Differences Platelet Indices In Hypoproliferative And Hyperdestructive Thrombocytopenia

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Abstract

Thrombocytopenia can increase the risk of bleeding. Determination of the type of thrombocytopenia is important because it will affect patient's treatment. The gold standard for distinguishing types of thrombocytopenia is bone marrow examination. This examination is invasive and carries risk of bleeding. Platelet indices are simple and less invasive and reliable in distinguishing the types of thrombocytopenia. The aim of this study is to evaluate the value of the platelet indices in differentiating types of thrombocytopenia.This study used retrospective cross sectional study. Subjects with leukemia, aplastic anemia, MDS for hypoproliferative thrombocytopenia (group 1), dengue fever, ITP, Evans syndrome, sepsis, pneumonia, and typhoid fever for hyperdestructive thrombocytopenia (group 2). Inclusion criteria were the subject's data with a platelet count <100,000 with data with name, age, sex, diagnosis and platelet count, PCT, MPV, PDW. Group 1 consisted of 103/150 (68.67%) subjects and group 2 47/150 31.33%) subjects. Platelet indices in group 1 vs group 2, MPV 10,02 □ 0,85 vs 11,72 □ 1,11 (p = 0,017); PDW 10,0 (7 – 15,70) vs 14,5 (10,40 – 19,40) (p <0,001) dan PCT 0,04 (0,01 – 0,19) vs 0.06 (0,01 – 0,10) (p = 0,208); Thrombocyte count 41 (11-97) vs 50 (8-90) (p = 0,380). MPV, PDW values were higher in hyperdestructive thrombocytopenia, because there was no thrombopoiesis abnormality in bone marrow to produce young platelets. PCT difference was not significant because platelet count was not significantly different and MPV was little significant. MPV and PDW values can differentiate types of thrombocytopenia.

Key words: Hyperdestructive, Hypoproliferative, Platelet indices, Thrombocytopenia

1. Main text

A state of thrombocytopenia may increase the risk of bleeding. The bleeding caused by thrombocytopenia usually will not occur until the total amount of platelet is less than 100.000/µL. The bleeding can be mild to severe and even can threaten life. According to ethio-pathology thrombocytopenia can be categorized into hypoproliperative and hyperdestructive type. The hyperdestructive type commonly caused by destruction of platelets extra medullar, the production of platelets are normal or increased in the marrow of the bone that can be found in Immune Thrombocitopenic Purpura (ITP) and infections. While, the

hypoproliperative type commonly is caused by a decrease in the production of platelets in the marrow of the bone and can be found in leukemia, Myelodisplasic Syndrome (MDS) and aplastic anemia. The determination of the thrombocytopenia type is very important; it is because it has an impact on the determination of which therapy the patient will get. 1,2,5

The examination of marrow bone until now is still being the gold standard to distinguish the type of thrombocytopenia hypoproliperative or hyperdestructive. However, this procedure is invasive and it has a risk of bleeding in patients with thrombocytopenia. There is a procedure that is simpler and less invasive and it can be relied upon to distinguish the type of thrombocytopenia, the procedure is checking the platelets index. The platelets indexes that can be used are Plateletcrit (PCT), Mean Platelet Volume (MPV) and Platelet Distribution Width (PDW). The parameter of PCT, MPV, and PDW is available in hematological examination at Dr. Hasan Sadikin Central Public Hospital (RSHS) Bandung, as the top referral hospital in West Java.1,3-5 The purpose of this research is to evaluate the value of the platelets indexes as a differentiator of thrombocytopenia hypoproliperative and hyperdestructive type..

Methods

The method in this study is a retrospective descriptive method with *cross sectional* form. This research is using the data subjects with a diagnosis of acute leukemia, aplastic anemia, *myelodisplastic syndrome* (MDS), *Immune Thrombocitopenic Purpura* (ITP), dengue fever, *Evans Syndrome,* sepsis, pneumonia, typhoid fever, pregnancies period in the period of August 1, 2018 to the July 31, 2019 at the central laboratory in RSHS Bandung. The criteria of inclusion in this research is the first data subject with the platelets <100.000 with the details data such as names, ages, gender, and the result of the examination of the total amount in plateletss PCT, MPV, PDW with the diagnosis of the latest laboratory examination in that period. Operational limitations on thrombocytopenia hypoproliperative are patients diagnosed with leukemia, MDS, and Aplastic anemia. Meanwhile, the operational limitations on thrombocytopenia hyperdestructive are patients diagnosed with ITP, dengue fever, Evans Syndrome, sepsis, pneumonia and typhoid fever. The exclusion criteria for this research are the subjects with primary diagnosis and comorbid diagnosis mixed up with the operational limitations for thrombocytopenia hypoproliperative and hyperdestructive type.[4,6]

