

[a] Pearson chi-square test. BMI = body mass index; BW = birth weight; LBW = low birth weight; PIH = pregnancy-induced hypertension.

Logistic Regression Results

In crude analyses, no BMI category reached statistical significance in either model (all p>0.05; AUC 0.523 vs. 0.524), confirming that BMI alone, without clinical context, has negligible discriminative power for LBW in this population. After adjustment for maternal age, gestational age, and PIH, both models improved substantially.

Across both adjusted models, preterm delivery was the dominant predictor (Model A: aOR 3.03, 95%CI 2.13–4.31, p<0.001; Model B: aOR 3.01, 95%CI 2.12–4.29, p<0.001). PIH was also independently significant (Model A: aOR 2.90, 95%CI 1.05–8.03, p=0.04; Model B: aOR 2.90, 95%CI 1.05–8.02, p=0.040). Maternal age was not significant in either model (p=0.333–0.338). BMI categories were not independently significant in either adjusted model (WHO Overweight: aOR 0.94, p=0.73; WHO Obese: aOR 1.19, p=0.45; AP Overweight: aOR 1.06, p=0.78; AP Obese: aOR 1.08, p=0.66).

Adjusted model performance was comparable between systems: AUC 0.646 (WHO Global) versus 0.634 (Asia-Pacific); Nagelkerke R² 0.095 versus 0.093; AIC 968.83 versus 969.56. At the default classification threshold (p=0.50), both adjusted models produced identical sensitivity (42.1%) and specificity (82.3%). All VIF values were <1.05, indicating no multicollinearity. Full results are presented in **Table 2**.

Table 2. Crude and adjusted logistic regression results: WHO Global vs. WHO Asia-Pacific BMI classification (N=729)

Variable	Crude OR	95% CI	aOR*	95% CI	p†
Covariates (same in both models)					
Maternal age (years)	—	—	0.99	0.96–1.01	0.33
PIH	—	—	2.90	1.05–8.03	0.04*
Preterm delivery (<37 wk)	—	—	3.03	2.13–4.31	<0.001*
Model A — WHO Global BMI Classification (ref: Normal weight, BMI <25.0 kg/m²)					
Overweight (BMI 25.0–29.9 kg/m²)	1.07	0.77–1.47	0.942	0.67–1.32	0.73
Obese (BMI ≥30.0 kg/m²)	1.37	0.89–2.11	1.192	0.74–1.91	0.45
AIC / BIC	1014.53 / 1028.30			968.83 / 996.38	
McFadden R² /Nagelkerke (R²)	0.003 / 0.004			0.053 / 0.095	
AUC	0.523			0.646	
Sensitivity / Specificity (at p=0.5)	—			42.1% / 82.3%	
Overall accuracy	—			62.0%	
Model B — WHO Asia-Pacific BMI Classification (ref: Normal weight, BMI <23.0 kg/m²)					
Overweight (BMI 23.0–24.9 kg/m²)	1.07	0.70–1.64	1.06	0.68–1.67	0.78
Obese (BMI ≥25.0 kg/m²)	1.22	0.88–1.68	1.08	0.75–1.54	0.67
AIC / BIC	1015.08 / 1028.86			969.56 / 997.11	
McFadden R² / Nagelkerke R²	0.002 / 0.003			0.052 / 0.093	
AUC	0.524			0.634	
Sensitivity / Specificity (at p=0.5)	—			42.1% / 82.3%	
Overall accuracy	—			62.0%	

* Adjusted for maternal age (continuous, years), gestational age (preterm vs. term [ref.]), and PIH (yes vs. no [ref.]). Reference categories for BMI: Normal weight in each system. * p<0.05; p<0.001 noted where applicable. aOR = adjusted odds ratio; AIC = Akaike Information Criterion; AUC = area under the ROC curve; CI = confidence interval. All analyses performed in JASP version 0.18.

Screening Diagnostic Performance

Table 3 presents the crude diagnostic performance when the obese category is used as the screen-positive threshold, directly mimicking a clinical screening scenario. The Asia-Pacific classification identified 49.5% of all LBW cases (sensitivity), compared to only 16.3% for the WHO Global system, an absolute improvement of 33.2 percentage points representing a three-fold increase. This corresponds to 345 versus 106 screen-positive women respectively.

The sensitivity gain was accompanied by a reduction in specificity: 54.8% for Asia-Pacific versus 87.3% for WHO Global. PPV (52.8% vs. 56.6%) and NPV (51.6% vs. 50.6%) were comparable between systems. In antenatal screening, where the primary objective is minimizing missed LBW cases, sensitivity is the priority metric.

Table 3. Crude diagnostic screening performance: WHO Global vs. WHO Asia-Pacific obesity thresholds for LBW detection

Classification / Screen-Positive Threshold	Sensitivity	Specificity	PPV	NPV	n screen+
WHO Global — Obese (BMI ≥30.0 kg/m²)	16.3%	87.3%	56.6%	50.6%	106
WHO Asia-Pacific — Obese (BMI ≥25.0 kg/m²)	49.5%	54.8%	52.8%	51.6%	345
Absolute difference (AP − WHO Global)	**+33.2%**	−32.5%	−3.8%	+1.0%	+239

*Screen-positive = classified as obese. WHO Global: BMI ≥30.0 kg/m² (n=106, 14.5% of sample). WHO Asia-Pacific: BMI ≥25.0 kg/m² (n=345, 47.3% of sample). Sensitivity = proportion of LBW cases correctly identified. Specificity = proportion of normal BW cases correctly excluded. NPV = negative predictive value; PPV = positive predictive value. Calculated from crude (unadjusted) classification data.

Reclassification Analysis and Summary

A total of 124 participants (17.0%) were classified as 'normal weight' under the WHO Global system but reclassified as 'overweight' or 'obese' under the Asia-Pacific system. Among these reclassified participants, 63 (50.8%) were LBW cases, a case proportion comparable to the overall case-to-control ratio in this study (50.5%), indicating these women carry substantial LBW risk that is invisible to WHO Global classification and would not be flagged for enhanced surveillance under current Indonesian guidelines. **Table 4** provides a comprehensive comparison of all performance metrics.

Table 4. Comprehensive model performance and screening comparison: WHO Global vs. WHO Asia-Pacific BMI classification

Performance Metric	WHO Global	Asia-Pacific	Interpretation
AIC (crude)	1014.53	1015.08	Similar, both poor without covariates
AIC (adjusted)	968.83	969.56	Similar, WHO marginally lower
Nagelkerke R^2 (crude)	0.004	0.003	Negligible explained variance
Nagelkerke R^2 (adjusted)	0.095	0.093	Comparable; covariates drive model

AUC (crude)	0.523	0.524	Near-chance; BMI alone insufficient
AUC (adjusted)	0.646	0.634	Moderate; dominated by maternal age & PIH
Sensitivity at p=0.5 (adjusted)	42.1%	42.1%	Identical in regression model
Specificity at p=0.5 (adjusted)	82.3%	82.3%	Identical in regression model
Screening sensitivity (Obese as +)	16.3%	49.5%	AP: 3× higher, as key advantage
Screening specificity (Obese as +)	87.3%	54.8%	Trade-off for sensitivity gain
Women reclassified WHO→AP	—	124 (17.0%)	Additional at-risk women identified
LBW rate in reclassified women	—	50.8%	Clinically meaningful

*AIC = Akaike Information Criterion; AP = Asia-Pacific; AUC = area under the ROC curve; PPV = positive predictive value. Logistic regression metrics from JASP version 0.18. Screening sensitivity/specificity computed from crude (unadjusted) classification with obese category as screen-positive threshold.

Discussion

This study compared the WHO Global and WHO Asia-Pacific BMI classifications for identifying pregnant women at risk of delivering low birth weight (LBW) infants in an urban Indonesian population. Two principal findings emerged. First, both BMI classifications demonstrated comparable predictive performance after adjustment for maternal age, preterm delivery, and pregnancy-induced hypertension, indicating that the choice of BMI classification had little influence on overall multivariable model performance. Second, when obesity was used as the screening threshold, the WHO Asia-Pacific classification identified substantially more women who subsequently delivered LBW infants than the WHO Global classification. These findings suggest that although the two BMI classifications perform similarly as predictive models, the Asia-Pacific classification provides greater clinical utility as a screening tool by improving the identification of women who may benefit from closer antenatal monitoring.[21,22]

The higher screening sensitivity observed with the WHO Asia-Pacific classification is consistent with its lower obesity threshold (BMI ≥25.0 kg/m²), which classifies a substantially larger proportion of women as overweight or obese than the WHO Global classification.[19] This broader definition increases the likelihood of identifying women who may already have obesity-related metabolic disturbances despite having BMI values below the conventional WHO obesity threshold.[23,24] Similar findings have been reported among Chinese, Korean, and other Asian populations, where lower BMI cut-offs improved the identification of women at risk of adverse pregnancy outcomes.[25–27] These observations support the use of ethnicity-specific BMI thresholds in Asian populations, where body composition and metabolic risk differ from those of Western populations.[28,29] Our findings are consistent with evidence from China indicating that lower BMI thresholds improve the identification of women at risk for adverse pregnancy outcomes. Wu et al. reported that using the WHO Asian obesity criterion (BMI ≥25 kg/m²) identified nearly four times more obese pregnant women than the Chinese criterion (BMI ≥28 kg/m²), while demonstrating superior predictive performance for obesity-related maternal and perinatal complications. Importantly, women with BMI between 25 and 28 kg/m² had risks comparable to those with BMI ≥28 kg/m², suggesting that reliance on higher BMI thresholds may underestimate clinically important risk among Asian pregnant women.[16] Similarly, Zhao et al. found that pregnancy complications began to increase significantly at BMI values around 23 kg/m², supporting lower BMI thresholds for risk stratification among women of reproductive age in Asian populations.[30]

In parallel, evidence from other Asian populations further demonstrates the clinical relevance of lower BMI thresholds. A nationwide Korean cohort reported that increasing pre-pregnancy BMI based on the WHO Asia-Pacific classification was associated with progressively higher risks of adverse maternal and neonatal outcomes, although LBW was not specifically evaluated.[27,31] Similarly, a recent systematic review and meta-analysis confirmed that higher pre-pregnancy BMI is associated with adverse neonatal outcomes, including LBW and preterm birth.[32] In Indonesia, Battung et al. further demonstrated that Asian-specific BMI criteria improved the identification of women at risk of adverse pregnancy outcomes compared with conventional WHO classifications, supporting the use of population-specific BMI thresholds in clinical practice.[19]

The improved screening performance of the WHO Asia-Pacific classification is biologically plausible because Asian populations have higher body fat percentages and greater cardiometabolic risk at lower BMI values than Western populations.[32,33] These metabolic disturbances may impair placental function and fetal nutrient transfer through chronic inflammation, oxidative stress, and endothelial dysfunction, thereby increasing the risk of fetal growth restriction and LBW.[34,35] Consequently, women with BMI 25.0–29.9 kg/m² may already carry clinically important metabolic risks despite being classified as overweight under WHO Global criteria.[25,26]

The biological rationale for lower BMI thresholds in Asian populations is well established. Asian individuals exhibit substantially higher percentage body fat, greater visceral adipose tissue accumulation, and elevated cardiometabolic risk at BMI values categorized as 'normal' or 'overweight' by WHO Global criteria, owing to lower skeletal muscle mass and differences in fat distribution and adipokine profiles.[36,37] These metabolic perturbations, particularly insulin resistance and low-grade inflammation adversely affect placental development, trophoblast invasion, and fetal nutrient delivery, increasing the risk of intrauterine growth restriction and LBW.[38,39] Women with BMI 25.0–29.9 kg/m² who are classified as 'overweight' under WHO Global criteria but 'obese' under Asia-Pacific criteria may already exhibit these adverse metabolic characteristics, justifying the Asia-Pacific classification's treatment of this stratum as high-risk.[40]

An important implication of this study is the distinction between predictive modelling and clinical screening. Although both BMI classifications demonstrated similar regression performance, the WHO Asia-Pacific classification substantially increased case detection, indicating greater utility for antenatal screening.[12,41,42] Adoption of this classification may facilitate earlier nutritional counselling, gestational weight monitoring, and closer surveillance among women at increased risk.[43,44] Nevertheless, BMI should be regarded as a population-level screening tool rather than a definitive measure of individual health and should be interpreted alongside other clinical assessments.[29,37] Consistent with this approach, the FIGO guideline recommends preconception BMI assessment and individualized nutritional counselling as key components of obesity management during pregnancy.[45]

This study has several strengths. To our knowledge, it is the first study in Indonesia to directly compare the screening performance of the WHO Global and WHO Asia-Pacific BMI classifications for identifying women at risk of low birth weight within the same population. Additional strengths include complete ascertainment of LBW cases across 10 primary healthcare centers, a relatively large sample size (N = 729), and the evaluation of both predictive model performance and diagnostic screening performance, providing a more comprehensive assessment of BMI classification utility.

