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BLOOD SMEAR PROFILE OF PATIENTS WITH DENGUE HEMORRHAGIC FEVER IN BALI ROYAL HOSPITAL

PROFIL APUSAN DARAH TEPI PENDERITA DEMAM BERDARAH DENGUE DI BALI ROYAL HOSPITAL

I Made Dwi Mertha Adnyana *, Ni Luh Gede Sudaryati, A.A. Komang Suardana

Departemen of Biology, Faculty of Information Technology and Science, Hindu University of Indonesia Denpasar City-Indonesia.

A B S T R A C T

Background: Each year, dengue hemorrhagic fever has grown. Clinical hematological examinations and blood preparations are used to confirm the diagnosis. **Purpose:** To detect, assess and characterize dengue hemorrhagic fever blood smear at Bali Royal Hospital. **Method:** Cross-sectional descriptive observational study-was conducted in April at Bali Royal Hospital on 37 patients with dengue hemorrhagic fever, clinical hematological tests and the manufacture of blood preparations identified using inclusion and exclusion criteria. Platelet counts, hemoglobin levels, hematocrit values, leukocyte counts, clinic degrees, gender and age, and blue plasma lymphocytes, are all used in hematological analyzed by univariate, ANOVA and BNT tests to analyze data. **Result:** Patients with dengue hemorrhagic fever are mostly toddlers and children (35.13%), women (54.0%), and dengue fever degree I (64.86%) with positive blue plasma lymphocytes (51.36%). Platelet counts, hemoglobin levels, hematocrit values, and leukocyte counts are significantly changed on days 3, 6, and 9, with probability values ($p = 0.000$) less than $p = 0.01$. The findings of the BNT test indicate that the number of platelets and haemoglobin on various days is significantly different ($p<0.01$), but the hematocrit value and leukocyte calculation are not significantly different ($p>0.01$). **Conclusion:** Clinical hematological tests and blood preparations reveal a blood component anomaly in Dengue Haemorragic Fever (DHF) patients at Bali Royal Hospital on days 3, 6, and 9.

A B S T R A K

Latar belakang: Penyakit demam berdarah dengue setiap tahun mengalami peningkatan. Penegakan diagnosis dilakukan dengan pemeriksaan hematologi klinik dan pembuatan Sediaan Apusan Darah Tepi (SADT). **Tujuan:** Untuk mengidentifikasi, mengevaluasi dan menggambarkan apusan darah tepi penderita demam berdarah dengue (DBD) di Bali Royal Hospital. **Metode:** Jenis penelitian deskriptif observasional dengan rancangan *cross-sectional*. Penelitian dilakukan selama bulan April bertempat di Bali Royal Hospital dengan pemeriksaan hematologi klinik dan pembuatan sediaan apusan darah tepi pada penderita DBD sebanyak 37 orang, penetapan sampel menggunakan kriteria inklusi dan eksklusi. Analisis hematologi berdasarkan parameter jumlah trombosit, haemoglobin, nilai hematokrit, jumlah leukosit, derajat klinik, jenis kelamin, usia dan limfosit plasma biru. Analisis data menggunakan uji univariat dan ANOVA serta uji BNT. **Hasil:** Penderita DBD didominasi oleh balita dan anak–anak (35.13%), jenis kelamin dominan adalah perempuan (54.0%), derajat klinik dominan adalah DBD Derajat I (64.86%) dengan Limfosit Plasma Biru (LPB) Positif (51.36%). Pemeriksaan jumlah trombosit, kadar haemoglobin, nilai hematokrit dan hitung leukosit pada hari ke 3, 6 dan 9 berbeda sangat nyata dengan nilai probabilitas ($p=0.000$) yakni lebih kecil dari $p<0.01$. Hasil uji BNT jumlah trombosit dan haemoglobin pada hari berbeda terdapat berbeda sangat nyata ($p<0.01$) sedangkan nilai hematokrit dan hitung leukosit berbeda nyata ($p>0.01$). **Kesimpulan:** Terdapat abnormalitas komponen darah pada penderita DBD di Bali Royal Hospital pada hari ke 3, 6 dan 9 yang dilakukan melalui pemeriksaan hematologi klinik dan sediaan apusan darah tepi (SADT).

