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Association between Nutritional Knowledge and Immunonutrients Intake with Immunity Status Post-Pandemic COVID-19 in College Students

Hubungan antara Pengetahuan Gizi dan Asupan Zat Imunonutrisi dengan Status Imunitas Pascapandemi Covid-19 pada Mahasiswa Fakultas Kedokteran Universitas Lampung

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ABSTRACT

Background: The occurrence of COVID-19 pandemic has affected various aspects of life. Several studies have shown that the ability to recover and avoid COVID-19 infection depends on the level of immunity, which is influenced by the intake of immunonutrients. However, healthy eating habits, such as the consumption of these immononutrients, are influenced by a good nutrition understanding.
Objectives: This study aimed to determine the association between nutritional knowledge and immunonutrients intake with immunity status post-pandemic COVID-19 in college students.
Methods: The study procedures were carried out using an observational analytical method with a cross-sectional design. The sample population comprised 104 first-year students from Medical Education Study Program at Medical Faculty of Lampung University. Students were determined using the unpaired categorical comparative analytics sample size formula and selected with a straightforward simple random sampling method. Data were collected using a questionnaire, including nutritional knowledge, immunonutrients intake, and immune status. Analysis was carried out using Chi-Square test and logistic regression.
Results: The result showed that 51.9% of respondents had decreased immunity status. The bivariate test revealed that protein intake (p-value<0.001), zinc (p-value=0.006), iron (p-value<0.001), vitamin A (p-value<0.001), and vitamin C (p-value=0.002) had a relationship with immunity status, while nutritional knowledge (p-value=0.708) had no association. In addition, the factors most related to immunity status were protein, iron, and vitamin C intake.
Conclusions: Immunonutrients intake is a factor that directly influenced immunity status, while nutritional knowledge is an indirect factor.

INTRODUCTION

Corona Virus Disease 2019 (COVID-19) is caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-Cov-2) virus. Based on the rapid spread and large number of cases, the World Health Organization (WHO) on March 11 2020 officially declared that COVID-19 outbreak was a global pandemic[1]. Consequently, Indonesia issued a policy of Large-Scale Social Restrictions, particularly on community activities. This policy mandated that teaching and learning, typically conducted in schools or campuses, be transitioned to online platforms. Workplaces also shifted to remote operations, and there were limitations on buying and selling activities in shopping centers, leading to their closure[2]. The online learning policy has several negative impacts on students, such as feeling frustrated and unable to focus due to network constraints, students becoming lazier and less motivated to learn, and a lack of understanding of the material being taught[4].

According to previous studies, COVID-19 and other infections caused by viruses have self-limiting properties or can heal spontaneously without the help of specific treatment. At present, no drug has the ability to cure COVID-19, and the speed of recovery largely

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depends on individual's immunity[5]. In addition to COVID-19, other infectious diseases can also infect individuals with low immune status. The human body's defense system commonly known as immunity can recognize viruses, bacteria, or other pathogens that enter the body. A good immune system helps the body fight infections caused by pathogens[6]. However, several factors can influence immune status including age, nutrition, mineral and vitamin intake, hormones, exercise habits, stress management[7], and COVID-19 vaccine.

A previous study conducted on 232 active students of the Public Health Undergraduate Program at UPN Veteran Jakarta in 2020 showed that there was a significant relationship between knowledge and preventive measures for COVID-19 through increasing body immunity[8]. Meanwhile, in another study conducted on 119 students at the Faculty of Public Health, Andalas University, there was no relationship between knowledge and behavior to prevent COVID-19 through increasing body immunity. This could be because respondents with poor knowledge had a higher percentage of having good behavior. The results also showed that 93.3% of respondents had good attitudes[9].

Nutritional consumption for immunity is called immunonutrients intake, which consists of a group of specific nutrients. This intake is very useful for improving the immune status or immunity of the body. Nutrients included in immunonutrients are protein as a building block, omega-3 fatty acids as an anti-inflammatory, anti-oxidants (vitamin A, vitamin C, and vitamin E) as antiviral substances, and minerals (zinc) to increase immunity.[7] This is consistent with a study conducted on 78 students from Medical Faculty of Lampung University in 2014. Among the 3 types of immunonutrients substances studied, namely protein, zinc, and iron, there was a significant relationship between protein and iron intake with immunity status. However, there was no significant relationship between zinc intake and immunity status[10]. Similar results were also obtained in another study conducted on 110 students residing in the FIKES dormitory at a University. The study showed that there was no significant relationship between the intake of micronutrients (vitamin A, vitamin C, vitamin D, vitamin E, iron, and zinc) with immune status among Legal and Human Rights Research and Development employees[11].

