

THE CORRELATION BETWEEN NUTRITIONAL STATUS WITH SEVERITY OF DENGUE INFECTION IN PEDIATRIC PATIENTS

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Abstract: Introduction: Dengue virus infection is a health problem, especially in tropical and subtropical countries, including Indonesia. The nutritional status of pediatric patients can affect the severity of this disease. This study aims to assess the correlation between nutritional status and the severity of dengue infection in pediatric patients. Methods: This study was an observational analytic with a cross-sectional approach. Inclusion criteria in this study were data on pediatric patients aged <18 years and treated at Lewoleba Hospital from January 2019-December 2021. Incomplete medical record data were excluded from this study. First, the diagnosis of dengue infection was established based on WHO criteria. Then, patients were grouped into DF and DHF grades I-IV. Next, nutritional status is calculated based on the WHO growth chart (weight/age), which is further grouped into underweight, normal, and overweight/obese. Finally, the analysis was carried out with the Chi-square test and Spearman Correlation Test. Results: A total of 81 patients were included in this study. The majority of patients were male (60.5%), in the age range of 5-10 years (46.9%), and had normal nutritional status (63%). There was a tendency for underweight patients to experience a more severe degree of DHF (DHF grade III-IV), which was 67.7% (p<0.0001). The nutritional status of the patients was also found to have a positive correlation with a moderate strength of correlation with the severity of dengue infection (r=0.556; p<0.0001). Conclusion: There was a positive correlation between nutritional status and dengue infection severity. Underweight patients tended to experience a more severe degree of dengue infection.

Keywords: dengue infection, dengue hemorrhagic fever, dengue fever, nutritional status, pediatric population.

I. INTRODUCTION

Dengue infection is a viral disease transmitted through the bite of the *Aedes aegypti* and *Aedes albopictus* mosquitoes. Dengue virus has 4 viral serotypes, namely DENV-1, DENV-2, DENV-3, and DENV-4, with high morbidity and mortality in many areas of the world. Dengue virus can cause various clinical manifestations from asymptomatic symptoms to dengue hemorrhagic fever (DHF) with plasma leakage that can cause hypovolemic shock, namely dengue shock syndrome (DSS).^{[1],[2]}

Dengue virus infection is a common health problem, especially in 100 tropical and subtropical countries in Southeast Asia, the Western Pacific, Central America, and South America. According to the World Health Organization (WHO), it is estimated that every year there are 50 to 100 million cases of dengue infection in the world. From that, 500,000 cases of DSS occurred, and 22,000 cases caused death.^{[3],[4]} Descriptive studies in Indonesia from 2010-2019 found that DHF cases still fluctuate yearly, with the lowest cases occurring in 2018 with 65,602 cases. The peak incidence occurred in 2016, with 78.85 cases per 100,000 population.^[5]

Many factors affect the severity of DHF, namely the immune status of each individual, the strain or serotype of the infecting virus, the patient's age, the patient's genetic background, and secondary dengue infection. Nutritional status also affects the degree of dengue infection in patients. The immunological theory states that good nutrition increases antibody response. The reaction of antigens and antibodies in the body due to viral infection causes dengue virus infection to be more severe. In the pathogenesis of DHF, the complement system plays an important role.^[6,7] The importance of nutritional status in the immunological process is crucial in the approach to dengue therapy in pediatric patients. Thus, this study aims to assess the correlation between nutritional status and the severity of dengue infection in pediatric patients.

II. METHODS

This study was an observational analytic with a cross-sectional approach. The research data was taken from the patient's medical record with a total sampling method. Inclusion criteria in this study were data on pediatric patients aged <18 years and admitted at Lewoleba Hospital from January 2019-December 2021. Incomplete medical record data were excluded from this study.

The diagnosis of dengue infection in patients at Lewoleba Hospital was established based on WHO criteria, and patients were grouped into DF and DHF grades I-IV. Nutritional status was calculated based on the WHO growth chart (weight/age), which is grouped into underweight, normal, and overweight/obese. The Chi-square and Spearman Correlation Test was done with a significance set point (α) of 0.05. This research received permission from the Ethics Committee of Lewoleba Hospital.