INTRODUCTION

Dengue Hemorrhagic Fever (DHF) is transmitted by *Aedes Aegypti* and *Aedes Albopictus* which bring the dengue virus into the human body through injection of probosis into the skin (Sudaryati et al., 2020). This virus is included in the genus flavivirus with family of flaviviridae (Khatroth, 2017). Dengue virus has four types of serotypes (DEN-1, DEN-2, DEN-3 and DEN-4) which lead to different clinical manifestations in each individual. Most of them are commonly found serotypes in the territory of Indonesia namely Serotype DEN-3 (Indriyani and Gustawan, 2020).

Dengue hemorrhagic fever is classified into four severity levels: I, II, III and IV (Ministry of Health of the Republic of Indonesia, 2019). Dengue hemorrhagic fever has been classified as an exceptional occurrence because to its fast spread, particularly during the rainy season, which results in a high incidence rate (IR), particularly in Indonesia (Suryani, 2018).

According to the Ministry of Health of the Republic of Indonesia (2019, 2018) the figure of the incidence rate (IR) dengue hemorrhagic fever in Indonesia per 100,000 population in 2015 was 50.75, in 2016 amounting to 78.85, 2017 amounted to 26.10 and 2018 of 24.73. In the last two years, the CFR figure has been decreased, namely in 2015 (0.83), 2016 (0.78), 2017 (0.72) and 2018 (0.70). However, there is an increase in cases, morbidity and mortality in several regions of Indonesia, one of which is Bali Province. The Province of Bali is designated as an extraordinary area of the dengue virus that has increased every year. Based on the Report of the Bali Provincial Health Office (2020) the prevalence of cases of dengue hemorrhagic fever reached 5.956 (2019) and 8.930 (2020) with the number morbidity of 137.3 (2019) and 153.3 (2020). Furthermore, Bali Province occupies the second position with the prevalence of the highest DHF in Indonesia (Sudaryati et al., 2020).

Dengue virus infection is a systemic illness with a wide variety of clinical manifestations. Clinically, dengue hemorrhagic fever is divided into three phases: febris, critical and rehabilitative (Ayuni et al., 2017). Management of DHF is generally carried out by clinical hematological examinations taken in the febrile phase (day 3-7). This examination aims to identify the abnormality of blood components in patients with dengue hemorrhagic fever such as platelets (MPC), hematocrit values (HCT), Haemoglobin (Hb), count leukocytes (WBC) and blue plasma lymphocytes (LPB) (Ali et al., 2021; Ayuni et al., 2017; Jayaprakash, 2020). Clinical hematology examinations are required to diagnose relative lymphocytosis in the blood and to identify blue plasma cells in dengue fever patients (Raditha et al., 2016). Clinical manifestations of dengue hemorrhagic fever include bleeding, hepatomegaly, circulatory failure, positive tornicet tests, eczemosis, epitaxis, gum bleeding and skin rashes (Alvinasyrah, 2021).

Clinical hematological tests are frequently used to compel medical staff to make a diagnosis. The inspection of the Blood Smear Peripheral is one of the exams performed. This examination is used to assess the proportion of relative present in the blood, to monitor for deficiency and to detect disruptions in the blood's cell activity (Arwie and Islawati, 2018; Satria et al., 2021).

Based on the findings of monitoring the process and the screening for dengue hemorrhagic fever in patients and or suspects in the dengue examination of clinical hematology and peripheral blood smear at Bali Royal Hospital. The purpose of this study is to detect, assess, and characterize dengue hemorrhagic fever (DHF) peripheral blood smear peripherals at Bali Royal Hospital. This research is critical because it will give scientific data on clinical hematological profiles associated with dengue hemorrhagic fever, particularly in Bali province.