In response to COVID-19 pandemic, ongoing improvements are being implemented across various sectors to enhance education, healthcare, and community welfare. This present study was carried out to evaluate students' knowledge following the return to in-person lectures, particularly focusing on nutrition and immunonutrients, and to assess the intake of immunonutrients in relation to their immune status. The study procedures were conducted with students from Medical Education Study Program at Medical Faculty of Lampung University (FM UNILA), who were considered a vulnerable group for immune deficiencies due to their prior history of infectious diseases, including COVID-19. First-year students were specifically selected due to their limited exposure to nutritional education, particularly in the area of immunonutrients. A pre-survey conducted on 30 students revealed that 10 respondents exhibited signs of decreased immune function, as indicated by frequent fevers, coughs, and colds over the past 12 months. Therefore, this study aims to assess the relationship between nutritional knowledge and intake of immunonutrients with immunity status after COVID-19 pandemic among first-year medical students at Lampung University in 2022 /2023.

METHODS

This study was an observational analytical investigation using a cross-sectional method, which was conducted From December 2022 to January 2023, at Medical Faculty of Lampung University. Students at Medical Faculty of Lampung University made up the study's population. Furthermore, the minimum sample requirement, as determined by the sample calculation findings, was 104 first-year Medical Faculty students. With a 95% confidence level and 80% test power, the sample size was determined using the unpaired categorical comparative analytics formula. The sampling process was carried out using a simple random method through a spin wheel online. Respondents who were willing to participate in this process were between the ages of 17 and 21 years old and met the inclusion criteria for this study sample. Students with COVID-19, diabetes mellitus (DM), hypertension, chronic infectious diseases, and those already on a weight loss diet program were excluded. The sampling frame consisted of data from first-year students obtained from the academic and student affairs units of Medical Faculty, Lampung University.

The independent variables in this study were nutrition knowledge and immunonutrients intake, while the dependent variable was immune status. Immune status was measured using Immune Status Questionnaire (ISQ) and assessed by adding up the scores according to the complaints respondents had experienced during the last 12 months. Data on knowledge was obtained from interviews using a validated questionnaire, which contained questions regarding food sources of protein, vitamin A, vitamin C, iron, zinc, as well as the function of immunonutrients and immunonutrients. In this questionnaire, each question had 1 correct answer and a score of 1 was obtained when answered correctly. A 2-day and 24-hour food recall questionnaire was used to measure immunonutrients intake (protein, zinc, iron, vitamin A, and vitamin C) in grams/day on weekdays and weekends. The results were compared to the recommended nutritional adequacy rate (RDA) to determine the nutritional adequacy level. A total of 2 enumerators who had previously received instruction and training assisted the study teams in gathering data. Furthermore, data were analyzed using univariate, bivariate (chi-square), and multivariate (logistic regression), yielding a substantial degree of 95% (p-value<0.05). This study was conducted after obtaining an ethical clearance letter from the Ethics Committee of Medical Faculty of Lampung University with number 78/UN26.18/PP.05.02.00/2022.

RESULTS AND DISCUSSIONS

The study results indicated that the immune status of 54 respondents (51.9%) had declined. While the majority of respondents, 79 (76.0%) showed good

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nutritional knowledge, many had inadequate intake of key nutrients. In this study, 51 (49.1%) had insufficient protein intake, 86 students (82.7%) had inadequate zinc intake, 65 (62.5%) had poor iron intake,92 (88.5%) had deficient vitamin A intake, and 87 (83.7%) had lacked sufficient vitamin C intake. On average, their daily intake of protein was 95. 07 grams, zinc was 26.05 mg, iron 42.93 mg, vitamin A 26.26 mcg, and vitamin C was 74.09 mg.

