RESEARCH ARTICLE

Correlation of Thrombocytopenia and Length of Hospitalization in Dengue Child Patient

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Abstract

Dengue virus infection (DVI) is one of the major health problems that cause 500 thousand patients hospitalized annually. Thrombocytopenia is one of the abnormal hematologic findings that is always found in DVI patients. This study aimed to determine the correlation of thrombocytopenia and length of hospitalization in dengue child patients. This retrospective analysis study used secondary data from seven major hospitals in Bandung with a total sampling method. The inclusion criteria were patients aged 0–18 years old diagnosed with dengue fever (DF), or dengue hemorrhagic fever (DHF), or dengue shock syndrome (DSS) who was admitted from January to December 2015 and excluded when there was comorbid as well as incomplete data. The correlation was analyzed by Spearman's rank correlation test. There were 2,025 samples from a total of 5,712 DVI cases during 2015. Among those who admitted, most of the patients experienced severe thrombocytopenia (40%) with the average length of hospitalization was 4.84 days. This result was not much different from the patients with moderate (38.1%) and mild (21.9%) thrombocytopenia who were treated for an average of 4.13 days and 4.08 days, respectively. The analysis of correlation obtained a significant relationship between thrombocytopenia and length of hospitalization despite showing a weak correlation (r=0.231, p=0.001). In conclusion, there is a weak correlation between thrombocytopenia and length of hospitalization among dengue child patients.

Key words: Dengue virus infection, length of hospitalization, thrombocytopenia

Korelasi Trombositopenia dengan Lama Rawat Inap pada Pasien Anak Terinfeksi Virus Dengue

Abstrak

Infeksi virus dengue (IVD) merupakan salah satu masalah kesehatan utama yang menyebabkan 500 ribu pasien dirawat di rumah sakit setiap tahun. Trombositopenia adalah salah satu temuan abnormal hematologi yang selalu ditemukan pada pasien IVD. Penelitian ini bertujuan mengetahui korelasi trombositopenia dengan lama rawat inap pada pasien anak terinfeksi virus dengue. Penelitian analitik retrospektif ini menggunakan data sekunder tujuh rumah sakit besar di Kota Bandung dengan metode *total sampling*. Kriteria inklusi adalah pasien anak usia 0–18 tahun yang didiagnosis demam dengue (DD), atau demam berdarah dengue (DBD), atau sindrom syok dengue (SSD) yang dirawat dari bulan Januari hingga Desember 2015. Kriteria eksklusi meliputi komorbiditas dan data rekam medis yang tidak lengkap. Analisis dilakukan dengan uji korelasi rank Spearman. Terdapat 2.025 sampel dari total 5.712 kasus IVD selama tahun 2015. Di antara yang dirawat, sebagian besar pasien mengalami trombositopenia berat (40%) dengan lama rawat inap rerata 4,84 hari. Hasil ini tidak jauh berbeda dengan pasien dengan trombositopenia sedang (38,1%) dan ringan (21,9%) yang dirawat selama rerata 4,13 hari dan 4,08 hari masing-masing. Analisis korelasi diperoleh hubungan yang bermakna antara trombositopenia dan lama rawat inap meskipun dengan nilai korelasi lemah (r=0,231; p=0,001). Simpulan, terdapat korelasi lemah antara trombositopenia dan lama rawat inap pada pasien anak terinfeksi virus dengue.

Kata kunci: Infeksi virus dengue, lama rawat inap, trombositopenia

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Introduction

Dengue virus infection (DVI) is a major public health problem in many tropical and sub-tropical countries.[1–3] It is estimated that 2.5 billion people are at risk of suffering from DVI and more than 75% of these people live in the Asia-Pacific region.[1,4,5] Indonesia as one of the countries with category A for endemicity of dengue fever (DF) and dengue hemorrhagic fever (DHF) shows that DVI is still the main health problem as well as the cause of hospitalization and death, especially among the children.[1,6] The incidence of DHF in 2018 reached 65,602 cases with the highest number of cases (8,732 cases) is in the West Java.[7] Based on WHO report, about half a million people suffering from DHF require hospitalization each year.[1]

Clinical manifestations of DVI are varying from mild to severe degrees which in some cases can cause fatal conditions and death.[8,9] Thrombocytopenia (thrombocyte level<150,000 cells/mm^3) is the most common finding in DVI patients and is one of the WHO criteria used as a potential indicator of clinical severity.[10–12]

The huge number of cases with a high need for health services such as hospitalization directly makes a disease costs even greater. This must be considered especially by a country implementing the universal health coverage system, such as Indonesia. So, it becomes important for clinicians to be able to determine which patients need to be hospitalized as well as determine the patient's length of stay effectively and efficiently.

Research in 2010 stated that there was a weak correlation between platelet counts with a length of stay (r=0.262).[13] This study was conducted to determine the correlation between thrombocytopenia and length of stay in dengue child patients who were admitted at the hospital in Bandung during 2015.