MATERIAL AND METHOD

The type of this researchwas observational descriptive using a cross sectional design (Darwin et al., 2021). The research was conducted by performing clinical hematological examinations and peripheral blood smear preparation for Dengue Hemorrhagic Fever patients on the third, sixth and ninth days, which were then analyzed for platelets, haemoglobin, hematocrit values, leukocytes, clinic degrees, gender and age, as well as lymphocytes blue plasma. Those periods were determined by the management of DHF patients in the critical phase, who underwent a hematological standard examination 3-9 days after passing through the Febris phase in order to detect clinically significant hematological abnormalities in patients with dengue hemorrhagic fever.

This research was conducted at the Clinical Hematology Laboratory, Bali Royal Hospital in April 2021. The sample of this study was the patient with dengue hemorrhagic fever treated in Bali Royal Hospital as many as 37 people consisting of 17 men and 20 women. The inclusion criteria for determining respondents, namely experiencing Febris >3-7 days, were torniquet test (+), the results of the analysis of positive hematology dengue and there is a rash on the skin. While the criteria for exclusion namely Dengue (-), Dengue Suspop, Test Tourniquet (-) and Febris < 3 days.

Tools and materials used in this study were masks, haircups, handscone, tweezers, needle frany, blood lancet, sterile cotton, alcohol 70-90% glass cover, pipette drops, aquadest, glass objects, 3% giemsa, emersion oil, tools such as cameras to record the data.

The data obtained were further tabulated and analyzed using SPSS version 25.0 software. Clinic degrees, gender, age and blue plasma cells were examined using univariate tests, assessed descriptively and presented as frequency tables. While the value of hematocrit, platelets, haemoglobin and leukocytes were analyzed using the One-Way Anova test to find out the difference in value in each day (day X) and continued with the BNT test with probability value ($p<0.01$) (Darwin et al., 2021).

RESULT

Based on the results of observations conducted on DHF sufferers in Bali Royal Hospital, 37 respondents were obtained by respondents (n=37). The characteristics of people with dengue hemorrhagic fever based on age and gender are presented in Table 1.

Table 1. Demographic characteristics of dengue hemorrhagic fever patients by age and sex

No	Age	Sex	
		Female	**Male**
1	≤ 1 – 10	8 (21.6%)	5 (13.5%)
2	≥11 – 30	6 (16.2%)	7 (18.9%)
3	≥ 31 – 50	3 (8.10%)	4 (10.8%)
4	> 50	3 (8.10%)	1 (2.70%)
	Total (n=37)	20 (54.0%)	17 (46.0%)

Source: Research results, 2021

The characteristics of people with dengue hemorrhagic fever (DHF) in Bali Royal Hospital during April 2021 based on the age level obtained the dominant age of contracted by the dengue virus which is <1-30 years with 13 people each.

Based on the sexual characteristics obtained by data 20 people (54.0%) patients of dengue hemorrhagic fever (DHF) female and 17 people (46.0%) male sex. Data from the characteristics of dengue hemorrhagic fever (DHF) based on clinical degrees are presented in Table 2.

Table 2. Characteristics of Patients with Dengue Hemorrhagic Fever (DHF) based on clinical degrees

No	Age	Total Cases	
		People	**Percentange (%)**
1	DHF degree I	24	64.86
2	DHF degree II	9	24.32
3	DHF degree III	4	10.81
4	DHF degree IV	0	0
	Total	(n=37)	100%

Source: Research results, 2021

Data from the characteristics of dengue hemorrhagic fever in Bali Royal Hospital based on clinic degrees (Table 2) obtained the highest number of cases in DHF degrees I with 24 people (64.86%) and no dengue hemorrhagic fever (DHF) sufferers with degrees of clinic IV.

Data characteristics of people with dengue hemorrhagic fever (DHF) based on blue plasma lymphocytes are presented in Table 3.

Table 3. Characteristics of DHF patients based on blue plasma lymphocytes

No	Blue Plasma Lymphocytes Interpretation	Total Cases	
		People	**Percentange (%)**
1	Positive	19	51.36
2	Negative	18	48.64
	Total	(n=37)	100%

Source: Research results, 2021

Data from the characteristics of dengue hemorrhagic fever (DHF) in Bali Royal Hospital based on blue plasma lymphocytes (Table 3) obtained 19 people (51.36%) with positive cases and 18 people (48.64%) with negative cases.

