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Relationship Between Nutritional Status and Severity of Dengue in Children

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ABSTRACT

Dengue infection, caused by the dengue virus, remains a global health concern, especially in developing countries like Indonesia. Children are the most vulnerable group, with cases often progressing to dengue fever, dengue hemorrhagic fever, or dengue shock syndrome. Although existing studies show inconsistent results, nutritional status is considered to influence the severity of dengue infection. This study aimed to examine the relationship between nutritional status and the severity of dengue infection in children aged 5–18 years. This analytical observational study used a cross-sectional design. Data were collected from the medical records of 119 pediatric patients diagnosed with dengue hemorrhagic fever at RSAB Harapan Kita, Jakarta, between January 2023 through December 2024. Patients who met the inclusion were included. Data analysis was performed using the Pearson Chi-Square test with a significance level of $p<0.05$. Most children were aged 10–18 years (64.7%) and male (62.2%). About 57.1% had poor nutritional status (undernutrition or overnutrition), and 89.1% were classified as having non-severe dengue. No significant association was found between nutritional status and dengue severity ($p=0.351$). There is no significant relationship between nutritional status and the severity of dengue infection in children

INTRODUCTION

Dengue infection is a disease originating from the dengue virus, the arbovirus family of the family Flaviviridae and the genus Flavivirus. (Ariyanti & Anggraini, 2022) Dengue infection is an acute disease that progresses rapidly and can cause a variety of clinical symptoms, ranging from mild undifferentiated febrile illness to dengue fever (DD), dengue hemorrhagic fever (DHF), to Dengue Shock Syndrome (DSS). (Novitasari A et al., 2015) Dengue virus is a significant health issue, especially in children in developing countries. (Yulianto A et al., 2016) World Health Organization has designated dengue infection as one of the 10 global health hazards that need serious attention. Dengue in children that is not handled adequately can cause extraordinary events, severe dengue and lead to death. (Kementerian Kesehatan RI, 2022)

Over the past five decades, the incidence of dengue virus infections has jumped up to thirtyfold, with an estimated 50 million people infected each year and 2.5 billion people living in endemic areas. (Yulianto A et al., 2016) According to the World Health Organization (WHO), dengue reached its highest recorded incidence within one year at 2024 which affecting more than 100 countries worldwide, continuous transmission an unexpected surge resulting in more than 14.6 million reported in cases and over 12,000 dengue related to death. Subsequently, from January to July 2025, more than 4 million cases and over 3,000 deaths were reported to the WHO from 97 countries. (Fasitasari M et al., 2024) With a prevalence of 51.53 cases per 100,000 people in 2019, dengue is endemic in Indonesia, a large archipelago country that has experienced repeated outbreaks for decades. (Santoso MS et al., 2025) According to data from the Ministry of Health of Indonesia in 2021, the incidence of dengue disease is more often experienced by children than in adults and cases reported are < 15 years old with a prevalence of 34.13% with an age range of 5-14 years. (Aliyyu H et al., 2023) In Indonesia at 2023, there are 114,720 dengue cases with a total number of deaths of 894 cases consisting of 35 provinces or 92% and having an incidence rate of dengue >10 per 100,000 population. (Sibuea, 2024)

LITERATURE REVIEW

Various studies on dengue infection have been conducted to identify factors that can affect the rate of dengue infection. Nutritional status is a factor that plays a big role in the occurrence of dengue infection. (Novitasari A et al., 2015) A study conducted by Permatasari DY, et al. shows that there is a relationship between poor nutritional status and the occurrence of dengue because of weak cellular immunity so that it is unable to inhibit the proliferation of viruses and inhibit the transmission of infection to other cells that have not been infected. (Permatasari DY et al., 2015) A study by Zulkipli, et al. shows that in obese children it can affect the severity of infection through the mechanism of inflammation pathways. (Zulkipli MS et al., 2018)

These results are different from the findings of a study conducted by Naiem et al. concluding that there is no significant relationship between nutritional status and severity of dengue infection in children treated at Prof. Dr. R. D. Kandou Manado Hospital. This is due to the equitable distribution of normal nutritional status in children with two severity levels of infection, where

61.1% of children with normal nutritional status fall into the category of severe dengue infection, while the other 63.3% have mild dengue infection.(Naiem RAA et al., 2022)

Based on those background and data that has been obtained, the author interest to conduct a study with the aim of determining the relationship between nutritional status and dengue infection in children aged 5-18 years using the WHO 2009 classification.

