

ADAPTIVE IMMUNE SYSTEM OF MALNUTRITION CHILDREN IN TEGALWANGI VILLAGE, CIREBON REGENCY

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Abstract. Malnutrition consisting of poor nutrition, stunting, and undernutrition is one of the most common health problems in Indonesia. Based on data on the number of malnourished toddlers in Cirebon district, Weru sub-district has a relatively high number, including 208 toddlers with malnutrition, 164 thin toddlers and 281 short toddlers. To determine the adaptive immune system as reviewed from the CD4+ and IgM levels of malnourished children in Tegalwangi Village, Weru District, Cirebon Regency. This type of research is observational research. By using 50 malnourished children as samples in this study. Measurement of CD4+ and IgM levels uses the Elisa (enzyme-linked immunosorbent assay) method. The data analysis technique used is the Chi Square test. From 50 samples of malnourished children in Tegalwangi Village, Weru District, Cirebon Regency, the results obtained were children at risk of low CD4+ levels were boys (OR=0.508, p value>0.05), children aged 42-60 months (OR=1.969, p value>0.05), children with short categories (OR=2.857, p value>0.05) and malnourished children (OR=2.000, p value>0.05). Children at risk of low IgM levels are boys (OR=0.692, p value>0.05), children aged 42-60 months (OR=1.444, p value>0.05), children in the short category (OR=2.550, p value>0.05) and malnourished children (OR=1.385, p value>0.05). It can be concluded that the adaptive immune system of malnourished children in Tegalwangi Village, Weru District, Cirebon Regency is not significant.

Keywords: *adaptive immune system, malnutrition, CD4+, IgM*

Introduction

Malnutrition can be defined as an imbalanced, excessive, or deficient nutritional intake (WHO, 2021). Child malnutrition is a major public health problem worldwide. Malnourished children have a higher risk of dying from infectious diseases. Malnutrition is estimated to be the main cause of 45% of deaths of children under 5 years of age worldwide. Malnutrition increases susceptibility to infection, infections worsens malnutrition by reducing appetite, causing catabolism and increasing nutrient requirements. More than 45 million children under 5 years of age (6.8 percent) are predicted to suffer from malnutrition in 2022. 13.6 million of them (2.1 percent) suffer from severe malnutrition. More than three-quarters of all children with severe malnutrition live in Asia and another 22% live in Africa. When children consume more calories from food and drinks than the amount of energy they need, they become overweight. Food system failures characterized by low affordability and access to nutritious food, marketing of nutritionally deficient foods, and lack of physical activity are the causes of malnutrition. Since 2000 there has been an increase of approximately 4 million. There are currently 37 million children under 5 years of age living with overweight worldwide (WHO et al., 2023). In previous research, malnutrition can have a detrimental effect on the immune system. Which suggests that malnourished children

may have impaired immune function, including decreased phagocytosis by leukocytes and altered levels of immune cells and factors. Malnutrition causes a decrease in the immune system's ability, which makes children more susceptible to infectious diseases. While the immune system plays an important role in maintaining overall health and protecting against infection and disease. The immune system also relies on soluble factors in the blood, such as antibodies and complement proteins, to help identify and eliminate pathogens. These components work together to neutralize or destroy invading microorganisms.

In the case of malnourished children suffering from bacterial infections, their peripheral blood mononuclear cells expressed high levels of the key cytokines required for Th1 differentiation, as well as overexpression of Th2 cytokines. Peripheral CD8+ and CD4++ T cell counts were unchanged in malnourished children hospitalized for bacterial infections. However, the number of CD4+ memory T cells and effector T cells is reduced. Malnutrition also impairs the ability of T cells to respond to inflammatory stimuli (Ibrahim et al., 2017). Newborn babies only have 10% of the IgM levels of adults, because the mother's IgM cannot penetrate the placenta. When an antigen first enters the body, a primary immune response occurs, characterized by the appearance of IgM several days after exposure. IgM levels peak after approximately 7 days. Six to seven days after exposure, IgG can be detected in serum, while IgM begins to decrease before IgG levels peak, which is 10-14 days after antigen exposure. and malnutrition is one of the most common health problems in Indonesia (Indonesian Ministry of Health, Antibody levels then decrease and generally only a few can be detected 4-5 weeks after exposure. Malnutrition consisting of poor nutrition (Mujahidah and Faizah, 2023), Indonesia is a developing country that still faces many nutritional problems (Triawanti et al., 2018). In Indonesia, stunting is a nutritional problem for toddlers that has not yet been resolved. According to Basic Health Research (Risikesdas) data, the prevalence of toddlers with short and very short status in Indonesia was 37.2% in 2013, then fell to 30.8% in 2018. Meanwhile, the prevalence of toddlers in Indonesia was 29.9% in 2018, a decrease from 32.8% in 2013. The Indonesian Nutritional Status Study (SSGI) conducted in 2021 was conducted in 34 provinces, but is still considered a high category (more than 20%) according to WHO standards. In addition, data in Indonesia does not yet differentiate between stunting caused by nutritional factors and non-nutritional factors, such as hormones, genetics, or family (Kemenkes, 2004). Berdasarkan data jumlah balita gizi buruk dikabupaten Cirebon, kecamatan weru mempunyai jumlah yang terbilang tinggi diantaranya yaitu 208 balita gizi kurang, 164 balita kurus dan 281 balita pendek.