Several limitations should also be acknowledged. First, parity, anemia, and gestational diabetes data were unavailable, leaving the possibility of residual confounding. Second, the unmatched case-control design limits causal inference and may introduce selection bias. Third, the findings were derived from urban primary healthcare centers in Jakarta and may not be fully generalizable to other populations; given Indonesia's substantial ethnic and geographic diversity, BMI–LBW associations and the relative performance of WHO Global versus Asia-Pacific thresholds may differ in rural, other-island, or ethnically distinct populations, and should be verified before national extrapolation. Finally, the retrospective use of routinely collected medical records may have introduced information bias despite standardized data extraction procedures. In addition, although anthropometric measurement followed a nationally standardized antenatal care protocol, facility-level equipment calibration records were not available for independent verification across the 10 Puskesmas, which may have introduced minor measurement variability. Prospective multicenter studies with more comprehensive clinical data are warranted to validate these findings.

Conclusions

In this urban Jakarta case-control population, the WHO Asia-Pacific BMI classification substantially improved the identification of pregnant women at risk of low birth weight while maintaining comparable predictive performance to the WHO Global classification. These findings support consideration of population-specific BMI thresholds in antenatal nutritional screening among Asian populations; however, given the ethnic and geographic diversity of Indonesia, further multicenter and rural studies are warranted before generalizing these findings nationally.

Conflict of interest

The authors declare that there are no conflicts of interest.

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Author Contributions

MIBP: Conceptualization, methodology, formal analysis, data curation, investigation, writing—original draft preparation, writing—review and editing, and final approval of the version to be published. DO: Conceptualization, methodology, validation, supervision, writing—review and editing, and final approval of the version to be published. RI: Data curation, validation, supervision, writing—review and editing, and final approval of the version to be published. DNC: Data curation, validation, supervision,

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ORIGINAL ARTICLE

Ultra-processed foods consumption and arterial elasticity among male medical students at Universitas Pembangunan Nasional Veteran Jakarta

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Abstract

Background : Medical students commonly consume ultra-processed foods (UPFs) because of demanding academic schedules. Excessive UPF consumption has been associated with vascular dysfunction, but evidence on arterial elasticity in healthy young adults remains limited.

Objective : This study investigated the association between UPF consumption and arterial elasticity among male medical students at Universitas Pembangunan Nasional Veteran Jakarta.

Methods : A cross-sectional study included 50 male medical students selected by simple random sampling. UPF consumption was assessed using a semi-quantitative food frequency questionnaire and analyzed with NutriSurvey software. Arterial elasticity was measured using an Accelerated Photoplethysmograph Analyzer SA-3000P. Participants were aged ≥18 years, non-smokers, and had no diabetes mellitus, hypertension, or alcohol consumption. Associations were analyzed using a Chi-square test.

Results : Sugar intake from UPFs was significantly associated with arterial elasticity (p = 0.041; PR = 2,256; 95% CI = 1,153 – 4.406). In contrast, total energy, salt, and fat intake from UPFs were not significantly associated with arterial elasticity (p = 0.471, p = 0.990, and p = 0.763, respectively).

Conclusions : Higher sugar intake from UPFs, rather than total energy, salt, or fat intake from UPFs, was associated with arterial elasticity. Limiting sugar intake from UPFs may help preserve vascular health in young adults.

Keywords: arterial elasticity, ultra-processed foods, medical students

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Introduction

Cardiovascular disease (CVD) remains the leading cause of death worldwide. In 2022, approximately 19.8 million deaths were attributed to CVD.[1] Reduced arterial elasticity is one of the earliest manifestations of vascular dysfunction that precedes the development of hypertension, atherosclerosis, and other cardiovascular diseases.[2] It is also recognized as a biomarker of early vascular aging (EVA), a condition in which vascular age exceeds chronological age.[3] Although vascular aging is typically associated with older adults, early changes in arterial elasticity have been observed in younger populations. Zheng et al.,[4] (2020) reported that 12.9% of adults under 30 years old already exhibited EVA. As these vascular changes occur before the onset of clinical CVD, identifying modifiable risk factors that contribute to reduced arterial elasticity is important for early prevention.

Among the modifiable risk factors, unhealthy diets account for an estimated 7.94 million CVD-related deaths each year.[5] Over the past three decades, the global burden of CVD has increased substantially due to a dietary shift toward high consumption of ultra-processed foods (UPF).[6,7] Ultra-processed foods are highly processed, industrially processed foods containing minimal whole food ingredients. They are typically high in additives, salt, fat, and cholesterol, while being low in dietary fiber and micronutrients.[8,9]

Several biological mechanisms may explain the association between UPF consumption and reduced arterial elasticity. Excess sodium intake promotes hypertension, which induces endothelial dysfunction and structural remodelling of the arterial wall.[10,11] High consumption of added sugars increases inflammation and oxidative stress, whereas high saturated fat levels impair endothelial nitric oxide bioavailability and reduce arterial elasticity.[3] Together, these mechanisms may accelerate vascular aging. High UPF consumption has been shown to accelerate vascular aging by up to 9.9 years among individuals in the highest consumption quintile.[12]

The consumption of UPF continues to increase because of its convenience, affordability, and palatability.[13] Young adults, particularly medical students, are more likely to consume UPF because of demanding academic schedules and limited time for preparing healthy meals.[14] A study conducted at Sam Ratulangi University reported that 36% of college students regularly consumed UPF.[15] Another study at Universitas Indonesia found that 61.2% of medical students had pre-hypertension.[11] These findings indicate that medical students may already be at risk of impaired vascular health.

Arterial elasticity can be assessed using non-invasive methods, including pulse wave velocity (PWV) and accelerated photoplethysmography (APG).[16] However, previous studies have reported inconsistent findings about the association between UPF consumption and arterial elasticity. While one study reported no significant association between UPF consumption and PWV,[17] another study found a significant relationship between weekly UPF consumption and increased PWV or reduced arterial elasticity.[18] These inconsistencies may reflect differences in study populations, dietary assessment methods, and techniques used to evaluate arterial elasticity. In addition, studies examining the association between UPF consumption and arterial elasticity measured using APG, particularly among medical students, remain limited. Previous studies have also reported sex differences in arterial elasticity. Estrogen enhances nitric oxide production, thereby enhancing endothelial function and preserving arterial elasticity.[19] Consequently, young females have higher arterial elasticity than young males.[20] Therefore, only male participants were included in the present study to minimize the potential confounding effects of sex hormones on arterial elasticity. Therefore, this study aimed to investigate

the association between UPF consumption and arterial elasticity among male medical students at Universitas Pembangunan Nasional Veteran Jakarta.

Methods

This is an analytical observational study with a cross-sectional design. The sample size was calculated using the two-proportion hypothesis formula with $\alpha = 5\%$, $\beta = 80\%$, $P_1 = 19.7\%$,[21] and $P_2 = 39.4\%$.[22] The sample size formula estimates the required number of participants for each comparison group. Therefore, the calculated sample size was doubled, resulting in a total sample size of 50 participants.

Participants were selected using a simple random sampling method. The inclusion criteria were male medical students at Universitas Pembangunan Nasional Veteran Jakarta aged 18–22 years who engaged in moderate physical activity, had either good or poor sleep quality, experienced low-to-moderate stress levels, and provided written informed consent. Exclusion criteria included current smoking, alcohol consumption, and a history of hypertension or diabetes mellitus.

The study was conducted from August to October 2025 at the Physiology and Nutrition Laboratory, Medical Education and Research Center (MERCe), Universitas Pembangunan Nasional Veteran Jakarta. The principal researcher conducted data collection. No enumerator or research assistants were involved in the study.

The independent variable of this study was UPF consumption, which was assessed using a semi-quantitative food frequency questionnaire (SQ-FFQ). This questionnaire was adapted from a previously published SQ-FFQ developed for Indonesian university students and modified to include 40 food and beverage items classified as UPF according to the NOVA classification. This questionnaire assessed dietary intake for the last 30 days.[23] The selected food items represent commonly consumed UPFs among Indonesian young adults, making the instrument culturally appropriate for the study populations. Frequency and household portion sizes were converted to grams using the midpoint method.[24] Ultra-processed foods (UPFs) were defined according to the NOVA classification as industrial formulations made predominantly from processed ingredients and additives, with little or no intact whole foods.[8] Total UPF intake was analyzed using NutriSurvey software to estimate total energy intake (kcal), percentage of energy derived from UPFs, and intake of sugar, salt, and fat from UPFs. The percentage of energy from UPFs was calculated by dividing the energy obtained from UPFs by the recommended daily energy intake for young adult males aged 19-24 years (2650 kcal), then multiplying by 100%. As no universally accepted cut-off for UPF intake is available, participants were categorized into lower and higher UPF intake groups using the sample median percentage of energy derived from UPFs. Sugar, salt, and fat intake from UPFs were categorized according to the Indonesian Ministry of Health Recommendation as ≤50 g/day or >50 g/day, ≤2000 mg/day or >2000 mg/day, and ≤67 g/day or >67 g/day, respectively.[25]

The dependent variable was arterial elasticity, which was measured using the Accelerated Photoplethysmograph SA-3000P (Tokyo Iken Co., Ltd., Japan), a non-invasive arterial assessment device. It performs automatic internal calibration before each measurement. All assessments were performed by the same trained examiner using a standardized protocol to ensure measurement reproducibility.

Arterial elasticity was categorized as suboptimal (<30), normal (30–70), or optimal (>70) according to the manufacturer's recommended classification for the APG device,[26] which has also been used in previous studies.[27] Participants'nutritional status, sleep

quality, and stress level data were collected to describe the study population. Nutritional status was assessed using body mass index (BMI) and classified as underweight (<18.5 kg/m²), normal (18.5–22.9 kg/m²), overweight (23.0–24.9 kg/m²), obese class I (25.0–29.9 kg/m²), or obese class II (≥30 kg/m²). Sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI) with Cronbach's α = 0.83, and categorized as good (≤5) or poor (>5). Stress levels were measured using the Perceived Stress Scale-10 (PSS-10) with Cronbach's α = 0.89, and categorized as low (1–14) or moderate (15–26).[25,28–31]

Descriptive analysis was conducted to examine participant characteristics. Associations between independent and dependent variables were analyzed using a Chi-square test. Because only a few participants had optimal arterial elasticity, the normal and optimal arterial elasticity categories were combined into a single category to meet the assumption of the Chi-square test. Statistical significance was set at $p < 0.05$. This study received ethical approval from the Ethics Committee of Universitas Pembangunan Nasional Veteran Jakarta (No. 290/XI/2025/KEP).

Results

A total of 50 participants were included in this study. Most participants were 20 years old. As shown in **Table 1**, most participants had normal BMI (38%), moderate stress levels (64%), and poor sleep quality (58%).

Table 1. Participant characteristics

No.	Charactheristics	Total (n = 50)
1.	Age, years	20 (18 – 22)
2.	Body Mass Index, n (%)	
	Underweight	3 (6.0)
	Normal	19 (38.0)
	Overweight	16 (32.0)
	Obese 1	7 (14.0)
	Obese 2	5 (10)
3.	Stress Level, n (%)	
	Moderate	32 (64.0)
	Low	18 (36.0)
4.	Sleep Quality, n (%)	
	Poor	29 (58.0)
	Good	21 (42)

Figure 1 illustrates that most participants exhibited suboptimal arterial elasticity (64%), followed by normal and optimal arterial elasticity. These findings indicate that reduced arterial elasticity was common in this young adult population.

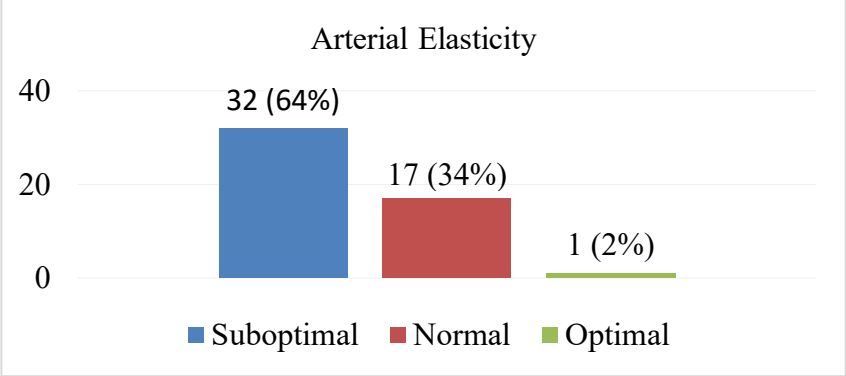

Figure 1. Arterial elasticity distribution among participants

Table 2 presents UPF intake among participants. Overall, participants consumed an average of 1327 ± 529.1 kcal/day from UPFs, accounting for approximately 50 ± 20% of total energy intake. The most consumed UPF foods were instant noodles and fried chicken. Meanwhile, the most-consumed UPF beverages were fruit-flavored, carbonated, and chocolate malt beverages.