METHODOLOGY

This study used a cross-sectional method and an observational analysis type. This research was conducted at RSAB Harapan Kita Jakarta in April - May 2025. The subjects of this study used the medical records of RSAB Harapan Kita Jakarta, namely pediatric patients aged 5-18 years who were diagnosed positive for dengue period infection from January 2023 through December 2024 which the total number of the patients was 345 subjects. From this total subjects were calculated using finite-infinite formula with the prevalence of children aged 5-18 years affected by dengue fever are 34.13% (Aliyyu H et al., 2023), the results obtained 119 subjects, using consecutive non-random sampling, with the inclusion criteria are pediatric patients aged 5-18 years and confirmed positive for dengue infection. Meanwhile, for the exclusion criteria are having comorbid diseases (bronchial asthma, heart disease, and diabetes mellitus) and using long-term corticosteroids. The nutritional data were calculated using BMI formula divided with their age, with the result poor nutritional if z score -3 SD through $< -2 \text{ SD}$ and good nutritional if -2 SD through $>+2 \text{ SD}$. (Putri MDGM et al., 2024) The severity of dengue infection were divided non severe dengue and severe dengue. Non severe dengue by covering with no warning sign of dengue shock syndrome and severe dengue with the sign of dengue infection or dengue shock syndrome.(Novitasari A et al., 2015)

The research data were analyzed using Chi-square test with a 95% confidence degree with a meaning limit of $p<0.05$ then the results of statistical calculations indicate a significant relationship between the two variables. Data processing in the study uses the statistical package for social sciences (SPSS) program with univariate analysis which functions to describe the free variable, namely nutritional status with a dependent variable, namely dengue infection, which will be written in the form of a distribution with percentage results and bivariate analysis with the aim of finding out whether there is a relationship between the free variable, namely nutritional status, and the independent variable, namely dengue infection.

This research was carried out when it had followed the stages of an ethics review from the Faculty of Medicine, Trisakti University with ethics number 011/KER/FK/02/2025 and had received approval from RSAB Harapan Kita with ethics number IRB/24/03/ETIK/2025. In this study, patient data will be guaranteed confidentiality.

RESULTS AND DISCUSSION

Based on Table 1, in the group of children with poor nutrition which includes malnutrition and overnutrition who experienced non-severe dengue there were 59 (49.6%) and those who experienced severe dengue there were 9 (7.6%). In children who have good nutritional status who experience non-severe dengue, there are 47 (39.5%) and 4 (3.4%) severe dengue.

Table 1. Respondent Characteristics (n=119)

Characteristics	Frequency	Percentage (%)
Age		
5-9 years	42	35.3%
10-18 years old	77	64.7%
Gender		
Man	74	62.2%
Woman	45	37.8%
Nutritional Status		
Poor	68	57.1%
Good	51	42.9%
Severity of Dengue Infection		
Non Severe Dengue	106	89.1%
Severe Dengue	13	10.9%

Based on the results of the analysis (Table 2) there was no relationship between nutritional status and the degree of severity of dengue infection in children, with a significance value of $p=0.351$.

Table 2. The Relationship Between Nutritional Status and the Degree of Severity of Dengue Infection in Children

Variabel	Severity of dengue infection		p -value*
	Non severe dengue n (%)	Severe dengue n (%)	
Nutritional Status			
Poor	59 (49.6%)	9 (7.6%)	
Good	47 (39.5%)	4 (3.4%)	0.351

*=Chi-square test (p -value >0.05)

DISCUSSION

In this study, a total of 119 data samples using medical records at RSAB Harapan Kita Jakarta showed that the majority of pediatric patients who experienced dengue infection were in the age range of 10-18 years, which was 64.7% (Table 1) These findings are in line with research by Putri et al. stating that the age group of 12-18 years is the group with the highest number of dengue cases.(Putri MDGM et al., 2024) A study conducted by Prayitno et al. on the serological prevalence of dengue and the strength of primary infection in

children in urban areas of Indonesia showed that more than 80% of children aged 10 years and above have been infected with dengue virus at least once.(Prayitno A et al., 2017) The increase in dengue cases in older children is caused by their high activity outside the home, such as in school environments or playgrounds, which increases the risk of exposure to mosquitoes that carry the dengue virus.(Islammia DPA et al., 2022) Children's lack of awareness in protecting themselves from mosquito bites is also a supporting factor. This illustrates the high burden of dengue disease in children in Indonesia and the importance of implementing effective prevention and control measures to reduce the incidence rate.(Prayitno A et al., 2017)

