Association of clinical symptoms and laboratory values with the severity of dengue infection in pediatric patients at H. Adam Malik Hospital

Desi Afnita Lubis[a*], Ayodhia Pitaloka Pasaribu[b], Rini Savitri Daulay[c] ,Lenny Evalina sihotang[d] , Indri Adriztina[e]

*desiafnitalubis@gmail.com

Master of Tropical Medicine, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia
JL.Dr. Mansyur No. 5 Padang bulan, Medan baru, Medan North sumatera, Indonesia

Abstract

Background: Dengue infection is an infectious disease caused by four dengue virus serotypes (DENV 1, 2, 3, and 4) which belong to the Flaviviridae family and are transmitted through mosquito vectors of the species Aedes aegypti or Aedes albopictus. Dengue has become a global public health problem, especially in most tropical and subtropical countries. Dengue hemorrhagic fever can attack all age groups. The majority of dengue hemorrhagic fever cases occur in children. The mortality rate in children tends to increase so it is necessary to pay more attention to clinical symptoms and laboratory values. Method: The research design used was descriptive-analytical with a cross-sectional design, with a sample size of 58 respondents. The sampling technique used was total sampling. Results: Statistical test results using the Fisher test. 37 people (63.8%) had clinical symptoms of vomiting, 20 people (34.5%) had a fever with a temperature of ≥ 400, and 15 people (25.9%) had bleeding manifestations. Laboratory results obtained hematocrit values $\geq 40\%$ were 27 people (48.3%), platelet values <150,000 were 46 people (79.3%), leukocytes <5,000 were obtained by 31 people (53.4%), and abnormal lymphocytes were obtained as many as 38 people (65.5%). Conclusion: In this study, there was no relationship between fever, signs of bleeding, hematocrit, leukocytes, and lymphocytes with the severity of dengue infection.

Keywords: Fever, signs of bleeding, hematocrit, leukocytes, lymphocytes, severity of dengue infection

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1. Introduction

Dengue infection is caused by one of four serotypes of viruses from the genus Flavivirus, family Flaviviridae. This virus can enter the human body through the Aedes aegypti and Aedes albopictus mosquitoes (Jayawera et al, 2021; Wen Hung et al, 2020). Over the past 60 years, the dengue virus has spread to more than 130 countries, causing nearly 10,000 deaths and 100 million symptomatic cases each year. Additionally, more than 50% of the global population is at risk of contracting dengue fever, with the majority in Asia, followed by Africa and the Americas. The first cases of dengue infection in Indonesia were reported in 1968 from the cities of Jakarta and Surabaya. The Indonesian Ministry of Health reported the highest number of cases in 2016 with 204,171 with a death rate of 1598 cases. In 2019, it reported 138,127 cases with a death rate of 919. Meanwhile, in 2020 the total number of cases was 103,509 with a death rate of 725. The role of vectors in the spread of disease causes many cases to be found in the rainy season when there are many puddles of water that become breeding places for mosquitoes. Apart from climate and environmental conditions, several studies show that dengue fever is related to population mobility and density and community behavior (Khan et al. 2021; Pasaribu et al. 2021; Lim et al. 2020; Faridah et al. 2022; Ministry of Health. 2021).

Dengue infection is currently recognized as the most common cause of hospitalization among acute fever cases in Indonesia. Data for 2020 in the province of North Sumatra includes the 10 provinces with the highest incidence of dengue hemorrhagic fever (DHF) with 3125 cases. Dengue fever has become a public health problem that continues to occur in the city of Medan, North Sumatra, despite the widespread implementation of dengue control (Pasaribu et al. 2021; Ministry of Health. 2021).

Almost 95% of cases of dengue hemorrhagic fever are less than 15 years old. Due to their immature hemodynamic systems, children especially infants, tend to develop more severe degrees of dengue disease. National surveillance data from Asian countries shows that infants under 1 year of age and children aged 4-9 years are consistently at high risk of developing more severe dengue hemorrhagic fever (Khan et al, 2021).

Dengue hemorrhagic fever can attack all age groups. The majority of dengue hemorrhagic fever cases occur in children. The mortality rate in children tends to increase so it is necessary to pay more attention to clinical symptoms and laboratory values. Examination of platelets and hematocrit plays an important role in helping early diagnosis if plasma leakage occurs in patients with dengue infection which can cause shock in the patient. A complete blood count can serve as an early indicator of the prognosis of dengue fever. (Handayani et al. 2021; Putri et al. 2019; Rao et al. 2020).

Many clinical and laboratory factors have been associated with disease severity. Practical clinical markers are needed to predict patient severity, as patients with mild clinical symptoms at the initial examination may experience deterioration. Early detection and appropriate management of severe dengue can reduce dengue-related mortality. Therefore, researchers are interested in examining the relationship between clinical symptoms and laboratory values with the degree of severity in dengue infection patients. (Khan et al. 2021; Te. et al, 2022; Handayani, et al, 2022).

