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Relationship Between Platelet, Hematocrit and Leukocyte with Dengue Severity in Bengkulu City, Indonesia

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ABSTRACT: Establishing the correct diagnosis of the clinical stage and the severity of dengue patients is very important to determine the prognosis. Examination of platelets, hematocrit and leukocytes for each clinical stage of dengue can help group and manage patients based on their clinical degree. This study aimed to determine the relationship between platelet, hematocrit and leukocyte examination results with the clinical degree of dengue based on WHO. This study used a cross-sectional study design with a sampling technique using consecutive sampling from July-November 2020 in 5 hospitals at Bengkulu City with total sample of 35 patients. The results found a strong relationship between hematocrit levels and the degree of severity of dengue (p = 0.001; r = 0.637). However, there was no significant relationship between the number of platelets (p = 0.826; r = -0.039) and leukocytes (p = 0.554; r = -0.103) with the severity of dengue. Laboratory tests are crucial to establish the clinical degree of dengue and disease's prognosis.

Key Words: dengue, hematocrit, platelets, leukocytes

1. INTRODUCTION

Dengue is emerging as a serious public health problem globally. It is estimated to occur annually in over 100 endemic countries, putting almost half of the world's population at risk.[1,2] The incidence rate (IR) of dengue by province in 2018 in Indonesia showed the highest incidence rate of dengue were East Kalimantan at 87.81 per 100,000 population, Central Kalimantan at 84.39 per 100,000 population, and Bengkulu at 72.28 per 100,000 population. The incidence rate in the province of Bengkulu increased twice to that in 2017, from 31.95 to 72.28 per 100,000 population. Bengkulu City, with 8,487 dengue patients and a mortality of 108, was designated as high risk region for dengue infection.[3]

Dengue is an endemic disease that occurs throughout the year. It commonly happens in the rainy season, the *Aedes* mosquito's population develops optimally in the community. In the past 50 years, the incidence of dengue has increased by 30 folds, with an increase in

geographical expansion to new countries and expansion from urban to rural areas. An estimated 50 million dengue infections occur every year and infected around 2.5 billion people live in the 128 endemic countries.[4]

Dengue Shock Syndrome (DSS) is a major problem in almost all DHF patients. Dengue shock syndrome occurs due to plasma leakage. Proper and early treatment on DHF patients is an important factor for successful recovery (5). According to WHO (2011), dengue is classified into four degrees, namely grade I, grade II, grade III, and grade IV, and DSS is included in degrees III and IV. Increased capillary permeability at this stage results in massive plasma infiltration into the interstitial space leading to hypovolemia resulting in a variety of complex manifestations and complications. [6–8]

Early and accurate diagnosis, and an accurate assessment of the stage and condition of the patient are very important factors in determining the patient's prognosis. The more severe the patient's disease, the worse the prognosis.[9,10] Therefore an accurate assessment of the risk of shock is essential for adequate management, preventing shock and further bleeding. The main pathophysiology of DHF are manifestations of bleeding and circulatory failure.[11,12] Bleeding is usually caused by thrombocytopaty and thrombocytopenia, therefore it is necessary to check platelets. Increased hematocrit indicates the degree of hemoconcentration, thus, it is important in assessing plasma permeation.[13] It is hoped that the examination of platelets and hematocrit for each clinical degree of dengue will greatly assist medical personnel to make a diagnosis and determine the prognosis of dengue.

World Health Orgnization (WHO) criterion for clinical degree of dengue do not provide a definite value from the results of the examination of platelets, hematocrit and leukocytes for each clinical degree. The medical staff determines the degree of the clinic only based on clinical signs and symptoms, even though the examination of platelets, hematocrit and leukocytes plays an important role in helping diagnose dengue, especially if there is a plasma leak which can trigger shock.[14] Based on this data, the study aimed to see the relationship between the examination of the platelet, the value of the hematocrit and the level of leukocytes with the clinical degree or severity levels of dengue in adult patients at Bengkulu City, Indonesia.