Most of the pediatric patients in this study were identified as having dengue infection with male sex as much as 62.2% (Table 1). These findings are in line with research conducted by Kharisma et al. which also showed that men show a higher tendency to suffer from dengue compared to women.(Kharisma PL et al., 2021) Overall, men showed higher rates of illness and death from infectious diseases than women throughout their lives. During infants and children, males tend to be more susceptible to infection because their humoral and cellular immune responses are lower than females. As we age, the differences in the immune system between men and women begin to form, influenced by sex steroid hormones that begin to increase slowly from infancy in a period referred to as minipuberty. Hormones such as testosterone, progesterone, and estradiol not only play a role in sexual development, but also affect the functioning of the immune system by modulating the activity of immune cells such as lymphocytes, dendritic cells, and macrophages interacting through specialized receptors as well as response elements to hormones.(Kharisma PL et al., 2021) Testosterone has been shown to have immunosuppressive effects, among other things, by lowering the secretion of IFN- γ and IL-4 and causing abnormal neutrophil activation. In addition, men have a lower efficiency in producing immunoglobulins that play an important role in fighting viral infections. (Muenchhoff & Goulder, 2014) In contrast, women produce more estrogen hormones that can stimulate the synthesis of IgG and IgA immunoglobulins, which provide more protection against dengue infection. (Muenchhoff & Goulder, 2014).

In children aged 5-18 years, it shows that most children who experience dengue infection have an overnutrition status, which is 45.4% (Table 1). This result is in line with the research that has been conducted by Putri et al. who also noted that most dengue patients in their study have an overweight status, which is as much as 40%.(Putri MDGM et al., 2024) The severity of dengue disease in children is greatly influenced by the body's immune system response. Children with less nutritional status tend to show milder manifestations of dengue fever than children with better nutritional status. This situation occurs because children with poor nutrition have lower lipid levels, so the replication of the dengue virus does not run optimally. This condition is suspected to be the reason why children with poor nutrition rarely experience severe dengue infection. In contrast, children with nutritional status experience more accumulation of excess fat in adipose tissue, which plays a role in immunological processes through the

secretion of the hormone leptin. This leptin can stimulate immune cells such as monocytes and macrophages to secrete pro-inflammatory cytokines such as TNF- α , IL-6, and IL-12. This excessive production of cytokines can trigger cytokine storms, which is one of the mechanisms that explain the occurrence of severe dengue infection. The inflammatory effects of this over-nutritional condition contribute to increased capillary permeability, which can eventually trigger plasma leakage and lead to DSS.(Andriawan FR et al., 2022)

The degree of severity of dengue infection in children, the majority is included in the non-severe dengue category, which is 89.1% (Table 1). These findings are in line with a study conducted by Putri et al. Grade I and II dengue is classified as Non-DSS, while grade III and IV are categorized as DSS. In the study, the proportion of patients with dengue of degrees I and II reached 83.2% (104 patients), higher than the patients of degrees III and IV of dengue which was only 16.8% (21 patients).(Putri MDGM et al., 2024) This shows that medical interventions carried out in a timely manner and according to protocols play a very important role in preventing the progression of the disease from worsening dengue conditions to become more severe. In addition, the level of knowledge of the public, especially parents or caregivers, in recognizing early clinical symptoms of dengue infection also affects early detection and treatment, so that it can prevent progression to a higher level of severity. Similar research by Idris et al. also supports these findings, where only 15.3% of the 254 pediatric patients were classified as severe dengue, while most were non-severe dengue cases.(Rezeki S et al., 2012) This is suspected because epidemiologically, most dengue infections are mild to moderate and do not develop into severe complications such as heavy bleeding or shock. The clinical spectrum of dengue is highly variable and often early symptoms such as fever, abdominal pain, or vomiting do not progress to severe conditions, especially if the patient seeks immediate medical attention. In the context of this study, patients who come to the emergency department are most likely to receive effective evaluation and early treatment, such as fluid therapy and close monitoring that play an important role in preventing the occurrence of critical phases of the disease. (Rezeki S et al., 2012)

