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The role of nutrition the COVID-19 pandemic

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ABSTRACT

In the ongoing coronavirus disease 19 (COVID-19) pandemic, the most vulnerable groups are those with pre-existing health problems and the elderly due to their reduced immune system to prevent infection. Nutrition plays a significant role in maintaining the immune system to prevent pathogen manifestation. This review aimed to identify and discuss the role of nutrients in COVID-19 in developing immunity. Studies included in this review were obtained from articles published in reputable journals accessed from the National Center for Biotechnology Information (NCBI) website, leading search engine, in a retrospective timeframe from January 1 to May 2, 2020, using specified keywords. The search resulted in seven articles relevant to the objective of the review. They highlighted the role of nutrients, namely the deficiency of essential nutrients that might exacerbate the health status. The consumption of certain nutrients, micronutrient and omega-3 might be tolerated up to the upper level of recommended dietary allowance (RDA) to benefit the health status. This review can assist in providing the prevention and mitigation approach to improve immunity amid the COVID-19 pandemic. The government should expand the continuous delivery of messages regarding the benefit of appropriate nutrients in maintaining health and immune system. Furthermore, the current condition gives the best opportunity to educate the community on a healthy and balanced diet for daily life.

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1. INTRODUCTION

The influenza pandemic has been repeatedly reported in global history. In 1918-1920, an influenza pandemic, which is referred to as the Spanish influenza pandemic, was reported to affect many countries globally. The Asian and Hong Kong flu this between 1957 and 1968 the H1N1 pandemic in 2009 [1]. In late 2019, the world was taken by surprise with the emergence of an influenza outbreak in Wuhan, Hubei Province, China, which eventually develops into a worldwide pandemic. The disease that causes this outbreak, which is then referred to as the coronavirus disease of 2019 or COVID-19, targets the human respiratory system [2]. More than ten million people worldwide are affected by this virus.

The virus's official name is severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) that belongs to the β-coronavirus class [3]. This type of virus shares the same genetic characteristics as coronavirus types, namely severe acute respiratory syndrome (SARS) virus and the Middle East respiratory syndrome (MERS) virus [4]. Indonesia declared the two first confirmed cases on March 2, 2020 in Depok, West Java. On March 29, 2020 the number of positive COVID-19 cases have reached almost 1,300 cases in

30 provinces. DKI Jakarta, West Java, Banten, East Java, and Central Java are the five provinces with the highest number of COVID-19 cases [5].

The SARS-Cov-2 virus-infects the respiratory tract and causes acute respiratory distress syndrome (ARDS), leading to a high amount of mortality. The World Health Organization (WHO) declared COVID-19 as a pandemic on March 12, 2020. Up to May 12, 2020, the John Hopkins Coronavirus Resource Centre has recorded 4,175,284 confirmation cases, making the disease an emerging public health problem in all countries in the world which heightens the need for preventive and curative actions to avoid further spread of the disease. The magnitude of this public health problem is overwhelming with more than 180 countries affected by the disease. Countries have started to implement policies to contain the pandemic, including encouraging people to stay at home and applying physical distancing [2].

Recent developments reveal that droplets are the medium for disease transmission and that the disease mostly manifests in people with impaired immune systems [6]. Virus-loaded droplets originate from the mucus environment and are expelled when someone coughs or sneezes. Early findings revealed that the elderly and people with comorbidities are more susceptible to develop more severe infections with increased risk for poor outcomes [7]-[9]. In China, patients with pre-existing comorbidities such as cardiovascular disease, diabetes mellitus, chronic respiratory disease, cancer, and hypertension are observed to have a high fatality rate [10].

Malnutrition is a condition where the balance between the macro-and micronutrients required for metabolism reactions is not achieved. The deficit of both types of nutrients will deteriorate the immune system and increase the disease's predisposition. In animal studies, protein deficits have been demonstrated to decrease virus-specific antibody responses and increase influenza infection possibility [11]. Virus manifestation, micronutrient deficiency, and pre-existing comorbidities signify disease severity and increase mortality. The nutrition- deficiency-related factors might worsen disease severity, but information on disease prevention from the nutrition perspective is limited during this pandemic. Since COVID-19 is a new disease with so many undisclosed aspects, a comprehensive approach, including prevention, is needed to reduce the impact of the outbreak [12].

