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EDITORIAL

Breastfeeding, complementary feeding practices, and management of wasting in the young children: The significances and the updates

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World breastfeeding week

Human milk is the standard for infant nutrition and growth. World Breastfeeding Week (WBW) is essential in raising awareness, providing support, and advocating for breastfeeding, which leads to healthier communities. Over recent decades, there has been a significant increase in breastfeeding rates, a broader acknowledgment of human milk as the primary food for infants, and a deeper understanding of breastfeeding's role in human development, ushering in a new era for breastfeeding.[1] The first World Breastfeeding Week (WBW) was celebrated in 1992. It was initiated by the World Alliance for Breastfeeding Action (WABA) to promote and support breastfeeding practices worldwide and is observed annually from August 1-7, aligning with the anniversary of the Innocenti Declaration adopted in August 1990.[2] **Table 1** shows a series of important historical milestones and collaborative efforts in the development of WBW into a global movement.

Over decades, the effects of WBW can be seen in several areas such as 1) increased awareness on benefits of breastfeeding for both infants and mothers, the importance of breastfeeding for infant health, reducing the risk of infections, malnutrition, and chronic diseases, while also benefiting maternal health, 2) support for breastfeeding mothers by encouraging the establishment of supportive environments for breastfeeding, including workplaces, healthcare settings, and communities, leading to improved policies and resources for breastfeeding mothers, such as maternity leave, breastfeeding-friendly workplaces, and access to lactation consultants, 3) advocacy and policy changes at local, national, and international levels, 4) community engagement through events, educational workshops, and campaigns that bring together parents, healthcare providers, and organizations to support breastfeeding initiatives which fosters a more supportive network for breastfeeding mothers, 5) improved health outcomes for both infants and mothers. A recent study on breastfeeding practices during COVID-19 pandemic highlights 81.3% of exclusive breastfeeding and 93.4% of continued breastfeeding which were both associated with intention to breastfeed.[3] And these figures may be attributed to over a three decades of WBW campaigns.

Complementary Feeding Practices: the 2021 IYCF Indicators

The WHO's guiding principles for complementary feeding of breastfed children and for feeding non-breastfed children aged 6–24 months provide global recommendations on optimal feeding practices to promote growth, health, and behavioral development in infants and young children under two years old. To aid in program implementation and track progress on infant and young child feeding (IYCF) both nationally and globally, indicators for evaluating IYCF practices were released in 2008. This guidance document outlined eight core indicators and seven optional ones, which have since become the benchmark for data collection and reporting on IYCF practices worldwide. In 2017 and 2018, WHO and UNICEF held two inter-agency technical consultations to review and update the IYCF indicators. These discussions addressed topics such as dietary diversity, food groups, additional breastfeeding indicators, and the consumption of unhealthy foods and beverages. A major takeaway from these consultations was the recommendation to include specific indicators for assessing unhealthy eating practices.[4]

The ASEAN guideline on the minimum standards for management of child wasting

On 7th August 2024, ASEAN Secretariate with WHO, UNICEF, and other development partners launched the four ASEAN guidelines and minimum standards on nutrition for its member states, among them is the guidelines on management of child wasting.

The aim of this guideline is to offer practical advice to help ASEAN Member States enhance efforts in preventing, detecting early, and managing child wasting through their national health systems, including incorporating child wasting treatment into regular primary healthcare services. It specifies the core principles and minimum standards for providing services to prevent, detect, and treat child wasting, and details key steps for integrating these services into routine primary healthcare. This guideline focuses solely on health system interventions to address wasting, with particular attention to Severe Acute Malnutrition (SAM). An important recommendation is to simplify management protocols to facilitate scaling up and integrating wasting services into national health programs. Common adaptations include family screening for MUAC, community health worker-led treatment, fewer follow-up visits, using a single treatment product, reducing therapeutic food dosages during treatment and recovery, and relying on MUAC and oedema as the only criteria for admission and discharge. It also suggests raising the MUAC cut-off for admitting children with wasting to those with a MUAC above 115 mm. For treating all children with wasting, a single therapeutic food product is recommended, preferably lipid-based nutrient supplements that meet the specifications of ready-to-use supplementary food (RUSF) or ready-to-use therapeutic food (RUTF). Adjustment may be adapted based on feasibility, acceptability, equity considerations, resource availability, and production capacity relevant to each ASEAN Member State.[5]

Conflict of interest

The authors declare that there is no conflict of interest related to the study.

Open Access

Table 1. Milestones and efforts in the history of WBW (synthesized from https://waba.org.my/wbw/)

Period	**Milestone and efforts**
1970s-1980s:	*Early advocacy and research*
The global breastfeeding movement gained momentum with the recognition of breastfeeding as a critical aspect of child health. The World Health Organization (WHO) and UNICEF began advocating for breastfeeding and addressing issues related to infant nutrition and maternal health.	
August 1990:	*Innocenti Declaration*
The Innocenti Declaration on the Protection, Promotion, and Support of Breastfeeding was adopted by the WHO and UNICEF at an international meeting in Innocenti, Italy. This declaration was a significant milestone in establishing breastfeeding as a fundamental right for infants and a critical public health issue.	
1992:	*Establishment of World Breastfeeding Week*
In response to the Innocenti Declaration, the World Alliance for Breastfeeding Action (WABA) was founded. WABA organized the first World Breastfeeding Week to promote breastfeeding awareness and support. The event was initially celebrated in more than 20 countries, highlighting its early international reach.	
1990s-2000s:	*Global support and expansion*
As the concept of WBW gained traction, it was embraced by more countries and organizations. The event became an annual observance, with increasing participation from governments, non-governmental organizations (NGOs), health professionals, and communities; focused on raising awareness, advocating for breastfeeding-friendly policies.	
2000s-Present:	*Integration with global health goals*
WBW continued to align with broader global health initiatives, including the Millennium Development Goals (MDGs) and later the Sustainable Development Goals (SDGs).	
Ongoing:	*Strengthened collaborations and advocacy*
WABA and other organizations have continued to work collaboratively to enhance the impact of WBW. This includes partnerships with international health organizations, advocacy for policy changes, and the use of media and technology to spread the message.	
Local Initiatives:	*Cultural and regional adaptation*
As WBW expanded globally, it adapted to various cultural contexts and regional needs. Local organizations and communities have developed tailored programs and events.	
Present Day:	*Global movement and recognition*
WBW is now celebrated in over 170 countries, involving a wide range of activities, from educational workshops to public campaigns. It has become a significant global movement that not only highlights the benefits of breastfeeding but also advocates for supportive environments and policies worldwide as shown in the 2024 WBW theme *"Closing the gap: Breastfeeding support for all"*	

Table 2. Some key changes between the 2008 and 2021 recommended IYCF indicators[4]

No.	Indicator	IYCF Version	
		2008	2021
1.	Exclusively breastfed for the first two days after birth		Available
2.	Mixed milk feeding under six months		Available
3.	Continued breastfeeding age	12-15 months	12-23 months
4.	Minimum dietary diversity (MDD) 6–23 months	No breastmilk in food group	Breast milk added in food group
5.	Minimum meal frequency (MMF) 6–23 months	Allowed children to achieve the minimum with milk feeds only	At least one non-milk feeding is required to meet minimum for non-breastfed children
6.	Minimum milk feeding frequency for non-breastfed children 6–23 months	Optional	Recommended
7.	Minimum acceptable diet (MAD) 6–23 months		Altered to reflect changes in MDD and MMF above
8.	Egg and/or flesh food consumption 6–23 months		Available
9.	Sweet beverage consumption 6–23 months		Available
10.	Unhealthy food consumption 6–23 months		Available
11.	Zero vegetable or fruit consumption 6–23 months		Available
12.	Bottle feeding 0–23 months	Optional	Recommended

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CASE REPORT

Effect of vitamin D supplementation on lung function in chronic obstructive pulmonary disease patients: An evidence-based case report

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Abstract

Background: Chronic obstructive pulmonary disease (COPD) is characterized by progressive and persistent airflow obstruction together with an increased chronic inflammatory response, primarily caused by environmental exposure and smoking habit. Vitamin D deficiency is associated with increased rates of exacerbation and hospitalization in COPD patients. Recent studies have indicated a direct correlation between vitamin D deficiency and the severity of COPD, suggesting that acute exacerbation could be prevented with vitamin D supplementation. Some studies propose that correcting the serum vitamin D level may improve the prognosis for COPD patients experiencing respiratory tract infections.

Objective: The aim of this study was to determine the effect of vitamin D supplementation for lung function in COPD patient.

Methods: Literature search was carried out by advanced searching on Pubmed, Cochrane Library, and Scopus using a combination of MeSH Terms and Title/Abstract. Following screening for duplications, the literature obtained then screened according to predetermined eligibility criteria. The appropriate literatures were critically reviewed and the level of evidence in accordance with the Oxford Center for Evidence Based Medicine.

Results: One meta-analysis and three randomized controlled trial (RCT) met the PICO and eligibility criteria that had been set. Three studies concluded that vitamin D supplementation enhanced lung function in COPD patient. Vitamin D deficiency is common in COPD patients, so it is recommended to check vitamin D levels before vitamin D supplementation.

Conclusion: Vitamin D administration can improve lung function and prevent acute exacerbation in COPD patients.

Keywords: COPD, lung function, vitamin D, vitamin D supplementation

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Clinical scenario

A 70-year-old patient complains of worsening shortness of breath over the past week. The patient has been diagnosed COPD for the past four years and has regular treatment. The patient has often reported experiencing dyspnea following physical exertion and upon awakening in the morning over the past month. Because they experience attacks of dyspnea frequently, the patient rarely doing activity outside the home. Patient complains of wheezing and a cough in addition to shortness of breath. There is no complaint of fever. Based on physical examination, the patient's respiratory rate is 28 breaths per minute, and oxygen saturation reaches 93%. The patient's weight is 45 kg, with a height of 165 cm, resulting in a body mass index of 16.5 kg/m2. Additional wheezing sounds are heard in both lung fields. Laboratory tests show albumin level of 2.9 g/dL and a vitamin D-25 OH level of 16.7 ng/mL, categorizing it as a vitamin D deficiency.

The patient is referred to the clinical nutrition department for nutritional therapy during treatment. During the course of treatment, the patient is provided with 5000 IU vitamin D supplementation per day, with the suggestion that this could improve the patient's lung function. The patient then asks the physician about vitamin D's advantages for lung health, as he was previously aware of its benefits for bone health.

Introduction

COPD is the top ten leading global causes of death, characterized by progressive and persistent airflow obstruction primarily caused by environmental exposure to smoke and smoking habit. COPD represents a significant global public health challenge in the 21st century. In 2005, COPD was responsible for 5% of all deaths worldwide. The Global Burden of Disease 2015 reported an alarming 11% rise in COPD-related mortality from 1990 to 2015, alongside a 44% increase in disease prevalence during the same period. If this trend persists, COPD is projected to become the third most common cause of death worldwide by 2030.[1,2] Most cases of COPD (85%) are associated with smoking. Tobacco smoke exposure triggers alterations in lung function, impeding growth, diminishing peak performance, and hastening the age-related decline.[3]

About one billion people worldwide are estimated to have 25(OH)D levels of less than 75 nmol/L.[4] COPD poses a high risk for vitamin D deficiency, which is thought to be caused by malnutrition, insufficient outdoor activity, kidney dysfunction, and high catabolism associated with steroid therapy. The occurrence of insufficient vitamin D levels among individuals with COPD ranges from 31% to 77%. Compared to a control group, COPD patients exhibit lower levels of vitamin D. Additionally, insufficient vitamin D is linked to higher rates of exacerbation and hospitalization in COPD patients.[6]

Currently, vitamin D is viewed has certain systemic effects in COPD patients. Additionally, due to its impact on gene regulation, vitamin D provides protective effects against pulmonary diseases. There is considerable interest in the potential administration of vitamin D in COPD_to improve controlled symptoms and to reduce the risk of acute exacerbation. Vitamin D deficiency is common among people with COPD, in whom it associates interdependently with worse lung function and increased risk of upper respiratory infections.[7] Evidence from two randomised controlled trials shows that vitamin D supplementation reduces the risk of acute exacerbation COPD in people with vitamin D deficiency and meta-analysis of individual participant data from RCTs shows that vitamin D supplementation reduces risk of acute respiratory infection.[8] Certain research suggests that adjusting the serum vitamin D levels could enhance the outlook for individuals with COPD.[9]

Clinical questions

P: Chronic obstructive pulmonary disease
I: Vitamin D supplementation
C: Placebo or no Vitamin D supplementation
O: Acute exacerbation

Clinical question: How are the effects of vitamin D supplementation in COPD patients?

Methods

The literature search was conducted on November 20, 2023, with advanced searching on Pubmed, Cochrane Library, and Scopus, using a combination of MeSH Terms and Title/Abstract from each PICO component and using boolean operators "OR" to increase sensitivity and "AND" to increase specificity (**Table 1**). Data extraction is performed based on the eligibility criteria and relevance to the PICO framework in the clinical scenario. We excluded articles that do not meet the inclusion criteria, not conducted in humans, and articles not available in full text. Critical appraisal was conducted on the four included articles. Critical appraisal tools and determination of levels of evidence are based on the Oxford Centre for Evidence Based Medicine.

Eligibility criteria

Inclusion criteria including subjects over 18 years of age with a diagnosis of COPD, the study used randomized controlled trial (RCT) design and systematic review/meta-analysis from RCT, the intervention is the supplementation of vitamin D, while the control group was given placebo or no vitamin D supplementation, published from 2017 to 2023, and was written in English. Exclusion criteria involve studies that were not conducted on human subjects and articles that are not accessible in full text.

Critical study method

The critical review methodology involved thoroughly all selected articles by examining the *validity*, *importance*, *applicability* (VIA) using CEBM (*Centre for Evidence Based medicine*) in accordance with the type of therapeutic study.

Results

Based on the results from the database conducted with advance searching, The author found 89 literatures, 80 literatures from Pubmed, 1 literature from Cochrane Library, and 8 literatures from Scopus. As shown in **Figure 1**, there are 1 SR/MA and 3 RCTs selected to be included in this Evidence Based Case Report. Based on criteria from the Oxford Centre for Evidence Based Medicine, the level of evidence of 1 article with the SR/MA study is level 1a, while 3 articles with the RCT study is level 1b. The subjects in 4 study articles were patients with COPD who received vitamin D supplementation in the intervention group, compared to the control group given placebo or no vitamin D supplementation, to assess the outcome of acute exacerbation. The study attributes of these articles were outlined in **Table 2**. The level of evidence for these articles is depicted in **Table 3**.

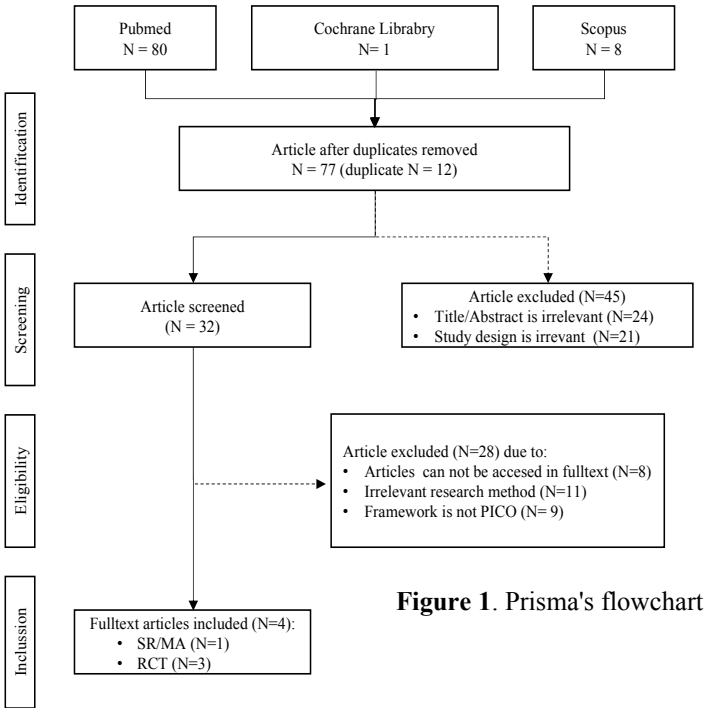

Figure 1. Prisma's flowchart

We performed an extensive review of the literature by utilizing advanced search methods on Pubmed, the Cochrane Library, and Scopus. This involved combining MeSH Terms and Title/Abstract searches. The advanced search strategy according to address the population, intervention, comparison, and outcome.

Table 1. Literature search strategy

Database	*Search Strategy*	*Hits*	*Selected Article*
Pubmed	((((((((((copd[MeSH Terms]) OR (chronic obstructive pulmonary disease[MeSH Terms])) OR (pulmonary emphysema[MeSH Terms])) OR (bronchitis, chronic[MeSH Terms])) OR (lung diseases, obstructive[MeSH Terms])) OR (copd[Title/Abstract])) OR (chronic obstructive pulmonary disease[Title/Abstract])) OR (bronchitis, chronic[Title/Abstract])) OR (pulmonary emphysema[Title/Abstract])) AND ((((((((((1 alpha, 25 dihydroxy 20 epi vitamin d3[MeSH Terms]) OR (vitamin d[MeSH Terms])) OR (cholecalciferol[MeSH Terms])) OR (cholecalciferol receptors[MeSH Terms])) OR (vitamin d receptor[MeSH Terms])) OR (vitamin d receptors[MeSH Terms])) OR (vitamin d[Title/Abstract])) OR (cholecalciferol[Title/Abstract])) OR (vitamin d receptor[Title/Abstract])) OR (vitamin d receptors[Title/Abstract]))) AND ((((((((((respiratory muscle[MeSH Terms]) OR (disease exacerbation[MeSH Terms])) OR (respiratory function test[MeSH Terms])) OR (lung function test[MeSH Terms])) OR (dyspnea[MeSH Terms])) OR (lung function[MeSH Terms])) OR (diaphragm, respiratory[Title/Abstract])) OR (respiratory muscle[Title/Abstract])) OR (disease exacerbation[Title/Abstract])) OR (lung function[Title/Abstract])) OR (respiratory[Title/Abstract]))	80	2
Cochrane Library	#1 MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] #2 MeSH descriptor: [Bronchitis, Chronic] explode all trees #3 MeSH descriptor: [Pulmonary Emphysema] explode all trees #4 MeSH descriptor: [Vitamin D] explode all trees #5 MeSH descriptor: [Cholecalciferol] 3 tree(s) exploded #6 MeSH descriptor: [Receptors, Calcitriol] this term only #7 MeSH descriptor: [Receptors, Calcitriol] explode all trees #8 MeSH descriptor: [Disease Progression] explode all trees #9MeSH descriptor: [Respiratory Function Tests] explode all trees #10#1 OR #2 OR #3 #11#4 OR #5 OR #6 OR #7 #12#8 OR #9 #13#10 AND #11 AND #12	1	1
Scopus	(((chronic AND obstructive AND pulmonary AND diseases) OR (copd) OR (pulmonary AND emphysema) OR (bronchitis AND chronic)) AND (cholecalciferol) AND (exacerbation)) AND PUBYEAR > 2017 AND PUBYEAR < 2024 AND (LIMIT-TO (SRCTYPE , "j")) AND (LIMIT-TO (OA , "all")) AND (LIMIT-TO (DOCTYPE , "ar")) AND (LIMIT-TO (SUBJAREA , "MEDI")) AND (LIMIT-TO (LANGUAGE , "English")) AND (LIMIT-TO (EXACTKEYWORD , "Chronic Obstructive Lung Disease"))	8	1

Table 2. Assessment of literature characteristics

Writer	Desain Studi	Characteristics of Populasi	Intervension	Outcomes	Research Results
Xiaoyan L, et al.[10] (2020)	Meta-analysis of RCT	Total 25 articles involving 2.670 participants diagnosed as COPD according to the Guidelines for the Diagnosis and Treatment of COPD.	Patients with COPD were given vitamin D dose 125-300000 IU/week supplementation compared to placebo.	COPD assessment test, exacerbations, sputum, forced expiratory volume in 1 second, 6-minute walking distance.	vitamin D supplementation in patients with COPD could improve the lung function 6MWD and reduce acute exacerbation.
Ali AF, et al.[11] (2019)	*Randomized Controlled Trial*	30 men (93.8%) and two women (6.3%) were in the intervention group and 30 men (96.8%) and a woman (3.2%) in the placebo group.	The intervention group took 50,000 IU vitamin D_3, and those in the control group received placebo once a week for 8 weeks, then once a month for 4 months.	COPD Assessment Test (CAT) score and lung function evaluated by spirometry of patients with COPD (FEV_1, FEV_1/FVC, number of exacerbation)	Consuming 50,000 IU vitamin D_3 increased quality of life in COPD. exacerbations had not worsened after 6 months.
Rachida R, et al.[12] (2022)	*Randomized Controlled Trial*	155 COPD patient aged 40 y or older, had a vitamin D deficiency [25(OH)D concentration <50 nmol/L], and had a confirmed history of a COPD exacerbation in the last 12 month before screening.	participants were allocated in a 1:1 ratio to receive either 16,800 IU vitamin D (3 tablets of 5600 IU) or a matching placebo orally once a week for 1 year.	exacerbation rate in 1 year. Plasma C- reactive protein (CRP), and interleukin-6	The study does not show that vitamin D supplementation reduces exacerbation rate in COPD patients with vitamin D deficiency.
Farzaneh D, et al.[13] (2019)	*Randomized Controlled Trial*	70 patients (35 participants in each group) with the COPD stages of II-IV according to the GOLD report, having VDD (serum 25(OH) vita- min D level of <20ng/ml) and an age of 40 years.	The patients were randomly allocated to receive 300,000 IU of vitamin D (25-hydroxycholecalciferol) (Daropakhsh-Iran) or placebo.	the serum levels of interleukin-6, IL-8, and CRP and based on the modified Medical Research Council (mMRC) dyspnea scale.	a significant correlation was found between the change of the vitamin D levels and the degree of decrease in the level of inflammatory biomarkers, but inadequate for evaluating the clinical outcome improvements

After completing the identification and screening process, eligible articles were chosen for critical evaluation. Four articles were found to have a PICO framework aligned with the clinical scenario. Among these, three were randomized controlled trials (RCTs), while one was a meta-analysis of RCTs. These four articles identified the validity criteria based on quality and level of evidence according to the Oxford Centre for Evidence-Based Medicine (CEBM).

Table 4. Validity criteria

	PICO	Review Strategy	Study Design	Study Quality Assessment	High Quality	Results in Tables/Forest Plots	Similarity of Study Results	Quality of evidence*	Level of evidence**
Xiaoyan L, et al.[10]	+	+	+	+	-	+	+	High	1a
Ali AF, et al.[11]	+	+	+	+	+	+	+	Moderate	1b
Rachida R, et al.[12]	+	+	+	+	-	+	+	Moderate	1b
Farzaneh D, et al.[13]	+	+	+	+	+	+	+	moderate	1b

*Quality of evidence according to GRADE guidelines, https://www.ncbi.nlm.nih.gov/pubmed/21208779
**Level of evidence according to Oxford Center of Evidence-based Medicine (CEBM), http://www.cebm.net.
+ clearly mentioned in the article; - not done; ? Not stated clearly

Discussion

Vitamin D deficiency is prevalent in individuals with COPD, correlating with impaired lung function and heightened susceptibility to upper respiratory infections. There is a focus on protective factors that may mitigate the frequency and severity of COPD exacerbations. Vitamin D is particularly compelling due to its varied effects on lung health, tissue remodelling, suppression of pro-inflammatory cytokines, and beneficial modulation of both innate and adaptive immune responses.[7,14]

Based on the results of SR/MA and RCT articles show that administration of vitamin D in increased circulating concentrations of 25(OH)D. This 25(OH)D acts as a substrate for CYP27B1 expressed in the kidney and multiple extra-renal tissues, including respiratory epithelium. CYP27B1 expression in respiratory epithelium and leucocytes is induced during infection and inflammation. The active form of vitamin D, known as 1,25(OH)2D, is produced locally within the lung. It binds to the vitamin D receptor, triggering antimicrobial and antiviral responses, such as the expression of antimicrobial peptides, apoptosis, and the production of reactive oxygen and nitrogen intermediates. Moreover, this active vitamin D metabolite demonstrates anti-inflammatory properties by promoting the production of the anti-inflammatory cytokine IL-10 while inhibiting proinflammatory cytokines released by type 1 helper T cells. This combined antimicrobial, antiviral, and anti-inflammatory action holds promise for reducing the risk of acute exacerbations in COPD, which are frequently triggered by viral respiratory infections and characterized by dysregulated pulmonary inflammation.[4,8]

Several biological mechanisms may explain the contribution of vitamin D deficiency to COPD. First, vitamin D acts as a potent inhibitor in either innate or adaptive immune response via activation of VDR. Second, vitamin D can upregulate the expression of antimicrobial peptides in response to infections. Third, vitamin D deficiency has an effect on airway smooth muscle by regulating the expression of genes related to cell proliferation, glucocorticoid response, and smooth muscle contraction.[15] Vitamin D deficiency increases the

susceptibility to respiratory infections and airway colonization leading to chronic inflammation.[16]

Study from Xiaoyan L, et al.[10] and Ali AF, et al.[11] showed that vitamin D supplementation in COPD patients could reduce their acute exacerbations. Vitamin D supplementation plays a very important role in various effects on lungs, tissue remodelling, reduction of pro-inflammatory cytokines and beneficial modulation of both innate and adaptive immune systems. Study Farzaneh D, et al.[13] show vitamin D supplementation can decrease in the level of inflammatory biomarkers. Increased inflammation in COPD patients affected disease progression and exacerbation and could worsen comorbidities. Relatively, short duration of monitoring had been inadequate for evaluating the maximum effects of vitamin D on the clinical outcome improvements, including acute exacerbation. However, different results were obtained from study from Rachida R, et al.[12] studied COPD patients with ≥1 exacerbations in the preceding year and a vitamin D deficiency (15–50 nmol/L) were randomly allocated in a 1:1 ratio to receive either 16,800 International Units (IU) vitamin D3 or placebo once a week in 1 years. In this study Vitamin D supplementation did not reduce exacerbation rate in COPD patients with a vitamin D deficiency.

Vitamin D has antimicrobial antibacterial and antiviral effects through several mechanisms, one of them is the control of activity of cathelicidin which is an antimicrobial polypeptide. Cathelicidin was shown to be active against mycobacteria and against other organisms causing COPD exacerbations including antibiotic resistant strains such as Pseudomonas aeruginosa, Staphylococcus aureus, chlamydia, and other groups of viruses. This mechanism could be an explanation for the increased frequency and severity of exacerbations associated with low vitamin D in COPD.[2,16]

Many COPD patients experience vitamin D deficiency, increased rates of exacerbation and hospitalization in COPD patients are attributed to vitamin D deficiency. Recent studies have concluded that vitamin D deficiency is directly related to the severity and acute exacerbation of a COPD patients and may be prevented with vitamin D supplementation. Some studies have suggested that prognosis for COPD patients who are suffering from respiratory tract infections may improve through correction of their serum vitamin D level. Different articles might draw different conclusions due to the dose of vitamin D used, the method of administering vitamin D, and individual differences, including age, gender and race.[10] Optimal body vitamin D status is very important to maintain lung function and prevent acute exacerbations of COPD. Fulfilment of vitamin D needs can be obtained from food sources and sun exposure.[16]

Foods rich in vitamin D include fatty fish such as trout, salmon, tuna, and mackerel, with fish liver oil being the top source. Beef liver, egg yolks, and cheese offer minimal amounts of vitamin D, particularly in the form of vitamin D3 and its metabolite 25(OH)D3. Additionally, low-fat or fat-free milk and egg yolks also contain vitamin D.[17] Many individuals worldwide fulfil a portion of their vitamin D requirements through exposure to sunlight. Type B ultraviolet (UVB) radiation, ranging from about 290 to 320 nanometers in wavelength, penetrates uncovered skin and converts 7-dehydrocholesterol into provitamin D3, subsequently transforming into vitamin D3. Some experts and researchers suggest approximately 5 to 30 minutes of sun exposure, particularly between 10 a.m. and 4 p.m., either daily or twice weekly, to the face, arms, hands, and feet without sunscreen to facilitate adequate vitamin D synthesis.[18]

A recent meta-analysis and systematic review conducted in 2017 revealed a notable protective effect of vitamin D supplementation in reducing the risk of acute respiratory tract infections, particularly among individuals with insufficient vitamin D levels.[9] Based on the critical studies above, it is recommended to check vitamin D levels before vitamin D supplementation. There is considerable variation from person to person, proper dosage should be determined by measuring a patient's vitamin D blood levels before, and several months after, taking vitamin D3 additions or increasing ultraviolet-B exposure. If there is insufficiency or deficiency, vitamin D supplementation can be given until vitamin D levels are optimal and normal.[7] Vitamin D levels above 30–40 ng/mL may reduce the risk of COPD.

patients with vitamin D deficiency can be given 2000–5000 international units per day of vitamin D3 for six months n to reduce acute exacerbations.[11,19]

Conclusion

Vitamin D levels tend to be diminished in patients experiencing acute exacerbation of COPD, and this association correlates directly with lung function, the severity of the disease, and the frequency of exacerbations. The potential of vitamin D to decrease exacerbations is notable, but its efficacy is contingent upon adequate dosage and sustained intake over an extended period. There's a need for additional research to substantiate the advantages of vitamin D supplementation in COPD management.

Conflict of interest

The authors declare there is no conflict of interest regarding this article.

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CASE REPORT

Role of folic acid supplementation in level of c-reactive protein in metabolic syndrome : evidence based case report

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Abstract

Introduction: The prevalence of metabolic syndrome is increasing, its progression involves an inflammatory response that has an important impact on the initiation, progressivity, and complications of several diseases such as heart disease, stroke, type 2 diabetes mellitus, and cancer. C-reactive protein (CRP) is one of the inflammation markers increased in patients with metabolic syndrome. Folic acid has a role in metabolizing homocysteine and improving endothelial function. There have been many studies conducted, but the results are still inconsistent.

Method: Literature searching was conducted using PubMed, Cochrane Library, and Embase databases. MeSH terms, advanced search and eligibility criteria were used for title/abstract screening before journal review.

Results: One systematic review and meta-analysis (SR-MA) and one RCT met the PICO and eligibility criteria. The SR-MA found that folic acid administration can reduce CRP level (WMD -0.94 (95% CI -1.56 – 0.32; p=0.00) at a dose of 0.15 mg/day for 12 weeks to 10 mg/day for 2 weeks, while the RCT found an insignificant result.

Conclusion: Folic acid supplementation has a potential benefit to decrease CRP levels in metabolic syndrome.

Keywords: folic acid, supplementation, CRP, metabolic syndrome, case report

Case Scenario

A 34-year-old woman came to clinical nutrition clinic for post-hospitalization consultation with diagnosis of Grade II Obesity in Mirizzi syndrome post laparotomy cholecystectomy adhesiolysis, common bile duct (CBD) exploration, bypass choledochoduodenostomy POD-11. The patient now has no complain, fever is absent, intake and toleration of oral route was good, hemodynamics was stable with blood pressure 134/77 mmHg, heart rate was 90 times per minute, respiratory rate was 20 times per minute, and temperature was 36.8^{o}C. On physical examination of abdomen, it found distended, intestinal noise within normal limits, tenderness is absent, in right hemiabdomen surgical wound looks clean and dry. On physical examination of extremities, no edema or muscle wasting was obtained. Anthropometric examination obtained the weight was 93 kg, height was 165 cm, waist circumference was 105

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cm. From laboratory examination it obtained that leucocyte was 9.300/µL, CRP 5.6 mg/L, triglyceride 155 mg/dL, HDL cholesterol 37 mg/dL, and fasting blood glucose was 110 mg/dL. The patient was given nutritional medical therapy of 1700 kcal according to total energy needs. Patients asked about recommended folic acid supplementation to support in reducing inflammation with metabolic comorbidities.

Introduction

Metabolic syndrome is still one of the main health problems. From 1999 to 2014, the prevalence of metabolic syndrome in US increased from 27.6% to 32.3% with mortality rate dropped dramatically from 29.6% to 2.7% owing to advances in health care.[1] Data in Indonesia shows similarities in prevalence with rate of 28% in men and 46% in women in 2020, but very different mortality with rate of 73%.[2,3]

The pathophysiology of metabolic syndrome involves an inflammatory response, which has an important impact on the initiation, progression, and complications of several diseases such as heart disease, stroke, type 2 diabetes mellitus and cancer. [4] C-reactive protein (CRP) as one of the acute phase proteins of inflammatory markers increases and can predict new or recurrent events in patients with metabolic syndrome. The inflammatory marker CRP has been widely used in epidemiological and interventional studies to assess and identify associations between systemic inflammation and metabolic syndrome.[5]

Folic acid has shown effect on decreasing homocysteine levels, improving endothelial function, and decreasing inflammatory reactions. A study conducted by Talari et al.,[6] in 2016 showed that folic acid can reduce CRP levels in patients with type 2 diabetes mellitus. However, a study from Spoelstra et al.,[7] in 2004 showed that supplementation of folic acid for 6 months did not improve CRP level in patients with type 2 diabetes mellitus. This difference creates uncertainty regarding the effect of folic acid on inflammatory response in patients with metabolic syndrome.

Therefore, the authors are interested in finding more information about the relationship between folic acid and inflammatory markers in patients with metabolic syndrome, in the hope of providing recommendation on the management of metabolic syndrome. This study aimed to assess the effect of folic acid supplementation on inflammatory marker of CRP in patients with metabolic syndrome. Because serum CRP level can be reflected by high sensitivity-CRP (hs-CRP) in clinical practice, this critical study included studies using hs-CRP as an outcome.[8]

Clinical question

P: Adult patients with metabolic syndrome

I: Folic acid supplementation

C: Without folic acid supplementation

O: Level of CRP

Clinical question:
could folic acid supplementation decrease the level of CRP in patients with metabolic syndrome?

Methods

Literature search was performed using combination of MeSH terms and Title/Abstract on three large databases: PubMed, Cochrane Library and Embase. Searching was carried out on 4th January 2024. The keywords used were "folic acid", "supplement", "C reactive protein" and "metabolic syndrome" (**Table 1**). Critical assessment tools and levels of evidence are based on the Oxford Center for Evidence-Based Medicine.

After obtaining the articles, filtering of duplication is carried out. If search results are found as SR-MA of RCT, the reviewer will exclude RCT that are included in the SR-MA to avoid duplication. The articles obtained are then selected by comparing the title and abstract with the PICO from predetermined clinical questions and with other eligibility criteria. After getting relevant articles then proceed with critical review by discussing with senior writers.

Table 1. Resources and Search Strategy

Database	Terminology	Hits	Eligible
PubMed	(("folic acid"[MeSH Terms] OR "folic acid"[Title/Abstract]) AND ("c reactive protein"[MeSH Terms] OR "c reactive protein"[Title/Abstract]) AND ("metabolic syndrome"[MeSH Terms] OR "metabolic syndrome"[Title/Abstract])) AND (randomizedcontrolledtrial[Filter] OR systematicreview[Filter])	4	2
Cochrane	#1 (metabolic syndrome):ti,ab,kw #2 (folic acid supplementation):ti,ab,kw #3 (CRP):ti,ab,kw #4 #1 #2 AND #3	6	1
Embase	#1 (metabolic syndrome):ti,ab,kw #2 (folic acid supplementation):ti,ab,kw #3 (CRP):ti,ab,kw #4 #1 #2 AND #3 #5 #4 AND ('meta analysis'de OR 'randomized controlled trial'/de OR 'systematic review'de)	3	1

Eligibility Criteria

Inclusion criteria including research with SR-MA of RCT dan RCT design, subjects over 18 years of age with metabolic syndrome, received folic acid supplementation, and the outcome was level of CRP. Exclusion criteria including animal study, article not available in full text and was written in other language than English and Indonesian.

Results

As shown in **Figure 1**, one SR-MA of RCT and one RCT were included in this Evidence-Based Case Report. Based on the criteria of the Oxford Centre for Evidence Based Medicine, the level of evidence of both articles is level 1. The subjects in both articles were adult patients with metabolic syndrome and received folic acid supplementation in the intervention group compared with no folic acid supplementation in the control group, to assess CRP level as the outcome.

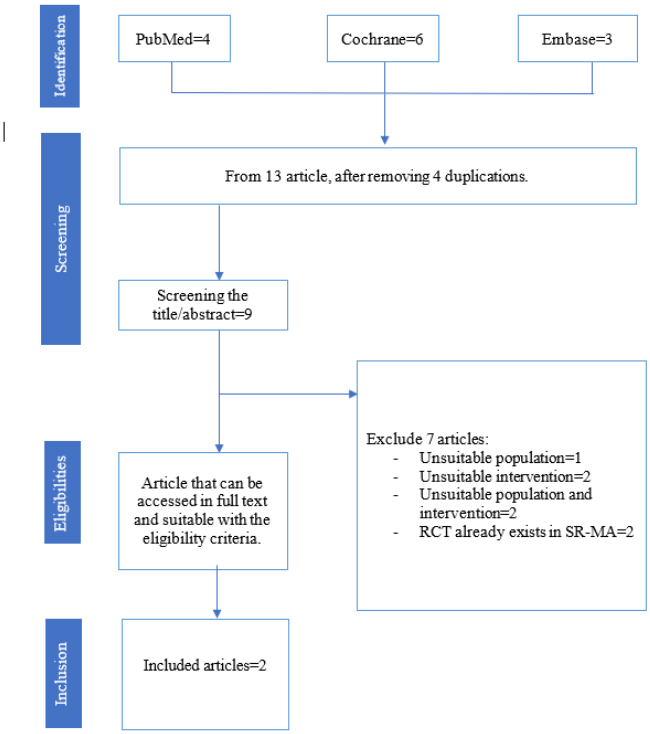

Figure 1. Prisma's Flow Chart

Critical appraisal

In the article by Jiang Z et al.[8], the authors assess using FAITH tools, while in the article by Schneider MP et al.,[9] the authors assess using CEBM tools from the University of Oxford. Before critical appraisal, an assessment of the relevance of the two articles to the clinical question using PICO was carried out. The articles obtained have good relevance to the established clinical question, namely the effect of folic acid supplementation on CRP level in adult patients with metabolic syndrome. This can be seen in

Table 2. Study Characteristic

Author	Study design	Population characteristic	Intervention	Outcome
Jiang Z, et al.,[8]	SR-MA of RCT	A total of 10 studies with a total of 511 patients. Adult patients (≥18 years old) with metabolic syndrome (with several conditions including overweight, obesity, PCOS, CAD, T2DM, and CHD).	Folic acid supplementation was given at a dose of 0.15 mg/day for 12 weeks up to 10 mg/day for 2 weeks, with 2 studies including vitamin B6 or B12 supplementation compared with placebo.	All studies had CRP/hs-CRP outcomes, 5 studies have variation in outcome (including other inflammatory markers in the form of IL-6 and/or TNF-α).
Schneider MP, et al.,[9]	Double-Blind RCT	A total of 75 adult male subjects (≥ 18 years old) with BMI > 25 kg/m^2.	Folic acid supplementation at a dose of 5 mg/day orally for 4 weeks.	The outcomes in this study consisted of: 1) inflammatory markers in the form of hs-CRP, IL-1β, and adiponectin; 2) oxidative stress markers in the form of GSH/GSSG ratio and total antioxidant capacity; 3) vascular tone in the retina and kidneys.

SR-MA, systematic review meta-analysis; RCT, randomized controlled trial; PCOS, polycystic ovarian syndrome; CAD, coronary arterial disease; T2DM, type 2 diabetes mellitus; CHD, chronic heart disease; hs-CRP, high sensitive C reactive protein; IL-6, interleukin-6; TNF-α, tumor necrotizing factor- α; BMI, body mass index; GSH/GSSG ratio, glutathione/oxidized glutathione ratio.

Table 3. Relevance Criteria

Authors	Population similarity	Determining Factor similarity	Outcome similarity
Jiang Z et al. (2022)	+	+	+
Schneider MP et al. (2011)	+	+	+

Table 3. However, there are several variations, such as variations in intervention in the SR-MA by Jiang et al.,[8] where two studies included vitamin B6 or B12 supplementation. In addition, there are variations in outcomes of the two studies with varying outcome including IL-6 and/or TNF-α. The outcomes in study by Schneider[9] had a variety including IL-1β, adiponectin, GSH/GSSG ratio, NOS-dependence vascular tone, dan total antioxidant capacity.

From a critical appraisal of the two articles, an assessment of validity was obtained. Article by Jiang Z et al.,[8] evaluated the risk of selection bias, performance bias, detection bias, and reporting bias in the studies included, and found that most of it had an unclear risk of bias (67,9%), followed by a low risk of bias (28,6%) and high bias (3,5%) in performance bias, where there were 2 studies conducted open label. Publication bias was assessed using funnel plots, Egger's test, and Begg-Mazumdar correlation test, and the result showed no publication bias. Meanwhile, in the article by Schneider MP et al.,[9] good validity was obtained, where randomization was carried out and the randomization list was sealed, research subjects were monitored for quite a long time and in detail, folic acid level were measured to ensure compliance with the intervention, subject did not know who received treatment and who received placebo, treatment beside the intervention in both groups was the same and comparable from the start of the trial where folic acid level were almost the same in both groups, and also all subjects involved taken into account in the final conclusion. Summary and details of the critical appraisal can those two articles can be seen in **Table 4, 5, and 6** below.

Table 4. Summary of Critical Appraisal of Validity, Importance, Applicability dan Level of Evidence (SR-MA) Criteria

	Questions	Jiang Z et al.,[8]
Validity	Does the SR-MA describe the clinical question (PICO) and is it used in article search and selection?	+
	Did the search uncover all relevant evidence?	+
	Have the selected studies been critically appraised?	+
	Does it only include high-quality studies?	-
	Are study results summarized in tables and diagrams and heterogeneity between studies assessed?	+
Importance	Do the research results have a big influence, and are they not due to chance?	+
	Are clinically important results statistically significant?	+
Applicability	Are the characteristics of the patients we will be dealing with similar to the characteristics of research patients?	+
	Are the exposures in the study similar to those in our patients?	+
	Level of evidence	1

Table 5. Summary of Critical Appraisal of Validity, Importance, Applicability dan Level of Evidence (RCT) Criteria

	Questions	Schneider MP et al.,[9]
Validity	Is patient therapy assigned randomly?	+
	And were the two groups similar at the start of treatment?	+
	Besides the treatment allocated, were both groups treated the same?	+
	Are all patients taking part in the trial counted? And were they analyzed in randomized groups?	+
	Are measurement objective or do patients and physicians remain blind to the therapy received?	+
Importance	How big is the impact?	The mean difference in intervention group was 0.3 and the control group was 0.6.
	What measurements are used, and what do they mean?	Mean difference in CRP level
	How precise are estimates of therapeutic effects?	Not statistically significant
Applicability	Can the study results help treat patient being treated?	+
	Is this treatment feasible in clinical practice?	+
	Do the potential benefits of therapy outweigh the potential harms of therapy for the patient being treated?	+
	Level of evidence	1

Literature 1: Jiang Z, Qu H, Chen K, Gao, Z. Beneficial Effect of Folic Acid on Inflammatory Markers in the Patient with Metabolic Syndrome: Meta-analysis and Meta-regression of Data from 511 Participants in 10 Randomized Controlled Trials. Critical Reviews in Food Science and Nutrition. 2022; 1-10.[3]

A. How well was the research done? **(INTERNAL VALIDITY)**

Question Does the systematic review address a focused question (PICO)?
The article: Yes ■ No ☐ Unclear ☐
Comment: In the title, abstract, and introduction, the authors have clearly stated the focus of the question under study, which consists of an intervention of providing folic acid supplementation, clinical outcome in the form of level of CRP (with variations of IL-6 and/or TNF- α), in the population metabolic syndrome patients (with variations of PCOS, CAD, stable CHD, and type 2 DM).
… and use it to direct the search and select articles for inclusion?
The article: Yes ■ No ☐ Unclear ☐
Comment: In the methods section, the authors explain the inclusion and exclusion criteria in accordance with the PICO mentioned above, with a clear definition of the population, and if there is uncertainty about the population in the study, a search is carried out to the authors of the RCT.
F Did the search find all the relevant evidence?
The article: Yes ■ No ☐ Unclear ☐
Comment: In the methods section, the authors state that a search was carried out in four databases, and identification and selection of studies according to eligibility criteria, resulting in 10 studies. The author will try to correspond to the experts if there are studies whose articles are unpublished. Apart from the narrative, this is also explained in the form of a flowchart.
A Have the studies been critically appraised?
The article: Yes ■ No ☐ Unclear ☐
Komentar: Dalam bagian metode, disebutkan penilaian kualitas metodologi studi dengan menilai ada atau tidaknya bias seleksi, bias performa, bias deteksi, dan bias *reporting*.
I Did they only include high quality studies?
The article: Yes ☐ No ■ Unclear ☐
Comment: There was a 3.5% high risk of bias from the risk of bias assessment of all studies, namely performance bias, where there were 2 studies conducted open label.
T Have the results been totalled up with appropriate summary tables and plot?
The article: Yes ■ No ☐ Unclear ☐
Comment: In the result section, the authors of this article display a summary of the data on the characteristics of the included studies in tabular form and the results are displayed in the form of a forest plot according to the outcomes of CRP, hs-CRP, and other variations in outcomes (IL-6 and TNF-α).
H … and heterogeneity between studies assessed and explained?
The article: Yes ■ No ☐ Unclear ☐
Comment: The author assessed and explained the heterogeneity of studies within the forest plot, namely that heterogeneity was found to be 46.34% between studies (heterogeneity $\chi 2=1.86$, p=0.03, I2=46.34%).

B. What were the results? **(IMPORTANCE)**

What measure was used, how large was the effect (could it have been due to chance)?
In this study, the weight-mean difference was -0.94 (95% CI -1.56, -0.32; p=0.00). Based on these results, it can be interpreted that the effect of folic acid supplementation on CRP is clinically important and statistically significant and not due to chance.
How are the results presented?
The author presents the pooled results in the form of a forest plot.

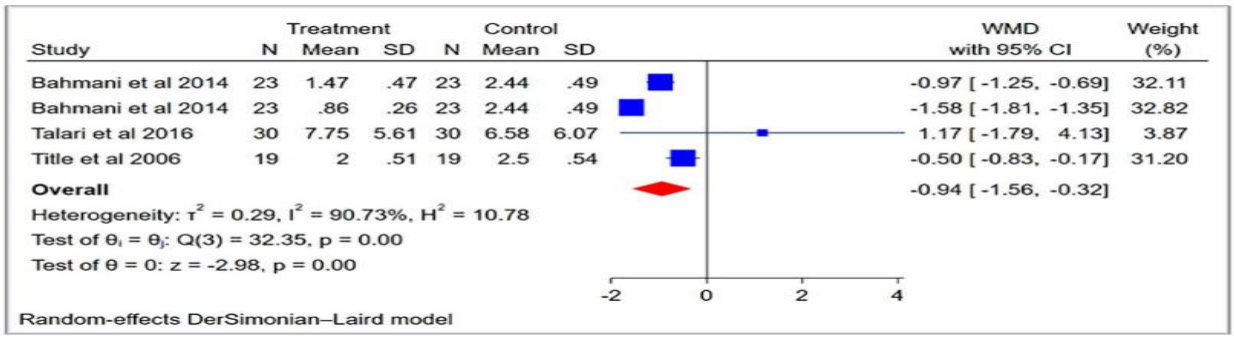

Figure 3. Forest plot for inflammatory marker hs-CRP

Are the clinically important result statistically significant?
Yes, the pooled result shows p = 0.00.

C. Can it be applied? **(APPLICABILITY)**

Are the clinical results applicable to our patients?	
Do the characteristics of the patients encountered resemble the characteristics of the research patient.	Yes, the patients encountered resemble the characteristics of research patients, namely patients with metabolic syndrome. Meanwhile, for other disease variations, the scenario patient has a history of multiple cholelithiasis (Mirizzi syndrome) post-operatively.
Are the exposures in the study similar to those in our patient?	Yes, folic acid supplementation has been applied to our patient.

Literature 2: Schneider MP, et al. Folic Acid Treatment Normalizes NOS-Dependence of Vascular Tone in the Metabolic Syndrome. Obesity; 2011; p. 963.

A. Are the results of this test valid? **(VALIDITY)**

R Was the assignment of patients to treatments randomized?
The article: Yes ■ No ☐ Unclear ☐
Comments: In the methodology section of the study protocol, it is stated that patients were devided into 2 groups, namely a group with metabolic syndrome and a group without metabolic syndrome, and then given therapy randomly between receiving folic acid and placebo for 4 weeks, paused with a wash out phase for 4 weeks between 2 therapy phase, which was carried out blindly.
R Were the groups similar at the start of the trial?
The article: Yes ■ No ☐ Unclear ☐
Comment: In the methods section, the authors explain the inclusion and exclusion criteria according to the PICO mentioned above, with a clear definition of the population. Metabolic syndrome is defined according to the US NCETP III guidelines which require a minimum of 3 of 5 criteria (WC > 102 cm, TGA ≥ 150 mg/dl, SBP ≥ 130 mmHg or DBP ≥ 85 mmHg, HDL < 40 mg/l, and FBG ≥ 100 mg/dl). Only male subjects were included because it was previously known that gender influences the outcome of endothelial function which is a variation in outcomes in this study apart from inflammatory markers. Other exclusion criteria were type 1 or 2 DM, kidney disease, liver disease, heart disease (myocardial infarction, coronary intervention, stroke, or peripheral vascular disease, or therapy with any antihypertensive, antidiabetic or antilipid). In addition, the characteristics of the two groups were summarized in a table, where there were no significant differences in the item age, weight, body surface area, body mass index, total cholesterol levels, LDL cholesterol, uric acid, creatinine, and urinary albumin excretion, as well as baseline folic acid levels.

A Aside from the allocated treatment, were groups treated equally?
The article: Yes ■ No ☐ Unclear ☐
Comment: Both groups were given a washout phase of the same duration, namely 4 weeks, and their baseline folic acid levels were also checked in both groups.
A Were all patients who entered the trial accounted for? And were they analyzed in the groups to which they were randomized?
The article: Yes ☐ No ☐ Unclear ■
Comment: In the result section, there is no mention of the number of subjects who took part on the final calculation or any information about loss to follow up, it is only stated directly in its entirety that the results showed no differences in inflammatory markers (including CRP) between the two groups. In the method section, it is stated that the subjects were analyzed in randomized group.
M Were measures objective or were the patients and clinicians kept "blind" to which treatment was being received?
The article: Yes ■ No ☐ Unclear ☐
Comment: In the method section, it is stated that measurements were carried out equally in both groups, and therapy was administered blindly (folic acid or placebo).

B. What were the results? **(IMPORTANCE)**

How large was the treatment effect?
In this study, the results were not significantly different between the two groups (therapy and control groups). The mean difference between the therapy group was 0.3 (CI 95%, p = 0.35) and the control group was 0.6 (CI 95%, p = 0.62).

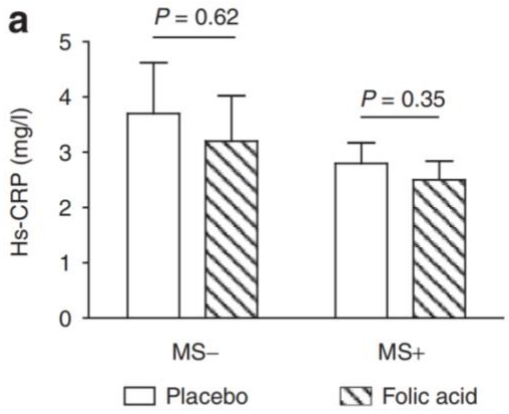

Figure 4 (**a**) High-sensitivity C-reactive protein (hs-CRP), (**b**) interleukin-1β (IL-1β), and (**c**) adiponectin levels in obese subjects with (MS+) and without (MS−) the metabolic syndrome during placebo (empty boxes), and folic acid treatment (shaded boxes).