Table 2. Energy and Nutrient Intake from UPF among Participants

No.	Energy and Nutrient Intake	Mean ± SD / Median (Min -Max)
1.	Energy (kcal)	1327 ± 529.1
2.	% UPF Consumption	50 ± 20
3.	Gram of UPF (g)	490.3 ± 206.7
4.	Sugar (g)	24.5 (0.9 – 137.4)
5.	Salt (mg)	1746.1 (560.6 – 5516.1)
6.	Fat (g)	58.7 (19.5 – 180.7)
7.	Carbohydrate (g)	116.6 (30 – 331.4)
8.	Protein (g)	73 ± 36.1
9.	Cholesterol (mg)	83.7 (35.9 – 1653.5)

Note: Normally distributed data are presented as mean ± SD and non-normally distributed data are presented as Median (Min -Max)

The median sugar intake derived from UPF was 24.5 g, with a wide range from 0.9 to 137.4 g, shown in Table 2. Similarly, the median salt intake from UPF was 1746.1 mg (range 560-5516.1 mg), corresponding to approximately 75.9 mmol of sodium. In addition, the median fat intake from UPF was 58.7 g, ranging from 19.5 to 180.7 g.

Table 3 shows there was no association between the percentage of energy derived from UPFs and arterial elasticity (PR = 0.803; p = 0.471). In contrast, sugar intake from UPFs demonstrated a significant association with arterial elasticity. Participants with sugar intake >50 g/day had a higher proportion of suboptimal arterial elasticity (63.6%) compared to those within the recommended intake or ≤50 g/day (28.2%), with a prevalence ratio indicating more than a twofold increased risk (PR = 2.256; 95% CI = 1.153-4.406; p = 0.041). Meanwhile, salt and fat intake from UPFs were not statistically significant (salt: PR = 1.131; p = 0.990; fat: PR 1.166; p =0.763).

Table 3. Association of energy, sugar, salt, and fat intake from ultra-processed foods with arterial elasticity

Variables	Arterial Elasticity				Total		PR (95% CI)	p-value
	Suboptimal		Normal + Optimal					
	N	%	N	%	N	%		
Percentage of energy derived from UPFs								
Higher (> median)	13	56.6	10	43.5	23	100	0.803	0.471
Lower (≤ median)	19	70.4	8	29.6	27	100		
Sugar intake from UPFs								
>50 g/day	7	63.6	4	34.4	11	100	2.256 (1.153 – 4.406)	0.041*
≤50 g/day	11	28.2	28	71.8	39	100		
Salt intake from UPFs								
>2,000 mg/day	7	38.9	11	61.1	18	100	1.131	0.990
≤2,000 mg/day	11	34.4	21	65.6	32	100		
Fat intake from UPFs								
>67 g/day	6	42.9	8	57.1	14	100	1.166	0.763
≤67 g/day	12	33.3	24	66.7	36	100		

Note: significant p<0.05, Chi-square test

Discussion

This study involved 50 male medical students aged 18 – 22 years, representing a young adult population generally considered to have a low risk of cardiovascular disease. Although arterial aging is typically present in older age, early alterations in arterial elasticity may occur in young adults due to risk factors such as hyperglycemia, adiposity, smoking, and lifestyle behaviors.[32] Decreased arterial elasticity is closely related to structural changes, particularly increased tunica intima thickness and endothelial dysfunction.[33]

The participants' characteristics in this study indicate the presence of several risk factors that may affect vascular health. Regarding nutritional status, more than half (56.0%) were classified as overweight or obese. This high proportion of excess body weight is consistent with findings among Indonesian university students, whereas overweight and obesity rates exceed 30%.[34] Increased adiposity has been associated with chronic inflammation, which contributes to reduced arterial elasticity.[35]

The majority of participants experienced moderate stress levels (64%), consistent with findings among medical students at Universitas Nusa Cendana (46,8%).[36] Medical students experienced heightened stress levels due to long study hours and high academic workload. Chronic stress may elevate cortisol levels and alter arterial tone, thereby decreasing arterial elasticity.[37]

Poor sleep quality was also common, affecting 58% of participants, which is comparable to the prevalence among medical students at Universitas Yarsi (57%).[38] The high prevalence of poor sleep quality is caused by high academic pressure, fear of failure, and hectic exam schedules. Inadequate sleep has been linked to increased sympathetic nervous system activity and oxidative stress, thereby impairing arterial elasticity.[39]

The participants' risk profile in this study was reflected in arterial elasticity findings, with 66% showing suboptimal elasticity despite their young age. This indicates the

presence of early vascular aging, likely influenced by dietary patterns, lifestyle, excess adiposity, psychological stress, and poor sleep quality.[27,40]Participants consumed an average of 1327 ± 529.1 kcal/day from UPFs. The majority of participants (54%) were classified as having lower total energy derived from UPF intake. This finding is consistent with a study reporting that UPFs contributed an average of 15.7% total energy intake among residents in Jakarta.[41]

Previous studies involving adults aged 18–45 years found no association between UPF consumption, accounting for approximately 50% of total daily energy intake, and arterial elasticity.[17] In the present study, although a higher proportion of participants had suboptimal arterial elasticity in the higher UPF consumption group than in the lower UPF consumption group, the difference was not statistically significant (56.5% vs. 43.5%; p = 0.471). Nevertheless, evidence from cohort studies has shown that each 10% increase in UPF intake raises CVD risk by 12%.[42] Ultra-processed foods are designed to be hyperpalatable, with high sugar, salt, and fat content, thereby stimulating the brain's reward system and food-regulation pathways.[43] This leads to increased appetite and reduced satiety responses, causing the body to consume more calories. The high content of processed carbohydrates, added sugars, salt, and saturated fat in UPF can cause metabolic and inflammatory disorders that can decrease arterial elasticity.[44] Consistent with these mechanisms, a cohort study found that high UPF consumption was significantly associated with cardiovascular disease even after adjusting for total energy intake.[45] Similarly, a meta-analysis study found that the adverse effects of UPF consumption were related to its high content of added sugar, salt, saturated fat, and low content of protective nutrients compared to the high total calories from UPF consumption.[46] These findings imply that the nutritional quality of UPFs may have a greater influence on cardiovascular health than energy intake per se.

The median sugar intake from UPFs in this study was 24.5 g (range: 0.9–137.4 g). Most participants (78%) consumed sugar within the recommended daily limit (≤50 g/day) established by the Indonesian Ministry of Health. Despite this, sugar intake from UPFs was significantly associated with arterial elasticity (p = 0.041). Participants with sugar intake >50 g/day had a 2.256 times higher prevalence of developing suboptimal arterial elasticity than those consuming ≤50 g/day (PR = 2.256; 95% CI: 1.153 – 4.406). This finding is consistent with a study in healthy adults showing that consumption of 20–25 g of glucose decreases brachial–ankle pulse wave velocity (baPWV), a marker of arterial elasticity, whereas no decrease in baPWV occurs after consuming 15 g of glucose.[47]

High sugar intake may induce postprandial hyperglycemia, which can reduce nitric oxide bioavailability. This effect is mediated by increased arginine catabolism, leading to the accumulation of asymmetric dimethylarginine (ADMA), a competitive inhibitor of endothelial nitric oxide synthase (eNOS).[48] Decreased nitric oxide bioavailability may enhance arterial matrix metalloproteinase (MMP) activity. Activation of MMP-2 and MMP-9 promotes elastin degradation, collagen deposition, and arterial smooth muscle cell migration within the arterial wall. These structural arterial alterations contribute to decreased arterial elasticity.[49] These biological pathways were not directly assessed in the present study. Therefore, further longitudinal and mechanistic studies are needed to confirm this association. The proposed mechanism by which glucose affects arterial elasticity is illustrated in **Figure 2.**

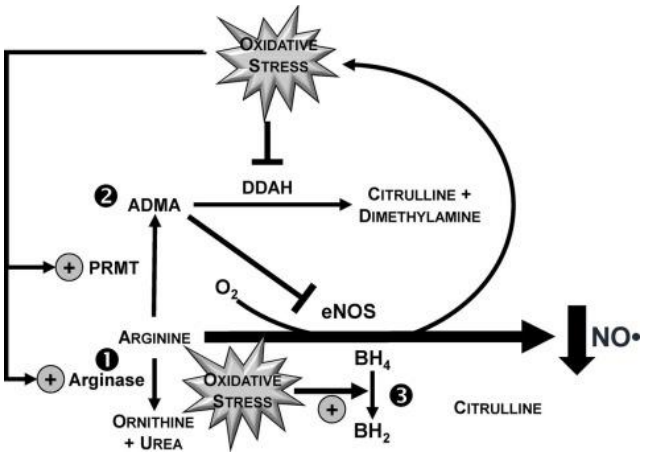

Figure 2. Mechanism of the Effect of Glucose on Arterial Elasticity[48]

These findings suggest the importance of limiting sugar intake from UPFs, even among apparently healthy young adults. Intervention through nutrition education and healthy food policies in universities may help preserve vascular health and reduce future cardiovascular risk.

The median salt intake from UPFs was 1746.1 mg (range: 560 – 5516.1 mg), equivalent to 75.9 mmol of sodium. Most participants (64%) consumed salt within the Indonesian Ministry of Health recommendation of ≤2,000 mg/day. In contrast, a national survey found that the average daily salt intake of Indonesians was 2,746 mg/day.[50]

A study conducted in healthy adults reported that an average salt intake of 1498 mg was positively associated with increased peripheral blood pressure but showed no association with PWV, a marker of arterial elasticity.[17] In the present study, the proportion of suboptimal arterial elasticity in the group with salt intake >2,000 mg/day was higher than that in those with salt intake ≤2,000 mg/day; however, the difference was not statistically significant (38.9% vs. 34.4%; p = 0.990).

Excessive salt intake may impair vascular function through several mechanisms. High salt intake can increase plasma volume and systemic vascular resistance, leading to increased blood pressure and decreased arterial wall elasticity.[51] In addition, excess salt can also increase superoxide (O^{2-}), which reacts directly with nitric oxide and inhibits its diffusion into vascular smooth muscle, preventing vasodilation and increasing blood pressure. Salt also disrupts the endothelial glycocalyx, which can interfere with vascular shear stress mechanotransduction and cause endothelial dysfunction. Intake of more than 150 mmol (3450 mg) of sodium can also increase epithelial sodium channel (eNaC) access, leading to increased intracellular sodium and decreased arterial elasticity.[52] In the present studies, these biological pathways were not assessed, so they should be considered as potential mechanisms.

However, these adverse vascular effects are more pronounced at substantially higher sodium intake. Consistent with this, a meta-analysis study found no significant association between usual salt intake and vascular structure as measured by carotid-femoral pulse wave velocity (cf-PWV).[51] In contrast, another meta-analysis reported that salt intake > 5000 mg per day was associated with reduced arterial elasticity.[53]

The median fat intake from UPF was 58.7 g (range: 19.5 – 180.7 g). One study demonstrated that consumption of high-fat meals (50 – 105 g of fat) could reduce arterial reactivity and flow-mediated dilation (FMD) due to reduced nitric oxide bioavailability.[54]

The majority of participants (72%) had fat intake categories in line with Ministry of Health recommendations (≤67 g/day). The proportion of suboptimal arterial elasticity was higher in the group with fat intake >67 g/day compared to the group with fat intake ≤67 g/day, although this difference was not statistically significant (42.9% vs. 33.3%; p = 0.763). Previous studies have suggested that high-fat foods are rich in saturated fatty acids (SFA) and trans fatty acids (TFA), which increase inflammation and oxidative stress. Fat consumption can increase postprandial triglyceride and lipoprotein levels, which decrease nitric oxide concentrations. Increased oxidative stress and decreased nitric oxide can disrupt the vascular endothelium through increased matrix metalloproteinase (MMP) activation. Matrix metalloproteinases increase elastin degradation and vascular smooth muscle cell migration, thereby decreasing arterial elasticity.[54]

Previous studies have reported inconsistent findings regarding the relationship between total fat intake and cardiovascular health. The Prospective Urban Rural Epidemiology (PURE) study, which included adults aged 35-70 years from 18 countries, found that total fat consumption and fat types such as SFA and TFA were not significantly associated with cardiovascular disease and mortality.[55] Similarly, a meta-analysis of 43 prospective cohort studies reported no significant associations between total fat, SFA, monounsaturated fatty acids (MUFA), or polyunsaturated fatty acids (PUFA) and cardiovascular disease.[56] In addition, the Tehran Lipid and Glucose Study found no significant association between total fat or individual fatty acids and incident cardiovascular disease after adjustment for potential confounders.[57] These findings should be interpreted cautiously because of methodological differences across studies. Previous studies primarily involved middle-aged and older adults and evaluated long-term cardiovascular outcomes, whereas the present study included healthy young adults and assessed arterial elasticity as an early marker of vascular dysfunction. Therefore, the absence of a significant association between total fat intake from UPFs and arterial elasticity does not necessarily contradict previous evidence.