The results of the research of Watuna et al. The level of education of parents also affects the severity of dengue fever in children. Highly educated parents know better what to do when their child is sick and show better knowledge, attitudes, and behavior. Parents who are highly educated are more likely to immediately take their children to the doctor for proper treatment, which will help manage dengue virus infections and reduce the severity of the disease.(Watuna MC et al., 2016)

Based on the results of a statistical test using the Chi-square method, which showed no significant relationship between the nutritional status of the child and the degree of severity of dengue infection in children ($p=0.351$) was found. These results are consistent with the study of Naiem et al. which found no association between the severity of dengue infection in pediatric patients at Prof. Dr. R. D. Kandou Manado General Hospital and nutritional status. Well-nourished children usually have stronger immune systems, which means they

can fight off disease more effectively and usually have milder symptoms.(Naiem RAA et al., 2022)

Similar study by Kharisma et al. showed consistent results, especially the absence of an association between dengue fever severity and nutritional status. The study found that children with good nutritional status had a 25.0% lower chance of developing dengue fever. Nutritional status does affect the immune system in fighting infections, where poor nutrition and good nutrition can have a protective effect against the risk of developing severe dengue. Dengue viruses that have RNA genetic material require support from host factors, such as lipids and fatty acids, to replicate. The fatty acid synthase (FASN) enzyme that functions in fatty acid synthesis also plays a role in supporting the dengue virus replication process. In individuals with low or normal nutritional status, lower lipid levels cause virus replication to be less than optimal, so the risk of developing severe dengue decreases.(Kharisma PL et al., 2021)

Normal nutritional status is often considered as a factor that provides protection against severe dengue, the results of this study show that the largest proportion of dengue infection sufferers are actually in the group with good nutritional status (39.5%), in line with the research of Kharisma et al. which recorded a similar percentage (25.0%).(Kharisma PL et al., 2021) This data shows that nutritional status does not always reflect the balance of nutritional components, both macronutrients and micronutrients, which play an important role in forming the immune system. Ahmed et al.'s research also states that micronutrients can modulate the immune system and influence the risk of infection and the course of dengue disease. (Ahmed S et al., 2014)

In this study, the majority of children aged 10–18 years had good nutritional status (39.5%). This group is thought to have a more balanced immune response, both humoral and cellular aspects that help suppress cytokine storms and reduce the risk of plasma leakage, one of the main characteristics of severe dengue.(Te H et al., 2022)

CONCLUSIONS AND RECOMMENDATIONS

The majority of children in this study were male (62.2%) and between the ages of 10 and 18 (64.7%), and 57.1% of pediatric patients had unnormal nutrition status, which included undernutrition and overnutrition. The majority of pediatric patients (89.1%) suffered from dengue fever which was considered not severe and there was no significant relationship between nutritional status and the degree of severity of dengue infection in children ($p=0.351$). For recommendations, the researcher need strengthening early detection for dengue fever, strict clinical monitoring such as spesific nutrition intake especially for school-aged children who have higher exposure risks.

FURTHER STUDY

Future research should involve more detailed measurements of nutritional status are needed to better understand their role in dengue pathophysiology.

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2
Relationship Between Nutritional Status and Severity of Dengue in Children

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ABSTRACT

Dengue infection, caused by the dengue virus, remains a global health concern, especially in developing countries like Indonesia. Children are the most vulnerable group, with cases often progressing to dengue fever, dengue hemorrhagic fever, or dengue shock syndrome. Although existing studies show inconsistent results, nutritional status is considered to influence the severity of dengue infection. This study aimed to examine the relationship between nutritional status and the severity of dengue infection in children aged 5-18 years. This analytical observational study used a cross-sectional design. Data were collected from the medical records of 119 pediatric patients diagnosed with dengue hemorrhagic fever at RSAB Harapan Kita, Jakarta, between January 2023 through December 2024. Patients who met the inclusion were included. Data analysis was performed using the Pearson Chi-Square test with a significance level of $p < 0.05$. Most children were aged 10-18 years (64.7%) and male (62.2%). About 57.1% had poor nutritional status (undernutrition or overnutrition), and 89.1% were classified as having non-severe dengue. No significant association was found between nutritional status and dengue severity ($p = 0.351$). There is no significant relationship between nutritional status and the severity of dengue infection in children.