The hematology examination is using the Sysmex XN-1000 tool, with the method of impedance and flow cytometry. The minimum samples that can be used in this research is determined by using a formula to test two proportions. In this study, the 95% confidence level was chosen. After the examination, the result showed at least 31 subjects patients for each group, so that this study requires 62 samples. The calculation of platelets index in thrombocytopenia hypoproliperative group and hyperdestructive group statistically tested by *unpaired t test,* when the data is distributed normally, and non-parametric test (test Mann-Whitney U) is used

when the data is not distributed normally. The results are considered significant by statistics when the p value < 0.05.

Results and Discussion

During the period of August 1, 2018 to July 31, 2019 found that there are 150 subjects that fulfill the inclusion criteria, 103 (68,7%) of hypoproliperative group and 47 (31,3%) for hyperdestructive group. The test for normality is using *Kolmogorov-Smirnov* method, and it shows the data of platelets index, PCT and PDW of whole subjects. The test for normality is using *Kolmogorov-Smirnov* and it shows the total amount of plateletss, PCT, and PDW from the whole subjects of abnormal distribution ($p<0,05$), while the MPV data from the whole subjects of normal distribution ($p>0,05$). The characteristics data subjects in this study is shown in Table 1.

Table 1. Patient Characteristics Data

Patient Characteristics	Hypoproliferative n (%)	Hyperdestructive n (%)	P value
Age :			
0 - <18 years	2 3 (22.3 %)	12 (25 , 5 %)	0.670
≥ 18 years	80 (77.7 %)	35 (7 4.5 %)	
Type Gender :			
Man	5 2 (50.5 %)	25 (5 3 , 2 %)	0, 760
Woman	51 (49.5 %)	2 2 (46.8 %)	
Diagnosis (%)			
Leukemia	62 (60.2 %)		
Aplastic anemia	25 (24.3 %)		
MDS	16 (15.5 %)		
ITP		19 (40.4 %)	
Dengue infection		13 (27 , 7 %)	
Evans syndrome		7 (14.9 %)	
Pneumonia		5 (10, 6)	
Sepsis		2 (4.3 %)	
Typhoid fever		1 (2 , 1 %)	

Information : MDS = Myelodysplastic syndromes, ITP = Immune thrombocytopenic purpura ,

From the Table 1, it can be seen that there is no significant difference in the gender and age of the subjects. The most common disease with thrombocytopenia hypoproliperative type in RSHS is leukemia and ITP for hyper destructive type. From the table, it can be concluded that there is no significance difference between thrombocytopenia hypoproliperative and hyperdestructive type based on age and gender of the subjects. The result of the plateletss index in thrombocytopenia hypoproliperative and hyperdestructive type can be seen in the Table 2 below.

Table 2. Platelet Index Test Results on Thrombocytopenia Type Hipoproliferatif and Hiperdestruktif

Platelet Index	Hypoproliferative	Hyperdestruction	P value
Platelet count (x10 3 / µL), Median (Range)	41 (11 - 97)	50 (8 - 90)	0, 3 8 0
PCT (fl), Median (Range)	0.04 (0.01 - 0.19)	0.06 (0.01 - 0.10)	0.20 8
MPV (fl), Mean ± SD	10.02 ± 0 , 85	11.7 2 ± 1.1 1	0.017
PDW (%), Median (Range)	10.0 (7 - 15.70)	14.5 (10.40 - 19.40)	<0 , 001

From the Table 2, it can be seen that the total platelets and PCT value was higher in hyperdestructive group compared to hypoproliperative group, however, it is not statistically significant. Meanwhile, the MPV value and PDW value in hyperdestructive group was higher and statistically significant difference compared to the hypoproliperative group.

