INDONESIAN JOURNAL OF
CLINICAL PATHOLOGY AND MEDICAL LABORATORY
Majalah Patologi Klinik Indonesia dan Laboratorium Medik

PAGE 46
2021 Nov; 28(1): 46-50
p-ISSN 0854-4263 e-ISSN 2477-4685
Available at www.indonesianjournalofclinicalpathology.org

Prognostic Value of Platelet-Lymphocyte Ratio and High-Density Lipoprotein in Patients with Acute Myocardial Infarct

Lestari[1], Sulina Yanti Wibawa[1,2], Amaliyah Tahir Lopa[1,3], Darmawaty Rauf[1,4]

[1] Department of Clinical Pathology, Faculty of Medicine, Hasanuddin University/Dr. Wahidin Sudirohusodo, Makassar, Indonesia. E-mail: alexanataniamarbun@gmail.com
[2] Pathology Clinic Installation, Stella Maris Hospital, Makassar, Indonesia
[3] Pathology Clinic Installation, dr. Tadjuddin Chalid Hospital, Makassar, Indonesia
[4] Pathology Clinic Installation, Faisal Islamic Hospital, Makassar, Indonesia

ABSTRACT

Acute Myocardial Infarct (AMI) is the main reason for mortality. Platelet to Lymphocyte Ratio (PLR) describes thrombocyte aggregation and inflammation that is linked to cardiovascular disease. High-Density Lipoprotein (HDL) is anti-atherogenic. This study aims to analyze the prognostic value of PLR and HDL in patients with AMI. This study was a retrospective observational study by obtaining laboratory results from complete blood count and lipid profiles from inpatients with AMI (STEMI and NSTEMI) medical records during Mei 2019–August 2020. Receiver Operating Characteristics (ROC) analysis was done to get the PLR and HDL cut-off. Prognostic value evaluation was based on sensitivity, specificity, positive and negative predictive value, and accuracy. Results obtained were from 302 subjects with a mean age of 58.4+9.6 years old, with most male patients (74.5%). Receiver operating characteristics curve analysis showed an 0.514 Area Under Curve (AUC) for PLR with p=0.685. High-density lipoprotein ROC was 0.573 with a p=0.033 (p< 0.05), with HDL cut-off = 50.0; sensitivity 72.7%, specificity 32.3%, positive predictive value 63.3%, negative predictive value 42.0% and 57.3% accuracy. Platelet to lymphocyte ratio mean was lower in the HDL <50 group (187.9) compared to the HDL > 50 (210.8), (p=0.009). High-density lipoprotein can be concluded as a potential prognostic factor of acute myocardial infarct. The lower the HDL, the greater the risk for a poor prognosis. A big-scale prospective study should be held to clarify and confirm these findings.

Keywords: High-density lipoprotein, platelet to lymphocyte ratio, NSTEMI, STEMI

INTRODUCTION

Acute Myocardial Infarct (AMI) is one of the world's leading causes of mortality and morbidity.[1] Mortality rate of AMI is around 10%-20% for the first six months since diagnosis, and half of all deaths happen in the first 30 days.[2] Acute myocardial infarct is also the leading cause of death in Indonesia. World Health Organization (WHO) reported that AMI caused 139,400 deaths in the Indonesian population during 2012.[3] Acute myocardial infarcts can be divided into two categories, Non-ST-Segment Elevation MI (NSTEMI) and ST-Segment Elevation MI (STEMI).[2]

Inflammation plays a vital role in initiating and propagating the complex atherosclerotic process that is the start of AMI.[4] Platelet to Lymphocyte Ratio (PLR) is a prognostic marker that describes the aggregation and inflammation pathway and is claimed to be more useful in predicting the atherosclerotic coronary burden. A higher PLR is identified as a significant independent predictor of the livelihood survival rate in patients with AMI. The PLR is also used to predict cardiovascular events that are harmful (AMI or relapse, the progressivity of heart failure, and mortality).[5]

High-Density Lipoprotein (HDL) is one of the main components of human lipoprotein classes, with its anti-atherogenic state giving protection to the heart. High-density lipoprotein prevents the oxidative modification of the arterial wall by Low-Density Lipoprotein (LDL). In addition, HDL also induces antithrombotic activity by preventing platelet aggregation.[6] Further research about the relationship of biomarker levels in patients with AMI is needed. This research aimed to analyze PLR and HDL that have prognostic value in patients with AMI, STEMI, or NSTEMI.