What is the measure? What does it mean?
The author did not directly mention the mean difference between the two therapy and control groups. The result data is presented in the form of a bar chart as above without mentioning the absolute number of the average hs-CRP level. Therefore, in this critical appraisal the author read the hs-CRP levels based on the bar diagram presented, where the average hs-CRP levels in the group that did not have metabolic syndrome who were given placebo and folic acid each was 3.8 mg/l and 3.2 mg/l, while in the group with metabolic syndrome given placebo and folic acid, hs-CRP levels were 2.8 mg/l and 2.5 mg/l, respectively. From this data it can be concluded that the mean difference in the group that does not have metabolic syndrome is 0.6 mg/l and is greater than the group that has metabolic syndrome, namely 0.3 mg/l. However, the P value in each group was > 0.05, which means the value is not statistically significant.
How precise was the estimate of the treatment effect?
In this study, p>0.05 was obtained in both groups, so it can be concluded that the results of the two mean differences were not statistically significant.

C. Will the result help me in caring for my patient? **(EXTERNAL VALIDITY/APPLICABILITY)**

Could the results of the study help treat case patients?	
Is my patient so different to those in the study that the results cannot apply?	No, the characteristics of the patients in the study resembled the case patients, namely having metabolic syndrome.
Is the treatment feasible in my setting?	Yes, administering folic acid can be done and is easy to obtain in clinical practice for case patients.
Will the potential benefits of treatment outweigh the potential harms of treatment for my patient?	Yes, folic acid has potential benefits in reducing CRP levels. It has high toxic levels, and the excess in the body will be excreted in the urine.

Discussion

Folic acid or vitamin B9 is a water-soluble vitamin that is essential for carbon metabolism. It plays roles in various cellular reactions such as DNA synthesis, repair, and methylation, thus supporting cell division.[4,10] Folic acid can be found in various food sources, such as nuts, spinach, asparagus, broccoli, green vegetables, and avocado. Folic acid cannot be synthesized in the body and depends entirely on intake from diet or supplementation.[4]

Folic acid also plays a role in the metabolism of homocysteine to methionine. Folic acid deficiency will result in increased levels of homocysteine in the blood and has been linked to metabolic syndrome. Levels of more than 11 µmol/l will increase the risk of cardiovascular disease. Hyperhomocysteinemia will result in impaired endothelial function, increased vascular lesions, and increased platelet adhesiveness.[10] This condition is associated with increased gene expression of proinflammatory cytokines, one of which is CRP, which is produced in the liver.[8,9]

C-reactive protein (CRP) has been shown to be prognostic of the incidence of various diseases in the metabolic syndrome population such as myocardial infarction, stroke, and type 2 DM.[5,8] C-reactive protein levels >3 mg/l are associated with a 1.7 times increased risk of cardiovascular disease in the metabolic syndrome.[5] It is said to has a higher predictive value compared to LDL cholesterol levels.[8] It is has also been shown to impair insulin signaling through the regulation of spleen tyrosine kinase (Syk) on small G-protein pA, jun N-terminal kinase (JNK) mitogen-activated protein kinase (MAPK), insulin receptor substrate-1 (IRS-1), and endothelial nitric oxide synthase (eNOS) in vascular endothelial cells. C-reactive protein has also been shown to contributes to atherothrombosis though endothelial cell activation and dysfunction in vitro as well as in vivo. Lowering the levels of CRP would reduce or prevent these adverse effects and hence reduce the incidence of cardiovascular diseases.[10,11]

Administration of folic acid can reduce CRP levels in metabolic syndrome. Based on the literature search, two articles were found that met the eligibility criteria, namely one systematic review and one randomized controlled trial (RCT). In a systematic review conducted by Jiang et al.,[8] in 2022, it was found that administration of folic acid with varying doses and duration (0.15 mg/day for 12 weeks to 10 mg/day for 2 weeks) significantly reduced CRP levels in metabolic syndrome (WMD= -0.94 95% CI -1.56, -0.32; p=0.00).[8] This supports the idea that administration of folic acid can reduce proinflammatory cytokines. The advantage of this article is that it includes RCTs that use a crossover design. However, there is a weakness, namely that it still includes RCTs with high bias (3.5%).

In the RCT conducted by Schneider et al.,[9] in 2011, each subject was given 5 mg folic acid per day or placebo each for 4 weeks with a wash-out phase between the second phase of the study for 4 weeks, and it was found that administration of folic acid had no effect to decrease CRP levels. According to this RCT, the mean difference of CRP in metabolic syndrome group is smaller than in non-metabolic syndrome group, and this result was not statistically significant.[9] The weakness of this article is that homocysteine levels were not checked, where its level can decrease with folic acid administration by various factors such as dose, absorption, and duration of supplementation. However, the strength of this

article is the method used a crossover design with a 4-week supplementation phase and a 4-week wash-out phase.

Based on these two articles, the effect of folic acid administration on CRP levels in patients with metabolic syndrome is still inconclusive. However, folic acid has the potential to reduce CRP levels, therefore further research is needed. The supplementation dose that can be given is 0.15 mg (150 μg) to 1 mg per day for a minimum of 8 weeks together with the use of statin as an anti-inflammatory agent[12] The upper limit of tolerable intake from supplementation is 1 mg, and acute side effects can occur at a dose of 15 mg (15 times the upper limit of tolerable intake).[13] It is recommended that if facilities are available, serum folic acid levels should be checked prior to supplementation.

Conclusion

Folic acid supplementation can potentially reduce CRP levels in patients with metabolic syndrome and grade 2 obesity. In patients in this case, folic acid supplementation can be given to support in reducing the patient's inflammatory condition.

Conflict of interest

The authors declare there is no conflict of interest regarding this article.

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CASE REPORT

The effect of vitamin D supplementation on increasing CD4 levels in human immunodeficiency virus: evidence-based report

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Abstract

Introduction: Human immunodeficiency virus (HIV) is a retrovirus infection that attacks the immune system. According to world data in 2016, the number of HIV-infected patients reached 36.7 million, and 10 million people died due to acquired immunodeficiency syndrome (AIDS). Patients with HIV infection are susceptible to decreased levels of vitamin D (25(OH)D) by proinflammatory cytokines or as a result of the use of antiretroviral drugs. Vitamin D plays an important role in immune system, including reducing the production of pro-inflammatory cytokines and increasing the production of cathelicidin that inhibit viral replication. Oral vitamin D supplementation is an effort that can be made to increase vitamin D. To date, the relationship between vitamin D sufficiency and CD4 T cell count remains unclear, although most studies have shown a positive association. This study wanted to determine the effect of oral vitamin D supplementation on increasing CD4 levels in patients with HIV infection.
Methods: Literature search was carried out by advanced searching on Pubmed, Cochrane Library, and Science Direct using eligibility criteria determined by the authors.
Result: One systematic review and three randomized controlled trials (RCT) met the PICO and eligibility criteria that had been set. Three studies concluded that vitamin D supplementation can increase CD4 levels. One study shows that vitamin D supplementation dose of 5,000 IU daily could not increase CD4 levels.
Conclusion: Providing vitamin D supplementation at appropriate dose can increase serum vitamin D levels so that it can increase CD4 levels.

Keywords: vitamin D supplementation, CD4, human immunodeficiency virus

Clinical Scenario

A 28-year-old woman has been suffering from HIV for 4 months. The patient has not received antiretroviral therapy. The patient was treated for complaints of weakness that had worsened since 4 days before entering the hospital. At admission, the patient experienced anemia (7.7 g/dL), hyponatremia (135 mEq/L), hypokalemia (2.9 mEq/L), hypoalbuminemia (2.8 g/dL), and vitamin D deficiency (4.6 ng/mL). The patient was consulted by an internist to a physician clinical nutrition specialist for nutritional management and

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asked whether giving vitamin D supplementation could help immunological recovery by increasing of CD4 levels?

Introduction

The human immunodeficiency virus (HIV) is a retrovirus infection that attacks the immune system. According to world data in 2016, the number of HIV-infected patients reached 36.7 million, and 10 million people died due to acquired immunodeficiency syndrome (AIDS). The prevalence of HIV cases in Indonesia from 2005–2019 data recorded 338,363 people suffering from HIV and 1,536 people with AIDS. Patients with HIV are susceptible to vitamin D deficiency, this is caused by impaired renal 1α-hydroxylation of 25-hydroxyvitamin D3 mediated by proinflammatory cytokines or as a result of the use of antiretroviral drugs. Vitamin D plays a role in the immune system, both the innate immune system and the adaptive immune system.[1,2] There is an increased risk of morbidity and mortality in HIV-infected patients with low levels of vitamin D.[3] CD4 T cell counts in peripheral blood are useful to determine immune status and stage of HIV infection.[4]

Vitamin D plays a role in the innate and adaptive immune system, and the vitamin D receptor (VDR) is expressed in almost all cells of the immune system, namely CD8+ T lymphocytes, CD4+ T lymphocytes, as well as B lymphocytes and monocyte/macrophage cells. The active form of vitamin D, namely 1,25(OH)2D, will influence the differentiation of innate immune cells, which increases the development of regulatory T lymphocytes with suppressive activity. Additionally, pathogen elimination is increased through increased intracrine 1,25(OH)2D production by monocytes and macrophages, leading to increased phagocytosis and expression of pathogen recognition receptors. This signaling will increase the transcription of cathelicidin, which have antimicrobial properties, and defensins, which has both antimicrobial and antiviral properties. Cathelicidin is also known to inhibit HIV replication in CD4+ T cells and macrophages.[5-7]

Based on previous research, vitamin D can influence both innate and adaptive responses through the expression of its receptors on various immune cells, such as monocytes, dendritic cells, and lymphocytes. Through this process, vitamin D is known to increase CD4 levels. According to two randomized controlled trials and one systematic review, vitamin D supplementation can increase CD4 levels in HIV patients. Several studies state that giving vitamin D supplementation at the appropriate dose can improve vitamin D levels and the patient's immune system.

Clinical Questions

P : Patients with HIV infection
I : Vitamin D supplementation
C : Placebo or no vitamin D supplementation
O : CD4 level
Clinical question: Can oral vitamin D supplementation reduce CRP levels in patients with HIV infection?

Methods

The literature search was carried out by advanced searching using a combination of MesH terms and title/abstract on the PubMed database, Cochrane Library, and advanced search on Science Direct. The search was carried out on January 4, 2024. The keywords used were vitamin D supplementation, CD4, and human immunodeficiency virus. Critical appraisal tools and determination of the level of evidence are based on the Oxford Center for Evidence Based Medicine.

Eligibility Criteria

Inclusion criteria included subjects over 18 years of age with a diagnosis of HIV infection. The study used a randomized controlled trial (RCT) design and systematic review/meta-analysis from an RCT. The intervention was the supplementation of vitamin D, while the control group was given placebo or no vitamin D supplementation, published from 2019 to 2024, and was written in English. Exclusion criteria include research that

was not conducted in humans and articles not available in full text.

Critical Study Method

The critical review method was carried out on all selected articles by examining the *validity*, *importance*, *applicability* (VIA) using CEBM (*Centre for Evidence Based medicine*) in accordance with the type of therapeutic study.

Results

Based on the results from the database, which was conducted with advance searching, the author found 9 literatures from PubMed, 65 literatures from Cochrane Library, and 147 literatures from Science Direct. As shown in **Figure 1**, there are1 SR/MA and 3 RCTs selected to be included in this evidence-based case report. Based on criteria from the Oxford Centre for Evidence Based Medicine, the level of evidence of 1 article with the SR/MA study is level 1a, while 3 articles with the RCT study is level 1b. The subjects in 4 study articles were patients with HIV infection who received vitamin D supplementation in the intervention group, compared to the control group given placebo or no vitamin D supplementation, to assess the outcome of CD4 levels. The study characteristics of these articles are listed in Table 2. The level of evidence for these articles is presented in **Table 3**.

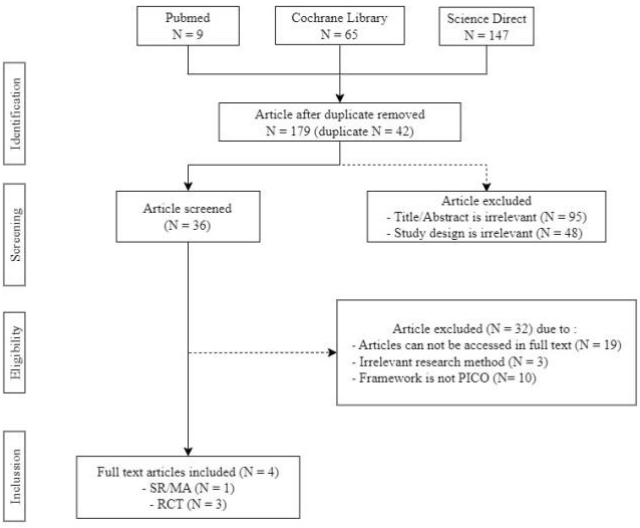

Figure 1. Prisma's Flowchart

Discussion

In HIV patients, the prevalence of vitamin D deficiency and insufficiency is quite high, ranging from 24% to 72%. This deficiency can be attributed to malabsorption, chronic inflammation, poor intake, and liver dysfunction. Vitamin D is a micronutrient that plays a role in regulating the innate and adaptive immune systems. One of its functions is to enhance the transcription of cathelicidin, which can inhibit HIV replication in CD4+ T cells and macrophages. The relationship between vitamin D sufficiency and the increase in CD4 levels in HIV patients is still uncertain, so further research on this matter is needed for clarification.[8]

CD4+ T cell counts and viral load are essential indicators for determining the clinical course of HIV-1 infection. CD4+ T lymphocytes are the primary target cells of HIV, followed by dendritic cells, monocytes, and macrophages. The acute infection is characterized by the destruction of gut-associated lymphoid tissue (GALT) that harbors a high number of CD4+ effector memory cells. Destruction leads to both anatomical and functional alterations of the gut mucosal barrier, facilitating the passage of commensal microorganisms into the circulation system, which in turn, promotes continuous immune activation.[9]

Vitamin D in humans is obtained through three main pathways: the synthesis of vitamin D in the skin, consuming food sources of vitamin D, and supplementation in the form of vitamin D2 or D3. Ultraviolet B (UVB) can convert 7-dehydrocholesterol into previtamin D3 in the skin, and then quickly converted it into cholecalciferol (D3). Vitamin D3 goes to the liver to be converted into 25-hydroxyvitamin D (calcidiol) by the enzyme 25-hydroxylase. Calcidiol goes to the kidneys and is converted into 1,25-dihydroxyvitamin D3 (calcitriol) by the enzyme 1-α-hydroxylase. Calcitriol is the active form of vitamin D which works on target cells and binds to the vitamin D receptor (VDR).[10]

Based on studies by Almeida-Afonso R, et al.,[11] Teixeira NDSCCA, et al.,[12] and Permata M, et al.,[13] vitamin D supplementation can increase

Table 1. Literature Search Strategy

We conducted a comprehensive analysis of existing research using advanced search methods in Pubmed, Cochrane Library, and Science Direct. This process includes combining MeSH Terms and Title/Abstract searches to ensure a thorough search strategy that targeted the population, intervention, comparison, and outcome.

Database	*Search Strategy*	*Hits*	*Selected Article*
Pubmed	("vitamin d supplementation"[Title/Abstract] OR "vitamin d3 supplementation"[Title/Abstract] OR "cholecalciferol supplementation"[Title/Abstract]) AND "2014/01/19 00:00":"3000/01/01 05:00"[Date - Publication] AND (("cd4 antigens"[MeSH Terms] OR "cd4"[Title/Abstract]) AND "2014/01/19 00:00":"3000/01/01 05:00"[Date - Publication]) AND (("hiv"[MeSH Terms] OR "human immunodeficiency virus"[Title/Abstract] OR "hiv"[Title/Abstract])	9	3
Cochrane Library	#1 (vitamin d supplementation):ti,ab,kw #2 (vitamin d3 supplementation):ti,ab,kw #3 (cholecalciferol supplementation):ti,ab,kw #4 MeSH descriptor: [CD4 Antigens] explode all trees #5 (cd4):ti,ab,kw #6 MeSH descriptor: [HIV] explode all trees #7 (human immunodeficiency virus):ti,ab,kw #8 (hiv):ti,ab,kw #9 #1 OR #2 OR #3 #10#4 OR #5 #11#6 OR #7 OR #8 #12#9 AND #10 AND #11	65	1
Science Direct	(vitamin d supplementation OR vitamin D3 supplementation OR cholecalciferol supplementation) AND (cd4) AND (human immunodeficiency virus OR HIV)	147	0

Table 2. Assessment of Literature Characteristics

Author	Study Design	Population Characteristics	Intervension	Outcomes	Research Results
Almeida-Afonso R, et al.[11] (2021)	*Randomized Controlled Trial*	37 patients in the intervention group (supplemented once a week with 50,000 IU vitamin D) and 36 patients in the placebo group	Patients with HIV infection were given vitamin D dose 50,000 IU/week supplementation compared to placebo for six months.	T CD4 cells count, vitamin D levels, calcium, phosphorus, glucose, urea, osteocalcin level	Supplemented active group achieved a small increase in T CD4+ lymphocytes at the end of the six months follow-up time, compared to the placebo group (p = 0.05)
Ashenafi S, et al.[14] (2019)	*Randomized Controlled Trial*	95 patients were allocated to the intervention group (daily oral supplementation 5,000 IU) and 102 patients were allocated to the placebo group.	The intervention group took daily dose vitamin D3 supplementation (5,000 IU), and those in the control group received matching placebo tablet from good	HIV viral load, CD4 T cell count, CD8 T cell count, BMI, MUAC, vitamin D status	The study does not show that vitamin D supplementation dose 5,000 IU daily can increase CD4 T cell count. There was no significant changes in CD4 T cell count in this study

Author	Study Design	Population Characteristics	Intervensions	Outcomes	Research Results
			manufacturing. The intervention was carried out for 16 weeks.		
Teixeira NDSCCA, et al.[12] (2019)	*Systematic Review*	Total 198 articles and after selection process 5 articles were identified eligible. Total sample from those 5 articles were 4470. The PICO strategy of the following guiding question: does vitamin D supplementation lead to improvements in the clinical picture of HIV patients?	The intervention group got vitamin D supplementation ranged from 2,000 to 50,000 IU per week, and the duration of intervention ranged from 12 weeks to 3 years	The main variables investigated were: 25(OH)D, BMI, CD4 count, but some studies went further and included biochemical tests and immunological data	The results of the five clinical trials demonstrated a positive effect of supplementation on CD4 lymphocytes count supporting the vitamin D benefit in immunological recovery.
Permata M, et al.[13] (2020)	*Randomized Controlled Trial*	10 patients in the intervention group (supplemented calcitriol 0,5 mcg per day for eight weeks) and 10 patients in the placebo group	The patients in intervention group received vitamin D (calcitriol 0,5 mcg per day) for 8 weeks.	This study aims to determine whether the addition of vitamin D affects increasing the CD4 counts of HIV/AIDS infection patients	There was a significant increase in the CD4 cell count of the vitamin D group, but not in the CD4 cell count of both groups. In the vitamin D group, the mean CD4 count before the addition of vitamin D was 361.3+185.2 cells/mm^3 increased to 400.1 + 185.2 cells/mm^3 ($p = 0.046$)

Table 3. Relevance Criteria

Authors	Population similarity	The similarity of the determining factors	Outcomes similarity
Almeida-Afonso R, et al. (2021)[11]	+	+	+
Ashenafi S, et al. (2019)[14]	+	+	+
Teixeira NDSCCA, et al. (2019)[12]	+	+	+
Permata M, et al. (2020)[13]	+	+	+

After the identification and screening process, articles that are suitable for population, intervention, comparison, and outcome are then critically reviewed. Four articles were found to have appropriate setting to the clinical scenario. Among these articles, three are randomized controlled trials (RCTs) and 1 is a systematic review (SR). These four articles identified the validity criteria based on quality and level of evidence according to the Oxford Center for Evidence-Based Medicine (CEBM).

Table 4. Validity Criteria

	PICO	Review Strategy	Study Design	Study Quality Assessment	High Quality	Results in Tables/Forest Plots	Similarity of Study Results	Quality of evidence*	Level of evidence**
Almeida-Afonso R, et al.[11]	+	+	+	+	-	+	+	Moderate	1b
Ashenafi S, et al.[14]	+	+	+	+	+	+	+	Moderate	1b
Teixeira NDSCCA, et al.[12]	+	+	+	+	-	+	+	High	1a
Permata M, et al.[13]	+	+	+	+	+	+	+	Moderate	1b

*Quality of evidence according to GRADE guidelines, https://www.ncbi.nlm.nih.gov/pubmed/21208779
**Level of evidence according to Oxford Center of Evidence-based Medicine (CEBM), http://www.cebm.net.
+ clearly mentioned in the article; - not done; ? Not stated clearly

CD4 levels significantly in HIV patients. Meanwhile, a different statement from a study by Ashenafi S, et al.,[14] shows that vitamin D supplementation does not show significant changes in CD4 levels in HIV patients.

The study by Almeida-Afonso R, et al.,[11] show that vitamin D supplementation was found to be effective in normalizing blood levels after six months (>30 ng/mL) for 80% of the patients in the study. None of the patients exhibited blood levels considered dangerous (>100 ng/mL). A weekly oral dose of 50,000 IU of vitamin D was sufficient to safely normalize vitamin deficiency with good adherence among HIV-1-infected subjects. The study also indicated that vitamin D supplementation in the intervention group achieved a small increase in T CD4+ lymphocytes at the end of the six-month follow-up period compared to the placebo group.

According to a systematic review by Teixeira NDSCCA, et al. with 5 eligible articles (4470 samples), it also states findings consistent with the Randomized Controlled Trial (RCT) by Almeida-Afonso R, et al. With vitamin D supplementation ranging from 2,000 to 50,000 IU per week, and the intervention duration ranging from 12 weeks to 3 years, it can improve vitamin D levels. The relationship between chronic viral infections and hypovitaminosis D is well known. Vitamin D deficiency is associated with a low TCD4 cell count and a viral load higher than 50 copies/mL. In addition, vitamin D deficiency occurs more frequently in patients with more severe disease progression. Thus, patients with vitamin D deficiency increase the risk of morbidity and mortality in HIV patients. Based on this systematic review, sufficient levels of 25(OH)D are positively correlated with the number of CD4+ cells and a reduction in infection levels.[12]

According to several previous studies, vitamin D deficiency is associated with increased inflammation and immune activation, low peripheral blood CD4+ T cells, faster progression

of HIV disease, and shorter survival time in HIV-infected patients.[15,16] A study by Ashenafi S, et al.,[14] states that supplementation with vitamin D3 at a dose of 5000 IU per day for 16 weeks can significantly increase serum vitamin D levels. Given these prior findings, the study hypothesized that daily nutritional supplementation with vitamin D3 could reduce viral replication and restore immune and nutritional status in HIV infection.

However, the results of the study by Ashenafi S, et al.,[14] indicate somewhat different outcomes. The study does not demonstrate that a daily vitamin D supplementation dose of 5,000 IU can increase CD4 T cell count. The difference in results from this study could be due to an inadequate number of doses or an insufficient length of intervention. Apart from that, when compared with research conducted by Permata, et al. even though the study was for a period of 8 weeks, the intervention given was vitamin D in the active form (calcitriol).[13]

In addition to supplementation, vitamin D needs can be fulfilled by consuming foods that are natural sources of vitamin D and by sun exposure. Vitamin D is a fat-soluble vitamin naturally present in some foods and is also produced endogenously when ultraviolet (UV) from sunlight hits the skin, triggering vitamin D synthesis. Fatty fish (such as trout, salmon, tuna, and mackerel) and fish liver oil are the best sources of vitamin D. Beef liver, egg yolks, and cheese contain small amounts of vitamin D. Some foods are fortified to provide vitamin D, such as beverages made from soy, almonds, oats, and cow's milk. Several studies suggest that approximately 5–30 minutes per day or at least twice a week, especially between 10 a.m. and 4 p.m., on the face, arms, hands, and legs without sunscreen usually leads to sufficient vitamin D synthesis.[17]

Conclusion

The relationship between chronic viral infections and hypovitaminosis D is well known. Patients with HIV are susceptible to vitamin D deficiency. Vitamin D deficiency is associated with a low TCD4 cell count and a higher viral load. Vitamin D supplementation can increase 25(OH)D levels in plasma, and adequate levels of 25(OH)D are positively associated with the number of CD4. Several articles state that vitamin D supplementation can increase serum vitamin D levels which has a positive relationship with increasing CD4 levels. However, some different results are still found so future trials need to be conducted to prove the benefits of vitamin D to increase CD4 levels in HIV.

Conflict of interest

The authors declare there is no conflict of interest regarding this article.

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LITERATURE REVIEW

Intermittent fasting-induced improving insulin resistance in healthy obese adults: A scoping review

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Abstract

Background: Obesity is a severe global public health problem linked to chronic noncommunicable disease and increased mortality. It has harmful effects on metabolic disorders via the insulin resistance pathway. Available guidelines recommend caloric reduction via intermittent fasting for obesity management. However, the available literature is less focused on the benefits of intermittent fasting on improved insulin resistance in healthy obese adults, especially related to an accumulation of free fatty acids. Therefore, a scoping review is necessary.

Objective: This review aims to collect evidence on the benefits of intermittent fasting on improved insulin resistance in healthy obese adults.

Methods: This scoping review followed the 5-step Arksey and O'Malley framework and was submitted following PRISMA ScR. Five electronic databases were thoroughly searched. Papers are included if they are eligible. The result was a synthesis of descriptive and narrative elements.

Results: 1117 papers were collected in total. Nine randomized controlled trial studies met the review's inclusion criteria. The papers included are sourced from reputable, relevant sources. As a whole, intermittent fasting appears to benefit improved insulin resistance in healthy obese adults. Intermittent fasting has been shown to reduce insulin levels while increasing insulin sensitivity, therefore improving insulin resistance.

Conclusion: Evidence suggests that intermittent fasting can help improve insulin resistance in healthy obese adults.

Keywords: Fasting, Insulin, Insulin Resistance, Obesity

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Introduction

Obesity is defined as excessive fat accumulation that is measured by a body mass index (BMI) of more than 30 kg/m^2 as a result of impaired energy balance and homeostatic processes.[1-4] Obesity prevalence is increasing globally. Apart from prevention and treatment, the World Obesity Federation predicts that more than half (51%) of the global population will be obese in the coming years.[5] Although the causes of obesity are multifactorial, an excess supply of caloric intake plays an important role in developing obesity.[6]

Obesity has negative consequences that present a risk to health. It was responsible for various metabolic dysfunctions and is a single risk factor for other diseases in current investigations.[7-8] Recent studies define obesity as a disease that is caused many as 21 diseases, including metabolic disorders, and is linked to insulin resistance.[7-9] Obese individuals had a higher probability of having simple (two diseases) and complicated (≥four diseases) multimorbidity than healthy weight ones.[9] The current study explains the global cost of overweight and obesity is expected to reach $4.32 trillion per year by 2035.[5]

Considering the risk of obesity-related comorbidities and cost consequences is increasing, obesity management focuses on realistic weight loss in order to trim it.[10] Therefore, adequate therapy is required. The Obesity Medicine Association (OMA) recommends the central management of obesity through a nutritional intervention approach, especially meal arrangements.[11-12] Numerous diets have been devised to treat obesity.[13-17] The treatment is based on calorie restriction using the principle of reducing calories, and the ultimate goal is to create a negative energy balance.[18]

The Obesity Medicine Association recommends intermittent fasting as one of ten takeaway messages in managing obesity. Obesity management with intermittent fasting is advantageous. Meta-analyses studies show that intermittent fasting therapy has beneficial outcomes for weight loss and chronic disease risk factors compared to daily calorie restriction. Intermittent fasting is characterized by recurring and periodic fasting periods, triggering adaptive changes in the body's physiological functions. Intermittent fasting modifies homeostatic, systemic, and metabolic processes, allowing the body to perform its recovery function.[19-22]

The benefits of intermittent fasting as a nutrition therapy for obesity are clear.[19,23] Nevertheless, to our knowledge, few discuss intermittent fasting on intermittent fasting on improved insulin resistance in healthy obese adults. Originally, managing obesity before moving to other diseases could significantly impact clinical results. We evaluated intermittent fasting on improving insulin resistance in healthy obese adults. As a result, this scoping review aims to investigate the function of intermittent fasting in improving insulin resistance in healthy obese adults.

Methods

Protocol design

This study was designed as a broad-scoping literature review to map pertinent evidence for intermittent fasting on improving insulin resistance in healthy obese adults. The review was carried out to summarize, map, and present evidence findings from various papers using descriptive methodologies. The 5-step Arksey and O'Malley framework was used for validation, and the results were published following PRISMA ScR (priority reporting item for systematic review and a meta-analysis extension for scoping reviews).[24]

Protocol design

We established inclusion criteria to select papers that were relevant to the review's purpose. The paper inclusion criteria were decided by publishing in English, internationally, accessible, full-text papers published after 2018, focusing on intermittent fasting to improve insulin resistance in healthy obese adults, design by randomized controlled trial (RCT), original research (protocols and review papers not permitted), the population consisted of people, the subject is overweight and obesity, and quality of evidence from reputable

journal indexed by Scopus. Exclusion criteria were set: articles with unclear results.

Information sources

We used primary papers of experimental RCTs design that met the eligibility requirement. Papers from four electronic databases, including Science Direct, Scopus, Wiley One Library, PubMed, and Google Scholar, were used to discover studies published in the last five years between January 2018 and January 2023. Five databases were chosen since they are all focused on nutrition and medical sciences and are relevant to the study's objectives.

Search strategy

A first exploratory search was conducted, which included electronic sources. The findings of this search were then utilized to build a scoping review search strategy. The database searches' keywords were as follows: "(fasting OR intermittent fasting OR time-restricted eating OR alternate day fasting) AND (obesity OR overweight) AND (insulin resistance OR insulin sensitivity) AND (RCT OR Randomized Controlled Trial)." Papers were collected, and the full text was screened for eligibility.

Result

Selection of evidence

A total of 1117 papers were identified from databases, including Science Direct 526, Scopus 73, Wiley One Library 261, PubMed 9, and Google Scholar 248 paper. In the total paper, 1117 of these, 371 items were eliminated during the initial assessment, and 113 papers were found to have a potential close match with the scoping review's emphasis. 21 paper is removed after duplicate, leaving 92 paper. Then, 58 papers are excluded by title and subject (non-human subject), leaving 37 papers eligible. Last, 18 papers are excluded by reputable evidence and subject (non-spesific evidence), leaving 19 papers suitable for analysis. Ten of them were excluded because the outcome

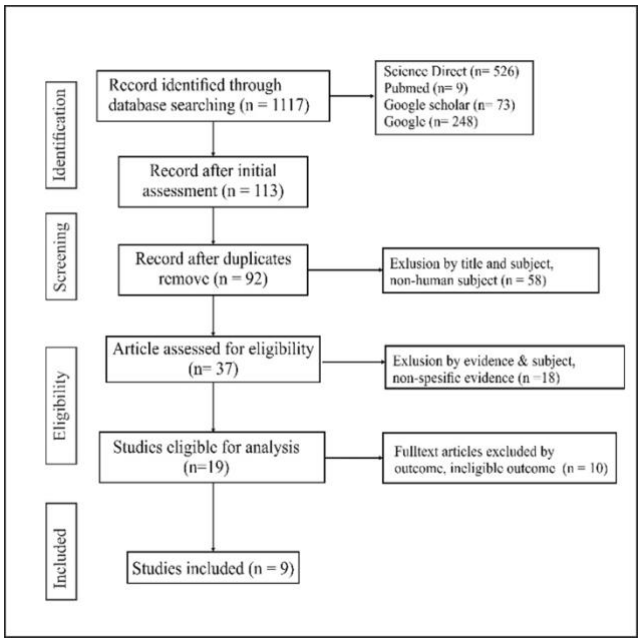

Figure 1. PRISMA flow chart.

did not match the scoping objectives. Finally, nine papers were included for a scoping review. **Figure 1** shows the PRISMA flowchart showing the search strategy used.

Characteristics of evidence

The following are the characteristics of the papers covered in this review: papers are based on research published in reputable Scopus-indexed journals. Papers is including Q1's (n = 8) and Q2's (n = 1). Papers originate from a variety of countries, including the USA (n=2), China (n=2), Iran, Portugal, South Korea, the UK, and German, respectively (n=1) are included in this scoping review (n=9). All research subjects a health, overweight or obese adults (n=9). The entire research evaluates the impact of intermittent fasting interventions. What distinguishes them is the type of intermittent fasting used. Interventions are typically classified into three types. One paper investigated alternate-day calorie restriction (ADCR). Four papers investigated time-restricted feeding/eating (TRF/TRE). Four papers investigated intermittent/continuous calorie restriction (I/CCR) or intermittent energy restriction (IER). The duration of the intervention varied from 37 days to one year. The subjects' ages varied from 18 to 75 years, with a total sample size

of 28-150. However, one paper disregards the variety of age subject requirements. BMI subject range from 23 to 50 kg/m^{2,} and one paper disregards the variety of BMI subject requirements.

Synthesis of results

The nine papers' findings support intermittent fasting's use to improve insulin resistance in healthy, obese adults. Overall, the nine papers demonstrated that after the intervention of three different types of intermittent fasting, there was a reduction in insulin resistance as measured using HOMA-IR. In other words, despite a scarcity of research, evidence suggests that intermittent fasting can aid in improving insulin resistance in healthy obese adults. **Table 1** shows the mapping, analysis, and synthesis of evidence.

Discussion

Summary of evidence

The summary of evidence is meant to summarize results following the scoping review's principal purpose. First and foremost, it should be highlighted that there aren't many papers on the use of intermittent fasting as a dietary therapy for obesity that can improve insulin resistance in healthy obese adults. The author acknowledges that the early findings of the paper may be appropriate. Exclusion techniques revealed, however, that while most papers focused RCTs on the benefits of intermittent fasting on weight reduction in obese persons, they did not focus on outcomes related to pathways linked to better insulin resistance owing to free fatty acid buildup. All of the presented investigations are only partially explained. The study's findings, on the other hand, can be woven into a crimson thread.

According to the author, there were initially 1117 documents from five electronic database sources possibly useful for study purposes. Despite hundreds of papers potentially based on the keywords we seek, the paper fails to focus on the topic, namely the effect of intermittent fasting therapies on insulin resistance in obese healthy individuals. As a result, the exclusion method used to establish eligibility excludes the paper. We are leaving only nine papers for us to cover.

Obese people are known to have a buildup of dietary fat. This buildup promotes adipose tissue expansion and increases free fatty acids in non-adipose tissue or organs, resulting in metabolic abnormalities due to impaired insulin signaling and sensitivity. This process is well-known to contribute to insulin resistance primarily.[7] Outstanding guidelines have recommended intermittent fasting as a treatment for obesity to reduce the supply of calories from dietary fat.[11] These findings may be related to the contribution of nutritional support through periodic dietary management and daily calorie restriction that modifies metabolic function.[22]

This review study found one paper with ADCR-type intermittent fasting intervention combined with exercise.[26] The second type of intermittent fasting we discovered is TRF/E.[27,28,33] And the last type is I/CCR or I/ECR.[25,29–31] Overall, the intervention of three types of intermittent fasting decreases insulin levels, enhances insulin sensitivity, and eventually improves insulin resistance. Previous systematic review studies have shown that intermittent fasting is beneficial glycemic and insulin levels control in people with type 2 diabetes and metabolic syndrome but did not focus on insulin resistance.[34] Three types of intermittent fasting (ADF, TRE, and Restriction) are known to decrease fasting glycemic levels, as well as other studies that show improved insulin sensitivity and a reduction in risk factors for chronic illness.[21,35]

Nine findings of the three types of intermittent fasting benefit insulin levels and sensitivity and insulin resistance. These findings are consistent with prior research, which found that ADF, TRF/E, and I/CCR can reduce insulin resistance.[36-37] ADCR-type intermittent fasting, although this intervention is a mix, it is not only intermittent fasting, yet it still contributes. This intervention focuses on energy conservation. Participants ingested 25% of the recommended daily calorie intake on three days of the week, alternating with 'fasting days,' and consumed ad libitum on the remaining four days ‘feed day’.[26]

Table 1. Mapping, synthesis, and analysis

Title	Country	Study type/subject	Intervention	Main findings	Reference
Effects of intermittent and continuous calorie restriction on body weight and metabolism over 50 wk: a randomized controlled trial	German	RCT/overweight/obese adult**.**	I/CCR 8 wk	Insulin concentrations and HOMA-ir were reduced in all research groups.	25
Effects of alternate day calorie restriction and exercise on cardio-metabolic risk factors in overweight and obese adults: an exploratory randomized controlled study.	South Korea	Randomized controlled study/overweight/obesity adult**.**	ADCR 50 wk	Significant insulin, glucose, and HOMA-ir reductions were observed after eight weeks of intervention.	26
Early time-restricted feeding improves insulin sensitivity, blood pressure, and oxidative stress even without weight loss in men with prediabetes.	USA	Randomized, crossover, control study/overweight/obese adult man with prediabetes.	TRF 37 d	eTRF lowers insulin levels and insulin resistance while increasing insulin sensitivity and cell responsiveness.	27.
Effects of four-hour and six-hour time-restricted feeding on weight and cardiometabolic health: a randomized controlled trial in adults with obesity.	USA	*RCT,* randomized parallel-arm trial/ adult obesity.	TRF 10 wk	TRF for 4 and 6 hours results in equal decreases in fasting insulin and insulin resistance.	28
Intermittent energy restriction is comparable to continuous energy restriction for cardiometabolic health in adults with central obesity: A randomized controlled trial; the Met-IER study.	UK	*RCT/adult with central obesity.*	I/CER 4 wk	On the whole, insulin sensitivity significantly increased and decreased insulin resistance and insulin level.	29
Effect of intermittent versus continuous calorie restriction on body weight and cardiometabolic risk markers in subjects with overweight or obesity and mild-to-moderate hypertriglyceridemia: a randomized trial.	Iran	*RCT*/overweight/obese adult.	I/CCR 8 wk	Intermittent calorie restriction improving HOMA-IR.	30
Intermittent energy restriction ameliorates adipose tissue-associated inflammation in adults with obesity: A randomized controlled trial.	Portugal	*RCT*/adult obesity.	I/CER 12 wk	Both dietary regimens improved glucose homeostasis and insulin sensitivity after 12 weeks, with a substantial drop in fasting glucose and insulin plasma concentrations and a significant rise in HOMA-β, HOMA-S, and a decrease in HOMA-IR.	31
Randomized controlled trial for time-restricted eating in overweight and obese young adults.	China	*RCT*/overweight and obese young adults.	TRE 8 wk	6-h eTRE lowered fasting insulin and insulin resistance when compared to the control.	32
Calorie Restriction with or without Time-Restricted Eating in Weight Loss.	China	*RCT*/adult obesity.	TRE 12 mth	Both time-restricted eating and calorie restriction daily were linked to lower HOMA-IR.	33

ADF reduces insulin resistance by enhancing insulin sensitivity and lowering glucotoxicity from calorie intake. [36]

TRF/E type intermittent fasting positively affected insulin resistance. The intervention focused on eTRF with a daily meal schedule of 6 hours and an early dinner before 15:00, TRF 4 hours and 6 hours, the 6-hour eTRE eats ad libitum from 07:00 to 13:00, whereas the 6-hour lTRE eats ad libitum from 12:00 to 18:00, both followed by complete fasting till tomorrow, and 8 hour period adopted from 8:00 to 16:00. It is believed that this good alteration is due to glucoregulatory factors. Fasting may help manage glucose by activating the metabolic switch. The metabolic transition that happens while going from fed to fasting causes hepatocytes to produce ketone bodies, enhancing insulin sensitivity. TRE works by restricting meals briefly, promoting glycemic control, and increasing insulin sensitivity. Zhang explains mechanism effect of TRF is the circadian rhythm system. The circadian system supports improved glucose tolerance and the body's physiological response to fasting at night and morning.[27,28,32,33]

While ADCR and TRF/E help with insulin resistance, I/CCR or I/CER does the same. In the dietary intervention, the ICR group consumed 25% of daily energy needs on two non-consecutive days, while the CCR group ingested 80%, the group's weekly energy intake was reduced by 3500 kcal, the CCR group was directed to consume 70% of total energy, while the ICR group consumed 100%, and IER adopted three non-consecutive fasting days per week (very low energy diet) and a daily low-calorie diet CER. Even though the underlying mechanism is unclear, all four studies imply that changes in insulin resistance occur primarily in those in the highest tertile of HOMA-IR due to changes in plasma TG concentrations linked with insulin, which can contribute to peripheral insulin resistance. Moreover, inflammation in adipose tissue is a root cause of poor insulin signaling, and it is essential for obesity-induced insulin resistance. Given the complex interactions, the more significant drop in HOMA-IR found in the IER group may be related to the inflammatory condition.[25,29–31]

Limitations and strengths

This present review has some limitations that must be recognized. The first review's limitations only applied to papers written in English. Second, despite the fact that the five prominent databases chosen were searched and identified, it only returned the first 15 pages based on relevancy. The third limitation we are aware of is that the available sources of information are relatively restricted, with most of the studies we identified describing insulin resistance as the secondary result. Finally, despite the study's limitations, to the author's knowledge, we believe that this is the first study to examine the effect of intermittent fasting on reducing insulin resistance in overweight or obese healthy individuals. Furthermore, the papers chosen for evidence synthesis are from relevant, recognized sources indexed by Scopus, ensuring that the evidence is of high quality.

Conclusions

In conclusion, according to the findings of this scoping study, the intervention of intermittent fasting has the potential to improve insulin resistance in healthy obese adults. This scoping study is considered to be one of the stepping stones for future research. It is hoped that more comprehensive research will be carried out to provide empirical evidence future on intermittent fasting to improve insulin resistance in clinical practice in healthy obese persons. As a consequence, it is possible to avoid the development of the consequent illness.

Conflict of interest

The author states that any known financial or personal conflicts of interest did not influence the work disclosed in this study.

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CASE REPORT

Effect of probiotic administration in adult atopic dermatitis patients: an evidence-based case report

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Abstract

Introduction: Atopic dermatitis (AD) is a chronic skin disease characterized by abnormal skin barrier function and heightened immunologic sensitization. Its incidence has surged recently, with approximately 60% of cases diagnosed within the first year of life. AD can persist or recur, significantly deteriorating the quality of life due to persistent itching and sleep disturbances. Individuals with AD are at increased risk of developing other atopic disorders like asthma and allergic rhinitis. Various dietary approaches, including low carbohydrate, calorie, and fat diets, have been associated with enhanced quality of life by regulating immune responses. Probiotics have been used as adjuvant therapy in allergic conditions, though their effectiveness varies due to the complex nature of allergies.
Method: A literature search was conducted using PubMed, Cochrane Library, and Google Scholar. MeSH terms, advanced search strategies, and predefined eligibility criteria were employed to identify relevant studies. Duplicate studies were excluded, and critical assessment tools and levels of evidence were defined per Oxford Center for Evidence-based Medicine standards.
Results: One systematic review and meta-analysis of randomized controlled trials (RCTs) met the PICO and eligibility criteria. The meta-analysis demonstrated that probiotics significantly decreased AD severity in adults, enhancing their overall quality of life. Other meta-analyses and systematic reviews supported that probiotics reduce clinical severity and improve life quality in adult AD patients.
Conclusion: Probiotic supplementation is a viable option to improve the quality of life for adult AD patients, offering potential therapeutic benefits in managing this condition.

Keywords: probiotic, allergy, atopic dermatitis

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Case scenario

Ms. TU, 23 years old, has been suffering from AD for the past 3 years. When symptoms arise, the patient often takes cetirizine 1x10 mg. The patient came for treatment due to unbearable itching. In addition to therapy and also allergen and stressor avoidance education by an Ear, Nose, and Throat specialist (ENT), the patient was referred to a

clinical nutrition specialist for nutrition education suitable for the patient's condition. The specialist was also consulted regarding whether probiotic supplementation could help improve the quality of life for the AD patient.

Introduction

Atopic Dermatitis (AD) is a chronic, recurrent inflammatory skin condition that not only disrupts the skin's barrier function but also involves immune dysregulation among other mechanisms.[1] In recent years, the prevalence of AD has increased significantly, with estimates suggesting that 3-10% of adults are affected, which is a notable increase compared to earlier statistics.[2] Approximately 60% of AD cases start in the first year of life, and while many children experience mild symptoms, the disease can persist into adulthood or recur, impacting life significantly.[3] The quality of life for individuals with AD can be severely compromised. The disease often coexists with other atopic disorders such as asthma, allergic rhinitis, and chronic sinusitis, further complicating patients' health scenarios.[4] The persistent itching and visible rash associated with AD can lead to sleep disturbances, anxiety, social withdrawal, and even asthma, underscoring the profound psychosocial impact of this condition.[5]

Atopic dermatitis can significantly impact the decrease in the quality of life for patients and their families. AD patients have an increased risk of experiencing other atopic disorders, such as asthma, allergic rhinitis, and chronic sinusitis.[5,6] Similar to other atopic disorders, the dominance of Th2 cells over Th1 cells leads to an imbalance that exacerbates the pathogenesis of AD, increases IgE, and activates interleukin (IL).[6-8]

Probiotics are living microorganisms administered in sufficient quantities to provide health benefits to the host. Several mechanisms regarding how probiotics reduce atopy have been outlined, including shifting the Th1/Th2 balance towards Th1, inhibiting Th2 cytokines, or increasing the production of regulatory cytokines such as IL-10 through dendritic cell maturation or its receptors.[9,10]

A systematic review conducted by Lopez et al.,[1] indicates that probiotics have beneficial effects on pediatric patients with AD. Oral probiotics, particularly strains of the *Lactobacillus* genus, help reduce the severity of AD.[1] A clinical trial administering a combination of oral probiotic strains to young patients with moderate AD demonstrates that this oral probiotic administration effectively reduces the SCORAD index and decreases the use of topical steroids in patients with moderate AD.[9]

Clinical Question

P : Adult patients with AD
I : Probiotic supplementation
C : Placebo
O : Quality of life

Clinical question: can probiotic supplementation improve the quality of life in adult patients with AD?

Methods

Literature search was conducted through advanced searching using a combination of MeSH terms and Title/Abstract in the PubMed, and Cochrane Library databases, and advanced search in Google Scholar. The search was performed on June 26, 2023. The keywords used were atopic dermatitis, probiotic, and quality of life. Critical appraisal tools and determination of the level of evidence were created based on the Oxford Centre for Evidence-Based Medicine.

Eligibility Criteria

Inclusion Criteria including subjects aged over 18 years with a diagnosis of AD, receiving probiotic therapy, and has presence of quality of life outcomes, study design was randomized clinical trial (RCT), systematic review, or meta-analysis design, published between year 2019 to 2023 and was written articles are in English. Exclusion criteria studies involving experimental animal subjects, and articles not available in full text.

Results

The author found 7 articles in Pubmed, 12 articles in Cochrane and 2 articles in Google Scholar. Duplicate removal was performed using Zotero. The articles were assessed for eligibility criteria based on PICO, resulting in the selection of four articlesas shown in **Figure 1**. One Systematic review and meta-analyses RCT and one Meta-analyses RCT that met the eligibility criteria. The study characteristics of these articles were listed in **Table 2**. The level of evidence for these articles is presented in Table 3, and all the articles were found to be relevant for answering the clinical question **(Table 4).**

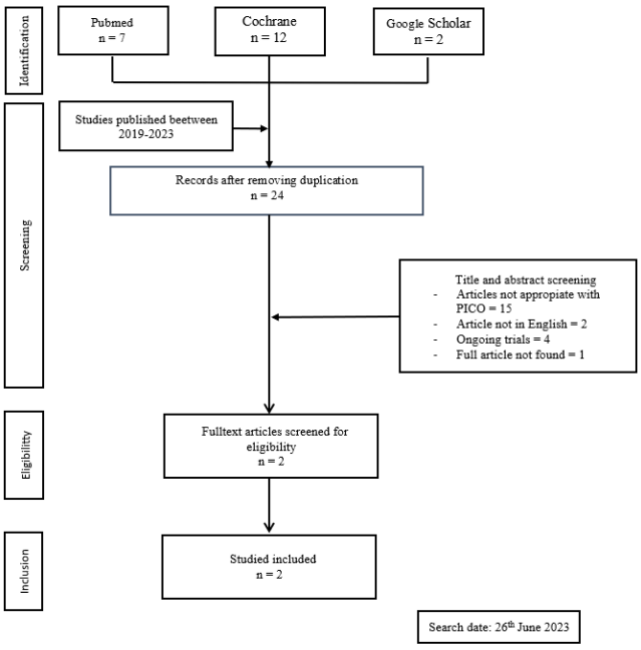

Figure 1. Prisma's flow chart

The literature search was conducted on June 26th, 2023, spanning three databases: PubMed, Cochrane, and Google Scholar. Initially, PubMed yielded 7 studies, Cochrane 12, and Google Scholar 2. After ensuring only studies published between 2019-2023 were considered, all found records were compiled and duplicates removed, resulting in a total of 24 unique records. These 24 records underwent a screening process based on the title and abstract, assessing their relevance to the predefined inclusion criteria (PICO). During this phase, 15 articles were excluded for not aligning with the PICO criteria, 2 for not being in English, 4 due to being ongoing trials, and 1 because the full article was unavailable. Subsequently, the remaining 2 articles were fully reviewed for eligibility. Both passed the eligibility criteria and were included in the final analysis of the study.

Table 1. Resources and Search Strategy

Database	Terminology	Hits	Eligible
PubMed	((probiotic[Title/Abstract]) AND (atopic dermatitis[Title/Abstract])) AND (quality of life[Title/Abstract]) Filters: Meta-Analysis, Randomized Controlled Trial, Systematic Review	7	2
Cochrane	#1 - (probiotic):ti,ab,kw AND (atopic dermatitis):ti,ab,kw AND (quality of life):ti,ab,kw" with Publication Year from 2019 to 2023, in Trials (Word variations have been searched)	12	0
Google Scholar	allintitle: atopic dermatitis probiotic quality of life	2	0

Table 1 presents the search strategy and outcomes of a systematic literature review focused on the effects of probiotics on quality of life for individuals with atopic dermatitis, utilizing three databases: PubMed, Cochrane, and Google Scholar, with searches conducted from 2019 to 2023. The search terms were specifically designed for each database to capture studies relevant to the predefined criteria. PubMed's search resulted in 7 hits with 2 studies meeting the eligibility criteria, utilizing terms within titles and abstracts along with filters for meta-analysis, randomized controlled trials, and systematic reviews. Cochrane identified 12 studies, but none were eligible, likely due to mismatches in study focus or quality despite using detailed indexing terms. Google Scholar, using a simpler title-focused search, also found 2 articles, but none qualified, pointing to the database's broader and less specialized content scope. The varying outcomes across databases underscore the need for precise and tailored search strategies to effectively identify relevant high-quality studies in systematic reviews.