2. Methods

The type of research used is analytical observational research using a cross-sectional study design. The study population consisted of all medical record data of pediatric patients diagnosed with dengue infection during the period 1 January 2021 to 31 December 2022 at H. Adam Malik General Hospital, Medan. Determination of the sample in this research was a total sampling technique and met the inclusion criteria. The inclusion criteria used in this study were pediatric patients < 18 years old with a diagnosis of dengue infection and patients who had medical records with good data including laboratory. Exclusion criteria in this study were patients ≥ 18 years old with a diagnosis of dengue infection and diseases such as hemophilia, leukemia, idiopathic thrombocytopenia purpura (ITP), and other hematological diseases.

Data analysis in this research uses data analysis to determine the correlation between variables, calculated using the statistical software Statistical Package for The Social Science (SPSS) version 25.0. The test used is the Fisher exact test. The basis for decision-making in this data analysis is based on the p-value, if the p-value is >0.05 then Ho is accepted and Ha is rejected. However, if the p-value <0.05 then Ho is rejected and Ha is accepted. In collecting data, researchers obtained ethical permission from the Research Ethics Committee, Faculty of Medicine, University of North Sumatra.

3. Results

58 research subjects met the inclusion criteria with sample data that had been observed as follows:

Table 1. Characteristics of research subjects

Characteristics		Frequency (N) (n;60)	Percentages (%)
Gender	Male	28	41,7
	Female	30	58,3
Age	Toddler (< 5 tahun)	5	8,6
	Children (5-11 tahun)	27	46,6
	Adolescent (12-17 tahun)	26	44,8
WHO 2009 Classification			
	Non-Severe	55	94,8
	Severe Dengue	3	5,2
Clinical Manifestation Vomiting	Ya	37	63,8
	Tidak	21	34,5
Fever	$\geq 40^0$C	20	34,5
	$< 40^0$C	38	65,5
Bleeding sign	Ya	15	25,9
	Tidak	43	74,1
Laboratory examination			
Hematocrit	$\geq 40\%$	27	46,6
	$< 40\%$	31	53,4
Platelets	< 150.000	46	79,3
	$\geq$150.000	12	20,7

Leukocytes	< 5.000	31	53,4
	≥ 5.000	27	46,6
Lymphocytes	Normal	20	34,5
	Abnormal	38	65,5

Based on data on patient characteristics, it was found that 30 (58.3%) were female and 28 (41.7%) were male, most of whom were 5-11 years old, namely 26 (44.8%). 37 people (63.8%) had clinical symptoms of vomiting, 20 people (34.5%) had a fever with a temperature of ≥ 400, and 15 people (25.9%) had bleeding manifestations. Laboratory results obtained hematocrit values ≥40% were 27 people (48.3%), platelet values <150,000 were 46 people (79.3%), leukocytes <5,000 were obtained by 31 people (53.4%), and abnormal lymphocytes were obtained as many as 38 people (65.5%).

Table 2. Correlation of clinical symptoms (vomiting, fever ≥400, and bleeding manifestations) with the severity of dengue infection

	Non-Severe Dengue		Severe dengue		*p-value**
	Frequency	%	Frequency	%	
Vomiting					
Yes	35	68,4	2	66,7	0,705
No	20	72,7	1	33,3	
Fever					
$\geq 40^0$	18	32,7	2	66,7	0,271
$<40^0$	37	67,3	1	33,3	
Bleeding sign					
Yes	13	23,6	2	66,7	0,161
No	42	76,4	1	33,3	

Based on the results of bivariate analysis, it was found that there was no significant relationship between fever $\geq 40^0$C, bleeding manifestations, and vomiting with the severity of dengue infection in pediatric patients at H. Adam Malik General Hospital (p-value >0.05).

Table 3. Association between laboratory values (Hematocrit, Platelets, Leukocytes, and Lymphocytes) with the severity of Dengue infection

	Non-Severe Dengue		Severe Dengue		*p-value**
	Frequency (n)	Percentages (%)	Frequency (n)	Percentages (%)	
Hematocrit					
≥ 40	25	45,5	2	66,7	0,447
< 40	30	54,5	1	33,3	
Platelets					

< 150.000	11	20	2	66,7	0,508
≥150.000	44	80	1	33,3	
Leukocytes					
<5000	30	54,5	1	33,3	0,447
≥ 5000	25	45,5	2	66,7	
Lymphocytes					
Abnormal	36	65,5	2	67,7	0.729
Normal	19	34,5	1	33,3	

Based on the results of bivariate analysis, it was found that there was no significant relationship between hematocrit, platelet, leukocytes, and lymphocyte values with the severity of dengue infection in pediatric patients at H. Adam Malik General Hospital (p-value >0.05).

