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THE DIFFERENCE OF MEAN PLATELET VOLUME AND PLATELET COUNT IN CORONARY HEART DISEASE PATIENTS WITH ACUTE CORONARY SYNDROME AND NON ACUTE CORONARY SYNDROME

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ABSTRACT

Background: CHD is currently one of main causes and the first death in developed and developing countries, including Indonesia. CHD appeared with the clinical appearance of asymptomatic, Stable Angina Pectoris until ACS. ACS is a progressively CHD and takes parameters that describe the process pathogenesis. Mean Platelet Volume and platelet count are two parameters in Complete Blood Count which reflect the activity of platelets in CHD. **Objective:** This study is to investigate the differences Mean Platelet Volume and Platelet Count in CHD with ACS compared to non-ACS. **Methods:** A cross-sectional study was conducted with collecting data from the medical records of patients with CHD who underwent treatment in the dr. Kariadi General Hospital Medical Center Semarang, the period of January-December 2019. Eighty subjects of 20 non-ACS patients and 60 ACS patients were included in this study which is Mean Platelet Volume and Platelet Count in hematology laboratory were analyzed. The Independent t-test were used for comparing the group means. **Results:** MPV was found to be higher significantly among ACS patients as compared to non ACS, 9,43 ± 0,3868 fl vs 10,23 ± 0,785 fl (p-value<0.01) while Platelet Count was lower significantly among ACS patients as compared to non ACS, 282,63 ± 75,084 10^9/L vs 322,30 ± 41,980 10^9/L. **Conclusion:** There were significantly differences in Mean Platelet Volume and Platelet count between patients with ACS and non-ACS.

Keywords: Acute Coronary Syndrome, Coronary Heart Disease, Mean Platelet Volume, Platelet Count, Stable Angina Pectoris

INTRODUCTION

Coronary Heart Disease (CHD) is one of the leading causes of death in both developed and developing countries, including Indonesia nowadays, including Indonesia. It is estimated that approximately 13 million people died as a result of it in 2010. Because of the high number of deaths, it made CHD become the leading cause of death in developing countries.[1]

Reported from the World Health Organization (WHO), in 2015, more than 17 million people died of heart and blood vessel disease. Accounting for about 31% of all deaths worldwide, which most of it, about 8,7 million of deaths is caused by CHD. According to the results of the Baseline Health Research 2018, 1,5 percent of Indonesians, or 15 out of 1000, suffer from CHD. Refers to the Sample Registration System survey 2014, CHD is the leading cause of death in Indonesia, accounting for 12,9% of all deaths.[2]

CHD can manifest itself in a number of ways, including asymptomatic, stable angina pectoris, acute coronary syndrome, and even sudden cardiac death.[3] 3 All situations in the coronary artery disease spectrum, other than an acute coronary syndrome, are classified as stable angina pectoris. Acute coronary syndrome must be avoided by proper diagnosis and risk stratification in patients with stable coronary artery disease. Acute Coronary Syndrome (ACS) is one of the clinical manifestations of CHD, which is the most common and deadly of all cardiovascular diseases.[4]

The primary cause of CHD is atherosclerosis. Atherosclerosis is a chronic inflammatory mechanism in which inflammation plays a key role at any stage of the disease, from plaque formation to plaque rupture, which can lead to thrombosis.[5]

Platelet activation and aggregation have long been considered in the pathophysiology of coronary heart disease because platelets play a key role in thrombus formation following plaque rupture in the coronary.[6] Variables The average size and amount of platelets in the blood are measured by Mean Platelet Volume (MPV) and Platelet Counts (PC). As a result, MPV and PC may reflect platelet activation.

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To the best of the author's knowledge, no data or analysis has been conducted at Dr. Kariadi Central Hospital in Semarang to investigate the discrepancies in MPV and PC between CHD with ACS and non-Acute Coronary Syndrome patients (non-ACS). In light of the above, the aim of this study is to see the differences in MPV and PC between Coronary Heart Disease patients with ACS and non-ACS patients with CHD.

METHODOLOGY

The aim of this study is to see if there were any differences in MPV and PC in CHD patients with ACS versus non-ACS patients in Indonesia, specifically in Semarang, Central Java. From January to December 2019, the data were gathered from the medical history of CHD patients at the Dr. Kariadi General Hospital Medical Center in Semarang. This study was a cross-sectional analysis with an analytical observational approach. The CHD patients which treated at the Dr. Kariadi General Hospital Medical Center were the subjects of this research. The subjects were separated into two groups; ACS and non-ACS.

The Health Research Ethics Committee of Diponegoro University's Medical Faculty provided ethical approval (No. 84/EC/KEPK/FK-UNDIP/V/2020). The study subjects' identities were kept private and were not revealed. All the research expenses were borne by the researcher. All the data in this research were secondary data which the data were obtained from the medical record patients. Exclusion criteria for this subject include severe infection, hematology disorder, hepatic impairment, renal impairment, oral contraception, malignancy disorders, and pregnancy complications.