Several limitations of this study should be acknowledged. First, overall dietary patterns were not assessed. There, the contribution of overall dietary quality to arterial elasticity could not be determined. Second, lipid profiles were not assessed, so the potential influence of undiagnosed dyslipidemia on arterial elasticity could not be excluded. Third, the small sample size limited the use of multivariable regression analysis to adjust for potential confounders, such as BMI and stress level. Fourth, the small sample size, involving only male medical students from a single university, may limit the external validity of the findings.

Conclusions

This study shows that higher sugar intake from UPFs was significantly associated with suboptimal arterial elasticity. However, no significant associations were observed between total energy, salt, or fat intake from UPFs and arterial elasticity. These findings suggest that limiting sugar intake from UPFs may support vascular health.

Conflict of interest

All authors declare no conflicts of interest

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Author Contributions

ASM: design of the study, data acquisition, interpretation of data, drafting the manuscript; NB: conceptualization, design of the study, interpretation of data, critical revision of the manuscript for important intellectual content, and final approval of the version to be published; EH: design of the study, interpretation of data; MD: design of the study, interpretation of data

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ORIGINAL PAPER

The effect of Ramadan fasting and physical exercise on fasting blood glucose in productive-age adults: A pilot study

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Abstract

Background: Productive-age adults are vulnerable to metabolic disorders due to unhealthy diets, low physical activity, which increase fasting blood glucose levels.
Objective: This study aims to analyze the effect of the combination of Ramadan fasting and physical exercise on fasting blood glucose levels in productive-age adults.
Methods: A quasi-experimental study with a non-equivalent control group design was conducted on 34 respondents aged 18-25 years with normal or prediabetes fasting blood glucose levels according to the American Diabetes Association classification. Participants underwent a two-week intervention during Ramadan. The intervention group fasted during Ramadan and underwent physical exercise, including walking and soleus push-ups, whereas the control group showed lower adherence to the intervention. Fasting blood glucose levels were measured at the beginning of Ramadan (T_o), the end of Ramadan (T_1), and one month after Ramadan (T_2). Analysis using Two-Way Repeated Measures ANOVA.
Results: Fasting glucose levels between the intervention and control groups at T_o, T_1, and T_2 showed no significant differences ($p>0.05$). Mixed ANOVA results also showed no effect of time ($p=0.159$), group effect ($p=0.855$), or interaction between time and group ($p=0.269$).
Conclusion: The combination of Ramadan fasting and physical exercise for two weeks did not result in significant changes in fasting blood glucose levels. However, both groups maintained glycemic homeostasis within the normal range.

Keywords: fasting blood glucose, Ramadan fasting, physical exercise, adults

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Introduction

Glucose metabolism disorders are a global health challenge that show an increasing trend year after year. The World Health Organization reports that more than 10% of the world's adult population lives with diabetes mellitus, while the International Diabetes Federation estimates that the proportion of individuals with prediabetes continues to increase globally.[1,2] Prediabetes conditions include impaired fasting glucose (IFG) and impaired glucose tolerance (IGT), which are major risk factors for the development of type 2 diabetes mellitus if not accompanied by appropriate lifestyle interventions.[3]

Southeast Asia is one of the fastest-growing regions in the world for cases of impaired glucose tolerance. The International Diabetes Federation reports that the prevalence of diabetes in adults in Southeast Asia continues to rise, accompanied by a high proportion of the population with prediabetes and impaired glucose tolerance.[2] Globally, an estimated 541 million adults have impaired glucose tolerance, and this number is projected to increase to more than 700 million by 2045 if effective preventive interventions are not implemented.[2] Furthermore, the global prevalence of impaired fasting glucose continues to increase, contributing to the high risk of developing type 2 diabetes mellitus in the adult population.[4]

The increasing prevalence of blood glucose disorders is inseparable from changes in modern lifestyles characterized by low physical activity, increased consumption of high-energy foods, obesity, and irregular sleep patterns.[5] Developing countries with high urbanization rates, including Indonesia, show a significant increase in the productive age group in the early stages of metabolic disorders.[2] This condition is a serious concern because diabetes mellitus is associated with various chronic complications such as cardiovascular disease, nephropathy, neuropathy, and retinopathy, which contribute to high global morbidity and mortality rates.[6]

At the national level, the prevalence of diabetes mellitus in Indonesia among people aged 15 years and older continues to increase. The Indonesian Ministry of Health, through the 2018 Basic Health Research (Riskesdas), reported that the prevalence of diabetes diagnosed by doctors was 2.0%, while the prevalence based on blood glucose levels reached 8.5%. These findings indicate a significant gap between diagnosed and undiagnosed cases in the community. Furthermore, the prevalence of impaired glucose tolerance in Indonesia aged 15 years and older reached 10.9%, while the prevalence of impaired fasting glucose was 26.3%.[7] These high proportions indicate that the number of individuals with prediabetes is much greater than the number of individuals with diagnosed diabetes.

Preliminary screening data from students at the Salewangang Maros Health Sciences College before Ramadan showed that 53.8% had fasting blood glucose levels in the prediabetes category, while 5.1% had fasting blood glucose levels within the diabetic range according to the American Diabetes Association classification.[3] These findings represent the results of initial screening in a limited population and do not reflect the general population prevalence. However, they do indicate potential impaired blood glucose regulation in young, productive-age adults. This indicates that metabolic disorders can begin at a young age and have the potential to worsen if not accompanied by healthy lifestyle management and adequate physical activity.

In Indonesia, young adults, particularly college students, are beginning to show an increase in risk factors for metabolic disorders due to changes in modern lifestyles. Various studies report that college students tend to experience low levels of physical

activity, high-energy diets, inadequate sleep duration, and increased sedentary behavior, all of which contribute to an increased risk of overweight, obesity, insulin resistance, and metabolic syndrome.[8,9,10] These conditions make college students a vulnerable population to blood glucose regulation disorders, even though they are still of productive age. Furthermore, changes in activity patterns during Ramadan also have the potential to affect metabolic balance if not accompanied by healthy lifestyle habits and adequate physical activity.[5]

The productive-age adult group with normal blood glucose levels and prediabetes is an important target in metabolic disease prevention strategies. Individuals with prediabetes have experienced progressive impairment of insulin sensitivity that can be improved through lifestyle modifications, while individuals with normal blood glucose remain at risk of decreased insulin sensitivity if exposed to risk factors continuously.[11] Therefore, early detection and preventive intervention in this group are crucial to suppress the increase in type 2 diabetes mellitus cases in the future.

The productive-age adult group was chosen in this study because it is a group with high mobility and academic activity, making it vulnerable to changes in modern lifestyle patterns such as a sedentary lifestyle, irregular eating patterns, lack of sleep, and decreased physical activity. According to the Central Statistics Agency, the productive age range is 15-64 years.[12,13] However, this study focused on the 18-25 age group because this age range falls within the emerging adulthood phase, a transitional period characterized by increased independence, lifestyle changes, intense academic activity, and an increased risk of metabolic disorders due to poor health behaviors.[14] Previous research has shown that the 18-25 age group is a critical period for weight gain, insulin resistance, and cardiometabolic disorders due to changes in activity patterns and lifestyle habits.[8] In addition, students in this age range tend to experience poor sleep patterns, low physical activity, and suboptimal diet quality, potentially affecting blood glucose regulation.[9]

Physical activity is a non-pharmacological intervention that plays a crucial role in regulating blood glucose levels and controlling nutritional status. Aerobic exercise has been shown to increase glucose uptake by skeletal muscle, increase insulin sensitivity, and improve glycemic control.[15] Light aerobic activity, such as walking, is an easy, inexpensive, and safe form of exercise for adults. Previous research has shown that regular 30 minutes of walking exercise can lower fasting and postprandial blood sugar levels in individuals with prediabetes and type 2 diabetes mellitus.[16,17]

Physiologically, muscle contractions during aerobic activity increase the translocation of glucose transporter type 4 (GLUT-4) to the muscle cell membrane, thereby increasing glucose uptake more efficiently.[18] These metabolic adaptations contribute to increased insulin sensitivity and decreased peripheral insulin resistance. In addition to walking exercise, postural muscle activation, such as through soleus push-ups, has also been reported to increase muscle oxidative metabolism and improve blood glucose regulation in individuals with prediabetes.[15,19] A recent meta-analysis also showed that aerobic exercise interventions provide significant improvements in glycemic control in individuals with prediabetes.[18]

In the context of Indonesia, a predominantly Muslim country, Ramadan is a period characterized by changes in eating patterns, sleep patterns, and metabolic rhythms due to daily fasting. Ramadan fasting can affect blood glucose regulation through changes in energy intake, metabolic hormones, and physical activity.[20] Several studies have shown that Ramadan fasting can have a positive effect on glycemic control when accompanied

by adequate physical activity and a healthy lifestyle.[21,22] Conversely, changes in consumption patterns without sufficient physical activity have the potential to cause blood glucose fluctuations and worsen insulin resistance.[23]

Ramadan fasting combined with structured physical activity has been reported to have better metabolic effects than fasting without physical activity.[24] Light aerobic activity during Ramadan can help maintain insulin sensitivity, improve glucose oxidation, and reduce the risk of increased blood glucose levels during the fasting period.[25]

Although various studies have examined the effects of intermittent fasting and physical activity on glycemic control, previous research has yielded mixed results regarding changes in fasting blood glucose levels during Ramadan.[21,24] Furthermore, research specifically evaluating the combination of Ramadan fasting and light physical exercise such as walking and soleus push-ups in young adults is still limited, particularly in Indonesia. Most previous studies have been conducted in patients with diabetes mellitus, while research in productive age populations with normal blood glucose levels or prediabetes is still relatively limited.

Based on the description, this study was conducted to analyze the effect of Ramadan fasting and physical exercise on fasting blood glucose levels in productive-age adults in Maros Regency, especially in students of the Salewangang Maros Health Sciences College in 2026.

Methods

This study was a quantitative study with a quasi-experimental design using a non-equivalent control group design approach, conducted from February to April 2026 at the Salewangang Maros Health Sciences College. This study aimed to analyze the effect of Ramadan fasting and physical exercise on fasting blood glucose (FBS) levels in productive-age adults. The independent variables in this study were Ramadan fasting and physical exercise in the form of walking exercise and soleus push-ups, while the dependent variable was fasting blood glucose levels. Control variables included age, gender, body mass index (BMI), energy intake, carbohydrate intake, and family history of diabetes mellitus.

The study population consisted of all active students in grades I-III aged 18-25 years. Participants aged 18-25 years were selected because this age group represents the emerging adulthood phase and was considered the most appropriate target population for the objectives of this study. The sample size was determined using the Lemeshow formula and obtained a total of 34 respondents who were divided into an intervention group (n=17) and a control group (n=17). The sampling technique used purposive sampling in accordance with the research inclusion and exclusion criteria. The inclusion criteria included: (1) active students aged 18-25 years, (2) having fasting blood glucose levels in the normal or prediabetes category (<126 mg/dL) based on the American Diabetes Association classification,[3] and (3) willing to participate in the entire series of studies by signing an informed consent. The exclusion criteria included: (1) having fasting blood glucose levels >126 mg/dL (2) not taking all measurements until the end of the study.

Group determination used a per-protocol analysis approach based on the level of respondent compliance with the Ramadan fasting and physical exercise intervention during the study.[26,27] The intervention group consisted of respondents who fully observed the Ramadan fast and complied with the physical exercise program, while the control

group consisted of respondents who did not meet optimal compliance with the intervention.

The physical exercise intervention was conducted over a two-week period during Ramadan. It consisted of walking exercises for 30 minutes per session, three times per week, performed before breaking the fast. The duration and frequency of the exercise were adjusted to the World Health Organization's recommendation of at least 150 minutes of moderate-intensity aerobic physical activity per week to maintain metabolic health.[28] In addition, respondents also performed soleus push-ups for 10 minutes per session, six times per week, performed after breaking the fast or after meals to help improve oxidative metabolism and muscle glucose utilization during sedentary periods.[15] Compliance with Ramadan fasting and physical exercise was collected through daily Google Form filling and active monitoring via WhatsApp group throughout the study period.

Fasting blood glucose levels were measured three times during the study: before the intervention (beginning of Ramadan/T0), after the intervention (end of Ramadan/T1), and one month post-intervention (T2). The tests were performed before breaking the fast after fasting for at least 8–12 hours without caloric intake, as recommended for Ramadan fasting metabolism.[29] The measurements were performed using a calibrated EasyTouch GCHb 3-in-1 device. The classification of fasting blood glucose levels refers to the American Diabetes Association, namely normal (<100 mg/dL), prediabetes (100-125 mg/dL), and diabetes mellitus (≥126 mg/dL).[3]

Anthropometric data were obtained by measuring body weight using a OneMed digital scale and height using a SAGA stadiometer to calculate body mass index (BMI), which was classified according to the WHO Asia-Pacific classification.[30] Energy and carbohydrate intake were assessed using a 2×24-hour food recall method conducted on weekdays and weekends at baseline (T_0) before the intervention. Respondent characteristics, including age, gender, BMI, energy intake, carbohydrate intake, and family history of diabetes mellitus, were obtained using a structured respondent characteristics form. All collected data were checked for completeness and accuracy before data processing.

