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Research Article

The Comparison Between Platelet Count and Hematocrit Levels in Primary and Secondary Dengue Hemorrhagic Fever Infection

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ABSTRACT

Background: Dengue hemorrhagic fever is an infectious ailment that exhibits a significantly elevated incidence rate in Indonesia. Dengue hemorrhagic fever can be classified into primary and secondary infection, where the secondary infection tends to cause more severe clinical manifestations. Hematocrit and platelet count are essential parameters observed in dengue hemorrhagic fever. This study aimed to analysed the existence of statistically significant differences in the level of hematocrit and platelet count between primary and secondary dengue hemorrhagic fever infections.
Methods: This study applied analytical observational cohort design with 60 samples in the form of medical record and laboratory data of hematocrit level and platelet count from patients diagnosed with dengue hemorrhagic fever.
Results: The results reveal significant differences in hematocrit and platelet values between primary and secondary DHF infection. Hematocrit value arises 2.73% higher ($p = 0.043$) and the platelet count drops 50,500/µl lower ($p = 0.00$) in secondary dengue hemorrhagic fever infection.
Conclusions: Significant differences of hematocrit and platelet values were found between primary and secondary dengue hemorrhagic infection. Clinicians should increase wary of secondary dengue hemorrhagic fever infected patients due to more severe clinical manifestations.

Keyword : Dengue Hemorrhagic Fever, Primary Infection, Secondary Infection, Hematocrit, Platelet

INTRODUCTION

Dengue Hemorrhagic Fever (DHF) is an infectious disease commonly found in tropical and subtropical countries [1]. Dengue virus is the aetiology of this disease and transmitted through mosquito bite of Aedes aegypti and Aedes albopictus species. There are 4 stereotypes of dengue virus, those are DENV-1, DENV-2, DENV-3, and DENV-4. Each stereotype only confers lifelong immunity to that stereotype, not to other stereotypes [2,3]. Infection with different stereotype or secondary infection leads to more severe clinical manifestation [4].

Asia, which is included in the area with tropical climate, ranks the first place in dengue hemorrhagic fever cases, with Indonesia as the country with one of the highest cases in Southeast Asia [5]. Indonesia experiences fluctuation in dengue hemorrhagic fever cases in the last 11 years, in the period of 2011-2021. The average number of dengue hemorrhagic fever cases in the last 11 years is around 105,132, with the highest cases occurring in 2016 [6].

Essential laboratory parameters that require routine monitoring are hematocrit and platelet count, due to hemoconcentration and thrombocytopenia being a definite clinical manifestation in dengue hemorrhagic fever [7,8]. Elevation in hematocrit level indicates plasma leakage caused by increase in vascular permeability due to infection. The elevation of the hematocrit value can reach more than 20% which signifies plasma volume decreased 20% due to leakage [9]. Platelet count usually decline until reaches a number below 100.000/µl. Thrombocytopenia is caused by enhancement of platelet destruction by reticuloendothelial system and direct bone marrow suppression by dengue virus [10].

The increase in hematocrit and decrease in platelet count tend to be more dramatic in secondary dengue hemorrhagic infection than in primary infection. This phenomenon caused by immunity enhancement due to antibody increasement formed as a result of prior infection/primary infection. Immunity enhancement causes exaggerated immune response which causes an increase in vascular permeability and platelet destruction by the reticuloendothelial system [5,9].

METHOD

This study applied a retrospective observational analytic cohort design and held in Cinta Kasih Tzu Chi hospital, Cengkareng, West Jakarta. Total samples for this study is 60, which consist 30 samples of primary infected dengue hemorrhagic fever and 30 for the secondary infection as well. The number of samples obtained by effect size equation, which quantifies the strength and differences in the incidence of effects between the experimental and control groups [11].

The inclusion criteria of this study were adult dengue hemorrhagic fever patients, specifically patients over 18 years old age. The exclusion criteria for this study are patients with co-infection or co-morbid, patients who are pregnant, and patients that are using certain drugs that could affect platelet count (abciximab, acetaminophen, quinidine, quinine, danazol, cimetidine, diclofenac, eptifibatide, methyldopa, rifampicin, tirofiban, trimethoprim, vancomycin) [12,13].

The data used for this study is medical record and laboratory data. The initial step for data collection is gathered all the test results of positive IgM/IgG dengue rapid test. After data from the laboratory was

collected, the data was filtered and confirmed in the medical record department and selected based on exclusion and inclusion criteria. Some data that does not fill the requirements of the inclusion criteria are excluded due to avoid false positive result.

This study utilized IBM SPSS version 26 application and utilize independent sample T-test method to analyzing the data. With this analytical method, a comparison of the average of the two case groups is carried out, which in this study are primary infected dengue hemorrhagic fever group and secondary infected dengue hemorrhagic fever group [14].

RESULTS

The number of samples collected after being filtered with the exclusion criteria are 60 in total, with 30 patients both in primary and secondary dengue hemorrhagic fever infection. Table 1 consists of patient's data distribution. The study results show men experienced more dengue hemorrhagic fever infections with more cases of primary infection. The total number of male patients who had dengue hemorrhagic fever infection was 34 (56,67%) and 26 for the woman (43,33%).

