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ANALYSIS OF MEAN PLATELET VOLUME, PLATELET DISTRIBUTION WIDTH, AND PLATELET COUNT IN HEMORRHAGIC AND NON-HEMORRHAGIC STROKE

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ABSTRACT

Stroke is a sudden and acute focal or global cerebral functional disorder lasting more than 24 hours due to cerebral blood flow impairment. Platelets play an essential role in the pathophysiology of non-hemorrhagic stroke by causing thrombus formation in blood vessels after erosion or rupture of atherosclerotic plaques. Mean platelet volume, PDW and platelet counts are hematological parameters that can be measured on routine blood tests that can describe platelet function and activity and are standard tests carried out in hospitals. The aim of this study was to analyze the differences in MPV, PDW and platelet count between non-hemorrhagic strokes and hemorrhagic strokes. This was a retrospective cross-sectional study conducted in the Dr. Wahidin Sudirohusodo General Hospital of Makassar. A total of 375 Non-Hemorrhagic Stroke (NHS) and 221 Hemorrhagic Stroke(HS) patients were included in this study. Mean platelet volume, PDW and platelet counts were obtained from complete blood count at the time of admission. There was a significant difference in platelet count between NHS and HS patients (p=0.01). Never the less, there were no significant differences between MPV and PDW between NHS and HS patients (p=0.19 and p=0.54, respectively). The results of this study indicated that there were significant differences in platelet counts in HS and NHS with increased platelet counts being a risk factor for NHS and a decrease in platelet counts as a risk factor for HS. However, there were no significant differences in the values of MPV and PDW in NHS and HS patients. It is recommended to study using a better sample selection method so that it can eliminate the occurrence of bias with other diseases which can also cause a decrease and increase in MPV values, PDW and platelet counts.

Key words: Mean platelet volume, platelet distribution width, platelet count, stroke

INTRODUCTION

According to the World Health Organization,a stroke is a sudden and acute functional focal and global brain disorder that lasts more than 24 hours due to a disruption of brain blood flow. Injuries that can occur in the brain and cause strokes are narrowing of blood vessels, blockage of blood vessels, as well as blockage or narrowing or rupture of blood vessels, so that the blood supply decreases. Stroke occupies the third position of the top ten causes of death after coronary heart and cancer in Indonesia.[1,2]

Stroke, moreover, can be divided into hemorrhagic stroke and non-hemorrhagic stroke. Eighty percent of stroke cases are non-hemorrhagic strokes, while 20% of cases are hemorrhagic ones. Non-hemorrhagic stroke causes a disruption of the supply of oxygen and nutrients to brain cells due to thrombus formation or embolism. Meanwhile, intracerebral and subarachnoid a hemorrhagic strokes are caused by cranial blood vessel rupture.[3,4]

Platelets have a significant role in maintaining blood vessel integrity during hemostasis process. The efficiency of circulating hemostatic cells depends on several vasoactive factors and prothrombotic agents, including thromboxane A2 and serotonin secreted from platelets. Thus, large platelets contain more granules,as well as produce and release more stimulators. Platelet volume, furthermore, is associated with shorter bleeding times, while Mean Platelet Volume (MPV) is considered as a determinant of platelet activities.[5-7]

The mean platelet volume not only can be used to assess changes in both stimulation level and platelet function level but can also be very useful in a variety of clinical conditions. In vascular disorders, the severity and extent of the disease are related to stimulation of platelet production, and MPV has a broader clinical application to detect and monitor this disorder. Therefore, a high-mean platelet volume not only can be associated with more platelet reactivity and aggregationbut can also be considered as an essential factor in hemostasis.[7-10,13]

Besides MPV, other main parameters that can detect platelet function and activity are Platelet Distribution Width (PDW) and platelet count. If platelet size is related to the function and activity of platelets, PDW is used to determine variations in platelet size. Next, platelet activation can cause changes in platelet count and morphology.[5,8-10]

Hence, platelet parameters, mean platelet volume, PDW, and platelet count, can be used to detect platelet function. The platelet parameters can be measured on routine blood tests which are standard examinations carried out in hospitals.[5,7-11] Based on the description of MPV, PDW and platelet count in the pathogenesis of stroke above, this research aimed to analyze differences in MPV values, PDW, and platelet counts between non-hemorrhagic and hemorrhagic strokes.