Data were analyzed using IBM SPSS Statistics 25. Univariate analysis was used to describe the distribution of respondent characteristics and research variables in the form of means and standard deviations (mean ± SD) as well as frequencies and percentages. Normality tests were performed using Shapiro–Wilk. Bivariate analysis used Two-Way Repeated Measures ANOVA to assess the effect of time (time effect), group effect (group effect), and time × group interaction on changes in fasting blood glucose levels at three measurement points (T0, T1, and T2).[31] A p-value <0.05 was considered statistically significant.

This study has been reviewed and approved by the Health Research Ethics Committee of the Muslim University of Indonesia (Approval Number 339/A.1/KEP-UMI/IV/2026). All respondents received an explanation of the study's objectives and procedures and provided written informed consent before participating. Respondent confidentiality and anonymity were maintained throughout the data collection, processing, and analysis.

Results

The characteristics of the study respondents are shown in **Table 1**. This study involved 34 respondents consisting of 17 respondents in the intervention group and 17 respondents in the control group. The average age of respondents in the intervention group was 20.06

± 1.088 years, while in the control group it was 20.24 ± 1.251 years. The average body mass index (BMI) in the intervention group was 20.847 ± 3.0845 kg/m² and in the control group it was 21.329 ± 2.9404 kg/m². The average energy intake of respondents in the intervention group was 1421.903 ± 314.5599 kcal, while in the control group it was 1569.432 ± 518.2053 kcal. The average carbohydrate intake in the intervention group was 180.303 ± 37.1373 grams, while in the control group it was 185.274 ± 56.1283 grams. Based on gender, the majority of respondents were female (33 people) (97.1%), while only one was male (2.9%). A family history of diabetes mellitus was found in 12 respondents (35.3%), while 22 respondents (64.7%) did not have a family history of diabetes mellitus.

Table 1. Respondent characteristics

Characteristics Respondents	Intervention (n=17)	Control (n=17)	Total (n=34)	*p*-value
Age (years), mean ± SD	20.0 ± 1.0	20.2 ± 1.2	20.1 ± 1.1	0,664
BMI (kg/m²), mean ± SD	20,8 ± 3,0	21,3 ± 2,9	21,0 ± 2,9	0,644
Energy intake (kcal), mean ± SD	1421,9 ± 314,5	1569,4 ± 518,2	1495,6 ± 429,9	0,323
Carbohydrate intake (g), mean ± SD	180,3 ± 37,1	185,2 ± 56,1	182,7 ± 47,1	0,763
Gender , n (%)				
Man	1 (5.9%)	0 (0.0%)	1 (2.9%)	1.000
Woman	16 (94.1%)	17 (100.0%)	33 (97.1%)	
Family history of DM, n (%)				
Presence	7 (41.2%)	5 (29.4%)	12 (35.3%)	0.720
None	10 (58.8%)	12 (70.6%)	22 (64.7%)	

Changes in fasting blood glucose levels during the study are presented in **Table 2**. Overall, fasting blood glucose levels remained relatively stable in both the intervention and control groups throughout the study period. Although the intervention group showed a slight decline in fasting blood glucose from baseline to one month after Ramadan, no statistically significant differences were observed between the two groups at any measurement time (all $p > 0.05$).

Table 2. Changes in fasting blood glucose levels based on measurement time

Measurement Time	Intervention (mean ± SD)	Control (mean ± SD)	*p*-value
T_0 (beginning of Ramadan)	98.8 ± 10.2	95.5 ± 16.5	0.497
T_1 (end of Ramadan)	98.0 ± 7.1	97.4 ± 11.8	0.862
T_2 (1 month post Ramadan)	89.7 ± 22.8	95.5 ± 13.0	0.366

The Mixed ANOVA results are presented in Table 3. No significant main effects of time or group were observed on fasting blood glucose levels. Likewise, no significant time × group interaction was found ($p > 0.05$), indicating that changes in fasting blood glucose over time were comparable between the intervention and control groups.

Table 3. Effect of Ramadan fasting and physical exercise on fasting blood glucose levels

Analysis Parameters	F value	*p*-value
Changes in fasting blood glucose levels based on measurement time (*time effect*)	1,892	0.159
Differences in fasting blood glucose levels between groups (*group effect*)	0.034	0.855
The effect of Ramadan fasting and physical exercise on changes in fasting blood glucose levels (*time × group interaction*)	1,339	0.269

Discussion

Fasting blood glucose (FBS) is an important indicator in assessing glucose homeostasis and insulin sensitivity in the body. Blood glucose regulation is influenced by various factors such as diet, physical activity, sleep quality, nutritional status, and fasting duration.[32] Impaired blood glucose regulation is a global concern because the prevalence of diabetes mellitus and prediabetes continues to increase in various countries, including in productive age groups.[1,2] This increase in cases is closely related to changes in modern lifestyles such as low physical activity, sedentary behavior, inadequate sleep patterns, and increased consumption of high-energy foods.[5,10]

The results of this study showed that the average fasting blood glucose levels in the intervention group experienced a gradual decrease from the beginning of Ramadan until one month after the intervention, although the changes were not statistically significant. These findings suggest that the combination of Ramadan fasting and light physical exercise can maintain stable blood glucose regulation in young adults. Physiologically, fasting causes the body to undergo metabolic adaptation through glycogenolysis and gluconeogenesis mechanisms to maintain blood glucose levels within the normal range.[29] In addition, intermittent fasting also triggers metabolic switching from glucose utilization to fatty acid oxidation and ketone bodies as alternative energy sources, thereby helping to increase the body's metabolic efficiency.[33,34]

The absence of significant differences in fasting blood glucose levels based on measurement time indicates that the body's glucose homeostasis was maintained throughout the study period. This can be explained by the fact that most respondents were in the normal and prediabetes categories, so that insulin compensatory mechanisms were still able to maintain stable blood glucose levels.[35] This study aligns with research by Pavlou et al., who reported that time-restricted eating did not significantly change fasting glucose levels in healthy adults.[36] Similar results were also reported by Yuan et al., who stated that intermittent fasting tends to have a stable effect on glycemic control in individuals with mild glucose intolerance.[37]

In addition to fasting, light physical activity performed during the study is thought to contribute to maintaining the stability of respondents' blood glucose.[18] Walking exercise and soleus push-ups are light aerobic activities that can increase glucose utilization by

skeletal muscle through increasing GLUT-4 translocation independently of insulin. Muscle contraction activity during exercise increases glucose uptake and insulin sensitivity, thereby helping maintain stable blood glucose levels during Ramadan fasting.[15,18] Previous research has shown that light to moderate intensity aerobic exercise can improve glycemic control and reduce insulin resistance in individuals with prediabetes.[16,38] In addition, soleus muscle activation has been reported to increase local oxidative metabolism and help regulate blood glucose during sedentary periods.[15,19]

However, the results of this study indicate that there were no significant differences between the intervention and control groups. A longer intervention duration may lead to more pronounced improvements in fasting blood glucose, as previous evidence suggests that exercise performed consistently over a longer period promotes metabolic adaptations and improves glycemic control in individuals with prediabetes.[18] Furthermore, respondents in the control group continued their routine daily activities during Ramadan, thus likely still experiencing the metabolic effects of Ramadan fasting even without structured physical exercise. Research by RezkAllah and Takla (2019) showed that interval training in individuals with prediabetes can improve glycemic control, as indicated by a significant decrease in fasting blood glucose (FBG) and HbA1c levels compared to the control group.[39] These results indicate that interval-based physical activity plays a crucial role in improving blood glucose regulation by increasing insulin sensitivity.

Another factor suspected of contributing to blood glucose stability in this study is hormonal adaptation and a reduced inflammatory response during Ramadan fasting. Intermittent fasting is known to affect the hormones leptin and ghrelin, which play a role in regulating appetite and energy balance.[20] In addition, Ramadan fasting has also been reported to reduce inflammatory mediators and increase insulin sensitivity through a mild metabolic adaptation mechanism (hormesis).[40,41] These adaptations allow the body to maintain stable blood glucose regulation despite changes in eating patterns and activity times during Ramadan.

The results of this study indicate that the combination of Ramadan fasting and light physical exercise is relatively safe for young adults with normal blood glucose levels or mild prediabetes. Although no statistically significant changes were found, this intervention has the potential to help maintain blood glucose homeostasis and prevent the worsening of metabolic disorders in productive age. These findings support the concept that lifestyle modification through dietary management and physical activity remains an important strategy in preventing type 2 diabetes mellitus from a young age.[7,38]

This study has several limitations, including a relatively small sample size, a short intervention duration, which may have limited the ability to detect significant changes in fasting blood glucose. In addition, physical activity and dietary intake were assessed using self-reported methods, which may be subject to recall and reporting bias. Future studies should consider using more objective measures of physical activity and dietary assessment to improve the accuracy of the findings.

Conclusion

This study shows that the combination of Ramadan fasting and physical exercise, such as walking and soleus push-ups, does not significantly change fasting blood glucose levels in productive-age adults. However, fasting blood glucose levels in both groups remained within the normal range throughout Ramadan and for one month after Ramadan,

indicating an adaptation of the body's glucose homeostasis during the fasting period. Further research is recommended using a larger sample size, longer intervention duration, and more comprehensive measurements of metabolic parameters to obtain a more in-depth picture of the effects of Ramadan fasting and physical exercise on blood glucose regulation.

Conflict of interest

The authors declared no conflict of interest regarding this article.

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Author Contributions

NI**:** Data acquisition, formal analysis, interpretation of results, drafting the manuscript, and final approval of the version to be published. SM: Conceptualization, supervision, critical revision of the manuscript, and final approval of the version to be published. FW**:** Conceptualization, supervision, critical revision of the manuscript, and final approval of the version to be published. S: Conceptualization, supervision, critical revision of the manuscript, and final approval of the version to be published.

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ORIGINAL PAPER

Association of vitamin E intake and malondialdehyde (MDA) levels with cognitive function in elderly residing at the Budi Mulia Tresna Werdha nursing home, East DKI Jakarta

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Abstract

Background: Cognitive dysfunction is one of the health problems associated with elderly. Oxidative stress is thought to play a role in the neurodegenerative process through increased production of free radicals that cause nerve cell damage. Vitamin E is an antioxidant that protects cell membranes from oxidative damage, whereas malondialdehyde (MDA) is a biomarker of oxidative stress produced by lipid peroxidation. The objective of this study is to analyze the association of vitamin E intake and MDA levels with cognitive function among elderly residents of Budi Mulia 1 Nursing Home in DKI Jakarta, Indonesia.

Methods: This secondary study employed a cross-sectional design using data derived from a primary study investigating the association between zinc intake, superoxide dismutase activity, and cognitive function among elderly. A total of 85 participants met the inclusion and exclusion criteria. Vitamin E intake was assessed using a Semi-Quantitative Food Frequency Questionnaire (SQ-FFQ), plasma MDA levels were measured from stored plasma samples, and cognitive function was evaluated using the Indonesian version of the Montreal Cognitive Assessment (MoCA-Ina).

Results: The median age of the participants was 69 years (range: 60–91 years). The median vitamin E intake, plasma MDA level, and cognitive function score were 3.7 mg/day (2.5–3.8), 2.85 nmol/mL (1.88–6.77), and 16 (1–30), respectively. No significant association was found between vitamin E intake and cognitive function ($r = 0.027$; $p = 0.806$), nor between plasma MDA levels and cognitive function ($r = 0.096$; $p = 0.380$).

Conclusion: There was no significant association between vitamin E intake or plasma MDA levels and cognitive function among elderly.

Keywords: vitamin E, malondialdehyde, oxidative stress, cognitive function, elderly

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Introduction

Elderly represent one of the population groups experiencing the most significant demographic shift worldwide. According to Indonesian Law Number 13 of 1998 concerning the Welfare of Older Persons, elderly are individuals aged 60 years and above.[1] It is estimated that by 2030, one in six people globally will be aged 60 years or older, and the number of individuals aged 60 years and above is projected to reach 2.1 billion by 2050.[2] Indonesia is currently entering an ageing population period, characterized by approximately 12% of its population being classified as elderly in 2024.[3] In DKI Jakarta, the proportion of elderly has reached 10.64% of the total population.[4]

The growing older adult population presents both opportunities and challenges for national development. If elderly remain healthy and productive, this demographic transition may provide Indonesia with a second demographic dividend.[5] However, the increasing number of elderly is accompanied by a higher prevalence of cognitive decline, characterized by impairments in memory, attention, language, and problem-solving abilities.[6,7] Such decline may limit individuals' participation in family and social activities, ultimately increasing the burden on caregivers and society.[8]

Micronutrients, including vitamins, minerals, and antioxidant compounds found in food, such as vitamins A, C, D, and E, as well as selenium, have received considerable attention because of their potential role in neuroprotection and the maintenance of cognitive function.[9] Devarshi, et al.[10] reported that higher intakes of vitamins C, D, and E, folate, and carotenoids among elderly were associated with better cognitive performance, particularly in memory and executive function. In addition, Devore, et al.[11] found that adequate intakes of vitamins C and E were associated with a lower risk of cognitive decline and Alzheimer's disease over time.