Table 1. Characteristic of respondents

Variable	n	%	Mean
Immune Status			
Decrease	54	51.9	5.38
Good	50	48.1	
Nutrition Knowledge			
Poor	7	6.7	
Sufficient	18	17.3	
Good	79	76	
Protein Intake			
Inadequate	51	49.1	95.07 g
Adequate	40	38.4	
Excessive	13	12.5	
Zinc Intake			
Inadequate	86	82.7	26.05 mg
Adequate	18	17.3	
Iron Intake			
Inadequate	65	62.5	42.93 mg
Adequate	39	37.5	
Vitamin A Intake			
Inadequate	92	88.5	26.26 mcg
Adequate	12	11.5	
Vitamin C Intake			
Inadequate	87	83.7	74.09 mg
Adequate	17	16.3	

The prevalence of declined immunity status among respondents was 51.9%, while the average final ISQ score was 5.38 with a standard deviation of 2.84. The results indicated that students had complaints that could be a parameter of their immunity status. The highest complaint in the almost always category (>6 incidents in the last 12 months) was a severe headache with a percentage of 7.7%, followed by muscle pain with a percentage of 6.7%. The highest complaint in the frequent category (5 to 6 incidents in the last 12 months) was severe headaches with a percentage of 22.1%, followed by complaints of colds at 16.3%. Meanwhile, the highest complaint in the regular category (3 to 4 incidents in the last 12 months) was colds with a percentage of 23.2%, followed by severe headaches at 20.2%. In complaints in the occasional category (1 to 2 incidents in the last 12 months), the highest percentage was cough complaints with a percentage of 56.7%, followed by cold complaints with a percentage of 53.8. Approximately 37.5% of respondents had never suffered from sudden high fever during the last 12 months, as well as acute diarrhea for 34.6% of respondents, severe headaches for 6.7%, acute skin problems for 72.1%, muscle pain for 24.1%, colds 2.9%, and coughs 12% of respondents. Therefore, it was concluded that the complaint that most respondents did not experience was acute skin problems.

Immunity referred the body's defense against disease, specifically infection. The most important function of immune system for the body was to prevent and eradicate infections and their causes[13]. Furthermore, immunity status was a marker of the condition of an individual immune system which could be measured using laboratory tests or questionnaires[14]. A good immune status helped the body fight exposure to microorganisms, specifically after the current pandemic. Previous studies showed that the body had 2 stages of immunity, namely specific and adaptive immunity. Specific immunity was in the form of the body's first defense, which were macrophages, dendritic cells, natural killer cells, neutrophils, as well as cytokine molecules, interleukins, and so on. Meanwhile, adaptive immunity was immunity that was more effective in warding off viral infections which was performed by Antigen Presenting Cells (APC), as well as B and T lymphocytes[15].

Decreased immune status could be caused by several factors such as lack of nutrition, stress, physiological conditions, genetic factors, lack of exercise, sleeplessness, and exposure to dangerous substances or use of drugs[16]. The effects included increased susceptibility to infections and diseases characterized by coughs, fever, colds, muscle aches, diarrhea, headaches, and the sudden appearance of skin problems[17].

This result showed that the majority of respondents' nutritional knowledge was in the good category (79%). Respondents were familiar with the definition and sources of intake of several nutrients (protein, vitamins, and minerals), the nutritional content of several food sources, and the function and use of nutrients, but did not understand the impact of deficiencies in nutrients and immunonutrients which exhibited antioxidant effects and as an enzyme cofactor.

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This good nutritional knowledge was obtained by respondents through memories related to previously studied material, social factors of education through social media, as well as other factors related to nutritional education. Meanwhile, nutritional knowledge was lacking because in general first-year students had not studied nutrition courses, in-depth there no good understanding of nutrition and immunonutrition was obtained[18].

In this study, 49% of respondents had inadequate protein intake. However, the average protein intake of respondents was 93.07 from the normal value of 90 to 119, indicating that the average protein intake of students met the criteria for the recommended %RDA. Protein was a nutrient that was useful as a building as well as a regulating substance for the body and was obtained from vegetable and animal sources. Animal protein was obtained through consuming beef, eggs, seafood, and fish. Sources of vegetable protein could be found in food ingredients such as tofu, tempeh, and broccoli. Lack of protein intake led to several health problems and reduced immunity[19]. Similar results were found in previous studies stating that the majority, comprising 46 respondents had insufficient levels of protein intake, 31 had insufficient protein intake (67.4%), 7 had sufficient protein intake (15.2%), and 15 had more protein intake (17.4%)[20].