INTRODUCTION

Dengue infection is a disease originating from the dengue virus, the arbovirus family of the family Flaviviridae and the genus Flavivirus. (Ariyanti & Anggraini, 2022) Dengue infection is an acute disease that progresses rapidly and can cause a variety of clinical symptoms, ranging from mild undifferentiated febrile illness to dengue fever (DD), dengue hemorrhagic fever (DHF), to Dengue Shock Syndrome (DSS). (Novitasari A et al., 2015) Dengue virus is a significant health issue, especially in children in developing countries. (Yulianto A et al., 2016) World Health Organization has designated dengue infection as one of the 10 global health hazards that need serious attention. Dengue in children that is not handled adequately can cause extraordinary events, severe dengue and lead to death. (Kementerian Kesehatan RI, 2022)

Over the past five decades, the incidence of dengue virus infections has jumped up to thirtyfold, with an estimated 50 million people infected each year and 2.5 billion people living in endemic areas. (Yulianto A et al., 2016) According to the World Health Organization (WHO), dengue reached its highest recorded incidence within one year at 2024 which affecting more than 100 countries worldwide, continuous transmission an unexpected surge resulting in more than 14.6 million reported in cases and over 12,000 dengue related to death. Subsequently, from January to July 2025, more than 4 million cases and over 3,000 deaths were reported to the WHO from 97 countries. (Fasitasari M et al., 2024) With a prevalence of 51.53 cases per 100,000 people in 2019, dengue is endemic in Indonesia, a large archipelago country that has experienced repeated outbreaks for decades. (Santoso MS et al., 2025) According to data from the Ministry of Health of Indonesia in 2021, the incidence of dengue disease is more often experienced by children than in adults and cases reported are < 15 years old with a prevalence of 34.13% with an age range of 5-14 years. (Aliyyu H et al., 2023) In Indonesia at 2023, there are 114,720 dengue cases with a total number of deaths of 894 cases consisting of 35 provinces or 92% and having an incidence rate of dengue >10 per 100,000 population. (Sibuea, 2024)

LITERATURE REVIEW

Various studies on dengue infection have been conducted to identify factors that can affect the rate of dengue infection. Nutritional status is a factor that plays a big role in the occurrence of dengue infection. (Novitasari A et al., 2015) A study conducted by Permatahari DY, et al. shows that there is a relationship between poor nutritional status and the occurrence of dengue because of weak cellular immunity so that it is unable to inhibit the proliferation of viruses and inhibit the transmission of infection to other cells that have not been infected. (Permatahari DY et al., 2015) A study by Zulkipli, et al. shows that in obese children it can affect the severity of infection through the mechanism of inflammation pathways. (Zulkipli MS et al., 2018)

These results are different from the findings of a study conducted by Naiem et al. concluding that there is no significant relationship between nutritional status and severity of dengue infection in children treated at Prof. Dr. R. D. Kandou Manado Hospital. This is due to the equitable distribution of normal nutritional status in children with two severity levels of infection, where

61.1% **of** children with normal nutritional status fall into the category of severe dengue infection, while the other 63.3% have mild dengue infection. (Naiem RAA et al., 2022)

Based on those background and data that has been obtained, the author interest to conduct a study with the aim of determining the **relationship between nutritional status and dengue infection in** children aged 5-18 years using the WHO 2009 classification.

METHODOLOGY

This study used a cross-sectional method and an observational analysis type. This research was conducted at RSAB Harapan Kita Jakarta in April – May 2025. The subjects of this study used the medical records of RSAB Harapan Kita Jakarta, namely pediatric patients aged 5-18 years who were diagnosed positive for dengue period infection from January 2023 through December 2024 which the total number of the patients was 345 subjects. From this total subjects were calculated using finite-infinite formula with the prevalence of children aged 5-18 years affected by dengue fever are 34.13% (Aliyyu H et al., 2023) the results obtained 119 subjects, using consecutive non-random sampling, with the inclusion criteria are pediatric patients aged 5-18 years and confirmed positive for dengue infection. Meanwhile, for the exclusion criteria are having comorbid diseases (bronchial asthma, heart disease, and diabetes mellitus) and using long-term corticosteroids. The nutritional data were calculated using BMI formula divided with their age, with the result poor nutritional if z score < -3 SD through < -2 SD and good nutritional if -2 SD through $> +2$ SD. (Putri MDGM et al., 2024) The severity of dengue infection were divided **non severe dengue** and **severe dengue**. Non severe dengue by covering with no warning sign of dengue shock syndrome and severe dengue with the sign of dengue infection or dengue shock syndrome. (Novitasari ¹⁴ A et al., 2015)