Cognitive function and oxidative stress are closely related, as oxidative stress may adversely affect cognitive performance. Oxidative stress is defined as an imbalance between free radicals (pro-oxidants) and antioxidants that can lead to tissue damage. [12] One of the biomarkers of oxidative stress is malondialdehyde (MDA), the final product of cellular lipid peroxidation derived from polyunsaturated fatty acids. [13,14] Numerous studies have demonstrated that MDA is a stable and reliable indicator of lipid peroxidation and serves as an accurate biomarker of oxidative stress.[15]

Vitamin E is a potent antioxidant capable of donating a hydrogen ion from its hydroxyl (OH) group to neutralize free radicals. Through this mechanism, vitamin E terminates lipid peroxidation chain reactions, protects cells from oxidative damage, and helps reduce oxidative stress and inflammation associated with ageing and age-related diseases.[16,17] Power, et al.[13] reported that vitamin E supplementation may provide beneficial effects on working memory among elderly. Furthermore, Ortega, et al.[18] demonstrated an association between vitamin E status and cognitive function in elderly aged 65–91 years.

Previous research conducted using the same cohort demonstrated that cognitive impairment was present in 84.7% of elderly, while superoxide dismutase (SOD) activity explained 15.9% of the variation in cognitive function. However, no significant association was observed between zinc intake and either SOD activity or cognitive function among elderly.[19] Since the primary study focused on zinc intake and SOD activity, the potential contribution of vitamin E intake, a major lipid-soluble antioxidant, and malondialdehyde (MDA), a biomarker of lipid peroxidation and oxidative stress, to cognitive function remains unclear.

The present study is a secondary analysis derived from the same cohort but addresses a different scientific question by examining the association between vitamin E intake, plasma MDA levels, and cognitive function. Unlike the primary study, which investigated zinc intake and SOD activity,[19] this study evaluates dietary antioxidant intake together with a biomarker of oxidative stress, thereby providing complementary evidence regarding the potential role of antioxidant nutrition and lipid peroxidation in cognitive ageing. Consequently, this secondary analysis extends the findings of the primary study by providing additional scientific evidence on nutritional and oxidative stress-related factors associated with cognitive function among elderly.

Therefore, this study aimed to analyze the association between vitamin E intake and malondialdehyde (MDA) levels, as a biomarker of oxidative stress, and cognitive function among elderly.

Methods

This secondary study employed a cross-sectional design to analyze the association between vitamin E intake, malondialdehyde (MDA) levels, and cognitive function among elderly. Both primary and secondary data were utilized. The primary data consisted of stored biological samples obtained from the primary study, specifically blood plasma samples used for the measurement of plasma MDA levels. Secondary data were derived from the primary study and included participant characteristics, energy intake, vitamin E intake, cognitive function, and physical activity.

The primary study was conducted at the Budi Mulia 1 Nursing Home in DKI Jakarta, Indonesia, between July and September 2024. Measurement of plasma MDA levels was performed at the Department of Biochemistry and Molecular Biology Laboratory, Faculty of Medicine, Universitas Indonesia.

The target population comprised all residents of the Budi Mulia 1 Nursing Home who had been enrolled as participants in the primary study. Study participants were selected from the target population based on the primary study inclusion criteria and the availability of stored plasma samples that met the required quality standards. Total sampling was applied to all eligible participants from the primary study who fulfilled the inclusion and exclusion criteria.

The inclusion criteria were: (1) male or female residents aged ≥60 years who had participated in the primary study; (2) willingness to participate as indicated by written informed consent; and (3) availability of stored plasma samples of adequate quality, defined as samples that had been stored continuously at −20°C since collection (approximately one year), had not undergone repeated freeze–thaw cycles, had sufficient volume for laboratory analysis, and showed no visible hemolysis. The exclusion criteria were: (1) acute illness or severe pain at the time of the primary study; (2) coagulation disorders; (3) smoking or alcohol consumption within one year before the primary study; (4) refusal to participate; and (5) plasma samples that showed hemolysis, had not been consistently stored at −20°C, had undergone repeated freeze–thaw cycles, or had insufficient volume for MDA measurement.

A total of 96 elderly were initially screened for participation in the primary study. Of these, 86 fulfilled the eligibility criteria and provided written informed consent. During the study period, one participant withdrew because they permanently left the nursing home, resulting in a final sample of 85 participants included in the present secondary analysis. No missing data were identified for variables included in the present analysis; therefore, all 85 participants were included in the statistical analyses.

Vitamin E intake was assessed using the validated Semi-Quantitative Food Frequency Questionnaire (SQ-FFQ). The SQ-FFQ was used to estimate habitual vitamin E intake based on the frequency and portion size of foods consumed. To improve the accuracy of dietary assessment, food photographs, food models, standard household measures, and the monthly nursing home menu were used during the interview. Daily nutrient intake was analyzed using NutriSurvey 2007 software, and information regarding the type, product, and daily dosage of dietary supplements was also recorded to estimate total nutrient intake.

Cognitive function was evaluated using the Indonesian version of the Montreal Cognitive Assessment (MoCA-Ina), a validated cognitive screening instrument with a total score ranging from 0 to 30, where higher scores indicate better cognitive function. Physical activity was assessed using the Physical Activity Scale for the Elderly (PASE), which evaluates leisure, household, and occupational activities performed during the previous seven days. PASE score was categorized as inactive (<125) or active (≥125).

Educational level, history of chronic diseases, age, and sex were obtained through interviewer-administered questionnaires completed during the primary study. Anthropometric measurements, including body weight and height (or estimated height using knee height for participants unable to stand upright), were performed by trained research personnel following standardized procedures. Body mass index (BMI) was calculated as body weight (kg) divided by height squared (m^2).

Plasma MDA levels were measured using stored plasma samples using the Wills thiobarbituric acid reactive substances (TBARS) spectrophotometric method. Plasma samples were reacted with thiobarbituric acid (TBA), and absorbance was measured at of 530 nm. MDA concentrations were calculated using a standard calibration curve and expressed as nmol/mL.

Data analysis was performed using IBM Statistical Package for the Social Sciences (SPSS) version 29. Data normality was assessed using the Kolmogorov–Smirnov test. Normally distributed continuous variables were presented as mean ± standard deviation, whereas non-normally distributed variables were presented as median (minimum–maximum). Categorical variables were expressed as frequencies and percentages. The associations between vitamin E intake and cognitive function, as well as between plasma MDA levels and cognitive function, were analyzed using Spearman's rank correlation test. A p-value of less than 0.05 was considered statistically significant.

This secondary study received ethical approval from the Health Research Ethics Committee of the Faculty of Medicine, Universitas Indonesia (Approval No. KET-496/UN2.F1/ETIK/ PPM.00.02/2026). Written informed consent had been obtained from all participants prior to their involvement in the study.

Results

A total of 85 participants were included in this study. Participant characteristics included age, sex, educational level, history of chronic diseases, body mass index (BMI), nutritional status, energy intake, energy intake status, fat intake, and physical activity as shown in **Table 1**. The data were obtained from our previous study.[19] The median age of the participants was 69 years (range: 60–91 years). The majority of participants were female (61.2%) and had a primary level of education (72.9%). Most participants had a history of chronic disease (87.1%), with hypertension being the most common condition (47.1%). The median BMI was 21 kg/m² (range: 17–35 kg/m²), and nearly half of the participants (49.4%) had normal nutritional status. The median energy intake was 1,928 kcal/day (range: 1,342–2,167 kcal/day), and most participants (76.5%) had adequate energy intake. In addition, the median fat intake was 64 g/day (range: 48–68 g/day). Based on physical activity level, the majority of participants (88.2%) were classified as physically inactive.

The median vitamin E intake among participants was 3.7 mg/day (range: 2.5–3.8 mg/day). Based on the Indonesian Recommended Dietary Allowance (RDA), all participants (100%) had inadequate vitamin E intake. The median cognitive function score was 16 (range: 1–30), and 72 participants (84.7%) were classified as having cognitive impairment. Vitamin E intake and cognitive function were obtained from our previous study.[19] Spearman's correlation analysis showed no significant association between vitamin E intake and cognitive function ($r = 0.027$; $p = 0.806$) as shown in **Table 2**.

Table 1. Characteristics of study participants (n = 85)

Variable	n%	Mean±SD / Median (min-max)
Age, *years*		69 (60-91)
Sex		
Male	33 (38.8)	
Female	52 (61.2)	
Educational level		
No formal education	13 (15.3)	
Primary education	62 (72.9)	
Secondary education	7 (8.2)	
Higher education	3 (3.5)	
History of chronic disease		
No	11 (12.9)	
Yes	74 (87.1)	
Schizophrenia	29 (34.1)	
Asthma	3 (3.5)	
Hypertension	40 (47.1)	
Hyperuricemia	21 (24.7)	
Dyslipidaemia	6 (7.1)	
Diabetes mellitus	7 (8.2)	
Gastritis	1 (1.2)	
Vertigo	1 (1.2)	
Parkinson's disease	1 (1.2)	
Dermatitis	1 (1.2)	
Heart disease	1 (1.2)	
Body mass index, kg/m^2		21 (17-35)
Nutritional status		
Underweight	19 (22.4)	
Normal	42 (49.4)	
Overweight	9 (10.6)	
Obese	15 (17.6)	
Energy intake, kcal/day		1928 (1342-2167)
Energy intake status		
Inadequate	20 (23.5)	
Adequate	65 (76.5)	
Fat intake, g/day		64 (48-68)
Physical activity		
Inactive	75 (88.2)	
Active	10 (11.8)	

**Data are presented as median (minimum–maximum).*

Table 2. Association between vitamin E intake and cognitive function

Variable	Cognitive function	
	r	p-value
Vitamin E intake, *mg/day*	0.027	0.806

r = correlation coefficient; p-value = level of statistical significance (p < 0.05); Spearman's rank correlation test.

The median plasma MDA level among participants was 2.85 nmol/mL (1.88–6.77 nmol/mL), while the median cognitive function score was 16 (range: 1–30). Spearman's correlation analysis demonstrated no significant association between plasma MDA levels and cognitive function (r = 0.096; p = 0.380) as shown in **Table 3**.

Table 3. Association between plasma malondialdehyde (MDA) levels and cognitive function

Variable	Cognitive function	
	r	p-value
MDA, *nmol/ml*	0.096	0.380

MDA = malondialdehyde; r = correlation coefficient; p-value = level of statistical significance (p < 0.05); Spearman's rank correlation test.

Discussion

This study found no significant association between vitamin E intake and cognitive function, as measured by the Indonesian version of the Montreal Cognitive Assessment (MoCA-Ina), among elderly (r = 0.027; p = 0.806). This finding is consistent with the study conducted by Hartati, which reported no significant association between serum vitamin E levels and cognitive function among elderly in Indonesia.[20] Theoretically, vitamin E is the primary lipid-soluble antioxidant that protects cell membranes from free radical-induced damage.[21] In the central nervous system, vitamin E inhibits lipid peroxidation in neuronal membranes, thereby helping to maintain neuronal integrity and function.[16,17] Long-term vitamin E deficiency may increase neuronal susceptibility to oxidative damage, potentially accelerating neurodegenerative processes and cognitive decline.[17,21]

The present findings are also in agreement with those reported by Cetin, et al.,[22] who demonstrated that increased vitamin E levels following supplementation were not accompanied by greater improvements in cognitive function compared with the control group. Similarly, a systematic review by Farina, et al.,[23] concluded that vitamin E supplementation did not significantly improve cognitive performance or reduce the risk of progression from mild cognitive impairment to dementia. Furthermore, Grundman reported that vitamin E has not been proven effective in preventing the progression of mild cognitive impairment to Alzheimer's disease.,[24] These findings suggest that cognitive function in elderly is a multifactorial condition influenced by various factors, including physical activity, health status, educational attainment, chronic diseases, genetic factors, and oxidative stress levels.