The most common diseases reported as a prompt to the development of ARDS in COVID-19 patients are hypertension, diabetes mellitus, cardiovascular diseases (CVD), coronary heart disease [9], [13]. Centre for Disease Prevention and Control (CDC) reported that diabetes mellitus is one of the most dangerous COVID-19 comorbidities as it stimulates CVD that causes one-third of the patients to be admitted to the intensive care unit (ICU) [14]. Patients with severe COVID-19 and diabetes conditions present severe inflammatory indicators and a higher mortality rate compared to non-diabetic patients. A New York hospital report stated that patients with a high body mass index (BMI) >40 kg/m^2 also have a high risk of being admitted to the hospital after older age. While in France, patients with a BMI ≥35 kg/m^2 require invasive mechanical ventilation [10]. Being obese would increase the probability of having a higher viral load, extend the virus shedding period to the community, and increase mortality [1]. In the progression of CVD, nutrient deficiencies worsen the severity of the disease. A review for the US Preventive Service Task Force suggested that the consumption of vitamins and minerals will create benefits in preventing chronic diseases and nurture health [15].

Obesity is a sign of excessive energy intake stored in the body, a situation that might increase micronutrient deficiency risk. People with obesity tend to have a lower vitamin D (1,25-dihydroxy vitamin D/calcitriol) level, which plays a role in pathogenicity and inflammation [16]. Therefore, nutrient shortage and malnutrition will increase disease severity. Low nutritional status is likely to be related to higher oxidative stress levels and inflammation status that can impair immune function. The immune system is highly dependent on sufficient nutrient intake and diet consumed to be optimum [17]. Sufficient energy intake to support care is also recommended by the National Health Commission of the People's Republic of China and the National Administration of Traditional Chinese Medicine to improve health outcomes [12].

In light of the important role of nutrition in driving COVID-19 progression, this paper aims to highlight the role of nutrients in addressing health issues linked the COVID-19 pandemic. This is a review that has a purpose to enrich and emphasize nutrition's role in preventing COVID-19 infection amidst this pandemic by elaborating the role of nutrients to improve the immune status and reduce mortality in COVID-19 patients. It is expected that the narrative in this paper will be able to assist the policymakers in deciding on the management of the COVID-19 pandemic, especially in developing preventive programs.

2. RESEARCH METHOD

This was a retrospective review of articles related to COVID-19 and nutrition published from January 1 to May 2, 2020. The literature search was performed using the search engine in the National Center for Biotechnology Information (NCBI) website (https://pubmed.ncbi.nlm.nih.gov) by inserting the keywords

of "COVID-19 and nutrition", "novel coronavirus and nutrition", "COVID-19 and public health", "novel coronavirus and public health". The NCBI website was selected because it is considered the leading search engine for biomedical journal articles with an excellent search engine [18]. Most of the published materials related to this topic were letters to the editor, short communication, editorial, statement, journal pre-proof, and comment. There were 1,673 articles identified by the search engine. Inclusion and exclusion criteria were then applied to shortlist the articles. The inclusion criteria used include: (1) published from January 1 to May 2, 2020, (2) article published in English, and (3) article highlights the role of nutrient in COVID-19. Meanwhile, the exclusion criteria were: (1) published prior to January 1, 2020 and after May 2, 2020, (2) article published in a non-English language, and (3) article does not present nutrition point of view.

Selected articles were sorted by looking at the exposure and outcome in the article and eventually seven articles were identified as suitable to the review objectives. A narrative review was then written to elaborate on the findings of these articles. This review emphasizes the benefits of good nutrition during the pandemic, including the role of nutrients in the immune system. In the writing process, the authors organized the references, identified the nutrient explored, and displayed the findings of each article. For analysis purpose, the author used nutrient as the study exposure and COVID-19 as the observed outcome.