METHODS

This research was a retrospective observational study using data of inpatients with stroke diagnosis at the Medical Record Installation of the Dr. Wahidin Sudirohusodo General Hospital in Makassar from January 2016 to December 2016. Inclusion criteria in this research were non-hemorrhagic stroke and hemorrhagic stroke patients who not only had been diagnosed by clinicians to undergo routine hematology with an onset of more than 24 hours but also had laboratory data for MPV values, PDW, and platelet counts. Hence, patients with incomplete medical record data, patients with disorders of thrombosis and coagulation system, patients with head injury, patients having surgery, patients using immunosuppressant, patients with hematological abnormalities, and patients with malignancies were excluded from this research. Mean platelet volume values, PDW, and platelet counts in this research were obtained from routine blood tests performed using Sysmex XN-1000 and ABX Pentra 80 hematology analyzer devices.

Subsequently, the normality of the data was tested using the Kolmogorov-Smirnov test. Based on the results of the Kolmogorov-Smirnov test, it was known that the data were not normally distributed. Thus, the data were presented in median form (the highest and lowest values). Afterwards, differences in MPV values, PDW, and platelet counts between NHS and HS patients were analyzed using the Mann-Whitney test. In this stage, the data were analyzed using a computer program with a significant p-valueof <0.05.

RESULTS AND DISCUSSION

The total number of stroke patients obtained in this research was 596, collected from 375 non-hemorrhagic stroke patients and 221 hemorrhagic stroke patients.

Based on Table 1, it was known that the number of male stroke patients was higher than the female ones. Besides, the age range of stroke patients in this research was 27-91 years old. It was also known that the stroke patients in this research were mostly from the age group of 61-70 years old as many as 163 patients (27.3%). These findings were in line with research conducted by Fusun *et al.* in Turkey reporting that stroke mostly attacked males as many as 313 (53%) with the highest number of incidence found in the age group of over 60 years old.[7]

Moreover, based on the results of the Mann-Whitney test on MPV values in hemorrhagic stroke and non-hemorrhagic stroke, there was no significant difference between HS and NHS patients (p=0.19) (Table 2). Similarly, research conducted by Tohgil *et al*. reported that a decrease in MPV value due to cerebral thrombosis illustrated many large

Table 1. Characteristics of samples of patients with hemorrhagic and non-hemorrhagic stroke

Characteristics		HS n (%)	NHS n (%)	Total n (%)
Sex	Male	133 (22.3)	209 (35.1)	342 (57.4)
	Female	88 (14,8)	166 (27.9)	254 (42.6)
Age (years)	21 - 30	2 (0.3)	2 (0.3)	4 (0.7)
	31 - 40	16 (2.7)	11 (1.8)	27 (4.5)
	41 - 50	54 (9.1)	62 (10.4)	116 (19.5)
	51 - 60	66 (11.1)	95 (15.9)	161 (27.0)
	61 - 70	49 (8.2)	114 (19.1)	163 (27.3)
	71 - 80	25 (4.2)	69 (11.6)	94 (15.8)
	81 - 90	9 (1.5)	18 (3)	27 (4.5)
	91 - 100	0 (0)	4 (0.7)	4 (0.7)
Total		221 (37.1)	375 (62.9)	

Note: HS, Hemorrhagic Stroke; NHS, Non-Hemorrhagic Stroke

and active platelet losses. Large platelets containing more adenosine, made aggregation easier than small platelets.[11]

Furthermore, based on the results of the Mann-Whitney test, there was no significant difference in PDW values between HS and NHS patients (p=0.54) (Table 3). This finding could be because this research used data from medical records. As a result, sampling time and routine blood test time could not be observed. Research conducted by Vagdatli *et al*. argued that PDW values decreased in the first, second, third and fourth hours which were calculated from the time of sampling due to reduced formation of platelet pseudopodia. However, according to Waseem *et al.*, there was no significant difference in PDW values between patients with the first-stroke attack and patients with more than one stroke attack. Unfortunately, there is still no literature investigating PDW as an indicator of the risk of developing symptomatic carotid artery stenosis.[5,12,13]

Also, based on the results of the Mann-Whitney test on platelet counts, it was known that there were significant differences between HS and NHS patients with a p-value of 0.01 (see Table 4). According to Du *et al*., an increase in platelet count is a risk for NHS, while a decrease in platelet counts can increase the risk for HS. Increased platelet counts then can trigger thrombus formation, which is a risk factor for NHS. Conversely, a decrease in platelet counts can result in a reduction of coagulation function and can also cause HS. This result indicates that the fragility of capillaries and thrombocytopenia at the same time can lead to cerebral hemorrhage even though the mechanism is clearly unknown. Platelet counts, consequently, are good predictors for predicting HS that can cause death within 24 hours after a stroke attack. Meanwhile, a significant decrease in platelet count can indicate NHS patients with a poor prognosis, leading to death.[9]

Next, Mann-Whitney posthoc test was performed to determine differences in platelet values between NHS patients and HS as illustrated in Figure 1.