The research **data** were analyzed using Chi-square test with a 95% **confidence degree** with a meaning limit of $p < 0.05$ then the results of statistical calculations indicate **a significant relationship** between the two variables. Data processing in the **study** uses the **statistical package for social sciences (SPSS) program with** univariate analysis which functions to describe the free variable, namely nutritional status with a dependent variable, namely dengue infection, which will be written in the form of a distribution ¹³ with percentage results and bivariate analysis with the aim of finding out **whether there is a relationship between the free variable**, namely nutritional status, **and the independent variable**, namely dengue infection.

This research was carried out when it had followed the stages of an ethics review from the Faculty of Medicine, Trisakti University with ethics number 011/KER/FK/02/2025 and had received approval from RSAB Harapan Kita with ethics number IRB/24/03/ETIK/2025. In this study, patient data will be guaranteed confidentiality.

RESULTS AND DISCUSSION

Based on Table 1, in the group of children with poor nutrition which includes malnutrition and overnutrition who experienced non-severe dengue there were 59 (49.6%) and those who experienced severe dengue there were 9 (7.6%). In children who have good nutritional status who experience non-severe dengue, there are 47 (39.5%) and 4 (3.4%) severe dengue.

1 Table 1. Respondent characteristics (n=119)

Characteristics	Frequency (n=119)	Percentage (%)
Age		
5-9 years	42	35,3%
10-18 years old	77	64,7%
Gender		
Man	74	62,2%
Woman	45	37,8%
Nutritional Status		
Poor	68	57,1%
4 Good	51	42,9%
Severity of Dengue		
Infection		
Non Severe Dengue	106	89,1%
Severe Dengue	13	10,9%

1 Based on the results of the analysis (Table 2) there was no relationship 2 between nutritional status and the degree of severity of dengue infection in children, with a significance value of p=0.351.

2 Table 2. The relationship between nutritional status and the degree of severity of dengue infection in children

Variabel	Severity of dengue infection		p-value*
	Non severe dengue n(%)	Severe dengue n(%)	
Nutritional Status			
Poor	59 (49,6%)	9 (7,6%)	
Good	47 (39,5%)	4 (3,4%)	0,351

5 *Chi-square test (p-value >0.05)

DISCUSSION

In this study, a total of 119 data samples using medical records at RSAB Harapan Kita Jakarta showed that the majority of pediatric patients who experienced dengue infection were in the age range of 10-18 years, which was 64.7% (Table 1) These findings are in line with research by Putri et al. stating that the age group of 12-18 years is the group with the highest number of dengue cases. (Putri MDGM et al., 2024) A study conducted by Prayitno et al. on the serological prevalence of dengue and the strength of primary infection in

children in urban areas of Indonesia showed that more than 80% of children aged 10 years and above have been infected with dengue virus at least once. (Prayitno A et al., 2017) The increase in dengue cases in older children is caused by their high activity outside the home, such as in school environments or playgrounds, which increases the risk of exposure to mosquitoes that carry the dengue virus. (Islamnia DPA et al., 2022) Children's lack of awareness in protecting themselves from mosquito bites is also a supporting factor. This illustrates the high burden of dengue disease in children in Indonesia and the importance of implementing effective prevention and control measures to reduce the incidence rate. (Prayitno A et al., 2017)

Most of the pediatric patients in this study were identified as having dengue infection with male sex as much as 62.2% (Table 1). These findings are in line with research conducted by Kharisma et al. which also showed that men show a higher tendency to suffer from dengue compared to women. (Kharisma PL et al., 2021) Overall, men showed higher rates of illness and death from infectious diseases than women throughout their lives. During infants and children, males tend to be more susceptible to infection because their humoral and cellular immune responses are lower than females. As we age, the differences in the immune system between men and women begin to form, influenced by sex steroid hormones that begin to increase slowly from infancy in a period referred to as minipuberty. Hormones such as testosterone, progesterone, and estradiol not only play a role in sexual development, but also affect the functioning of the immune system by modulating the activity of immune cells such as lymphocytes, dendritic cells, and macrophages interacting through specialized receptors as well as response elements to hormones. (Kharisma PL et al., 2021) Testosterone has been shown to have immunosuppressive effects, among other things, by lowering the secretion of IFN- γ and IL-4 and causing abnormal neutrophil activation. In addition, men have a lower efficiency in producing immunoglobulins that play an important role in fighting viral infections. (Muenchhoff & Goulder, 2014) In contrast, women produce more estrogen hormones that can stimulate the synthesis of IgG and IgA immunoglobulins, which provide more protection against dengue infection. (Muenchhoff & Goulder, 2014)