Methods

This study was a correlational analysis with a retrospective cross-sectional design to determine the correlation of thrombocytopenia with a length of hospitalization in child patients infected with dengue virus.

The instrument used in this study was secondary data from the main research on "Hospital-based surveillance: accuracy, adequacy, and timeliness of dengue case reports in Bandung, West Java, Indonesia of 2015" in the

form of medical records from a database of seven major hospitals in Bandung city (St. Borromeus Hospital, Advent Hospital, Hermina Pasteur Mother and Child Hospital, Hermina Arcamanik Hospital, Limijati Mother and Child Hospital, Santo Yusuf Hospital, and Dr. Hasan Sadikin General Hospital Bandung) in the period of January to December 2015. The inclusion criteria were data of child patients aged 0–18 years who were diagnosed with DF, or DHF, or dengue shock syndrome (DSS). The exclusion criteria were patients with comorbid and incomplete medical record data. The number of samples was determined through the total sampling method. The variables assessed in this study were the degree of thrombocytopenia as the independent variable and length of hospitalization as the dependent variable. The length of hospitalization was arbitrarily determined and grouped into <3 days, 3–5 days, and >5 days.

The correlation of thrombocytopenia with a length of hospitalization was analyzed using the Spearman's rank test. The hypothesis test is significant if it meets the p value<0.05. The strength of correlation between thrombocytopenia and length of hospitalization in child patients infected with dengue virus is expressed by the correlation coefficient (r). Data analysis was performed using IBM® SPSS® version 25 and the results were presented in the form of tables.

This research was conducted after obtaining approval from the Health Research Ethics Committee of Faculty of Medicine of Universitas Padjadjaran Bandung with the letter number: 1371/UN6.KEP/EC/2019.

Results

From 1 January to 31 December 2015 there were 5,712 DVI cases collected from the database of seven major hospitals in Bandung. This study only involved 2,025 samples, all of which were child patients aged 0–18 years old with a diagnosis of DF, or DHF, or DSS. Based on Table 1, the sample that had the most characteristic value was male (51.7%), age≤15 years old (89.1%), DHF (59.2%), and severe thrombocytopenia (40%).

The clinical diagnosis terminology used in this study follows the WHO 2011 guideline criteria. Thrombocytopenia is established when the number of thrombocyte/platelets in the blood <150,000 cells/mm^3.[1] It can be identified through the results of hematological laboratory

Table 1 Characteristics of the Subjects by Gender, Age, Clinical Diagnosis and Degree of Thrombocytopenia

Variables	Categories	n=2,025	Persentage
Gender	Male	1,046	51.7
	Female	979	48.3
Age (years)	≤15	1,804	89.1
	>15	221	10.9
Clinical diagnosis	Dengue fever (DF)	714	35.3
	Dengue hemorrhagic fever (DHF)	1,199	59.2
	Dengue shock syndrome (DSS)	112	5.5
Thrombocytopenia	Mild (100,000–<150,000 cells/mm³)	444	21.9
	Moderate (50,000–<100,000 cells/mm³)	772	38.1
	Severe (<50,000 cells/mm³)	809	40.0

Table 2 The Degree of Thrombocytopenia in Various Clinical Diagnoses

Severity of Infection	Thrombocytopenia						Total	
	Mild		Moderate		Severe			
	n	%	n	%	n	%	n	%
DF	238	33.3	292	40.9	184	25.8	714	35.3
DHF	204	17.0	472	39.4	523	43.6	1,199	59.2
DSS	2	1.8	8	7.1	102	91.1	112	5.5
Total	444	21.9	772	38.1	809	40.0	2,025	100.0

Table 3 Duration of Hospitalization of Dengue Child Patients by the Degree of Thrombocytopenia

Thrombocytopenia	Duration of Hospitalization					
	<3 Days		3–5 Days		>5 Days	
	n	%	n	%	n	%
Mild (100,000–<150,000 cells/mm³)	84	18.9	282	63.5	78	17.6
Moderate (50,000–<100,000 cells/mm³)	90	11.7	546	70.7	136	17.6
Severe (<50,000 cells/mm³)	36	4.4	540	66.7	233	28.8

tests. The platelet value used in this study was the lowest platelet level of the entire platelet serial examination during hospitalization.

The occurrence of thrombocytopenia in various clinical conditions of patients is further presented in Table 2. According to the table, this study found that most of the DF patients (40.9%) had moderate thrombocytopenia. While the majority of both DHF (43.6%) and DSS (91.1%) patients have experienced severe thrombocytopenia.

From the analysis of the data, the average length of hospitalization of the dengue patient was 4 (±2 days). Based on Table 3, most of the patients with mild, moderate, and severe thrombocytopenia were treated for the same period of 3–5 days. Furthermore, the average length of hospitalization of dengue patients based on the degree of thrombocytopenia showed that patients with mild thrombocytopenia underwent hospitalization for an average of 4.08 days. Whereas in patients with moderate and severe thrombocytopenia underwent hospitalization for an average of 4.13 days and 4.84 days,

respectively.