2. METHODS

This research was conducted in July 2020 and has been approved by Health Research Ethics Commite of the Faculty of Medicine and Health Sciences Universitas Bengkulu, by numbers 306/UN30.14.9/LT/2020. The study used an analytic observational study with cross-sectional design.[15] The target population in this study was all adult patients with dengue in Bengkulu City. The accessible population in this study was all patient with dengue at Harapan dan Do'a Hospital, Ummi Hospital, Gading Medika Hospital, Dr. M. Yunus Hospital and Bhayangkara Hospital, Bengkulu City, Indonesia, between July 2020 to November 2020.

The research sample was 26 people. The research sampling technique used consecutive sampling for 5 months at 5 hospitals. Data collection begins with the signing of the consent sheet by the respondent and then completes the identity data sheet, then the characteristics of the research subject. Measurement of thrombocyte, hematocrit, and

leukocyte levels in research subjects was carried out by using spectrophotometer method in the Clinical Pathology Laboratory of Bhayangkara Hospital and Harapan and Do'a Hospital, Bengkulu City. The respondents' vein bloods were collected from the cubital fossa after disinfection. Hypothesis testing used was bivariate analysis with Rank Spearman nonparametric hypothesis testing. Data analysis was performed by using SPSS version 23 software.[15]

3. RESULT

Table 1 shows the characteristics of the research subjects. Patients age ranged was from 19 years to 57 years of age. Mean ± SD age was 34.03 ± 11.29 years of age. The number of male was 15 patients (57.7%). The highest degree of dengue severity in grade I was 19 patients (54.29%).

Table 1. Frequency Distribution of Research Subjects

Characteristic	n (%)	Mean± SD
Age		
▪ 17-37 years	22 (62.86)	33.08±10.40
▪ 38-58 years	13 (37.14)	
▪ >58 years	0 (0)	
Sex		
▪ Laki-laki	22 (62.86)	
▪ Perempuan	13 (37.14)	
Tingkat Keparahan DBD		
▪ Grade I	19 (54.29)	
▪ Grade II	11 (31.43)	
▪ Grade III	5 (14.28)	
▪ Grade IV	0 (0)	

Platelet level (x1000 / mm3) was 8 for minimum and 312 for maximum with the average platelet of 144.51 ± 76. Platelet levels decrease according to the increase in the severity of DHF. There is no significant relationship between the platelet count and the severity of DHF. The strength of the relationship is inversely related, the lower the platelet count, the more severe the clinical degree of dengue. Data can be seen in table 2.

Table 2. Relationship between Platelets and Dengue Severity

Severity Level of Dengue	Platelets Level (x1000/mm^3)
▪ Grade I	152.95±75.97
▪ Grade II	142.18±62.68
▪ Grade III	117.60±94.07
Rank Spearman Correlation Test	p= 0.825; r= -0.39

Hematocrits level (%) was 27 for minimum and 57 for maximum with the average platelet of 40.34 ± 5.58. There is a significant relationship between the number of hematocrit and the severity of DHF. The strength of the relationship was strong and directly

proportional, the higher the hematocrit level, and the more severe the clinical degree of dengue was. Data can be seen in table 3.

Table 3. Relationship between Hematocrit and Dengue Severity

Severity Level of Dengue	Hematrocyt Level (%)
▪ Grade I ▪ Grade II ▪ Grade III	39.89±4.73 41.18±7.38 40.20±3.25
Rank Spearman Correlation Test	p= 0.001 ; r= 0.637

Leukocyte level (x1000/mm3) was 2.8 for minimum and 19.1 for maximum with the average platelet of 5.98 ± 3.69. There was no significant relationship between the number of leukocytes and the severity of DHF. The strength of the relationship is inversely related, the lower the level of leukocytes, and the more severe the clinical degree of dengue. Data can be seen in table 4.