In children aged 5–18 years, it shows that most children who experience dengue infection have an overnutrition status, which is 45.4% (Table 1). This result is in line with the research that has been conducted by Putri et al. who also noted that most dengue patients in their study have an overweight status, which is as much as 40%. (Putri MDGM et al., 2024) The severity of dengue disease in children is greatly influenced by the body's immune system response. Children with less nutritional status tend to show milder manifestations of dengue fever than children with better nutritional status. This situation occurs because children with poor nutrition have lower lipid levels, so the replication of the dengue virus does not run optimally. This condition is suspected to be the reason why children with poor nutrition rarely experience severe dengue infection. In contrast, children with nutritional status experience more accumulation of excess fat in adipose tissue, which plays a role in immunological processes through the

secretion of the ⁶hormone leptin. This leptin can stimulate immune cells such as monocytes and ⁷macrophages to secrete pro-inflammatory cytokines such as ⁸TNF- α , ⁹IL-6, and ¹⁰IL-12. This excessive production of cytokines can trigger ¹¹cytokine storms, which is one of the mechanisms that explain the occurrence of ¹²severe dengue infection. The inflammatory effects ¹³of this over-nutritional condition contribute to increased capillary permeability, which can eventually trigger ¹⁴plasma leakage and lead to DSS. (Andriawan FR et al., 2022)

¹⁵The degree of severity of dengue infection in children, the majority ¹⁶is included ¹⁷in the non-severe dengue category, which is 89.1% (Table 1). These findings are in line with a study conducted by Putri et al. Grade I and II dengue is classified as Non-DSS, while grade III and IV are categorized as DSS. In the study, the proportion of patients with dengue of degrees I and II reached 83.2% (104 patients), higher than the patients of degrees III and IV of dengue which was only 16.8% (21 patients). (Putri MDGM et al., 2024) This shows that medical interventions carried out in a timely manner and according to protocols play a very important role in preventing the progression of the disease from worsening dengue conditions to become more severe. In addition, the level of knowledge of the public, especially parents or caregivers, in recognizing early clinical symptoms of dengue infection also affects early detection and treatment, so that it can prevent progression to a higher level of severity. Similar research by Idris et al. also supports these findings, where only 15.3% of the 254 pediatric patients were classified as severe dengue, while most were non-severe dengue cases. (Rezeki S et al., 2012) This is suspected because epidemiologically, most dengue infections are mild to moderate and do not develop into severe complications such as heavy bleeding or shock. The clinical spectrum of dengue is highly variable and often early symptoms such as fever, abdominal pain, or vomiting do not progress to severe conditions, especially if the patient seeks immediate medical attention. In the context of this study, patients who come to the emergency department are most likely to receive effective ²²valuation and early treatment, such as fluid therapy and close monitoring that play an important role ²³in preventing the occurrence of critical phases of the disease. (Rezeki S et al., 2012)

The results of the research of Watuna et al. The level of education of parents also affects the severity of dengue fever in children. Highly educated parents know better what to do when their child is sick and show better knowledge, attitudes, and behavior. Parents who are highly educated are more likely to immediately take their children to the doctor for proper treatment, which will help manage dengue virus infections and reduce the severity of the disease. (Watuna MC et al., 2016)

¹⁶Based on the ¹⁷results of a statistical ¹⁸test using the Chi-square method, which showed no ¹⁹significant relationship between the nutritional status of the child ²⁰and the degree ²¹severity of dengue infection in children ($p=0.351$) was found. These results are ²²consistent with the study of Naiem et al. which found no association between the severity of dengue infection in pediatric patients at Prof. Dr. R. D. Kandou Manado General Hospital and nutritional status. Well-nourished children usually have stronger immune systems, which means they

can fight off disease more effectively and usually have milder symptoms. (Naiem RAA et al., 2022)