3. RESULTS AND DISCUSSION

The results of the elaboration of the articles selected for the review are summarized in Table 1. The reviewed paper expressed that corroborate the role of nutrients in avoiding the progression of disease-related immune functions that could lead to serious health status. The role of vitamins and minerals is deemed to be important to enhance the immune status by modulating the mechanism. Calder *et al.* [19] suggested the consumption of essential fatty acid, such as alpha-linolenic acid (ALA) omega-3, up to the upper limit of the safe range for daily consumption. Essential fatty acids are not the only nutrients recommended. Other micronutrients are also proposed to be consumed to support the immune function, one of which is vitamin D. The low concentration of vitamin D is commonly found in cardiovascular disease patients and will affect its role in the immune system. For patients with cardiovascular cases, it is mandatory to reduce sodium consumption that links to the tissue expression of the ACE2 receptor. The increment of body weight can increase the susceptibility to hospitalization, which may relate to the recommendation to stay at home. Staying at home tends to reduce physical activity and increase food intake, resulting in susceptibility to obesity. In public health approaches, nutrition and immunity should be included in the integrative program for preventing COVID-19 due to its fundamental role in reducing morbidity and mortality related to this disease. Both macro-and micronutrients will impact how the immune function deals with SARS-CoV-2 infection.

ESPEN experts have issued a nutrition recommendation for several conditions, i.e., individuals at risk or infected by SARS-CoV-2 and ICU patients infected with SARS-CoV-2 during pre-intubation, ventilation, post-mechanical ventilation, and dysphagia period. Attention should be given to the intakes of energy, protein, fat and carbohydrate, and micronutrients to meet the daily need requirements.

Table 1. Summary of articles identified as discussing the relationship between nutrition and COVID-19

Author	Type of article	Outcome observed	Result
Calder *et al.*[19]	Review	Immune system	Micronutrient and omega-3 supplements will benefit the immune system; the amount above RDA and within the safety limit is recommended. Further actions for responding to public health problems should include nutrition frameworks to improve public health outcomes.
Frühbeck *et al.*[20]	Statement	Risk factor	Obesity with malnutrition might increase the severity of disease and the possibility to require intensive care
Grant *et al.* [21]	Review	Risk factor	Vitamin D deficiency increases the susceptibility to ARDS. Those who are at risk of having infection to influenza/COVID-19 should increase the 25(OH)D concentration to more than 40-60 ng/mL
Butler and Barrientos [22]	Article	Impact of malnutrition on a patient of COVID-19	An unhealthy diet will increase the chance for the inflammatory onset and deteriorate the host defense. A healthy and balanced diet should be a concern for reducing predisposition to serious illnesses
Muscogiuri *et al.* [2]	Perspective	The recommendation of nutrition intake during the pandemic	Consuming food from good sources will support immune function. Arranging the activity for maintaining weight will assist to avoid negative health effects during the pandemic.
Post *et al.* [23]	Journal pre-proof	Risk factor	High sodium intake might link to down-regulation of the ACE2 receptor expressed in internal organ
Barazzoni *et al.* [24]	Editorial	Preventive and curative actions related to COVID-19	European Society for Clinical Nutrition and Metabolism (ESPEN) experts stated that providing concise guidance proposing ten practical recommendations for the nutritional management of COVID-19 patients

is necessary.

Table 2 elaborates the benefit of macro-and micronutrient consumption in maintaining the immune system as explained in the reviewed articles. The shortage of macro-and micronutrients will increase the risk of having the severe type of the disease suffered. Efforts to meet nutrient requirements will stimulate the immune system to function better that will benefit the health status amid this pandemic.

Table 2. Nutrient, food group, and food-related benefits for the immune system

Nutrient	Food source	Benefit
Energy	Total energy intake of food consumed	Adequate energy intake will support immunity [24].
Protein	Animal and plant-based food	Protein intake will benefit the immune system [24].
Fat and carbohydrate	Fat and staple food	To meet the energy requirement [24].
Vitamin A	Carrots, green leafy vegetables, sweet potatoes (β-carotene), red meat, egg, and poultry (retinol)	B-carotene and retinol are anti-infective agents against viral infection [2].
Vitamin Bs	Liver, green leafy vegetables, egg, and red meat	Deficient status of vitamin B can deteriorate innate and adaptive immunity that can increase susceptibility to infection [19].
Vitamin D	Liver, fish, egg yolk, dairy (e.g., milk, yogurt), and sun exposure to activating 7-dehydrocholesterol in the skin	Sufficient vitamin D reduces the risk of developing several chronic diseases such as cardiovascular disease, diabetes mellitus, cancers, and hypertension that create a significantly higher risk of death from respiratory tract infections [2, 21].
Vitamin C	Red peppers, broccoli, strawberries, oranges, mangoes, lemons, and other fruits and vegetables[2]	Adequate intake of vitamin C will aid in reducing cold severity and duration [2].
Vitamin E	Vegetable oils (soybean, sunflower, corn, wheat germ, and walnut), nuts, seeds, spinach, and broccoli.[2]	The deficiency of vitamin E will impair both humoral and cell-mediated immune functions [2].
Zinc	Animal source	A trace element that has an important role in developing immune cells and enzymes co-factors [19]
Fatty acid	Fish and fish oil containing omega 3, polyunsaturated fatty acid (PUFA), docosahexaenoic acid (DHA)	Anti-inflammatory and immunomodulatory properties of fatty acids could give a protecting factor against infection [19].