METHODS

This was a retrospective observational study using data from the medical records. This study obtained patients with an AMI diagnosis medical

record through the May 2019-August 2020 period at the Medial Records Installation of Dr. Wahidin Sudirohusodo Hospital, Makassar. The inclusion criteria were AMI patients diagnosed by clinicians that had complete blood count and lipid profile laboratory results. In addition, patients who had coronary intervention/coronary artery bypass and a history of heart failure were excluded from this study.

Complete blood count was done with a venous blood sample collected in a tube containing Dipotassium Ethylene Diamine Tetra Acetic Acid (K2EDTA) anticoagulant and measured using the Sysmex XN-1000 analyzer. The PLR was calculated by dividing the platelet count by the lymphocytes. High-density lipoprotein cholesterol was measured by collecting venous blood in a Serum Separating Tube (SST) and running it in the BioMajesty JCA-BM6010/C.

Statistical analysis used were descriptive statistics, frequency distribution statistics, independent T-test, and Mann-Whitney test. The cut-off of PLR and HDL were obtained by a Receiver Operating Characteristics (ROC) analysis. Prognostic value evaluation was based on sensitivity, specificity, positive and negative predictive value, and accuracy. Results were significant if $p < 0.05$. The Ethical Study Committee of the Medical Faculty of Hasanuddin University/Dr. Wahidin Sudhirohusodo Hospital gave authorization for this study with article no. 432/UN4.6.5.31/PP36/2020.

RESULTS AND DISCUSSIONS

There were 302 samples that fulfilled the inclusion criteria, with 187 patients with NSTEMI and 117 patients with STEMI from the inpatients of a referral hospital.

The age of the subjects was 38–87 years old (mean of 58.4±9.6 years old), the highest frequencies were in the 50–59 years old group (41.4%), and most of them were male (74.5%) (Table 1).

There were more patients with NSTEMI compared to STEMI, and 61.9% of subjects with NSTEMI had a higher PLR mean (195.7) compared to those with STEMI (192.8), but statistical tests showed that the difference was insignificant ($p > 0.05$). This fact showed that this study did not find a significant relationship between PLR and AMI. High-density lipoprotein concentration was lower in NSTEMI (mean of 42.8 mg/dL) compared to those with STEMI (mean 46.5 mg/dL). This study found a statistically significant relationship between HDL and AMI ($p < 0.05$) (Table 2).

Table 1. Characteristic distribution of study sample

Variable		n	%
Gender			
	Male	225	74.5
	Female	77	25.5
	Total	302	100.0
Age			
	<50 y.o.	51	16.9
	50-59 y.o.	125	41.4
	60-69 y.o.	77	25.5
	>=70 y.o.	49	16.2
	Min-max	38	87
	Mean±SD	58.4 ± 9.6	
AMI diagnosis			
	NSTEMI	187	61.9
	STEMI	115	38.1
	Total	302	100.0

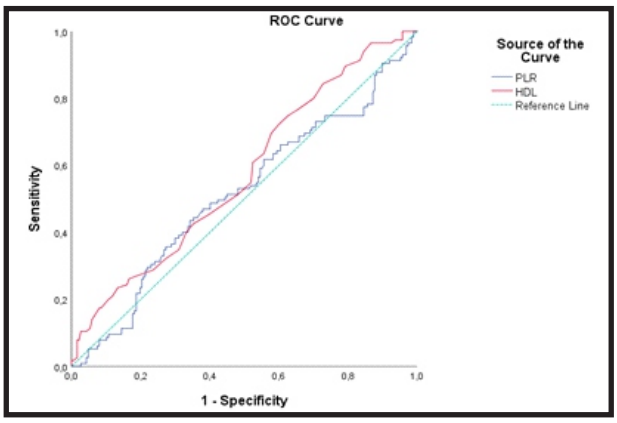

Figure 1. PLR and HDL ROC graph

Table 2. Comparison of PLR and HDL in NSTEMI and STEMI patients

Variable	AMI	n	SD	p
PLR	NSTEMI	187	107.3	0.685
	STEMI	115	90.1	
	Total	302	101.0	
HDL (mg/dL)	NSTEMI	187	11.0	0.006
	STEMI	115	11.7	
	Total	302	11.4	

The ROC analysis had an area under the curve (AUR) of 0.514 with p=0.685 (not significant) for PLR (Figure 1). This result showed that PLR could not be a prognostic marker for AMI, causing the inability to calculate the cut-off for PLR. The Area Under Curve (AUC) for HDL was 0.573 with p=0.033 (significant if p < 0.05). These results show that HDL concentration can be a prognostic marker for AMI. The cut-off for HDL was 50.0 mg/dL that gave the most optimal sensitivity and specificity, with a sensitivity of 72.7% and specificity of 2.2%, the positive predictive value of 63.3%, the negative predictive value of 42.0%, and accuracy of 57.3%. These results give an impression that HDL dysfunction has clinical significance for cardiovascular disease prognosis.