Table 4. Relationship between Leukocytes and Dengue Severity

Severity Level of Dengue	Leukocyt Level (x1000/mm^3)
▪ Grade I ▪ Grade II ▪ Grade III	62.36±38.47 57.70±39.03 54.80±22.48
Rank Spearman Correlation Test	p=0.554 ; r= -0.103

4. DISCUSSION

Diagnosis of dengue and the course of the disease must be done accurately. In patients with DHF, laboratory examination shows thrombocytopenia and hemoconcentration.[16,17] The amount of platelet and hematocrit levels is often used as indicators of the severity of the disease. The number of leukocytes to see the cause of the infection (virus / bacteria).[7]

In this study, there was a significant relationship between hematocrit and the severity of dengue, but there was no insignificant relationship between platelets and leukocytes and the severity of dengue. Based on this study the decrease in leukocyte levels and platelet levels cannot provide an idea of the degree of severity of dengue.

The results of the correlation between leukocytes and the clinical degree of dengue shows the mean number of leukocytes in grade I (62.36±38.47x1000/mm^3) and decreased in grade II (57.70±39.0 x1000/mm^3), and grade III (54.80±22.48 x1000/mm^3). The average number of leukocytes at each clinical degree was still within normal limits. This is because the patient came for treatment not on the first day of fever. Similar results were drawn by Idris (2017) in Samarinda and Dewi (2013) in Jakarta, there was no significant relationship between leukocyte levels and dengue severity, but the risk of shock in leukopenia was lower than those without leucopenia.[18,19]

The first day to the third day of fever is usually found leukopenia within normal limits. Leukopenia occurs due to bone marrow depression due to a direct or indirect viral infection process through the production of pro-inflammatory cytokines that suppress the

bone marrow. [20–22] In severe shock, leukocytosis can be found, characterized by a large number of a typical transformed lymphocytes and absolute neutropenia.[23]

The results of platelet correlation and clinical degree of dengue shows mean platelet count at grade I (152.95±75.97 x1000 /mm^3) and decreased in grade II (142.18±62.68 /mm^3) and grade III (103.66 x1000 /mm^3). Platelet levels in this study decreased at each degree, but the results of statistical analysis showed that there was no significant relationship between platelets and the severity of dengue in this study. The results of this study are similar to those of Syumarta (2014) in Padang, Aziz (2019) and Ayunani (2017).[9,22,24] A reduced amount of platelet is an indicator of plasma seepage. Plasma permeation is the result of an immunological reaction between the dengue virus and the body's defense system, which causes changes in the nature of the blood vessel walls, making it easier for fluids to penetrate. This is in line with previous studies that reported thrombocytopenia as a parameter of haematological abnormalities in dengue patients.[25–27]

The results of the correlation between hematocrit and clinical degree of dengue shows mean hematocrit levels were at grade I (39.89±4.73%) and slightly increased in grade II (41.18±7.38%) and slightly decreased grade III (40.20±3.25%). Hemoconcentration or an increase in the percentage of hematocrit is caused by deficient blood plasma and is related to blood viscosity. Hemoconcentration can occur suddenly after a decrease in the number of platelets. Hemoconcentration in dengue patients is associated with vascular leakage.[28] Based on the research, there was a significant relationship between hematocrit levels and the degree of severity of dengue, with a strong and directly proportional relationship strength. The results of this study are similar to research conducted by Ulhaq (2019) in Padang, Cahyani (2019) in Jakarta and Ayunani (2017) in Lampung, Ikrima (2017) in Aceh.[24,29–31] Hemoconcentration is a sensitive indicator of plasma leakage, it is necessary to carry out periodic hematocrit examinations. The hematocrit value will decrease if hemodilution occurs, due to a decrease in blood cellular levels or an increase in blood plasma levels.[32,33]

5. CONCLUSIONS

There is no relationship between the number of leukocytes and platelets with the severity of dengue. There is a relationship between hematocrit levels and the degree of severity of dengue with a strong relationship. This means that the higher the hematocrit level, the heavier the clinical degree of dengue.

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