This study revealed that the intake of zinc was inadequate by 82.7%. The average student intake level was 39.54 from the minimum zinc adequacy value of 77%. Zinc referred to a micronutrient that played an important role in mediating immunity of the body. Furthermore, it was a cofactor for various enzymes in the body and played a significant role in the metabolism of nutrients and activating immune cells that fight infectious pathogens. Zinc had a role in immune function, which was a constituent of the enzyme superoxide dismutase (SOD). SOD was an endogenous antioxidant that functioned as a cell protector against oxidant disorders and oxidative stress. This ensured that zinc deficiency could result in diseases of immune system. Zinc nutritional sources were found in food sources of protein, this was because zinc bonded to amino acids, peptides, and nucleic acids. Food sources that contained zinc included meat, shellfish, poultry, liver, nuts, and seeds[21].

The intake of iron was insufficient in this study by 62.5%. This study indicated that the average level of nutritional adequacy according to the history of iron intake of the respondents was 60.34% per day, the level of adequacy of iron intake was declared sufficient when the intake reached ≥90% per day, this indicated that the average iron intake of students was still inadequate from need. Iron was a micronutrient that functioned as a binder for oxygen in the blood which could be distributed in red blood cells by 60% and 25% was in the storage area, in the body, specifically the liver. Another small portion was distributed to muscles (8%) and enzymes (5%). The role of iron in immunity was that it contributed to the production and development of lymphocyte cells which were one of the components of immunity. Iron from food could be found in 2 types, namely heme iron (meat, fish, chicken, and squid) and non-heme iron (vegetables, fruit, rice, pasta, and nuts)[22]. Iron deficiency, apart from causing iron anemia, also had an impact on reducing the ability of neutrophils to carry out activities and kill pathogens that invaded the body[23].

This study indicated that vitamin A intake was 88.5% below average. Furthermore, the average amount of vitamin A consumed by respondents was 26.26 mg, which was less than the recommended daily allowance. Antioxidants such as vitamin A were crucial for immunity. The role of vitamin A in immunity was maintaining epithelial cells, one of the body's tissues involved in non-specific immunity. Furthermore, vitamin A contributed to cellular immunity by inhibiting the activity of natural killer cells, neutrophils, and macrophages to stop cytokine storms. Food sources containing vitamin A were generally animal foods that contained fat such as liver, fish oil, milk, processed products, butter, and eggs. Vegetable foods that contain vitamin A included yellow or orange vegetables and fruits such as carrots, tomatoes, and sweet potatoes, as well as dark green vegetables such as spinach and cassava leaves. Vitamin A deficiency could cause problems with the eye, respiratory, and digestive immune systems. Vitamin A deficiency also caused increased susceptibility to pathogenic infections[24].

In this study, vitamin C intake was inadequate by 83.7%, with an average intake of 74.09 mg, lower than the nutritional adequacy figure. Vitamin C intake was very important for the body, as it played a significant role in regulating genes responsible for B cell and T cell generation, as well as increasing proliferation differentiation. Furthermore, it functioned as an antioxidant and also a cofactor for several enzymes in the body. Vitamin C also helped the body in the absorption and metabolism of iron. Lack of vitamin C intake could cause symptoms of scurvy which were characterized by fatigue, weakness, shortness of breath, muscle spasms, decreased appetite, dry skin, bleeding from the gums, and hair loss. Sources of vitamin C were found in vegetables and fruit such as oranges, pineapples, tomatoes, papaya, cassava, katuk leaves, and papaya leaves[25].

The association between the post-COVID-19 pandemic immunity status of respondents and their nutritional knowledge and immunonutrient intake was examined using bivariate analysis. According to the study results, 3 respondents (42.86%) had inadequate nutritional knowledge, which was lower than the 51 respondents (52.58%) who had a high understanding of nutrition and had suffered a decline in their immunological health. Those with inadequate dietary knowledge were more than those with good knowledge, 46 (47.42%), by 4 (57.14%) in the group of respondents with good immune status. Based on the results of the Chi-square test, a p-value of 0.708 (>0.05) was obtained, so it could be concluded that there was no relationship between nutritional knowledge and post-COVID-19 pandemic immunity status in first-year medical students at Lampung University.