Acute myocardial infarct was higher in the group with HDL < 50 mg/dL (214 patients) compared to the group with HDL < 50 mg/dL (88 patients). Most patients with HDL < 50 mg/dL were diagnosed with NSTEMI (136 patients) (Table 3).

Platelet to lymphocyte ratio was lower in the group with HDL < 50 mg/dL (187.9) compared to the group with HDL >50 mg/dL (210.8). Statistic results show a significant difference with p < 0.05. It can be interpreted that there is a significant relationship between PLR and HDL (Table 4).

There has been proof that has confirmed the potential of several components in circulating as an effective marker of the atherosclerotic process, such as subtypes of white blood cells (neutrophils, lymphocytes, eosinophils, and monocytes), thrombocytes, and lipid profile.[2,7] Platelet to lymphocyte ratio calculated by the number of platelets and lymphocytes has been deemed an efficient biomarker of inflammation that is both cheap and easy to calculate. The PLR is a hematological parameter for inflammatory status associated with poor prognosis in heart disease patients. Previous studies reported a correlation between PLR and coronary artery narrowing in coronary heart disease patients.[8] Other literature have confirmed the potential of PLR as an inflammation marker that is significantly and independently related to the severity and prognosis of patients with AMI.[9]

Unfortunately, this study showed that PLR does not have a significant prognostic value towards AMI. It might be due to the multifactorial mechanism of the relationship of PLR and poor prognosis in AMI. First of all, the number of thrombocytes is an outcome and a factor that causes the inflammatory response. Megakaryocytes can be stimulated by inflammation mediators and cause rapid proliferation and platelet production.[10] Response towards stress during ischemia of myocardial infarct is the release of cortisol and catecholamines, redistribution of lymphocytes to lymphatic organs, and apoptosis, all causing lymphopenia. Other factors that can affect this condition are high physiologic stress levels causing high cortisol and catecholamine levels, causing a decrease in the number of lymphocytes.[11]

Previous studies state that NSTEMI patients with lower HDL levels are linked to higher mortality risk during hospital admission.[12] This is related to the dysfunction of an HDL subfraction, causing a decrease in the pro-oxidative effect and an increase in the proinflammation effect. Li *et al*. also states that HDL is an important parameter to predict the risk, prognosis, and clinical outcome of AMI.[13]

The crucial role of HDL in AMI is its ability to induce Reverse Cholesterol Transport (RCT). The decrease of HDL in the efflux capacity of cholesterol is linked to cardiovascular disease, including AMI. High-density lipoprotein has several benefits to protect the cardiovascular system, such as an antioxidant, anti-inflammation, vasodilator, antithrombotic, immunomodulator, and endothelial

Table 3. Distribution of AMI patients according to HDL category

Cut-off HDL (mg/dL)	AMI		Total
	NSTEMI	STEMI	
< 50	136	78	214
≥ 50	51	37	88
Total	187	115	302

Table 4. Mean Difference of PLR based on HDL cut-off

Cut-off HDL (mg/dL)	n	Mean	SD	P
< 50	214	187.9	101.8	0.009
≥ 50	88	210.8	97.6	

repair and recruiting endothelial progenitor cells.[14]

The HDL cut-off alone can affect clinical studies' results. A cut-off value is ideally calculated with a ROC analysis, but confounding factors (eating habits, nutritional and socio-economy factors, and cardiovascular risks) remain.[15] Even though there are studies that use a lower HDL cut-off of 40 mg/dL, they still showed that lower HDL concentrations are an independent risk predictor in cardiovascular disease. The cut-off of this study is not consistent with previous studies due to several differences. First of all, race, lifestyle, life habits, and environment can contribute to these differences. For example, the Caucasian race has a higher metabolic syndrome incidence linked to lipid metabolism. Second, genetic factors, especially genes involved in lipid metabolisms, such as Peroxisome Proliferators Activated Receptors (PPAR) and Apolipoprotein A-V (APOA5) genetic polymorphism, must be kept in mind.[16]

National guidelines in several countries showed a variation in cut-offs. Indonesian Heart Association 2017 guidelines targeted a cut-off of HDL > 40 mg/dL for male and HDL > 50 mg/dL for female patients to lower cardiovascular risks; while the American Heart Association (AHA)/American College of Cardiology (ACC) 2019 guidelines stated that low HDL levels were defined as < 40 mg/dL for male patients and < 50 mg/dL in female patients.[17,18] These cut-offs were the limit for low-risk dyslipidemia, while a cut-off of 50 mg/dL in this study was linked directly to the prognosis of AMI.