Understanding the immune system is essential to developing strategies to prevent and treat disease and improve overall health. Every child deserves good nutrition. Children who receive good nutrition will grow and develop optimally. They are better prepared to live healthy lives, free from poverty, learn and participate, and continue to develop throughout their lives, with benefits that continue from generation to generation (WHO, 2021). Based on the description presented, the researcher intends to conduct a study that aims to determine the description of the adaptive immune system of malnourished children in Cirebon Regency.

Materials and Methods

The type of research used is observational research where researchers do not intervene or treat variables. This study has obtained ethical clearance from the Health Research Ethics Commission of the Faculty of Pharmacy, YPIB University with registration number 003/KEPK/EC/III/2023. In this study, the independent variables studied were CD4+ and IgM levels as indicators of the adaptive immune system. The dependent variable in this study was malnourished children. The inclusion criteria in this study were malnourished children aged 24-60 months, not disabled and parents willing to be respondents. The exclusion criteria in this study were parents who did not agree to their children being research subjects and moved domicile. In this study, data were obtained from medical records of the Karang Sari Health Center. Data analysis used in this study was univariate and bivariate analysis. Univariate analysis was used for age and gender data. Bivariate analysis in this study used the Chi Square test. The results of the analysis were the relationship between age, gender, TB/A, BB/A with CD4+ and IgM levels.

Results and Discussion

Based on the data obtained from malnourished children in Tegalwangi Village, Weru District, Cirebon Regency, *Table 1* shows that the frequency of malnourished children in Tegalwangi Village, Weru District, Cirebon Regency is 58.0% for boys and 42.0% for girls. So that malnourished children in Tegalwangi Village, Weru District, Cirebon Regency are more boys than girls. This is in line with research conducted by Aprilia (2022) which shows a p value of 0.003 that there is a relationship between gender and the incidence of stunting. The percentage of data shows that boys experience more stunting. Likewise, the results of research conducted by Thurstans et al. (2022) stated the same thing that boys are more likely to experience stunting than girls, in other words, boys are more susceptible to malnutrition than girls. This is because there is one hormone that plays a role in the growth process, namely the hormone Insulin-like growth factor (IGF)-1, this hormone can trigger bone elongation. It was found that the hormone Insulin-like growth factor (IGF)-1 in girls is higher than in boys so that the frequency of boys experiencing stunting is greater than in girls.

Table 1. Demographics of malnourished children in Tegalwangi Village, Weru District, Cirebon Regency.

Category	Frequency (N)	Percentage (%)
Gender		
Boys	29	58.0
Girls	21	42.0
Age		
24-41 months	21	42.0
42-60 months	29	58.0
Height for age		
Very short >-3 (Z-score)	6	12.0
Short - <- 2 SD (Z-score)	44	88.0
Weight for age		
Malnutrition	20	40.0
Adequate nutrition	30	60.0