The primary cause of stroke is atherosclerotic lesions. Platelets are nucleated cells which have an essential role in the pathogenesis of atherothrombosis. Platelets can cause thrombus formation and also play a role in the inflammatory process. Platelets after activation are larger than normal size. Larger platelets will be more active in metabolic and enzymatic processes. Platelets will more quickly bind to collagen, produce more thromboxane A2, and express more glycoprotein Ib as well as IIb/IIIa receptors. Large platelets also contain more granules and cause platelet aggregation with faster adenosine diphosphate, but less sensitive to the inhibitory effects of prostacyclin aggregation.[5]

Mean platelet volume, Platelet distribution width, and platelet counts are parameters that can be used to evaluate the function of platelets. An increase in MPV is known to increase the risk of NHS significantly. As an essential marker of indicators that describe platelet function and activity, MPV is also known to have a relationship with platelet activity. Some previous researches have already evaluated the role of MPV in HS, but the relationship between changes in MPV and HS values is still controversial.

Table 2. Analysis of differences in MPV values of hemorrhagic and non-hemorrhagic stroke

	HS Median (Min-Max)	NHS Median (Min-Max)	p-value*
MPV	7.9 (6.0- 12.3)	8.4 (4.6- 12.7)	0.19

Note: HS: Hemorrhagic Stroke; NHS: Non-Hemorrhagic Stroke; p *: Mann-Whitney test

Table 3. Analysis of differences in PDW values ofhemorrhagic and non-hemorrhagic stroke

	HS Median (Min-Max)	NHS Median (Min-Max)	p-value*
PDW	11.8 (6.6- 28.0)	11.8 (4.8- 26.3)	0.54

Note: HS: Hemorrhagic Stroke; NHS: Non-Hemorrhagic Stroke; p *: Mann Whitney test

Table 4. Analysis of differences in platelet values of hemorrhagic and non-hemorrhagic stroke

	HS Median (Min-Max)	NHS Median (Min-Max)	p-value*
Platelets	261 (10- 1556)	240 (56- 839)	0.01

Note: HS: Hemorrhagic Stroke; NHS: Non-Hemorrhagic Stroke; p *: Mann Whitney test

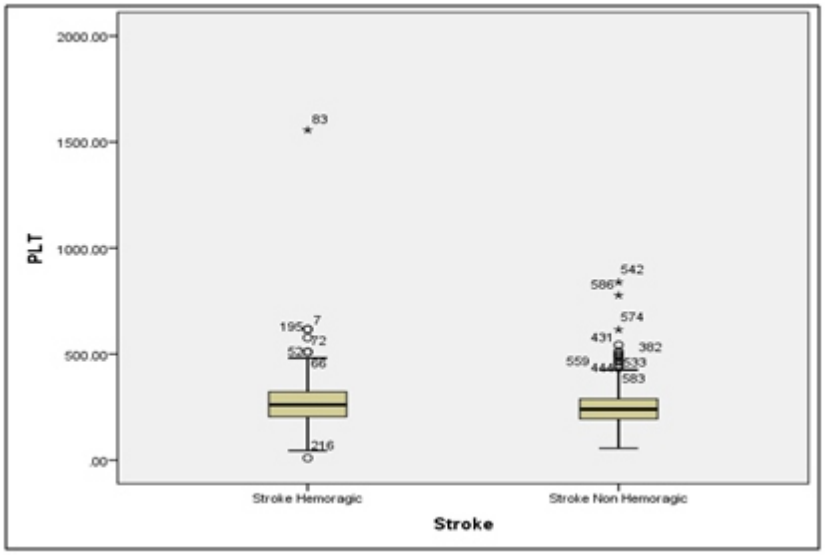

Figure 1. Post hoc Mann-Whitney test on platelets in NHS and HS

The association between MPV and HS risk is still not clear. Never the less, research carried out by Du *et al.* stated that a decrease in MPV value could reduce the risk of HS, while an increase in MPV value could increase the risk of HS. It means that patients with decreased MPV values may have a higher risk of bleeding than patients with increased MPV values. As a result, MPV can be used to evaluate the possibility of bleeding, and can also become a parameter to assess bone marrow hematopoietic function.[9]

Platelet distribution width can indicate variations in platelet size. Increased PDW can be an indicator of prothrombotic conditions. Variations in platelet size cause high PDW values. The causes of platelet morphological changes in the form of pseudopodia and spherical transformation causing platelet size to vary can be considered as a result of progressive platelet activation.[5] However, this research still has limited data, and it is difficult to avoid bias in medical record data.

