Research Article

HEMATOCRITE LEVEL AND TROMBOCYTE INDEX OF DENGUE HEMORRHAGIC FEVER PATIENTS IN KENDARI CITY REGIONAL GENERAL HOSPITAL

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ABSTRACT

Background: Dengue Hemorrhagic Fever (DHF) is an infectious disease caused by dengue virus which is characterized by plasma leakage. An examination of hematocrit and platelets is a routine blood test performed as a diagnosis criteria for DHF. **Aim:** The purpose of this study was to determine the relationship between elevated hematocrit levels and trombocyte index (MPV and PDW) in patients with DHF (Dengue Hemorrhagic Fever). **Method:** This study is an observational analytic study with a cross-sectional design, with 73 samples that have been diagnosed with dengue hemorrhagic fever. This study uses Quota sampling. Data were analyzed using the Spearman statistical test and if the value was ≤0.05. **Results:** The results of the study showed that dengue hemorrhagic fever patients had increased hematocrit levels by 91.8%, normal hematocrit by 8.2% and the increase in platelet index by 84.9% and the increase in platelet distribution width. 89.0%. Based on statistical tests obtained a positive correlation between hematocrit levels and trombocyte index (mean platelet volume) with p = 0,000 and r = 0,571. A positive correlation between hematocrit levels and trombocyte index (platelet distribution width) with p = 0,000 and r = 0,693. **Conclusion:** The conclusions of this study were that there was a significant correlation between hematocrit levels and trombocyte index (Mean Platelet Volume and Platelet distribution width) in dengue hemorrhagic fever patients in Kendari City Hospital.

Keywords: Hematocrit, Dengue Hemorrhagic Fever Patients, trombocyte Index (MPV and PDW).

INTRODUCTION

Dengue hemorrhagic fever is one of the most common tropical infectious diseases in Indonesia caused by the dengue virus. The classic symptoms of dengue fever are fever, headache, back pain, pain behind the eyeball, photophobia, and muscle/joint/bone pain. The disease may occur with or without hemorrhagic manifestations. With clinical signs found bleeding manifestations are petechiae, epistaxis, hypermenorrhea, and gastrointestinal bleeding. (WHO) WHO data in 2015, the incidence of dengue fever (DD) or dengue hemorrhagic fever (DHF) increases every 10 years. The incidence of dengue fever in the Western Pacific and Southeast Asia in 2008 exceeded 1.2 million cases, in 2020 it exceeded 2.3 million cases, in 2016 there were 37,687 severe cases of dengue from 2.3 million cases of dengue. In 2015 there were five provinces that had the highest mortality rate, namely Maluku (7.69%), Gorontalo (6.06%), West Papua (4.55%), North Sulawesi (2.33%), and Bengkulu (1.99%) (Ministry of Health RI, 2016). According to the Health Office, in 2016 the number of DHF sufferers in Southeast Sulawesi reported as many as 3,433 cases, an increase of more than 2 times compared to the previous year, 33 cases of which died Incidence Rate (IR) / Sickness Rate of 132.5 per 100,000 population and Case Fatality Rate (CFR) / Mortality Rate is 1.0%, this figure is lower than the previous year which reached 1.4%. The diagnosis of DHF can be made based on clinical criteria plus thrombocytopenia (≤100,000/mm3) and hemoconcentration/increased hematocrit 20%. The hematocrit value is the concentration (expressed in percent) of erythrocytes in 100 mL of whole blood. The hematocrit value will increase (hemoconcentration) due to an increase in blood cell levels

or a decrease in blood plasma volume, for example in the case of DHF. On the other hand, the hematocrit value will decrease (hemodilution) due to a decrease in blood cellularity or an increase in blood plasma levels, such as in anemia [1] .The suspected mechanism of thrombocytopenia in patients with DHF is depression of megakaryocyte function. There are several platelet indices that are known as indicators of platelet activation, namely Mean Platelet Volume (MPV), and Platelet Distribution Width (PDW). The higher MPV level indicates the number of large platelets which is a sign of increased platelet turnover. Meanwhile, Platelet Distribution Width (PDW) indicates the level of anisocytosis of platelets[2]. The results of initial data collection in 2019 at the Kendari City Regional General Hospital obtained as many as 268 people diagnosed with Dengue Hemorrhagic Fever. Therefore, the authors are interested in conducting research on the relationship between hematocrit levels and the platelet index of dengue hemorrhagic fever patients at the Kendari City Regional General Hospital.