3.1. Discussions

COVID-19 has become a new emerging public health problem, requiring serious campaigns to increase public awareness on how to prevent the disease. Personal hygiene, sanitation, face mask use, cough etiquette, and physical distancing are among the measures that are commonly promoted in these campaigns. Nutrition plays a significant role in improving the immune response against viral infection. It is important to meet the RDA requirements up to the upper limit to optimize the defense mechanism. A continuous and extensive national program is needed to get the most benefit from a nutrition program to reduce the burden of the health system during this pandemic. Some nutrients are already highlighted for their role in improving the immune response, emphasizing the importance of consuming a healthy and balanced diet to meet nutrient requirements to maintain the immune system's optimal function.

Vitamin B group plays a vital role in amino acid synthesis, tissue formation, and epigenetic mechanisms [25]. Vitamin B_6 (pyridoxal 50-phosphate/PLP) regulates the immune function as a co-factor in generating metabolites with immunomodulating effects. The intake of PLP above the RDA will maximize the lymphocyte mitogen response [26]. The insufficient intake of these nutrients will deteriorate protein mechanism and synthesis. Vitamin C supports the immune system by synthesizing the antioxidant in the skin and optimizing the barrier function to protect from pathogen infection. The shortage of vitamin C will impair the immune system and increase the predisposition to infection. In treating respiratory infection diseases, vitamin C requirements above 100-200 mg/day should be met to balance the metabolic demand and inflammation [27]. Vitamin D is another micronutrient that independently correlates with CVD prevalence. The low concentration of serum 25-hydroxyvitamin D (25(OH)D) is inversely associated with diabetes, hypertension, myocardial infarction, congestive heart failure, carotid atherosclerosis, microalbuminuria, stroke, and kidney dysfunction [28]. Vitamin D is clinically proven to reduce infection risk by modulating antimicrobial peptides, defensins, and cathelicidins formations. Vitamin D also strengthens cellular immunity by minimizing the production of proinflammatory Th1 agents such as tumor necrosis factor α (TNFα) and interferon γ [21].

Other micronutrients also significantly contribute to supporting the immune system. Vitamin E, A, iron, zinc, magnesium, copper, and selenium have been proven to reinforce the immune system [19]. Better micronutrient status will accelerate the diminish of inflammation and improve the immune system status. For patients with comorbidities, selected micronutrients will improve the immune function against the infection. Patients with hypertension are commonly treated with angiotensin receptor blockers (ARBs) and angiotensin-

converting enzyme (ACE) inhibitors to reduce inflammation [9]. Some findings from several studies have demonstrated that ACE2 is a suitable receptor and entry point for the spike protein of virus SARS-CoV-2 to enter the cell [29]. The binding of virus with ACE2 receptors is mainly contained in the alveolar cells of the lower respiratory tract. During the binding process, the inflammation process can interfere with the immune system, engaged for antigen-presenting materials [30]. The high sodium intake also contributes to the ACE2 receptor expression which will lower the risk for being contracted and for more severe COVID-19 [23]. A meta-analysis of eight reports, that cover more than 45,000 patients with COVID-19, confirmed that hypertension has a higher risk of COVID-19 disease that increase the mortality rate [31], followed by diabetes mellitus and other diseases [10].

Macronutrients also play a major role in supporting the immune system. Low protein status that originated from inadequate protein intake is commonly found in Indonesia because protein sources are deficient. The Indonesian population consumed a minimum quantity of protein-rich vegetable and animal products. On average, Indonesians consume 2.2kg of fish and 9.4kg of meat per year per capita [32]. The protein requirement for Indonesian adults ranges from 56-60g for daily consumption [33]. Protein is needed to form an infection defense agent by exerting the gut-associated lymphoid tissue (GALT) and functional, active immunoglobulins. Deficient protein intake will increase the susceptibility to lung infection, hyper-inflammation, and generate mortality [17].