Table 2 provides a detailed summary of two studies evaluating the effects of probiotics on atopic dermatitis (AD) and quality of life in adult populations. In the first study, Li et al.,[22] conducted a systematic review and meta-analysis involving 402 participants across 9 studies, demonstrating both short-term and long-term reductions in AD

Table 2. Study characteristic

No	Author	Study design	Population characteristics	Number of subjects	Outcomes	Results
1	Li *et al.* (2022)[22]	Systematic review and meta-analyses RCT	Adult participants with recorded criteria for the diagnosis of atopic dermatitis (AD) and relevant information regarding probiotic administration.	402 (9 studies)	The level of clinical severity and quality of life	The reduction in the severity of AD in the probiotic supplementation group compared to the control occurred in the short term (SMD: 0.63; 95% CI: 0.02-1.25) and long term (SMD: 1.57; 95% CI: 0.66-2.49). There was a significant long-term improvement in quality of life after probiotic supplementation compared to the control (SMD: 0.74; 95% CI: 0.39-1.09). A combination of L. salivarius (LS01) and Bifidobacterium (BR03) was identified as the best supplementation with the highest probability.
2	Umborowati *et al.* (2022)[20]	Meta-analyses RCT	Adult participants of any gender diagnosed with atopic dermatitis or eczema by a doctor.	241 (6 studies)	SCORAD and quality of life	Probiotics have been proven effective in managing AD in adult patients, as evidenced by a reduction in SCORAD (Mean Difference -7.90; 95% CI -7.25 to -6.92; p<0.00001; I2=96%) and an improvement in quality of life (Mean Difference -7.68; 95% CI -14.08 to -1.29; p=0.02; I2=47%), which is statistically significant.

CI, confidence interval; RCT, randomized controlled trial; SCORAD, scoring atopic dermatitis; AD, atopic dermatitis; SMD, standard mean difference; MD, mean difference

severity through probiotic supplementation, with significant long-term improvements in quality of life. Notably, a specific combination of L. salivarius (LS01) and Bifidobacterium (BR03) was identified as the most effective. The second study by Umborowati et al.,[20] included a meta-analysis of 6 studies with 241 participants, showing statistically significant improvements in AD symptoms and quality of life, as evidenced by reductions in SCORAD (scoring atopic dermatitis) and enhancements in life quality scores. Both studies underscore the therapeutic potential of probiotics in managing AD symptoms and improving the quality of life among adults.

Table 3 evaluates the validity criteria for two systematic reviews and meta-analyses conducted by Li et al.,[22] and Umborowati et al.,[20], both of which assess the impact of probiotics on atopic dermatitis. Each study was thoroughly analyzed for multiple aspects of research design and

methodology, including study design, number of patients, randomization, comparability in treatment and control groups, blinding, domain-specific considerations, determinant factors, and outcome measurements. Both studies scored positively across all criteria, indicating robust design and execution. The quality of evidence for each was rated as moderate, and they both achieved a level of evidence classified as 1A

Table 3. Validity criteria

	Study design	Number of patients	Randomization	Similarity treatment and control	Blinding comparable treatment	Domain	Determinant	Measurement of outcomes	Quality of evidence	Level of evidence
Li *et al.* (2022)[25]	+	+	+	+	+	+	+	+	Moderate	1A
Umborowati *et al.* (2022)[20]	+	+	+	+	+	+	+	+	Moderate	1A

* Quality of evidence according to GRADE guidelines, https://www.ncbi.nlm.nih.gov/pubmed/21208779
**Level of evidence according to Oxford Center of Evidence-based Medicine (CEBM), http://www.cebm.net.
+ clearly mentioned in the article; - not done; ? Not stated clearly
- Systematic review and meta-analysis with troublesome heterogeneity

according to the Oxford Center of Evidence-based Medicine guidelines, suggesting a high standard of reliability in their findings.

Table 4 outlines the relevance criteria assessed for two systematic review studies: Li et al.,[22] and Umborowati et al.,[20] Both articles were evaluated on several dimensions to determine their relevance to the field of study. These dimensions include similarity in population studied, determinants/interventions/indicators used, outcomes measured, and overall importance to the research question. Each study scored positively across all assessed criteria, indicating a high level of relevance.

Table 4. Relevance criteria

Article	Similarity Population	Similarity determinant/intervention/indicators	Similarity outcome	Importance
Li *et al.* (2022)[22]	+	+	+	+
Umborowati *et al.* (2022)[20]	+	+	+	+

Discussion

Atopic dermatitis can significantly impact the quality of life of affected individuals. The chronic and relapsing nature of AD has a profound effect on the quality of life of patients and their families. A study involving adolescents with mild-to-moderate AD showed that they had

a lower quality of life, as measured by the Children's Dermatology Life Quality Index.[12] Similar to other atopic disorders, the dominance of Th2 cells over Th1 cells leads to an imbalance that exacerbates the pathogenesis of AD, increases IgE, and activates interleukin (IL).[7–9]

The prevalence of this disease has increased 2 to 3 times in recent years, with adult AD ranging from 3-10%, while in children, the prevalence of AD can reach 20%.[3,4] About 60% of AD cases manifest in the first year of life. The onset of AD often occurs at the age of 3 to 6 months. The course of this disease can be continuous over a long period or recurrent.[1,2] The main complaints of AD patients may include recurring itching, dry skin, and redness. Several therapeutic approaches for AD have been implemented to support skin hydration, such as the use of emollients, allergen avoidance, and the use of antihistamines or corticosteroids during exacerbation phases. Despite these therapeutic approaches alleviating symptoms, their frequent use is often not sufficiently effective, and the recurrence rate remains high.[13]

Several dietary approaches, such as low carbohydrate, low calorie, low fat, and combinations, were related to improved quality of life. Dietary approaches may impact the patient's social interactions, personal satisfaction, economics, physical and psychological. Diet acts as a crucial supplier of nutrients that can affect the cellular microenvironment. Metabolic reprogramming, a significant characteristic linked with disease advancement, can influence both cell metabolism and immune system functionality. Various dietary approaches, such as caloric restriction (CR), fasting-mimicking diets (FMD), and ketogenic diets (KD), have the potential to alter the progression and responsiveness to the treatment of different diseases, including AD. Furthermore, these dietary approaches can modify the composition and functional abilities of the gut microbiome, thus indirectly affecting disease progression and treatment outcomes. These direct and indirect impacts of dietary approaches may affect metabolic changes, regulate immune responses, and potentially improve the effectiveness of treatments for a range of diseases.[14,15]

Numerous studies have provided information on the use of probiotics in AD, but the reported results are not consistent, especially in the adult population.[16] Probiotics have been widely used as adjuvant therapy in allergic cases with results that are still inconsistent due to the multifactorial mechanisms of allergy.[17] Probiotics are living microorganisms administered in sufficient quantities to provide health benefits to the host. Several mechanisms regarding how probiotics reduce atopy have been outlined, including shifting the Th1/Th2 balance towards Th1, inhibiting Th2 cytokines, or increasing the production of regulatory cytokines, such as IL-10, through dendritic cell maturation or its receptors.[9,10]

A systematic review conducted by *Lopez et al.*,[1] indicates that probiotics have beneficial effects on pediatric patients with AD. Oral probiotics, particularly strains of the *Lactobacillus* genus, help reduce the severity of AD.[1] A clinical trial administering a combination of oral probiotic strains to young patients with moderate AD demonstrates that this oral probiotic administration effectively reduces the SCORAD index and decreases the use of topical steroids in patients with moderate AD.[9]

In a comprehensive meta-analysis involving six randomized controlled trials with a total of 241 adult patients suffering from atopic dermatitis (AD), the administration of various probiotic strains demonstrated significant therapeutic benefits. The studies evaluated the effects of different probiotics, including *Lactobacillus plantarum* (2 × 10^10 CFU/day for 8 weeks), *Lactobacillus salivarius* (1 × 10^9 CFU/g twice daily for 16 weeks), a combination of *Lactobacillus salivarius* (LS01 DSM 2275) and *Bifidobacterium breve* (BR03 DSM 11,604) (each with a dose of 1 × 10^9 CFU/g twice daily for 12 weeks), *Lactobacillus acidophilus* (L-92) (20.7 mg/day in tablet form for 8 weeks), *Lactobacillus paracasei* (K71) (5 × 100 mg daily for 12 weeks), and *Bifidobacterium animalis subsp. lactis* (LKM 512) (6 × 10^9 CFU daily for 8 weeks). These probiotics were administered

over periods ranging from 8 to 16 weeks. The primary outcomes measured included the Scoring Atopic Dermatitis (SCORAD) index, quality of life (QoL) assessments, itch severity, skin lesion area, immunological markers such as IgE and various interleukins, and safety assessments. The meta-analysis revealed that probiotics significantly reduced the SCORAD index with a mean difference (MD) of -7.90 (95% CI -7.25 to -6.92; $p < 0.00001$; $I^2 = 96\%$) and improved the quality of life of the patients with a MD of -7.68 (95% CI -14.08 to -1.29; $p = 0.02$; $I^2 = 47\%$). These results indicate that probiotics can effectively decrease the clinical severity of AD and enhance the overall well-being of affected individuals. However, the analysis did not show significant changes in other parameters like serum IgE levels, interleukin-4 (IL-4), and tumor necrosis factor-alpha (TNF-α), suggesting that the impact of probiotics may be more pronounced on clinical symptoms rather than on underlying immunological markers. The clinical improvement in AD is determined by assessing changes in the severity of the disease.The SCORAD assessment index is used to evaluate the severity of AD by combining the extent, severity (intensity) of skin lesions (erythema, edema/papules, crusts, excoriation, lichenification, dryness), and symptomatic patient symptoms (itching, sleep disturbance) in the calculation. The higher the score, the more severe the disease experienced by the patient.[18]

Atopic dermatitis patient's quality of life assessment is performed using the Dermatology Life Quality Index (DLQI). The decrease in quality of life in AD patients is related to a decrease in sleep quality and depressive symptoms due to chronic itching, potentially affecting AD therapy. Chronic sleep quality reduction in AD patients contributes to the emergence of emotional and physical fatigue conditions that negatively impact social relationships and social sensitivity. Sleep quality is also inversely related to the severity of the disease in AD patients. The DLQI questionnaire consists of 10 questions with ratings ranging from 0, 1, 2, and 3. Improvement in quality of life is indicated by a high score, where scores 0-10 are categorized as low DLQI, while scores 11-30 are classified as high DLQI.[18,19] This questionnaire assesses six aspects: symptoms and feelings, daily activities, leisure time, work and school, personal relationships, and therapy for 7 days. Q1 evaluates itching, Q2 assesses embarrassment, Q3 assesses problems in shopping/house/garden, Q4 assesses clothing choices, Q5 evaluates social activities, Q6 assesses sports activities, Q7 discusses work/learning limitations, Q8 focuses on relationships with partners/close friends/colleagues, Q9 is related to sexual difficulties, and Q10 assesses problems arising from therapy.[19]

Prakoeswa et al.,[21] used the probiotic *Lactobacillus plantarum* IS-10506, isolated from traditional fermented buffalo milk curd in Indonesia, for administration to adults with AD. The study reported a significant increase in Foxp3 and IL-10. *Lactobacillus sp.* serves as an important adjuvant therapy for AD and plays a role in preventing AD recurrence by modulating the Th1 and Th2 cytokine profiles. Probiotics can reduce clinical symptoms by suppressing the Th2 adaptive immune response without enhancing the Th1 adaptive immune response.[20,21]

Conclusion

The systematic review and meta-analysis offer compelling evidence that probiotic supplementation can significantly enhance the quality of life (QoL) for adult patients with atopic dermatitis (AD). The critical review indicates that probiotics, such as *Lactobacillus plantarum, Lactobacillus salivarius, Bifidobacterium breve, Lactobacillus acidophilus, Lactobacillus paracasei,* and *Bifidobacterium animalis subsp. lactis*, administered over periods ranging from 8 to 16 weeks, effectively reduce the clinical severity of AD as measured by the SCORAD index. The improvements in QoL were reflected in several dimensions, including a reduction in itching, better sleep quality, and overall improvement in daily functioning and psychological well-being.

Conflict of interest

The authors declare there is no conflict of interest regarding this article.

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CASE REPORT

Vitamin D deficiency and risk of myasthenia gravis: An evidence-based case report

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Abstract

Background: An autoimmune condition known as myasthenia gravis (MG) targets the receptors for neurotransmitter acetylcholine at the neuromuscular junction, resulting in inhibition of muscle contraction. This results in muscle weakness resulting in a decrease in quality of life. Immunoregulation and muscle contractility are known to play a role in vitamin D. Literature on how vitamin D affects myasthenia gravis risk has not been widely carried out and the results are still controversial.
Objective: To evaluate the association between vitamin D and MG risk.
Methods: The search of the literature was conducted from PubMed, Cochrane Library, Embase, and EBSCOhost with the eligibility criteria determined by the authors. The literature search was using MeSH Term, text word, and title/abstract.
Results: Two articles were selected and critically appraised. The first article shows an odds ratio of 3.96 (CI95 1.26 to 12.52), which means that myasthenia gravis has vitamin D levels almost 4 times lower than healthy population. A case-control study that followed described a comparison of mean levels of vitamin D (25(OH)D) in myasthenia gravis (mean, 18.8±8.4 ng/mL) compared to healthy controls (26.3±6.1). ng/mL) ($p < 0.05$). Both studies revealed a strong interaction between MG and vitamin D inadequacy.
Conclusion: Both studies above support the theory that vitamin D deficiency is associated with the risk of developing MG.

Keywords: myasthenia gravis, vitamin D, adults, risk

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Introduction

Known as a rare disease, Myasthenia gravis (MG), research has shown that respiratory muscle exhaustion is increasing prevalence and mortality rates. Myasthenia gravis's prevalence worldwide varied from 2.17 to 32.0 per 100,000 population.[1] Department of Health United States estimates MG patients accounted for 5 to 14 for every 100,000 population from every ethnicity or gender.[2] In Indonesia, accurate data on MG prevalence was not available. However, based on 2016 research, 65 MG patients were living on Java Island.[3] Female to male ratio was estimated at around 3:1 at the age of less than 40-year-old. A similar ratio was estimated for the age of 40 – 50-year-old and puberty. But in people aged more than 50-year-old MG often occurred in males.[4]

Myasthenia gravis developed due to autoantibody bonded with acetylcholinesterase receptors on neuromuscular junction causing local and systemic muscle weakness.[5,6] Although the prevalence is not high, MG may cause severe mobility disability. If not properly managed, MG may lead to paralysis or mortality. Its chronic disease course required long-term therapy with adequate therapy management. Survivors often complained of difficulties in maintaining a good quality of life.[7] Therefore, it is important to discover the risk factor causing this disease.

Vitamin D deficiency was reported in almost every population in the world, both in terms of age and ethnicity. There are several factors associated with it, including environmental impact, habit, and lifestyle.[8] Low vitamin D is linked to a higher risk of developing a variety of illnesses. The significant health issue of vitamin D insufficiency is its great incidence. Lack of vitamin D levels causes a non-optimal immunity system, therefore, more vulnerable to several diseases.[9]

Through mechanisms in the muscle's vitamin D receptors, vitamin D controls the autoimmune response in MG and maintains muscular function.[10] The active form of vitamin D, 25(OH)D, was thought to regulate the immune system by raising the number of regulatory T-cells.[11] According to Asmark et al.,[12] the mean 25(OH)D in MG patients without supplementation was 5119 nM (range 27-96 nM), which is considerably lower than the mean of 6921 nM (range 29-133 nM) in healthy controls ($p = 0.017$). Guan et al.,[13] found that 69.8% and 23.2 %, respectively, of MG patients, had vitamin D deficiency and insufficiency. Furthermore, MG patients' vitamin D levels were found to be lower than those of healthy controls (17.366.64 vs. 22.117.28 ng/mL, p 0.001).

The author is searching for research to support the association between vitamin D deficiency and the risk of MG based on these descriptions.

Case

A 24-year-old female came to the hospital with dyspnea, worsening for 1 day before admission. For the last 3 weeks before presenting to our hospital, she complained of fever for 1 day, followed by coughing and an itchy throat. At the beginning of the disease course, there was no nausea, vomiting, diarrhea, sore throat, or dyspnea. Two weeks before coming to our hospital, her voice disappeared gradually. She also started to complain of difficulty in swallowing and dyspnea. Food intake started to decrease. She was diagnosed with dysphagia and dysphonia.

Five days before hospitalization, her complaint of difficulty in swallowing was increasing and she often spits. Dyspnea was becoming more severe and her body weakened. Her eyelids tend to drop, and difficult to open her eyes. Food intake was decreased further. At the time, she was still able to spontaneously open her eyes and followed orders. Weakness on all four extremities and cannot speak were also reported. The neurology division examined her and decided that she got impending myasthenia gravis.

On physical examination she was compos mentis, blood pressure 130/80 mmHg, pulse 88 beats/min, respiratory 32 beats/min, and temperature 37^0C. Anthropometry examination showed a body weight of 50 kg, and a height of 155 cm. Laboratory examination revealed Hb: 12.7 g/dL, leucocyte 18,000/µL, platelets 171,000 /µL, and total vitamin D 25-OH was 18.5 ng/mL. She was interested in learning how vitamin D and the prevalence of MG are related.

Methods

The literature search was done independently by 2 authors from 4 databases PubMed, Cochrane Library, Embase, and EBSCOhost. The search was performed using advanced searching on 22 March 2022 combining MesH Terms and abstracts/titles from each PICO component. Authors also used the Boolean operator "OR" to increase sensitivity and "AND" to raise specificity. Keywords used were "myasthenia gravis", "generalized myasthenia gravis", "myasthenia gravis paralytic", "myasthenic crisis", "vitamin D", "cholecalciferol", "1 alpha, 25 dihydroxy 20 epi vitamin d3". Literature obtained from those databases was screened based on inclusion and exclusion criteria. Inclusion criteria include MG patients aged >18-year-old, vitamin D deficiency as the main risk factor and MG as the main outcome in the research, articles with research design systematic review-meta-analysis, RCT, case-control, or cohort, in English, and research on the human subject.

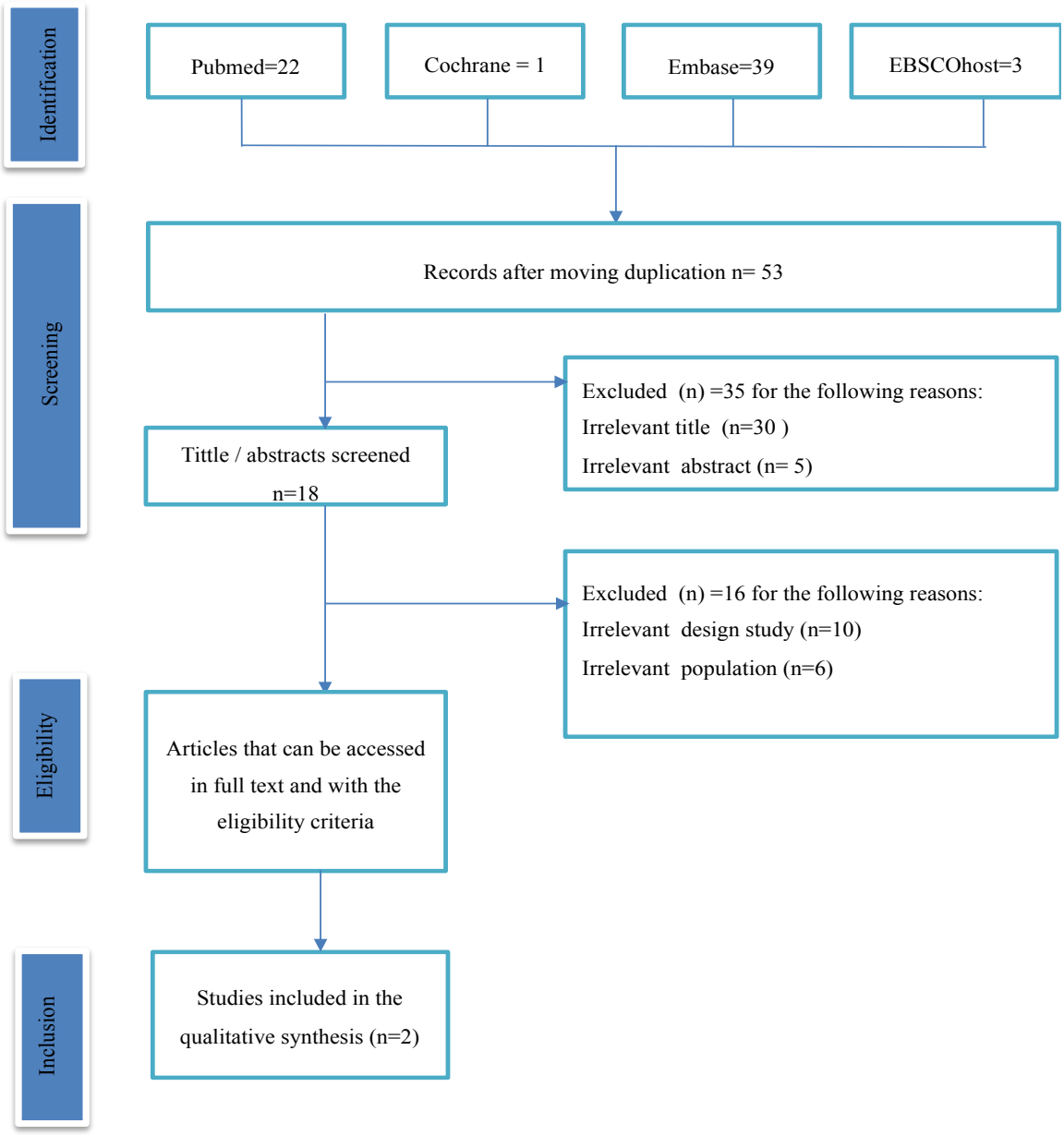

Figure 1. Prisma Flow Diagram on Literature Searching

Exclusion criteria are articles that were not available in full text, screened duplication, and availability of complete text in that literature. The literature search pathway is depicted in **Figure 1**. The critical review used in this study is based on a case-control literature guideline using the Critical Assessment Skills Programme (CASP) worksheet.

Critical appraisal was done with vitamin D deficiency as the main risk factor and myasthenia gravis as the main outcome of the research. Selection based on eligibility criteria was done to all articles available. The process was continued with critical appraisal and agreement between the 2 authors.

Result

In this study, we were able to obtain several articles: 22 from PubMed, 1 from Cochrane Library, 39 from Embase, and 3 from EBSCOhost (**Table 1**). Filtering for duplication was done with Mendeley. After that, each article was filtered based on methods, title abstract, PICO criteria, and full-text availability. The result was presented in **Figure 1**.

The research design selected in the Evidence-Based Case Report is 2 case-control studies. Literature's characteristics were displayed in **Table 2**. Moreover, both articles had a great relevance with PICO from predefined research questions (**Table 3**).

Table 1. Literature searching strategy

Database	Search Strategy		Hits
Pubmed	Search: ((((((myasthenia gravis[MeSH Terms]) OR (myasthenia gravis[Title/Abstract])) OR (Myasthenia gravis paralytica[MeSH Terms])) OR (Myasthenia gravis paralytica[Title/Abstract])) OR (generalized myasthenia gravis[MeSH Terms])) OR (generalized myasthenia gravis[Title/Abstract])) AND (((((vitamin D[Title/Abstract])) OR vitamin D[MeSH Terms]) OR (1 alpha, 25 dihydroxy 20 epi vitamin d3[MeSH Terms])) OR (1 alpha, 25 dihydroxy 20 epi vitamin d3[Title/Abstract])) Filters: Full text		22
Cochrane Library	ID		1
	#1	(Myasthenia gravis):ti,ab,kw	699
	#2	("myasthenia gravis paralytica"):ti,ab,kw	0
	#3	#1 OR #2	699
	#4	Vitamin D):ti,ab,kw	15694
	#5	#3 And #4	1
EBSCOhost	ID		3
	S1	AB myasthenia gravis OR AB myasthenia gravis paralytica OR AB myasthenic crisis	575
	S2	AB vitamin d OR AB cholecalciferol	4.104
	S3	S1 AND S2	3
Embase			39
	#1	'vitamin d'/exp	164.703
	#2	'myasthenia gravis'/exp	26.800
	#3	#1 AND #2	139
	#4	#3 AND ('cholecalciferol'/dd OR 'vitamin d'/dd) AND 'human'/de AND [adult]/lim	39

Table 2. Study characteristics

Characteristics	Justo, et al. 2021	Kang, et al. 2018
Study des	*Case-control*	*Case-Control*
Population	Patients of MG (n = 66) and healthy individuals (n = 25)	Patients of MG (n=25) and healthy individuals (n=40).
Determinant	Anti-acetylcholine receptor antibodies, complement factor C5a, and serum levels of 25(OH)D. Consumption of vitamin D and sunlight exposure.	1,25-dihydroxy vitamin D concentration [1,25(OH)2D] and 25(OH)D, a form of vitamin D.
Outcome	• Compared to 68.0 percent of the group of healthy adults, 89.4 percent of MG participants had insufficient levels of vitamin D (OR = 3.96; P = 0.024). • There was no statistically significant difference in the median serum 25(OH)D levels between the healthy group and the MG patients.	• Plasma 25(OH)D levels were lower in MG patients (18.8 8.4 ng/mL on average) than in healthy controls (26.3 6.1 ng/mL) (p 0.05). • MG patients had somewhat higher 1,25(OH)2D levels than did healthy controls. However, there was no identifiable difference between the groups.

Table 3. Relevance criteria

Authors	Similarity population	Similarity determinant	Similarity outcome	Level of evidence
Justo et al.	+	+	+	4
Kang et al.	+	+	+	4

Discussion

The literature search turned up 2 case-control studies that met the eligibility requirements. In case-control research, Justo et al.,[14] investigated the association between low vitamin D levels and a higher incidence of MG in the population of Argentina. A case-control research was also carried out by Kang et al.,[15] to examine the relationship between MG patients and vitamin D insufficiency.

The study by Justo et al.,[14] included 25 healthy controls and 66 patients with MG diagnosis. In this study, patients with chronic diseases causing severe deficiency in vitamin D were excluded. Vitamin D level was tested in all subjects using the chemiluminescence method. Research results showed an odds ratio of 3.96 (CI95 1.26–12.52) implying MG patients had vitamin D levels almost 4 times lower compared to the healthy population. A statistically significant positive link between vitamin D deficit and MG patients (p=0.024) was also established in one study, which indicated that 89.4% of MG patients and 68.0% of healthy controls had vitamin D deficiency.

The advantage of the study by Justo et al.,[14] is the author identified seasons as a confounding factor where there are 4 seasons in Argentine and vitamin D concentration also depended on sun exposure. However, statistically, no significant vitamin D fluctuation in MG patients in this research. In healthy controls, there was a change in vitamin D levels, with summer being the peak and spring being the lowest. Another advantage of this study is there was a questionnaire on vitamin D intake and sun exposure. However, one of the limitations of this study was limited patient and control, and patients were only included from 1 hospital. Based on the review, we concluded this

study has good validity and importance, however, it cannot be applied in Indonesia due to differences in season and sun exposure intensity.

Myashthenia gravis patients' mean vitamin D levels were compared to those of healthy controls in a case-control study by Kang, et al., [15] Patients with MG were shown to have lower plasma concentrations of 25(OH)D than healthy controls (18.88.4 ng/mL and 26.36.1 ng/mL, respectively, p 0.05). Myasthenia gravis patients had slightly greater 1,25(OH)2D levels than healthy controls, but there was no discernible difference between the two groups. Patients with generalized myasthenia gravis and ocular myasthenia gravis were separated. Ocular MG (50.9 28.7 ng/mL) and generalized MG (48.6 25.7 ng/mL) had similar 1,25(OH)2D levels. A similar outcome was also observed in 25(OH)D (generalized MG: 19.810.1 ng/mL; ocular MG: 17.24.9 ng/mL).[15]

Twenty-five MG patients were grouped as cases and did not consume vitamin D. Control group was gained of healthy volunteers with no medical history and no vitamin D supplementation. Vitamin D level was measured by chemiluminescence microparticle immunoassay. The blood sample was taken directly to hospital for testing. Several limitations in this study included a small number of patients, only performed in 1 hospital, and there was no odds ratio of vitamin D deficiency in case and control groups, therefore, the risk cannot be assessed.[15] Based on critical appraisal, study validity was good, however, the study result was not presented completely and cannot be applied in Indonesia due to climate differences.

According to Askmark et al.,[12] MG patients in Sweden had a vitamin D deficiency, and vitamin D therapy was linked to a reduction in muscle tiredness. This review supports their findings. In MG patients who were not receiving any supplements, the mean value of 25(OH)D was 51 19 nM (range 27 - 95 nM). With a mean value of 69 21 nM (range: 29–133 nM) and a significant difference from healthy controls (p = 0.017).

Additionally, vitamin D deficiency was found in studies of the Tiongkok community. Guan et al.,[13] found that 23.2% of MG patients had vitamin D insufficiency and that 69.8% of MG patients had a vitamin D shortage. In addition, patients with MG had lower levels of vitamin D (17.36 6.64 vs. 22.11 7.28 ng/mL, p 0.001) than healthy controls. Patients with MG may experience altered muscular function due to vitamin D's capacity to regulate adaptive immune response. The amount of vitamin D a person has varies on their race, age, sex, weight, creatinine status, color of skin, nutrition, exposure to sunlight, and use of sunscreen. As a result, vitamin D status may differ between nations.[16,17]

Vitamin D is an important nutrient needed for muscle contraction and preventing autoimmune disease. In addition to directly influencing cellular functions, vitamin D also conducts its biological effects by modulating gene expression via the vitamin D receptor. The central nervous system, Schwann cells, muscles, and peripheral neurons all express vitamin D receptors.[18] The immune system is regulated by vitamin D, which also inhibits plasma cells and B-cell activation promotes T-cell modulation and regulates T-cell reactivity, which in turn prevents an autoimmune reaction.[19]

Both studies mentioned above support the theory stating vitamin D was related to the risk of myasthenia gravis incidence. This may be the basis for testing vitamin D status in the adult population and suggesting consuming food with high vitamin D levels and adequate sun exposure.

Conclusion and recommendation

Based on this journal review, it was concluded that vitamin D deficiency was associated with MG incidence. Vitamin D deficiency may be prevented through adequate intake of high vitamin D food sources and sun exposure. Vitamin D supplementation can be given in vitamin D deficiency cases. It may be possible to do more studies using a cohort, RCT, systematic review, or meta-analysis design to examine the relationship between vitamin D insufficiency and the risk of MG.

Conflict of interest

The authors declare that there is no conflict of interest.

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ORIGINAL ARTICLE

Validity test of the Global Leadership Initiative on Malnutrition (GLIM) diagnostic criteria compared with the American Society for Parenteral and Enteral Nutrition (ASPEN) criteria in inpatients at Dr. Cipto Mangunkusumo hospital: A cross-sectional study

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Abstract

Background: Malnutrition experienced by numerous inpatients is linked to various complications. The Global Leadership Initiative on Malnutrition (GLIM), which established the latest malnutrition criteria, recommends a two-step methodology for diagnosing malnutrition in adult inpatients. This study aims to evaluate the validity of the GLIM criteria for the diagnosis of malnutrition in hospitalized patients at Cipto Mangunkusomo Hospital Jakarta by comparing them with the ASPEN criteria.

Methods: This cross-sectional study was conducted at Cipto Mangunkusomo Hospital, Jakarta. Secondary data was taken from 100 inpatients from October 2021 to February 2022 selected by consecutive sampling technique. The diagnosis of malnutrition in the patients applied the ASPEN and GLIM criteria. Furthermore, data were analyzed using Cohen's Kappa and chi-square tests.

Results: Of 100 inpatients, 63% were diagnosed with malnutrition according to the GLIM diagnostic criteria. Meanwhile, 48% of them were found to be malnourished according to the ASPEN criteria. The GLIM criteria have a specificity of 69.2%, a sensitivity of 97.9%, a PPV of 74.6%, and an NPV of 97.3%.

Conclusion: The GLIM diagnostic criteria are valid as an instrument for diagnosing malnutrition but require further research to assess the severity of malnutrition.

Keywords: Malnutrition, inpatient, diagnostic criteria of malnutrition, ASPEN, GLIM

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Introduction

According to WHO, malnutrition is a condition characterized by inadequate or excessive nutrient intake, an imbalance of critical nutrients, or poor nutrient use. The prevalence of malnutrition abroad ranges from 33-54% and between 33-70% in Indonesia.[1] Meanwhile, the prevalence of malnutrition in patients at Cipto Mangunkusomo Hospital (*Rumah Sakit Cipto Mangunkusumo*/RSCM) is 20.1% based on the WHO criteria, 42.8% based on the European Society for Clinical Nutrition and Metabolism (ESPEN) criteria, and 48.5% based on the American Society for Parenteral and Enteral Nutrition (ASPEN) criteria.[2]

The fundamental physiopathology of malnutrition involves a reduction in nutrient intake caused by anorexia (often seen in inflammatory conditions) and/or an inability to eat, although there may also be poor nutrient absorption. Inflammation is a recognized factor that leads to higher energy and protein needs. When coupled by reduced food intake, it results in an unfavorable nutritional balance and subsequent loss of fat-free mass, which is a key indicator of malnutrition. Adult malnutrition associated inpatient hospital has been linked to a higher likelihood of death, infection, hospital readmission, and various other consequences that have a financial impact on healthcare systems.[3]

Since there has been no widely approved method for diagnosing malnutrition in adults, differences in definitions of malnutrition diagnosis, patient demographics, and nutrition assessment methodologies result in substantial heterogeneity in the prevalence of malnutrition among the results of previous studies.[2–6] Currently, the diagnosis of malnutrition commonly employ criteria from ASPEN, ESPEN, and other organizations. In Indonesia itself, the National Guidelines for Malnutrition Health Services implemented though the Decree of the Minister of Health of the Republic of Indonesia adopted ASPEN's six diagnostic criteria derived from anamnesis, anthropometric assessment, and clinical examination. To diagnose malnutrition, at least two of the six criteria must be present.[3]

In 2016, the most recent criteria for the diagnosis of malnutrition on a global scale were established by representatives of major clinical nutrition groups in the world namely the Global Leadership Initiative on Malnutrition (GLIM) criteria. GLIM proposed a two-step model covering an initial screening with validated instruments for broad identification and diagnostic assessment of the patient at risk. GLIM employed a consensus method to establish operational criteria for the diagnosis of various types of malnutrition with inpatient subjects, i.e., imbalances in energy, protein, and other nutrients, based on at least one phenotypic criterion and one etiologic criterion.[7]

The GLIM diagnostic criteria are shorter and easier to classify than the ASPEN criteria, thus accelerating the diagnosis of malnutrition. Despite being the most modern diagnostic criteria established by numerous international clinical nutrition societies including ASPEN, the GLIM diagnostic criteria have not been widely used in Indonesia and GLIM-based statistics on the prevalence of malnutrition in this country are currently not available. Therefore, this study aims to examine the validity of the GLIM criteria for the diagnosis of malnutrition in adult inpatients at RSCM by comparing them with the ASPEN criteria.

Methods

Study design and population

This cross-sectional study was conducted at RSCM Jakarta, with a population of all adult inpatients at the Integrated Inpatient Service Installation, Building A, RSCM for the period of October 2021 to February 2022. The samples of this study were 100 participants who met the inclusion and exclusion criteria and were selected using a sequential sampling technique.

The inclusion criteria were aged between 18 and 60 years, treated at the Integrated Inpatient Service Installation, Building A, RSCM during the study period, and willing to participate in this study by signing an informed consent. Meanwhile, the exclusion criteria were suffering from skin diseases of the upper and lower extremities, having metal

implants or pacemakers, being in a psychiatric inpatient unit, intensive care unit or high care unit (ICU or HCU), or inpatient obstetrics and gynecology unit, experiencing burns, or being uncooperative during examination. This study has obtained research permit from Research Ethics Committee at the Faculty of Medicine, Universitas Indonesia with a research protocol KET-933/UN2.F1/ETIK/PPM.00.021/2021.

GLIM Validity Test Procedure

1) Two clinicians diagnosed malnutrition in the patients by adopting the GLIM criteria in the first diagnosis and the ASPEN criteria in the second, with an interval of one to two hours between the two diagnoses. Both clinicians did the same method for each patient.
2) Result of agreement has been trained well before the study began. The findings from both assessments were recorded, then the amount of agreement between the two evaluators was determined using Cohen's Kappa test.
3) The results of malnutrition diagnosis based on the GLIM criteria were compared with those of the ASPEN criteria in terms of sensitivity, specificity, PPV, and NPV.

Statistical analysis

The statistical analyses utilized SPSS for Windows (20th version). This study employed univariate chi-square test to evaluate patient characteristics and the k = 0 and k = 1 interpretations of Cohen's Kappa test to measure the independent variables. Data on subject parameters with normal distribution, such as sex, albumin level, and total lymphocytes, are presented as mean and standard deviation, whereas those with a distorted distribution are presented as median (minimum and maximum values). The validity of the GLIM diagnostic criteria of malnutrition was expressed in k values, and their sensitivity, specificity, positive predictive value, and negative predictive value were examined and reported as percentages in a 2 x 2 table.

Results

Among the 112 respondents who consented to having their data collected, 12 were excluded because the BIA tool did not provide access to their body composition information. Thus, 100 individuals participated in this study, 47 of whom were male and 53 were female. The age of the participants ranged from 20 to 59 years, with a median age of 44.5 years. Most of the patients (n=29, or 29%) were diagnosed with gastrointestinal, hepatobiliary, or pancreatic diseases. The characteristics of the patients and the prevalence of malnutrition are displayed in **Table 1** and **Table 2**, respectively.

Table 1. Characteristics of patients

Variable	Value
Age, median (min-max)	44.5 (20-59)
Sex	
- Female, n (%)	53 (53%)
- Male, n (%)	47 (47%)
Diagnosis, n (%)	
- Gastrointestinal tract, Hepatobiliary, Pancreas	29 (29%)
- Malignancy	21 (21%)
- Neuromuscular	15 (15%)
- ENT	14 (14%)
- Kidneys and urogenital tract	7 (7%)
- Immune and allergies	6 (6%)
- Endocrine metabolism	3 (3%)
- Cardiovascular	3 (3%)
- Teeth and mouth	2 (2%)

In this study, 48% of the total sample suffered from malnutrition based on the ASPEN diagnostic criteria, with 22 patients (45.8%) suffering from moderate malnutrition and 26 patients (54.2%) suffering from severe malnutrition. Meanwhile, 63% of the patients were severely malnourished based on the GLIM diagnostic criteria.

Table 2. Prevalence of malnutrition based on ASPEN, GLIM, Albumin, and TLC

Malnutrition criteria	Prevalence
ASPEN criteria, n (%)	
- Good nutrition	52 (52%)
- Malnutrition	48 (48%)
o Moderate malnutrition	22 (45.8%)
o Severe malnutrition	26 (54.2%)
GLIM criteria, n (%)	
- Good nutrition	37 (37%)
- Malnutrition	63 (63%)
o Severe malnutrition	63 (100%)
Albumin, n (%)	
- Mild malnutrition	14 (14%)
- Moderate malnutrition	11 (11%)
- Severe malnutrition	10 (10%)
TLC, n (%)	
- Mild malnutrition	18 (18%)
- Moderate malnutrition	9 (9%)
- Severe malnutrition	2 (2%)

Note: ASPEN = American Society for Parenteral and Enteral Nutrition; GLIM = Global Leadership Initiative on Malnutrition; TLC = Total Lymphocyte Count

Table 3. Prevalence of malnutrition by diagnosis

Diagnosis	Number of malnourished patients	Percentage (%)
GI tract, Hepatobiliary, pancreas	20	69
ENT	7	50
Teeth and mouth	1	50
Malignancy	10	47
Kidneys and urogenital tract	3	43
Endocrine metabolism	1	33
Cardiovascular	1	33
Immune and allergies	2	33
Neuromuscular	3	20
Total	**48**	**48**

Gastrointestinal, hepatobiliary, and pancreatic diseases were shown to be the most common in malnourished patients among the nine diagnoses examined in this study. As seen in **Table 3**, 20 patients (69%) of the 29 patients diagnosed with gastrointestinal, hepatobiliary, and pancreatic diseases also suffered from malnutrition.

Table 4. Degree of malnutrition based on GLIM component criteria

GLIM Criteria	n (%)
Weight loss	
- Moderate malnutrition	17 (27)
- Severe malnutrition	19 (30.2)
BMI	
- Moderate malnutrition	8 (12.7)
- Severe malnutrition	12 (19)
ALMI	
- Severe malnutrition	63 (100)

Note: GLIM = Global Leadership Initiative on Malnutrition; BMI = Body Mass Index; ALMI = Appendicular Lean Mass Index

Table 5. Cross-tabulation of ASPEN and GLIM diagnostic criteria of malnutrition

		ASPEN	
		Malnutrition	Good nutrition
GLIM	Malnutrition	47	16
	Good nutrition	1	36

Note: ASPEN = American Society for Parenteral and Enteral Nutrition; GLIM = Global Leadership Initiative on Malnutrition

According the GLIM criteria, weight loss, BMI, and ALMI determine the severity of malnutrition. **Table 4** describes the severity of malnutrition in the observed inpatients based on weight loss, BMI, and ALMI.

The GLIM diagnostic criteria have a sensitivity of 97.9%, a specificity of 69.2%, a PPV of 74.6%, and an NPV of 97.3% in detecting malnutrition, as shown in **Table 5**.

Discussion

In Southeast and East Asian countries, malnutrition is extremely common in adult inpatients [8] The elderly and those with chronic diseases such as cancer are more susceptible to malnutrition.[9] A prior study conducted in Vietnam revealed that most of the malnourished individuals in the study were women (58%) and the average age was 80.2 years (±10.2).[9] However, although female individuals are at risk for malnutrition, another previous study has found that only males were substantially associated with a greater prevalence of malnutrition (OR 10.06, CI 95%, p = 0.008).[10] Another study at Mexico shows malnourished patient vary from age 56-83 years old and has higher prevalence at post operative population. The GLIM criteria for malnutrition exhibit a link with bad short-term (in-hospital) outcomes that is dependent on both the dosage and duration of exposure. The findings were noted in individuals who had elevated levels of inflammation and reduced muscular mass.[11]

The highest prevalence of malnutrition in this study was in the gastrointestinal, hepatobiliary, and pancreatic disease group, with the highest incidence being in patients with gastrointestinal disease associated with aging. This is consistent with the age characteristic of the patients in this study (median > 40 years). In line with the results of a previous study carried out at the same hospital, acute gastrointestinal diseases, including hematemesis, melena, cholangitis, cholecystitis, and obstructive jaundice, remain the most inpatient diagnoses at RSCM during this study (48.3%).[12] Changes in the aging gastrointestinal tract are found in the mechanical disintegration of food, gastrointestinal motor functions, food transit, chemical digestion of food, and intestinal wall function. Meanwhile, the main age-related changes in the oral cavity are a decrease in bite force and the occurrence of mandibular reflexes. This is

caused by a decrease in the number of orosensory receptors which leads to increased sensory thresholds and decreased secretion of saliva, thus reducing the motor activity of the tongue and the masticatory muscles.[13]

The GLIM criteria have comparable evaluation points and parameters to those of the ASPEN criteria, but their cut-off values are different. In addition, the ASPEN criteria evaluate subcutaneous fat loss, presence or absence of fluid buildup, and functional condition of the patient, whereas the GLIM criteria do not. Therefore, the validity and reliability tests of the GLIM diagnostic criteria must be done in various sectors and sample groups.[5]

Comparatively, several previous studies have examined the validity of the GLIM criteria using different reference standards from this study. A systematic review and meta-analysis by Huo et al. indicated combined sensitivity of the GLIM criteria of 0.72 (95% CI, 0.64-0.78) and specificity of 0.82 (95% CI, 0.72-0.88).[15] Meanwhile, based on the results of the subgroup analysis (SGA), the GLIM criteria had higher diagnostic values (sensitivity of 0.81 and specificity of 0.80).[15] Another study by Balci et al. compared the GLIM criteria with SGA and NRS-2002 in the diagnosis of malnutrition and found that they had a sensitivity of 86.05% (95% CI 76.89–92.58), a specificity of 93.79% (95% CI 88.54–97.12), an PPV 89.16% (95% CI 81.28–93.96), and a NPV of 91.89% (95% CI 87–95.05).[16]

The GLIM approach for diagnosing malnutrition is more rapid than the ASPEN method as it uses fewer diagnostic criteria. In the process of establishing a diagnosis of malnutrition according to GLIM, there is a validated method for measuring muscle mass by using the Appendicular Lean Mass Index (ALMI) measured by dual-energy absorptiometry (DXA), bioelectrical impedance analysis (BIA), CT scan, or MRI.[7] Of the various reference values issued by malnutrition-related guidelines or associations to determine decreased muscle mass, the widely used ones are the normal values above 5.6 kg/m2 for women and 7.4 kg/m2 for men[17]. In this study, only 5 patients were found with ALMI values above 5 kg/m2, which were below normal values. This indicates that all samples in this study are malnourished.

The limitations of the current study include its observational design, being biased among examiner even though both examiners already trained before, conducted at a single facility, the absence of post-discharge follow-up, and the uncertainty regarding whether patients received nutritional support throughout their hospitalization. By considering all the criteria, clinicians can obtain a comprehensive understanding of malnutrition, including its causes and implications. Future studies should focus on investigating the relationship between malnutrition and nutritional interventions that take into account each criterion. This will help improve the clinical outcomes for every patient. These conclusions need to be confirmed through multicentric investigations with a larger sample size.

Conclusion

The GLIM criteria are valid for diagnosing malnutrition in patients compared to ASPEN criteria in hospital settings. Multicenter data and extrapolation analysis are needed to strengthen the validity of this study.

Limitation of study

This study is the first study ever conducted in Indonesia to compare the validity of the GLIM and ASPEN diagnostic criteria. The difficulty of blinding the evaluators limits this study to diagnosing malnutrition based on the GLIM or ASPEN criteria. Another limitation is the lack of an ALMI cut-off recommendation for the Indonesian population.

Conflict of interest

The authors declare that there is no conflict of interest.

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LITERATURE REVIEW

A review of anticaking agents in the realm of digital food printing

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Abstract

Background: Various food additives including anticaking agents have been in use since the second half of last century and digital printing of food is in practice. Concerns on food borne disease transmission following COVID-19 accelerated research in the direction of 3D printing. Objective: 3D printing of food depends on the rheological property of the dough. In addition to enhance the flow, anticaking agents which have other properties too can be exploited in 3D printing. Artificial intelligence (AI) assisted printing, targeting sustainability and customizability is in progress which needs data of food additives. The review has been done to consolidate data of the authorised anticaking agents used in food.

Methods: Using terms according to the criteria, a literature search was conducted with the data bases: Google Scholar, PubMed, ScienceDirect and Web of Science. Literature for full text analysis were selected from abstracts of 420 papers and books resulted on search, eliminating those prior to 2014, which were out of scope of the journal

Results: Consolidated literature about the anticaking agents authorised in Codex, is made discussing the deficiencies in the existing evaluation and highlighting the use of anticaking agents in 3D food printing. Promising application of the anticaking agents in AI assisted food printing has been observed.

Conclusion: This review being the first of its kind, consolidates the data of the anticaking agents including the current utility in 3D printing. It may instigate further research in this regard.

Keywords: Anticaking agents, 3D Food printing, Artificial intelligence, Ferrocyanides

Introduction

Quality of food is not easily definable as it is based on its organoleptic characteristics and nutritional value. Food additives are substances that are added to food for particular purposes to increase the shelf life and to improve the customizability. Innovation in food technology has crossed nanoencapsulation, ultra processing and has reached up to a stage of AI assisted digital printing of food.

3D printing of food (additive manufacturing) involves computer controlled material deposition such that products with definite composition and

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microstructure are formed without much human intervention. It offers the users to fabricate more customized foods, which depends on the rheological properties of the food material, printing and post printing parameters.[1] The raw material for food printing need to be in a state that allows them to be easily printed, whether it is in liquid or powder form, but should possess flowing property.[2] 4D printing refers to the change of shape, physical or chemical properties and functionality of the printed material over time in an ingredient of the food product.[3] Anticaking agents enhance the flow of the host particles by reducing the tendency to adhere to one another and hence have definitely crucial role in the properties of the material to be printed. Thisbecomes all the more true in the sintering techniques which make use of the powder deposition.[4] Further, the anticaking agents have many other characteristic properties which may find printing applications. Most essential aspect of digital food printing lies in the selection and utilization of the ingredients and their compatibility with the printing process. Artificial intelligence, with the enriched data base manages the printing process ensuring high quality, safety and personalization of the food.[5] Substances that modify acidity, viscosity, flavour, texture, mouth feel or probiotics could be added to the basic ingredients namely; carbohydrates, proteins, fats to enhance their properties and nutritional value.[6] The scope of the review is to summarize the literature about the anticaking agents listed in Codex7 highlighting their applicability in 3D printing of food and to provide insights for researchers from both the fields of food additives and digital printing of food.

Methods

A systematic review of the anticaking agents used in food industry was conducted through the online databases (Google Scholar, PubMed, Science Direct, Web of Science). The key words used were ‘Anticaking agent’, ‘Digital printing of food’ ‘AI and Food’, in general and the name of the specific anticaking agent as listed in Codex. Searches were also done using the names with synonyms wherever necessary. Relevant data from 1940s were reviewed and those within the scope of the journal are incorporated. Appropriate data up to March 2024 are included after screening the literature by title and abstract followed by full text review.

Anticaking Agents

The use of substances to prevent clumping predates written records and probably natural substances like flour might be used to prevent caking. Beyond preventing caking, the interest was to develop anticaking agents that offer additional benefits. There are 34 substances listed in the functional category of ‘anticaking agents’ in Codex including 7 exclusive anticaking agents. The rest of the compounds have more functions which consist of 16 emulsifying agents, 15 each of stabilizers and thickeners, 14 acidity regulators, 7 raising agents, 6 each of glazing agents and humectants, 5 flour treatment agents, 4 each of bulking agents and carriers, 3 each of firming agents, and colouring agents, 2 each of sweetening agents and antifoaming agents, 1 each of flavour enhancer, foaming agent and sequestrant7. An anticaking agent by technological perspective may be an anti-stick agent, drying agent or a dusting agent. Though advancement has reached up to microencapsulation for many of them, no data was available on some and hence are excluded in the review. We have discussed the anticaking agents under different groups, though not done so in Codex. All the additives are discussed with International Numbering System (INS) numbers along with Chemical Abstract Numbers (CAS). Table 1 summarises the important anticaking agents discussed in the review.