Hematocrit

Hematocrit examination is one of the most accurate and simple methods in detecting the degree of anemia or polycythemia. The hematocrit value is also used to calculate the average erythrocyte value. Usually this value is determined by venous blood or capillary blood[3]. When whole blood is centrifuged, the heavier particles fall to the bottom of the capillary tube and the lighter particles settle on top. Then the hematocrit value can be immediately measured. Normal hematocrit values differ in gender. In men the hematocrit value is 40% - 48% while for women the hematocrit value is 37% - 43%[4]. The hematocrit is normal in the early phase of fever. Small increases may occur due to high fever, anorexia, and vomiting. A sudden increase in hematocrit is seen after the platelet count is reduced. Hemoconcentration or an increase in hematocrit by 20% of the

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normal range, such as a hematocrit of 35% = 42% is objective evidence of plasma leakage[5]. Factors that affect the first hematocrit examination are Invivo factors in the form of erythrocytes, blood viscosity, plasma. And the second factor is centrifugation, anti-coagulant, temperature and time of sample storage, the examination material is not mixed until homogeneous before the examination is carried out, the hematocrit tube, when using capillary blood, the first drop of blood must be discarded because it contains interstitial fluid and inaccurate readings[6].

MPV and PDW against DHF

Platelets not only act as hemostatic cells, but also play a role in immune defense and inflammatory processes. Platelets are also able to bind to other cells such as leukocytes and vascular cells[7]. When the body is exposed to infection, a complex series of regulatory interactions occur, resulting in an irregular host response, inflammation and immunosuppression. The pro-inflammatory response to infection causes activation of the coagulation system and fibrinolysis[7]. There are three theories related to thrombocytopenia in dengue fever, namely a decrease in the number of platelets due to bone marrow suppression, increased platelet destruction and excessive use of platelets. Differences in the size of platelets in patients with dengue hemorrhagic fever are caused by thrombocytopenia[8]. PDW examination is a description of the short platelet life span that arises due to increased platelet destructive activity. As compensation for the occurrence of platelet destructive activity, there will be a thrombopoietic process or the formation of new platelets to overcome the thrombocytopenia state. If the thrombocytopenia process continues, the bone marrow will release younger, larger megakaryocytes as compensation for the continuous thrombocytopenia, resulting in variations in the diameter of the platelets in the circulation[9].

Hematocrit and Platelet Index to DHF

Plasma leakage that occurs in DHF causes hemoconcentration, namely an increase in the value of platelets. Together with this, erythrocytes release ADP (Adenosine diphosphate) which is one of the agonists of platelet aggregation, the release of ADP by red blood cells results in an increase in platelet aggregation. This theory is in accordance with the theory of secondary heterologous infection which states that increased platelet aggregation results in the destruction of platelets by the reticuloendothelial system (RES) resulting in thrombocytopenia. Then there is a process of thrombopoiesis by the bone marrow as compensation from the body, with this formation, it results in an increase in the variation of the platelet index[10].

METHOD

This study used an observational analytic research method with a cross sectional research design. This research was conducted in July 2020. The population in this study were patients diagnosed with Dengue Hemorrhagic Fever at the Kendari City Hospital in 2019 with a total population of 268 people. The number of samples as many as 73 people with the Quota sampling method. Inclusion criteria diagnosed with Dengue Hemorrhagic Fever, medical records of DHF patients in 2019 complete with laboratory results (hematocrit value and platelet count). Exclusion criteria were diagnosed with DHF with other diseases. Data analysis using Pearson Correlation test.

RESULTS

Characteristics of Samples Based on Gender, Age, Time of Fever, Hematocrit Level, MPV and PDW

Table 1. Distribution of Characteristics by Gender, Age, Time of Fever, Hematocrit, MPV and PDW.