Weight management is another crucial issue to be discussed in terms of COVID-19 pandemic. The quarantine period may result in unhealthy eating behavior and a sedentary lifestyle which may predispose a new clinical condition [34]. The overweight-obesity patients are at risk of increased susceptibility and prone to die. Encouraging the community to apply a healthy and balanced diet and increasing physical activity will provide an advantage in the pandemic season. The long period of staying at home discourages people from allocating extra time for exercising and increases the tendency to sit, watch television, play games, and operate electronic gadgets. [16]. The increment of BMI is significantly associated with the primary endpoint for the overweight and obesity category, odds ratio (OR) [95% confidence interval (CI)], 1.58 [0.77–3.24] and 2.58 [1.28–5.31], respectively. ESPEN is an international society that put this knowledge into consideration and issued a nutritional recommendation for those with or without COVID-19 risk. Those with one or more morbidities (polymorbid) and elderly should pay more attention to nutrition to reduce the risk of infection [24].

Those who consumed the modern diet consisting of high saturated fats, sugars, refined carbohydrates, and salts have an increased risk of obesity and cardiovascular disease, increased risk for being infected by COVID-19, and, when infected, increased risk of mortality and severe diseases [22]. A study in Seattle found that obese patients with COVID-19 have a high risk of having to receive ventilation treatment and died. Overweight and obesity in COVID-19 also increase the susceptibility to developing severe pneumonia when compared to the normal body weight [10]. Hence, it is mandatory to consume a healthy and balanced diet to meet the requirements of nutrients to maintain the optimum immune system function. The modern dietary pattern tends to contain high fat and low fiber. The excessive intake of food containing saturated fatty acid (SFA) may become the precursor for proinflammatory indicator modulation and might worsen the disease severity [35]. Nutrients that are involved in antioxidant and anti-inflammatory production include, vitamin A, vitamin C, omega-3-fatty acid, polyphenols, and carotenoids from a plant-based diet. Dietary fiber is also the potential source for short-chain fatty acids (SCFA) production from the gut microbiome activity in the colon [17].

Furthermore, this circumstance also lead to unhealthy eating behavior. The reluctance to engage in physical activities will worsen the chronic health condition. Having regular exercise at home will be beneficial for avoiding the coronavirus infection and maintain physical fitness [36].

Indonesia has implemented a national program called *GERMAS* (*Gerakan Masyarakat Sehat*/Healthy Community Movement) as a preventive action by promoting a healthy lifestyle. Optimizing this program through extensive nutrition education at the national level will help to improve the healthy lifestyle to reduce chronic disease incidence. Furthermore, Indonesia has also developed a Healthy and Balanced Diet Guideline (*Pedoman Gizi Seimban*g) and My Plate (*Isi Piringku*) as a daily consumption guideline. It is mandatory to have regular and massive nutrition education programs through digital platforms and to evaluate the programs routinely.

The government should continuously promote the benefit of nutrients in maintaining the health and immune system. This pandemic has offered the best opportunity to drive the population towards a healthy and balanced diet. Furthermore, the policy brief that reinforces the existing program, *GERMAS*, and the hygiene awareness program should be updated to achieve better wellbeing and adoption of a healthy lifestyle. Since there are things that remains a mystery with regards to the preemptive efforts and treatment of COVID-19, relying on the immune system is the possible prevention effort to be considered. This pandemic taught us to complete the puzzle of knowledge and put the best effort to find the most effective medicine.

4. CONCLUSION

Nutrition plays a major role in improving the immune response against viral infection. It is important to meet the RDA requirements for nutrition intake, even up to the upper level to optimize the defense mechanism. A continuous and extensive national nutrition program will result in enhanced health, reducing the burden of the health system. In the Indonesian context, the *GERMAS* program, which is a program that encourages people to adopt a healthy lifestyle, and a hygiene awareness program must be strengthened to reinforce wellbeing and a healthy lifestyle. The absence of the definitive preemptive and treatment for COVID-19 emphasizes the importance of improving the immune system as a part of the prevention efforts and policymakers need to formulate an effective and efficient strategy for the implementation of nutrition-related health promotion.

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