Table 1 Distribution of patient's gender and age based on infection type

Variabel	Primary Infection		Secondary Infection		Jumlah	
	n	%	n	%	n	%
Male	19	63.37	15	50	34	56,67
Female	11	36.67	15	50	26	43,33
Total	**30**	**100**	**30**	**100**	**60**	**100**

Source: Primary Data

The results of the study regarding hematocrit level in primary and secondary dengue hemorrhagic infections are shown in Table 2. There is a significant difference in hematocrit level between primary and secondary infection as evidenced by the p value below 0.05, with 0.043 result obtained from IBM SPSS version 26 analysis. Hematocrit level tend to be 2,73% higher in secondary infected dengue hemorrhagic fever patients. IBM also analyses confidence intervals in populations and stated we can be 95% confident that in the populations, patients with secondary dengue hemorrhagic infection have a higher hematocrit level in the range of 0.92-5.375% than primary infection.

Parameter: Hematocrit	
Variables	**Mean (%)**
Primary Infection	41.7
Male	42.58
Female	40.18
Secondary Infection	44.43
Male	47.13
Female	41.73
95% Coincidence Interval of the Differences	
Lower	**Higher**
0.92	5.375

Source: Primary Data

Study results regarding platelet count between primary and secondary dengue hemorrhagic fever are shown in Table 3. Significance difference in platelet count between primary and secondary dengue hemorrhagic fever were found in this study. This statement proven by analysis result with IBM SPSS that shows p-value below 0.05 which is 0.00. Platelet count drops more dramatically in secondary dengue hemorrhagic fever infection than in secondary infection, with a mean difference

of 50,500/µl. SPSS analysis also shows 95% confidence rate of platelet count drops lower in secondary dengue hemorrhagic infection than primary infection in the range of 36,066 – 64,934/µl.

Parameter: Platelet (/µl)	
Variables	**Mean (%)**
Primary Infection	94,700
Male	101,684
Female	82,636
Secondary Infection	44,200
Male	47,000
Female	41,400
95% Coincidence Interval of the Differences	
Lower	**Higher**
36,066	64,934

DISCUSSION

The elevation in hematocrit level occurs due to plasma leakage caused by viral protein NS1. The NS1 protein caused increase in vascular permeability resulting in plasma leakage. This phenomenon applies to both primary and secondary dengue hemorrhagic infection. Besides the NS1 viral protein, another factor that causes an increase in hematocrit level in secondary dengue hemorrhagic infection is immune enhancement. Preformed antibodies from the primary infection increase rapidly in response to resistance to the secondary infection. This "immune-boosting" event causing increased in cytokine response that leads to exaggerated increase in vascular permeability and higher hematocrit elevation in secondary infection [5,9].

The results of this study are supported by the results of previous research which stated that there is a significance difference in hematocrit level and platelet count in dengue hemorrhagic fever, proven by the p value below 0.05 [15].

Thrombocytopenia in dengue hemorrhagic fever occurs due to direct suppression of bone marrow by dengue virus, where the bone marrow is the site of thrombopoiesis [10]. Immune activation also occurs, in which dengue virus antigen binds to platelets and platelets bind to complement fragments. This phenomenon causes increased destruction of antigen-bound platelets and complement fragments in the reticuloendothelial system [16]. There is an increase of immunity in secondary dengue hemorrhagic fever infection, which activates more complement system and resulting in increased of platelet destruction by the reticuloendothelial system [17]. This incidence leads to more severe thrombocytopenia in secondary infection.

The results of this study are in line with many results of previous research that also found significant difference on platelet count between primary and secondary dengue hemorrhagic fever. Previous studies have stated that in secondary dengue hemorrhagic fever infection, the decrease in platelet count occurs more drastically than in secondary infection [15,18-20].

One other important finding in this study is the platelet count falls below the critical value. The critical value, referrals from Cinta Kasih Tzu Chi hospital is under 20,000/µl. This study found 3 patients with platelet count drops below the critical value. Seeing from the results of the p-value between hematocrit and platelet count in this study, platelet count has a p-value that is far below 0.05 (0.00), while the p value of hematocrit is almost 0.05 (0.043). From this, we can assume that the platelet count is a very important parameter for observing the course of dengue hemorrhagic fever.

Awareness to a decrease value in this parameter need to be improved so that the value does not drop below the critical value.

CONCLUSION

This study led to the conclusion that there are significant differences in hematocrit level and platelet count between primary and secondary infected dengue hemorrhagic fever patients. Significance is proven by both p-value of hematocrit and platelet count are below 0.05, sequentially 0.043 and 0.00. This study found that the average hematocrit level in secondary dengue hemorrhagic fever infection elevate 2.73% higher than primary infection. Platelet count in secondary dengue hemorrhagic fever infection decline by an average of 50,500/µl lower than the primary infection. This research may be furthered through the acquisition of additional research samples and inclusion of boarder populations, thereby the outcomes could be more significant and precise.

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