Characteristics	Amount (n = 73)	Percentage (%)
Gender		
Male	41	56,2
Female	32	43,8
Age		
< 18	26	35,6
> 18	47	64,4
Fever time		
1 – 5 days	61	83,6
> 5 days	12	16,4
Hematokrit		
Normal	6	8,2
Increase	67	91,8
Mean Platelet Volume (MPV)		
Normal	11	15,1
Increase	62	84,9
Platelet Distribution Width (PDW)		
Normal	8	11,0
Increase	65	89,0

Based on Table 1, the distribution of sample characteristics is based on gender, which is the largest sample with male sex of 41 samples (56.2%). The sample based on age was mostly found in adults who were more than 18 years old (47 people, 64.4%). Samples based on the duration of fever in dengue hemorrhagic fever patients were 61 samples with a duration of fever 1-5 days and as many as 12 samples with a duration of fever >5 days. The sample description is based on the increase in hematocrit levels that have increased above 20% as many as 67 samples (91.8), with a hematocrit value that did not increase 20% as many as 6 samples (8.2%). The MPV values that did not increase were 11 samples (15.1%) while those who experienced an increase in the MPV values were 62 samples (84.9%). The PDW value that did not increase was 8 samples (11.0%) while those who experienced an increase were 65 samples (89.0%).

Table 2. Analysis of the relationship between hematocrit levels and the platelet index (Mean Platelet Volume) of DHF (Dengue Hemorrhagic Fever) patients at the Kendari City Hospital in 2019

Increased Hematocrit	Mean Platelet Volume		Spearman Test*
	Normal	Increase	
Normal	5	1	p = 0,000
Increase	6	61	r = 0,571

Based on Table 2, it was found that there was a relationship between the increase in hematocrit and MPV value of p = 0.000 (p<0.05) with a correlation strength of r = 0.571. Thus, it can be concluded that there is a significant relationship between the hematocrit level and the platelet index (MPV) of dengue hemorrhagic fever patients at the Kendari City General Hospital with a strong correlation strength.

Table 3. Analysis of the relationship between hematocrit levels and the platelet index (Platelet Distribution Width) of DHF (Dengue Hemorrhagic Fever) patients at the Kendari City Hospital in 2019

Increased Hematocrit	Platelet distribution width		Spearman Test*
	Normal	Increase	
Normal	5	1	p = 0,000
Increase	3	64	r = 0,693

Based on Table 3, it was found that the relationship between an increase in hematocrit and PDW value was p = 0.000 (p<0.05) with the strength of the correlation, the value of r = 0.693. Thus, it can be concluded that there is a correlation between the hematocrit level and the platelet index (PDW) of dengue hemorrhagic fever patients at the Kendari City Regional General Hospital.

DISCUSSION

In this study, for age, the highest number of DHF patients was aged more than 18 years with a total of 47 patients (64.4%) and patients aged less than 18 years as many as 26 patients (35.6%), this is slightly different from the theory that reveals that the most DHF sufferers are children or at the age of < 10 years. For the duration of fever, the results were very clear, namely 61 patients (83.6%) this was in accordance with the theory that when the fever was on 3-5 days the fever fell and where at this time there was a critical phase of plasma leakage.

Increased hematocrit levels of patients with DHF (Dengue Hemorrhagic Fever) at the Kendari City Hospital.

Based on the research conducted to assess the increase in hematocrit levels of DHF patients at the Kendari City Hospital with numbers meeting the inclusion criteria, a picture of an increase in hematocrit was obtained as in Table 2 where the results of the study of a total of 73 samples of DHF patients at Kendari City Hospital, 6 samples did not experience an increase in blood levels. hematocrit and 67 samples experienced an increase in hematocrit 20%. The theory of the results of this study is in line with[11] which showed that most DHF patients experienced an increase in hematocrit above 20%. However, this research theory is not in line[12] where there was an increase in hematocrit above 30% in most samples. The hematocrit value is the volume of erythrocyte cells in 100 mm3 of blood and is expressed in percent. In the case of DHF, an increase in the hematocrit value (hemoconcentration) is due to a decrease in blood plasma levels due to vascular leakage. The hematocrit value will decrease when hemodilution occurs, due to a decrease in blood cellular levels or an increase in blood plasma levels, as in anemia.

Analysis of MPV and PDW Platelet Index of Dengue Hemorrhagic Fever Patients in Kendari City Hospital

Based on the research conducted to assess the MPV and PDW levels of DHF patients at the Kendari City Hospital who met the inclusion criteria, a picture of the platelet index was obtained as in Table 2 where the results of the study of a total of 73 samples of DHF patients at Kendari City Hospital, 11 samples did not experience an increase in the value. MPV and 62 samples with an increase in MPV value, for the results of the study the PDW value of 73 samples of DHF patients at the Kendari City Hospital, as many as 8 samples did not experience an increase in PDW value and 65 samples with an increase in PDW value. The theory of the results of this study is in line[13] that, it is known that the lowest MPV value variation is 8.6 m and the highest is 14.2 m. The lowest PDW value was 11.9 fl and the highest was 26.1 fl. However, the theory of this study is not in line with [14] which obtained an average MPV value of 9.9 fL and an average PDW value of 14.1 fl where these values did not indicate an increase in the two platelet indices.