Platelets play an important role in hemostasis system. The total platelets with less than 150.000/µL is called thrombocytopenia. Thrombocytopenia is caused by the destruction of platelets in the peripheral blood flow (hyperdestructive type) or inadequate rate production (hypoproliperative). Index of platelets is a parameter that is obtained through the measurement of blood platelets and using PCT, PDW, MPV examination.[5,6,7]

In the study, the result found that the male subjects had almost equal state of thrombocytopenia with the female subjects. Based on the age, the adult subjects (≥18 years) is more than the infant and children subjects (0 - <18 years) with no significant difference.

In this study, the number of subjects with thrombocytopenia hypoproliperative type (68,7%) more than the hyperdestructive (31,3%). The most common diseases found in the thrombocytopenia hypoproliperative is leukemia, meanwhile for the hyperdestructive type is ITP.

This research obtained that there is no significant difference from PCT value to distinguish thrombocytopenia hypoproliperative and hyperdestructive. It is in accordance with the research conducted by Parveen, he stated that the PCT value cannot distinguish the type of thrombocytopenia. The PCT value reflects the percentage of the platelets in the blood. The result of PCT can be obtained through the PCT formula = total platelets x MPV / 10. 000. Therefore, in a low platelets amount (thrombocytopenia) a low PCT value will be obtained. [4,6,8]

In this study, the average value of MPV on hypoproliperative including the normal category (10,02 $\pm$ 0,85) while, the MPV value on hyperdestructive type including the increase category (11,72 $\pm$ 1,11) with the p value 0,017, therefore, it can be concluded that MPV values were significantly higher in the hyperdestructive group than in the hypoproliperative group. This result is similar with some of the literature that stated the MPV is a test that can be relied to distinguish the type of thrombocytopenia. In the thrombocytopenia hyperdestructive type, the total platelets were decrease due to excessive destruction on peripheral blood flow. When the number of platelets decreased megakaryocytes in the marrow of the bone will be stimulated by thrombopoietin, thus causing hyperlobulacy in the megakaryocyte nucleus. Stimulation on megakaryocytes will lead to an increase on the rate of production of bigger size of platelets. MPV is a parameter to measure the volume or size of platelets, so that, the MPV value can be a marker of the

production rate and platelets activation. IN the other hand, the low MPV value in thrombocytopenia is indicated to hypoplasia or aplasia marrow bone. [7,9-12]

This study had found the median value of PDW on hypoproliperative categorized normal (10,0 (7 – 15,70) while, the PDW value in hyperdestructive categorized increase (14,5 (10,40 – 19,40) with the p value < 0,001, so that it can be concluded that the PDW value was significantly higher in the hyperdestructive group than in the hypoproliperative group. It is in accordance with the research that conducted by Shah et al and Borkataky et al, they concluded that the value of PDW is higher in thrombocytopenia hyperdestructive group than the hypopro liperative group. PDW parameter reflects the variability of platelet size in blood circulation, so that the PDW value will increase in the condition of platelet anisocytosis. Platelet anisocytosis increases with the production of young platelets that are larger in size than older platelets. Thus, in the hyperdestructive group where there is an increase in the number of young platelets, the PDW value will increase.[3,7,10,13]

In the thrombocytopenia type happened disruption of platelets in the marrow of the bone that may be caused by a decrease in the number of functions of the progenitor cell. It can cause disruption of megakaryocytepoiesis such as in a state of aplastic anemia, or inveteracy cell leukemia in marrow bone in the state of leukemia or an increase in apoptosis megakaryocyte and interference maturation and proliferation of megakaryocyte as in MDS. The circumstances that would cause the young platelets have bigger size or less formed so the anisositosis platelets would not be formed and the platelets is dominated by mature platelets which have smaller size. So that, in the thrombocytopenia hypoproliperative type obtained lower PDW and MPV results than the hyperdestructive type.[6,10,12]

The research has several limitations that the number of subjects who are in thrombocytopenia hyperdestructive type only determined based on the primary diagnosis without the confirmation of the examination of the marrow of the bone.

Conclusion and Suggestion

This study suggested that the value of MPV and PDW is a perimeter that can be used to distinguish the type of thrombocytopenia hypoproliperative and hyperdestructive type. Further studies with confirmation of examination marrow of the bone are needed to ascertain the cause of the thrombocytopenia state.

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