Carbonates, bicarbonate and sesquicarbona

Calcium carbonate [170(i): (CAS: 471-34-1)], sodium carbonate [500(i): (CAS: 497-18-8)] and magnesium carbonate [504(i): (CAS: 546-93-0)] are natural, hygroscopic substances with established safety profiles. Carbonates of calcium and magnesium are authorised flour treatment agents. Hickman et al[9], reported that biogenic

Table 1. Summary of the major anticaking agents discussed in the review

Anticaking agent	INS number	CAS number	Other functions*	Status in digital printing of food
Calcium carbonate	170(i)	471-34-1	Ar, C, Fa, Ft, S	White pigment in food printing ink
Sodium carbonate	500(i)	497-18-8	Ar, Ea, Ra, S,T	Altering gelation rheology and texture
Magnesium carbonate		546-93-0	Ar,C,Ft	Not used
Sodium bicarbonate	500(ii)	144-55-8	Ar,Ra,S,T	Used as smart ingredient for 4D printing
Monocalcium phosphate	341(i)	7758-23-8	Ar, Ea, Fa, Ft, H, Ra, S, Sa,T	High prospects in 3D printing
Dicalcium phosphate	341(ii)	7757-93-9	Ar, Ea, Fa, Ft, H, Ra, S,T	High prospects in 3D printing
Tricalcium phosphate	341(iii)	7758-87-4	Ar, Ea, Fa, Ft, H, Ra, S,T	High prospects in 3D printing
Hydroxypropyl distarch phosphate	1442	53124-00-8	Ea, S,T	Under research for flow property modification
Synthetic amorphous silica	551	7631-86-9	Af, Ca	Under research for preventing solidification
Calcium silicate	552	1344-95-2	Nil	Used in 3D printing as part of baking powder
Polydimethyl siloxane	900	9006-65-9	Af, Ea	No use
Cellulose	460(ii)	9004-34-6	Ba, Ca, Ea, Fa, Ga, S, T	Used as rheological modifier
Mannitol	421	69-65-8	Ba, H, St, Sw, T	Used as rheological modifier
Isomalt	953	64519-82-0	Ba, Fa, Ga, Sw, T	Used as sweetening agent
Magnesium stearate	470(iii)	557-04-0	Ea,T	Used for chocolate printing
Carnauba wax	903	8015-86-9	Ar, Ba, Ca, Ga	Used for enhancement of appearance and texture
Ferric ammonium citrate	381	1185-57-5	Nil	Used as anticaking agent for common salt which modify the viscoelastic properties of gels
Cyanides of sodium, potassium and calcium	535,536,538	14434-22-1 14459-95-1 1327-39-5	Nil	Used as anticaking agent for common salt which modify the viscoelastic properties of gels

*Af-antifoamimg agent; Ar-acidity regulator; Ba-bulking agent; Co-Colouring agent; Ca-carrier; Ea –emulsifying agent; Fa-firming agent; :Ft-flour treatment; Ga-glazing agent; H-humectants; Ra-raising agent; S-stabilizer; Sq- sequestrating agent; Sw –sweetener; T- thickener

carbonates are reported to have, sustainability and green credentials making them very prospective agents in the 3D printing of foods. Non edible food wastes containing calcium carbonate are reported as suitable ink for extrusion 3D printing. Calcium carbonate is used in the edible ink formulations as a white pigment and is also reported to reduce caking to improve the fluidity of tamarind paste at various concentrations.

Sodium carbonate, bicarbonate and the sesquicarbonate have been used as raising agents.[7-12]

The interaction between starch and gluten is affected by sodium carbonate and sodium bicarbonate with the increase of the swelling power and dough development time. The alkaline solution containing sodium carbonate and potassium carbonate named 'kansui' have been traditionally used to regulate the acidity and rheology of dough.[13-15]

In an investigation of the effect of sodium bicarbonate (baking soda) [500(ii) (CAS: 144-55-8)] on meat protein, Lizou et al.,[16] reported that it overall enhanced the processing performance of the meat. The leavening effect of it finds use in 4D printing.[17] The pH change time during mixing and bench time may be exploited in 4D printing especially for instant preparations.[3,18] 4D printed food need a smart ingredient and a stimulus ingredient which reacts to environmental stimuli, human intervention or internal stimuli. Sodium bicarbonate is a smart ingredient and is reportedto cause spontaneous change of the colour of natural powders exemplifying 4D printing.[3, 19] Carbonate and bicarbonate additives as such can be used in food only when they have low moisture content

and encapsulated carbonate based materials with a coating of lecithin, mineral or vegetable oil when the moisture is high as in cheese.[20]

Since digital printing of starchy foods is common, care is to be taken on the release of toxic acrylamide, an invariable product formed during frying and baking of starch in presence of sodium bicarbonate.[21] While using magnesium hydroxide carbonate, it is to be noted that it inactivate yeast, impart bitter taste and change the rheology of the dough badly.

The natural non marine evaporate mineral, sodium sesquicarbonate[500(iii)(CAS:533-96-0)] containing 90-95% of sodium bicarbonate, named 'trona' has been used as food tenderizer.[22]

Phosphates

Technological details of baking are out of scope of the review but involve lot of chemistry of phosphates. Phosphates have a series of excellent physicochemical properties. Phosphate additives are good acidity regulators that match pH 4-12. Further, the excellent water holding capacity, increased emulsification power, strengthening effect on protein, chelating effect on ions of copper and iron, leavening effect of the acidic phosphates, the cryoprotective power, texture development capacity, the foam stability and mineral nutritional enhancement make them versatile food additives which may find use in 3D printing.[6,18,23] Majority of packed food stuffs including baby formulae contain added phosphate.[24-25] Monocalcium monophosphate (MCP) [341(i) (CAS: 7758-23-8)] and dicalcium phosphates (DCP) [341(ii CAS: 7757-93-9] are hygroscopic white crystalline or granular powders. The hydrated form of MCP is fast acting and is used in combination with slower acting leavening agents. MCP is cited in more than hundred patented inventions disclosed on leavening agents.[26] DCP is used in combination with other phosphates and sodium bicarbonate, which require a baking time in excess of 30 min. It is used along with a faster acting raising agent where it provides last minute expansion of the cake batter. Microcrystalline form of tricalcium phosphate (TCP) [341(iii) (CAS 7758-87-4)] is thermally more stable and reacts only very slowly with water vapour or moisture during storage and hence used as an anticaking agent in dry beverage mixes. AI has been in use for whisky productionand one can expect developments towards 3D printing also in near future.[27] Food grade phosphates have been reviewed on their properties and uses.[28]

TCP has larger specific surface area and hence commonly used to bind water. Since moisture content of printing inks significantly affects the physical properties of food materials, TCP may find use in 3D printing.[29] The moisture absorption capacity of TCP is utilised in extending the shelf life of many fruit products.[30] The physical characteristics of amorphous and crystalline coconut sugar powder after the addition of TCP were studied by Nurhadi et al. TCP was found significantly to reduce water sorption of the coconut sugar powder.[31]

Starchy materials are often employed as printing inks and hydroxypropyl distarch phosphate (HDSP)[1442 (CAS: 53124-00-8)] is a prospective ingredient in digital printing. It is

insoluble in cold water and has the properties of both cross linked starch and hydroxypropyl starch with excellent shear and acid resistance and stability to heat.[32] HDSP exists in various forms and is mainly used to prevent water leakage from frozen foods and to improve stability of sauces, processed meat and dairy products. Diet rich in it is dysphagia friendly and hence satisfies the requirements for personalized food.[33] It is suggested to have beneficial implications in the treatment of obesity. Zhang et al.,[34] reported inhibitory effect of HDSP on the retrogradation properties of sterilized pea starch jelly. Very recently Xu et al.[35] reported the use of HDSP in 3D printing of ice cream inks. Phosphates in ultra processed food is suspected to cause many diseases like type 2 diabetes and chronic kidney disease.[36-37] Nutritional requirements of astronauts during long-term stay utilize fruits, vegetables, meat products and nutrients as printing ingredients but the 3D printing is still limited due to technological limitations38. The outstanding properties of phosphate may be technologically explored with due consideration to the adverse effects too.[39]

Silicon derivatives

Silica, silicates and polydimethyl siloxane(PDMS) fit in this category of anticaking agents. Synthetic amorphous silica (SAS)[551 (CAS: 7631-86-9)] is a white fluffy amorphous powder or granules consisting of agglomerated aggregates greater than 100nm. Among various forms of silica, only SAS is authorised as a food additive. It can be used according to good manufacturing practice, in large categories of foods.[40-41] Calcium silicate[552 (CAS 1344-95-2)] is a water insoluble white fine powder capable of high water and oil absorption capacity due to the porous structure and hence can compete with the host powder for existing moisture in the environment.[42] In a study on the effect of anticaking agents and relative humidity on the physical and chemical stability of powdered vitamin C using different anticaking agents in various ratios Lipasek et al.,[43] observed that calcium silicate and silicon dioxide, 50% by weight, improved the physical stability of sodium ascorbate. Calcium silicate and magnesium silicate are reported to lower free fatty acids from cooking oils.[44] Calcium silicate being a part of baking powder is being used in 3D printing of food.[8]

Polydimethylsiloxane (PDMS) [900 (CAS: 9006-65-9)] is a non nutritional, processing aid, added to oils as an antifoaming agent. The capacity of PDMS to protect oils from oxidation during deep frying operations has been studied extensively.[45] The Acceptable Daily Intake (ADI) for PDMS is not fixed even after half a century of evaluations.[46]

Carbohydrate compounds

Microcrystalline cellulose (MCC)[460 (ii) (CAS: 9004-34-6)][, powdered cellulose [460 (ii) (CAS: 9004-34-6)], mannitol[421 (CAS: 69-65-8)] and isomalt [953 (CAS: 64519-82-0)] are carbohydrate anticaking agents specified.[7] Microcrystalline cellulose and powdered cellulose are essentially the same, only slightly differing in the specifications. Cellulose without chemical modification are practically useless in 3D printing as they thermally decompose before getting melted and become flowable but surface modified MCC finds applications in 3D printing.[47-48] Various carbohydrates such as gelatine, wheat flour and starch serve as printing materials in 3D food printing.[6] MCC dietary fibres have similarity in texture to fat and have been used to prepare low fat mayonnaise emulsion with required consistency, thermal stability and improved antioxidant and flow characteristics.[49]

The carbohydrate alcohols mannitol and isomalt are ‘bulk sweeteners’ which can provide volume and mouth feel.[7] They are orally non fermentable and hence noncariogenic carbohydrate sweeteners due to the low calories.[50] Kou et al.,[51] reportedexcellent anticaking effect of mannitol compared to stearates of calcium and magnesium. Ruiz-Ojeda et al.,[52] reported that isomalt could increase the number of bifida bacteria in human gut. Isomalt absorbs very little water during storage and well suited for wafers and has stability in baking with no browning. It helps to maintain the shape and structure of the

3D printed food.[53] It is very suitable for people who are willing to make moderate life-style change in the diet and can be blend with other sweeteners to adjust the intensity of sweetness.[50,54] Isomalt is expected to be explored in research for the production of personalized food. The cooling effect in mouth and sweetness of mannitol and isomalt make them important constituents of health mints and cough drops.[6,55] While considering isomalt and mannitol for digital printing, the side effects of the sugar alcohols namely osmotic diarrhoea and bloating effect are to be considered.[56]

Salts of fatty acids and Carnauba Wax

Salts of myristic, palmitic and stearic acids with ammonia, calcium, potassium and sodium (470(i)); salts of oleic acid with calcium, potassium and sodium (470(ii)) and magnesium stearate [(470(iii) CAS:557-04-0, 91031-63-9)] are the authorised anticaking agents with other suitable printing functions, especially chocolates, which is a food material used with a certain degree of success in 3D printing.[57] Among the salts of fatty acids, magnesium stearate is in fact a mixture with magnesium palmitate has been incorporated into chocolate inks and chewing gum formulations for 3D printing.[58,59]

Carnauba wax [903 (CAS: 8015-86-9)] with an ADI 7mg/kg bw/day is used in digital printing as a coating agent and to provide glossy finish to enhance stability and viscosity.[6,60] When used in food, it is not significantly absorbed from diet and even if absorbed, would be hydrolysed and the products are incorporated in to metabolic pathways.[61] Many reports are seen about the use of carnauba wax in enhancing the shelf life of fruits.[59,62] Carnauba wax was tested for encapsulation of water-soluble compounds and as a matrix in microencapsulation of flavours.[63]

Other Anticaking agents

Out of the anticaking agents authorised in Codex, ferric ammonium citrate [381); (CAS :1185-57-5)] and ferrocyanides of sodium, potassium and calcium [535, 536 and 538)(CAS 14434-22-1, 14459-95-1,and 1327-39-5)] are not directly used in 3D printing, but used in sodium chloride which modify the viscoelastic properties of the gel.[6,2] Ferric ammonium citrate is a green powder with a faint odour of ammonia and saline ferruginous taste is authorised as an anticaking agent, nutrient, dietary supplement and acidity regulator.[7] The specifications for sodium ferrocyanide, potassium ferrocyanide, and calcium ferrocyanide have been established.[64] In the presence of ferrocyanides, sodium chloride crystals grow dendritically instead of its native cubic form and when a salt contains one or more ferrocyanide salts as anticaking agents, the term ‘ dendritic’ should be included.[7] The mechanisms of the anticaking effect of the ferrocyanide on sodium chloride were studied in details.[65] The group ADI is fixed for sodium, potassium and calcium ferrocyanide as 0.03 mg/kg/ day expressed as ferrocyanide ion on the assumption that the absorption of ferrocyanides from the gastrointestinal(GI) tract is low.[64] The use of ferrocyanides in salt is much debated.[66-67] Based on the toxicity studies done in a span of 8 decades, using bacteria, animals and humans; Joint FAO/WHO Expert Committee on Food Additives (JECFA) arrived at a conclusion that ferrocyanides are safe at the present use level.

Discussion

Changing food habits with advancing technology has brought with it thousands of approved food additives though with controversy on the use and use levels of some of them.[8] Out of different categories of additives authorised, only substances under the functional category of anticaking agents have been reviewed here focussing on the properties of them and their use in digital printing of food. Evaluation of an additive is a long procedure some of which needed decades and still resulted in confusions and difference in specifications by various regulating bodies exist.[46,64,68] A group ADI for sodium, potassium and calcium ferrocyanides is fixed, but calcium ferrocyanide was used in none of the toxicological studies though they vary widely in their action towards heat.[64] Ferrocyanides are not involved in the normal biological processes. Further, infrared

lasers employed in the sintering process in 3D printing may decompose the ferrocyanide ion and release cyanide, if not precisely controlled.

Artificially sweetened beverages, ice creams, industrial sandwiches, biscuits and cakes are the most frequently used categories of food and these contain some clusters of additives but no detailed studies are seen on the interaction between them.[69]

3D printing of food aiming at automation, customizability and sustainability in the food sector has a history of only few years thrust mainly on the most frequently used categories of food. The most important parameter in the success of 3D printing is the ingredient selection for which the physico-chemical properties of substances are to be well understood.[2] Currently carbonates, bicarbonates, stearates, carbohydrates, calcium silicate as part of baking powder, HDSP and carnauba wax are found used in 3D printing of food but only limited research literature is available on the uses of anticaking agents. Due to the multifaceted properties, phosphates seem to have of immense potential in 3D and 4D printing of food. AI has prospects in design, production, quality control and sustainability in digital printing leading to personalized foods.[27] To achieve the goal, many limitations are to be attended.

Food safety discussions on 3D printed foods are in the early stages. Rigorous safety standards are to be accepted in the printing components and printers in order to avoid contamination with bacteria that may lead to food borne diseases. Further, nutritional value of the food and the micro biome may also be affected. Intestinal micro biome plays a very important role in modulating risk of many diseases.[70, 71] The texture of printed food differs from the conventional food, indigestion, osmotic diarrhoea and blotting may result. Short term consumption can cause food poisoning, whereas use of it for long term can result in permanent changes within the body.[72] Selection and utilization of the printing materials and their compatibility with the printing process is to be thoroughly monitored.[6,21]

More data on; environmentally sustainable sourcing materials, particle size of additives, health effects due to the printed food, the effect of inorganic salts in dough properties, cause and effect relationship between consumption and effect of substances, effect of dietary components on gut microbiota and microencapsulation of additives are the bare minimum requirement of AI in 4D printing of food.[2,22,28] This together with the incorporation of bio medical data of diseases like coronary artery disease, chronic kidney disease, cancer and metabolic disorders which are common due to food additives are inevitable for successful AI assisted food printing in future.

Conclusion

Food habits often change with changes in technology. Processed food manufacture was triggered by the discovery of making bread. Later ultra processed foods entered the market on the shoulders of thousands of food additives of various categories which are merely used to improve the shelf life and palatability of food without proper health risk assessments. Anticaking agents were incorporated in to food to enhance the flow many of which have other desirable properties. A systematic review of literature about the anticaking agents authorised in Codex, is made discussing the limitations in the existing specification and highlighting the scope of them in digital printing of food.

3D printing of food which presently depends on the rheological properties has a history of only less than two decades and the food manufacture is on the way to 4D and 5D printing incorporating AI which aims at automation, sustainability, customizability and precise ingredient control. Ingredient control and automation can only be attained by feeding maximum relevant data of all categories of food additives and other desirable dietary materials. It is the first exhaustive review in this regard and may instigate further research to yield much more appreciable output. Though, no time frame can be set, AI assisted food printing can increase customizability and sustainability reducing health risks.

Conflict of interest

The authors declare that there is no conflict of interest.

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ORIGINAL ARTICLE

Lipid profile and anthropometry indices of franchised fast-food consumers in South Western states in Nigeria

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Abstract

Background: Franchised fast foods are known for their unique tastes as it contains a number of spices that makes it delicious. Daily busy schedules have made consumption of franchised fast foods (FFFs) an easy option and control of our food choices even at home.

Objective: This research investigated the lipid profile and anthropometric indices of consumers of franchised fast foods (FFFs) in South-Western States in Nigeria.

Methods: This was a cross-sectional study in South-West Nigeria and comprised three states: Lagos, Oyo, and Ogun. 300 respondents were recruited from ten (10) purposively selected fast-food outlets in Ikeja, Abeokuta and Ibadan cities, Nigeria. Standardized method for assessing plasma lipid profile was used. A well-structured and pretested questionnaire was used for the survey. The statistical analysis was done using 95% confidence interval and an error percentage of 5%.

Results: The major consumers of FFFs are single, younger adults, educated, and relatively high-income earners. Majority of male (39% and 23%) and females (33% and 41%) have excellent and good health status respectively. Significant association was observed between BMI and HDL-C ($p=0.009$) of male, and Significant differences existed among the BMI and all lipid profiles of female respondents ($p<0.050$).

Conclusion: The study conclude that both genders are at risk of age-related NCDs in the future due to inadequate physical activity and dependence on FFFs. The consumption of FFFs is common among young people, high-income earners and educated people.

Keywords: lipid profile, blood pressure, franchised fast-food, nutrition related health status

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Introduction

Fast foods are known for their unique tastes as it contains a number of spices that makes it delicious. Beyond that, many restaurants provide transport services, thereby making the food readily available for consumption. Daily busy schedules have made consumption of franchised fast foods (FFFs) an easy option to make, so much that it controls our food choices even at home. Economic objectives play a prime position in eating fast foods.[1,2] There are several reasons why human beings eat franchised fast foods (FFFs), although they are not oblivious to its dreadful outcomes on their health and family. When people consume junk foods consistently, it predisposes a person to an increased risk of cardiovascular disease, obesity and other chronic non-communicable diseases.

Fast foods have many compromising effects on health, either long term or short.[3] These foods are high in salt, fat and sugar content, and excess cholesterol level, leading to weight problems and a risk factor for many heart conditions.[4,5] Excessive salt intake especially from processed foods can deteriorate one's health including kidney impairment, if taken regularly.[1] Therefore, should be avoided as best as possible so as to enjoy full health and a happy life all through life.

Lipids are heterogeneous group of water insoluble organic molecules providing the body with the major source of energy.[6] More so, serving as carriers of fat-soluble vitamins, providing regulatory or coenzyme functions and synthesis of prostaglandins, bile salts and steroid hormones, which play a major role in maintaining body homeostasis.[7] An imbalance of lipids leads to major clinical problems.[7] A lipid profile measures total cholesterol (TC) which is sum of high-density lipoprotein cholesterol (HDLC), Low density lipoprotein cholesterol (LDLC), very low-density lipoproteins (VLDL) and triglycerides (TG).[6,7,8] Studies show that high Triglycerides (TG) often cause metabolic syndrome. Metabolic syndrome is a condition characterized by increased blood pressure, hyperglycemia, excess weight, low HDL and high TG. Excess TG are stored as fat in fat cells for later use regardless of what kind of calorie source a person eats (carbohydrate or protein).[7,10] Furthermore, cholesterol has been implicated to increase the risk of atherosclerosis, blood clots, heart attack, and stroke if present in high levels.[12] Elevated low-density lipoprotein (LDL) and cholesterol concentration are risk factors for CVD and a decrease in LDL reduces the progression of plaques, atherosclerosis and risk of heart attack and death.[7]

Hyperlipidemia is another adjustable risk factor in the etiology of CVD. Elevated lipid profile is the main contributor to the development of myocardial infarction worldwide.[7] Various authorities like United States National Cholesterol Education Program, Adult Treatment Panel III (NCEP ATP III) and the Joint European Task Force (JETF) have developed standard clinical parameters for CVD risk management.[7,11] Studies on both genders have revealed risk for atherosclerotic disease, an inverse relation to blood levels of HDL-C.[7,12] In general, the higher the HDL-C, the greater its capacity to perform its antioxidant and anti-inflammatory functions.

Problem statement and justification

Researchers suggested that approximately 25 percent (25%) of the adult population from twenty years old have high blood cholesterol levels. Initially, research focus was only on older adults of forty-five years and above because by that age, heart disease may become the leading threat for death.[7,13] Meanwhile, new compelling evidence suggests that heart disease may begin as early as two years of age, thus interventions may be needed at a younger age.[7,14] Besides, it has been reported that most children and adolescents with risk factors for heart disease are more likely to experience heart disease in adulthood. These same risk factors and predictors of heart disease commonly associated with adulthood are now being discovered in youths.

As a consequence, this research investigated the lipid profile and anthropometric indices of consumers of franchised fast foods (FFFs) in South-Western States in Nigeria.

Methods

Study area

Nigeria is made up of six geo-political zones, 36 states and Federal Capital Territory.[15] The South-West zone comprises six states (Lagos, Ekiti, Ondo, Oyo, Ogun and Osun) with an estimated population of 28 million people. The study areas are Ikeja Local Government Area in Lagos State, Abeokuta South Local Government Area in Ogun State and Ibadan the capital of Oyo State.

Study design and population

This cross-sectional study was carried out among consumers of franchised fast food (FFFs) in South-Western States in Nigeria. Respondents were recruited from ten (10) purposely selected fast-food outlets in Ikeja, Abeokuta and Ibadan cities, Nigeria.

Inclusive and exclusive criteria

Inclusive criteria:

- Respondents who were healthy.
- Respondents within the age range of 18 to 70 years old.
- Respondents without chronic illness, food allergies, dietary restriction and others stated in the exclusive criteria.

Exclusive criteria:

- Respondents with chronic illness, food allergies, on dietary restriction.
- Respondents on recreational medication that can affect the weight.
- Respondents who did not consent to partake in the study.

Sample size determination

Minimum sample size was calculated using the formula below:

$$N = \frac{Z^2 \times (p \times q)}{d^2}$$

Where,

N = the minimum sample size

Z^2= the standard normal deviate corresponding to a level of significance of 0.05 is 1.96

p = Prevalence of overweight in Nigeria is 26%.

q = 1-p (i.e. 0.74)

d = the desired precision: 5%

Applying the formula, the minimum sample size is:

$$N = \frac{(1.96)^2 \times (0.26 \times 0.74)}{(0.05)^2}$$

$$N = 295$$

Adjusted sample size was calculated for 15% attrition rate using:

$$\text{Adjusted Sample Size} = \frac{\text{Minimum Sample Size}}{\text{(1-Attrition rate)}}$$

$$\text{Adjusted Sample Size} = \frac{295}{(1-0.15)} = 347.06$$

Therefore, the adjusted sample size, considering a 15% attrition rate is approximately 347 to compensate for non-response rate for the purpose of this study. However, data was only computed for 300 respondents.

Sampling techniques

A multi-stage sampling procedure was used. First stage included random selection of three (3) states (Lagos, Oyo and Ogun) in South-West. In the second stage, the state capital (Ikeja, Ibadan and Abeokuta) were purposely selected. In the third stage, thirty-four (34) registered FFFs outlets in Lagos, twenty-seven (27) in Ibadan and thirteen (13) in Abeokuta and ten (10) FFFs centers were purposely selected. These ten selected FFFs outlets were divided in ratio 5:3:2 respectively.[16] The total number of FFFs outlets in each state capital was divided by Total number of FFFs outlets in the three (3) state capitals and multiplied by sample size. Final stage was a simple random sampling technique to draw the sample for the purpose of the study.

Data collection procedure

Data was collected from 10 food outlets. One hundred respondents were randomly selected from the three selected state capitals. A well-structured and pretested questionnaire was prepared for the survey. Consent was obtained from the consumers of FFFs after the purpose of the study had been explained and thereby, interviewed them directly. The questionnaire was used to collect data on the socio-economic and demographic characteristics of the respondents such as age, marital status, employment status, educational level and average household income. Assessment for lipid profile and anthropometric measurements for weight, height, and 4-site skinfold thickness for body fat percentage was conducted by trained personnels. Anthropometric measurements were conducted using standard procedures by trained personnels.[17,18] Measurements included: height using a stadiometer, weight using a weighing balance, body mass index (BMI) by dividing weight by square of height, and waist and hip using a non-stretchable measuring tape. All measurements were taken twice using standard procedures by trained personnels.

Body fat measurement (4-site skinfold thickness for body fat percentage)[19,20]

Biceps skinfold (front side middle upper arm), Triceps skinfold (back side middle upper arm), Subscapular skinfold (under the lowest point of the shoulder blade) and suprailiac skinfold (above the upper bone of hip) were estimated for total body fat. The sum of the measurements is inputted in a formula called the DURNIN formula.

- Body Density: 1.1620-0.0630 log (SF)
- The body fat % is calculated from: % Body Fat = 495/BD-450

Biochemical assays – extraction

Collection of blood sample

Venipuncture method was used, a cubital vein using a 20-gauge needle (diameter: 0.9 mm e.g., butterfly system maximum tubing length of 6cm). Tourniquet that was used was removed in less than one minute to avoid error due to hemoconcentration. After venipuncture, plasma is obtained by centrifugation for 10 minutes at 2000 x g at room temperature. The resulting plasma sample was transferred for biochemical assay for lipid profile analysis.

Isolation of high-density lipoproteins (HDL)[21]

HDL was isolated according to the method of Gidez *et al*., after precipitating very low-density lipoprotein (VLDL) and low-density lipoprotein (LDL) with heparin – manganese chloride solution.[22] An aliquot of heparin – manganese chloride solution was vortexed and left to stand at room temperature for 10 minutes, centrifuged at 4000 rpm for 10 minutes. The clear supernatant was removed into clean Eppendorf tubes, the precipitated (VLDL + LDL) returned to the first plasma volume taken with 0.1M phosphate buffer pH 7.4 and stored at – 2^{o}C until analysis.

Isolation of low-density lipoprotein (LDL) and very low-density lipoprotein (VLDL)[23]

The plasma LDL/VLDL fraction was separated using the Ononogbu and Lewis technique, which was precipitated with different concentrations of sodium dodecyl sulfate (SDS). 0.075ml of 100/0 SDS in 0.15 M sodium chloride was added to Iml of plasma in an Eppendorf tube, thoroughly mixed, and the tube was kept at 35^{0}C in bath water for 2 hours. A high-speed bench centrifuge was used to separate precipitated VLDL at 10,000rpm for 10 minutes at room temperature. Using a syringe, the SDS-soluble fraction was extracted, and the sides of the tube were thoroughly flushed with 0.5ml of 0.10/0 SDS in 0.15M sodium chloride to avoid washing off the precipitate.[23] The precipitated VLDL was dissolved in Iml of 1% SDS in 0.15M sodium chloride after centrifugation and stored at 20^{0}C until analysis.

Determination of plasma cholesterol[24]

This was determined spectrophotometrically according to the method of Allain et al. The reagent

was made with three enzymes: cholesterol esterase (Ce), cholesterol oxidase (CO) and peroxidase (POD); and two substrates 4 – amino antipyrine (4 – AA) and phenol.[23] A red dye quinoneimine dye was formed of which the intensity was proportional to the cholesterol concentration.

Determination of HDL cholesterol[21]

This was determined in the HDL-C fraction as described in the Isolation of HDL-C substituting HDL for plasma in the assay according to the method of Gidez *et al*.

Determination of LDL/VLDL cholesterol

0.l ml of VLDL and LDL extract was evaporated to dryness at 60^0C, alongside the standard cholesterol extract and the blank. Dried extracts were dissolved in cholesterol reagents as estimated. Cholesterol was calculated thus:
LDL cholesterol (mg/dl) = TC - HDL-C –TG/5
TC = Total cholesterol
HDL-C = High density lipoprotein cholesterol
TG = Triglycerides

Determination of plasma triglyceride[25]

This was determined spectrophotometrically according to Buccolo & David, using a diagnostic kit based on enzymatic hydrolysis of plasma triglycerides to glycerol and free fatty acids (FFA) by lipoprotein lipase (LPL). The H_2O_2 concentration was determined through the Trinder's reaction which results in a red color dye. The intensity of the color formed was proportional to the triglyceride concentration in the sample.
This questionnaire was structured and adapted from previous questionnaires. Secondary data for this study were collected from different websites, portals, textbooks and published articles.

Data analysis

The data collected from the respondents were analyzed using the statistical software, Microsoft Excel 2016, and IBM SPSS (Statistical Product and Service Solutions) version 25.0. Descriptive statistics (mean, standard deviation, frequency, percentages) and inferential statistics (chi-square and independent t test) were done. The statistical analysis was done using 95% confidence interval and an error percentage of 5%. Statistically the level of significance is set at $p<0.05$.

Results

Socio-demographic and economic characteristics

Table 1 presented the socio-demographic and economic characteristics of the respondents. Of the total 300 selected populations, 56.7% were female and 43.3% were male. The majority (39.3%) belong to the age group 25-37. The mean and standard deviation age of the study population is 33.42±10.66. The ethnicity distribution of the study population shows that the Southwest region represents a mix of diverse cultures of Nigeria. From the total population, the majority (70.5%) were Yoruba, and from Lagos state (36.9%). Most (46.3%) of the respondents had university education, and more than half (54.4%) never married. Half (50%) of the study population have an average household income of ₦500,000 thousand naira and more.

Anthropometric indices for male

Table 2 described the anthropometric indices of the male population which had a mean and standard deviation of 100 ± 16 for mean arterial pressure. Body mass index (BMI) results show that the majority (80%) of the male respondents were beyond normal weight. The male population has a mean and standard deviation of 31.70±06.68 for BMI. More than half of the respondents had a high risk of developing cardiovascular diseases with a significantly high borderline result (63.1%) of waist-hip-ratio, and the majority of the study population (94.8%) had excess body fat percentage. The male population has a mean and standard deviation of 1.01±0.05 and 36±6 for waist-to-hip ratio and body fat percentage respectively.

Table 1. Socio demographic and economic status of the respondents

Socio demographic and economic variables	Frequency	Valid percentage (%)
Sex		
Male	130	43.3
Female	170	56.7
Total	**300**	**100.0**
Age		
18-25	86	28.7
26-39	116	38.7
40-59	72	24.0
60-69	26	8.6
Total	**300**	**100.0**
Level of education		
Primary School	10	3.3
Secondary School	72	24.0
First Degree	138	46.0
Post-Graduate degree	72	24.0
Preferred not to state	8	2.7
Total	**300**	**100.0**
Location		
Ogun State	106	35.4
Oyo State	82	27.3
Lagos State	112	37.3
Total	**300**	**100.0**
Marital status		
Never Married	162	54.0
Married	106	35.2
Separated	14	4.7
Divorced	2	0.7
Widowed	8	2.7
Cohabiting	6	2.0
Preferred not to state	2	0.7
Total	**300**	**100.0**
Work status		
Government Employee	76	25.3
Private Sector	58	19.3
Self Employed	46	15.3
Homemaker	112	37.3
Unemployed	2	0.7
Preferred not to state	6	2.0
Total	**300**	**100.0**
Ethnicity		
Igbo	72	24.0
Hausa	14	4.7
Yoruba	206	68.6
Refuse to state	8	2.7
Total	**300**	**100.0**
Average monthly household income		
₦10,000-150,000	70	23.3
₦151,000-250,000	42	14.0
₦251,000-500,000	36	12.0
More than ₦500,000	150	50.0
Preferred not to state	2	0.7
Total	**300**	**100.0**

NOTE: *All total frequency that is less than 300 is due to non-responses of the respondents.*

Table 2. Anthropometric indices for male

Variable	Frequency	Percentage	$\underline{x}$±S.D
Body mass index			
Normal weight	26	20.0	**31.70 ± 06.68**
Overweight	36	27.7	
Grade i obesity	38	29.2	
Grade ii obesity	18	13.8	
Morbid obesity	12	9.2	
Total	**130**	**100.0**	
Waist-to-hip ratio (male)			
Low risk	16	12.3	**1.01 ± 0.05**
Moderate risk	32	24.6	
High risk	82	63.1	
Total	**130**	**100**	
Body fat percentage			
Below average/athletes	0	0	**36 ± 60**
General fitness	0	0	
Moderate/acceptable	6	4.6	
Obese/excessive fat	110	84.6	
Refuse	14	10.8	
Total	120	100.0	

$\underline{x}$±*sd* (mean±standard deviation)

Plasma lipid profile of male respondents

Table 3 revealed the plasma lipid profile of the study population. Majority (33.8%) of the male respondents were at the borderline of high TC in the blood. Majority (44.6%) had acceptable plasma levels of HDL-C while more than average (53.8%) had desirable plasma levels of LDL-C. Few (13.8%) of the respondents were classified to have high plasma levels of high-density lipoprotein and even less (3.1%) had very high LDL-C making them at risk of cardiovascular disease. Table 4 also shows that more than half of the population (83.1%) had normal TG results. The male population has a mean and standard deviation of 172±38, 57±22, 102±37, and 113±33 for TC, HDL-C, LDL-C and TG.

Anthropometric indices of female respondents

Table 4 showed the BMI of the female respondents. Result shows that the majority (35.3%) of the female respondents were overweight. 91.8% had high risk of developing cardiovascular diseases with a significantly high borderline result of waist-hip-ratio. More than half (61.1%) of the female population had an excess body fat percentage. The female population has a mean and standard deviation of 29.31±06.05, 0.94±0.06 and 30±7 for body mass index, waist-to-hip ratio and body fat percentage respectively.

Plasma lipid profile of female respondents

Table 5 showed the Plasma lipid profile for female respondents including the TC, LDL-C, HDL-C and TG. The percentage of the TC shows that 4.9% has desirable blood cholesterol, 42.0% being the highest blood cholesterol above desirable, 33.3% were at the borderline of having high TC in their blood, 11.1% had high blood cholesterol, and 8.6% blood cholesterol was very high. Majority (46.9%) had acceptable HDL-C. The table also shows that most of the population (91.8%) had normal TG results. The female population has a mean and standard deviation of 167±31, 58±15, 98±37, and 107±55 for TC, HDL-C, LDL-C and TG.

Table 3. Plasma lipid profile of male respondents

Plasma lipid	Frequency	Percentage	$\underline{x} \pm s.d$
Total Cholesterol			
Desirable	4	6.2	***172 ± 38***
Above desirable	21	32.3	
Borderline high	22	33.8	
High	10	15.4	
Very high	8	12.3	
Total	**65**	**100**	
High Density Lipoprotein			
Desirable (high)	27	41.5	***57 ± 22***
Acceptable	29	44.6	
Low	9	13.8	
Total	**65**	**100**	
Low Density Lipoprotein			
Desirable	35	53.8	***102 ± 37***
Above desirable	18	27.7	
Borderline high	5	7.7	
High	5	7.7	
Very high	2	3.1	
Total	**65**	**100**	
Triglyceride			
Normal	54	83.1	***113 ± 33***
Borderline high	11	16.9	
Total	**65**	**100**	

$\underline{x} \pm s.d$ (mean±standard deviation)

Table 4. Anthropometric indices of female respondents

Variable	Frequency	Percentage	$\underline{x} \pm s.d$
Body mass index			
Normal weight	34	20.0	***29.31 ± 06.05***
Overweight	60	35.3	
Grade I obesity	42	24.7	
Grade II obesity	26	15.3	
Morbid obesity	8	4.7	
Total	**170**	**100.0**	
Waist-to-hip ratio (female)			
Low risk	2	1.2	***0.94 ± 0.06***
Moderate risk	12	7.1	
High risk	156	91.8	
Total	**170**	**100**	
Body fat percentage			
Below average/athletes	2	1.4	***30.00 ± 07.00***
General fitness	18	12.5	
Moderate/acceptable	36	25.0	
Obese/excessive fat	88	61.1	
Total	**144**	**100.0**	

$\underline{x} \pm s.d$ (mean±standard deviation)

Table 5. Plasma lipid profile of female respondents

Plasma lipid	Frequency	Percentage	$\underline{x} \pm s.d$
Total Cholesterol			
Desirable	4	4.9	***167 ± 31***
Above desirable	34	42.0	
Borderline high	27	33.3	
High	9	11.1	
Very high	7	8.6	
Total	**81**	**100**	
High Density Lipoprotein			
Desirable (high)	38	46.9	***58 ± 15***
Acceptable	31	38.3	
Low	12	14.8	
Total	**81**	**100**	
Low Density Lipoprotein			
Desirable	49	60.5	***98 ± 37***
Above desirable	20	24.7	
Borderline high	4	4.9	
High	7	8.6	
Very high	1	1.2	
Total	**81**	**100**	
Triglyceride			
Normal	73	91.3	***107 ± 55***
Borderline high	7	8.8	
Total	**80**	**100**	

$\underline{x} \pm s.d$ (mean±standard deviation)

Association between body mass index (BMI), and plasma lipid profile among respondents

Table 6 revealed the association between BMI and plasma lipid profile for male respondents. A significant association was observed between BMI and HDL-C ($p=0.009$), while significant association was not observed between the BMI and TC, LDL-C and TG ($p>0.05$).

Association between BMI with plasma lipid profile among the female respondents

From the study carried out, **Table 7** revealed the significant differences that existed among the BMI and all plasma lipid profile tests that were carried out on female respondents ($p\leq0.05$).

Discussion

There is an increasing burden of non-communicable disease in Africa, including South-Western parts of Nigeria where this recent study was conducted.[26] This study demography mirrors the study population of Uthman-Akinhanmi on nutrient composition of selected snacks in South-West Nigeria. The mean and standard deviation of this study reveal most of the population that patronized franchised fast food are youths (33.42 ± 10.66), unmarried (54.4%) and people with higher income.

The majority of the respondents in this study were obese (52.2%) followed by overweight (27.7%).[27] This ascertained that increase in body weight is directly linked with excessive calorie intake and lack of physical exercise.[28] In contrast to Dsouza & Dsouza, obesity was more predominant in female respondents than male but in the study, it was revealed that the body mass index of both genders were beyond normal weight, in that majority (80%) of the respondents, both male and female are either overweight or obese.

Table 6. Association between BMI and plasma lipid profile among male respondents

Body mass index	**TC**						
	Desirable	**Above desirable**	**Borderline high**	**High**	**Very high**	**Total**	**p.Value**
Normal weight	2 (3.1)	7 (10.8)	2(3.1)	0(0.0)	2(3.1)	13(20.2).	0.250
Overweight	1(1.5)	7(10.8)	6(9.2)	2(3.1)	2(3.1)	18(27.7)	
Grade 1 obesity	1(1.5)	4(6.2)	10(15.4)	3(4.6)	1(1.5)	19(29.2)	
Grade 2 obesity	0(0.0)	1(1.5)	2(3.1)	4(6.2)	2(3.1)	9(13.8)	
Total	4(6.2)	21(32.3)	22(33.8)	10(15.4)	8(12.3)	65(100.0)	
	LDL-C						
	Desirable	**Above desirable**	**Borderline high**	**High**	**Very high**	**Total**	**p.Value**
Normal weight	9(13.8)	2(3.1)	0(0.0)	1(1.5)	1(1.5)	13(20.0)	0.141
Overweight	12(18.5)	3(4.6)	2(3.1)	1(1.5)	0(0.0)	18(27.7)	
Grade 1 obesity	9(13.8)	8(12.3)	1(1.5)	1(1.5)	0(0.0)	19(29.2)	
Grade 2 obesity	1(1.5)	4(6.2)	2(3.1)	2(3.1)	0(0.0)	9(13.8)	
Morbid obesity	4(6.2)	1(1.5)	0(0.0)	0(0.0)	1(1.5)	6(9.2)	
Total	35(53.8)	18(27.7)	5(7.7)	5(7.7)	2(3.1)	65(100.0)	
	HDL-C					**TG**			
	Desirable (high)	**Acceptable**	**Low**	**Total**	**p-Value**	**Normal**	**Borderline high**	**Total**	**p.Value**
Normal weight	8(12.3)	2(3.1)	3(4.6)	13(20.0)	*0.009	11(16.9)	2(3.1)	13(20)	0.772
Overweight	12(18.5)	6(9.2)	0(0.0)	18(27.7)		16(24.6)	2 (3.1)	18(27.7)	
Grade 1 obesity	4(6.2)	12(18.5)	3(4.6)	19(29.2)		16(24.6)	3(3.1)	19(27.7)	
Grade 2 obesity	0(0.0)	7(10.8)	2(3.1)	9(13.8)		7(10.8)	2(3.1)	9(13.8)	
Morbid obesity	3(4.6)	2(3.1)	1(1.5)	6(9.2)		4(6.2)	2(3.1)	6(6.2)	
Total	27(41.5)	29(44.6)	9(13.8)	65(100.0)		54(83.1)	11(16.9)	65(100)	

Values with asterisk (*) are statistically significant.

Table 7. Association between BMI, with plasma lipid profile among the female respondents

			TC				
Body mass index	**Desirable**	**Above desirable**	**Borderline high**	**High**	**Very high**	**Total**	**p.Value**
Normal weight	1(1.2)	10(12.3)	3(3.7)	0(0.0)	1(1.2)	15(18.5)	0.019
Overweight	1(1.2)	15(18.5)	10(12.3)	1(1.2)	2(2.5)	29(35.8)	
Grade 1 obesity	1(1.2)	6(7.4)	8(9.9)	3(3.7)	2(2.5)	20(24.7)	
Grade 2 obesity	1(1.2)	2(2.5)	5(6.2)	5(6.2)	0(0.0)	13(16.0)	
Morbid obesity	0(0.0)	1(1.2)	1(1.2)	0(0.0)	2(2.5)	4(4.9)	
Total	4(4.9)	34(42.0)	27(33.3)	9(11.1)	7(8.6)	81(100.0)	
			LDL-C				
	Desirable	**Above desirable**	**Borderline high**	**High**	**Very high**	**Total**	**p.Value**
Normal weight	11(13.6)	3(3.7)	0(0.0)	1(1.2)	0(0.0)	15(18.5)	*0.005
Overweight	23(28.4)	3(3.7)	1(1.2)	2(2.5)	0(0.0)	29(35.8)	
Grade 1 obesity	9(11.1)	6(7.4)	1(1.2)	3(3.7)	1(1.2)	20(24.7)	
Grade 2 obesity	5(6.2)	7(8.6)	0(0.0)	1(1.2)	0(0.0)	13(16.0)	
Morbid obesity	1(1.2)	1(1.2)	2(2.5)	0(0.0)	0(0.0)	4(4.9)	
Total	49(60.5)	20(24.7)	4(4.9)	7(8.6)	1(1.2)	81(100.0)	
		HDL-C				TG			
	Desirable	**Acceptable**	**Low**	**Total**	**p-Value**	**Normal**	**Borderline high**	**Total**	**p.Value**
Normal weight	10(12.3)	4(4.9)	1(1.2)	15(18.5)	0.025	15(18.8)	0(0.0)	15(18.8)	0.025
Overweight	15(18.5)	12(14.8)	2(2.5)	29(35.8)		26(32.5)	2(2.5)	28(35.0)	
Grade 1 obesity	8(9.9)	9(11.1)	3(3.7)	20(24.7)		19(23.8)	1(1.2)	20(25.0)	
Grade 2 obesity	4(4.9)	6(7.4)	3(3.7)	13(16.0)		11(13.8)	2(2.5)	13(16.2)	
Morbid obesity	1(1.2)	0(0.0)	3(3.7)	4(4.9)		2(2.5)	2(2.5)	4(5.0)	
Total	38(46.9)	31(38.3)	12(14.8)	81(100.0)		73(91.2)	7(8.8)	80(100.0)	

Values with asterisk (*) are statistically significant

According to WHO standard for measurement of waist to hip circumference, it was revealed in this study that 91.8% and 63.1% of the female and male respondents respectively, had high risk of developing cardiovascular diseases with a significantly high borderline result of waist-hip-ratio.[29]

Mohammadbeigi *et al.*, study confirms this in that fast food consumption was associated with abdominal obesity based on WHR, but not related to general obesity based on BMI.[30,31]

FFFs are rich in salt, saturated fats and added sugar which in turn implicates the nutritional health status of people negatively. The health status rating revealed that 41.3% and 29.0% of the female and male respondents were reported to have very good ratings.[32] Since fast food consumption has increased dramatically from the early 1970s its impact on social health status has also increased. From the percentage plasma cholesterol, triglyceride, HDL-C and LDL-C of the respondents from this study, there is a possible risk factor for non-communicable diseases (NCDs) in the near future if nutritional and lifestyle changes are not put in place. This is because the majority of the study participants are younger adults, university graduates and high-income earners (see **Table 1**),[33] and based on previous studies, the major risk factors of NCDs include dyslipidemia, obesity, physical inactivity, and poor to dietary practices among others.[31,33]

The association of a high fat intake with obesity and heart disease is well known and may contribute to the burden of obesity and non-communicable diseases.[34] According to WHO report, more than five (5) out of every ten (10) deaths in developing countries occur due to NCDs, accounting for 80% of the global burden of diseases. Most of these deaths occur in persons less than 70 years old.

It can be deduced from this study that foods that contain saturated fats can cause an increase in plasma cholesterol level. FFFs have been associated with high fat, salt, added sugar and very low dietary fiber that are abundant in fruits and vegetables.[31] Nutritional analysis shows that fast foods are generally high in fat, especially saturated fats, energy dense, high in fructose and glycemic index, but poor in fiber, vitamins A and C, and mineral calcium. About 62% and 54% of the male and female respondents respectively fall in between borderline to very high plasma level for TC.[31] This finding agrees with the previous study that shows that the cholesterol, and LDL-C increases with increased consumption of FFFs in a week, such that within a year the plasma level of total cholesterol LDL-C, TG are increased.

This study validates the effect of FFFs on the plasma lipid level and nutritional status of the consumers as there is significant difference in the association between body mass index (BMI) and HDL-C. Aside that, it revealed a significant association between body mass index and high-density lipoprotein ($p=0.009$) (see **Table 6 and 7**).[3] This finding however is in contrast with the findings of Nascimento *et al*., which reported obesity as associated with TG and LDL-C with decreased HDL-C.[3]

Dyslipidemia that has been associated with obesity are elevated triglycerides (TGs), LDL-C and decreased HDL-C levels.[35,36] As evidence suggests, high HDL-C and LDL-C levels are associated with longevity in that low HDL-C level is associated with an increased cardiovascular risk, particularly if cholesterol and TGs are also elevated.

From this present study, a significant difference existed among the body mass index and all plasma lipid profile tests that were carried out on female respondents ($p<0.050$). TC, TG, LDL-C and HDL-C were significantly associated with BMI (refer to **Table 6 and 7**).[37] This finding is in line with numerous studies that have concluded that the poor nutritional value, the excessive salt, saturated fats and trans fatty acid are associated with FFFs and are likely to perpetuate the prevalence of hypercholesterolemia, hypertriglyceridemia and with low plasma level in HDL-C.[35] Hypercholesterolemia has been associated with cardiovascular disease (CVD). Similarly, formation of atherosclerotic plaque has been linked with the elevation of non-high density lipoprotein cholesterol.

The mean of plasma lipid for male respondents are [TC-167, HDL-C-58, LDL-C-98 and Tg-107 (mg/d)] while the mean for the female respondents is [TC-172, HDL-C-57, LDL-C-102 and Tg-113

(mg/dl)].[38] Increase in cholesterol levels can be caused by eating fast food on a regular basis. This finding also confirms that foods that contain saturated fat can cause a relative increase in cholesterol. It has been well proven and established in previous studies that FFFs are rich in saturated fat, and they are mostly found in animal-based food products such as cheese, milk, butter and steak.[35,39] It has also been discovered that some plant-based foods, such as palm oil and coconut oil, contain saturated fats. Trans Fats, or trans-fatty acids, have undergone a hydrogenation process. Some trans fats are found in animal and plant products such as peanut butter, margarine, and potato chips.[35,40] Fast foods, although delicious, have been proven to be dangerous to the health of its consumers and may cause arteriosclerosis, hypertension, high blood pressure, diabetes, cholesterol, cancer, gallbladder disease, and liver damage. This cross-sectional study does not assess the factors influencing the consumption of FFFs by participants. This limitation should be noted in understanding the inference of this study.

Conclusion

This study focused on the lipid profile and anthropometric indices of consumers of franchised fast foods (FFFs) in South-Western Nigeria. Our findings revealed that the major consumers of FFFs are single, younger adults, educated, and relatively high-income earners. Significant participants have good health status but a higher percentage from both genders are at risk of age-related NCDs in the future due to inadequate physical activity and dependence on FFFs. To address the public health implications of FFF consumption, it is recommended to implement targeted nutrition and health education programs to promote healthier dietary choices and increase public awareness. Additionally, fostering community-based physical activity initiatives and ensuring the availability of healthier food options in fast food outlets are essential steps to mitigate future risks of age-related NCDs. Further research is needed to explore the factors influencing FFF consumption and to design effective preventive strategies against diet-related non-communicable diseases that might results from consumption of FFF.

Conflict of interest

The authors declare that there is no conflict of interest.

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ORIGINAL ARTICLE

Relation between nutrition intake, prediabetes, and central obesity with handgrip strength in Indonesian medical student

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Abstract

Background: Muscles are crucial in creating movement, stabilising body posture, and regulating body temperature. Muscle strength can be assessed using handgrip strength. Handgrip strength can predict muscle function, nutritional status, diabetes risk, and the risk of metabolic syndrome. Handgrip strength can be influenced by muscle mass, nutritional intake, fat mass, physical activity level, and metabolic syndrome.
Objective: This research is to find relationship between handgrip strength and nutritional intake, muscle mass, and central obesity.
Methods: The research was conducted as a cross-sectional study using observational analytical methods. The sample consisted of 53 individuals selected through purposive sampling. Handgrip strength can be measured using a hand dynamometer, nutritional intake using a 2x24 hour food recall, muscle mass using a body composition analyzer, central obesity using waist to hip ratio, and fasting blood sugar using a glucometer. Statistical data analysis employed the chi-square test and independent T-test.
Results: The results indicated a relationship between central obesity and handgrip strength ($p = 0.006$). Researchers are interested in studying muscle strength and its predictors concerning central obesity, prediabetes, and nutritional status in medical students. The results indicated a relationship between handgrip strength and central obesity ($p = 0.006$), but no relationship was found between handgrip strength and energy intake ($p = 0.235$), protein intake ($p = 0.524$), and prediabetes ($p = 0.272$).
Conclusion: There is a relationship between central obesity and handgrip strength. Future researchers are encouraged to consider additional factors, including physical activity, muscle mass index, and comorbidities.

Keywords: handgrip strength, energy intake, protein intake, central obesity, prediabetes

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Introduction

Muscles facilitate movement, stabilise body posture, and regulate body temperature. All muscle tissue in the body is called muscle mass.[1] If muscle mass increases, muscle strength also tends to increase.[2] Likewise, if muscle mass decreases, muscle strength will also decrease.[3] Muscle mass is influenced by an individual's nutritional intake and lifestyle, with the availability of nutrients affecting the muscle's ability to contract.