The relationship between increased hematocrit levels and the platelet index (MPV and PDW) in DHF patients at the Kendari City Hospital

The results in Tables 3 and 4 show that there is a significant relationship between the hematocrit level and the platelet index (MPV

and PDW) of dengue hemorrhagic fever patients at the Kendari City Hospital. This research theory is in line with[15] that the positive correlation between the relationship between the increase in hematocrit and PDW and MPV values, means that the higher the increase in hematocrit that occurs, the higher the PDW and MPV values. However, this research theory is not in line with[16],that there is no relationship The significant difference between the platelet distribution width and the mean platelet volume on the hematocrit in DHF patients was influenced by the number of samples studied by the researcher. The results of the analysis showed that the value of p = 0.000 with the strength of the correlation value of r = 0.571 hematocrit to MPV while the value of p = 0.000 with the strength of the correlation value of r = 0.693 hematocrit to PDW which means there is a significant relationship between hematocrit levels and the platelet index (MPV and PDW) of fever patients. dengue hemorrhagic fever in Kendari City Hospital. This is evidenced by the Spearman correlation statistical test in Tables 3 and 4 which shows a significant value (p) of 0.000 (p <0.05). This is in line with the WHO diagnostic criteria (2011) that an increase in hematocrit levels as a diagnostic parameter for dengue fever. An increase in the hematocrit value illustrates that hemoconcentration is always found in DHF, which is an indicator of plasma leakage, so it is necessary to carry out periodic hematocrit examinations. Hemoconcentration with an increase in hematocrit of 20% reflects increased capillary permeability and plasma permeation. Dengue virus infection begins when the vector takes the host's blood and introduces the virus into it. Dengue virus binds to and enters host cells through an endocytosis process mediated by low affinity receptors such as dendritic cells. The mechanism of immunopathogenesis of dengue virus infection involves a humoral response in the form of antibody formation that plays a role in the virus neutralization process, complement-mediated cytolysis and antibody-mediated cytotoxicity[17] or by binding of the viral antibody complex to the Fc receptor. This infection directly activates helper T cells (CD4) and T-cytotoxic cells (CD8) which produce lymphokines and interferon. These inflammatory mediators result in endothelial cell dysfunction and plasma leakage and will activate the complement system by secreting C3a and C5a, which results in increased permeability of blood vessel walls resulting in extravasation of plasma from intravascular to extravascular. In addition to endothelial dysfunction, namely an increase in vascular permeability, the antibody virus complex that is formed also activates the coagulation system, the fibrinolysis system, kinins, and interferes with the platelet aggregation process, which will overall result in bleeding manifestations that occur in DHF. According to [18], MPV is the average size of platelets/platelets. New platelets are larger, and an increase in MPV occurs when there is an increase in the number of platelets produced, otherwise a decrease in MPV is an indication of a decrease in the number of platelets (thrombocytopenia) as well as MPV, PDW is an indication of variations in platelet size which can be a sign of the release of active platelets. Mean Platelet Volume (MPV) and Platelet Distribution Width (PDW) are platelet indices that are better known as indicators of platelet activation compared to other platelet indices. Platelet distribution width (PDW) is the variation in the diameter of platelets circulating in peripheral blood. PDW indicates the level of anisocytosis of platelets. Young platelets are larger in size and old platelets are smaller in size. Thus, in the blood circulation there are biphasic platelets, young platelets have a larger size. As a result of increasing the proportion of young platelets, there is also an increase in the average diameter of platelets circulating in peripheral blood[19].

CONCLUSION

There is a significant relationship between the relationship between Hematocrit Levels and Platelet Index of Dengue Hemorrhagic Fever

Patients at the Kendari City Hospital with the strength of the correlation - each r = 0.571 and r = 0.693.

Acknowledgement

Conflict of Interest

All authors confirm there are no conflicts of interest related to this manuscript.

Author's Contribution

All authors in this review contributed equally. All authors prepared, drafted, structured research, critically read and revised manuscripts and gave final approval for publication.

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