In contrast, the findings of this study differ from those reported by Ortega, et al.,[18] who found that higher vitamin E status was associated with better cognitive function among elderly. This discrepancy may be explained by differences in the methods used to assess vitamin E status. In the present study, vitamin E intake was estimated from dietary intake using a Semi-Quantitative Food Frequency Questionnaire (SQ-FFQ), which may not accurately reflect actual vitamin E status in the body because it is influenced by absorption, metabolism, distribution, and storage processes.[18,25] Furthermore, the median vitamin E intake of participants was only 3.7 mg/day, substantially lower than the recommended dietary allowance for elderly, which is 15 mg/day.[26]

This study also found no significant association between plasma malondialdehyde (MDA) levels and cognitive function among elderly (r = 0.096; p = 0.380). The median plasma MDA concentration was 2.85 nmol/mL, with values ranging from 1.88 to 6.77 nmol/mL. MDA is a final product of lipid peroxidation and is widely used as a biomarker of oxidative stress. Elevated MDA levels reflect increased oxidative damage within the body and are thought to contribute to neuronal membrane damage, impaired cellular function, and accelerated neurodegenerative processes associated with cognitive decline.[27-29] Nevertheless, the relationship between MDA levels and cognitive function has not been consistently demonstrated across studies, as cognitive performance is influenced by multiple factors, including age, sex, chronic diseases, nutritional status, antioxidant capacity, and genetic predisposition.[28]

The present findings are consistent with those of Abdul Sani, et al.,[30] who reported no significant association between MDA levels and cognitive function among elderly. In contrast, Papathanasiou, et al.,[29] found that individuals with higher MDA levels tended to have poorer cognitive performance or more severe cognitive impairment. In the current study, most participants had a history of chronic diseases (87.1%), low educational attainment (72.9% with primary education), and low levels of physical activity (88.2%), all of which may influence cognitive function through mechanisms that are not necessarily directly related to MDA levels.

This study has several limitations. First, the cross-sectional design only allows assessment of associations between variables at a single point in time and therefore cannot establish causal relationships. Second, vitamin E intake was assessed using a Semi-Quantitative Food Frequency Questionnaire (SQ-FFQ), which relies on participants' ability to recall their habitual dietary intake and may therefore be subject to recall bias. Third, the study evaluated vitamin E intake solely from dietary sources and did not measure circulating vitamin E concentrations, which may better reflect vitamin E status in the body. Finally, oxidative stress was assessed using plasma MDA as a single biomarker, which may not fully represent the overall oxidative stress burden and antioxidant defense system.

Conclusion

The findings showed no significant association between vitamin E intake and cognitive function among elderly (r = 0.027; p = 0.806). Likewise, no significant association was observed between plasma MDA levels and cognitive function among elderly (r = 0.096; p = 0.380). These results indicate that vitamin E intake and plasma MDA levels were not associated with cognitive function among elderly residing at the Budi Mulia 1 Nursing Home in DKI Jakarta, Indonesia.

Conflict of interest

The authors declared no conflict of interest regarding this study.

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Author Contributions

All authors contributed equally to the study conception and design, data acquisition, analysis and interpretation, manuscript drafting and critical revision, and final approval of the manuscript. All authors reviewed and approved the final version of the manuscript.

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LITERATURE REVIEW

Nutraceutical potential of propolis for cardiometabolic improvement in type 2 diabetes mellitus: A literature review

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Abstract

Background: Type 2 Diabetes Mellitus (T2DM) is associated with chronic hyperglycemia and cardiometabolic complications. Nutraceuticals rich in flavonoids, such as propolis, have emerged as potential adjunctive strategies to improve cardiometabolic outcomes in T2DM patients. However, human clinical evidence remains limited and inconsistent. Therefore, this review evaluates the potential effects of propolis supplementation on cardiometabolic outcomes in patients with T2DM.
Methods: Literature searches were conducted in PubMed, ScienceDirect, and Wiley Library for studies published between 2015 and 2025 using keywords related to "Propolis," "Type 2 Diabetes Mellitus," "Cardiometabolic benefits", "oxidative stress", "glycemic control", and "lipid profile". Eight studies were included in this review, including randomized controlled trials published in English.
Results: Propolis, which is rich in flavonoids and phenolic compounds, exerts antioxidant, anti-inflammatory, and lipid-lowering effects. Supplementation improved fasting glucose, postprandial glucose, lipid profile, antioxidant and anti-inflammatory markers in several trials. Although, results remain heterogeneous due to differences in botanical sources and dosages.
Conclusions: Propolis demonstrates potential as a nutraceutical adjunct for cardiometabolic management in T2DM. Standardization of its composition and dosage remain essential for consistent therapeutic efficacy.

Keywords: cardiometabolic health, flavonoids, nutraceutical, propolis, type 2 diabetes mellitus

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Introduction

Type 2 Diabetes Mellitus (T2DM) is one of the leading causes of mortality in Indonesia. Based on the Indonesian Health Survey (2023), the prevalence of T2DM increased from 10.8% in 2018 to 11.7%. As of 2024, diabetes remains the main contributor to both mortality rate and healthcare cost burden in Indonesia.[1–3] Type 2 Diabetes Mellitus is a metabolic disorder characterized by elevated blood glucose levels caused by insulin resistance. Several factors contribute to its complications, including uncontrolled glycemic index, dyslipidemia, increased oxidative stress, and inflammation.[4]

The American Diabetes Association (ADA) recommends that adults with diabetes consume 14 grams of fiber/1000 kcal/day, or at least five portions (approximately 400 grams) of fruits and vegetables daily. However, based on the Individual Food Consumption Survey (SKMI) in 2014, the consumption of fruits and vegetables in Indonesia remains below recommended levels.[5] In addition to being the source of dietary fibers, fruits and vegetables are also the major sources of flavonoids in daily diets. [6]

Flavonoids are natural compounds formed by a phenolic structure and are secondary metabolites derived from plants. Their characteristic varies according to the arrangement of their phenyl and carbon rings.[6] Flavonoids are known to exert antioxidant, anti-inflammatory, and cardioprotective effects.[7]

One emerging nutraceutical rich in flavonoids is propolis, a resinous substance produced through a mixture of resin and bee saliva.[8] Each gram of *Apis mellifera* propolis contains approximately 1990 mg of flavonoid, while *Trigona* sp. contains 1000 mg.[6] The biological properties of propolis vary according to its flavonoid content, which depends on plant origin and extraction method.[9] Compared with other flavonoid-rich nutraceuticals, propolis contains unique bioactives such as caffeic acid phenethyl ester (CAPE) and artepillin C, which show dual hypolipidemic and anti-inflammatory effects.[10]

However, human clinical evidence regarding standardized propolis supplementation and its impact on cardiometabolic biomarkers in T2DM remains limited and inconsistent. This review aims to evaluate the potential effects of propolis supplementation on cardiometabolic outcomes by maintaining glycemic control, improving lipid profiles, and reducing oxidative stress in T2DM patients.

Methods

This study was conducted as a narrative literature review following predefined search and selection criteria. Search was conducted in PubMed, ScienceDirect, and Wiley Library, covering databases from the last ten years (2015-2025). The search included the following keywords: “Propolis”, “Type 2 Diabetes Mellitus”, “Cardiometabolic benefits”, “oxidative stress”, “glycemic control”, and “lipid profile”. Studies were included based on these criteria (1) The study design was a randomized clinical trial, (2) The literature was published in English and full-text accessible, and (3) The study was relevant to the main topic. This review included eight studies investigating the role of propolis, primarily in subjects with Type 2 Diabetes Mellitus (**Figure 1**)

Results

A total of 360 studies were identified through database searching. After removal of duplicates (n=6), 354 articles were screened for eligibility and 338 papers were excluded.

Sixteen full-text articles were assessed for eligibility. Eight articles were excluded for not meeting inclusion criteria, including non-randomized controlled trial design (n=2), non-type 2 diabetes mellitus (n=5), and outcomes not of interest (n=1). Ultimately, eight studies were included in the final review. Study inclusion details are shown in **Figure 1**.

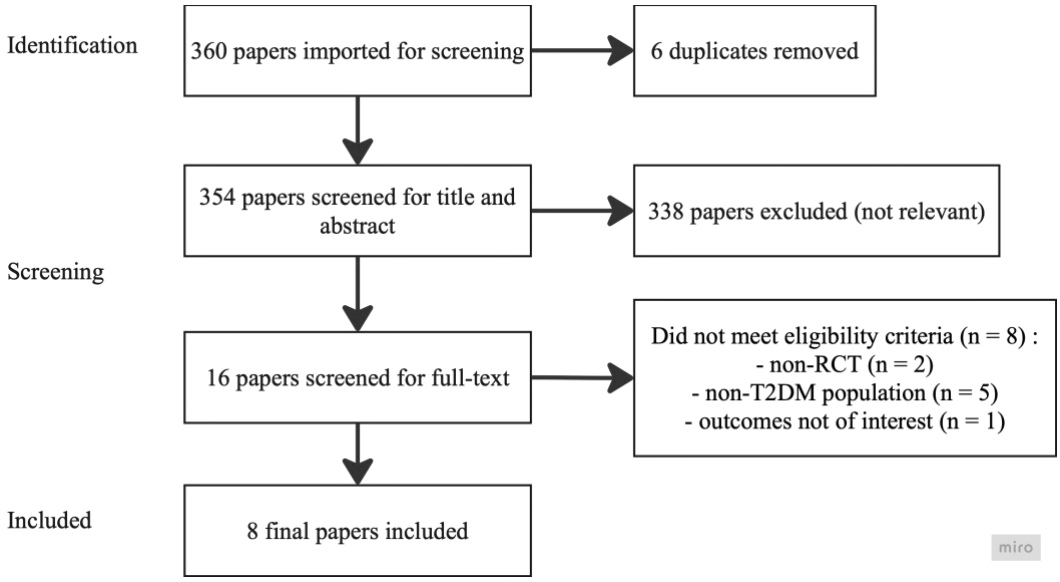

Figure 1. PRISMA Flow Diagram Study

Literature Review

1. Type 2 Diabetes Mellitus and cardiometabolic complications

Persistent hyperglycemia in T2DM promotes de novo lipogenesis, resulting in triglyceride dysregulation, reduced high-density lipoprotein (HDL), and increased low-density lipoprotein (LDL) levels.[11] Insulin resistance further stimulates lipolysis through hormone-sensitive lipase (HSL), increasing free fatty acids that are re-esterified into triglycerides and contribute to hypertriglyceridemia.[12,13] Elevated triglyceride-rich lipoproteins increase hepatic lipase activity and promote the formation of small dense LDL (sdLDL). These particles may undergo structural modifications, including oxidation, desialylation, glycation, and the formation of electronegative LDL—modified LDL particles with increased negative charge—making them highly atherogenic.[11,12]

In addition to dyslipidemia, chronic hyperglycemia induces low-grade inflammation through the release of pro-inflammatory cytokines such as tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6). The interaction between oxidative stress, inflammation, and dyslipidemia contributes to endothelial dysfunction and increases the risk of macrovascular complications, including stroke, myocardial infarction, and peripheral artery disease.[11]

The primary macrovascular complication of diabetes mellitus is diabetic dyslipidemia.[14] Newly diagnosed type 2 diabetes has a prevalence of 67.7% high cholesterol, mainly high LDL, which accounts for 91,7%. Adults with diabetes have a 2 to 4 times higher risk of developing cardiovascular disease; the main contributing factors are obesity, hyperglycemia, hypertension, and dyslipidemia.[12,13,15] Main dyslipidemia characteristics were increased triglyceride, remnant lipoprotein, and sdLDL; decreased

HDL, and postprandial dyslipidemia.[12] These changes made dyslipidemia in diabetic patients more atherogenic than other types of dyslipidemia.[16]

Lipoprotein alterations in diabetic dyslipidemia occur both qualitatively and quantitatively. Triglycerides will increase, and HDL will decrease as a result of insulin resistance in diabetes. The changes in lipoprotein particles happen to be increased sdLDL, very low-density lipoprotein (VLDL), and dysfunction of HDL.[12]

Despite pharmacological management, cardiometabolic disturbances in T2DM often persist and contribute to endothelial dysfunction and cardiovascular disease. Therefore, addressing cardiometabolic factors remains essential to reduce cardiovascular mortality and morbidity.[11]

2. *Propolis: Composition and Nutritional Bioactive*

Propolis is a resinous substance produced by bees and used to seal and protect the hive. It was formed by a mixture of resins originating from flowers, leaves, and plants with *Apis mellifera* bee saliva. Most of propolis consists of 50-55% resin, beeswax (30%), and pollen (5-10%), and others such as amino acids, minerals, sugar, vitamins, flavonoids, and phenols. The characteristic and profile of propolis were determined by the amounts of flavone, flavonols, flavonones, dihydroflavonoles, and total phenolic compound.[17] The composition of each propolis varies according to its geographical origin, bee species, botanical source, climatic condition extracted, and extraction method.[18,19]

Generally, propolis has three types based on botanical sources: poplar, Baccharis, and Dalbergia.[10] Different types of propolis based on their geographical origin, botanical source, and main flavonoid composition are presented in the **Table 1**.[17,18,20]