Based on the results of the analysis of the characteristics of dengue hemorrhagic fever (DHF) in terms of value, platelets, haemoglobin, hematocrit and leukocytes analyzed using the one-way Anova test presented in Table 4.

Based on the results of the data normality test using Shapiro Wilk Test obtained probability value (p>0.01) as such, platelet value parameters, haemoglobin, hematocrit and leukocytes on day 3, 6 and 9 are normally distributed. The time period was chosen by the treatment of DHF patients in the critical phase, who underwent a hematological standard examination 3-9 days after passing through the Febris phase in order to detect clinically significant hematological abnormalities in patients with dengue hemorrhagic fever. The results of the homogeneity test using the Levene test obtained probability value (p>0.01) as such, data distribution in value parameters thrombocytes (p=0.043), haemoglobin (p=0.311), hematocrit (p=0.169) and leukocytes (p=0.100) are homogeneous. The one-way ANOVA test results obtained the value of the platelet value (12.009), the value of haemoglobin (26.510), hematocrit value (23.040), count leukocytes (11.052) with table in a row, the platelet value, haemoglobin and hematocrit (p=0.000) and leukocytes of (0.005). Thus, platelet value parameters, haemoglobin, hematocrit and leukocytes in each unit of treatment (Day 3, 6, 9) are very different with probability values (p<0.01). The results of the BNT test parameters of platelets, haemoglobin, hematocrit and leukocytes are presented in Table 5.

Based on the results of the smallest different tests obtained platelet value parameters in the day 6 compared to day 9 obtained probability value (p=0.122), haemoglobin value in day 6 compared to day 9 probability value (p= 0.055), hematocrit value at day 3 compared day 6 probability value (p=0.031) and the value of the leukocyte day 3 count compared to day 6 probability value (p=0.471) and day 6 compared to day 9 probability value (p=0.569). So, examination of platelets, haemoglobin, hematocrit and leukocyte count based on day 3, 6 and 9 are significantly different but not significant with probability (p> 0.01).

Table 4. Characteristics of DHF patients based on platelet value, haemoglobin, hematocrit and leukocytes

No	Parameter	Day	N	Mean ± S. E	Shapiro-Wilk	Levene test	ANOVA
1	Thrombocytes	Day 3	37	191.3 ± 18.92a	0.021	0.043	0.000**
		Day 6		272.1 ± 10.09b	0.039		
		Day 9		311.0 ± 14.48b	0.061		
2	Haemoglobin	Day 3	37	11.72 ± 0.274a	0.040	0.311	0.000**
		Day 6		13.22 ± 0.179b	0.123		
		Day 9		13.78 ± 0.146b	0.029		
3	Hematocrit	Day 3	37	32.73 ± 0.957a	0.023	0.169	0.000**
		Day 6		35.08 ± 0.593a	0.104		
		Day 9		39.89 ± 0.684a	0.199		
4	Leukocytes	Day 3	37	9.41 ± 0.577a	0.039	0.100	0.005**
		Day 6		10.42 ± 0.441a	0.804		
		Day 9		9.91 ± 0.287a	0.546		

Description: ** = Different very real (P <0.01); Different letters = There is a significant difference

Table 5. The result of the smallest real difference test on platelet value parameters, haemoglobin, hematocrit and leukocytes on 3rd day, 6 and 9

Parameter	Day	Day -3	Day -6	Day -9	Levene test	ANOVA
Trombosit	Day -3	-	0.004**	0.000**	0.043	0.000**
	Day -6		-	0.122*		
	Day -9			-		
Haemoglobin	Day -3	-	0.000**	0.000**	0.311	0.000**
	Day -6		-	0.055*		
	Day -9			-		
Hematokrit	Day -3	-	0.031*	0.000**	0.169	0.000**
	Day -6		-	0.000**		
	Day -9			-		
Leukosit	Day -3	-	0.015**	0.471*	0.100	0.005**
	Day -6		-	0.469*		
	Day -9			-		