Adequate protein intake is vital in muscle synthesis.[4] On the other hand, excess energy intake, particularly from foods high in calories and low in nutrients, will increase the triglycerides, thereby increasing the incidence of metabolic syndrome.[5, 6]

According to the International Diabetes Federation (IDF), some metabolic syndrome symptoms are central obesity and increased fasting blood sugar levels.[7] In Indonesia, the prevalence of obesity and diabetes mellitus continues to increase.[8] Central obesity is a condition where fat accumulates in the middle of the stomach (intra-abdominal fat) (Lestari et al., 2021). The diagnosis of central obesity is made if waist to hip ratio ≥0.95 in men, or ≥80 in women. Central obesity triggers a pro-inflammatory state caused by cytokine release, resulting in a decrease in muscle strength, muscle function, and muscle mass.[9]

Indonesian National Health Survey 2018 shows that the proportion of impaired fasting blood sugar (fasting blood sugar = 100-125 mg/dL) in the population aged >15 years is 26.3%[8]. Increasing blood sugar levels can have a negative impact on muscle health, causing a decrease in muscle mass so that muscle strength will also decrease.[10,11] Muscle strength can be measured using the handgrip strength method.[12]

Handgrip strength is a method for measuring muscle strength and function.[12] Handgrip strength can be influenced by several factors, for example, muscle mass, nutritional intake, body mass index, metabolic syndrome, fat mass, age, and physical activity level.[13–16] Previous research has demonstrated that handgrip strength can predict muscle function, nutritional status, and several diseases, such as the risk of diabetes, the risk of metabolic syndrome, and even a person's mortality.[17–19]

Medical students have high academic demands. The time spent on average used for studying and completing assignments makes it difficult to engage in physical activities.[20,21] This can decrease muscle function due to infrequent use.[22] Additionally, a hectic schedule and numerous course assignments cause students to neglect meals, reducing the frequency and quantity of meals, which can impact nutritional intake.[23]

Convenience in accessing sweet and fatty foods, along with strong media influence in promoting these foods, can trigger the formation of unbalanced eating habits. This leads to a tendency to consume high-calorie but low-protein foods.[23] All these risk factors collectively contribute to decreased muscle strength, central obesity, and prediabetes. Previous research indicates a prevalence of metabolic syndrome in adolescents at 15.8%,[24] prompting researchers to explore the relationship between central obesity, prediabetes, nutritional intake, and handgrip strength.

Previous research has had a narrower scope, focusing on specific diseases with elderly and adult respondents. The planned study targets adolescents, an area with limited current research. Additionally, research on handgrip strength and the chosen independent variables –nutritional intake, fasting blood sugar, and central obesity – is still very limited, especially in Indonesia. Therefore, researchers are interested in studying muscle strength and its predictors concerning central obesity, prediabetes, and nutritional status in medical students. With this research, it is hoped that it can increase public knowledge about central obesity, prediabetes, muscle strength, and the importance of maintaining diet to improve lifestyle and prevent disease as early as possible.

Methods

The research followed a quantitative approach with observational analytical methods, employing a cross-sectional design. The data analysis employs the Chi-Square test and independent T-test. The chosen significance level for the p-value is 0.05.

The sample consisted of medical students from Universitas Pembangunan Nasional Veteran Jakarta (UPNVJ), selected using the purposive sampling method. Sample size estimation with two proportions and the minimum sample is 46. Sampling involved distributing questionnaires to the population and selecting samples that met the inclusion and exclusion criteria. Inclusion criteria for this study were individuals aged 18-24 years with a body mass index of more than 23 kg/m^2. BMI around 23- 24,9 with Asian Pacific classification is categorized as overweight thereby the risk of cardiovascular disease is increase. The selection of BMI ≥ 23 it is hoped that it will include respondents with metabolic syndrome. Exclusion criteria included those with a history of upper extremity injuries, deformities of the hands and fingers, neurological and motor disorders, arthritis, and chronic diseases. The research took place at UPNVJ's Pondok Labu and Limo campuses over three months, from October 2023 to December 2023.

Data collection involved measuring handgrip strength using a hand dynamometer, specifically a mechanical/Smedley type with the Camry Hand Dynamometer brand. The result will be categorized into 2 groups, low (< 35,7kg in men and <19,2 in women) and normal (35,7- 56,6 kg in men and 19,2- 35,3 in women).

Energy and protein intake measurements were obtained through interviews between nutritionists and respondents, recorded on the 2x24-hour Food Recall to document all food and drink consumed within two 24-hour periods, one on a weekday and one on a weekend taken by. The data was analyzed in Nutrisurvey application. Protein intake is divided into 2 groups, low (<0.8 g/kg) and normal (≥0,8 g/kg). Meanwhile, energy intake divided into 3 groups based on Indonesian Dietary Recommendation, low (<80%), normal (80-110%), and high (>110%).

Central obesity was measured using the waist-to-hip ratio. The diagnosis of central obesity is made if waist to hip ratio ≥0.95 in men, or ≥80 in women. Prediabetes was determined based on fasting blood sugar using a glucometer with the Easy Touch GCU brand. If glucose fasting level ≥100 mg/dL, it is categorized as a prediabetes condition. Before the examination, respondents were required to fast for at least 8 hours.

Results

Data collection took place in October - December 2023 at the Faculty of Medicine, UPN "Veteran" Jakarta, involving 53 respondents. Among the respondents, there were nine males (16.9%) and 44 females (83.1%). The age range of the respondents was 18 to 22 years, with the most common age being 20 years. All respondents had a BMI >23 kg/m^2 with 19 people (35.8%) in the overweight category, 21 people (39.6%) classified as grade 1 obesity, and 13 people (24.5%) classified as grade 2 obesity (**Table 1**).

In the distribution of handgrip strength among medical students at UPNVJ, the majority, 30 respondents (56.6%), had normal handgrip strength. Meanwhile, 23 respondents (43.4%) had low handgrip strength, and none had high handgrip strength. The average handgrip strength obtained in this study was 24.5 kg, with the highest value of 46.6 kg and the lowest value of 10.4 kg.

Energy intake is divided into three categories: excessive, sufficient, and insufficient. A total of 13 respondents (24.5%) were in the excessive energy intake category, 22 respondents (41.5%) had sufficient energy intake, and 18 respondents (34%) had insufficient energy intake. The average energy intake was 1,917 kcal, with a maximum value of 13,180 kcal and a minimum of 1,007 kcal.

Protein intake is divided into two categories: normal and low. Most respondents had sufficient protein intake (69.8%), while the remaining 30.2% had low protein intake. The average protein intake was 63.4 grams, with a maximum value of 156.9 grams and a minimum of 32.6 grams.

The average waist circumference of female respondents was 84.3 cm, and for male respondents, it was 82.7 cm. Meanwhile, the average waist-to-hip ratio for female respondents was 0.82, and for male respondents, it was 0.87. Thirty-four respondents (64.2%) did not have central obesity, while 19 (35.8%) had central obesity.

A total of 45 respondents (84.9%) had normal fasting blood glucose, while 8 respondents (15.1%)

had increased fasting blood glucose or could be said to be in prediabetes. The mean fasting blood glucose in this study was 87.3 mg/dL, with a minimum value of 64 mg/dL and a maximum of 108 mg/dL. When prediabetes condition is adjusted for nutritional status, the prediabetes in the overweight group is 37.5%, in the degree 1 obesity group is 25%, and in the degree 2 obesity group is 37.5%.

The group with sufficient energy intake showed a 20.8% distribution for both normal and low handgrip strength. Meanwhile, groups with higher and lower energy intake demonstrated a relatively even distribution of handgrip strength, except for the group with lower energy intake, which exhibited lower handgrip strength with a percentage of 5.7%. The chi-square test analysis resulted in a p-value of 0.235 ($p > 0.05$), signifying no statistically significant relationship between energy intake and handgrip strength. (**Table 2**)

The group with sufficient protein intake and normal handgrip strength constituted 41.5%. Conversely, the group with insufficient protein intake displayed equal percentages for low and normal handgrip strength, both at 15.1%.

Table 1. Characteristics of the respondents

Characteristics	n	%
Sex		
Male	9	16.9
Female	44	83
Age		
18 years	2	3.7
19 years	13	24.5
20 years	18	33.96
21 years	17	32
22 years	3	5.6
BMI		
Overweight	19	35.8
Obesity grade 1	21	39.6
Obesity grade 2	13	24.5
Handgrip Strength		
Normal	30	56.6
Low	23	43.4
Protein Intake		
Normal	37	69.8
Low	16	30.2
Energy Intake		
Excess	13	24.5
Sufficient	22	41.5
Insufficient	18	34
Fasting Blood Glucose		
Normal	45	84.9
Increase	8	15.1
Central Obesity		
No	34	64.2
Yes	19	35.8

Table 2. Bivariate analysis result (Chi Square test)

Characteristics	Handgrip strength				p- value
	Normal		Low		
	n	%	n	%	
Protein Intake					
Normal	22	41.5	15	28.3	0.524
Low	8	15.1	8	15.1	
Energy Intake					
High	10	18.9	3	17	0.235
Normal	11	20.8	11	20.8	
Low	9	17	9	5.7	
Prediabetes					
No	27	50.9	18	34	0.272
Yes	3	5.7	5	9.4	
Central Obesity					
No	24	45.3	10	18.9	0.006
Yes	6	11.3	13	24.5	

The chi-square test analysis yielded a p-value of 0.524 (p>0.05), indicating no statistically significant relationship between protein intake and handgrip strength.

The group without central obesity and normal handgrip strength accounted for 45.3%. On the other hand, the central obesity group with low handgrip strength constituted 24.5%. The chi-square test analysis resulted in a p-value of 0.006 (p<0.05), suggesting a statistically significant relationship between central obesity status and handgrip strength.

More than half of the respondents were represented in the group without prediabetes condition and normal handgrip strength (50.9%). The group with prediabetes conditions and low handgrip strength had a percentage of 9.4%. The group with the lowest percentage was the prediabetes group with normal handgrip strength, at 5.7%. Due to the expected count value being 50% (>20%) with a value of less than 5, the chi-square test requirements were not met. Therefore, the Fisher exact test was employed as an alternative to the chi-square test. The obtained p-value was 0.272 (p>0.05), signifying no statistically significant relationship between prediabetes and handgrip strength.

Discussion

Energy intake and handgrip strength

Bivariate analysis showed that the p-value obtained was 0.235 (p>0.05), concluding no relationship between energy intake and handgrip strength. These findings align with a study conducted by Lisnawati,[29] indicating no correlation between energy intake and handgrip strength in junior high school children, with a p-value of 0.770. In contrast, research conducted on teenagers in Malaysia demonstrated a positive relationship and correlation between energy intake and handgrip strength.[25]

Energy restriction may occur in respondents with low energy intake and low handgrip strength, leading to a decrease in protein synthesis. Especially when energy intake is insufficient for the body's physiological functions, muscles may undergo catabolism to provide energy, ultimately reducing muscle strength.[26] Additionally, inadequate energy intake results in low energy availability and insufficient for proper muscle contractions.[27] This theory is supported by research on children and adolescents with poor nutritional intake and insufficient energy intake, leading to decreased handgrip strength.[28] Therefore, ensuring adequate energy intake is crucial to enable protein to enhance muscle formation and strength.[25]

Protein intake and handgrip strength

Bivariate analysis showed a p-value of 0.524 (p>0.005), so it can be concluded that there is no significant relationship between protein intake and

handgrip strength. These findings align with a study conducted by Lisnawati,[29] demonstrating no correlation between protein intake and handgrip strength in junior high school children, with a p-value of 0.663. Similarly, Andarbeni's [29] research found no relationship between protein intake and handgrip strength in adolescent girls aged 12-15 years (p=0.074). However, this contrasts with a study conducted by Fitriani [23], which states that late adolescents with low handgrip strength correlate with less protein intake (p=0.0).

Increased protein intake is associated with increased muscle mass, resulting in muscle strength. However, it is crucial to balance increased protein intake with sufficient energy intake to impact muscle mass positively.[29] The results of this study may be linked to the quality of the protein intake consumed. Animal and vegetable proteins have different capacities for increasing muscle mass and strength. Empirical studies indicate that consuming at least 25 grams of high-quality protein (8-10 grams of essential amino acids and high in leucine) can enhance muscle protein synthesis and improve muscle strength.[25] Notably, this study did not consider muscle quality, which could be influenced by the type of protein consumed (animal/vegetable protein), potentially as a contributing factor. Furthermore, muscle strength is not only influenced by energy intake but also by nutritional status, physical activity, body fat percentage,[23] and hand anthropometry.[30]

Central obesity and handgrip strength

This study identified a relationship between central obesity and handgrip strength with a p-value of 0.006 ($p<0.05$). These findings align with research conducted in Chile involving subjects from adolescents to the elderly, demonstrating a correlation between central obesity and handgrip strength.[32] The decline in handgrip strength observed in individuals with central obesity is attributed to excessive adiposity, which hinders the regulation of testosterone, growth hormone, and insulin, leading to a reduction in muscle mass and function. Moreover, excessive adiposity can induce a pro-inflammatory state through the release of cytokines such as TNF-α and IL-6, further contributing to a decrease in muscle strength.[33]

According to research, elevated adipose tissue from a young age can negatively impact muscle performance, even with an increase in muscle mass. Conditions of central obesity trigger inflammation and insulin resistance, affecting muscle function.[32] Previous studies have indicated that excessive adipose tissue induces a pro-inflammatory state mediated by cytokines (tumour necrosis factor-alpha and interleukin-6). Elevated plasma cytokine levels are associated with a decrease in muscle strength, function, and mass.[9]

Prediabetes and handgrip strength

In this study, a p-value of 0.272 was obtained, indicating no significant relation between prediabetes and handgrip strength. This finding aligns with research conducted by Astrom on adult respondents, which showed no association between prediabetes and low handgrip strength.[34] However, this study contradicts research conducted in Korea, which asserted a negative relationship between handgrip strength and fasting blood sugar.[35] Another study on Korean adults indicates a negative relationship between prediabetes and handgrip strength in men but not in women.[17]

According to research by Astrom et al.,[34] individuals with diabetes, whether newly diagnosed or with a long-standing diagnosis, tend to exhibit lower handgrip strength compared to those with normal blood sugar levels. This is attributed to an accelerated decrease in skeletal muscle mass and increased intramuscular fat infiltration in individuals with diabetes. Not only does muscle strength decrease, but insulin resistance also worsens due to the suboptimal functioning of skeletal muscle tissue as a site for glucose absorption. Furthermore, chronic hyperglycemia can lead to the accumulation of advanced glycosylation end products (AGEs) in skeletal muscles, resulting in decreased handgrip strength, leg extension strength, and walking speed. In this study, none of the respondents was diagnosed with diabetes, so the AGEs might not have fully accumulated. However, individuals in the early stages of impaired glucose regulation,

such as prediabetes, may not experience a significant decline in grip strength.[34] Prediabetes conditions can still be addressed through lifestyle changes, including nutritional intake and exercise[36]

Conclusion

Based on research that has been conducted, a relationship was found between central obesity and handgrip strength. Central obesity conditions can reduce handgrip strength. Meanwhile, no associations were found between energy intake, protein intake and prediabetes with handgrip strength. The limitation of this study is that there is the possibility of flat slope syndrome. Flat slope syndrome is the tendency of underweight respondents to report consuming more food, while respondents who are overweight tend to report consuming less food. In addition, other variables such as physical activity, muscle quality, BMI, fat mass, and comorbidities that could influence hand grip strength were not studied. Other researchers conducting related research are expected to consider other factors, such as physical activity, muscle quality and comorbidities.

Conflict of interest

The authors declare that there is no conflict of interest.

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ORIGINAL ARTICLE

High blood pressure is correlated with anthropometric status in adults in Gribig district, Central Java, Indonesia

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Abstract

Background: More than 17 million deaths worldwide are caused by cardiovascular disease due to high blood pressure. According to the World Health Organization (WHO), around 1.3 billion adults will have high blood pressure in 2021. Obesity is a significant factor influencing blood pressure. Waist circumference measurements and body mass index (BMI) can be used to identify obesity issues.
Objective: The aim was to analyze the correlation between BMI, waist circumference, and blood pressure among adults at Primary Health Care in Kudus, Central Java, Indonesia.
Methods: This cross-sectional study evaluated BMI, waist circumference, blood pressure, and questionnaire. Men and women aged 18-59 (healthcare staff, patient caregivers, and patients) who agreed to become study subjects were included. Participants with a history of diseases, current conditions, medication intake that affects blood pressure, and pregnancy were excluded. Samples were taken using purposive sampling and the Pearson test as a statistical analysis.
Results: The analysis showed a significant correlation between the BMI of patients with systolic blood pressure (p=0.000) and diastolic blood pressure (p=0.000). A moderate relationship was found between BMI and systolic blood pressure(r=0.473) and diastolic blood pressure (r=0.439). Moreover, waist circumference was significantly correlated with systolic blood pressure (p=0.000) and diastolic blood pressure (p=0.000).
Conclusion: A significant correlation exists between BMI and waist circumference with blood pressure among adults at the Primary Health Care in Kudus, Central Java, Indonesia.

Keywords: Body mass index, waist circumference, blood pressure

Introduction

High blood pressure is a significant risk factor for cardiovascular disease that caused more than 17 million deaths globally in 2019.1 In 2021, the World Health Organization (WHO) stated that nearly 1.3 billion adults experienced high blood pressure. It was estimated that 46% of them were unaware of this condition.2 High blood pressure also plays some roles that may cause an economic burden on the health system both in a country and society.3 The increase in the economic burden is often the result of complications of high blood pressure, and it occurs in several countries, including Indonesia.[4,5]

In 2018, the Result of Nasional Basic Health Research (*Riskesdas*) showed that there was an increase in the prevalence of high blood pressure in Indonesian adults aged 18 years and over; it was from 25.8% in 2013 to 34.1% in 2018.[6] Based on Central Java's health profile in 2019, high blood pressure became one of the top priorities for non-infectious disease control in Central Java with the most significant proportion, which was 68.6%.[7] In 2021, the Health Service Report of Kudus Regency showed that cases of high blood pressure in Kudus Regency had the highest number compared to other non-infectious diseases, which was more than 200 thousand people.[8]

Factors that affect changes in blood pressure are divided into unmodifiable and modifiable factors.[1] Obesity is a factor that can be modified. It may affect blood pressure since it is assumed to underlie the mechanisms of altered secretion in adipose tissue. One of the most frequent examinations that are used to detect obesity is the measurement of body mass index (BMI). BMI measures a person's level of adiposity or body fat accumulation.[9] However, BMI cannot differentiate between body fat and lean muscle mass and does not discriminate the central fat or visceral fat distribution information.[10] Therefore, other measurements are needed to complete the BMI measurement, which is the measurement of waist circumference.[11] Waist circumference shows the accumulation of visceral fat, in which, when it is excessive, it may be associated with the accumulation of ectopic fat, or retroperitoneal fat in particular.[12]

A prospective cohort study of more than 4 thousand individuals in China shows that the emergence of the overweight condition at a younger age is associated with increased hypertension risk.[13] Research on adolescents in Indonesia also shows that obesity is a risk factor for prehypertension among them.[14] Treatment for hypertension must be the government's priority to prevent and control non-communicable diseases from an early age. One of the health service facilities that prioritize promotive and preventive efforts is a community health center (*Puskesmas*).[15] Therefore, preventive efforts in health centers in the form of early detection, control of modifiable risk factors, and changes in healthy lifestyle can reduce the risk of hypertension and prevent the disease from becoming more severe. This study aims to analyze the relationship between body mass index and waist circumference with adult blood pressure at the Gribig Health Center, Kudus Regency.

Methods

Study designs and participants

This research is an observational analytic study with a cross-sectional approach. The study measured the research subject's height, weight, waist circumference, and blood pressure and distributed questionnaires containing subject characteristics. The sample calculation utilized the formula developed by Sastroasmoro.[16] The minimum correlation considered significant is based on previous research17. A minimum sample of 65 subjects is idealized, assuming a significance level of 5% and a confidence interval of 95%. The population of this study were men and women aged 18-59 years at the Gribig Health Center, Kudus Regency. Ninety-two people became research subjects. The sample was collected using a purposive sampling technique. Written informed consent was obtained from all study subjects, and research protocols were approved by the Research Ethics Committee Faculty of Medicine and Health (Medical and Health Research Ethics Committee). Faculty of Medicine, Public Health and Nursing, Gadjah Mada University, Yogyakarta, with the number KE/FK/1676/EC/2022.

The study included men and women aged 18-59 who were either health center staff, patient escorts, or registered patients at the Gribig Health Center in Kudus District. They were willing to become research subjects by filling out informed consent. Exclusion criteria included respondents with a history of diabetes, cardiovascular disease, kidney disease, thyroid disorders, obstructive sleep apnea, sleeping less than <6 hours before measurement, taking medications that affect blood pressure (thiazide diuretics, Angiotensin Converting Enzyme Inhibitors (ACEI), Calcium Channel Blockers (CCB), Angiotensin Receptor Blockers

(ARB), pseudoephedrine), and in the pregnant state.

Measurements

Blood pressure is measured at the brachial artery in the right arm in the supine position using a digital sphygmomanometer (YuWell YE680), and it is recorded as systolic blood pressure to diastolic blood pressure. The accuracy maintained in this research uses a new unit digital sphygmomanometer and is charged using a new battery. Also, the unit has been validated. Prior to blood pressure measurement, the subject should rest for at least 5 minutes, should not consume caffeine, should not smoke, and should not do sports activities for at least 30 minutes before measurement, not in the condition of holding back urination and defecation. Measure blood pressure using an appropriate cuff to the circumference of the subject's upper arm. Subjects must be seated back in a chair, arms arranged at heart level, and feet touching the floor. Blood pressure is measured twice at 1-2 minutes. Then the average is taken. Additional measurements are made if the results of the first and second measurements are different with the range of >10 mmHg.

Body mass index (BMI) is calculated from the formula of a person's weight in kilograms divided by the square of the height in meters. BMI measurement consists of body weight and height. In measuring body weight, the subject must remove his shoes and jacket, put down his bag, and remove the contents. The subject then climbs onto a digital scale (OneMed Digital Bathroom Scale EF812) in a static state, upright, with the view facing forward and the position of the feet in the middle of the weighing machine. Weight is recorded up to 1 digit after the decimal point. Measurement is performed two times, and then the average is taken. The third measurement is carried out if the difference between the two measurements is >0.2 kg. The subject should remove the footwear and cover the head at the height measurement. The subject stands upright, feet together, hands by side with palms facing the thigh, and looks straight ahead. Back of the head and shoulders, heels, and butt against the wall to which the microtoise (GEA) is attached. Microtoise horizontal iron is pulled and then pressed until it touches the crown of the head. Height is recorded up to 1 decimal place. Repeat the measurement two times and then take the average. The third measurement is taken if the difference is >0.5 cm.

Waist circumference is measured at the midpoint between the lower border of the XII costal arch and the crest iliac using a measuring tape (OneMed Waist Ruler OD 235). Measurements are taken at the end of the normal expiration in an upright standing position with parallel feet. Measurements are conducted twice, and then the average is taken. The third measurement is taken if the difference between the two measurements is> 1 cm.

Data Analysis

Data analysis is performed using the Statistical Analysis Software Package for software Windows (SPSS) version 25. Descriptive statistics such as median, mean, and standard deviation are then analyzed to evaluate the mean of systolic blood pressure, diastolic blood pressure, BMI, waist circumference, and age of the participants. Whole variables are tested for data normality. The normality of the data distribution in this study was analyzed using a Kolmogorov-Smirnov test, resulting in a p-value greater than 0.05. Therefore, the data distribution is considered normal. Bivariate analysis was conducted using the Pearson correlation test to investigate the relationship between blood pressure, BMI, and waist circumference. Correlation is deemed significant if the p-value is less than 0.05.

Results

This study had 92 participants aged 18-59, categorized into early (26-35 years) and late adulthood (36-45 years).[18] Based on Table 1, the average of respondents aged 36-45 years as many 29 people (31.5%), and respondents aged 36-45 years as many 16 (17.4%). Respondents comprised 64 women (69.6%) and 28 men (30.4%). Most of their jobs are private, consisting of private employees, civil servant employees (PNS),

entrepreneurs, and laborers, as many as 47 people (51.1%). Most of their educational background is High School graduates, as many as 32 people (34.8%). Those who are married are 70 people (76%). This study found that of the research subjects, 14 people (15.2%) are smokers, and the remaining 78 do not smoke (84.8%). In this study, no research subjects consume alcohol (0%). As many as 27 of the 92 study subjects have a family history of hypertension (29.3%) (**Table 1**).

The average BMI of the research subjects was 24.47 kg/m2. The average waist circumference (WC) is 84.16 cm. The average systolic blood pressure (SBP) is 129.33 mmHg. The average diastolic blood pressure (DBP) is 79.56 mmHg (**Table 1**).

The analysis of the relationship between BMI and systolic blood pressure obtains a p-value of 0.000 ($p < 0.05$), indicating a significant correlation between BMI and systolic blood pressure. A correlation strength (r) of 0.473 indicates a positive correlation between BMI and systolic blood pressure with moderate correlation strength. The correlation between BMI and diastolic blood pressure is also considered significant, as indicated by a p-value of 0.000 ($p<0.05$). The correlation value of 0.439 also shows a positive correlation between BMI and diastolic blood pressure with moderate correlation strength (**Table 2**).

The analysis of the relationship between waist circumference and systolic blood pressure obtains a p-value of 0.000 ($p<0.05$), indicating a significant correlation between waist circumference and systolic blood pressure. The correlation value 0.659 indicates a positive correlation between waist circumference and systolic blood pressure with a muscular correlation strength. The correlation between waist circumference and diastolic blood pressure is also considered significant, as indicated by a p-value of 0.000 ($p<0.05$). The correlation value obtained was 0.588, which showed a positive correlation between waist circumference and diastolic blood pressure with moderate correlation strength (**Table 2**).

Discussion

This study found a significant correlation (p=0.000) between BMI and systolic blood pressure in the study subjects at the Gribig Health Center, Kudus District, with moderate correlation strength (r=0.473). Likewise, a significant correlation (p=0.000) is found between BMI and diastolic blood pressure in the study subjects at the Gribig Health Center, Kudus Regency, with moderate correlation strength (r=0.439). A positive correlation is found between BMI and systolic and diastolic blood pressure. The results of this study mean that the higher the BMI, the higher the blood pressure. The results of this study align with those of other studies conducted by Linderman et al. This study shows a positive relationship between BMI and blood pressure.[19] Research conducted by Saguaro et al shows that BMI positively correlates with systolic and diastolic blood pressure (r=0.336 and r=0.344, respectively).[17]

Based on the results of data analysis between BMI and systolic and diastolic blood pressure, the correlation's strength is considered moderate. This result is caused by several factors, including an increase in BMI, which may result from an imbalance between diet and activity or is influenced by genetics.[20] Increased BMI, through the mechanism of the sympathetic nervous system pathway, the renin-angiotensin system, and vascular inflammation can affect and even increase blood pressure.[21]

This study gives different results from the research conducted by Khalid et al. The study states that BMI negatively correlates with men's systolic and diastolic blood pressure. There is no significant correlation in women concluding that BMI does not affect blood pressure. The study by Khalid et al used respondents with high blood pressure, while this study used respondents who both suffered from high blood pressure and did not. The different research results are also caused by differences in the number of respondents, in which the study used 337 adult respondents consisting of 52.2% male and 47.8% female. This study uses 92 respondents, 30.4% male and 69.6% female.[22]

Table 1. Sociodemographic and clinical characteristics of research subjects

Characteristics	Total (N= 92)
Age, median (min-max)	35 (18-59)
26-35, n (%)	29 (31.5)
36-45, n (%)	16 (17.4)
Sex, n (%)	
Male	28 (30.4)
Female	64 (69.6)
Occupation, n (%)	
Unemployed	19 (20.7)
Students	9 (9.8)
Civil servant employees	17 (18.5)
Private employees	47 (51.1)
Education, n (%)	
Elementary	14 (15.2)
Junior high school	17 (18.5)
Senior high school	32 (34,8)
Diploma (D3)	10 (10.9)
Bachelor (S1)	19 (20.7)
Master's degree (S2/S3)	0
Marital status, n (%)	
Married	70 (76)
Single	22 (24)
Smoker, n (%)	
Yes	14 (15.2)
No	78 (84.8)
Alcoholic, n (%)	
Yes	0
No	92 (100)
Hypertension history, n (%)	
Yes	27 (29.3)
No	65 (70.7)
Clinical characteristics	
BMI, mean (SD), kg/m^2	24.47 (4.77)
WC, mean (SD), cm	84.16 (11.37)
SBP, mean (SD), mmHg	129.33 (20.77)
DBP, mean (SD), mmHg	79.56 (13.24)

Source: *Primary Data in Gribig Health Center year 2022*
SD: Standard Deviation.

Table 2. The correlation between BMI and waist circumference and blood pressure

	SBP		DBP	
	r	p	r	p
BMI	0.473	0.000	0.439	0.000
Waist Circumference	0.659	0.000	0.588	0.000

This study reports a strong correlation (r=0.659, p=0.000) between waist circumference and systolic blood pressure in the study subjects at Gribig Health Center in Kudus Regency. The correlation between waist circumference and diastolic blood pressure in study subjects at the Gribig Health Center, Kudus Regency, is also significant (p=0.000) with moderate correlation strength (r=0.588). The relationship between waist circumference and systolic and diastolic blood pressure in this study is positively correlated, and it is found that the correlation between waist circumference and systolic blood pressure is stronger than the correlation with diastolic blood pressure. The positive correlation between waist circumference and blood pressure indicates that the

higher the waist circumference, the higher the blood pressure.

This study found results similar to those of a study conducted in Nepal by Chaudhary et al. The study shows a clear relationship between waist circumference and systolic and diastolic blood pressure. The correlation between waist circumference and systolic blood pressure is positive and significant, and the same applies to the correlation between waist circumference and diastolic blood pressure.[23] The correlation of systolic blood pressure is also found to be stronger for waist circumference than diastolic blood pressure. These results are also supported by previous research conducted by Fu, et al. The study shows that waist circumference positively correlates with systolic and diastolic blood pressure, especially in men. This result is because men are more often associated with smoking, consuming alcohol, and doing less physical activity, which affects the increase in waist circumference.[24]

This research has several limitations. First, there is inequality in the participation of men and women, where women are far more dominant. The study design only uses cross-sectional data, meaning a causal relationship between BMI, waist circumference, and blood pressure cannot be established. Third, time constraints mean this study only takes a small portion of the population as a sample. Fourth, regarding blood pressure, this study is limited to only examining BMI and waist circumference variables. Therefore, further research is needed on factors outside this study that affect blood pressure, such as diet, salt intake, stress, and genetics. In addition, future research should use a larger sample size and other research designs that can explain the causal relationship between BMI, waist circumference, and blood pressure.

Conclusion

This study establishes a significant relationship between body mass index (BMI) and waist circumference with blood pressure among adolescents in the Gribig Health Center, Kudus Regency.

Conflict of interest

The authors declare that no conflict of interest with another person or institution.

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ORIGINAL ARTICLE

Development of a sports nutrition knowledge questionnaire for elite track and field athletes

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Abstract

Background: Satisfactory nutrition knowledge among athletes is important to encourage proper dietary habits to overcome deficiencies and enhance sports performance. Identifying knowledge gaps in sports nutrition is essential for improving athletes' understanding through a tool that evaluates both general nutrition knowledge (GNK) and sports nutrition knowledge (SNK).

Objective: This study aims to develop the Athletic Sports Nutrition Knowledge Questionnaire (A-SNKQ) specifically for Sri Lankan track and field athletes.

Methods: The development of the A-SNKQ followed an extensive step-wise approach. Firstly, a systematic literature review was conducted on existing SNK questionnaires for athletes. Secondly, sports nutrition guidelines were incorporated into the questionnaire. Thirdly, information from local literature was gathered to ensure contextual relevance. Lastly, a qualitative study involving key athletic stakeholders was conducted to gain cultural insights.

Results: The final version of the questionnaire consists of 32 questions in 12 sub-sections under two main sections: GNK section covers macronutrients, micronutrients, energy balance, hydration, and weight management, SNK section addresses carbohydrate loading, pre-training, training and post-training meals, sports supplements, supplement label reading, isotonic drinks, doping, and relative energy deficiency syndrome in sports.

Conclusion: A-SNKQ is a culturally tailored questionnaire which includes 32 questions across two major sections, designed to assess the GNK and SNK among track and field athletes in Sri Lanka. This was developed through a systematic literature review, examination of nutrition guidelines, exploration of local literature, and insights from a qualitative study with athletic stakeholders.

Keywords: knowledge, questionnaire, sports nutrition, Sri Lanka, athletics

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Introduction

Athletics is one of the most common sports worldwide.[1] The International Association of Athletics Federations (IAAF) recognizes several distinct athletic disciplines, including track sprints, middle/long distance hurdles, and relays; field throws and jumps; heptathlon and decathlon combined events; road running; race walks; cross-country; and mountain running and ultra-running.[1] Utilizing evidence-based, sports-specific nutrition practices is extremely valuable for enhancing sports performance and maintaining overall health.[2]

Sprinters heavily rely on response time, acceleration, and the capacity to maintain them despite increasing fatigue. There is common agreement that training nutrition should take priority over competition nutrition to ensure the athlete meets the higher metabolic demands of training.[3] Further, in order to optimize training capacity, recovery, and body composition, nutrient intake should be strategically timed before, during, and after exercise.[3] Energy intake should be personalized according to variability in training regimens, seasonality, and training volumes during the preparation period or the competition phase. In addition to energy supply, micronutrients are essential for energy metabolism, haemoglobin synthesis, bone health, and immune system stimulation.[4]

Further, hydration is essential for optimal sports performance and to prevent adverse events. Several ergogenic supplements, which can be defined as performance-enhancing substances, nutritional supplements, and a variety of techniques aimed at improving an athlete's exercise performance capacity[5] such as caffeine, creatine, beta-alanine, and bicarbonate—can benefit athletes depending on the event.[3] While there is no nationally published data on the dietary habits of athletes, a study on the nutritional intake of the undergraduate Sri Lankan athletic community found that they do not get sufficient energy or protein, and do not meet daily requirements for micronutrients, including vitamins B_1, B_2, B_9, B_{12}, and C and calcium, magnesium, and potassium.[6] While the majority of Sri Lankan athletes take nutrition supplements, including multivitamins (51.8%), creatine (37.3%), and protein powders (14.8%), they buy these supplements without recommendations from qualified professionals.[7]

Increasing evidence suggests that the nutrition knowledge of athletes is generally insufficient. [8] In a systematic review, Trakman and colleagues reported that athletes' sports nutrition knowledge (SNK) test scores ranged from 33% to 84%,[9] with more than half of the included studies reporting nutrition knowledge scores below 50%. suggesting that the majority of the athletic population may be at risk for chronic, inappropriate nutrition choices due to a lack of SNK. Indeed, a systematic review of twenty-nine original studies showed that athletes with strong nutrition knowledge are more likely to follow dietary recommendations,[10] which can improve athletes' performance and overall health.[11]

The development of a questionnaire begins with generating items, then moves on to the design of the questionnaire itself, and finishes with a thorough scientific assessment.[12] The structured approach to creating a questionnaire involves generating items, formatting these items, and refining the initial draft to ensure it is clear, engaging, and free of specialized language.[12]

Trakman and colleagues developed a questionnaire informed by recent updates in sports nutrition guidelines to evaluate SNK.[13] This tool has undergone validation through rigorous methods that include both classical test theory (CTT) and item response theory (IRT), specifically using Rasch analysis. This questionnaire consists of 89 questions divided into six categories: weight management, macronutrients, micronutrients, sports nutrition, supplements, and alcohol.[13] Similarly, Furber et al. have developed a psychometrically sound tool designed to measure general and SNK.[14] This instrument, consisting of 85 questions, was formulated with the guidance of an expert panel.[14] Tam and his team developed an electronically administered sports nutrition knowledge tool called the Platform to Evaluate Athlete Knowledge of Sports Nutrition Questionnaire (PEAKS-NQ), which consisted of 94 items.[15] The questionnaire was developed using focus group data from 16 high-level sports nutritionists, scientific literature, and an up-to-date

sports nutrition position stand. It was modified in cooperation with two experienced sports nutritionists to ensure its applicability to the intended population.[15]

In the Sri Lankan context, nutrition knowledge questionnaires for adolescents[16] and reproductive-age women[17] have been developed. However, to date, no published evidence exists for an SNKQ to assess the SNK in Sri Lankan athletics. Therefore, the aim of this study is to design and validate a culturally appropriate, comprehensive questionnaire that assesses both general and sports-specific nutrition knowledge among track and field athletes in Sri Lanka. This tool is intended to bridge the gap in current nutritional assessment methodologies by incorporating insights from systematic literature reviews, guidelines from authoritative bodies such as the International Olympic Committee (IOC), local dietary practices, and direct stakeholder inputs. Ultimately, this questionnaire aims to enhance the accuracy and relevance of nutrition knowledge evaluation within the athletic community, contributing to targeted nutritional interventions and improved athletic performance.

Methods

A mixed-methods approach was designed based on an extensive review of the literature [18] and used for the development of the questions (in English) for the current A-SNKQ. The reporting of the present study fulfils the design and conduct of GUIDED – a guideline for reporting for intervention development studies, in the EQUATOR library of reporting guidelines[19] (**Supplementary material 1**). The approach for developing the items in the tool comprised the following steps: (1)Conducting a systematic review of previous literature on SNKQs used in athletic sports; (2)Reviewing athletic-related SN guidelines; (3)Searching for local literature; (4)Conducting in-depth interviews with athletic stakeholders in Sri Lanka. This process was followed by an additional four steps to format and translate the questionnaire as follows: categorization into sections and subsections; implementation of branching logic; translation and cultural adaptation; and making the tool available online.

1. Systematic review of literature

A systematic review was conducted to synthesize data regarding existing questionnaires used to assess the SNK of athletes worldwide. Detailed information regarding this review has been published elsewhere.[20] In summary, the PubMed®, Web of Science®, and SciVerse Scopus® databases were searched using the keywords "sport" AND "nutrition" OR "diet" AND "knowledge" AND "questionnaire" OR "assessment" OR "survey". The titles, abstracts, and full texts of the identified articles were screened by two team members (RJ and KW). The principal investigator (RJ) carefully examined each questionnaire and extracted the most relevant questions for the Sri Lankan context. Subsequently, prior permission to use each question was sought from the respective authors, resulting in the compilation of a pool of questions.

2. Review of sports nutrition guidelines

Recent athletic-related sports nutrition guidelines[21] and educational materials related to athletics, including the International Olympic Committee (IOC) recommendations were closely reviewed to further modify the questions.

3. Search for local literature

Thirdly, to make the instrument culturally appropriate, two literature search strategies were used. First, searches were undertaken in index databases such as PubMed® and Scopus® using "Sri Lanka" as a keyword along with other sports and nutrition-related keywords, such as "sport," "athletic," "nutrition," and "dietary." Second, using the same set of keywords, non-index publications relevant to the Sri Lankan context were identified using Google Scholar (Google LLC, Mountain View, CA, USA).

4. Qualitative exploration

In this step, in-depth interviews were conducted with support staff (n = 11) and elite-level athletes in Sri Lanka (n = 4), involving human participants, to investigate practices and perceptions concerning four key areas of sports nutrition at the ground level.[22] These areas encompassed opinions regarding dietary practices, sports supplements, hydration, and other habits such as alcohol consumption and doping. The findings of this study have been previously published.[22] Informed written consent was obtained from each participant after giving them adequate time to ask questions and clarify doubts about the research.

All methods were performed in accordance with the declaration of Helsinki and ethical approval for the study was obtained from the Ethics Review Committee, Faculty of Medicine, University of Peradeniya, Sri Lanka [Ref No. 2022/EC/66].

Categorization of the pooled questions

After careful consideration of the pooled list of questions, the principal investigator (RJ) categorized them into two main sections, namely GNK and SNK, based on robust theoretical nutritional concepts. The commonly consumed local foods to be included in the questionnaire were identified based on in-depth interviews with support staff and elite-level athletes conducted during the qualitative study[22] and by using the food exchange atlas for Sri Lankan adults.[23] The general nutrition section included questions related to a non-athlete population's understanding of key nutrition concepts, with sub-sections on macronutrients, micronutrients, energy balance, hydration, and weight management. The sports nutrition section focused on the nutrition knowledge associated with sporting performance among athletes, such as carbohydrate loading, pre-training meals, meals during training, post-training meals, sports supplements, supplement label reading, alcohol, isotonic drinks, doping, and relative energy deficiency syndrome in sports (RED-S). The research team determined the number of questions in each sub-section, taking into account the relevance of individual items to the Sri Lankan population, the scientific credibility of the items, and the practicality of the overall number of items in the final tool.

Implementation of branching logic for questions

Branching logic, or skip logic, is a feature in survey design that changes the questions presented based on a participant's response to previous questions.[28] This method is particularly useful in tailoring the questionnaire to be more relevant and less burdensome to respondents by avoiding unnecessary questions.[28]

Given the diversity within the athletic population, it was not anticipated that athletes would possess comprehensive nutrition knowledge regarding the use of various supplements across all events. Hence, a decision was made to employ branching logic for questions related to supplement usage, where only the relevant supplements based on their sporting event were displayed. For instance, if an individual selects the 100 m event, questions related to supplements for other events will be disabled, allowing them to answer solely in relation to the selected event. This tailored approach enhances the questionnaire's relevance for each athlete's specific needs.

Translation and cultural adaptation

First, a forward translation was conducted from English to Sinhala by an independent translator who was a native Sinhalese speaker and had a good understanding of the instrument's domains. The translator was instructed to focus on capturing the conceptual equivalence rather than a literal word-for-word translation. Then a bilingual expert panel (n= 4), convened by the principal investigator (RJ), reviewed the translation and addressed any inadequacies in expressions or concepts. The panel consisted of the original translator, experts in sports nutrition (n=4), and individuals experienced in instrument development and translation (n=2). They also made modifications to individual questions to ensure cultural adaptation of the questionnaire. The third stage involved the back-translation of the instrument from Sinhala to English. It was carried out by a second independent

translator who had no prior knowledge of the original questionnaire. Any discrepancies identified in the back translation were discussed with the expert panel, and revisions were made until a satisfactory Sinhalese version of the A-SNKQ was obtained. A similar procedure was performed for the translation of the Tamil language.

Making the tool available online

Subsequently, an online version of the questionnaire was developed using Google Forms (platform: Google Forms, Google LLC, California, USA) to facilitate easy accessibility and data collection. It was made available in all three official languages of Sri Lanka: English, Sinhala, and Tamil ensuring inclusivity for participants across different language backgrounds.

Results

The systematic literature review (step 1) revealed a total of 11 studies on questionnaires assessing SNK. Among these, eight studies focused only on athletic disciplines, while three encompassed athletics and other sports. 26 questions from these studies were deemed appropriate and relevant for the Sri Lankan athletic population. By incorporating recent sports nutrition guidelines including IOC recommendations (step 2), we developed an additional 10 questions, resulting in an updated and evidence-based draft questionnaire consisting of 36 questions. The Google Scholar search (step 3) that was conducted specifically targeting local literature for contextual modifications resulted in a total of five articles, of which the first 100 search hits were examined. This led to an additional three items for the question pool. Finally, the in-depth interviews conducted with athletic stakeholders contributed two items, which were predominately related to the selection of food items according to the local setting and cultural practices on dietary practices, sports supplementation, and hydration. For the sports supplement questions, sports supplement labels (n=3) were collected from local stores and websites to be included in the current questionnaire (**Figure 1**). A total of eight draft items were excluded due to their lack of applicability within the local context and being beyond the scope of the A-SNKQ. The final version of the questionnaire comprises a total of 32 questions.

The final compiled SNKQ comprises 33 questions covering 12 sub-sections that are divided into two main sections: GNK and SNK. The general nutrition section comprises 15 questions distributed among sub-sections covering macronutrients (n=4), micronutrients (n=3), energy balance (n=4), hydration (n=3), and weight management (n=1). Within the sports nutrition section (n=17), specific emphasis is placed on carbohydrate loading, pre-training meals, and meals during training, each represented by one question. Post-training meals and RED-S are addressed with two questions, followed by sports supplements (n=6), supplement label reading, alcohol, isotonic drinks, and doping (n=4) in subsequent sub-sections. The questionnaire employed the main two-question formats of single-best response questions (SBRQs: n=29) and multiple-choice questions (MCQs: n=3) with no open-ended questions.

The structure of these questions varied, with some having three options, such as 'agree,' 'disagree,' and 'unsure,' while others had five responses carrying the most accurate answer. A plus mark (+1) was awarded for the correct answers and a negative mark (-1) for the wrong answers; zero marks (0) were given for an unsure response. The estimated time required to complete the questionnaire was approximately 10 - 15 minutes. A comprehensive overview of the A-SNKQ is represented in **Table 1**.

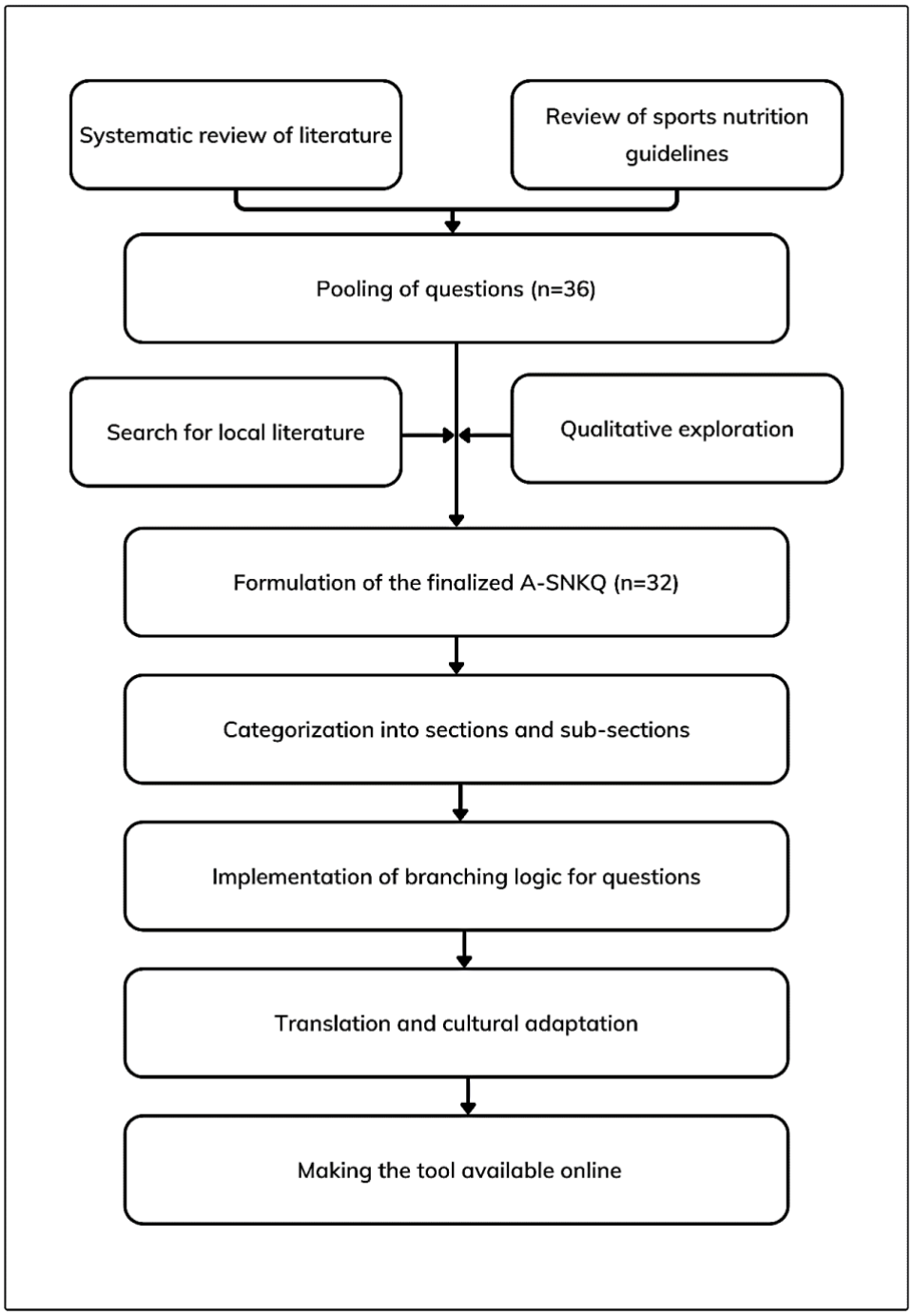

Figure 1. The step-wise approach for the development process of the A-SNKQ (Athletic Sports Nutrition Knowledge Questionnaire)

Table 1. Summary of A-SNKQ

Sections and sub-sections	Source of questions	Number of items	Question format
1. GNK			
Macronutrients	1,2,3,4	27	SBRQs
Micronutrients	1,2,3	08	SBRQs
Energy balance	1,2,4	09	SBRQs
Hydration	2,3,4	11	SBRQs
Weight management	3	01	SBRQs
2. SNK			
Carbohydrate loading	2	01	SBRQs
Pre-training meals	3,4	04	SBRQs
Training meals	2,4	06	MCQs
Post-training meals	2,3,4	11	MCQs, SBRQs
Sports supplements	2,4	26	SBRQs
Supplement label reading, alcohol, isotonic drink, and doping	1,2,3,4	16	SBRQs
RED-S	2	02	SBRQs

The four-step approach followed during the development of A-SNKQ: 1. Systematic review of literature, 2. Review of sports nutrition guidelines, 3. Search for local literature, 4. Qualitative exploration.
Abbreviations: GNK= General nutrition knowledge, MCQs= Multiple-choice questions, RED-S= Relative energy deficiency syndrome in sports, SBRQs= Single-best response questions, SNK= Sports nutrition knowledge.

Section 1: General Nutrition Knowledge

The initial question presents 20 common food items and asks respondents to identify the most abundant macronutrient. Eleven, five, and four food items predominantly contain carbohydrates, proteins, and fats, respectively. The second question focuses on dietary fibre, while the third and fourth questions address protein distribution and recommendations. In the micronutrient sub-topic, we listed six common food items and asked participants to identify the most abundant micronutrients, including calcium, iron, and vitamin C. Other questions in this sub-section explored participants' understanding of the availability of antioxidants in local sour fruits and the recommendation of micronutrient supplements for athletics. The subsequent sub-section covered knowledge of energy in nutrients and balance, as well as post-exercise recovery requirements, including the importance of consuming adequate amounts of carbohydrates and protein following exercise. The 'hydration' sub-section assessed participants' knowledge of signs of dehydration, food sources of salt, and the recommended post-training fluid intake. Lastly, participants' knowledge of weight management was evaluated through a separate question on appropriate low-energy, high-volume foods that can be used as a rice substitute.

Section 2: Sports Nutrition Knowledge

The sports nutrition section covered a range of topics related to carbohydrate loading, training-related meals, sports supplements efficacy and comprehension of supplement labels, the impacts of alcohol on performance and recovery, isotonic drinks, doping, and RED-S. Athletes' awareness of the importance of nutrition before training was assessed via a question that listed food items and inquired about the recommended intervals at which they should be consumed. Likewise, in order to evaluate participants' knowledge about the

appropriate food and beverage choices during an intense 2-hour training session and post-training meals, they were presented with 6 and 9 options, respectively, and asked to select appropriate choices, with several possible correct answers. Further, an MCQ format was utilized to evaluate the SNK of the respondent regarding the importance of having a recovery meal.

Four SBRQs were used to assess the understanding of recommended doses for whey protein, creatine, beta-alanine, and bicarbonate supplementation. An additional question was incorporated to specifically identify any misconceptions about the use of supplements. Recognizing that not all ergogenic supplements are equally effective for every sporting event, participants were provided with a list of events and asked to select their main athletic contest. Following that, they were provided with five supplement options, namely caffeine, creatine, nitrate, beta-alanine, and bicarbonates, and allowed to select the most appropriate supplement for their particular event.