Good nutritional knowledge did not make an individual exhibit good eating behavior and comply with existing recommendations when this knowledge was not based on desires or attitudes to fulfill their needs[26]. The reason there was no relationship in this study was because nutritional knowledge had an indirect influence on immune status. Furthermore, the main factors that

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could influence immune status were nutritional intake and disease infections[27] The relationship between knowledge and immunonutrient intake and immune status in students was presented in Table 2. Factors mostly associated with immunity status of post-pandemic COVID-19 in college students were presented in Table 3.

Table 2. Association between nutritional knowledge and immunonutrients intake with immunity status post-pandemic COVID-19 in college students

Variable	Decrease Immune Status		Good Immune Status		p-value	OR	95% CI
	n	%	n	%			
Nutritional Knowledge					0.708	0.67	0.14-3.18
Poor	3	42.86	4	57.14			
Good	51	52.58	46	47.42			
Protein Intake					<0.001*	612.5	66.1-5675.9
Inadequate	50	98.04	1	1.96			
Adequate	4	7.55	49	92.45			
Zinc Intake					0.012*	4.8	1.47-15.99
Inadequate	50	58.1	36	49.1			
Adequate	4	22.2	14	77.8			
Iron Intake					<0.001*	43.7	11.7-163.3
Inadequate	51	78.5	14	21.5			
Adequate	3	7.7	36	92.3			
Vitamin A Intake					<0.001*	-	0.32-527
Inadequate	54	58.7	38	41.3			
Adequate	0	0	12	100			
Vitamin C Intake					0.005*	6.6	1.77-24.69
Inadequate	51	58.6	36	41.4			
Adequate	3	17.6	14	82.4			

OR = odds ratio
95% CI = 95% Confidence interval
*chi-square test, significant if p-value<0.05

The study results indicated that 50 respondents (98.04%), who experienced a decrease in their immune status had an inadequate protein intake than 4 respondents who had adequate protein intake (7.55%). In the group of respondents who had good immunity status, only 1 had inadequate protein intake (1.96%) which was lower than those who had adequate protein intake, that was 49 people (92.45%). Based on the results of the Chi-square test, the p-value was <0.001, it can be concluded that there was a relationship between protein intake and immunity status after COVID-19 pandemic in first-year medical students at Lampung University. From the results of statistical tests, an OR value of 612.5 (95% CI= 66.1-5675.9) was obtained, which suggested that students with inadequate protein intake were 612.5 times more likely to experience a decreased immune status compared to students who had adequate protein intake.

Protein functioned as a maintainer of cells in body tissues and played a major role in helping the formation of immunoglobulin antibodies, which was one part of immunity. Furthermore, protein intake could be obtained in 2 ways, namely, through intake from outside the body and protein synthesized directly by the body. Those that could only be obtained from food intake were in the form of essential amino acids such as arginine, histidine, leucine, lysine, and others. Food ingredients were obtained from vegetable protein (nuts and seeds) and animal protein (red meat, eggs, chicken, shrimp, and fish,). Proteins that were synthesized by the body were called non-essential amino acids, such as glutamine, serine, and so on[28].

All respondents who had less protein intake experienced a decrease in their immune status. Lack of protein intake could make a person more susceptible to infection or disease. Furthermore, it was the largest component in the formation of antibodies. Proteins of the transferrin and lactoferrin types were iron-binding proteins that could prevent infection by separating iron, which was needed by microorganisms to reproduce [29].

The results showed that respondents who experienced a decrease in their immune status had an inadequate zinc intake of 50 people (58.1%), higher than those who had adequate zinc intake, which was 4 (22.2%). In the group of respondents who had good immunity status, those with inadequate zinc intake were 36 (41.9%), which was lower than 14 with adequate zinc intake, (77.8%). Based on the results of the Chi-square test, a p-value was obtained of 0.012, therefore, it was concluded that there was a relationship between zinc intake and post-COVID-19 pandemic immunity status in first-year medical students at Lampung University. From the results of statistical tests, an OR value of 4.8 (95% CI= 1.47-15.99) was obtained, which suggested that students with an inadequate zinc intake were 4.8 times more likely to have a decreased immune status compared to students who had an adequate zinc intake.