Description = ** = Very different (p <0.01); * = Real difference (p> 0.01)

DISCUSSION

Patients with dengue hemorrhagic fever (DHF) generally experience abnormalities in blood components when clinical hematological examinations with venous blood taking and making a blood smear peripheral preparation (SADT). Abnormality of blood components is caused by infection due to pathogens and/or dengue viruses in the blood. In this study there were 37 people (n=37) which were declared positive as people with dengue hemorrhagic fever that had different clinical characteristics and manifestations (Khatroth, 2017; Sumampouw, 2020; Suryawanshi et al., 2017).

According to the research findings in Table 1, the age distribution is driven by the dengue virus being more prevalent in toddlers and children, but the incidence of dengue hemorrhagic fever is determined by women having a greater prevalence than males. This is consistent with studies done by Rajpoot (2020) who reveals the age distribution of dengue hemorrhagic fever is dominated by toddlers and children with a group of age ≤ 15 years with a percentage of 86-95%. Research conducted by Anwari et al (2020) dan Ayuni et al (2017) indicated a greater prevalence of DHF patients among toddlers and children than in adults. This is reinforced by the propensity of communities bordering children to engage in more physical activity indoors, resulting in higher contact with *Aedes Aegypti* mosquitoes than adults who engage in outside activities.

The proportion of sufferers of DHF disease with the age range of <15 years is vulnerable to contracting the

dengue virus this is caused by the immune response with the specificity and immunological memory stored in dendrit cells and the lymph gland has not been firm. In addition, the function of the macrophages and the formation of specific antibody of certain antigens is still weak, so the cytokine secretion by macrophages due to lack of dengue virus infection which causes a lack of production of interferon (IFN) which functions to inhibit viral replication and prevent the spread of infection to cells that have not been infected (Ali et al., 2021; Halstead, 2017; Raditha et al., 2016; Rena et al., 2019)

In terms of gender, the majority of patients who contracted DHF were female. This is consistent with Wowor's research (2017) which indicates that gender is a risk factor for contracting dengue virus with or without reflection. The proportion of women's opportunities to becoming infected is 3,34 times that of men. This scenario is governed by glycoprotein hormones, which regulate the formation of mononuclear phagocytic cells and granulocytes in response to infections in general, particular proteins called receptors have an effect on the hormone process. In women, the plasma membranes of gonad cells contain glycoprotein hormone receptors for Folicle Stimulating Hormone (FSH) and Luteinizing Hormone (LH). The hypothalamic-mediated stimulation of FSH and LH can be inhibited with gonad steroids, resulting in very low levels of the estrogen hormone child. Estrogen has an effect on the storage of fat in the body and low estrogen levels in girls cause leptin production by fat cells in the body to remain somewhat elevated (Sumampouw, 2020).

Leptin is a hormone protein that governs weight, so girls tend to have less body weight with low immunity will be susceptible to disease because it has low cellular immunity so that immunological immunological responses and immunological memory has not developed perfectly and the decline in immunity characterized by reduced helper T-cells is able to disrupt the phagocytosis and development of immunological memory which results in T-lymphocytes not able to produce cytokines and mediators as body defenses (Indriyani and Gustawan, 2020; Satria et al., 2021).

Based on the observation results and grouping of dengue hemorrhagic fever based on clinic degrees (Table 2) obtained the highest number of cases in DHF degrees I reached 64.86%. The research of Sakinah (2019) stated the degree of DHF I generally present with a high temperature of 38°C, along with additional symptoms such as nausea, vomiting, pain in the ulcer area of the heart, headache, muscle discomfort and a rash on the skin, but without spontaneous bleeding through the mucosa, epistaxis, or melena hematemesis.

The clinical manifestation of DHF degrees I occurs due to the reaction of the body which is reduced by the virus through blood circulation and is digested by macrophages. On the early two days there was a buildup of viral material in the blood (viremia) and ended after five days embossed symptoms of fever.