To assess knowledge of banned substances, participants were presented with six substances and asked to identify the three banned items among them, alongside three safe items. Additionally, participants were shown three "real-life" supplement labels in the form of images to read the product labels and identify them. The final subtopic on RED-S was concerned with the impact on performance and health caused by athletes failing to meet their daily calorie needs.

Discussion

This study presents the first SNKQ developed in Sri Lanka, specifically tailored for track and field athletes. To ensure an extensive, locally acceptable tool, we employed four comprehensive strategies that combined cultural acceptance and the latest evidence. Consequently, the development of the A-SNKQ in this study addresses a significant gap in the existing literature and offers a valuable instrument for assessing SNK within the local athletic context.

Furber and colleagues (2017) listed Weetabix, chocolate spread, whole meal bread, and jelly beans as food items for participants to choose between high or low carbohydrates.[14] However, in the Sri Lankan context, during our in-depth interviews and literature review, these food items did not emerge. Hence, we incorporated bread, cooked rice, string hoppers, and sweet potatoes as examples of carbohydrate-rich foods in our study. Similarly, while they listed kidney beans and tuna as foods rich in proteins, we have included chickpeas and fish as corresponding items in our SNKQ.[14] Similarly, we substituted canola margarine, cottage cheese, and sunflower seeds with coconut oil and coconut sambal as sources of dietary fats. This replacement was implemented based on the prevalent use of coconut oil as the primary fat source in Sri Lanka.[27, 8]

Trakman and colleagues utilized a specific question within the SNK section to evaluate the approximate daily protein requirements of well-trained resistance athletes. In general, Sri Lankans have a low daily protein intake.[13]

Furber and his team employed a separate question to assess the participant's knowledge regarding vitamins B, C, calcium, and iron. [14] However, in order to prevent excessive length, we have chosen to consolidate the various subcategories of vitamins into two questions.

Engaging in intense training while maintaining a low energy intake can present substantial health risks, including the potential development of adverse conditions such as low energy availability (LEA).[26]

Proper hydration for sports is an essential area to access in any questionnaire related to sports nutrition. Previous studies have primarily concentrated on various aspects of hydration, including the determination of optimal fluid intake during exercise sessions,[25] the composition of sports drinks,[25] the myths and importance of hydration for sports performance,[13] and the identification of dehydration signs.[14] Hence, the subtopic 'hydration' was subsequently employed in our work to evaluate various aspects, including the identification of dehydration symptoms, the recognition of salt-rich sources, and the recommended post-training fluid intake for athletes. Our previous studies have also identified

limitations in knowledge regarding hydration within a similar population.[22]

The A-SNKQ developed in the current study has some limitations to consider. While it is a comprehensive tool, it contains knowledge items that may not be equally important for every athlete. As well, the length and technical nature of the questionnaire might pose challenges for athletes who lack motivation or have lower literacy levels. By implementing evidence-based interventions based on the findings of the SNK assessment tool, national athletic programs can optimize their athletes' nutrition knowledge and practices, leading to improved performance and overall success in the sporting arena. However, it is crucial to emphasize the need for proper validation of the current A-SNKQ, followed by the process of development. Precise validation of this developed questionnaire is important to ensure its relevance and significance in future research and practical applications.

Conclusion

In conclusion, we aimed to develop a culturally acceptable tool to assess SNK among track and field athletes in Sri Lanka. The questionnaire encompasses a total of 32 questions, categorized into two major sections: GNK and SNK. The development process followed a four-step approach that incorporated sources of information to formulate the current questionnaire. This involved conducting a systematic literature review, reviewing sports nutrition guidelines, searching for local literature, and gathering insights from a qualitative study involving relevant athletic stakeholders. These areas are considered fundamental to awareness of the overall nutrition principles applicable to athletes.

Conflict of interest

The authors declare there is no conflict of interest regarding this article.

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Athletic Sports Nutrition Knowledge Questionnaire (A-SNKQ)

This short survey is designed to assess the knowledge of Sri Lankan elite athletes regarding general and sports nutrition. Your participation and honest responses will be highly appreciated. The questionnaire takes about 10-15 minutes to complete. For statement-based questions, please indicate whether you agree with the given statements or not. If you do not know the answer to any question, please select the "unsure" option. The information you provide will be kept strictly confidential.

Section 1 – General Nutrition Knowledge

1. Macronutrients

1. Please consider the following food items and select **the most abundant** macro-nutrient in each food. **(Check the one that applies the most)**

Food item	Carbohydrates	Proteins	Fats	Unsure
Banana	☒	☐	☐	☐
Beef	☐	☒	☐	☐
Bread	☒	☐	☐	☐
Chicken	☐	☒	☐	☐
Chickpeas	☒	☐	☐	☐
Coconut oil	☐	☐	☒	☐
Coconut *sambal*	☐	☐	☒	☐
Corn flakes	☒	☐	☐	☐
Dates	☒	☐	☐	☐
Dhal	☒	☐	☐	☐
Dried fish	☐	☒	☐	☐
Egg white	☐	☒	☐	☐
Fish	☐	☒	☐	☐
Oats	☒	☐	☐	☐
Olive oil	☐	☐	☒	☐

Pasta	☒	☐	☐	☐
Peanuts	☐	☐	☒	☐
Rice	☒	☐	☐	☐
String Hoppers	☒	☐	☐	☐
Sweet Potatoes	☒	☐	☐	☐

2. Please consider the following food items and indicate whether they are a good source of dietary fibre source or not.

Food item	Yes	No	Unsure
Beef	☐	☒	☐
Fruits	☒	☐	☐
Green leafy vegetables (*mallum)*	☒	☐	☐
Milk	☐	☒	☐
Vegetables	☒	☐	☐

3. For athletes wanting to enhance recovery from physical activity and optimize muscle growth, spreading out protein consumption throughout the day is more effective than consuming it all at once.

   Agree ☒

   Disagree ☐

   Unsure ☐

4. The optimum daily protein intake for athletes who have a goal of weight maintenance or weight gain is (in grams per kilogram of body weight per day),

   0.3 g/kg BM/day ☐

   0.8 g/kg BM/day ☐

   1.5 g/kg BM/day ☒

   2.5 g/kg BM/day ☐

   Unsure ☐

2. Micronutrients

5. Select the micronutrient of which the following foods are a rich source,
   (Check the one that applies the most)

Food item	Calcium	Iron	Vitamin C	Unsure
Banana	☐	☐	☒	☐
Beef	☐	☒	☐	☐
Curd	☒	☐	☐	☐
Full cream milk powder	☒	☐	☐	☐
Local mandarins	☐	☐	☒	☐
Sweet potatoes	☐	☐	☒	☐

6. Most of the local sour fruits contain a **high amount** of antioxidants.

   Agree ☒

   Disagree ☐

   Unsure ☐

7. You should take vitamin supplements if,

1. You feel tired ☐
2. You are getting sick often ☐
3. Your colleagues also take the same ☐
4. You have been told you have a deficiency by a medical professional ☒
5. Unsure ☐

3. Energy balance

8. Please consider the following nutrient or substance and indicate whether it provides energy.

Type of nutrient/substance	Yes	No	Unsure
Alcohol	☒	☐	☐
Carbohydrate	☒	☐	☐
Fats	☒	☐	☐
Iron	☐	☒	☐
Proteins	☒	☐	☐
Vitamin B_{12}	☐	☒	☐

9. Feeling tired midway through a workout might be a sign of insufficient energy-rich food in one's diet.

   Agree ☒

   Disagree ☐

   Unsure ☐

10. Consuming a sufficient amount of carbohydrates helps to reduce protein breakdown in the body.

    Agree ☒

    Disagree ☐

    Unsure ☐

11. During resistance exercises, the body tends to use protein as the main energy source.

    Agree ☐

    Disagree ☒

    Unsure ☐

4. Hydration

12. Please read each of the following signs and state whether it is a method/sign of dehydration after an intense training session.

Method/Sign	Yes	No	Unsure
Assessing urine colour after training	☒	☐	☐
Presence of dry mouth	☒	☐	☐
Presence of loose stools	☐	☒	☐
Feeling of thirst	☒	☐	☐
Measuring urine-specific gravity	☒	☐	☐

13. If you lost one kilogram of weight during a training session, how much water do you need to consume after training (in liters)?

1. 0.5 L ☐
2. 1.0 L ☐
3. 1.5 L ☒
4. 2.0 L ☐
5. Unsure ☐

14. Please consider the following food items and indicate whether it is a rich source of salt.

Food item	Yes	No	Unsure
Jeewani	☒	☐	☐
King coconut water	☐	☒	☐
Marmite	☒	☐	☐
Milk	☐	☐	☐
Watermelon juice	☐	☒	☐

5. Weight management

15. If you want to lose weight, rice should be replaced with which of the following food items? **(Check the one that applies the most)**.

1. Chicken curry ☐
2. Potato curry ☐
3. Dhal curry ☐
4. Vegetable salad ☒
5. Unsure ☐

Section 2 – Sports Nutrition Knowledge

6. Carbohydrate loading

16. To maximize muscle glycogen stores, carbohydrate loading is best followed by how many hours before the competition (in hours)?

1. 6-12 h ☐
2. 12–24 h ☐
3. 24–48 h ☒
4. 168 h ☐
5. Unsure ☐

7. Pre-training meals

17. Please indicate the correct time gap for the pre-training meals given below.

Food item	4-hours before exercise	½-1-hour before exercise	Unsure
Rice and curry	☒	☐	☐
A banana	☐	☒	☐
Boiled chickpeas with coconut	☒	☐	☐
A jam sandwich	☐	☒	☐

8. Training meals

Check all that apply. Please note that minus marks will be given for each incorrect answer.

18. Which of the following food/beverage can be taken in the middle of an intense 2-hour training session?

1. A banana ☒
2. A small sandwich ☐
3. Nuts ☐
4. Raw eggs ☐
5. *Jeewani*/ORS ☐
6. Unsure ☐

9. Post-training meals

This section consists of multiple-choice questions, you can select one or more answers for each question.

Please note that minus marks will be given for each incorrect answer.

19. Recommended meal/s after two hours of an intense training session is/are,

1. A glass of *kola kanda* ☐
2. Milk packet ☐
3. A piece of fried chicken ☐
4. Boiled chickpeas ☒
5. Boiled sweet potatoes ☐
6. Bowl of cornflakes with non-fat milk ☒
7. Bread with jam ☐
8. Two boiled eggs ☐
9. White rice with dhal and chicken ☒
10. Unsure ☐

20. After heavy training athletes should,

1. Drink fluids but avoid eating as digestion is impaired after exercise ☐
2. Wait until your next meal to avoid overeating and gaining weight ☐
3. Eat foods high in carbohydrates and proteins within 30 minutes to 2 hours and eat sooner rather than later if you are training/competing again on the next day ☒
4. Eat whatever you can find as soon as possible to avoid low blood glucose ☐
5. Unsure ☐

10. Sports supplements

21. What is the amount of whey proteins that should be consumed per serving for optimum muscle building/muscle protein synthesis/recovery (in grammes)?
    1. 5 g ☐
    2. 10 g ☐
    3. 15 g ☐
    4. 20 g ☒
    5. Unsure ☐

22. What is the recommended daily creatine maintenance dose (in grams)?
    1. 2 g ☐
    2. 5 g ☒
    3. 7 g ☐
    4. 10 g ☐
    5. Unsure ☐

23. What is the recommended daily dose of beta-alanine (in grammes)?
    1. 1 g ☐
    2. 2 g ☐
    3. 3 g ☐
    4. 4 g ☒
    5. Unsure ☐

24. How do you calculate the recommended total dose of the bicarbonate according to body weight (in grammes per kilogram of the body weight per day)?
    1. 0.05 g/kg BM/day ☐
    2. 0.15 g/kg BM/day ☐
    3. 0.3 g/kg BM/day ☒
    4. 0.5 g/kg BM/day ☐
    5. Unsure ☐
25. Which statement about the contribution of sports supplements to your sports performance is true?
    1. Taking supplements is more important than changing your diet if you want to improve your sports performance ☐
    2. Taking supplements is equally as important as improving your diet if you want to improve your sports performance ☐
    3. Supplements do not benefit performance and are never needed ☐
    4. Some supplements can have a small impact on performance but the contribution will depend on the type of supplement and what sport you play ☒
    5. Unsure ☐

26. Select your primary sporting event and the corresponding optimal sports supplement.

(Certain sporting events may have multiple suitable sports supplements.)

Event	Caffeine	Creatine	Nitrate	Beta-alanine	Bicarbonate
100 m	☒	☒	☐	☐	☐
200 m	☒	☒	☐	☐	☐
100/110 m hurdles	☒	☒	☐	☐	☐
400 m	☒	☒	☐	☒	☒
400 m hurdles	☒	☒	☐	☒	☒
800 m	☒	☒	☒	☒	☒
1500 m	☒	☐	☒	☒	☒
3,000 m steeple chase	☒	☐	☒	☒	☒
5,000 m	☒	☐	☒	☐	☐
10,000 m	☒	☐	☒	☐	☐
Race walking	☒	☐	☒	☐	☐
Half marathon	☒	☐	☒	☐	☐
Marathon	☒	☐	☒	☐	☐
Long jump	☒	☒	☐	☐	☐
High jump	☒	☒	☐	☐	☐
Triple jump	☒	☒	☐	☐	☐
Pole vault	☒	☒	☐	☐	☐
Throws (discus, hammer, javelin and shot put)	☒	☒	☐	☐	☐
Heptathlon	☒	☒	☒	☒	☒
Decathlon	☒	☒	☒	☒	☒

11. Supplement label reading, alcohol, isotonic drink, and doping

27. Which of the following is banned by the World Anti-Doping Agency (WADA) for use before the competition?
    1. Bicarbonate ☐
    2. Caffeine tablets ☐
    3. Iron-IV infusion ☒
4. Polybion-IV infusion ☒
    5. Steroid injections ☒
    6. Whey protein ☐
    7. Unsure ☐

28. Drinking alcohol slows down recovery after training.
    Agree ☒
    Disagree ☐
    Unsure ☐

29. Identify the safe to use supplement put of the following three labels.

1. ☐

Supplement Facts

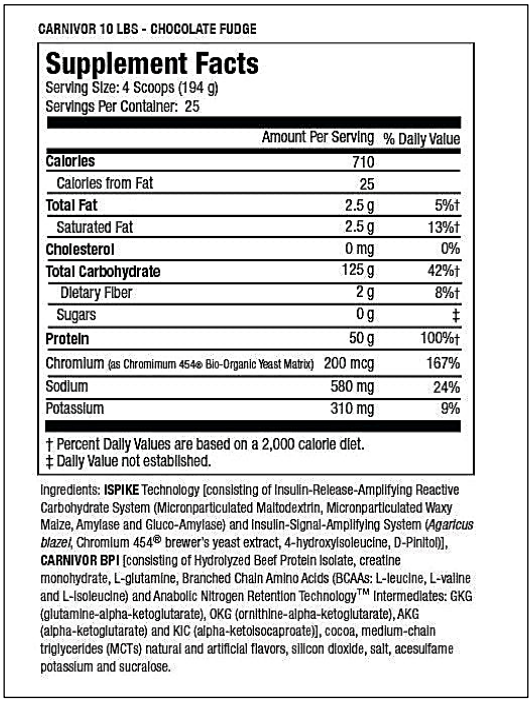
Serving Size: 1-3 Scoops (5.55g-16.65g)
Servings Per Container: 15-45

Amount Per Serving:		%DV
Proprietary Blend: 4,145mg *	12,435mg	*
(Arginine Alpha-Ketoglutarate, Creatine Monohydrate, Beta Alanine, Caffeine, 2-Aminoisoheptane HCl, Geranium Extract (stem & leaves), Yohimbe Extract (bark)(Standardized for Yohimbine Alkaloids)), Schisandra Chinensis (berry) Extract (Standardized for Schizandrol A)		
Caffeine 135mg *	405mg	*

*Daily value not established

Other Ingredients: Citric Acid, Natural and Artificial Flavors, Acesulfame-K, Sucralose, Silicon Dioxide, FD&C Red #40 and FD&C Blue #1

2. ☐



CARNIVOR 10 LBS - CHOCOLATE FUDGE

Supplement Facts
Serving Size: 4 Scoops (194 g)
Servings Per Container: 25

	Amount Per Serving	% Daily Value
Calories	710	
Calories from Fat	25	
Total Fat	2.5 g	5%†
Saturated Fat	2.5 g	13%†
Cholesterol	0 mg	0%
Total Carbohydrate	125 g	42%†
Dietary Fiber	2 g	8%†
Sugars	0 g	‡
Protein	50 g	100%†
Chromium (as Chromimum 454® Bio-Organic Yeast Matrix)	200 mcg	167%
Sodium	580 mg	24%
Potassium	310 mg	9%

† Percent Daily Values are based on a 2,000 calorie diet.
‡ Daily Value not established.

Ingredients: **ISPIKE** Technology [consisting of Insulin-Release-Amplifying Reactive Carbohydrate System (Micronparticulated Maltodextrin, Micronparticulated Waxy Maize, Amylase and Gluco-Amylase) and Insulin-Signal-Amplifying System (*Agaricus blazei*, Chromium 454® brewer's yeast extract, 4-hydroxyisoleucine, D-Pinitol)], **CARNIVOR BPI** [consisting of Hydrolyzed Beef Protein Isolate, creatine monohydrate, L-glutamine, Branched Chain Amino Acids (BCAAs: L-leucine, L-valine and L-isoleucine) and Anabolic Nitrogen Retention Technology™ Intermediates: GKG (glutamine-alpha-ketoglutarate), OKG (ornithine-alpha-ketoglutarate), AKG (alpha-ketoglutarate) and KIC (alpha-ketoisocaproate)], cocoa, medium-chain triglycerides (MCTs) natural and artificial flavors, silicon dioxide, salt, acesulfame potassium and sucralose.

3. ☐

NUTRITION INFORMATION

Servings Per Container: Approx. 42
Serving Size: 1 Rounded Scoop (43 g)

	Quantity Per Serving	Quantity Per 100g
Energy	710kJ/170 cal	1652kJ/395 cal
Protein	30g	70g
Total Fat	4g	9.3g
Cholesterol	85mg	198mg
Total Carbohydrate	4g	9.3g
Dietary Fiber	1g	2.3g
Sugars	2g	4.7g
Vitamin C	5mg	11.6mg
Calcium	210mg	488mg
Iron	0.72mg	1.7mg
Sodium	140mg	326mg
Ripped⁺ Matrix		
L-Carnitine L-Tartrate	500mg	1163mg
CLA (Conjugated Linoleic Acid)	250mg	581mg
***C. canephora robusta* Extract** (bean)	250mg	581mg
(Robusta Coffee) Standardized for 45% Chlorogenic Acids		
Green Tea Extract (as Camellia senensis) (leaf)		
Standardized for 15% EGCG	100mg	233mg
Rose Hip Extract (as Rosa canina) (fruit)		
Kelp (as Laminaria digitata) (stem and leaf)	100mg	233mg
All specified values are averages	20mg	47mg

Ingredients: Isolate Protein & Peptide Blend (Whey Peptides, Whey Protein Isolate, Whey Protein Isolate 97%), Cocoa (Processed with Alkali), Natural and Artificial Flavours, Gum Blend (Cellulose Gum, Xanthan Gum, Carrageenan), Salt, Soy or Sunflower Lecithin, Flaxseed, Medium Chain Triglycerides, Silicon Dioxide, Sucralose, Acesulfame-Potassium.

4. None of the above ☒
5. Unsure ☐

30. Which of the following is/ are examples of an isotonic solution (A solution with a concentration roughly equal to the composition of body fluids)?
    1. Dextrose ☐
    2. Fruit juice ☐
    3. *Jeewani* (ORS) ☒
    4. Water ☐
    5. Unsure ☐

12. RED-S

31. 'Meeting relatively lesser energy than the required amount causes poor performance and serious health issues.'

    Agree ☒

    Disagree ☐

    Unsure ☐

32. 'It is important not to change your dietary habits during overseas competitions.'

    Please indicate whether you agree with this statement by checking the appropriate box.

    Agree ☒

    Disagree ☐

    Unsure ☐

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LITERATURE REVIEW

Child rearing workplace policy for working mothers: a scoping review

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Abstract

Introduction: Straddling work and childcare harms working moms' health, potentially their children too. To address this, child rearing workplace policies are needed. These would promote work-life balance and ensure both mothers' and children's well-being, ultimately protecting pregnant and parenting women at work.

Objective: This study aims to explore the gaps between available child rearing workplace policy for working mothers and the implementation on the field while taking its implications into account.

Methods: We reviewed literature from PubMed electronic database. Predefined keywords were developed and chosen. Relevant articles were filtered according to the inclusion and exclusion criteria. Furthermore, all articles were reviewed independently and those that match were included and charted through Microsoft Excel based on each articles' characteristics.

Results: There are 13 workplace policies related to childcare for working mothers in the included articles. The most common policy was paid maternity leave. Other frequently mentioned policies included lactation support and facilities, flexible work arrangements, and daycare facilities. All policies have different implementation rates and implications to both working mothers and their children.

Conclusion: Supportive child rearing policies at work benefit everyone: employers, employees, and their families, leading to a better nutritional and health status, hence increase overall quality of life.

Keywords: workplace policy, working mothers, childcare, maternal employment

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Introduction

Globally, women workers shoulder more childcare responsibilities than men due to persistent gender norms across all countries. Women all around the world were subjected to triple roles: domestic worker, income earner outside household chores, and caregivers for family members.[1] Health problems among the female labour arise from the inability to juggle between the roles of nurturing

and working, therefore jeopardising the nutritional and health status of the working mom and their child. Mothers who were working and not protected by policy in their workplace could face "pregnancy discrimination" which defined as disadvantageous treatment of women in the workplace due to pregnancy, childbirth, and requestion or taking childcare/ family care/ other family related leave. Pregnancy discrimination could lead to maternal postpartum depression, impaired mother-child bonding, infant death, and hospitalisation during the first year of the child's life. Moreover, children of working mothers have been reported to have nearly twice the odds of being stunted than children of non-working mothers.[2] A systematic review reported that informal employment of mothers had a negative effect and significantly associated with higher risks of being underweight and stunting.[3] Another study in the U.S. revealed that approximately 74% of U.S. mothers work full-time where employment was identified as one of the reasons working mothers had to stop breastfeeding. [4]

Due to the importance of work and family life balance, health and safety of mother and children, also in the course of the attempt to protect women in workplaces who are pregnant and/or child rearing, United Nations with all representatives of every country adopted The Convention on the Elimination of All Forms of Discrimination against Women (CEDAW) in 1979. Convention on the Elimination of All Forms of Discrimination against Women (CEDAW) is an international treaty that focuses on comprehensive guarantees regarding women's right to equality in all spheres of life, including the reproductive rights of women in employment places. It has been a tool to tackle discrimination at workplaces. [5] International Labor Organization or ILO also declared an international Maternity Protection Convention No. 183 year 2000. This convention is a set of recommendations to support women and their children through health protection, paid maternity leave (prepartum and postpartum), benefits (e.g., cash benefits, medical benefits, etc.), employment protection and non-discrimination (the right to return to the same position or equivalent at the end of the maternity leave), and daily reduction of working hours (to breastfeed her child) or nursing breaks.[6]

United Nations International Children's Emergency Fund (UNICEF) also developed a set of policies known as family-friendly policies (FFP) to address the significance of achieving a balance between work and family life. The aim of FFP is to assist employees in managing the responsibilities of raising children from pregnancy to the early school years. Family-friendly policies recognizes the essential needs of parents and caregivers of young children, encompassing time, resources, and services. By actively investing in this critical phase of early childhood, families, businesses, and the government contribute to the overall success of children in education, the productivity of adults in the workforce, the potential for families to escape poverty, and the attainment of lifelong well-being.[7]

As demands for female workers' keeps adding up over the years, the consequences to this phenomenon, especially to their health and nutrition, cannot be ignored. Female workers spend most of their day in their workplace and it is important to see this as an opportunity for health and nutrition promotion. The prevalence of workplace wellness programs is on the rise due to a growing recognition among employers of the advantages they offer, including enhanced productivity and reduced healthcare expenses. Family oriented and maternal policies are also proven to have an impact at the organisational/ institutional level where it can help retain talent and effectively improve organizational performance.[8,9]

The aim of this scoping review was to explore the gaps between available child rearing workplace policy for working mothers and the implementation on the field while taking its implications for both the working mothers and children into account. Deciphering what drives or impedes policy all around the world could unveil crucial steps toward a supportive workplace for mothers who handled both work and motherhood. Identifying factors that boost or block policy realisation can pave the way for actionable strategies to optimize workplace policy related to child rearing toward better health and welfare for both working mothers and their children.

Methods

This scoping review adapted the method from Ziolkowski et al.,10 We modified the protocol, which was originally used to conduct a nationwide breastfeeding policy scoping review. The stages taken in this study are: (1) identify research questions, (2) identify the policies (3) study selection (4) charting the data, and lastly (5) combining, summarising, and reporting data.

1. **Research Question**
   Based on our analysis of the available data, key questions emerged concerning workplace policy and its impact for complementary feeding practices among working mothers:
   1. What is the workplace policy for working mothers that supports their children's health and welfare?
   2. How is the implementation of workplace policy in supporting working mothers to fulfil their children's health and welfare?
   3. What are the implications of child rearing workplace policy for the mothers and their children?
2. **Search Strategy**
   PubMed was chosen as the database of search due to its high numbers of indexed journals, ease of access, and available quality assessment to ensure the excellence of articles contained in the database.[11] The search function "AND" was used to identify articles with the predefined keywords, which are: policy, working mother, child health. Variations for the keyword were combined with the "OR" operation to maximize results which are: policies and regulations. This review only considered articles in English and was published in the last 10 years between December 2013 – January 2024.
3. **Inclusion and Exclusion Criteria**
   Inclusion criteria that were implemented for the search were: studies related to any scope of public policy (international, national, or regional) and any level of occupations (skilled, semi-skilled, or basic-skilled) in any country using any type of methodology. This review included implementation and/or implication of policies, regulations, guidelines, or recommendations applicable in workplace settings.

   Whereas the exclusion criteria of this review consisted of: COVID-19 or pandemic regulations, non-working mothers or fathers as respondents, self-employed respondents, articles with non-English language, unavailable abstract and manuscripts, and publications before 2013 or after January 2024.
4. **Data Selection**
   All articles were reviewed independently through electronic databases. Final articles that match the inclusion and exclusion criteria of this study were included and charted through Microsoft Excel. Each article's characteristics, such as: aims of the study, type of policy, methodology, and location were sorted by reviewer.

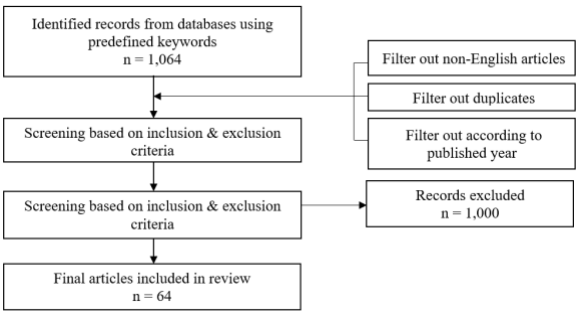

Figure 1. Flowchart of data selection process

The flowchart (**Figure 1**) depicts the process of data selection graphically. As shown in the flowchart, a rigorous multi-stage assessment was carried out. A sum of 1,064 emerged from PubMed using the predefined keyword. Further screening was conducted and we found several articles were irrelevant, not in English language, respondents were non-working mothers, published outside the 2013–2024-year range, also articles with unavailable abstract and manuscript. Further filtering based on the inclusion and exclusion criteria led us to exclude 1,000 articles. Therefore, there were 64 articles focused on workplace policy, working mother, and/or its implications for the mother and their children. We scrutinized titles, abstracts, and full texts against predefined inclusion-exclusion criteria to meticulously select

relevant articles for the review. Through this multifaceted approach, we conducted a thorough assessment of all articles, thereby securing the inclusion of solely pertinent studies within the review.

Results and Discussions

1. Child Rearing Workplace Policy for Mothers

There were 32 countries or regions that focused on the topic and two unspecified locations of study due to its research nature (worldwide-based review). Several articles did its research on more than one country, namely: one article addressed Brazil & Ghana, one article addressed India & South Africa, one article included UN member countries and one article included all staff of WHO in the Western Pacific Region. Most of the articles explored the USA as their location of research with 22 articles, followed by Kenya with three articles. Europe, Indonesia, South Korea, Thailand, and the UK had two articles addressing this topic. While the rest of these following countries or regions had one article: Bangladesh, Bhutan, Cambodia, China, East Africa, Ecuador, Egypt, Ethiopia, France, Germany, Ghana, Guatemala, India, Jerusalem, Mexico, Oman, Pakistan, South Africa, Sri Lanka, Sweden, and Taiwan. Location of the studies indicated the said countries or regions have had come to attention regarding the importance of child rearing workplace policy for mothers, despite its availability and factual implementations in the said countries or regions.

Table 1. Publications included in analysis

Policy: 1) Paid maternity leave 2) Childcare subsidy 3) Breast-pumping breaks 4) Breast-pumping facilities 5) Breast-pumping education & support 6) Flexible working arrangements 7) Paid sick/ medical leave 8) Daycare facility 9) IYCF practices & support 10) Bringing children to workplace 11) Paid childbearing leave 12) Unpaid leave 13) Paid parental leave (mother and father)

No	Authors	Year	Location	Study Aims	Methodology	Policy
1	Guendelman et al[12]	2013	USA	Relationship between access to employer-offered maternity leave (EOML) (both paid and unpaid) and uptake and duration of maternity leave following childbirth in a socio-economically diverse sample of full-time working women	Case control	1
2	Sheperd-Banigan & Bell[13]	2014	USA	Examine the associations between socio-demographic factors and employment leave variables (paid maternity, sick and personal leave)	Cross-sectional	1
3	Herbst & Tekin[14]	2014	USA	Examining the impact of childcare subsidy receipt on maternal health and the quality of child–parent interactions	Cross-sectional	2
4	Tsai[15]	2014	Taiwan	Explore the impact of employee's perceived breastfeeding support from the workplace and the benefits of breastfeeding on a woman's intention to use breast-pumping breaks after returning to work	Cross-sectional	3, 5
5	Smith-Gagen et al[16]	2014	USA	Relationship between breastfeeding initiation and duration with laws supportive of breastfeeding enacted at the state level.	Cross-sectional	3, 4
6	Aikawa et al[17]	2015	Thailand	Association between mothers' work-related factors and breastfeeding practices	Cross-sectional	1
7	Bai et al[18]	2015	USA	Examine the nature and extent of accommodations offered to breastfeeding employees among New Jersey employers since the US federal Reasonable Break Time for Nursing Mothers law enactment.	Cross-sectional	3, 4, 5

No	Authors	Year	Location	Study Aims	Methodology	Policy
8	Atabay et al[19]	2015	UN member countries	Assess the trends in the share of countries guaranteeing breastfeeding breaks in the workplace and paid maternal leave that lasts until the infant is 6 months old	Cross-sectional	1, 3
9	Iellamo et al[20]	2015	WHO, Western Pacific Region	Determine the extent to which World Health Organization (WHO) policies protect, promote, and support breastfeeding women working at the WHO, Western Pacific Region	Cross-sectional	4
10	Kumar et al[21]	2015	India	Working women in India constitute a dominant and expanding pool of mothers. There is paucity of research focused on feeding behavior within this group.	Cross-sectional	1, 5
11	Avendano et al[22]	2015	Europe	Examines whether maternity leave policies influence women's mental health in older age	Cross-sectional	1
12	Shepherd-Banigan et al[23]	2016	USA	Examines the impact of workplace attributes on changes in depressive symptoms among working women with young children between 6 and 24 months of age	Cross-sectional	6
13	Andres et al[24]	2016	USA	The relationship between maternity leave and health outcomes has not been formally and comprehensively assessed to guide public health research and policy in this area. This review aims to address this gap by investigating both the correlates of maternity leave utilization in the us and the related health benefits for mother and child	Systematic Narrative Review	1
14	Majee et al[25]	2016	USA	Examine workplace barriers and facilitators to breastfeeding in a small rural American community following the passage of the Affordable Care Act in 2010	Qualitative: IDI	3, 4, 5
15	Zoritch et al[26]	2016	USA	To quantify the effects of out-of-home day-care for preschool children on educational, health and welfare outcomes for children and their families	Review	8
16	Shepherd-Banigan et al[27]	2017	USA	Examines whether paid sick leave and hours worked per week are associated with receipt of recommended well-child visits, preventive dental care, influenza vaccines, obesity screening, and vision screening among U.S. children aged 0 to 17 years whose mothers were employed using data from the Medical Expenditure Panel Survey	Cross-sectional	7
17	Rasheed et al[28]	2017	Bangladesh	To assess the support for IYCF in the national policy environment through policy analysis and stakeholder analysis and in so doing identify opportunities to strengthen the policy environment	Qualitative study	9
18	Kavle et al[29]	2017	Unspecified	To determine barriers to exclusive breast-feeding in twenty-five low- and middle-income countries and discuss implications for programs	Systematic review	1, 3
19	Oddo et al[30]	2018	Guatemala	Explore the pathways by which maternal employment might influence bodyweight in children	Qualitative	6
20	Jou et al[31]	2018	USA	To predict the likelihood of outcomes related to infant health, maternal physical and mental health, and maternal health behaviors by the use and duration of paid maternity leave	Cross-sectional	1

No	Authors	Year	Location	Study Aims	Methodology	Policy
21	Avendano & Panico[32]	2018	UK	Examined whether a policy that grants parents the right to request flexible work influences their health and well-being	Cohort	6
22	Wainaina et al[33]	2018	Kenya	Explores the experiences of middle-income women to understand their attitudes and practices of EBF and to contribute toward the Baby Friendly Hospital (BFHI) and Baby Friendly Community Initiatives (BFCI) programs in Kenya	Qualitative	1, 3, 4, 6
23	Tshering et al[34]	2018	Bhutan	To examine the prevalence of exclusive breastfeeding and its associated factors	Cross-sectional	1
24	Zhang et al[35]	2018	China	To explore mothers' breastfeeding experience throughout the breastfeeding period and to understand their challenges and support service needs at each stage	Qualitative	1, 3, 4, 5
25	Basrowi et al[36]	2018	Indonesia	To achieve expert consensus on developing a workplace-based lactation promotion model	Delphi method	1, 3, 4, 5
26	Li et al[37]	2018	Germany	To examine the impact of maternal and paternal work hours on overweight/obesity among children aged 1–6 years in Germany using longitudinal data.	Longitudinal study	6
27	Riaz & Condon[38]	2019	Pakistan	To describe the attitudes and experiences of breastfeeding mothers returning to full-time work as nurses in a tertiary hospital in Pakistan.	Qualitative	1, 3, 4, 6, 8, 10
28	Abou-ElWafa & El-Gilany[39]	2019	Egypt	To describe EBF rate using the 24-hour recall method and factors influencing breastfeeding practices among working women	Cross-sectional	1, 3, 4, 5
29	Morain et al[40]	2019	USA	To describe policies related to parental leave, breastfeeding, and childcare for faculty and staff at top schools of public health in the United States	Cross-sectional	1, 7, 8, 11, 12, 14
30	Stack et al[41]	2019	USA	To characterize determinants of resident maternity, leave and the effect of length of leave on maternal well-being	Cross-sectional	1, 7
31	Jameel et al[42]	2019	Cambodia	Investigated the health-seeking behaviors for maternal and infant care of female garment factory workers in Kampong Tralach district, Cambodia	Qualitative Study	1, 4, 7, 8
32	Widiastuti et al[43]	2019	Indonesia	To look at the relationship between exclusive breastfeeding practices and frequency of sick children and the productivity of health-care provider mothers	Cross-sectional	1, 11
33	Clark et al[44]	2019	Kenya	Demonstrates that limited access to affordable early childcare inhibits poor urban women's participation in paid work	RCT	2
34	Szczesna et al[45]	2019	Europe	To analyse the risks and consequences of working in the operating theatre during pregnancy	Literature review	6
35	Slopen[46]	2020	USA	Explores the links of employment and demographic characteristics on leave type and lengths of overall, paid, and unpaid leave in a large city in the United States	Cross-sectional	1, 12
36	Niel et al[47]	2020	USA	Reviewed recent studies on the possible effects of paid maternity leave on the mental and physical health of mothers and children	Literature review	1
37	Doran et al[48]	2020	USA	To study the effect of California's first in the nation paid family leave policy on maternal postpartum psychological distress for women overall and for disadvantaged groups	Cross-sectional	1, 11

No	Authors	Year	Location	Study Aims	Methodology	Policy
38	Horwood et al[49]	2020	India & South Africa	To explore attitudes and perceptions towards breastfeeding in the informal work environment among male and female informal workers	Qualitative	4, 6, 12
39	Luthuli et al[8]	2020	South Africa	This study explored how mothers navigate the tension between the need to work and the need to take care of a newborn baby, and how this affects their feeding plans and practices	Mixed-method longitudinal cohort	1, 5, 6, 11
40	Elsey et al[50]	2020	Bangladesh	To understand perceptions of, and demand for, center-based child-care in Dhaka, Bangladesh among poor, urban households, and test the feasibility of delivering sustainable center-based child-care	Mixed methods	8
41	Schafer et al[4]	2021	USA	Explore the themes of comfort with human milk and formula feeding among childcare administrators near Tampa, Florida	Qualitative	8
42	Kraus et al[51]	2021	USA	To determine the current state of parental leave policies for medical students at medical schools in the United States	Comparative study	1, 13
43	Agampodi et al[52]	2021	Sri Lanka	To identify barriers and facilitators for early initiation of breastfeeding and exclusive breastfeeding for 6 months in rural Sri Lanka	Qualitative study	1, 5
44	Vilar-Compte et al[53]	2021	Unspecified	To review workplace interventions to promote, protect and support breastfeeding practices among working mothers globally	Systematic review	3, 4, 5, 6
45	Ickes et al[54]	2021	Kenya	To understand the barriers and facilitating factors on the capacity to maintain EBF for the recommended 6-month duration among women employed in the commercial agriculture and tourism industries.	Qualitative study	1, 3, 4, 5, 6, 7, 8
46	Ahn et al[55]	2021	South Korea	To summarize the current state of the science on maternal adaptation for working mothers with infants or young toddlers in Korea and to analyze various influencing factors of maternal adaptation based on the ecological systems theory	Systematic review	5, 6, 7
47	Juarez et al[56]	2021	Sweden	To assess the unintended health consequences of various components of Sweden's parental leave policy, including eligibility for and uptake of earnings-based benefits	Quasi-experimental study	1, 13
48	Kebede & Seifu[57]	2021	Ethiopia	Compared the breastfeeding laws, policies, and arrangements in Ethiopia with international standards, recommendations, and evidence-based practices	Commentary	1, 4, 5, 10
49	Chen et al[58]	2021	USA	Describes an integrated dataset that was used to understand the relationship between participation in a nutrition assistance program and low-income children's breastfeeding outcomes	Descriptive study	5
50	Ongprasert & Siviroj[59]	2021	Thailand	To investigate factors associated with breastfeeding for at least one year among women in Chiang Mai, Thailand	Cross-sectional	6
51	Campos & Hawkins[60]	2022	Mexico	To determine whether household income moderated the association between maternal employment status (defined as unemployed, formal, and informal full- and part-time employed) and any breastfeeding for ≥ 6 months.	Cross-sectional	6
52	Carroll et al[61]	2022	Brazil & Ghana	To test the adaptability of the costing approach in countries with different informal sector challenges.	costing methodology	2

No	Authors	Year	Location	Study Aims	Methodology	Policy
53	Tomori et al[62]	2022	USA	To update the evidence base since 2016 using a review of reviews approach	Review of reviews	3, 4, 5
54	Gbagbo & Nkrumah[63]	2022	Ghana	To assess availability and implementation of breastfeeding policies and programs in three public universities in Ghana	exploratory-descriptive-case study	4, 5
55	Barasinski et al[64]	2022	France	To assess the percentage of departments in Auvergne with an appropriate space for pumping milk at work	Cross-sectional	3, 4
56	Walker et al[65]	2022	Texas	To provide an overview of essential areas of knowledge related to practice for neonatal nurses and midwives who care for breastfeeding mothers and babies	Discussion paper	5
57	Kim et al[66]	2023	South Korea	To shed light on how the work hour reduction policy may differently affect workers with different levels of resources and support by demographic and socioeconomic status	Quantitative study	6
58	Amer & Kateeb[67]	2023	Jerusalem	To describe breastfeeding habits and demographic factors influencing these practices in Jerusalem Governorate.	Cross-sectional	6
59	Al-Ghannami et al [68]	2023	Oman	To examine individual barriers and supports to exclusive breastfeeding (EBF) and identify potential policy and programmatic interventions in Oman	Mixed method	5
60	Andrade & Gil[69]	2023	Ecuador	To understand the trade-off between the time mother, devote to work and child-caring activities	Quantitative study	5
61	Namiiro et al[70]	2023	East Africa	To explore and document the unpriced costs parents incur following birth of a preterm infant in the first year of life in a low resource setting.	Qualitative study	5
62	Pac et al[71]	2023	California	To examine the effects of paid parental leave policies on health	Cross-sectional	13
63	Borrell-Porta et al[72]	2023	UK	To study whether the experience of 'employment during motherhood' (EDM) exerts an effect on attitudes towards the welfare effects of EDM, which proxy gender norms with regards to employment	Quantitative study	5
64	Sprague et al[73]	2024	USA	To investigate how eligibility criteria in the Family and Medical Leave Act (FMLA) and Affordable Care Act (ACA) affect access to unpaid parental leave and breastfeeding breaks and assessed affordability and alternative policy models	Quantitative study	13

From 64 literatures which were elaborated in **Table 1**, we managed to identify 13 policies related to child rearing for working mothers in the workplace. The distribution of policy included in the literature were presented in **Table 2.** Some literature included more than one policy; hence the frequency was based on the occurrence of the policy across the 64 studies.

From **Table 2** we can see the most policy was "paid maternity leave", being the most common policy that was regulated throughout the globe. A Delphi method study in Indonesia found that "paid maternity leave" was 1 out of 2 most important indicators of a workplace-based lactation promotion.[36] Followed by breast-pumping education and support (including but not limited to the availability of policy for breastfeeding, health, and nutrition counselling also encouragement from employers and work peers) along with breast-pumping facilities (comfortable and sufficient breast-pumping room, including refrigerator for breastmilk storage). The least talked about policies was "IYCF practice &

support among working mothers" with only one literature focusing on this topic.

Regarding implementations and implications of each policy, we classified them into 6 groups and detailed each in the next part of the article. First group, employee leave policy, including: paid maternity leave, paid sick/ medical leave, paid childbearing leave, also paid and unpaid parental leave. The second group is the breastfeeding related policy, which includes: breast-pumping education and support, facilities, also breaks during working hours. The third group focuses on flexible working arrangements policy, which covers flexible time/ schedule work arrangements and flexible place of work (work from home). Fourth group is day care policy. Childcare policy which covers childcare subsidies and bringing children to work is the fifth group. The last group will cover the IYCF practices and support policy in workplaces.

Table 2. Available workplace policy for working mothers

No	Policy	Frequency
1	Paid maternity leave (pre- and post-partum)	30
2	Breast-pumping education and support	21
3	Breast-pumping facilities	17
4	Breast-pumping breaks	16
5	Flexible working (time and/or place)	16
6	Daycare facility	7
7	Paid sick/ medical leave	6
8	Paid childbearing leave	4
9	Paid parental leave (mother and father)	4
10	Unpaid parental leave (mother and father)	3
11	Childcare subsidy	3
12	Bringing child to workplace	2
13	Infant and Young Children Feeding practices & support	1

2. Implementation and Implications of Child Rearing Workplace Policy

2.1 Employee Leave Policy

Employee leave policy includes paid maternity leave, paid sick/ medical leave, paid childbearing leave, unpaid parental leave, and unpaid parental leave. The International Labor Organization, which covers 178 countries as their member, has been in an agreement for Maternity Protection Convention No. 183 since the year 2000. In which paid maternity leave was obligated to working mothers with a duration of not less than 14 weeks.[6] Atabay et al.,[19] explored the implementation of maternity leave in UN countries and revealed that in 2014, 48 countries did not provide paid maternity leave as their policy. Sadly, this policy was proven to be discriminatory. In Bhutan, South Asia, this policy differentiates between civil servants (6 months) and corporate/private employees (3 months), resulting in numbers of nonexclusive breastfeeding.[34] The discrimination was most prominent for informal working mothers in South Africa and Ethiopia due to unavailable paid maternity leave. Their financial conditions forced them to return to work early because they could not afford taking an unpaid leave. This condition resulted in shorter duration of breastfeeding or even as far as abandoning breastfeeding practices for their child.[8,57]

The American Academy of Paediatrics recommended 12 weeks paid parental leave based on previous studies and its advantages for the child. The United States of America was one of the countries that have a paid parental leave policy. Nevertheless, a study in their 12 top medical schools along with a different study in 25 top schools of public health reported that employers only offered a mean length of 8.6 weeks of paid maternity leave for their staff.[40,74]

This implementation gap also existed in Pakistan. The Maternity Benefit Ordinance of Pakistan ordered that full-time working mothers were eligible for 12 weeks of paid maternity leave, but a study by Riaz & Condon[38] in a tertiary hospital of Pakistan revealed that none of it was provided by the hospital as the employer.

Among the included studies, China held the longest paid maternity leave with a length of 98 days and an extra 15 days for mothers who went through caesarean delivery or multiple

deliveries.[35] A more prevailing effort was displayed by South Korea as they granted paid vacation breaks in addition to paid sick leave and maternity leave. They believe promoting a thriving maternal transition experience for working mothers was not only beneficial for the mother/family's health but might increase women's willingness to give birth to subsequent children and further contribute to overcoming the historically low birthrate in Korea.[55]

Several studies explored the relationship between employee leave policy implementation and its implications for working mothers and their children. Paid maternity leave has been proven to have several benefits for both working mothers and their children, namely:[22,47,48,75]

1. Mental health quality: a decrease in maternal postpartum depression and domestic abuse at home, also an increase in children's attachment and development along with better stress management. Paid and longer maternity leaves also associated with a reduction of postpartum depression symptoms in high-income countries, which could protect mothers, especially new mothers, in adjusting to motherhood.
2. Physical health quality: a decrease in infant mortality and rehospitalisation of mothers and infants, in addition to an increase in paediatric visit attendance and punctual infant immunisations.
3. Breastfeeding practice: an increase of practice initiation and longer duration of breastfeeding for infants. Aikawa et al.,[17] revealed that mothers who returned to employment more than equal to 3 months after giving birth proved to practice a longer exclusive breastfeeding than mothers who returned less than 3 months.[17] Not only was paid maternity leave beneficial for the employees and their children, a study in the USA suggested that working mothers who were offered 6-12 weeks maternity leave by their employment place were 6 times more likely to return to work,[12] decreasing the employee turnover.
4. Productivity of the mother: extended paid leave for the mother might strengthened the labour market attachment of mother and increased maternal income, especially on first time mothers. A study found the relative productivity of women without children is significantly higher than women with children even generally higher than the productivity of men in the same occupation. However, women were reported to be less productive than men in low skilled jobs. This indicated women with children were not adequately facilitated in workplaces. [76]

Whereas it was suggested that unpaid leave, may benefited wealthier working women but had a different outcome for low-income family children where it could potentially exacerbate health disparities.[24] A study by Khan[77] found a decrease of 1.9–5.2 percent in the infant, neonatal, and under-five mortality rates following the implementation of paid maternity leave. Although other findings by Huebener et al.,[78] found there were no effects of the changes in parental leave benefits on child development across various socio-economic groups, and consequently no effects on socio-economic development gaps. Mixed findings regarding parental leave policy and health outcomes on children were found in previous studies, but it was apparent that the timing of the parental leave policy mattered.

2.2 Breast-pumping Related Policy

Atabay et al.,[19] noted that in 2014, 51 countries did not guarantee breastfeeding breaks in any form and 4 countries provided only unpaid breaks or breaks that did not cover the first 6 months of life. An expert panel study in Indonesia expressed that employees should have breast-pumping breaks every 3 hours at the workplace and deemed it as one of the two most important indicators for a workplace-based lactation promotion model.[36] Kavle et al.,[29] expressed the implementation of breast-feeding breaks in low-and middle-income countries required more attention, as it was reported to be one of the barriers toward exclusive breastfeeding practices barrier for them.[29]

Policy concerning breast-pumping physical facilities in workplaces was as important as the breast-pumping breaks. Working mothers of Egypt reported that their workplace had no breastfeeding facilities and support apart from nursing breaks for mothers in the formal sector.[39] China was an exemplary country for raising breast-pumping related policies. Chinese female employees were entitled for an hour breastfeeding break every day for the first year after giving birth. However, emotional pressure and discouragement from colleagues and higher-ups were reported in workplaces.[35] Which indicates that education to raise awareness on the importance of breastfeeding was not to be limited to the mothers but also to the surrounding environment.

Working mothers of Western Pacific WHO suggested that having a private room with a chair, table, electric outlet, and refrigerator were much needed physical facilities for comfort and convenience while expressing breastmilk.[79] The importance of support and trust from employers were apparently important, as the working mothers in Cambodia garment factory workers were equipped with breast-feeding facilities but they were refusing to use it due to lack of trust and support.[42]

Breast-pumping education and support policy ranging from encouragement and support from peers, education regarding breastfeeding, to counselling with lactation experts. The United States of America recognized the importance of breast-pumping education and support policy; therefore, The Affordable Care Act was enacted in year 2010. Unfortunately, some employers in the rural communities showed lacked compliance to the law by not providing sufficient education and support for their working mothers.[25]

A study among health-care workers mothers in Indonesia reported that healthcare workers mothers who practiced exclusive breastfeeding were 3.22 times less likely to experience sick children, compared to those who did not practice exclusive breastfeeding. There was also a significant relationship between breastfeeding practice and the productivity of healthcare working mothers. Healthcare working mothers who practiced exclusive breastfeeding were 2.99 times more productive than those who did not.[43] This highlighted the importance of breastfeeding feasibility for working mothers through breast-pumping related policy, including: facilities, paid breaks, reduced working hours, education & support.