III. RESULTS

In this study, 81 respondents had a dengue infection, with DHF grade III being the most common case (38.3%). The majority of patients were male (60.5%), in the age range of 5-10 years (46.9%), and had normal nutritional status (63%). Abdominal pain and vomiting became the two most symptoms experienced by the patient. The median patient's length of stay was 3 days, and all patients (100%) survived until the end of the study (TABLE 1).

TABLE 1. The characteristics of patients

Variables	Total patients (N=81)
Sex, n (%)	
• Male	49 (60.5)
• female	32 (39.5)
Agent (%)	
• 0-5 years old	29 (35.8)
• 5-10 years old	38 (46.9)
• >10 years old	14 (17.3)
Nutritional status, n (%)	
• Underweight	27 (33.3)
• Normal	51 (63)
• Overweight/Obese	3 (3.7)
Infection status, n (%)	
• DHF grade IV	-
• DHF grade III	31 (38.3)
• DHF grade II	27.2 (22)
• DHF grade I	24 (29.6)
• DF	4 (4.9)
Signs and symptoms, n (%)	
• Headache	40 (49.4)
• Abdominal pain	62 (76.5)
• Muscle pain	30 (37)
• Vomiting	61 (75.3)
• Hepatomegaly	45 (55.6)

• Palpebral edema	10 (12.3)
• Pleural effusion	3 (3.7)
• Ascites	2 (2.5)
• Petechia	27 (33.3)
• Spontaneous bleeding	21 (25.9)
• Lethargy	20 (24.7)
LOS (day), median (min-max)	3 (1-7)
Outcomes (survived), n (%)	81 (100)

From laboratory examination, the median value of white blood cells (WBC) was 5,600/ μ l, haemoglobin 11.9 g/dl, platelets 59,000/ μ l, and hematocrit (HCT) 35%. From the serological examination, the positive values for NS-1, IgM, and IgG markers were 51.9%, 44.4%, and 54.4%, respectively (TABLE 2).

TABLE 2. Laboratory results

Variables	Total patients (N=81)
Complete blood counts, median (min-max)	
• WBC ($10^3/\mu$ l)	5.6 (1.9-18)
• Haemoglobin (g/dl)	11.9 (2.5-16.9)
• Platelets ($10^3/\mu$ l)	59 (15-157)
• HCT (%)	35 (12.4-47.9)
Serology, n (%)	
NS-1	
• Positive	42 (51.9)
• negative	3 (3.7)
• Not examined	36 (44.4)
IgM	
• Positive	36 (44.4)
• negative	32 (39.6)
• Not examined	13 (16)
IgG	
• Positive	44 (54.4)
• negative	24 (29.6)
• Not examined	13 (16)

From the results of the Chi-square test analysis (TABLE 3), it was found that there was no significant relationship ($p=0.148$) between the nutritional status of patients and the incidence of plasma leakage in cases of dengue infection (DHF and DF). However, the analysis of disparity in the group with plasma leakage (DHF) found that there was a tendency for underweight patients to experience a more severe degree of DHF (DHF grade III-IV), which was 67.7%. Meanwhile, most patients with grade I-II DHF had a normal nutritional status (80.4%). This result was statistically significant ($p<0.0001$).

TABLE 3. The association between nutritional status with the severity of dengue infection

Nutritional status	DHF, n (%)	DF, n (%)	p-value
Underweight	27 (35.1)	-	0.148
Normal	47 (61)	4 (100)	
Overweight/Obese	3 (3.9)	-	
Nutritional status	DHF grade III-IV, n (%)	DHF grade I-II, n (%)	p-value
Underweight	21 (67.7)	6 (13)	<0.0001*
Normal	10 (32.3)	37 (80.4)	
Overweight/Obese	-	3 (6.5)	

*) statistically significant

The correlation test results using the Spearman Correlation Test (TABLE 4) on the research variables on the severity of dengue infection experienced by patients. The variables of age and sex were found to have a negative correlation with the severity of dengue infection. However, this result was not statistically significant. Meanwhile, the nutritional status variable of the patient had a positive correlation with a moderate strength of correlation with the severity of dengue infection ($r=0.556$; $p<0.0001$).