Table 1 shows the frequency of children aged 24-41 months at 42.0% and children aged 42-60 months at 58.0%. So that malnourished children in Tegalwangi Village, Weru District, Cirebon Regency are more children aged 42-60 months compared to children aged 24-41 months. The results of this study are different from previous research conducted by in their research showing that malnourished children are more common in children aged 7-23 months, as well as the results of research by Mustakim et al. (2022) in their research showing that stunting occurs more often in children aged 6-36 months. This is because parents are willing for their children to be subjects in this study. The basis for assessing nutritional status is anthropometric parameters. The combination of several parameters is called the Anthropometric Index. Several anthropometric indices that are often used are body weight and according to age (BB/A), height according to age (TB/A) (Winowatan et al., 2017). Height according to age is known as one of the indicators of growth in toddlers. Height according to age can also describe the adequacy of nutrition in toddlers. Toddlers whose nutritional needs are not met can affect growth, development, and intelligence (Puspito Panggih Rahayu, 2020). In this study, to assess or determine the nutritional status of malnourished children in Tegalwangi Village, Weru District, Cirebon Regency, researchers used standard anthropometric measurements of children as reviewed from TB/A and BB/A. The nutritional status category is indicated by the threshold value (Z-Score). In the TB/A index, there are very short categories (<-3 SD) and short (-3 SD to <-2). And in the BB/U index there are categories of malnutrition (-3 SD to <-2 SD) and adequate nutrition (-2 SD to $+1$ SD) (Kemenkes, 2004). The age used in this child anthropometric standard starts from children aged 24-60 months. For height measurements using an infanometer for children who cannot stand and a stadiometer for children who can stand upright while for weight measurements using scales. Based on research that has been conducted on 50 malnourished children in Tegalwangi Village, Weru District, Cirebon Regency, the demographic results of malnourished children were obtained from the results of anthropometric measurements.

The results of the data in *Table 1* show that malnourished children in Tegalwangi Village, Weru District, Cirebon Regency, are still relatively high because the standard anthropometric data on the TB/U index with a very short category that has a threshold value (Z-Score) <-3 SD as many as 6 people (12%) and on the BB/U index with the undernourished category that has a threshold value (Z-Score) -3 SD to <-2 SD as many as 20 people (40%). The results of this study are in accordance with research conducted by Mujahidah and Faizah (2023) in her research showed that children with undernourishment are still quite high, namely 51.5% and those who experience stunting are 98.1%. Then in the study of Sartika et al. (2024) concluded that nutrient intake in toddlers is very important to support the growth of nutritional status so that toddlers grow according to the growth chart so that growth failure does not occur (growth faltering) which can cause stunting. This can be caused by low parental education which is the main cause of stunting in toddlers. Because the level of parental education greatly determines the ease of parents in responding to and understanding the nutritional knowledge obtained regarding the nutritional status of toddlers. Likewise, the level of income or earnings of parents is a benchmark for the economic status of the family. Low levels of parental income can result in a decrease in the family's purchasing power and food consumption, causing nutritional conditions to worsen regarding the nutritional status of toddlers. Sufficient income to meet family needs is generally obtained from working family members or from their own sources of income.

Measurement of CD4+ and IgM levels in this study was measured using the Elisa (Enzyme-Linked Immunosorbent Assay) method. The Elisa technique is an immunological method that aims to determine or measure the activity and response of protein expression and the immune reaction status of individual reactions/responses (Santosa et al., 2019). Elisa (Enzyme-Linked Immunosorbent Assay) is based on the antigen-antibody reaction, namely the chemical interaction between antigens and antibodies made by leukocyte B cells. This specific immune response is very important to protect the body from threats such as pathogens and toxins. Therefore, Elisa allows antigen analysis through this reaction (Sakamoto et al., 2018). Based on the results of the CD4+ and IgM level measurements obtained, *Table 2* shows that CD4+ levels show the highest percentage of abnormal CD4+ levels. Because in this study, the research used for the whole study was malnourished children in Tegalwangi Village, Weru District, Cirebon Regency, *Table 2* shows normal and abnormal CD4+ levels. The normal CD4+ count ranges from 410-1,590 cells/mL of blood (Widiyanti and Sandy, 2016). In a study conducted by Luckheeram et al. (2012) it was stated that malnutrition itself can cause a decrease in CD4+ levels and impaired immune function. Lack of essential nutrients, such as vitamins and minerals, can contribute to a decrease in CD4+ levels. Malnutrition can interfere with the body's ability to produce and maintain adequate numbers of CD4+ T cells, which are essential for the immune response. Malnutrition can weaken the immune system, making individuals more susceptible to infection and reducing the body's ability to mount an effective immune response.

Table 2. Frequency of CD4+ levels in malnourished children in Tegalwangi Village, Weru District, Cirebon Regency.