Breastfeeding workplace intervention, mainly: lactation room, lactation breaks, and organizational policies were key strategies to help increase the duration of breastfeeding and prevented early introduction of age inappropriate feeding.[53]

2.3 Flexible Working Arrangement Policy

Flexible working arrangement whether as time or place of work for the working mothers, reported in result in more time spent for early childhood education and care (ECEC) by the parents. In Poland it was recognized as a law for breastfeeding working mothers to cut back their working hours, but it seemed this law was not implemented for healthcare professionals.[45] The Kenya Bill of Health also supported working mothers to breastfeed. Farm and hotel managers reported to support the bill through flexible work schedules, in which they revealed that mothers prefer to arrive later to work to ensure their child was breastfed properly.[54]

A flexible working policy in India, which was working from home, enabled working mothers to breastfeed their children during work hours and granted them privacy to do so. This was important because it was reported that male vendors in India disliked the idea of mothers to breastfeeding in the public due to privacy and respect concerns.[49]

This policy did not come with its inhibitions. In lower-income households displayed that children were less likely to be breastfed for more than 6 months when the mothers were an informal part-time employee. Whereas among higher-income households, children were less likely to be breastfed for more than 6 months when the mothers were a formal full-time employee. This outcome was also observed in a study based on maternal employment study in Jerusalem.[67] It

seemed that the working hours affected different demographics of working mothers differently.[80]

Reduction in working hours for mothers in employment should be considered by workplaces as a study in Germany indicated that 35 or more maternal work hours per week was associated with an elevated risk of childhood overweight and obesity (OR=1.64, 95% CI 1.10 to 2.44, p=0.02). Maternal full-time work hours were also associated with higher risk for childhood overweight and obesity. Although these findings were only in families with medium to high income but not in families below the income median.[37]

Flexible working place or work from home arrangements proved to have benefits not only for the children, but also the mothers. A decrease in depression score was observed in working mothers with children between 6-24 months in the USA.[23] A different outcome was reported in working mothers in the UK who were protected under The Flexible Working Act. They stated that flexible working arrangements had no impact on mothers' health and well-being.[32]

2.4 Daycare Policy

High quality and affordable childcare facilities were available to support working families within diverse European countries.[55] Meanwhile, only several farms in Kenya that reported to have subsidised on-site daycare. This arrangement allowed mothers to breastfeed during working hours. Unfortunately, not all farms in Kenya were equipped with on-site daycare facilities.[54] Some of the mothers had to travel from their workplace to the daycare which prevented them from practicing exclusive breastfeeding. Hence the distance of the daycare combined with transportation measures was crucial to the success of this policy.

The implementation of daycare policy was urgently needed for low-income families in Bangladesh, since it was reported the need for daycare among slum households was 3.8 times higher than those of non-slum households in Dakha area. Approximately 24% of working mothers in Dakha had been turning-down paid work due to lack of childcare and the other 84% were willing to pay up to ~$3.30 per month to use a daycare.[50] Women in sub-Saharan Africa also expressed the conflict between day care and paid work responsibilities. As quoted from Clark et al.,[44] from his study in Kenya, "Yet, ironically, in the continent with the highest fertility rates, NGOs, policymakers, and researchers generally perceive the least conflict between women's childcare responsibilities and their engagement with paid work. Programmes that fall under the umbrella of WEE in sub-Saharan Africa typically emphasise increasing women's education, job training, and access to microcredit, but they do not focus on providing subsidized daycare." Expressing urgency for emergence of daycare, preferably subsidised.

One of the challenges of on-site daycare in workplaces was identified by Gbagbo & Nkrumah.[63] They stated financial feasibility proved to be a major hurdle for employers to launch childcare policy/programs. Not to be disheartened, subsidized day care was proven to be cost-effective, due to the effects that it would bring which was increased maternal employment and human capital development, which could far outweigh the cost of its implementation.[44]

2.5 Childcare Policy

Some studies included childcare policy as one of the child rearing workplace policies. Childcare policy in this study consisted of childcare subsidy and bringing child to work. In Germany, childcare subsidies were offered by the German government through Parental Allowance Plus and Partnership Bonus. This initiative provided financial aid for mothers and fathers to work part-time.

The effect of childcare subsidy was important to be seen from an economic perspective. Carroll et al.,[61] used an estimation model to predict the cost of maternity cash transfer or childcare subsidy in informal sectors of Brazil and Ghana, where it respectively would cost them 0.004-0.02% of the GDP and 0.076-0.28% of the GDP, respectively. These shares reflect lower investments in accordance with the estimated cost of not breastfeeding.

A study in the USA revealed that childcare subsidies were associated with a decrease in physical and mental health of the working mothers. They even reported an increase in anxiety, depression, and parenting stress in mothers. Increased psychological and physical aggression towards children were also observed in this condition. A close and thorough evaluation was much needed so that this policy would not have such detrimental effects on the well-being of children.[14]

As for the bringing child to work policy, some employers prohibited this action. In a tertiary hospital in Pakistan, bringing a baby to work was apparently a routine occurrence amongst nurses even though it was against the hospital's permission. Fortunately, the nurse management tolerated it to some degree as a means for the nurses to work.[38]

2.6 IYCF Practices & Support Policy

IYCF or known for Infant and Young Children Feeding has been known to impact children in a positive light. Improvement of health, development, nutritional status was reported therefore increasing their chance of survival.[81] Enhancing nutrition, health, and overall development in children aged 0 to 23 months is of utmost importance to prevent inadequate feeding practices during this critical period.

Lack of awareness regarding IYCF practices was shown in working mothers of informal work environments in India and South Africa. Upon return to their workplaces many mothers changed their infant feeding practices by adding breastmilk substitutes. Non-breastmilk fluids such as formula milk, buffalo milk, and non-nutritive fluids (Rooibos tea) were reported to be some of them. Some mothers also raised their concerns regarding 'spoilt' breastmilk if they express it during working hours. Hygiene and safety were also some of the problems that caused working mothers in informal work environments to avoid expressing breastmilk in workplaces. Counselling mothers on optimal feeding behaviour was a potentially a successful intervention to convert awareness into actual practice for working mothers in India,[21] opening opportunities for other workplaces to start implementing this policy.

Woldetensay et al.,[82] reported better maternal social support were associated with higher scores of infant feedings. This highlighted how important it is to support mothers from all sectors possible. The attention of primary caregiver, mainly mothers in some cultures, is essential to ensure the child received proper practices of IYCF, including the monitoring of the child's feeding to ensure the frequency also quality of feeding and diet during the complementary feeding period. A proper IYCF practice can lower the risk of child malnutrition, reduced the vulnerability to illnesses (such as acute respiratory infections, diarrheal diseases), and reduced the risk of childhood mortality.[83] Moreover, low variety complementary feeding (related to Minimum Dietary Diversity) had been linked to incidence of stunting by 1.72 times, compared to those who ate various type of complementary feeding. Frequency of complementary feeding also had association with increase incidence of stunting by 1.85 times.[84]

Due to the importance of IYCF practices and yet the lack of literature in this sector, development of IYCF supporting policies in the workplaces was much needed and encouraged for further research.

Conclusion

Child rearing workplace policies are a complex multisectoral effort. The proper implementation could result in positive implications for working mothers and their children. This scoping review explored the available child rearing workplace policy and how those current policies are implemented. Its implications could go beyond employers, the employees, but also their families by increasing nutritional and health status of the child, hence increasing the quality of life of the people surrounding it. Opportunities for actions to facilitate a better motherhood and working experience must come in awareness to better support working mothers.

Further research and effort into the development, implementation, and evaluation of the topic may result in increased productivity for workplaces and healthier outcomes for working mothers and their children.

Conflict of interest

The authors declare there is no conflict of interest regarding this article.

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ORIGINAL ARTICLE

Impact of an oral nutritional supplement on nutritional status in older adults with malnutrition: A randomized controlled trial

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Abstract

Background: The aging population is expanding at an unprecedented rate, leading to a significant increase in the prevalence of malnutrition among older adults. Oral Nutritional Supplements (ONS) have emerged as a widely accepted strategy to address the nutritional needs of this demographic.

Objective: This study aimed to evaluate the impact of an ONS on the nutritional status of malnourished older adults.

Methods: This was an open-label, randomized-controlled, parallel-group, single-centered study. Recruitment criteria were age ≥60 years, and mini nutrition assessment-short form (MNA-SF) score ≤11. A total of 50 participants were randomly assigned to the intervention (IG) and control (CG) groups (1:1 ratio). The IG received 200 mL of ONS as a bedtime drink for 12 weeks, while the CG received 200 mL of water. Nutrition status, biochemical analysis, and dietary assessment were performed at the beginning and end of the study.

Results: Forty-two participants (IG: n=20, and CG: n=22) completed the study. After 12 weeks, the IG showed a significant improvement in the MNA-SF score ($p<0.001$) compared to the CG ($p=0.118$). The IG experienced a substantial increment in the vitamin D level ($p=0.002$). No significant improvements were found in the serum albumin and haemoglobin levels in either group. The intervention led to significant increases in daily intake of energy ($p<0.001$), carbohydrate ($p=0.013$), protein ($p<0.001$), and fat ($p<0.001$) in comparison to the control group.

Conclusion: Supplementing with an ONS, along with a regular diet, significantly improved nutritional status, some biochemical parameters, and daily intake of energy and macronutrients in older adults with malnutrition.

Keywords: biochemical parameters, malnutrition, nutritional status, older adults, oral nutritional supplement

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Introduction

Nutritional assessment is crucial for assessing nutritional status and planning necessary interventions. A comprehensive assessment of nutritional status requires several measurements including anthropometry, biochemical, clinical, and dietary details. Consequently, various nutritional screening tools have been validated for different populations. The mini nutritional assessment (MNA) has been widely recommended as a valid tool for screening malnutrition among older adults.[1]

The risk of malnutrition can be accurately, specifically, and sensitively identified using the MNA. The MNA allows for the detection of cognitive and functional impairments and difficulties in eating, which is often associated with malnutrition in older adults before a severe change in weight or serum protein occurs.[2] Guigoz Y. et al.,[3] suggested that the MNA is a reliable screening and assessment with clearly defined thresholds and it should be incorporated in the geriatric assessment and proposed in the minimum data set for nutritional interventions. Interventional studies suggest that timely intervention is associated with increases in MNA scores and prevents weight loss in malnourished older adults.[3]

Improving nutritional status in older adults is important for the maintenance of good health, functional independence, lower disease risk, and quality of life.[4] A quantum of studies has used the MNA to evaluate the effectiveness of various nutritional interventions on the nutritional status of older adults. As a potential nutritional intervention, the efficacy of using an ONS has been evaluated in several studies involving malnourished older adults and has shown beneficial effects on nutritional status as measured by improvement in MNA scores.[5-7] A recent interventional study by Na et al.,[5] studied the impact of using an oral nutritional supplement (ONS) on nutritional status in malnourished older adults. The intervention group showed a significant increase in the MNA score from 19.7±3.0 to 21.1±2.6 (p=0.004), while the control group showed no significant change (p=0.90).

To date, only a limited number of studies have explored the impact of ONS on biochemical parameters in older adults, with reported findings contradicting each other. Pereira et al.,[8] reported that ONS increases serum immunoglobulin, myoglobin, total protein, vitamin E, and magnesium in malnourished older adults. Another extensive study done by Chew et al.,[9] observed the beneficial effect on vitamin D levels in response to 24-week oral nutritional supplementation. Conversely, a study done by Huynh et al.,[10] among malnourished older adults reported no significant difference in biochemical parameters between the intervention and control group after 12-week supplementation. As a form of enteral nutrition, ONSs provide calories, high-quality protein, and micronutrients that are recommended to fulfill the basic nutritional requirements of malnourished older adults when regular diet alone is insufficient.[11]

Previous studies have also demonstrated significant increases in the intake of energy, carbohydrate, protein, and fat.[9, 12] In this context, the purpose of the current study was to evaluate the impact of an ONS as a bedtime drink for malnourished older adults, on MNA score, biochemical parameters, and energy and nutrient intake.

Methods

Study design

This study was an open-label, parallel-group, randomized-controlled clinical trial conducted among institutionalised Sri Lankan older adults with or at risk of malnutrition between January 2023 and May 2023. The study protocol was reviewed and approved by the ethics review committee of the Sri Lanka Medical Association (ERC/22-005). Prior to study participation, each participant voluntarily provided written informed consent. The detailed protocol regarding the methodology has been published elsewhere [13] and a summary is given below. This clinical trial is registered at Sri Lanka Clinical Trials Registry (SLCTR/2022/021).

Participants

Participants were recruited from the Moratuwa Social Service Elderly Care Home, a long-term care facility in Western Province, Sri Lanka. Participants were screened for malnutrition using the mini nutrition assessment short form (MNA-SF) questionnaire. Older adults with malnutrition or at risk of malnutrition (MNA-SF score ≤ 11) were recruited. Inclusion criteria were age ≥ 60 years and residing in the selected elderly care institution for more than one year. Exclusion criteria were inability to consume food orally, being bedridden, intolerance to milk products, being on an end-of-life care pathway, having no capacity to consent, or any acute medical conditions.

Sample size

The main outcome was the percentage who achieved at least 5% weight gain in the intervention group (IG) compared to the control group (CG). Considering the 5% weight gain in the IG compared to the CG, 25 participants were required in each group (5% alpha, 80% power, drop-out rate 20%). The detailed sample size calculation is presented previously published study protocol [13].

Intervention

Participants were randomly assigned to the IG or CG, to receive an ONS dissolved in 200 mL of water [Entrasol Platinum, Kalbe Pvt. Ltd., Indonesia] or 200 mL of water, respectively. The detailed nutritional composition of the ONS is summarized in Supplementary **Table 1**. Participants were instructed to consume the ONS daily before bedtime (between 9-10 pm) for 12 weeks. Both IG and CG consumed the same diet during the intervention period as all participants received the standard menu served in the institution.

Outcome measures

Nutritional status, biochemical assessment, and dietary assessment were performed at baseline (week 0), and post-intervention (week 12) visits.

- *Nutritional status*
  The MNA-SF questionnaire was used to determine the nutritional status. The MNA score indicates three different levels of nutritional status; well-nourished (12-14 points), risk for malnutrition (8 – 11 pints), and malnourished (0-7 points) [14]. MNA-SF score was measured on all participants in both groups, at baseline and after 12 weeks.

- *Biochemical parameters*
  All biochemical parameters were tested at an accredited laboratory (Nawaloka Metropolis laboratory, Nawaloka Hospital PLC, Sri Lanka) following the standard procedures. A venous blood sample of 10 – 12 mL was collected for the assessment of the following biochemical parameters.
  - Full blood count: Full blood count was analyzed using SYSMEX XE-2100 Haematology Automated Analyser.
  - Total 25-(OH) vitamin D: The serum was separated from the venous blood sample collected and tested within 3 hours using MAGMLUMI 2000 analyzer by Competitive Chemiluminescence Immunoassay (CLIA). This test quantitatively measures the sum of both 25-(OH) vitamin D3 (cholecalciferol) and 25-(OH) vitamin D2 (Ergocalciferol) in the specimen.
  - Serum albumin: The serum was separated from the venous blood sample and mixed with a bromcresol green dye reagent. The resulting colour change was measured using a spectrophotometer (Shimadzu 1800UV/Visible Scanning Spectrophotometer, Japan). The absorbance was converted into albumin concentration.
  - Total serum cholesterol: Total cholesterol was determined using a Cobas c501 auto analyzer using an electrochemiluminescent immunoassay (ECLIA, Roche Diagnostics).

- High sensitivity C - reactive protein (hCRP): The Roche Cobas c501, which is an in vitro diagnostic test system, was used to quantitatively determine the C reactive protein (CRP) in human capillary whole blood and serum, EDTA K2/K3 and lithium heparin anti-coagulated whole blood and plasma by photometric measurement.

- *Dietary intake*
  A 24-hour dietary recall was conducted by trained dieticians to assess the daily dietary intake of the study participants. The quantity of food was recorded using household measures (teaspoon, tablespoon, teacup, coconut spoon, etc.) with the help of caregivers. The domestic measures of the consumed solid foods were weighed in grams using a digital kitchen scale and the liquid foods were measured in millilitres. The recorded weights and volumes of the consumed food items were entered into Nutri-Survey (EBISpro), which was adjusted with Sri Lankan food composition data [15] to calculate the daily intake of energy, carbohydrate, protein, and fat.

Statistical analysis

Participants who may have deviated from the study protocol or dropped out during the study were excluded and per-protocol analysis was performed. Data analysis was performed using IBM SPSS version 23 statistical software package (SPSS Inc., Chicago, IL, USA). Given the small sample size (n=50), the Shapiro-Wilk test was conducted to assess the normality, with a significance level set at a p value less than 0.05 indicating a significant deviation from normality. Baseline values were compared using independent sample t-test and expressed as the mean and standard deviation (mean±SD) for continuous variables, while categorical variables were compared using chi-square test and presented as values and percentages.

To analyze the changes in measurements between the two groups, different statistical tests were used based on the distribution of the data. The independent sample t-test was used for parametric distributions, while for non-parametric distributions, the Mann-Whitney U test was used. When comparing the pre-and post-intervention mean values of the measurements, the paired sample t-test was applied for parametric distributions, and for non-parametric distributions, the Wilcoxon Signed Rank test was applied. A value less than 0.05 was considered statistically significant.

Results

Baseline characteristics

At the end of the 12th week, out of the total fifty participants initially enrolled, twenty in the IG and twenty-two in the CG completed the study. The CONSORT flow diagram depicting the progress through the phases of the study for the two parallel groups is shown in **Supplementary Figure 1**. The following results are based on the analysis of data from forty-two participants who completed the study. The mean age of the IG was 75.4±6.1 years, and the CG was 74.8±5.2 years (p=0.732). At the baseline, there was no significant difference in MNA-SF scores between the two groups (IG; 8.72±1.95 vs. CG; 9.56±1.45, p=0.090) (**Supplementary Table 2**).

Nutritional status

The IG showed a significant improvement in mean MNA-SF score (8.75±1.83 to 10.85±1.57; p<0.001) compared to the CG (9.27±1.24 to 8.77±1.68; p=0.118) (**Figure 1**). All the participants had a low MNA-SF (≤11) on inclusion. At the end of the 12th week, 45% of the participants in the IG had achieved normal nutritional status according to the mini nutrition assessment short form (MNA-SF score range of 12-14) (Figure 2). In the CG, only 5% of the participants reached normal nutritional status, while 23% were malnourished and 72% were at risk of malnutrition.

Biochemical parameters

Table 1 presents the pre- and post-interventional changes in biochemical parameters within and between the two groups.

A significant increase in vitamin D level was observed in both the IG (14.76±4.70 to 23.96±4.18 ng/mL; p<0.001) and CG (15.36±5.65 to 19.32±7.20 ng/mL; p<0.001), with the IG showing a significantly higher increase than the control group (IG: 9.20±5.29 vs. CG: 3.96±4.85 ng/mL; p=0.002) **Figure 3**. Serum albumin levels decreased in both groups, but CG lost significantly more than IG (IG: -0.20±0.26 vs. CG: -0.40±0.19 g/dL; p=0.006).

The pre- to post-intervention total serum cholesterol level was significantly reduced by -21.2±16.3 mg/dL (p<0.001) in the IG and by -17.4±38.0 mg/dL (p=0.044) in the CG. However, there was no significant difference in the changes of total serum cholesterol levels between the two groups (p=0.679). An elevation in hCRP was observed in both groups (IG: 3.12±7.97 vs. CG: 3.03±10.04 mg/L; p=0.974), but it was not significant.

Dietary intake

The changes in dietary intake after nutritional intervention are shown in **Table 2**. The levels of energy (p<0.001), carbohydrate (p=0.013), protein (p<0.001), and fat (p<0.001) were significantly increased in the IG compared to the CG.

Adverse events

The ONS was well tolerated, and no serious adverse effects were reported.

Discussion

In this study, we observed that supplementation with an ONS specifically designed for malnourished older adults improves the nutritional status, biochemical parameters, and dietary intake, of the participants in the IG compared to the CG participants.

Poor nutritional status is a common cause for concern in older adults and their caregivers, particularly those who are hospitalized or institutionalized, as it is strongly associated with elevated morbidity and mortality. The current study observed an increment of 2.1 score points in the mean MNA-SF within the IG. This aligns with previous research indicating that ONSs yield positive effects on the nutritional status of malnourished older adults. For instance, Zhang and colleagues observed a 2.1-point rise in MNA-SF score among community-dwelling older adults with malnutrition who received the supplementation.[6] Chen et al.,[16] similarly reported a significant improvement in MNA-SF score (from 9.07±1.83 to 12.04±1.31) in participants who received nutritional supplement drinks compared to those receiving nutritional education instead. Na et al.,[5] used MNA long form, revealing a notable increase in nutritional status among frail older adults at risk of malnutrition with the use of oral nutritional supplementation. An observational study done in 38 nursing homes in Spain, reported that malnourished older adults increased their MNA-SF score by 4 points in response to energy and protein-rich ONS for 3 months.[17] It is important to note that variations in MNA score changes across studies may arise from differences in ONS nutritional composition, study duration, sample size, and participants' health status. Nevertheless, the collective evidence supports the crucial role of ONS in enhancing the nutritional status of older adults with malnutrition.

In turn, the impact of the ONS on biochemical parameters showed a substantial improvement in the vitamin D level in the IG. At the baseline, the study sample was deficient in vitamin D (Supplementary Table 2). Within the relatively short study period, the mean vitamin D level increased by 9.20 ng/mL in the IG, and this increment is significantly high when compared to the CG. One serving of the intervention product provides 2.8 mcg (112 IU) of vitamin D (Supplementary Table 1). Although there is an improvement in vitamin D levels, still many participants remain deficient in vitamin D.

Table 1. Changes in biochemical parameters over 12-weeks

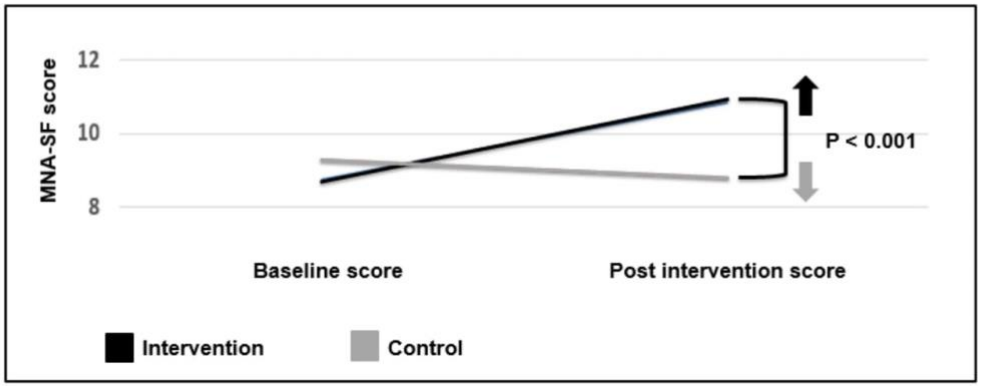
Serum Biomarker	Intervention group (n=20)		p value[(a)]	Control group (n=22)		p value[(a)]	p value[(b)]
	Pre-value	Post-value		Pre-value	Post-value		
WBC (Per Cu mm)	7638±2104	6772±1655	0.013	7450±1940	6265±1547	<0.001	
WBC change (Per Cu mm)	-866±1422			-1185±1126			0.422
Haemoglobin (g/dl)	11.22±1.11	11.34±1.04	0.378	11.67±1.16	11.66±1.02	0.940	
Haemoglobin change (g/dl)	0.12±0.59			-0.01±0.56			0.473
RBC (10^6 /UL)	3.93±0.48	3.76±0.45	0.004	4.05±0.48	3.89±0.44	0.004	
RBC change (10^6 /UL)	-0.17±0.23			-0.16±0.23			0.930
Platelet count (Per Cu mm)	300000±94780	287000±87647	0.184	293000±58899	290000±112669	0.832	
Platelet count change (Per Cu mm)	-13000±42541			-3273±71261			0.595
Vitamin D (ng/mL)	14.76±4.70	23.96±4.18	<0.001	15.36±5.65	19.32±7.20	0.001	
Vitamin D change (ng/mL)	9.20±5.29			3.96±4.85			0.002*
Serum albumin (g/dl)	4.28±0.23	4.08±0.24	0.003	4.38±0.35	3.98±0.43	<0.001	
Serum albumin change (g/dl)	-0.20±0.26			-0.40±0.19			0.006*
Total serum cholesterol (mg/dl)	166.2±44.2	145.0±45.0	<0.001	208.4±53.1	191.0±51.84	0.044	
Total serum cholesterol change (mg/dl)	-21.2±16.3			-17.4±38.0			0.679
Hs-CRP (mg/L)	1.28±1.46	4.40±8.57	0.105	1.49±1.52	4.52±10.12	0.182	
Hs-CRP change (mg/L)	3.12±7.97			3.03±10.04			0.974

Values are mean ± standard deviation, *, p value statistically significant. [a], Paired sample t-test or Wilcoxon signed rank test. [b], Independent sample t-test or Mann-Whitney U test. WBC; white blood cell, RBC; red blood cell, Hs-CRP; high sensitivity C reactive protein.

Table 2. Comparison of the impact of ONS on daily dietary intake between the two groups

Energy and macronutrient	Intervention group (n=20)		p value[(a)]	Control group (n=22)		p value[(a)]	p value[(b)]
	Pre-value	Post-value		Pre-value	Post-value		
Energy (kcal)	1346.20±157.33	1651.60±162.54	<0.001	1381.10±143.58	1379.10±160.56	0.901	
Difference in energy intake (kcal)	305.40±68.03			-1.99±74.22			<0.001*
Carbohydrate (g)	212.58±34.64	250.85±42.47	<0.001	219.43±36.68	225.63±42.15	0.522	
Difference in carbohydrate intake (g)	38.27±34.20			6.19±44.64			0.013*
Fat (g)	39.12±6.89	57.79±10.16	<0.001	40.06±7.55	34.81±15.20	0.089	
Difference in fat intake (g)	18.66±10.41			-5.24±13.80			<0.001*
Protein (g)	33.84±6.04	48.46±7.91	<0.001	35.48±6.41	38.05±5.63	0.171	
Difference in protein intake (g)	14.62±8.82			2.57±8.51			<0.001*

Values are mean ± standard deviation, *, p value statistically significant. [a], Paired sample t-test or Wilcoxon signed rank test. [b], Independent sample t-test or Mann-Whitney U test.



Nutritional Status	Intervention (n=20)		p value (a)	Control (n=22)		p value (a)	p value (b)
	Pre-value	Post-value		Pre-value	Post-value		
MNA-SF score	8.75±1.83	10.85±1.57	<0.001	9.27±1.24	8.77±1.68	0.118	
△MNA-SF score	2.10±0.97			-0.50±1.44			<0.001

Figure 1: Change in the MNA-SF score between the intervention and control group. MNA-SF; mini nutrition assessment short form. a, Paired sample t-test. b, Independent sample t-test.

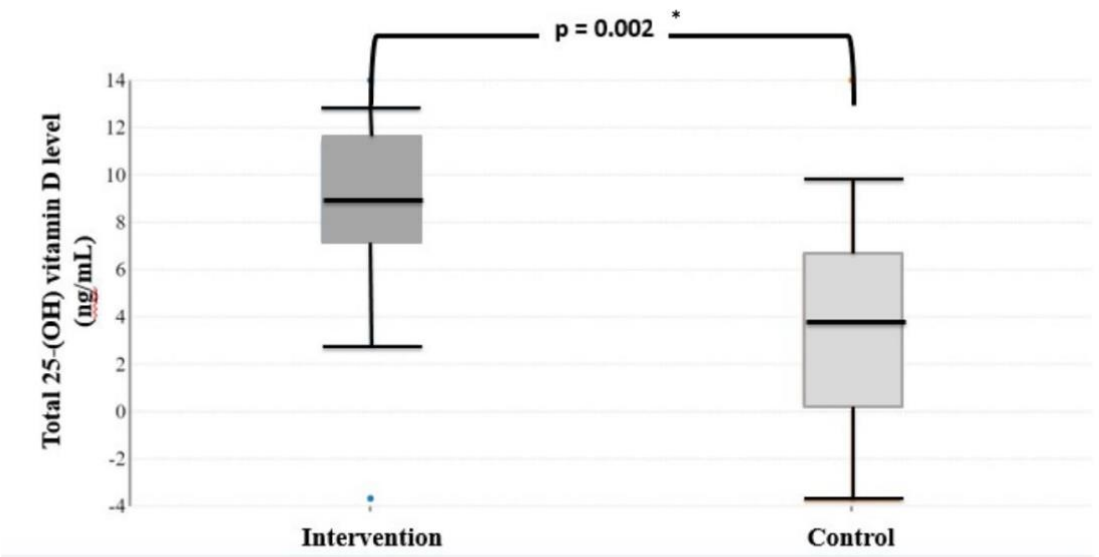


Figure 3: Change in total 25-(OH) vitamin D level between the intervention and control group. *, p value statistically significant. Independent sample t-test was used to analyze the difference in changes in vitamin D levels between the two groups.

Supplementary Table 1. Nutritional composition (serving size: 4scoops (57g) of the ONS

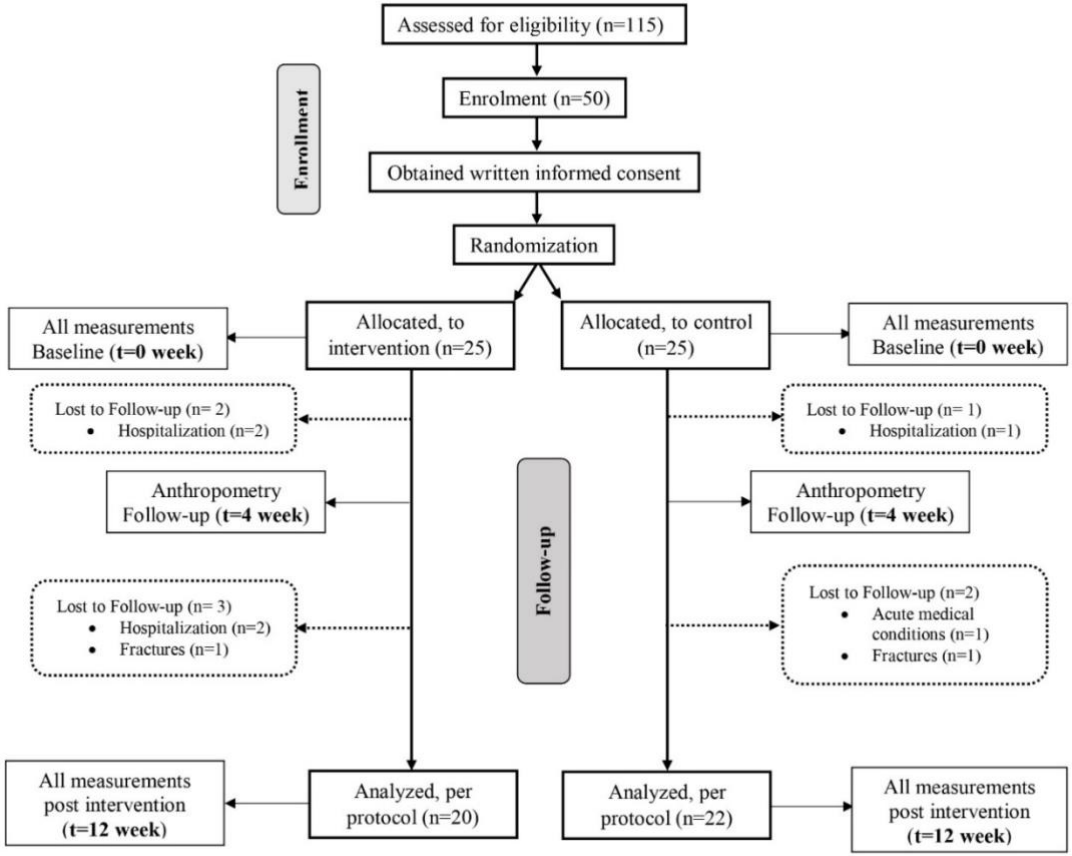
		% DV	Per serving	Per 100 g
Total Calories	kcal		247	434
Total fat	g	12	8	14
SFA	g	23	4.5	8
MUFA	g		2	3
PUFA	g		1	2
Trans Fatty Acids	g		< 0.5	< 0.5
Cholesterol	mg		< 0.5	< 0.5
Protein	g	20	12	21
Total Carbohydrate	g	10	32	55
Dietary fiber	g	17	5	9
Sucrose	g		7	12.5
Sodium	mg	10	153	268
Potassium	mg	2.5	126	221
Vitamin A	mcg	30	184	323
Vitamin B_1	mg	25	0.3	0.55
Vitamin B_2	mg	25	0.4	0.71
Vitamin B_3	mg	30	4.7	8.2
Vitamin B_5	mg	40	2.1	3.6
Vitamin B_6	mg	35	0.4	0.75
Vitamin B_7*/Biotin*	mg	60	17.6	30.7
Folic acid	mcg	30	125	220
Vitamin B_{12}	mcg	30	0.7	1.3
Vitamin C	mg	40	26.8	64.5
Vitamin D_3	mcg	20	2.8	4.9
Vitamin E	mg	30	4.6	8.1
Calcium	mg	20	219	384
Magnesium	mg	8	26.6	46.6
Phosphorus	mg	15	88.7	156
Iron	mg	9	2.1	2.7
Iodine	mcg	30	46.2	81
Zinc	mg	30	3.9	6.8
Chromium	mcg	15	3.3	5.8
Selenium	mcg	15	4.1	7.2

SFA - Saturated Fatty Acids, *MUFA* - Monounsaturated Fatty Acids, *PUFA* - Polyunsaturated Fatty Acids

Supplementary Table 2. Demographic and baseline clinical characteristics of biochemical parameters, and daily dietary intake

Variable	Intervention group (n=20)	Control group (n=22)	p value[(a)]
Age (Years)	75.4±6.1	74.8±5.2	0.732
Gender n (%)			0.588
Male	7 (35%)	6 (27%)	
Female	13 (65%)	16 (73%)	
Duration of staying at the elderly care residence (Years)	5.20±5.23	4.49±4.22	0.599
MNA-SF score	8.72±1.95	9.56±1.45	0.118
Blood parameters			
WBC (Per Cu mm)	7638±2104	7450±1940	0.765
Hemoglobin (g/dl)	11.22±1.11	11.67±1.16	0.209
RBC (10 6 /UL)	3.93±0.48	4.05±0.48	0.404
Platelet count (Per Cu mm)	300000±94780	293000±58899	0.776
Serum albumin (g/dl)	4.28±0.23	4.38±0.35	0.275
Total serum cholesterol (mg/dl)	166.2±44.2	208.4±53.1	0.008*
hCRP (mg/L)	1.28±1.46	1.49±1.52	0.659
Vitamin D level (ng/mL)	14.76±4.70	15.36±5.65	0.710
Dietary intake per day			
Energy intake (kcal)	1346.20±157.33	1381.10±143.58	0.457
Carbohydrate intake (g)	212.58±34.64	219.43±36.68	0.538
Fat intake (g)	39.12±6.89	40.06±7.55	0.677
Protein intake (g)	33.84±6.04	35.48±6.41	0.400

Values are mean ± standard deviation for continuous variables and n (%) for categorical variables. *, p value statistically significant. [a], Independent sample t-test or chi-square test. MNA-SF; mini nutrition assessment short form, BMI; body mass index, WBC; white blood cell, RBC; red blood cell, Hs-CRP; high sensitivity C reactive protein.



Supplementary Figure 1: CONSORT flow diagram

To address this, ONS may need to incorporate higher amounts of vitamin D to more effectively meet the needs of individuals and mitigate deficiencies. A recent study done by Chew et al.,[9] showed significant improvements in the vitamin D deficiency and insufficiency status in the IG, in contrast to a worsening vitamin D status in the placebo group. Nevertheless, it is worth noting that the previous study utilized an ONS containing 15.5 mcg (620 IU) of vitamin D over a relatively longer supplementation period of 24 weeks.

Albumin, the most abundant protein in human serum, has been used as an indicator of malnutrition.[18] In the current study, a decline in serum albumin levels was observed in both IG and CG, with the CG experiencing a significant decrease. However, serum albumin levels were still within a normal range in both the IG and CG. These findings are consistent with those of Chen and Lee (2023), who reported a decrease of -0.09 g/dL in participants who received a nutritional supplement and -0.02 g/dL in those who received nutritional education only.[16] Nevertheless, serum albumin is no longer regarded as a precise indicator of nutritional status due to its lack of specificity and long half-life.[19] Furthermore, serum albumin concentration is not solely indicative of poor nutritional status, as it can also be influenced by factors such as inflammation, hepatic insufficiency, and renal losses in nephrotic syndrome.[20] Aging is another factor contributing to the decrease in serum albumin levels, with levels decreasing by approximately 0.1 g/L per year.[21] In light of these findings, the current study suggests investigating the impact of ONS on valid prognostic indicators such as serum pre-albumin and transferrin level as well rather than relying only on serum albumin level.

Haemoglobin is another good marker of nutritional status in older adults. The study's findings of relatively unchanged Haemoglobin levels in both groups suggest that the impact of the ONS may not have been immediately discernible within the short study duration.

The majority of the study participants were taking statin medication to manage their altered cholesterol levels. Consequently, we observed a significant difference in total serum cholesterol levels between the two groups at the study's outset. Therefore, we did not anticipate any significant impact on their total cholesterol levels.

ONSs are specifically designed to provide calories, high-quality protein, and micronutrients that are recommended to fulfil the basic nutritional requirements of individuals when a regular diet alone is insufficient. The given ONS contributed to the observed significant increase in carbohydrate, fat, and protein intake in the IG. Following the present results, previous studies have also demonstrated a significant increase in energy, carbohydrate, fat, and protein intake in the treatment group compared to the control group.[9]

The main strength of this study is the high follow-up rate with 100% compliance, which can be attributed to the extensive support provided by caregivers who routinely monitored the ONS consumption. A higher follow-up rate is crucial for minimizing potential bias and ensuring the accuracy of the study findings. Additionally, the controlled environment in which the study was conducted helped to minimize confounding factors, particularly dietary intake, further strengthening the study's validity.

However, the study is subject to certain limitations. Conducting the study in a single elderly care institution limits the generalizability of the findings. Despite this, the institution accommodated nearly 200 older adults at the time of the intervention, a significantly high number compared to other institutions in Sri Lanka. The institution is representative of various demographics, including urban, rural, and suburban areas, and encompasses major ethnic groups in Sri Lanka (Sinhala, Tamil, and Muslim). Therefore, we believe the findings are applicable to other elderly care and community settings. Additionally, the older adults in this institution exhibit a wide range of medical conditions and comorbidities, suggesting that the findings may also be relevant to other healthcare settings. Another limitation is the inability to assess vitamin D intake from food sources and measure sun exposure among subjects. Furthermore, the short duration of ONS administration in our study limits our ability to assess the sustainable effects of ONS.

Conclusion

In conclusion, ONSs show promising improvements in nutritional status, beneficial effects on some biochemical parameters, and a significant increase in nutrient intake among malnourished older adults. Future studies should include multiple elderly care institutions and community settings to enhance the generalizability of the findings. Extending the duration of ONS administration will help assess the long-term sustainability and effectiveness of ONS. Incorporating measures to assess vitamin D intake from food sources and sun exposure will provide a more comprehensive nutritional evaluation. Additionally, evaluating more biomarkers related to inflammation and other health conditions will offer a detailed understanding of the effects of nutritional interventions. These improvements will provide deeper insights into the impact of ONS and help develop tailored, effective strategies to combat malnutrition in older adults.

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Author contributions

R.Jayawardena was involved in conceptualization of the study, supervision, data interpretation and review of the manuscript. P.Wickramawardhane was involved in data curation, data analysis and writing the manuscript.

Conflict of interest

The authors declare there is no conflict of interest regarding this article.

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LITERATURE REVIEW

The roles of growing up milk on growth and anemia prevention in children under 5 years of age

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Abstract

Background: Adequate nutrition during the early years of life is necessary for good growth, development, and long-term health outcomes. The first 1000 days of life are a critical time for nutrition.

Aims: This literature review aimed to evaluate the role of growing up milk on growth, stunting, and anemia prevention of under-five children.

Methodology: This study used a literature review approach, searching three databases: PubMed, Google Scholar, and Cochrane. The inclusion criteria in this literature review were 1) randomized clinical trials, systematic review, and meta-analysis, 2) studies conducted over the last 10 years, 3) available in full text, 4) written in Indonesian or English, and 5) Research studies conducted in humans.

Result: We identified 3 publications, that matched the inclusion criteria and research aims, including 2 original articles from Lovell AL, et al and Cervo MCM, et al, and 1 meta-analysis by Brooker PG et al. Fortified milk (GUM) consumption significantly had a positive impact on nutritional status, especially growth and hemoglobin status (anemia).

Conclusion: Fortified milk (GUM) consumption is a solution to macro-micronutrient adequacy in under five children. More efforts are needed to conduct studies in Indonesia on GUM and address specific nutrients that may promote linear growth, reverse stunting and anemia in children.

Keywords: growing up milk, growth, anemia

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Introduction

The period from a baby's conception to their second birthday, commonly known as the first 1000 days, plays a critical role in determining their future health. As a result, global health organizations like the World Health Organization (WHO) have developed guidelines aimed at promoting optimal nutrition for infants and young children during this crucial timeframe.[1]

At 12 months of age, it's important for them to consume a variety of nutritious solid foods adhere to dietary guidelines and provide the appropriate balance of nutrients.[2-4] However, compliance with dietary guidelines is known to be low in both higher- and lower-income countries, which places young children at risk of missing out on essential macro- and micro-nutrients during this critical developmental period.[5-6]

Early in life, proper nutrition is essential for the best possible growth, development, and long-term health results.[7] Unfortunately, a lot of kids, especially younger ones under five, don't get enough macro and micronutrients, which can cause stunting, growth failure, and an increased risk of infections and anemia.[8] Malnutrition is defined as an inadequate or unbalanced nutrient intake. If this condition persists, children under five years old are at risk for stunting and anemia.[9] Malnutrition has long-term effects on a child's growth and development during the first 1000 days of life.

The goal of this literature review is to examine how growing up milk affects the adequacy of macro-micronutrients and how it affects the growth, stunting, and prevention of anemia in children under five.

Methods

This literature review uses three databases, PubMed, Google Scholar, and Cochrane, with PICO as listed below:

P: under five children
I: growing up milk
C: none growing up milk
O: growth and development

The inclusion criteria in this literature review were 1) randomized clinical trials, systematic review and meta-analysis, 2) studies conducted over the last 10 years, 3) available in full text, 4) written in Indonesian or English, and 5) Research studies conducted in humans. Articles with a lack of available data were excluded. Keywords of "growing up milk", "fortified milk", "stunting", "anemia", and "under five children", were used—literature search process presented in **Figure 1**.

Results

We have found 3 publications, that matched our criteria and the aim of this literature review (**Table 1**). The articles were 2 original articles from Cervo MCM, et al.[10] and Lovell AL, et al.[11] Also, there was 1 meta-analysis from Brooker PG, et al.[12]

In their ten-week nutrient-fortified milk-based formula study, Cervo MCM et al.[10] found that preschoolers who drank two servings of fortified milk a day for twelve weeks had a significant increase in height (1.40 cm), weight (1.35 kg), body mass index (0.96 kg/m2), mid-upper arm circumference (0.66 cm), and psychomotor scores (13.74% higher) compared to those who did not drink fortified milk ($p < 0.0001$).[10] A long with that, Lovell et al.[11] RCT study comparing Cow Milk and Growing-Up Milk revealed that GUM enhances Vitamin D and Iron status in healthy 2-year-old children. Brooker et al.[12] meta-analysis on the impact of fortified formula on growth and nutritional status of young children demonstrate that fortified milk leads to increased weight gain (MD = 0.14 kg [95% CI 0.06, 0.21], $p = 0.0003$) compared to control milk. Results from subgroup analyses indicate improved weight gain in lower-income countries and in studies with intervention periods exceeding 6 months. However, no effects on other anthropometric measures were observed. Furthermore, infants consuming fortified milk exhibited increased hemoglobin (MD = 3.76 g/L [95% CI 0.17, 7.34], $p = 0.04$) and ferritin (MD = 0.01 nmol/L [95% CI 0.00, 0.02], $p = 0.02$) concentrations.[12]

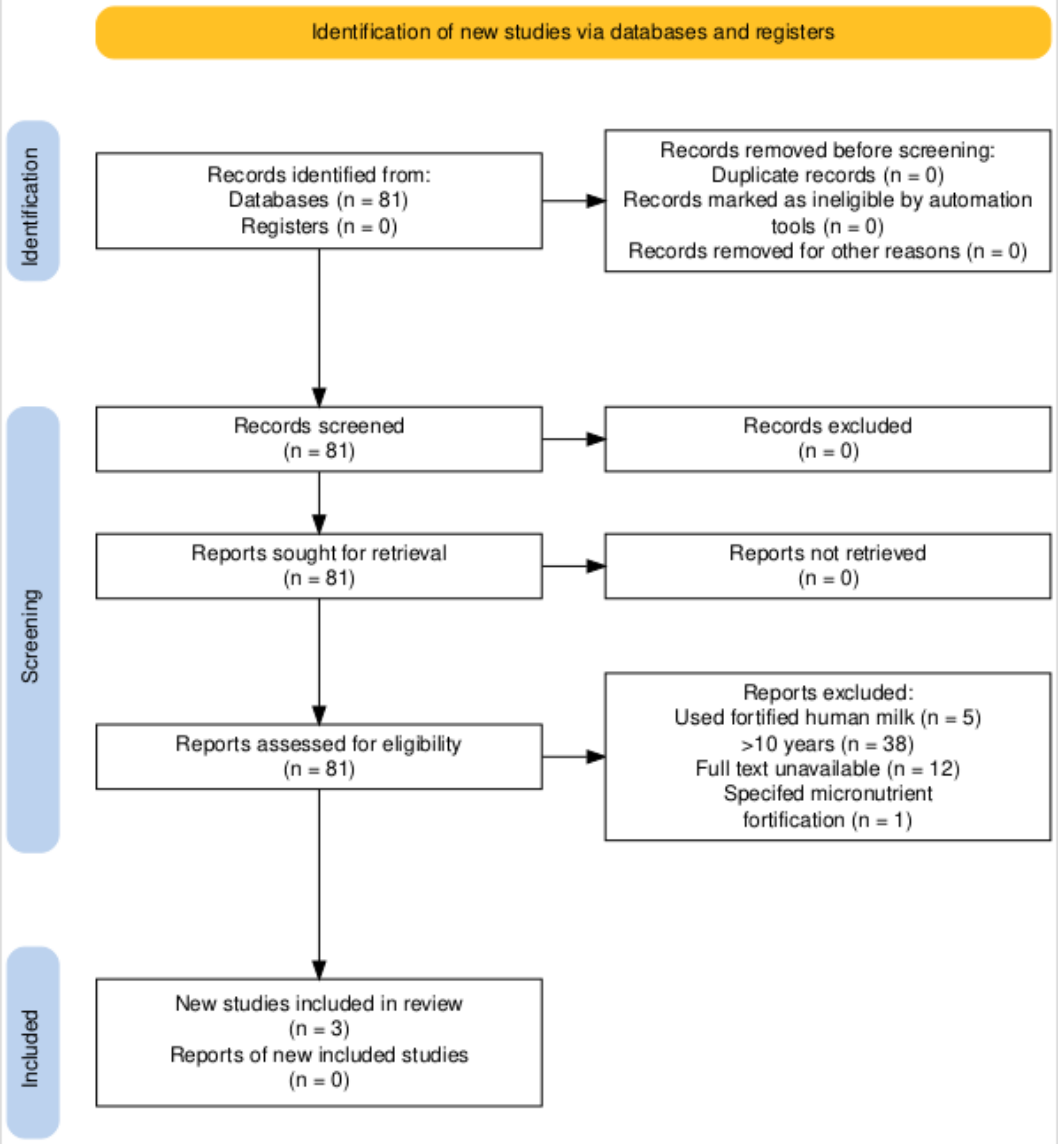

Figure 1. PRISMA flow chart for study selection

Table 1. Characteristics of included studies

No	Author	Title	Subjects	Intervention	Results
1.	Cervo MCM, et al	Effects of Nutrient-Fortified Milk Based Formula on the Nuritional Status and Psychomotor Skills of Preschool Children	One hundred twenty (120) preschools children, aged 3–5 years, with mean age of 4.10 ± 0.14 years were recruited for the study.	This randomized, single-masked, controlled trial examined the effects of nutrient-fortified milk-based formula supplementation on nutritional status, nutrient intake, and psychomotor skills. Study participants were divided equally into three major groups, normal, underweight, and severely underweight based on WHO-Child Growth Standards, and were further divided into two groups: fortified milk group who was given two glasses of fortified milk (50 g of powdered milk/serving) a day for twelve weeks in addition to their usual diet and the nonintervention group who was not given fortified milk and thus maintained their usual intake.	Results showed that consumption of two servings of fortified milk a day for twelve weeks significantly increased the height of preschool children by 1.40 cm, weight by 1.35 kg, body mass index by 0.96 kg/m2, mid-upper arm circumference by 0.66 cm, and psychomotor scores by 13.74% more than those children who did not consume fortified milk ($p < 0.0001$). Hence, fortified milk-based supplement in the diet of preschool children improved overall nutritional status, nutrient intake, and performance in psychomotor scale.

No	Author	Title	Subjects	Intervention	Results
2.	Lovell AL, et al	Compared with Cow Milk, a Growing-Up Milk Increases Vitamin D and Iron Status in Healthy Children at 2 Years of Age: The Growing-Up Milk-Lite (GumLi) Randomized Controlled Trial	160 healthy 1-y-old	Participants were randomly assigned 1:1 to receive GUMLi (1.7 mg Fe/100 mL; 1.3 μg cholecalciferol/100 mL) or CM (0.02 mg Fe/100 mL; 0.06 μg cholecalciferol/ 100 mL) for 12 mo.	GUMLi was a large contributor to dietary intakes of iron and vitamin D after 12 mo when compared with intakes from food and CM. The adjusted mean difference between groups for serum ferritin concentrations was 17.8 μg/L (95% CI: 13.6, 22.0 μg/L; P < 0.0001), and for 25(OH)D it was 16.6 nmol/L (95% CI: 9.9, 23.3 nmol/L; P < 0.0001). After 12 mo, ID was present in 16 (24%) participants in the CM group and 5 (7%) participants in the GUMLi group (P = 0.009), and the prevalence of VDD in the CM group increased to 14% (n = 10) and decreased to 3% (n = 2) (P = 0.03) in the GUMLi group.
3.	Brooker PG, et al	Effect of Fortified Formula on Growth and Nutritional Status in Young Children: A systematic Review and Meta-Analysis.	A total of 12 studies reported across 19 publications met the eligibility criteria and were included in the review	The systematic review and meta-analyses were conducted and reported in accordance with the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement	Fortified milk was associated with increased weight gain (MD = 0.14 kg [95% CI 0.06, 021], p = 0.0003) compared with control milk. Subgroup analyses demonstrated increases in weight in lower-income countries, and in studies with intervention periods > 6 months. There were no effects of fortified milks on other anthropometric measures. Haemoglobin (MD = 3.76 g/L [95% CI 0.17, 7.34], p = 0.04) and ferritin (MD = 0.01 nmol/L [95% CI 0.00, 0.02], p = 0.02) concentrations were increased in infants consuming fortified milks.