4. Discussion

This study aims to analyze the relationship between clinical symptoms (fever, signs of bleeding, and vomiting) and laboratory results (hematocrit platelets, leukocytes, and lymphocytes) with the severity of dengue infection. Of the 58 research subjects, based on data on patient characteristics, 30 (58.3%) were female, and 28 (41.7%) were male, but Khan et al's research reported that men were more likely to be infected with dengue. amounting to 57%, while research by Senavong et al reported that cases of dengue infection were 57% in women and 43% in men (Khan et al. 2021; Senavong et al. 2020).

It was found that the majority of people diagnosed with dengue infection were 5-11 years old, namely 26 people (44.8%). whereas in another study by Khan et al, the maximum age was 10-14 years, amounting to 52.6%, while in Senavong et al's research, the maximum age was 5-14 years, namely 93.9%, (Khan et al. 2021; Senavong et al. 2020).

From this study, the highest number of non-severe dengue infections were diagnosed, namely 94.8%. From Senavong et al's research, the most frequent diagnoses were severe dengue as much as 69.8%. In a study by Arora et al., the number of confirmed cases of dengue without warning signs was 17.65%, dengue with warning signs was 62.35% and 20% was severe dengue. The research was conducted at New Delhi Hospital, India (Khan et al. 2021; Senavong et al. 2020; Arora et al. 2021).

From this study, it was found that those who had clinical symptoms of vomiting (63.8%), fever with a temperature of ≥ 400 (34.5%), and bleeding manifestations (25.9%) while in Senavong et al's research, it was found that 51.8% experienced vomiting. %, and signs of bleeding at 53.6% (Senavong et al. 2020).

Based on statistical analysis using the Fisher exact test, it was found that there was no significant relationship between fever ≥ 40^0C, signs of bleeding, vomiting, platelet, hematocrit, leukocyte, and lymphocyte values with the severity of dengue infection in pediatric patients at H. Adam Malik General Hospital (p-value>0.05). Khan et al. reported the results of their study that there was a significant relationship between fever and hematocrit values. Resource and Medical reports that there is a significant relationship between the hematocrit value and the severity of dengue infection. Cahyani et al also reported a relationship between hematocrit and dengue infection (Khan et al. 2021; Cahyani. 2019; Resource and Medical. 2020).

According to WHO 2017, the hematocrit value usually begins to increase on the third day of the course of dengue infection, the hematocrit number must be monitored at least every 24 hours to recognize dengue infection early. In severe dengue, the hematocrit is checked every 3-4 hours. An increase in the hematocrit value reflects the condition of hemoconcentration which is always found in dengue infection patients.

Meanwhile, in another study, namely Resource and Medical, there was a significant relationship between vomiting and the severity of dengue infection, but for platelet values and mucosal bleeding, there was no significant relationship. Vomiting is an important danger sign in predicting the risk of severe dengue but was not found in our study. This may be because complete medical record data has not been recorded on

how many times and how much vomiting occurred in 24 hours. Senavong et al, in their study, showed a significant relationship between vomiting and the severity of dengue fever. Khan et al reported the results of their study that there was a significant relationship between platelets and the severity of dengue infection. In Arora et al's study also showed that vomiting and thrombocytopenia were significantly related to the severity of dengue infection, while in Cahyani et al's study, there was a relationship between platelets and lymphocytes in dengue infection. Tasya et al's research found that there was no significant relationship between dengue infection and lymphocytes, but in Nainggolan et al's research, there was a relationship between lymphocytes and plasma leakage. Putri et al's research found a relationship between the number of leukocytes and the incidence of dengue shock syndrome, but in Pasaribu et al's research there was no relationship between the severity of dengue infection and leukocytes (Khan et al. 2021; Senavong. 2020; Arora et al. 2021; Putri et al. 2019; Cahyani et al. 2019; Pasaribu. 2023; Resource and Medical. 2020).

5. Conclusion

Based on the results of the data analysis that has been carried out, the results obtained are that 38 people (63.8%) had clinical symptoms of vomiting, 20 people (34.5%) had fever with a temperature of $\geq 40^0$ C, and 15 people (25.9%) had bleeding manifestations). Laboratory results obtained hematocrit values $\geq 40\%$ for 27 people (48.3%), platelet values <150,000 for 46 people (79.3%), leukocytes < 5,000 for 31 people (53.4%), and abnormal lymphocytes for 30 people (51.7%) obtained 38 people (65.5%). There was no significant relationship between fever $\geq 40^0$C, bleeding manifestations, vomiting, platelet, hematocrit, leukocyte, and lymphocyte values with the severity of dengue infection in pediatric patients at H. Adam Malik General Hospital (p-value >0.05).

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