Category	Normal		Abnormal	
	N	%	N	%
Gender				
Boys	8	16.0	21	42.0
Girls	9	18.0	12	24.0
Age				
24-41 months	9	18.0	12	24.0
42-60 months	8	16.0	21	42.0
Height for age				
Very short >-3 (Z-score)	16	32.0	28	56.0
Short - <- 2 SD (Z-score)	1	2.0	5	10.0
Weight for age				
Malnutrition	12	24.9	18	36.0
Adequate nutrition	5	10.0	15	30.0

IgM levels show the highest percentage of abnormal IgM levels. Because in this study, the research used for the whole study were malnourished children in Tegalwangi Village, Weru District, Cirebon Regency, as shown in *Table 3*, normal and abnormal IgM levels. Normal IgM levels in children range from 16.5±13.8 mg/dL (mean±SD). In the study by Gaayeb et al. (2014), it was stated that malnutrition causes a decrease in immunoglobulin levels. And the impact of malnutrition on immunoglobulin levels can vary depending on the specific antigen and nutritional status of the individual. Based on the results of the analysis test, *Table 1* shows that malnourished children in Tegalwangi Village, Weru District, Cirebon Regency in the category of male gender are 0.508 times at risk of having lower CD4 + levels compared to girls (the value is not significant

because the p value is >0.05). This is in line with research conducted by Yogani et al. (2015) in their research, showing that CD4 levels are lower in men compared to women due to several factors, such as genetics, hormones, and body condition. This has shown that female gender has a positive relationship with increasing CD4. Malnourished children in Tegalwangi Village, Weru District, Cirebon Regency, *Table 4* shows the frequency of children aged 42-60 months 1,969 times at risk of having lower CD4 + levels compared to children aged 24-41 months (value is not significant because p value >0.05). This study is in line with research conducted by Aulia and Rahayu (2021) stating the same thing, that there is no relationship between age and changes in CD4 levels. Likewise, research conducted by Yogani et al. (2015) states that age has no relationship with CD4 + levels as indicated by a p value >0.05. Age is not a determining factor in increasing children's weight and CD4 count (Nugroho et al., 2014).

Table 3. Frequency of IgM levels in malnourished children in Tegalwangi Village, Weru District, Cirebon Regency.

Category	Normal		Abnormal	
	N	%	N	%
Gender				
Boys	3	6.0	26	52.0
Girls	3	6.0	18	36.0
Age				
24-41 months	3	6.0	18	36.0
42-60 months	3	6.0	26	52.0
Height for age				
Very short >-3 (Z-score)	6	12.0	38	76.0
Short - <- 2 SD (Z-score)	0	0.0	6	12.0
Weight for age				
Malnutrition	4	8.0	26	52.0
Adequate nutrition	2	4.0	18	36.0

Table 4. Analysis of CD4+ levels in malnourished children in Tegalwangi Village, Weru District, Cirebon Regency.

Category	N	%	Mean±SD	Odds ratio	p value
Gender					
Boys	29	58.0	259.505±257.622	0.508 (0.155±1.665)	0.261
Girls	21	42.0	341.109±242.691		
Age					
24-41 months	21	42.0	309.670±283.835	1.969 (0.600±6.455)	0.261
42-60 months	29	58.0	282.270±231.226		
Height for age					
Very short >-3 (Z-score)	6	12.0	297.244±213.339	0.350 (0.038±3.265)	0.339
Short - <- 2 SD (Z-score)	44	88.0	293.306±259.237		
Weight for age					
Malnutrition	20	60.0	235.426±211.845	0.500 (0.144±1.742)	0.273
Adequate nutrition	30	40.0	332.680±272.361		

The results of measuring malnourished children reviewed from TB/A and BB/A at CD4+ levels in *Table 4* show that very short children are 0.350 times at risk of having lower CD4+ levels compared to short children (value is not significant because p value >0.05). And children with poor nutritional status are 0.500 times at risk of having lower CD4+ levels compared to children with sufficient nutritional status (value is not significant because p value >0.05). In a study (Indrawanti et al., 2021) showed that CD4+ levels in stunted children cannot be directly linked to stunting conditions.