Discussion

Even though the rate of malnutrition in Southeast Asia has decreased, it is expected that over 25% or 165 million children under the age of 5 around the world are suffering from stunted growth. This is particularly prevalent in Africa and Asia, with 90% of affected children residing in these regions. For children to grow and develop in a healthy way, nutrition is crucial. Malnutrition in children is still a serious issue in developing nations like Indonesia. Several research works have indicated a relationship between children's cognitive ability and growth factors such as height, weight, and head circumference. Inadequate nutrition has been found to lead to decreased academic performance, increased absenteeism, and lower intelligence. Nutrition also significantly impacts the development of cognitive and psychomotor skills, with iron being especially essential for neurotransmitter production and energy metabolism. Preschool-age children (those under five years old) are particularly susceptible to nutritional deficiencies during this time, especially after weaning. Although their need for calories remains high, young children may refuse to eat nutrient-rich foods due to picky eating habits or limited food options, making it difficult to ensure they receive the necessary nutrients for healthy growth and development. Thus, supplementing a child's usual diet with significant amounts of nutrients in the form of energy and nutrient-dense food could be quite beneficial.[10]

In the first two years of life, linear growth retardation can have significant consequences; these effects typically manifest during the supplementary feeding period. Lack of diversity in the diet and insufficient quantities of complementary foods have been linked to stunted growth in children. Dietary diversity is a crucial aspect of a healthy diet, and a more varied diet is strongly correlated with adequate intake of energy, protein, and micronutrients. Insufficient consumption of these vital nutrients over a prolonged period puts children at risk of stunted growth.[12,13] Due to their ability to regulate IGF-1 levels, macronutrient components like high-quality protein and necessary amino acids have been identified as critical components that support childhood growth. It has been demonstrated that children with low protein consumption have poor linear growth.[15] Furthermore, energy deficiency in these children can also result in suboptimal growth, loss of body fat, and muscle. Ensuring adequate intake of both macronutrients and micronutrients, such as iron, zinc, phosphorus, and vitamins, is crucial for proper growth.[14-20]

Anemia affects around 300 million preschool-aged children worldwide, with a significant prevalence among children in underdeveloped nations. Children's cognitive and physical development is negatively impacted by anemia, which can also have long-term effects on an adult's physical productivity and ability to reproduce. It is often believed that iron deficiency, primarily from inadequate dietary intake or lack of iron, accounts for roughly half of instances of anemia. [21-23]

According to studies conducted in Indonesia, the majority of children under five were unable to satisfy their daily needs for macro- and micronutrients. Research conducted in Sumbawa by Limardi et al. discovered that while 14% of children who were not stunted obtained appropriate supplemental dietary diversity, just 6% of stunted children did. Compared to the non-stunted group, the stunted group consumed much less flesh foods (beef, fish, poultry, organ meat, and other types of meat). Additionally, compared to children who are not stunted, the median consumption of total protein was considerably lower in stunted children.[24] A study by Semba et al. showed that kids between the ages of 6 and 59 months who drank iron-fortified milk had a lower risk of anemia than kids who didn't.[25] However, a meta-analysis by Matsuyama et al. on the impact of fortified milk on young children's growth and nutritional status discovered that, when compared to control milk, the effects of fortified milk on weight gain were negligible. When compared to control groups, the risk of anemia was lower in the fortified milk groups. There were no appreciable effects on changes in body composition, Hb concentration, or height gain that could have been impacted by the fortification type. When fortified milk is fully absorbed and combined with a regular diet, it can

serve as a useful supplemental nutrition source for children who may benefit from it.[26]

Growing-up milk (GUMs), also known as young-child formula (YCF), are milk-based beverages that supply nutrients for which there may occasionally be only a minimal intake during the early childhood dietary transition period.[26,27] Supplementation may offer substantial nutritional and energy benefits, thereby enhancing dietary adequacy. Milk has a lot of different nutrients. Additional nutrients found in the powdered fortified milk-based formula (GUM) include energy, protein, fat, carbohydrates, vitamin A, thiamine, riboflavin, niacin, vitamins B6, B12, C, D, E, and K, folic acid, pantothenic acid, biotin, calcium, phosphorus, chloride, iodine, iron, zinc, manganese, copper, choline, dietary fiber, and linoleic acid. These nutrients are all essential for a child's growth and development, as controlled by CODEX.[10]

Lovell et al.[11] research revealed that when given to 12-month-old children as a complete meal, GUM maintains iron stores and considerably lowers the occurrence of iron insufficiency as compared to CM consumption at two years of age. The results of the study were also observed, showing that GUM considerably increased total iron intakes, suggesting that supplying a fortified diet by consumption of ≥300 mL GUMLi/d was a suitable approach. These results suggest that GUM may be utilized as a tactic to raise dietary iron levels and lower the incidence of ID anemia. Cervo MMC, et al[10] Research indicates that giving three to five-year-old children an oral nutrition supplement consisting of two servings of a fortified milk-based formula for a duration of twelve weeks is linked to enhancements in certain anthropometric metrics and psychomotor abilities. It is clear that all groups that drank fortified milk-based formula were able to meet and even surpass the standard or expected average gain in height and weight for a preschooler, compared to the non-intervention group, which only increased in height within the expected range and did not even meet the standard or average weight gain for a preschooler. The group that had fortified milk had higher energy and nutritional consumption. The nutrients included in the milk included carbs, protein, lipids, calcium, phosphorus, magnesium, zinc, copper, and vitamins C, D, and K. The recommended energy and nutrition intake (RENI) and estimated average requirement (EAR) for all essential nutrients—energy, protein, calcium, iron, vitamin A, thiamine, riboflavin, niacin, and vitamin C—were met by the participants who drank fortified milk. Therefore, adding fortified milk-based formula to preschoolers' diets may assist to enhance their overall nutritional status as well as their psychomotor skills, which are essential for meeting developmental milestones. These two RCTs were consistent with a meta-analysis conducted by Brooker PG et al.[12] which discovered that drinking fortified milk may help young children's growth and nutritional status in certain areas, especially in study groups where undernutrition was a concern. It is important to note, however, that there is a wide range of these products available, with variable compositions, therefore, it is important to consult with a qualified healthcare provider when choosing the most suitable product

Cross sectional studies in Indonesia showed a positive impact of GUM on nutritional status. Unpublished data of Sasmiati et al, in Yogyakarta, found that there was correlation between formula milk consumption and under-five children nutritional status.[28] And a cross-sectional study from Sjarif DR et al showed that two protein sources had a significant association with stunting, namely, GUM as a protective factor. This result shows that a GUM consumption of 300 ml/day is associated with less stunting.[29]

The present literature review found that consuming GUM can improve nutritional status, including iron in young children. Considering that iron deficiency is the most common nutrient deficiency among children in the world, it is an important public health concern to be addressed. Especially, when adequate nutritious complementary foods are unavailable or fussy eating behaviour is prevalent during dietary transition, children may not be meeting nutritional requirements for optimal growth and development. Under such circumstances, fortified milk (GUM) may be a safe, acceptable, and effective source of nutrients to supplement those children in need, to

provide essential nutrients to these children in need, until they can establish healthier eating habits.

This paper has both strengths and limitations. One strength is that the authors independently screened articles and extracted data from all the included papers. Results were discussed at a designated time between all authors, and a consensus was reached regarding each paper. However, there are some limitations to this review. The only search engines utilized for this literature evaluation were PubMed, Google Scholar, and the Cochrane database; hence, not all pertinent papers in Indonesian may have been found. Furthermore, the analysis was restricted to research papers released between 2014 and 2024; a larger time range would have produced additional or different findings.

Conclusion

Fortified milk (GUM) consumption had a significant positive impact on nutritional status, especially growth and hemoglobin status (anemia). Fortified milk (GUM) consumption is a solution to macro-micronutrient adequacy in under five children. More efforts are needed to conduct studies in Indonesia on GUM and address specific nutrients that may promote linear growth, reverse stunting anemia in children.

Conflict of interest

The authors declare there is no conflict of interest regarding this article.

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ORIGINAL ARTICLE

Changes in nutritional status, risk factors and food intake in stroke subjects: cohort study analysis of non-communicable disease risk factors

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Abstract

Background: Stroke is a major cause of death and disability worldwide, affecting 15 million people annually. In Indonesia, the prevalence is 10.9%. Major risk factors include high blood pressure, obesity, inactivity, poor diet, and smoking.
Objective: This study aims to analyze long-term trends in risk factors, nutritional status, and food intake among stroke patients from 2011-2021, assessing their impact on stroke incidence.
Methods: Data from a longitudinal cohort study of 5,329 subjects, including 215 stroke patients, were analyzed using Microsoft Excel 2019 and SAS software. ANOVA was used to assess annual changes in risk factors, nutritional status, and food intake. Survival analysis was conducted with SAS PROC LIFETEST and PROC LIFEREG.
Results: The cohort was primarily female (62.8%), aged 60 or older (57.2%), senior high school education (25.6%), civil servants (30.7%), and low income (57.2%). Significant changes were noted in BMI (p=0.037), fasting blood glucose (FBG) (p=0.001), HDL (p=0.049), abdominal circumference, smoking habits, physical activity (p<0.001), protein intake (p=0.026), and intake of energy, fat, carbohydrates, and sodium (p<0.001). Factors significantly associated with stroke included age, FBG, postprandial glucose, smoking (p<0.0001), LDL (p=0.0380), HDL (p=0.0126), physical activity (p=0.0455), energy intake (p=0.0002), fat intake (p=0.0007), and sodium intake (p=0.0012).
Conclusions: The study highlights significant changes in nutritional status, glucose levels, HDL cholesterol, physical activity, and smoking habits. These factors, along with age, cholesterol levels, and dietary intake, impact stroke incidence, underscoring the need for comprehensive stroke prevention strategies.

Keywords: stroke prevention, risk factors, longitudinal study, nutritional status, food intake, stroke incidence

Introduction

Stroke is a leading cause of death and disability worldwide with dramatic impacts on millions of lives annually. WHO (2023) reports that stroke affects 15 million people globally annually, resulting in 5 million deaths and 5 million permanent disabilities.[1] In Indonesia, according Riskesdas (2018) 10.9% of the population affected by stroke and 11.4% in West Java, representing about 131,846 individuals stroke.[2]

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Understanding stroke risk factors is crucial for the effective prevention and treatment of stroke. These factors are categorized as modifiable or non-modifiable. Modifiable factors, such as high blood pressure, smoking, poor diet, and physical inactivity, account for 82–90% of stroke cases. Non-modifiable factors include age, sex, and ethnicity.[3,4] Additionally, conditions such as hypertension, diabetes mellitus, high cholesterol, coronary heart disease, atrial fibrillation, and heart valve disease further elevate the stroke risk.[4]

A cohort study is required to gain deeper insights into these factors. In 2011, the Ministry of Health, Republic of Indonesia initiated a cohort study in Bogor City, West Java, involving 5,329 participants. This study examined the impact of behavioral, biomedical, and genomic factors on non-communicable diseases (NCDs), such as stroke. BADAN LITBANGKES (2018) reported a cumulative incidence of metabolic syndrome of 6.8%, diabetes mellitus of 7%, coronary heart disease of 5.3%, stroke of 2.08%, suspected cervical cancer of 2.2%, and breast cancer of 1.9%.[5] Over a 10-year period, this study provides valuable insights into changes in risk factors, nutritional status, and food intake among stroke patients, thereby enhancing our understanding of stroke risk factors specific to Indonesia.

Methods

Study population

This study used secondary data from the FRPTM cohort study conducted by the Research and Development Center for Public Health Efforts of the Indonesian Ministry of Health in Bogor, West Java. The study included adults aged 25 years and older who possessed an Indonesian Identity Card and resided in five selected sub-districts of the Central Bogor District. A total of 5,329 participants were analyzed, of whom 215 experienced a stroke between 2011 and 2021. This study was approved by the Health Research Ethics Committee of the Health Research and Development Agency (numbers: LB.02.01/5.2/KE.143/2014 and LB.02.01/5.2/KE.042/2016). Confidentiality was ensured by anonymizing health data, restricting access to authorized personnel, encrypting digital records, and securely storing physical records

Data collection

Data collection for this study followed the WHO STEP-wise approach, a standardized method for assessing non-communicable disease (NCD) risk factors. This approach involves three key steps. Step 1 involved collecting lifestyle data through questionnaires to assess factors such as physical activity, smoking, and dietary habits (24-hour food recall and a Food Frequency Questionnaire). Step 2 included physical measurements, where anthropometric data, such as weight, height, abdominal circumference, and Body Mass Index (BMI), were recorded. Step 3 involves biochemical measurements, including laboratory tests for biomarkers such as Fasting Blood Glucose (FBG), 2-hour Postprandial Glucose, cholesterol, triglycerides, LDL, and HDL levels. Stroke was defined based on neurological examinations by a specialist and the presence of residual stroke symptoms, supported by patient history and anamnesis. Interviewers were trained staff with at least a diploma in their health. Blood draws are performed by ISO-certified private lab technicians, while anthropometric measurements, blood pressure, and abdominal circumference are assessed by local community health center

Statistical analysis

Data processing and analysis were performed using Microsoft Excel 2019 and SAS software, respectively. Excel was used for the initial data organization and descriptive statistics because of its user-friendly interface and effective tools for basic statistical operations and data visualization. SAS software was selected for its advanced capabilities in managing complex datasets and performing sophisticated statistical analyses. Specifically, SAS PROC LIFETEST was employed for survival analysis to estimate the survival and density functions, providing insights into stroke incidence over time. SAS PROC LIFEREG was used to analyze the factors influencing stroke risk, offering a detailed

examination of survival data and hazard functions. Statistical analyses included univariate analysis to assess the individual risk factor characteristics and their prevalence within the study population. Analysis of Variance (ANOVA) was used to examine changes in risk factors and nutritional status over time, identify significant differences among groups, and help to understand how these factors impact stroke risk. Survival analysis assessed how various factors influence the time until stroke onset, incorporating the survival function to estimate the probability of remaining stroke-free, the probability density function to visualize the likelihood of stroke over time, and the hazard function to estimate the rate at which strokes occur, thus providing insights into periods of increased risk.

Results

Demographic data revealed that the population was predominantly female (62.8%), with males representing 37.2%. Age-wise, the majority were 60 years and older (57.2%), followed by those aged 51-60 years (28.4%), with smaller percentages in the younger age groups. Educationally, most individuals had completed elementary school (31.6%) or junior high school (20.5%), while a small fraction had higher education (3.3%). Domestic workers (27.9%) and civil servants (30.7%) were the most common, while students and private employees were less frequent (0.5% each). Income distribution shows a significant portion of the population with low income (57.2%), contrasted by smaller proportions in the medium (25.1%), high (9.3%), and very high income brackets (8.4%).

Table 1. Individual and socio-economic characteristics of stroke subjects

Variabel	%
Gender	
Male	37.2
Female	62.8
Age	
31-40 years	1.9
41-50 years	12.6
51-60 t years	28.4
≥ 60 years	57.2
Education	
Not school	1.9
Didn't finish elementary school	17.2
Elementary school graduate	31.6
Junior high school graduate	20.5
Senior high school graduate	25.6
University graduate	3.3
Occupation	
Driver	4.7
Domestic worker	27.9
Student	0.5
TNI/POLRI	2.8
Civil Servants	30.7
Self-employed/ Service/Trader	5.1
Private Employee	0.5
Farmer	0.5
Factory worker	2.3
Construction worker	4.2
Retiree	12.1
Other	4.7
Income	
Very high	8.4
High	9.3
Medium	25.1
Low	57.2

Of the 5,329 participants in the FRPTM cohort study, 215 experienced stroke over a 10-year period from 2011 to 2021. **Figure 1** shows the trends in risk factors and nutritional status among stroke subjects. At baseline, the obesity prevalence was 58.1%, decreasing to 20.9% at the 10-year follow-up. Central obesity started at 56.7%, but varied before ending at 21.4%. Low physical activity decreased from 13% to 5.1% and moderate smoking decreased from 10.7% to 4.2%. Diabetes prevalence, as indicated by fasting blood glucose (FBG) and 2-hour postprandial glucose (2h-BG) levels, remained relatively stable, with FBG falling from 13.5% to 6% and 2h-BG from 15.8% to 7%. High triglyceride levels decreased from 27.9% to 12.6%, high total cholesterol levels from 67% to 19.1%, LDL cholesterol levels from 91.2% to 25.6%, and low HDL levels from 55.3% to 14%. These findings reflect improvements in some risk factors, such as reduced obesity and better lipid profiles, but highlight the need for a continued focus on diabetes management and central obesity.

Table 2 presents the significant changes in nutritional status and risk factors for stroke subjects over a 10-year follow-up period, with p-values

indicating statistical significance ($p<0.05$). Notable changes were observed in body mass index (BMI) ($F=2.385$, $p=0.037$), abdominal circumference

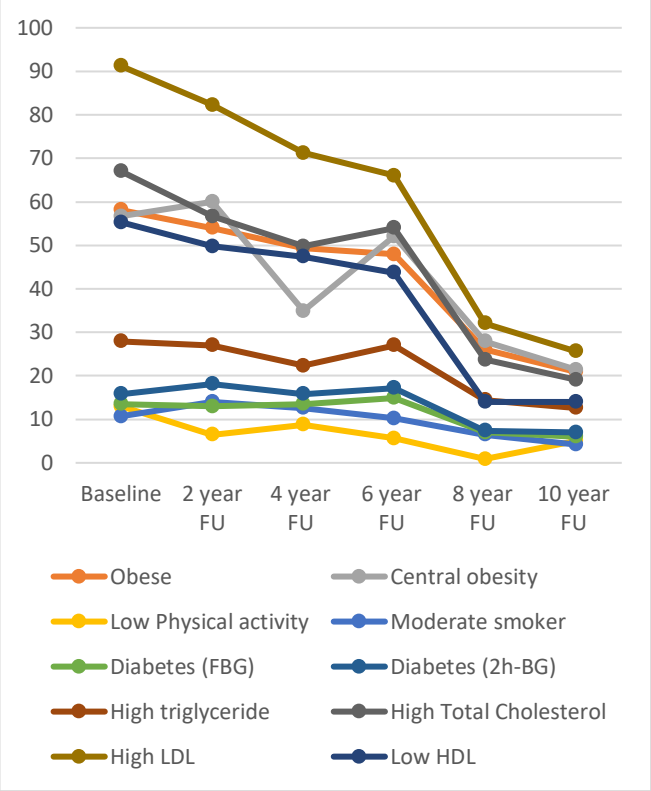

Figure 1. Trends in Risk Factors and Nutritional Status in Stroke Subjects Over a 10-Year Follow-Up Period

($F=13.551$, $p<0.001$), fasting blood glucose (FBG) ($F=4.313$, $p=0.001$), HDL cholesterol ($F=2.240$, $p=0.049$), smoking habits ($F=10.073$, $p<0.001$), and physical activity levels ($F=5.207$, $p<0.001$). A significant decrease in BMI and abdominal circumference suggests improvements in weight management, which can reduce the risk of stroke. A decrease in FBG indicates better glucose control, which is crucial for reducing stroke risk. The significant change in HDL levels reflects alterations in lipid profiles, with increased HDL being associated with a reduced risk of stroke owing to its role in clearing LDL cholesterol from the bloodstream. Changes in smoking and physical activity levels also reflect the impact of lifestyle modifications.

Table 3 shows the significant changes in dietary intake over the 10-year follow-up period, with p-values demonstrating statistical significance ($p<0.05$) for energy intake ($F=11.692$, $p<0.001$),

Table 4. Factors affected the incidence of stroke

Table 2. ANOVA results of changes in nutritional status and risk factors of stroke subjects over 10 years *follow up*

Variable	F	Sig
IMT	2.385	0.037
Abdominal Circumference	13.551	0.000
Total cholesterol	1.464	0.199
Fasting Blood Glucose	4.313	0.001
Variable	F	Sig
2-hour Postprandial Glucose	0.909	0.474
Triglycerides	2.065	0.068
LDL	1.259	0.280
HDL	2.240	0.049
Smoking habit	10.073	0.000
Physical activity	5.207	0.000

**significant ($p<0.05$)*

fat intake ($F=70.207$, $p<0.001$), carbohydrate intake ($F=49.187$, $p<0.001$), and sodium intake ($F=20.509$, $p<0.001$). These results highlight the significant adjustments in dietary patterns, which are essential for evaluating their impact on stroke risk.

Table 3. ANOVA results of changes in nutritional intake of stroke subjects over 10 years

Food Intake	F	Sig
Energy	11.692	0.000
Protein	1.835	0.058
Fat	70.207	0.000
Carbohydrate	49.187	0.000
Sodium	20.509	0.000

Table 4 identifies several factors that significantly affected stroke incidence, with p-values less than 0.05. The significant predictors included age ($p<0.0001$), fasting blood glucose (FBG) ($p<0.0001$), 2-hour postprandial glucose (2h-BG) ($p<0.0001$), LDL cholesterol ($p=0.0380$), HDL cholesterol ($p=0.0126$), smoking habits ($p<0.0001$), physical activity ($p=0.0455$), energy intake ($p=0.0999$), and sodium intake ($p<0.0001$). Additionally, LDL and HDL levels, smoking habits, physical activity, and dietary factors, such as energy, fat, and sodium intake, were assessed. These findings higlight the importance of managing glucose levels, promoting physical activity, and making dietary adjustments in stroke prevention

Variable	Estimate	Standard Error	95% confidence Limits		Chi-Square	Sig
Age	-0.0115	0.0019	-0.0153	-0.0077	35.65	0.0001
IMT	-0.0102	0.0059	-0.0218	0.0014	2.98	0.0842
Abdominal circumference	0.0019	0.0026	-0.0033	0.0070	0.51	0.4768
Total cholesterol	-0.0005	0.0005	-0.0016	0.0005	1.09	0.2975
Fasting Blood Glucose	0.0023	0.0003	0.0017	0.0030	52.59	**0.0001**
2-hour Postprandial Glucose	-0.0008	0.0002	-0.0011	-0.0005	29.69	**0.0001**
Triglycerides	0.0000	0.0002	-0.0004	0.0004	0.00	0.9858
LDL	-0.0012	0.0006	-0.0023	-0.0001	4.30	0.0380
HDL	0.0040	0.0016	0.0009	0.0072	6.23	0.0126
Smoking habit	-0.0003	0.0000	-0.0003	-0.0002	59.55	**0.0001**
Physical activity	0.0000	0.0000	0.0000	0.0000	4.00	**0.0455**
Energy intake	0.0002	0.0000	0.0000	0.0002	6.65	**0.0002**
Protein intake	-0.0008	0.0004	-0.0016	0.0001	2.92	0.0873
Fat Intake	-0.0030	0.0009	-0.0024	0.0011	0.56	**0.0007**
Carbohydrate Intake	-0.0000	0.0001	-0.0002	0.0001	0.12	0.7237
Sodium intake	-0.0001	0.0000	-0.0001	-0.0000	33.08	**0.0012**

Discussion

Individual and socioeconomic subjects

Over a 10-year period, 4.04% of the participants in the cohort study experienced stroke. At baseline, 86 subjects had already suffered a stroke, and this number increased to 215 over the decade. Stroke incidence was higher in women (62.8%) than in men (37.2%). Some studies have reported that women have a higher risk of stroke than men.[6,7] Most stroke patients were elderly (57.2% aged 60 years or older), highlighting age as a risk factor for stroke. The risk of stroke increases with age, and individuals older than 45 years have a higher risk of stroke.[8] In this study, age significantly affected the incidence of stroke ($P < 0.0001$). The risk of stroke increases with age, with the odds doubling after 55 years of age.[9] Aging leads to the deterioration of body organs, including the blood vessels in the brain, which lose elasticity over time. This decline in vascular function is closely linked to the increased risk of stroke as individuals get older. [10,11]

Most stroke patients had an elementary school education level (31.6%) or high school (25.6%). The majority of the participants were employed as civil servants (30.7%) or domestic workers (27.9%). These job types reflect different levels of physical activity and exposure to risk factors such as work-related stress and access to healthcare. Income analysis revealed that most stroke subjects were in the low-income group, with 57.2% having a low income, which may indicate limited access to preventive and adequate medical care.

Nutritional factors

Obesity is defined by a Body Mass Index (BMI) exceeding 25 kg/m², while central obesity is specifically indicated by an abdominal circumference greater than 90 cm in men and over 80 cm in women. Over the course of a 10-year study, data revealed statistically significant changes in both BMI and abdominal circumference, with BMI showing a significant decrease ($F=2.385$, $p=0.037$) and abdominal circumference demonstrating even more pronounced changes ($F=13.551$, $p<0.001$). Despite these changes, obesity and central obesity persisted as common issues throughout the study period. Obesity worsens ischemic stroke by increasing both systemic and local inflammation.[12] Weight loss and malnutrition are associated with greater neurological impairment and worse clinical outcomes in stroke patients.[13] Poor nutrition during a stroke's acute phase can lead to further malnutrition, complicating recovery and daily functioning.[14]

Lifestyle factors

Physical activity and smoking are significant risk factors for stroke. Physical activity was measured in MET-min/week and smoking was assessed using the Brinkman Index. Over the 10-year follow-up period, there were notable changes in both physical activity ($F = 5.207$, $p<0.001$) and smoking habits ($F = 10.073$, $p<0.001$). These changes suggest an increased awareness of stroke risks and the benefits of lifestyle modifications, consistent with the Health Belief Model (HBM), which posits that individuals alter behaviors based on perceived risks and benefits. Improving patient communication about stroke recurrence risks and implementing a Comprehensive Reminder System based on the HBM could enhance stroke prevention efforts.[15]

This study showed that smoking ($p < 0.0001$) and physical activity ($p = 0.0455$) significantly affected the incidence of stroke. Higher levels of physical activity are associated with a reduced incidence of stroke.[16] Regular exercise is crucial for preventing stroke and aiding recovery by lowering cardiovascular risk, enhancing lung capacity, and improving cognitive function.[17,18] Physical activity is important to prevent secondary complications such as cardiovascular diseases and death.[19] Smoking decreased over the follow-up period, which is important because smoking increases stroke risk through oxidative stress, arterial damage, and plaque buildup. Quitting smoking improves HDL function and lowers cholesterol levels, further reducing stroke risk. [20,21]

Biochemical markers

Blood levels of total cholesterol, triglycerides, LDL, and HDL are useful for diagnosing dyslipidemia. In this study, subjects with stroke had the highest prevalence of elevated cholesterol levels over the 10-year period. High total cholesterol levels are associated with atherosclerosis, which increases stroke risk.[9] Triglycerides stored in fat cells and released for energy are typically normal in stroke patients. However, elevated triglyceride levels can also contribute to arterial plaque formation and inflammation.[22]

Over the 10-year period, HDL levels decreased significantly ($F = 2.240$, $P = 0.049$). The proportion of individuals with low HDL levels decreased from 55.3% to 14.0%, while those with normal HDL levels decreased from 44.7% to 14.0%. HDL plays a crucial role in transporting cholesterol from the tissues back to the liver, preventing atherosclerosis, and protecting against heart diseases.[23] Decreasing HDL levels may suggest a rising public health challenge as low HDL levels are associated with a higher risk of heart disease and stroke. Public health strategies should focus on increasing HDL levels through lifestyle changes such as improved diet, increased physical activity, and smoking cessation.

Both LDL ($p = 0.0380$) and HDL ($p = 0.0126$) levels significantly affected the stroke incidence. LDL is a degradation product of very low-density lipoprotein (VLDL), is associated with higher mortality and decreased blood vessel resilience owing to cell necrosis.[24] Low HDL levels are associated with a high risk of heart disease and stroke.[25] An HDL level of at least 60 mg/dL reduces heart disease risk, whereas levels below 40 mg/dL increase this risk.[23]

Hyperglycemia can damage large blood vessels, increase blood viscosity, raise blood pressure, and elevate stroke risk.[26] During the 10-year follow-up, the highest prevalence of normal fasting blood glucose (FBG) levels was noted. Stroke can result from plaque buildup, which blocks blood vessels in the brain.[27] Stroke patients with high blood sugar levels had a lower risk of FBG levels and showed a significant decrease over the 10 years ($F = 4.313$, $P = 0.001$). Lowering FBG levels positively affects stroke patients, as high FBG levels are independently linked to an increased risk of stroke.[28]

Fasting blood glucose (FBG) and 2-hour postprandial glucose measurements significantly affected the incidence of stroke ($p < 0.0001$). This finding suggests a clear link between diabetes mellitus and stroke. Elevated blood sugar levels can worsen stroke outcome. Diabetes contributes to stroke through several mechanisms, including atherosclerosis, cerebral small-vessel disease (SVD), and impaired blood flow. Individuals with diabetes are at a higher risk for stroke, and high

blood sugar can exacerbate brain damage, increase bleeding risk, and hinder recovery.[11,29]

Dietary intake

Food intake significantly affects the stroke risk. High energy and fat consumption can lead to obesity and dyslipidemia, whereas excessive carbohydrates may cause hyperglycemia. The results showed significant decreases in energy ($F=11.692$, $p<0.001$), fat ($F=70.207$, $p<0.001$), carbohydrate ($F=49.187$, $p<0.001$), and sodium ($F = 20.509$, $p<0.001$) intake. Stroke can cause complications, such as paralysis, neuropsychological issues, and dysphagia, which worsen nutritional deficiencies by limiting movement, disrupting eating habits, and increasing the risk of aspiration.[30]

Nutrient intake is crucial for recovery from stroke. Energy intake ($p = 0.0002$) and fat intake ($p = 0.0007$) significantly affected stroke incidence. Reducing saturated fat may reduce cardiovascular events.[31] Sodium intake also played a significant role ($P =0.0012$). High sodium intake increases blood pressure by causing water retention, increasing systemic resistance, altering endothelial function, and affecting large arteries, all of which contribute to hypertension and stroke.[32] The Indonesian Ministry of Health recommends limiting the sodium intake to 2000 mg per day.[33]

The study's findings are limited by missing data due to incomplete measurements and disruptions from the COVID-19 pandemic in 2020, potentially affecting the accuracy of the results on lifestyle factors and stroke risk. Future research should investigate the long-term effects of physical activity and dietary changes on stroke recovery, and consider socioeconomic factors and healthcare access. Expanding and continuing this cohort study is crucial for a deeper understanding of NCDs in Indonesia, with a focus on integrating comprehensive data and overcoming pandemic-related disruptions to improve the validity and applicability of the findings.

Conclusion

Over a 10-year follow-up period, significant changes were noted in nutritional status, fasting blood glucose (FBG) levels, high-density lipoprotein (HDL) cholesterol, physical activity, and smoking habits among stroke subjects. Key risk factors influencing stroke incidence include advanced age, elevated blood sugar levels, imbalanced cholesterol levels (LDL and HDL), smoking, physical activity, and dietary intake (energy, fat, and sodium). This study highlights how sustained lifestyle modifications such as controlling smoking habits, improving diet, and increasing physical activity are crucial for reducing stroke risk. It provides valuable insights into the long-term impact of these modifications on stroke prevention. These findings underscore the need for proactive management of stroke risk factors and suggest that comprehensive, sustainable prevention strategies are essential. Future research should explore the effectiveness of specific interventions across diverse populations to refine stroke prevention approaches and address the risk factors that evolve with age and lifestyle changes.

Conflict of interest

The authors declare that no conflict of interest with another person or institution

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ORIGINAL ARTICLE

Correlation between food preferences and nutritional intake in food service at KH Mas Mansur Student Dormitory of Universitas Muhammadiyah

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Abstract

Background: Having good nutritional knowledge is not enough to form a healthy diet in students, it needs to be supported by a good consumption environment, such as food service in dormitories. Providing healthy food and having good preferences needs to be conducted to increase students' food intake.

Objective: The purpose of this study was to see how the correlation of food preferences in the dormitory with the amount of nutrient intake in students who lived in the KH dormitory

Methods: This study used an analytic observational design with a cross sectional approach. The subjects of this study were students who lived in dormitories with a total population of 365 students. Data collection was carried out by direct interview method with a 24-hour recall form instrumen for 3 days.

Results: The results of the correlation test showed that food preferences in the dormitory were positively correlated with total energy (p=0.032) and protein (p=0.012) intake. There was no correlation between food preferences in the dormitory with intake of fat and carbohydrate.

Conclusion: This study showed that the better the students' preferred food in the dormitory, the higher the amount of energy and protein intake. The results of this study was limited to the relationship of food preference factors to student food intake, so it is still necessary to conduct further studies on other internal and external factors that are also related to the level of student intake. Thus the amount of intake obtained by students living in dormitories can be maximised.

Keywords: food service, food preference, nutrition intake

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Introduction

Based on data from *Badan Pusat Statistik Indonesia* (BPS Indonesia), the student population is increasing every year. It is known that in 2022 the population reach 9.23 million students. [1] This population is part of the young adult population and has a risk of nutritional problems that need adequate attention.[2] In the young adult age range, students experience a transition in life from adolescence to adulthood. Students begin to

experience several changes and adjustments to social, psychological, and biological interactions in the environment. These situations can lead to changes in unbalanced consumption behavior. [3],[4] Therefore, it is important to make efforts to improve healthy eating patterns in order to meet the nutritional needs of students and establish healthy eating habits that continue into adulthood.[5] This is also to reduce the burden of chronic diseases that continue to increase in the long term.[6]

College students are part of a nutritionally vulnerable group. This is triggered by inadequate food intake and lack of control over food. Students are more likely to consume food that is easily accessible and in a short time, causing the formation of the habit of consuming fast food, eating at restaurants / food stalls.[7] This phenomenon is increasing because it is supported by the increasing number of fast food stalls and high-energy foods/ drinks.[8] Based on research conducted in 2020 by Tambun et al.[9] at Sebelas Maret University Surakarta (UNS) on food consumption in migrant students showed that students' energy intake was still relatively low, this was indicated by the average value of Total Energy Consumption (TKE) of 74.6%. In addition, other research conducted in 2018 by Nurkhopipah et al.[10] on the undergraduate student population of Sebelas Maret University Surakarta showed that almost half of the student sample (44.95%) had poor eating habits.

Nutritional knowledge is significantly associated with healthy eating, but knowledge about healthy eating alone cannot guarantee adherence to a healthy diet.[3] The environment may influence the availability and access of food consumption among students. Therefore, in order to improve nutritional knowledge, it is also important to improve the environmental sector that can provide convenience and affordability of healthy foods. By changing environmental factors, it will be able to influence the consumption habits of students.[11]

One approach to influencing the food consumption environment on campus can be accomplished by organising meals in student dormitories.[11] Student dormitories with food service can better support the nutritional adequacy of students compared to dormitories without food service,[12] However the organising of meal is not enough if it does not pay attention to the elements of nutritional fulfilment, good management and good acceptance (preferences) by students. Therefore, it is important to consider students' preferences for food, as well as see the amount of intake consumed by students, so that they can see how much the food preferences affect the nutritional intake of students in the dormitory.

One of the internal/individual factors that can determine a person's food consumption is food preference. A good preference level for a food can enhance the level of food intake. A person will tend to prefer consuming preferred foods (with greater quantity and frequency) compared to foods that are not preferred.[13] The higher a person's level of food preference, the higher the level of satisfaction with food consumption.[14] Therefore, it is recognised that the preferences towards a food will affect the amount of food intake that is consumed, as well as describing the level of satisfaction of the individual.

KH. Mas Mansur Student Dormitory is a student dormitory of Universitas Muhammadiyah Surakarta which is equipped with food service. This dormitory accommodates students from various study programmes and semester grades. This dormitory is conventionally service-oriented. So that the implementation of this food is specifically only for student of the dormitory. The food service system in this dormitory is carried out from Monday to Friday by serving two main menus a day, than besides consuming food from the dormitory, students can also consume food outside the dormitory to fulfill their daily nutrition needs.

Based on the information above, the researcher is interested in seeing how the relationship between the level of food preference in student dormitories and the level of intake of calories (energy), protein, fat, and carbohydrates in the food served in the dormitory KH Mas Mansur UMS.

Methods

This type of research is quantitative research with a cross sectional design. This study was conducted in the area of Universitas Muhammadiyah

Surakarta, namely in the KH Mas Mansur student dormitory located on Kartasura, Sukoharjo, Central Java, Indonesia. The Data collection was carried out in March 2023. The population of students in the dormitory is 365 students, consists of 157 men and 208 women. In the dormitory building, the students are spread over two buildings (male dormitory and female dormitory) and each building consists of four floors of dormitories. From this population, the sample size was calculated using the Slovin method and obtained from as many as 83 research subjects, then the sample was taken using proportional random sampling technique. The inclusion criteria in this study were students aged 18-25 years, had lived in the dormitory for at least 3 months, in good health, not taking medication and not running a special diet programme. While the exclusion criteria are suffering from chronic diseases.

The independent variable in this study is food preference in the dormitory and the dependent variable is the level of nutrient intake food dormitory (total energy, protein, fat and carbohydrate intake). Data collection of food preferences in the dormitory was carried out using the hedonic test method with a linkert scale (1-5).[15] The assessment was conducted on all menu items served in one day and each menu item served was rated on a linkert scale (1-5), and the results of the assessment were recorded in the form food recall 24 hours. This assessment was conducted for 3 days randomly from Monday to Friday. Then from the assessment data collected, calculations were made to be able to see the accumulation of food preference evaluations in one day. The formula used for accumulating students' food preferences is based on the calculation below:

$$\%food\ preferences = \frac{(\text{total score} - \text{minimum score})}{(\text{maximum score} - \text{minimum score})} x100\%$$

Description:

Total score : Is the overall result of the scoring of all food items that are served

Minimal score : Is the minimum score (1) summed as many food items are assessed.

Maksimal score: Is the maximum score (5) summed up as many food items are assessed

Data on total energy, protein, fat and carbohydrate intake were obtained through interviews using the 24-hour food recall method. Data collection of each element (energy, protein, fat, and carbohydrates) was carried out in 3 days. Determination of the day of data collection was carried out randomly by the researcher in the range of Monday to Friday. The data from the 24-hour food recall interview was then inputted into the Nutrisurvey application in order to determine the amount of energy, protein, fat and carbohydrates. Then to find out the level / amount of nutrient intake, it is needes to be compared with the Recommended Dietary Allowance (RDA). Then the level / amount of nutrient intake will be obtained in the form of %.

All data obtained were analysed to determine the relationship between variables using the Pearson product moment correlation statistical test (α=0.05) with the help of SPSS 25 software. This study has obtained an ethical eligibility test from the Health Research Ethics Commission of Dr. Moewardi Hospital Number 321/III/HREC/2023.

Results

The food service in the KH Mansur student dormitory is a conventional food service that is administered directly by the dormitory with the system is service oriented. This system does not serve the generally in public, but specifically to particular consumers, in this case students who live in the KH Mas Mansur dormitory. The food service system is not organised to serve students' intake needs in a day, but only serves two main menus so with this system to fulfill their daily needs, students also consume food from outside the dormitory. Student food services can be accessed from Monday to Friday and with canteen operating time is from 06.30-20.00. The food service uses a weekly menu cycle system and there are also some menus that use a monthly cycle. The food distribution system is self-service, so the portioning is done directly by the students. The size

of the food portioning will certainly affect the intake of nutrients / food. So that the size of the amount of nutrient / food intake depends on the portioning and student preferences.

Table 1. Characteristics of Research Subjects

Category	Frequency	
	N	%
Gender		
Male	35	42,2
Female	48	57,8
Faculty		
Health	11	13,3
Non-health	72	86,7
Dormitory Food Preferences		
Low (<37%)	0	00,0
Medium (37-77%)	46	55,4
High (>77%)	37	44,6

Table 1 presents data on the characteristics of the research subjects. Based on gender, there were more female subjects than male. There were 48 female respondents (57.8%) while 35 male respondents (42.2%). When viewed based on faculty distribution, most respondents were in the non-health faculty category with a total of 72 subjects (86.7%) while the health faculty was only a small proportion, as many as 11 subjects (13.3%). In addition, when viewed from food preferences in the dormitory, most were in the moderate category, as many as 46 people (55.4%), and the remaining 37 people (44.6%) were in the high preference category. No students were found in the category of low food preference rating in the dormitory.

Food preference is an assessment of the level of like or dislike for a food (12). **Table 2** shows the mean value of food preference assessment by students, which is a percentage of 73.44%. The percentage value of food preference is included in the low category if it is <37% and is said to be high if >77%. When this value is categorised in the food preference assessment category, this value falls into the moderate preference category (37-77%).

Table 2 shows that the average level of food energy intake in the dormitory is 64.60% RDA. The highest percentage of macronutrient adequacy is carbohydrates with an acquisition of 68.38% RDA, then protein intake is 56.86% RDA, and the lowest level of fat intake is 55.59% RDA. When viewed from the percentage of fulfilment of student intake needs, from two times serving the main menu by organising food in the dormitory, the contribution to student food intake is said to be sufficient if the percentage of intake is obtained at 60-70% of the RDA. Based on the average results of the acquisition of food intake figures in the dormitory, energy and carbohydrate intake are sufficient, while protein and fat are still insufficient.

The intake of students from outside the dormitory obtained an average energy of 28.39%, protein 20.66%, fat 32.04% and carbohydrates 28.35%. The provision of meals in the dormitory meets the intake needs of 60-70% RDA, so to meet the amount of food intake obtained from outside the dormitory in the range of 30-40% RDA. When viewed from the average acquisition of food intake outside the dormitory, it can be said that fat intake is appropriate, while energy, protein and carbohydrate intake is still considered insufficient.

When viewed based on the accumulated value of food intake in the dormitory and food outside the dormitory, it can see the level a day of nutritional adequacy of students. By the accumulation of food in the dormitory and outside the dormitory, it can see the adequacy of energy and macronutrients of students. The average student energy adequacy is 91.80%, protein is 76.69%, fat is 86.05% and carbohydrate is 95.63%. Nutritional adequacy is said to be normal if it can be fulfilled as much as

Tabel 2. Preference Score and Nutritional Intake

Variable	*Mean±SD*		
	Food in dormitory	Food outside dormitory	Total
Dietary energy intake (%RDA)	64,60±12,11	28,39±11,91	91,80±17,05
Dietary protein intake (%RDA)	56,86±09,41	20,66±11,68	76,69±13,79
Dietary fat intake (%RDA)	55,59±11,7	32,04±16,76	86,05±20,15
Dietary carbohydrate intake (%RDA)	68,38±16,14	28,35±12,39	95,63±21,34
Food preferences (%)	73,44±14,41	-	-

(90-119%RDA), severe deficit (<70%RDA), moderate deficit (70-79%RDA), mild deficit (80-89%RDA) and excess (≥120%RDA). Based on these mean values, it can be seen that the adequacy of energy and carbohydrates is in the normal category, protein is in the moderate deficit category, and fat is in the mild deficit category.

preferences are the level of likes and dislikes towards a food, so that preferences can affect food consumption including the selection of diet frequency, nutrient intake, and food adequacy of a person.[20] Increased food preferences will increase the size of a person's meal, so the higher the food preference, the higher the portioning that is carried

Table 3. Relationship between food preferences in dormitories and nutritional adequacy

Variabel	r	*p-value*
Dietary energy intake level in the dormitory (%RDA)	0,235	0,032*
Dietary protein intake level in the dormitory (%RDA)	0,274	0,012*
Dietary fat intake level in the dormitory (%RDA)	0,200	0,070
Dietary carbohydrate intake level in the dormitory (%RDA)	0,207	0,060

** Significant relationship if p value <0.05 (Pearson Product Moment analysis test)*

Table 3 presents data from the statistical analysis of the correlation between food preferences and macronutrient adequacy. Based on the table, it can be seen that food preferences have a significant correlation in energy (p=0.32) and protein (p=0.012), while there is no correlation between food preferences in the dormitory with the level of fat and carbohydrate intake.

Discussion

The Correlation between Food Preferences and Dietary Energy Adequacy in Dormitories

Based on **Table 3**, it is evident that food preferences are related to the level of energy intake of students (p=0.032). So it can be seen that the higher the preference for food in the dormitory, the higher the energy intake of students. Energy intake is the total of macronutrient components in food that are supplied to the body, including carbohydrates, protein and fat.

The correlation between food preferences in dormitories and energy adequacy is in line with research conducted in 2013 by Sutyawan & Setiawan [17] on high school students living in student dormitories and as well as research in 2017 by Tinah [19] on Polytechnic students living in dormitories. The results of both studies show that the level of preference for food served by the food provider is related to energy adequacy. This is certainly in line with the theory stating that food out and will also increase the amount of energy intake.[14]

If viewed from the overall average energy adequacy of students who live in dormitories, it can be seen that the nutritional adequacy of students is still in the good category, this is marked by the average acquisition of energy intake of 91.80%RDA. Furthermore, when comparing with previous research conducted in 2020 by Tambun et al. [9] on UNS migrants who did not live in dormitories, it was classified as low, which is 74.6%. Than as well as the results of research conducted on students of UIN Walisongo Semarang in 2021 by sholicah[21] found that 72.72% of students had deficiency in energy intake. Therefore, the provision of food in the dormitory and good eating preferences can lead to better energy intake adequacy.

The correlation between food preferences and the level of energy intake indicated the importance of attention from food service organisers to the preferences of the menu served to students. So that in pursuing to meet the adequacy of students, it is necessary to get good food preferences. The organising of meals in dormitories with two main meals can contribute to energy adequacy of 60-70% of the RDA. Based on the data obtained, the average student adequacy of food in the dormitory is 64.60%RDA. This indicates that the food service in the dormitory is in the normal range, but this percentage can still be optimised to reach the maximum percentage.

Food preferences in dormitories are an important factor in the energy intake of students. So that the organised food needs to pay attention to the acceptance of food in the dormitory. However, there are also other factors that can also affect the nutritional intake of students, including the composition of food components and menu preparation.[22]

The correlation between food preferences and dietary protein adequacy in dormitories

Based on **Table 3**, it is determined that food preference in dormitories is related to students' protein intake (p=0.012). This indicates that the higher the preference for food in the dormitory, the higher the protein intake of students. Similar research has been conducted in 2013 by Sutyawan & Setiawan [17], with the subject of student senior high school who living in student dormitories. The study proved the similar result that the level of food preference in dormitories is related to protein intake, which can be explained by the relationship between protein and umami flavour in food.

Umami flavours tend to indicate the existence of proteins or amino acids.[23] Umami compounds in foods include free amino acids, nucleotides, peptides, organic acids and their derivatives. They can enhance the flavour of food, such as regulating sweetness, enhancing saltiness and suppressing sourness and bitterness.[24, 25] Umami flavour is commonly found in protein-containing foods such as fish, chicken, shrimp, mushrooms. With a high food preference, it can be associated with protein source foods in the diet.

Proteins are comprised of 20 different amino acids. Most proteins contain glutamate. Glutamate is the major umami flavour component in most proteins. Glutamate is a precursor to protein and a component of protein hydrolysates, so the umami flavour is a signal of the existence of protein in food [26]. However, some high-protein foods do not have a strong umami flavour. The umami flavour quality can be perceived by humans because of the easily digestible proteins that are formed due to cooking or fermentation.[27]

The impact of umami taste sensitivity on food behaviour relates to an individual's ability to perceive taste stimulation. Umami flavour sensitivity is associated with preference, acceptance and food intake. The association may be influenced by the palatability of the individuals. Palatability is one of the mechanisms of increasing liking or preference produced by umami compounds.[28]

Food materials that contain protein tend to deliver umami flavour into foods. Umami flavour increases the palatability of food, which subsequently increases food acceptance, and influences food intake.[23] The umami flavour can provide an appetite for food, which tends to indicate the existence of protein, so the high preference for food in the dormitory can be associated with the existence of protein nutrients in food. The higher the level of liking for food, the higher the nutrients in the food consumed.

There is a relationship between food preferences and protein intake in the food service in the dormitory, it can be concluded that with a mean scoring of food preferences of 73.44%, where this figure is included in the moderate category (37-77%), it was achieved a mean value of protein intake of 56.86% RDA, this figure is lower than the target adequacy of the food service in the dormitory which is 60-70%RDA. So that the organisation of food in the dormitory can strive to increase food preferences in the dormitory in order to increase the adequacy of student protein intake.

Next, it is seen that the mean protein intake obtained from outside the dormitory is 20.66% RDA. When the two are summed up, the total value of the adequacy of student protein intake is 76.69% RDA. From this figure, it is known that the adequacy of protein intake of students living in dormitories is in the category of moderate deficit (70-79% RDA). Something similar happened in another study in 2021 conducted by Patimbano et al.[29] in Public Health students at Sam Ratulangi University Manado, many students were found having an insufficient level of protein intake, which was 66.1%. In addition, another similar study in 2020 conducted by Cholidah et al.[30] on medical students at Mataram University found that some students (51.14%) were also found were also found having inadequate protein intake.

The correlation between food preferences and dietary fat and carbohydrate intake levels in dormitories

Table 3 shows that there is no relationship between food preference and fat (p=0.70) and no relationship between food preference and carbohydrate (p=0.60). Both p values showed p>0.05. This shows that the value of food preference in KH Mas Mansur dormitory is not related to the level of fat and carbohydrate intake. However, this study found a relationship between preference and energy intake, where energi intake is the total amount intake of fat, carbohydrate and protein.

The existence of a relationship between food preferences with energy, but there is no relationship between preferences with fat and carbohydrates can be due to the composition of nutrients in each food that students consume differently. In addition, the amount of energy in a food depends on the nutrient content of protein, fat and carbohydrates. When properly digested in the body, one gram of protein provides about 4 kcal of energy; one gram of fat provides about 9 kcal of energy; and one gram of carbohydrate provides about 4 kcal of energy.[31]

Food materials can be categorised as sources of carbohydrates, fat or protein. There are some foods that are sources of carbohydrates such as rice, flour, sweet potatoes, sugar. In addition, there are also sources of protein such as eggs, meat, fish, nuts. While sources of fat such as fish, eggs, meat, soya, fried foods and foods processed with oil. It can be said that each food has its own nutritional value. Thus there is a possibility that someone consumes the same energy but with a different macronutrient composition. So that the amount of fat and carbohydrate intake depends on the type of food consumed by students. Although students consume food on the same day and with the same food menu presentation, there is a possibility that they consume fat and carbohydrate intake with different compositions. It depends on the food chosen and the portioning conducted.

The absence of a relationship may be because of other factors that influence food preferences. It is known that there is a significant relationship between food preferences and genetic variants. The existence of genetic variants makes each individual have certain preferences and tendencies towards sweet and fatty foods.[32] Moreover, genetic factors in umami flavour sensitivity are also related to, socio-demographics and individual status. These factors lead to the different umami flavour sensitivities of foods.[24] Furthermore, the intensity of sweet and salty flavours can also indicate the presence of certain nutrients in foods. Carbohydrates (mono and disaccharides) are associated with sweet flavour intensity, while fat, protein, energy and sodium are associated with salt flavour intensity.[25]

Another possible reason is that the researcher also found a wide variety of portioning done by students. There is no standard measurement in portioning. It all depends on the portioning carried out by students, because the provision of food in the KH Mas Mansur student dormitory with a self-service system. Students do their own portioning, so this can lead to different sizes of menu items taken by each student. This difference can lead to a comparison of the different amounts of macronutrient intake in students.

Another possible factor is that there were findings during data collection where students gave a good preference value for a food in the dormitory but did not consume the food because they did not want to consume the food and there were also those who said because the food did not match with other foods. For example, in the dormitory there is a menu of krispy chicken and clear vegetables. Both get a good preference value but do not take clear vegetables because it is not suitable when consumed with krispy chicken because it can eliminate the krispy texture of the chicken. So that the compatibility in the preparation of the menu needs to be arranged properly.

In this study, it can be seen that students who live in the KH Mas Mansur student dormitory which is equipped with a food service system obtain a mean fat intake adequacy of 86.05%RDA with a category included in a slight deficit (80-89%RDA) and carbohydrate intake adequacy of 95.63%RDA including in the normal category (90-119%RDA). When compared to research in 2021 conducted by Patimbano et al.[29] on Public Health

students at Sam Ratulangi University Manado, it was found that most of the adequacy of students' fat and carbohydrate intake was still classified as insufficient with a total percentage of students of 75.4% and 84.7%. This shows that to meet the intake needs of students not only considers providing access to consumption for students but also from internal and external factors.

Conclusions

In this study, it can be seen that the average value of food preferences in the dormitory is in the moderate category. The result of this study is that there is a relationship between food preferences in the dormitory with the level of energy and protein intake, but there is no relationship with the level of fat and carbohydrate adequacy. So it can be concluded that in the implementation of food in the KH Mas Mansur student dormitory, if the higher the assessment of student preferences for food in the dormitory, the more energy and protein adequacy in students will increase, so that the organizers of meals in the dormitory must continue to make efforts to increase preferences for food in the dormitory in order to further increase the adequacy of energy and protein intake. As for further research to be able to see the relationship to other external and internal factors that can affect the adequacy of student intake.

Conflict of interest

The authors declare that there is no conflict of interest.

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