Zinc played an important role in physiological health, growth, and immune development. Furthermore, it was known to act as an anti-inflammatory, immunomodulatory, and anti-viral agent. The role of zinc in immunity was in controlling the function and proliferation of neutrophils, natural killer cells (NK cells),

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macrophages, T and B lymphocytes, as well as cytokine production. Zinc nutritional sources could be found in food sources of protein, this was because zinc binded to amino acids, peptides, and nucleic acids. Some food sources that contained zinc included meat, shellfish, poultry, liver, nuts, and seeds. Respondents who had a history of zinc intake experienced less decline in immune status. This was caused by zinc deficiency which could suppress humoral and adaptive immune responses, causing increased susceptibility to infection. Zinc deficiency was also associated with risk factors for pneumonia and increased inflammation[30].

The results indicated that 51 respondents who experienced decreased immune status had an inadequate iron intake, (78.5%), higher than 3 who had an adequate iron intake, that was 3 people (7.7%). In the group of respondents who had good immunity status, 14 (21.5%) had less iron intake than 36 respondents with adequate iron (92.3%). Based on the results of the Chi-square test, the p-value was <0.001, so it could be concluded that there was a relationship between iron intake and immunity status after COVID-19 pandemic among first-year medical students. From the results of statistical tests, an OR value of 43.7 (95% CI= 11.7-163.3) was obtained, which indicated that students with inadequate iron intake were 43.7 times more likely to have a decreased immune status compared to students who have adequate iron intake.

Iron played an active role in the synthesis of hemoglobin in the blood-bound oxygen and carried it from the lungs to all body tissues and carbon dioxide from all cells to the lungs to be excreted by the body. Furthermore, it also functioned in the formation of lymphocyte cells which was an indicator of immune status. Iron deficiency, apart from causing anemia, could also had an impact on immune reactions, which were decreasing neutrophil activity and decreasing the ability of NK cells. Decreased neutrophil activity could significantly disrupt the ability to kill intracellular bacteria. Iron deficiency also had an impact on reducing the ability of NK cells to kill bacteria[31].

The results of the study indicated that 54 respondents who experienced a decrease in immune status had inadequate vitamin A intake (58.7%), higher than none who had adequate vitamin A intake (0%). In the group of respondents who had good immunity status, those with inadequate vitamin A intake were 38 (41.3%) lower than those with adequate vitamin A intake, which was 12 (100%). Based on the results of the Chi-square test, the p-value was <0.001, therefore it could be concluded that there was a relationship between vitamin A intake and immunity status after the COVID-19 pandemic in first-year medical students at Lampung University.

The results of this study followed the theory stating that vitamin A had important effects on innate, humoral, and specific immunity. Although the mechanism of vitamin A in influencing immune system was not known with certainty, some scientists believed that retinol was thought to influence the growth and differentiation of B lymphocyte cells which played a role in the humoral immune system. This provided antibody responses related to T lymphocyte cells which played a major role in the cellular immune system[24]. Food sources of vitamin A were generally found in fat sources such as liver, fish oil, dairy products, butter, and eggs. Vitamin A was known as an anti-infective vitamin because it functioned as natural immunity as well as a protector for epithelial cells and was useful for fighting several bacterial and viral infections. The role of vitamin A in non-specific immunity could be seen in the integrity of the mucosal epithelial cells. Furthermore, its role in cellular immunity was to reduce the function of neutrophils, macrophages, and natural killer cells to prevent cytokine storms. Vitamin A deficiency could cause severe disorders of the eye, respiratory, and digestive immune systems. This could also cause an individual's increased susceptibility to common pathogens that infect cells [32].

The results revealed that respondents who had decreased immune status had inadequate vitamin C intake, as many as 51 people (58.6%), higher than those who had adequate vitamin C intake, that was 3 people (17.6%). In the group of respondents who had good immunity status, 36 people (41.4%) exhibited inadequate vitamin C intake compared to 14 people (82.4%) who had adequate vitamin C intake. Based on the results of the Chi-square test, a p-value was obtained of 0.005, therefore, it could be concluded that there was a relationship between vitamin C intake and immunity status after COVID-19 pandemic of first-year medical students at Lampung University. From the results of statistical tests, an OR value of 6.6 (95% CI= 1.77-24.69) was obtained, which indicated that students with inadequate vitamin C intake were 6.6 times more likely to have a declined immune status compared to students who had adequate vitamin C intake.