TABLE 4. The correlation test between research variables with the severity of dengue infection

Variables	p-value	r
Age	0.066	-0.205
Sex	0.876	-0.018
Nutritional status	<0.0001*	0.556

*) statistically significant

IV. DISCUSSION

In this study, the majority of patients with dengue infection were male. Several previous studies also found the same results. Research at Tugurejo Hospital, Semarang, showed that patients with dengue infection were predominantly male (50.6%; $p=0.026$).^[8] Research at UKI General Hospital, Jakarta, also found that most DF and DHF patients were males (60%).^[9] However, a study at Sanglah Hospital, Denpasar, found that female patients had a more significant proportion than males (54.5% vs 45.5%).^[10] Dengue infection did not differ for either males or females. This variation occurred possibly due to the demographic differences between the sexes of the population in each region.

Most patients (46.9%) with dengue in this study were aged 5-10 years. Research at Roemani Hospital, Semarang, found similar results, where patients aged 4-9 years were found to have the highest proportion (39.6%) experiencing dengue infection.^[11] Another study at Sanglah Hospital, Denpasar, described similar results, where most dengue infection patients were children aged 5-10 years (52.2%).^[10] Those are because children have immune systems that tend to be more vulnerable than adults, so children are more susceptible to infection.

Based on the proportion of nutritional status, almost two-thirds of patients have a normal nutritional status. Research at the Gambiran Hospital, Kediri, and Samarinda City described the same results, where pediatric patients with dengue infection were mainly categorized as having normal nutritional status, namely 53.5% and 80.5%, respectively.^{[12],[13]} In statistical analysis, a significant relationship was found between nutritional status with the severity of dengue infection, where there was a tendency for underweight patients to experience a more severe degree of dengue infection ($p<0.0001$). The correlation test also showed a positive correlation between those two variables. Several previous similar studies showed quite varied results. Permatasari et al.^[8] depicted that bivariate analysis showed a significant relationship between nutritional status ($p=0.013$) and the severity of dengue infection in Tugurejo Hospital, Semarang. In multivariate analysis, the OR 9.474 (95% CI: 1.177-76.227) showed that underweight patients had a 9.474 times greater chance of suffering more severe dengue infection.⁸ A similar study in Cirebon, West Java, also obtained similar results. In this study, underweight patients had a 2.2-fold risk of experiencing a more severe degree of DHF infection status ($p=0.004$).^[14] This result follows the theory that nutritional status is less susceptible to dengue virus infection because it has low cellular immunity. So, the immune response and immunologic memory are not fully developed. In underweight conditions, there is a decreased immunity with a reduced number of CD4 + T-helper cells and a lower CD4 + /CD8 + ratio. In addition, the production of secretory IgA, complement components (C3, C4, and factor B), specific cytokines (such as IL-2 and TNF), and phagocytosis have decreased. The presence of memory cells of antigens stored in dendritic cells and lymph nodes will start their functions if there is a viral infection. Thus, if the immunologic memory is not completely gained, the body's immune response centre, T lymphocytes, cannot produce cytokines and mediators as the body's defence.^[8]

Several other studies showed result that contradicts this study. For example, a study in Thailand showed that patients with overweight nutritional status had a higher tendency to develop grade III-IV DHF infection than grade I-II DHF (45.5% vs 18.8%), but the results of this study were not statistically significant.^[15] A study in Baubau Hospital explained a correlation ($p=0.014$; $r=0.476$) between overweight and obese nutritional status and the severity of dengue infection.^[16] The hypothesis that supports the two studies is that in patients with excess nutrition, fat adipocytes also release pro-inflammatory cytokines as in the pathogenesis of DHF, namely TNF- α , IL-1 β , IL-6, and IL-8. The synergistically will result in the accumulation of cytokines which causes an increase in capillary permeability, triggering plasma leakage and exacerbating the course of DHF to cause Dengue Syndrome Shock.^{[17],[18]}

V. CONCLUSION

In this study, it was found that there was a positive correlation between nutritional status and the severity of dengue infection. In addition, there was a tendency for underweight patients to experience a more severe degree of dengue infection. However, research with larger sample size is still needed to infer these results from a wider population.

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