Similar study by Kharisma et al. showed consistent results, especially the absence of an association between dengue fever severity and nutritional status. The study found that children with good nutritional status had a 25.0% lower chance of developing dengue fever. Nutritional status does affect the immune system in fighting infections, where poor nutrition and good nutrition can have a protective effect against the risk of developing severe dengue. Dengue viruses that have RNA genetic material require support from host factors, such as lipids and fatty acids, to replicate. The fatty acid synthase (FASN) enzyme that functions in fatty acid synthesis also plays a role in supporting the dengue virus replication process. In individuals with low or normal nutritional status lower lipid levels cause virus replication to be less than optimal, so the risk of developing severe dengue decreases. (Kharisma PL et al., 2021)

Normal nutritional status is often considered as a factor that provides protection against severe dengue, the results of this study show that the largest proportion of dengue infection sufferers are actually in the group with good nutritional status (39.5%), in line with the research of Kharisma et al. which recorded a similar percentage (25.0%). (Kharisma PL et al., 2021) This data shows that nutritional status does not always reflect the balance of nutritional components, both macronutrients and micronutrients, which play an important role in forming the immune system. Ahmed et al.'s research also states that micronutrients can modulate the immune system and influence the risk of infection and the course of dengue disease. (Ahmed S et al., 2014)

In this study, the majority of children aged 10-18 years had good nutritional status (39.5%). This group is thought to have a more balanced immune response, both humoral and cellular aspects that help suppress cytokine storms and reduce the risk of plasma leakage, one of the main characteristics of severe dengue. (Te H et al., 2022)

CONCLUSIONS AND RECOMMENDATIONS

The majority of children in this study were male (62.2%) and between the ages of 10 and 18 (64.7%), and 57.1% of pediatric patients had malnutrition status, which included undernutrition and overnutrition. The majority of pediatric patients (89.1%) suffered from dengue fever which was considered not severe and there was no significant relationship between nutritional status and the degree of severity of dengue infection in children ($p=351$). For recommendations, the researcher need strengthening early detection for dengue fever, strict clinical monitoring such as spesific nutrition intake especially for school-aged children who have higher exposure risks.

FURTHER STUDY

Future research should involve more detailed measurements of nutritional status are needed to better understand their role in dengue pathophysiology.

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Relationship Between Nutritional Status and Severity of Dengue in Children

原創性報告



主要來源

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Part I

Article Assessment Form

No	Evaluation Item	Assessment Column*			Reviewer Advise	Author Response
		1	2	3		
A.	ABSTRACT					
1	The abstract contains the following main elements: a) Research objectives, b) Methods used, c) Results obtained, and d) brief conclusions/interpretations of the results obtained.			x		
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1	Submission of research methods is presented in full (allowed in the form of a narrative or a combination of tables and figures).		x		Explain in more detail about the methodology	
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1	The conclusions have answered all research objectives and provided reasons for the research results		x		Please explain the conclusions and provide recommendations from the author	
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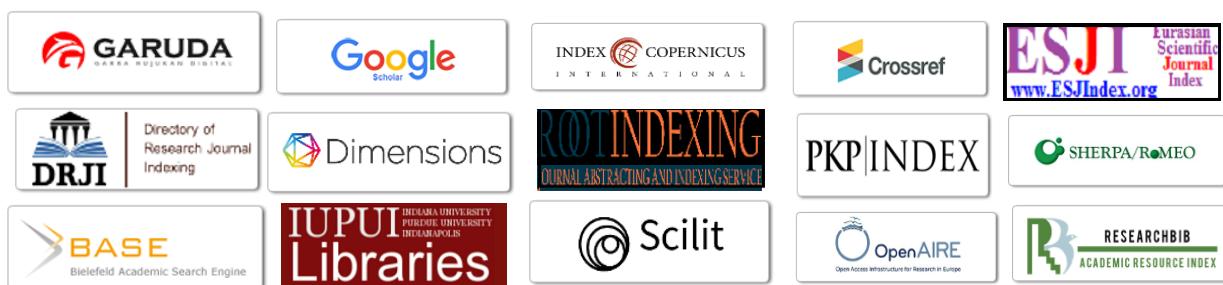
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