Table 1. Major Types of Propolis and Their Nutraceutical Relevance

Propolis type	Geographical origin	Botanical source	Main composition	Potential Nutraceutical Relevance
Poplar	Europe, North America, Non-tropical area of Asia, New Zealand	*Populus* spp., *Populus nigra* L.	Flavones, flavonones, cinnamic acid and its esters (e.g., chrysin, galangin, pinocembrin, pinobanksin-3O-acetate, quercetin, kaempferol, apigenin, naringenin)	Antioxidant, anti-atherogenic
Green (Alecrim) Brazilian	Brazil	*Baccharis* spp. *(*B. *dracunculifolia)*	Prenylated p-coumaric acid, diterpenoid acid (e.g., Artepilin C)	Antioxidant, anti-inflammatory
Red propolis	Cuba, Brazil, Mexico	*Dalbergia* spp.	Isoflavonoid, (isovlavans and pterocarpans)	Estrogenic modulation, anti-obesity
Mediterranean	Sicily, Greece, Algeria, Malta, Turkey	*Cupressaceae* spp.	Diterpenes such as totarol and totarolone	Antimicrobial, antioxidant
"Pacific"	Pacific region (Okinawa, Taiwan, Indonesia)	*Macaranga tanarius*	C-Prenyl-flavonones (propolins, prokinawan, nymphaeol, isonymphaeol)	Lipid-lowering, glycemic control

3. *Mechanism Relevant to T2DM*

a. *Propolis and Lipid Modulation*

Some previous studies in type 2 diabetes patients reveal the mechanism in which propolis could lower lipid levels. A possible mechanism shows that flavonoids in propolis may inhibit the hepatic 3-hydroxy-3-methylglutaryl-CoA reductase (HMG CoA reductase), acyl CoA cholesterol-acyltransferase (ACAT), acetyl-CoA carboxylase α (ACAC), and fatty acid synthase (FAS). Therefore, it will reduce cholesterol availability to produce VLDL. In addition, propolis may also decrease the activity of phosphatidylcholine-specific phospholipase C and increase the level of annexin A7.[21]

Propolis also contributes to increasing HDL level. It increases the expression of liver ATP-binding cassette transporter A1 and G1 protein, which will increase the formation of HDL particles.[21] A previous study in mice showed some properties of lipid-lowering effect of propolis, such as increasing the inhibition activity of enzymes involved in cholesterol biosynthesis and reducing hormone-sensitive lipase.[22]

The main bioactive component of propolis that has hypolipidemic activity is caffeic acid. The ester form, caffeic acid phenethyl ester (CAPE), inhibits the differentiation of adipocytes by blocking the expression of PPAR-γ, *adipocyte-specific fatty binding protein* (aP2), CEBP-α, and *fatty acid synthase* (FAS) that lower the triglyceride storage. It also inhibits the phosphorylation of extracellular signal-regulated kinase (ERK) and Akt to decrease the expression of cyclin D1 downstream, therefore suppressing the fat production.[18]

A study by Zakerkish et al.,[23] administered 1000 mg of Iranian propolis supplementation and compared to a placebo group, with a total of 94 participants diagnosed with T2DM aged 35 to 85 years old, analyzed the lipid profile alteration before and after intervention of Iranian propolis 500 mg capsules twice daily as an adjunctive to standard therapy. In the final week of the study, a 90-day period, both glycemic and lipid indicators were measured.Click or tap here to enter text.

Compared to the placebo group, the propolis group showed significant improvement of HDL cholesterol (p=0.024), with basal levels of 44.66 ±8.69 and 43.98 ±10.21 in the propolis and placebo group, respectively. The HDL cholesterol improved by 10.6%. Other cholesterol, such as triglycerides, total cholesterol, LDL cholesterol, and VLDL cholesterol, shows no significant changes.[23]

This result is in accordance with a previous study by Afsharpour et al.,[24] which showed a significant increase of HDL level (p=0.045) and a decrease of LDL (p=0.039), triglycerides (p=0.034), and total cholesterol (p=0.021). On the other hand, Samadi et al.,[25] showed the significant alteration of total cholesterol (p=0.01) and LDL (p=0.04), but not in HDL (p=0.27) and triglyceride level (p=0.17) compared to the placebo group. The propolis used in this study was 300 mg Iranian propolis pills, three times a day for 12 weeks.Click or tap here to enter text.

b. *Glycemic Regulation*

Propolis may improve glycemic control through several mechanisms. Flavonoids present in propolis act as α-glucosidase and α-amylase inhibitors, reducing intestinal glucose absorption and postprandial hyperglycemia.[19,22,26] In addition, compounds such as galangin and pinocembrin modulate insulin signaling through the Akt/mTOR pathway,

while caffeic acid phenethyl ester (CAPE) activates the AMPK pathway, which enhances glucose uptake and improves energy homeostasis.[17]

Clinical trials have demonstrated improvements in glycemic parameters following propolis supplementation. A previous study by Ochoa-Morales et al.,[27] in Mexico showed the supplementation effect of propolis compared to monotherapy metformin and placebo. The propolis used in the study was 600 mg (given in divided doses) produced in Chicago, Illinois, USA, in addition to base therapy of 850 mg metformin twice daily. A total of 36 participants were recruited in the study and were subjects with T2DM aged 30-60 years old, men and women. Participants then were randomly assigned to 3 groups: placebo group, metformin group, and propolis group. Supplementation was given for 12 weeks, and glycemic and lipid alteration was analyzed.

The result showed that the fasting plasma glucose (FPG) compared to placebo, both the metformin ($p=0.002$) and propolis groups ($p=0.004$) showed significant reduction. However, no significant differences were observed between the placebo and metformin group for FPG level ($p=0.13$), 2-hour postprandial ($p=0.347$), and HbA1c level ($p=0.617$).[27]

This study showed that propolis supplementation could lower the FPG and 2-hour postprandial blood glucose. The possible mechanism was reduced glucose-6 phosphatase, translocation of glucose transporter 4 (GLUT-4) in skeletal muscle, and increased glucose uptake in peripheral tissue. Propolis also inhibits the alpha amylase, beta glucosidase, and intestinal maltase, which explains the decreased postprandial glucose.[27]

Similarly, Zakerkish et al.,[24] showed that there were also significant decreases of HOMA-IR by 46.6% ($p<0.0001$), HbA1C by 8% ($p=0.006$), FPG by 28.6% ($p<0.0001$), and 2-hour postprandial glucose by 50.8% ($p<0.0001$).[23] Comparable findings were reported by Afsharpour et al., who found significant reductions in fasting and postprandial glucose levels following propolis intake.

c. Anti-inflammatory Effect

Persistent hyperglycemia in T2DM promotes the formation of advanced glycation end products (AGEs), which contribute to oxidative stress and vascular inflammation. This process stimulates the release of pro-inflammatory cytokines, including TNF-α, IL-1β, and IL-6, which accelerate endothelial dysfunction and atherosclerotic plaque development.[28]

Polyphenolic compounds in propolis exert anti-inflammatory effects by inhibiting key signaling pathways such as nuclear factor-kappa B (NF-κB), cyclooxygenase-2 (COX-2), and mitogen-activated protein kinase (MAPK). These mechanisms suppress the production of inflammatory cytokines and may reduce the progression of vascular inflammation.[18]

Cinnamic acid and coumarate in propolis inhibit the production of IL-6; therefore, the production of macrophages decreases, and IL-17 increases as a protective cytokine against myocardial infarction.[17] The bioactive compounds in propolis with anti-inflammatory properties include caffeic acid phenethyl ester (CAPE), terpenoids, steroids, and amino acids.[29]

Yousefi et al.,[29] showed that 8 weeks of propolis supplementation could lower the IL-6 ($p=0.017$) and IL-17 ($p=0.02$) significantly. This study used propolis capsules from Alamut, Qazvin, Iran, with each consumption containing 1500 mg/day, divided into 500 mg capsules three times a day. The study includes participants with T2DM diagnosed less than ten years ago, aged 35-55 years old, in Iran.

Another study by Zakerkish et al.,[23] showed no significant change of IL-6 and TNF-α levels after supplementation of Iranian propolis for 90 days. Zhao et al.,[30] showed that supplementation of 900 mg of Brazilian propolis for 18 weeks shows a significant reduction of IL-6 and TNF-α levels compared to the control group. This study shows that Brazilian propolis intake for 18 weeks results in a favorable anti-inflammatory effect in T2DM patients. IL-1β and TNF-α as pro-inflammatory cytokines were inversely correlated with IL-6 as anti-inflammatory in this study.

d. Antioxidant Mechanism

Oxidative stress plays an important role in the pathogenesis of T2DM and its cardiovascular complications. Persistent hyperglycemia increases the production of reactive oxygen species (ROS), which damage cellular structures and impair endothelial function.[29,31] Propolis contains flavonoids and polyphenols with strong antioxidant properties that scavenge free radicals, inhibit lipid peroxidation, and enhance the activity of endogenous antioxidant enzymes such as superoxide dismutase (SOD), catalase, and glutathione peroxidase (GPx).[22,32] The hydroxyl group of flavonoid has high reactivity to free radicals so that it could bind and form a more stable and less reactive particle.[31]

Polyphenolic compounds in propolis can neutralize reactive species such as superoxide (·O2−), hydroxyl radicals (·OH), and hydrogen peroxide (H2O2), and may inhibit pro-oxidant enzymes including NADPH oxidase and xanthine oxidase while enhancing antioxidant enzyme expression. Certain polyphenols, such as kaempferol, may also form metal-chelating complexes that contribute to antioxidant activity.[18]

In addition, flavonoids inhibit lipid peroxidation, platelet aggregation, and cyclooxygenase and lipoxygenase activity. These compounds may also suppress LDL oxidation through activation of the nuclear factor erythroid-2 related factor-2 (Nrf2) pathway, thereby reducing oxidative stress and the risk of atherosclerosis.[22,33]

Several propolis constituents, including 3,5-dicaffeoylquinic acid and 1,4,5-tricaffeoylquinic acid (art-C), further contribute to antioxidant activity by scavenging superoxide and hydroxyl radicals in vascular tissues.[17]

Afsharpour et al.,[31] conducted a randomized, double-blind study in Iran involving 62 T2DM patients, who were randomly assigned to a propolis or placebo group. Subjects were male and female patients aged 33 to 55 years old. The propolis used in this study was in capsule form with a 500 mg dose each, three times a day for 8 weeks. Oxidative stress parameters that were analyzed in the study are plasma levels of total antioxidant capacity, glutathione (GPx), and superoxide dismutase. In the study, after 8 weeks of propolis supplementation, there was a significant increase of total antioxidant capacity ($p=0.042$), superoxide dismutase ($p=0.034$), and glutathione ($p=0.028$).

Hesami et al.,[34] also showed the effect of propolis supplementation on oxidized LDL and catalase activity as an antioxidant, using the same dose of capsule propolis for 8 weeks in an Iranian population. The result showed that catalase activity increased significantly ($p=0.041$) and oxidized LDL decreased significantly ($p=0.031$). This could lower the risk of atherosclerotic plaque formation. A similar result was obtained by Moayedi et al.,[35] who analyzed the result of propolis supplementation compared to standard, exercise and placebo groups.

Sixty women participated in the study and were given 4 treatments: a control group, which was given nothing; an exercise group, which was asked to perform combined aerobic and resistance training; a propolis-only group, which was given supplementation only; and a combined exercise and propolis supplementation group. Propolis was given

in encapsulated form three times daily with a total of 1500 mg/day for 8 weeks. The result shows significant upregulation of SOD ($p<0.05$) and TAC ($p<0.05$), while MDA ($p<0.05$) was downregulated in the propolis supplementation group compared to the control. A more significant result was shown in the exercise combined with the propolis group, which shows an increase in SOD and TAC and reduced MDA.[35]

Strength and limitation

This literature review has several strengths. It focuses on randomized controlled trials evaluating propolis supplementation in patients with type 2 diabetes mellitus and integrates clinical findings with mechanistic explanations, including lipid modulation, glycemic regulation, anti-inflammatory, and antioxidant effects. In addition, multiple cardiometabolic outcomes were evaluated, providing a comprehensive overview of the potential role of propolis as a nutraceutical adjunct in T2DM management. However, this review has limitations, including the absence of a formal risk-of-bias assessment and heterogeneity among the included studies in terms of propolis composition, dosage, and intervention duration.

Conclusion

Type 2 Diabetes Mellitus (T2DM) is a metabolic disease characterized by elevated blood glucose levels resulting from insulin resistance. Despite the availability of T2DM treatment, nutraceuticals such as propolis have shown promising potential as adjunctive therapies for improving metabolic control and preventing complications.

Propolis has demonstrated measurable benefits on glycemic control, lipid modulation, and antioxidant balance among patients with type 2 diabetes mellitus when used as adjunct to standard therapy. However, current clinical studies are characterized by heterogeneity in propolis composition and the absence of standardized formulation, which limit clinical translation. Current evidence also showed limited intervention period and relatively small sample size, therefore limiting conclusions on long-term cardiometabolic outcomes. Future research should prioritize comprehensive bioactive profiling and well-designed long-term intervention to establish clinically relevant therapeutic thresholds.

Conflict of interest

The authors declared no conflict of interest regarding this article.

Ethic Statement

Ethical approval was not required for this study because it is a literature review based exclusively on previously published study and does not involve human participants or animals.

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Author Contributions

WS : Conceptualization, data acquisition, formal analysis, interpretation of results, drafting the manuscript, and final approval of the version to be published; DRG, NRMM: Supervision, critical revision of the manuscript, interpretation of data, and final approval of the version to be published.

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