The collected data was entered in the Microsoft Excel sheet and analyzed using the Social Sciences Statistical Package software (SPSS). Quantitative data were summarized in the form of Mean and Standard Deviation (SD) and the differences were analyzed using the Independent Sample t-Test. To see the distribution of data, Shapiro-Wilk and Kolgomorov-Smirnov tests were used to see if the data was normal. The differences between groups were investigated using a parametric Independent Sample T-test on data with ratio scales that were normally distributed. The results of the Independent Sample T-Test would have shown major differences if $p<0.05$

RESULT

In this study, the sampling technique was carried out by consecutive sampling and a total of 80 CHD patients were assigned as study subjects. Eighty subjects comprising of 60 ACS and 20 non-ACS patients were included in the present study. Demographic characteristics of CHD patients are shown in Table 1. As described in Table 1, the mean age of subjects is 57 years with a range of 36 to 87 yrs. The male to female ratio is 1,75 : 1 with 51 males and 29 females.

Table 1. The Characteristic of Research Subjects

Sex	**Num**
Males (n)	51
Females (n)	29
Mean Age (years)	57,30 ± 11.06
Hematology Lab	**Mean**
Hb (g/dl)	13,56 ± 1,58
Ht %	40,28 ± 4,30
Erythrocyte (10^6 / ul)	4,59 ± 0.60
MCH (pg)	29,65 ± 2,04
MCV (fl)	88,36 ± 4,48
MCHC (g/dl)	33,64 ± 1,07
Leukocyte (10^3/ul)	9,91 ± 3,72
Platelets (10^3/ul)	292,55 ± 70,24
RDW (%)	13,06 ± 0,98
MPV (fl)	10,03 ± 0,78
Coronary Heart Disease	**Num**
Non ACS (n)	20
ACS (n)	60
UAP (n)	20
AMI (n)	40

As shown in Table 2, MPV was found to be higher among ACS patients as compared to non ACS patients which is statistically significant (10,23 ± 0,79 vs 9,43 ± 0,39 fl , p-value <0.001. PC was found to be lower among ACS patients as compared to non ACS patients which is statistically significant (282,63 ± 75,08 vs 322,30 ± 41,98 x 10^9/L), p-value<0.01.

As shown in Table 3, there were statistically significant differences MPV and PC among the 3 groups ($p<0.001$ and $p <0,05$).

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Table 2. Differences MPV and PC in ACS and Non-ACS

Variabel	Non- ACS	ACS	*p**
MPV (fl)	9,43 ± 0,39	10,23 ± 0,79	0,000
PC (10^9/L)	322,30 ± 41,98	282,63 ± 75,08	0,001

*Independent Sample T-Test

Table 3. Differences MPV and PC in ACS sub-groups and Non-ACS

Variabel	Non-ACS (A)	UAP (B)	AMI (C)	*p*
MPV (fl)	(9,43 ± 0,39)	(10,06 ± 0,73)	(10,32 ± 0,80)	*0,000
PC (10^9/L)	(322,30 ± 41,98)	(304,90 ± 78,06)	(271,50 ± 11,38)	**0,038

*One-way ANOVA + Post-Hoc Games Howell
A:B < **0,01**, B:C = **NS**, A:C < **0,01**
**Kruskall Wallis + Post-Hoc Mann Whitney
A:B = **NS**, B:C = **NS**, A:C < **0,01**

DISCUSSION

In our study, MPV was significantly higher in ACS patients than non-ACS. Our results are similar to Khandekar et al., who also showed higher MPV in ACS patients than stable CAD.[7] Pal et al. and Ahamed et. al. also found higher MPV in ACS patients.[8,9]

Our study reveals that Platelet Counts was significantly lower in ACS patients than non-ACS. Our results are synergic with Ranjith et al. and Majumder, et al.[10,11]

Increased MPV and decreased PC have a relationship in the process pathogenesis of ACS. Evidenced by the results of this study, indicates the presence of a negative correlation exists between MPV and PC. It is caused by platelets play an important role in the pathogenesis of ACS. Increased platelet aggregation has occurred proven leads on the formation and propagation of intracoronary thrombus, larger and hyperactive platelets can accelerate the appearance of the features clinical called as acute coronary syndrome.[8,12] The function of platelets is very associated with the process of atherogenesis and athethrombosis in pathogenesis of ACS. Greater platelets are more reactive because of the concentration of active substances is high in micro granules (for example thromboxane A2 and B2, factor platelet-4, *P-selectin*, growth factor-derived platelets) and expression of the GP IIb/IIIa receptor.[8]

These finding the mechanism to explain MPV enhancement in ACS. Therefore in ACS, platelet count decreased suggest that activated platelets are common occurrence during the pathogenesis of ACS where increase in the rate of consumption of platelets at the site of rupture of the plaque.