After being tested by the macrophage, the macrophage automatically became a presenting cell (APC) antigen and activated T-helper cells. Active T-helper cells will phagocyte more dengue viruses. Furthermore, helper cells can activate the cytotoxic cells that will lyse macrophages. T cells also activate the B cell to release antibodies. Eliminible inflammatory mediators cause systemic symptoms such as joint pain, fever, malaise, muscle pain and others. In dengue fever can occur bleeding because of the platelet aggregation that causes thrombocytopenia, but is still mild (Indriyani and Gustawan, 2020).

The results of the examination of blue plasma lymphocytes in patients with dengue hemorrhagic fever treated in Bali Royal Hospital (Table 3) obtained 51.36% of positive sufferers with blue plasma lymphocytes seen in clinical examinations with the blood smear peripheral dosage method (SADT). Blue plasma lymphocytes are mononuclear cells with fine and solid chromatin structures and relatively width and dark blue cytoplasms found since the day three fever (Raditha et al., 2016). Blue plasma lymphocytes are found in the Blood Smear Peripheral with an average of 8.3% in sufferers contracting DHF and will experience the peak of fever on day six and nine so that routine checks on the day are highly recommended for the accuracy in the management of DHF citizens. The increase in blue plasma lymphocytes in the blood of DHF patients is a response to the transformation of lymphocyte cells to stimulation of dengue virus antigens (Arruan et al., 2015; Ayuni et al., 2017).

Examination of blood components in the form of platelet counts, hematocrit hemoglobin levels, and the count of leukocytes is a crucial thing to uphold the diagnosis in patients with dengue hemorrhagic fever. The results of the statistical analysis of the number of platelets in dengue sufferers in Bali Royal Hospital, the probability value (p=0.000) is smaller than (p<0.01) which indicates the number of platelets in day 3, 6 and 9 different very real inter-day examinations. The results showed the day 3 platelet values with DHF patients tended to be lower than normal namely <150×103/µL with a 21-person frequency (56.77%). At Day 6 platelets tended to increase and had entered the normal value (150-440) with a frequency of 28 people (75.67%) while in the day 9 normal platelet frequencies reached 36 people (97.29%). This is influenced by the condition of DHF sufferers increasingly improving every day.

According to the management of dengue hemorrhagic fever in Indonesia stated the criteria for repatriating post-DHF patients examining platelet platelets >50,000/µL (Ayuni et al., 2017; Halstead, 2017). Thrombocytopenia plays a critical role in the etiology of DHF and in the pathophysiology of dengue infection. Thrombocytopenia is defined as a decrease in platelet count below 150.000/L. In dengue infection, thrombocytopenia arises as a result of bone marrow suppression, destruction and shortening

of the spococial spirit. Thrombocytopenia is caused by the creation of an antibody virus complex that induces platelet aggregation in DHF patients. The aggregate is eliminated when it goes through RES (Reticulo Endothelial System). Thrombocytopenia on DHF is also caused by increased platelet breakdown in peripheral circulation. Platelet aggregation results in factor III expenditure, which culminates in consumptive coagulopathy. Thrombocytopenia is typically discovered between days 3 and 9 as a result of the patient's pain and as an indication of plasma leaks in the blood (Adarsh et al., 2021; Alvinasyrah, 2021; Roganovic, 2020).

The results of the examination of haemoglobin levels in the blood in patients with dengue hemorrhagic fever (DHF) shows day 3, 6 and 9 there are very real differences in each day with a probability value (p=0.000) smaller than (p<0.01). The results showed the average haemoglobin sufferer of DHF at day 3 lower than the normal value of 11.72 gr/dl while in the day 6 haemoglobin value of 13.22 gr/dl and at day 9 of 13.78 gr/dl. The results of clinical hematology examinations found 6 people (16.21%) have hemoglobin levels above normal namely >16 gr/dl, this occurs due to the proinflammatory mediator's cross reaction (TNF-α) and anti-NS1 antibodies with protein on endothelical cell mucosa which results in cell apoptosis which then has an impact on plasma leakage and increased levels of haemoglobin (Jayaprakash, 2020).