Based on the Spearman's rank test, this study found a significant relationship between thrombocytopenia and length of hospitalization (p<0.001) with the weak correlation (r =0.231).

Discussion

In this study, as presented in Table 1, the majority of DVI cases (59.2%) in hospitalized child patient was the DHF. This finding was likely due to the majority of mild cases of DVI (DF) could be treated as an outpatient as stated in one of study in 2015.[14] Moreover, this result was also consistent with the reference stating that children become the most impatient patient in the case of DHF.[15]

The majority of patients in this study had a severe degree of thrombocytopenia (40.0%). This result was in line with the proportion of diagnosis the majority of patients involved in this study which mostly were severe cases (DHF) patients. This finding seemed consistent with the study stating that thrombocytopenia was seen to be more relevant in those with severe dengue.[16,17]

From the data presented in Table 2, this study found that patients with DHF and DSS had more severe conditions compared with DF patients. It was known from the finding of severe thrombocytopenia both in DHF (43.6%) and DSS (91.1%) patients, while most of the DF patients experienced moderate thrombocytopenia (40.9%). This result was in line with the WHO guideline which considered thrombocytopenia as one of the criteria indeterminate the clinical severity of DVI.[1]

The length of hospitalization represents the time in a treatment period that was calculated by the subtraction of the date of discharge and the date of admission the patient was hospitalized.[15] In this study, the patient's length of hospitalization was stated in the unit of the day. Further analysis from the results of this study showed that most of the patients with mild, moderate, or severe thrombocytopenia were treated for an average of 4 days (range in 2–6 days). Another study that was conducted in Semarang (2015–2016) found that the average length of hospitalization of 137 child patients was 5.47 days. This difference of an average length of hospitalization may be due to criteria inclusion used in this study which only included DHF patients as the subject.[15]

This length of hospitalization was further classified into 3 groups, <3 days, 3–5 days, and >5 days. This classification is based on the average length of hospitalization of dengue patients in Dr. Hasan Sadikin General Hospital Bandung. In mild thrombocytopenia, the average length of stay of the patient was 4.08 (97 hours) days. Whereas in patients with moderate and severe thrombocytopenia the average length of hospitalization was 4.13 days (99 hours) and 4.84 days (116 hours), respectively. This result showed that the difference in duration of hospitalization between the patients with mild, moderate, and severe thrombocytopenia was not more than 24 hours. In general, the result indicated that all of the patients with mild, moderate, and severe thrombocytopenia were hospitalized for 4 days. But with more detailed calculations, this study found that there was a little difference in length of stay among patients. The more severe degree of thrombocytopenia the longer duration of hospitalization.

This finding was confirmed by the result from Spearman's rank correlation test. In this study, it was found that there was a relationship between thrombocytopenia with a length of stay in child patients infected with dengue virus (p<0.001) with a weak correlation (r=0.231) as presented in Table 4. The results of this study are in accordance with previous studies which showed an association between thrombocytopenia and length of stay but with weak correlation (r=0.262).[13]

The health system problem currently being faced by Indonesia today is the Social Security Administrator (*Badan Penyelenggara Jaminan Sosial*, BPJS) budget deficit which reaches 28 trillion IDR. Dengue virus infection is one of the diseases borne by the BPJS, so health services for dengue cases including hospitalization directly contribute to the costs incurred, and the deficit currently being experienced by BPJS. Indonesia was the country with the highest economic burden of dengue in the region, followed by Thailand, representing about 34% and 31% of the total economic burden of dengue, respectively.[18] Inpatients that are actually not needed by DVI patients are often performed especially in child dengue patients.[14] This is caused by parents concerns about uncertain conditions and the potential for fatal outcomes due to dengue infection.[14] Hospitalization that is too early makes the long duration of hospitalization of patients becomes longer and consequently, the burden of costs incurred becomes even greater. Total

2015 economic burden of dengue in Indonesia was estimated at 381.15 million USD which comprised 355.2 million USD for hospitalized and 26.2 million USD for ambulatory care cases.[19] In addition, the number of beds available for inpatients in hospitals is limited. The ratio of beds in hospitals in Indonesia in 2015 was 1.21 per 1,000 population. This ratio increased compared to 2014, which was 1.07 per 1,000 population. Although the ratio of beds to the population in Indonesia in 2015 was sufficient, there are still six provinces with insufficient ratios of beds to population, one of which is the province of West Java (0.84).[20]

Limitations of this study were in the use of cross-sectional study design so the results show less interrelationship between variables.

Conclusion

From this study there is weak correlation between thrombocytopenia and hospitalization duration of dengue child patients. However, the difference in length of hospitalization between mild and severe thrombocytopenia is less than 24 hours. We proved that the degree of thrombocytopenia is not predictive of length of hospitalization among dengue child patients.

Conflict of Interest

The authors declare that there was no conflict of interest.

Acknowledgment

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