This study is also comparing MPV and platelet counts between non-ACS and subgroup-ACS, namely Unstable Angina Pectoris (UAP) and Acute Myocardial Infarction (AMI). This study proved significant differences in the value of MPV and platelet count among the three groups with $p < 0.05$

In our study, MPV was significantly higher in UAP patients than non-ACS. Our results are similar to L. Pizzuli et al., who also showed higher MPV in UAP patients than non-ACS.[13] Cengiz Demir, et. al also found higher MPV in UAP patients.[14]

Our study reveals that Platelet Counts was lower in UAP patients than non-ACS but non-significantly. Our results are synergic with Mercan et. al.[14]

Activation of platelets play a major role in the cascade of complex events derived from ruptured plaque atherosclerosis and resulting in thrombus formation. Activation of platelets at the site of the lesion coronary atherosclerosis may contribute to the formation of platelet coronary artery in unstable angina so that it increases the level of consumption of platelets. UAP is a clinical entity bridging the gap between the Stable Angina Pectoris and AMI.[15]

Increased the rate of platelets consumption at the site of rupture of atherosclerotic plaque leads to release the large platelets of the bone marrow. The process of injury of the monolayer cells in vascular endothelium is considered as the events underlying the initiation and progression of coronary atherosclerosis. The contact between platelets and collagen fibers of the subendothelial produces adhesion and reversible aggregation of platelets to collagen, but it can be irreversed if the stimulus pro-aggregation is strong enough. Platelets aggregation

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irreversibly release a variety of active proteins, i.e. adenosine diphosphate (ADP), serotonin, and thromboxane A2. As well as platelets 3, which activates the intrinsic pathway of coagulation. And also growth factors derived from platelets, which stimulate the proliferation of smooth muscle cells and vascular fibroblasts.

Aggregation of platelets to each other resulting in the formation of thrombus primary mechanically still unstable. In some patients, it can lead to intermittent or temporary vessel occlusion and ischemia by platelets labile; in others the formation of platelets may be progressive and lead to occlusion partial/total with myocardial infarction manifestations. Because the formation of platelets in the APTS in homeostatic will be more reactive.[16]

In our study, MPV was significantly higher in AMI patients than non-ACS . Our results are similar to that of Pizzuli et al., who also showed higher MPV in AMI patients than non-ACS.[13] Ding, et. al and Khode et.al also found higher MPV in AMI patients.[12,17]

Our study reveals that Platelet Counts was significantly lower in AMI than non-ACS. Our results are synergic with Khandekar et. al, Mercan et. al, and Ding, et. al.[7,12,14]

Increased MPV and decreased PC on AMI reflects the platelets activation level and is considered as a marker of important AMI. Furthermore, it can be used in the prediction of risk, diagnosis, and assessment of prognosis of AMI. Increased MPV is likely correlated with the inflammatory response intensity in the body during the process of pathogenesis AMI.[12] Another theory also shows it is caused by the consumption of platelets during an attack of acute myocardial to stimulate the proliferation of megakayocytes. Evidenced based on the interaction between thrombopoietin and its receptors on the platelets surface will reduce the thrombopoietin, resulting in low production of platelets. Higher MPV will have a lot of receptors to induce feedback inhibition resulted lower platelet count.[18]

In our study, MPV was non-significantly higher in AMI than UAP. Our results are similar to Khandekar et al. and Mercan et al., who also showed non-significantly higher MPV in AMI patients than non-ACS.[7,14]

Our study reveals that Platelet Counts was non-significantly lower in AMI patients than UAP. Our results are synergic with Khandekar et. al, Mercan et. al, and Syahrir et. al.[7,14,19]

Highest MPV was found in the myocardial infarction group. According to previous research, MPV is a strong indicator for assessing the incidence of endothelial injury in ACS patients. MPV is also contribute to prothrombotic status in ACS incidents and large platelets even play a specific role in infarction incidents.[20]

Platelet activation generally occurs before an acute coronary event. The increased use of platelets at the site of atherosclerotic plaques, can cause the bone marrow release the large platelets to the edge of lesion. High MPV, on the other side, have higher thrombotic potential due to higher density, faster aggregation, higher levels of thromboxane-A2, and greater expression of glycoprotein Ib and IIb / IIIa receptors.[21]

Therefore, if atherosclerotic plaques experienced a fissure, rupture or ulceration, both local and systemic, it can trigger a thrombogenesis, platelet activation, aggregation, and platelet secretion, and the platelets formation on the location ruptured, and it cause a total occlusion of the coronary arteries. Platelets will also produce disruption of coronary blood flow, and it cause an imbalance between oxygen supply and demand. Conditions of severe and persistent imbalance of oxygen supply and demand can lead to myocardial infarction.[22]

As a result, higher MPV in AMI group of ACS, may be caused by atherosclerotic plaques triggered platelet activation. This condition will make the bone marrow secrete the immature platelets to the peripherals with a larger size than the mature ones.

CONCLUSION

From this study, we conclude there were significantly differences MPV and PC between CHD patients with ACS and non-ACS.

However, this study has some limitations. The limitation in this research is the research design which is considered weak in showing the differences between the variables of the ACS sub-group. This research used a cross-sectional design, due to time constraints during the Covid-19 pandemic. Another limitation is the incomplete medical record that

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available at Dr. Kariadi Semarang is one of the reasons. Also lack adequate journal about the differences between NSTEMI / STEMI and CHD Non-ACS if we want to research the AMI sub-groups with non-ACS.

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