Vitamin C (ascorbic acid) was an antioxidant that could be used to increase immunity and useful for treating infections. Vitamin C regulated genes responsible for B cell and T cell generation and increased proliferation differentiation. The mechanism for increasing body immunity through vitamin C was through increasing collagen synthesis, reducing ROS and damage due to ROS, accelerating healing due to ROS, and increasing cytokine production to kill microbes.[25] This study stated that giving 200 mg of vitamin C per day could reduce the severity of infection symptoms in adults. During COVID-19 pandemic, high-dose vitamin C injections given to COVID-19 patients with severe symptoms in Wuhan were proven to relieve cytokine storms. For healthy people and infections with mild symptoms, giving high doses of vitamin C injections was not recommended. Lack of vitamin C intake could cause clinical symptoms in the form of bleeding swollen gums and joint pain because the concentration of vitamin C in blood plasma and leukocytes was very low. Acute vitamin C deficiency could also cause scurvy disease and cause a decrease in cellular immunity[33].

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Table 3. Factors Most Associated with Immunity Status Post-Pandemic COVID-19 In College Students

Variable	Initial Model			Final Model		
	p-value	OR	95% CI	p-value	OR	95% CI
Nutritional Knowledge	0.112	0.20	0.02-1.44	-	-	-
Protein Intake	0.000	178	11.5-2753	0.000	155	13.8-1757
Zinc Intake	0.458	5.75	0.05-588	-	-	-
Iron Intake	0.091	18.15	0.62-525	0.012	22.3	1.99-251
Vitamin A Intake	0.998	137	0.00-0.00	-	-	-
Vitamin C Intake	0.021	46.8	1.79-1223	0.028	35.8	1.48-867

The results of the logistic regression analysis revealed that the factors most related to Post-Pandemic COVID-19 immunity status in students were protein, iron, and vitamin C intake. Inadequate protein intake could make an individual more susceptible to infection or disease. Protein was the largest component in the formation of antibodies. Furthermore, proteins of the transferrin and lactoferrin types were iron-binding proteins that prevented infection by separating iron from microorganisms[33]. Iron was essential for many physiological processes in the body including erythropoiesis, immune function, and host defense, as well as essential cellular activities such as DNA replication and repair, mitochondrial function including OXPHOS and enzymatic reactions which required iron as a cofactor[33]. Vitamin C was a potent antioxidant due to its ability to donate electrons, which allowed for protection against oxidant-related stress. This occurred in the stabilization of the fourth structure of collagen, which could help to maintain barrier function. Another critical role of vitamin C was the regulation of DNA and histone methylation in immune cells, which highlighted that vitamin C could, in part, mediate epigenetic regulation of antioxidant defenses. Recent studies showed that vitamin C was an important co-factor for the regulation of the transcription factor hypoxia-inducible factor-1α (HIF-1α), and maintenance of HIF-1α had shown to be protective against COVID-19-related symptoms[33].

The weakness of this study was that the assessment of immune status variables using a questionnaire was only qualitative and could not fully confirm the condition of immunity. Further studies suggested assessing immunity using complete blood tests, vitamin A levels, vitamin C levels, and zinc levels. This study did not ask about previous history of COVID-19 and also did not assess differences in immune status between students who had a history of COVID-19 or not. Therefore, it was recommended for further study to assess this.

CONCLUSIONS

In conclusion, immunonutrients intake was directly related to immune status, while nutritional knowledge was not related. Furthermore, it was recommended that respondents were able to improve their eating behavior according to balanced nutrition every day, as well as apply their nutritional knowledge to good and appropriate eating behavior. Medical Faculty of Lampung University was advised to educate canteen managers to ensure that a varied menu was served following the principles of balanced nutrition, including containing immunonutrients in the form of food or drinks. These results had direct implications for the knowledge and eating behavior of students to improve their immune status and could be supported by the faculty regarding education and provision of healthy food in the canteen. In this study, there were limitations in the form of measuring each variable using a questionnaire, which had the potential to bias information because the accuracy of the answer is influenced by the honesty and memory of respondents.

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CONFLICT OF INTEREST AND FUNDING DISCLOSURE

The authors declare no conflict of interest. Furthermore, the authors funded this study.

AUTHOR CONTRIBUTIONS

DIA: conceptualization, data curation, methodology, supervision, writing–review and editing; AM: data curation, investigation, methodology, writing–original draft; S: methodology; formal analysis.

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