Results Examination of Hematocrit Values in DHF patients in Bali Royal Hospital show there is a very real difference in hematocrit values in day 3, 6 and 9 with probability value (p=0.000) smaller than p<0.01. Hematocrit Value of DHF patients in day 3 obtained a series of 32.73%, in day 6 obtained a series of 35.08% and day 9 obtained at 39.89%. There were 7 people (18.91%) DHF sufferers experienced a surge in hematocrit values in day 6 and 9. Increasing hematocrit values interpreting hemoconcentration that occurred due to plasma leaks to extra vascular spaces accompanied by serous liquid effusion, through damaged capillaries. As a result of this leak, the plasma volume is reduced which can result in hypovolemic shock and circulation failure (Alvinasyrah, 2021; Rahayu et al., 2018). Increased hemoconcentration associated with a 20% increase in hematocrit values suggests an increase in capillary permeability and plasma receipt in the blood (Patel and Patel, 2020).

The results of the leukocyte count count on the blood of DHF patients showed that there was a very real difference in the value of leukocytes in day 3, 6 and 9 with a probability value (p=0.005) smaller than the p value <0.01. The results showed the average counting Leukost on Day 3 of 9.41×103/μl, day 6 of 10.42×103/μl and day 9 of 9.91×103/μL. There were 17 people (45.94%) in day 3, 12 people (32.43%) in day 6 and 8 people (21.62%) experienced the number of leukocytes below normal namely <3.6×103/μl which indicated that the DHF sufferer experienced leukopenia. In sufferers with dengue infections the number of leukocytes is generally normal or decreasing with the dominance of neutrophil cells. The occurrence of leukopenia in dengue infection is caused by the emphasis of bone marrow due to the process of viral infection directly or because of the indirect mechanism through the production of proinflammatory cytokines that suppress the bone marrow (Arruan et al., 2015; Satria et al., 2021).

The decline in leukocyte in DHF patients is caused by the weak immunological system in the blood. Decreasing leukocyte, netrophil and relative lymphocytosis occurs if DHF sufferers experience fever and leukopenia occur at day 3-5 after defervescence (Arwie and Islawati, 2018). The phagocytocyte process by leukocytes occur with the mechanime of the arrest of dengue virus by macrophages. Furthermore, infected macrophages will become active and release cytokines that have vasoactive or proxical properties including IL-1, IL-6, TNF Alpha and Platelet Activating Factor (PAF). The mediator material will affect the endothelial cells of blood vessel walls and hemostatic systems (Khatroth, 2017; Patel and Patel, 2020; Satria et al., 2021)

Macrophages process the dengue virus and scalp into APC (Presenting Cell antigen). The antigen attached to this macrophage will activate T-helper cells and attract other macrophages to phagocyte more viruses. T-helper will activate T-cytotoxic cells that will melisis macrophages that have phagocytes viruses (Arwie and Islawati, 2018; Buoro et al., 2016). A research conducted by Patel and Patel (2020) that Leukocytosis and neutrophilia occur and appear at the beginning of the development of dengue infection in the human body. Atypical and plasmasitoid lymphocytes in the blood smear peripheral preparation are the interpretation of lymphocytosis. This happens due to an increase in cellular immune responses to suppress and control cells that are infected with dengue viruses (Buoro et al., 2016; Meilanie, 2019; Patel et al., 2016; Retnowati et al., 2018; Roganovic, 2020).

CONCLUSION

Based on the results of the study there was a blood component abnormality in DHF patients in Bali Royal Hospital in Day 3, 6 and 9 which were carried out through clinical hematological examinations and blood-smear peripheral preparations (SADT). DHF patients are dominated by toddlers and children (35.13%), the dominant gender is a woman (54.0%), the dominant clinic degree is DHF degree I (64.86%) with positive blue plasma lymphocytes (LPB) (51.36%). Examination of platelet counts, Hemoglobin levels, hematocrit values and leukocyte count in day 3, 6 and 9 are very different with probability values (p=0.000) smaller than p<0.01.

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