However, stunting is one of the factors that can affect the health condition of the body, including CD4+ levels. Stunting is a low height based on age that occurs due to malnutrition. Likewise, in a study conducted by Maragareth et al. (2019) which stated that in addition to general health conditions, there are nutritional conditions that can affect CD4+ levels. Many factors can affect linear growth or height in children under five years of age, including the characteristics of toddlers and their parents, the level of toddler nutrient consumption, history of breastfeeding and toddler consumption patterns, family parenting patterns for toddlers, infectious disease infections, and hygiene and sanitation practices (Aprilia, 2022). Based on the results of the analysis test carried out. *Table 5* shows that malnourished children in Tegalwangi Village, Weru District, Cirebon Regency in the category of male gender are 0.692 times at risk of having lower IgM levels compared to girls (the value is not significant because the p value is >0.05). The results of this study are in line with research conducted in a research showing that boys have lower IgM levels compared to girls. Gender differences in immunoglobulin concentrations, especially high IgM levels in women, have been associated with hormonal effects on B lymphocytes. These gender differences may be very important when interpreting immunoglobulin levels in diseases with unequal gender distribution. For example, increased serum IgM levels are a typical diagnostic feature of primary biliary cirrhosis, which has a strong predominance in women.

Table 5. Analysis of IgM levels in malnourished children in Tegalwangi Village, Weru District, Cirebon Regency.

Category	N	%	Mean±SD	Odds ratio	p value
Gender				0.692 (0.125±3.826)	0.672
Boys	29	58.0	11.201±7.976		
Girls	21	42.0	12.158±6.600		
Age				1.444 (0.261±7.982)	0.672
24-41 months	21	42.0	12.705±9.030		
42-60 months	29	58.0	10.805±5.941		
Height for age				0.000	0.999
Very short >-3 (Z-score)	6	12.0	10.048±1.999		
Short - <- 2 SD (Z-score)	44	88.0	11.815±7.816		
Weight for age				0.722 (0.119±4.372)	0.722
Malnutrition	20	60.0	10.960±5.594		
Adequate nutrition	30	40.0	12.031±8.418		

Malnourished children in Tegalwangi Village, Weru District, Cirebon Regency in *Table 5* show the frequency of children aged 42-60 months 1.444 times at risk of having lower IgM levels compared to children aged 24-41 months (value is not significant because p value >0.05). The results of this study differ from the results of previous studies conducted by Bayram et al. (2019) in their research showed a significant relationship between age and IgM levels. This is because IgM levels will continue to increase after the neonatal period but are slightly lower in the age group 25 to 36 months and after 6 years to 11 years compared to the age group 25 to 36 months and after 6 years to 11 years of age other age groups. After the age of 11, the figure increases again and reaches its maximum value in the age group 16 to 18 years. The results of measuring malnourished children reviewed from TB/A and BB/A at IgM levels in *Table 5* show that very short children are 0.000 times at risk of having lower IgM levels compared to short children (value is not significant because p value >0.05). And children with poor nutritional status are 0.722 times at risk of having lower IgM levels compared to children with sufficient nutritional status (value is not significant because p value >0.05). This study is in line with research conducted by Meinapuri and

Putri (2018) which shows that IgM levels in children can be influenced by nutritional status. This shows that the relationship between nutritional status and IgM anti-phenolic glycolipid-1 (PGL-1) levels in children shows a correlation between nutritional status and IgM levels. Then in a study conducted by Indrawanti et al. (2021) stated in their study that there is a relationship between IgM levels and stunting in children. Stunting is a condition of failure to thrive in toddlers due to chronic malnutrition so that children become too short for their age. This shows that stunting can affect the nutritional status of children, such as chronic malnutrition which can affect IgM levels. In addition, stunting is usually associated with poverty, poor maternal health and nutrition, frequent illnesses, and improper feeding or care in early life. Therefore, stunting in children can affect their nutritional status, which can then affect IgM levels in the body.

Conclusion

Based on the results of research conducted on malnourished children in Tegalwangi Village, Weru District, Cirebon Regency, the conclusion obtained is that children at risk of low CD4+ levels are boys (OR=0.508, p value>0.05), children aged 42-60 months (OR=1.969, p value>0.05), children in the short category (OR=2.857, p value>0.05) and malnourished children (OR=2.000, p value >0.05). Children at risk of low IgM levels are boys (OR=0.692, p value>0.05), children aged 42-60 months (OR=1.444, p value>0.05), children with short category (OR=2.550, p value>0.05) and malnourished children (OR=1.385, p value>0.05). It can be concluded that the adaptive immune system of malnourished children in Tegalwangi Village, Weru District, Cirebon Regency is not significant.

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Conflict of interest

The authors confirm that there is no conflict of interest involve with any parties in this research study.

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