CONCLUSION AND SUGGESTIONS

Finally, it can be concluded that there are significant differences in platelet counts in HS and NHS. Increased platelet counts are known to be a risk factor for NHS, while a decrease in platelet counts can be considered as a risk factor for HS. Besides, it is also known that there is no significant difference in the values of MPV and PDW in NHS and HS patients. Never the less, it is still recommended for further research to use a better sample selection method so that it can eliminate bias with other diseases which can also cause a decrease and increase in MPV values, PDW and platelet counts.

REFERENCES

1. Setyopranoto I. Stroke: Gejala dan penatalaksanaan. Available at www.kalbemed.com/portals/6/1_05_185strokegejalapenatalaksanaan. Accessed on October 14th, 2016.
2. Brainin M, Heiss WD. Textbook of stroke medicine. New York, Cambridge University Press, 2010; 1-3.
3. Tanujaya TH, Indranila, Rahayu M. Hubungan antara PDW (Platelet Distribution Width) dengan TAT (Tes Agregasi Trombosit) pada penderita stroke iskemik di RSUP Dr. Kariadi Semarang. Available at https://ejournal.unpatti.ac.id/ppr_paperinfo_lnk.php?id=586. Accessed on October 24th, 2016.
4. Oz IB, Yucel M, Bilici M, Serifoglu I, Sayin R, *et al.* Is mean platelet volume a reliable marker to predict ischemic stroke in the follow-up of patients with carotid stenosis?. Available at www.ncbi.nlm.nih.gov/pubmed/26576699. Accessed on October 8th, 2016.
5. Koklu E, Yuksel IO, Arslan S, Cagrid G, Gencer ES, *et al.* Predictor of symptom development in intermediate carotid artery stenosis: Mean platelet volume and platelet distribution width. Available at www.ang.sagepub.com. Accessed on September 25th, 2016.
6. Gideon CS, Ibioku E, Achor OU, Prisca AC. Changes in hematological parameters in stroke patients in Port Harcourt, Nigeria. Available at https://www.ijsr.net/archive/v5i3/NOV161970.pdf. Accessed on June 29th, 2016.
7. Domac FM, Misirli H, Yilmaz M. Prognostic role mean platelet volume and platelet count in ischemic and hemorrhagic stroke. Available at www.ncbi.nlm.nih.gov/pubmed/20123229. Accessed on June 29th, 2016.
8. Chen Y, Xiao Y, Lin Z, Xiao X, He C, *et al.* The role of circulating platelets microparticles and platelet parameters in acute ischemic stroke patients.

Available at www.ncbi.nlm.nih.gov/pubmed/26169549. Accessed on September 16th, 2016.
9. Du J, Wang Q, He B, Liu P, Chen JY, *et al.* Association of mean platelet volume and platelet count with the development and prognosis of ischemic and hemorrhagic stroke. Available atwww.ncbi.nlm.nih.gov/pubmed/26992440. Accessed on October 11th, 2016.
10. Tamer D, Fevzi Y, Deniz AE, Cemil K, Fatih B, *et al*. The value of serum mean platelet volume in ischemic stroke patient. Available at www.jpma.org.pk/full_article_text.php?article_id=5512. Accessed on October 11th, 2016.
11. Tohgi H, Hajime S, Tamura K, Kimura B. Platelet volume, aggregation, and adenosine triphosphate release in cerebral thrombosis. Available at http://stroke.ahajournals.org. Accessed on September 31st, 2017.
12. Vagdalti E, Gounari E, Lazaridou E, Katsibourlia E, Tsikopoulou F, Labrianou I. Platelet distribution width: A simple, practical and specific marker of activation of coagulation. Available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2843567. Accessed on 18th, October 2016
13. Al-Tameemi WF, Ameen AMM. Significance of platelet indices in patients with acute ischemic stroke. Available at http://www.colmed-nahrain.edu.iq/. Accessed on August 23rd, 2017.