CONCLUSIONS AND SUGGESTIONS

This study concludes that HDL is a prognostic factor in acute myocardial infarct with an HCL cut-off of 50.0 mg/dL. The lower the HDL concentrations, the higher the risk for a bad prognosis in that patient. This study did not have a significant prognostic value in PLR as a potential inflammation marker in identifying high-risk AMI patients. Complete blood count and lipid profile laboratory examinations are feasible methods and can identify high-risk AMI patients. A large-scale prospective study is needed to clarify and confirm these findings.

REFERENCES

1. Putranto A, Suparyatmo J, Ariningrum D. Serum copeptin as the predictor for acute heart failure complication of acute myocardial infarction in patients with ST-segment elevation. Indones J Clin Pathol Med Lab, 2020; 26(3): 362-8.
2. Adam AM, Rizvi AH, Haq A, Naseem R, Rehan A, Shaikh AT, *et al*. Prognostic value of blood count parameters in patients with acute coronary syndrome. Indian Heart J, 2018; 70(2): 233-40.
3. Luke K, Purwanto B, Herawati L, Al-farabi MJ. Predictive value of hematologic indices in the diagnosis of acute coronary syndrome. Clin Sci, 2019; 7(15): 2428-33.
4. de Almeida AJPO, de Almeida Rezende MS, Dantas SH, de Lima Silva S, de Oliveira JCPL, *et al*. Unveiling the role of inflammation and oxidative stress on age-related cardiovascular diseases. Oxid Med Cell Longev, 2020; 2020: 1-20.
5. Karakurt A, Yildiz C. Predictive values of inflammatory cell ratios for complexity of coronary artery disease in patients with acute coronary syndrome. Int J Cardiovasc Acad, 2018; 4: 70-6.
6. Tanaka S, Couret D, Tran-Dinh A, Duranteau J, Montravers P, *et al*. High-density lipoproteins during sepsis: From bench to bedside. Crit Care, 2020; 24(1): 134.
7. Lassale C, Curtis A, Abete I, van der Schouw YT, Verschuren WMM, *et al*. Elements of the complete blood count associated with cardiovascular disease incidence: Findings from the EPIC-NL cohort study. Sci Rep, 2018; 8(1): 3290.
8. Marziah E, Aman AK, Ketaren AP. Correlation between platelet to lymphocyte ratio and coronary artery narrowing. Indones J Clin Pathol Med Lab, 2018; 24(3): 219-22.
9. Li X, Fang H, Li D, Xu F, Yang B, *et al*. Association of platelet-to-lymphocyte ratio with in-hospital major adverse cardiovascular events and the severity of coronary artery disease assessed by the Gensini score in patients with acute myocardial infarction. Chin Med J (Engl), 2020; 0(4): 3-9.
10. Shawky A, Radwan H. The prognostic value of Platelet-lymphocyte Ratio (PLR) in patients with Non-ST Segment Elevation Myocardial Infarction (NSTEMI). Cardiol Vasc Res, 2018; 2(2): 1-5.
11. Bolatkale M, Acara AC. A novel index for prompt prediction of severity in patients with unstable angina pectoris. Emerg Med Int, 2020; (7651610): 1-7.
12. Sia C, Zheng H, Ho AF, Bulluck H, Chong J, *et al*. The lipid paradox is present in ST-elevation but not in non-ST- elevation myocardial infarction patients: Insights from the Singapore Myocardial Infarction Registry. Sci Rep, 2020; 1-13.
13. Li Z, Huang J, Li N. predictive and prognostic value of high-density lipoprotein cholesterol in young male patients with acute myocardial infarction. Chin Med J (Engl), 2017; 130(1): 77-82.
14. Ben-Aicha S, Badimon L, Vilahur G. Advances in HDL: Much more than lipid transporters. Int J Mol Sci, 2020; 21(732): 1-18.
15. Wakabayashi I, Daimon T. Comparison of discrimination for cardio-metabolic risk by different cut-off values of the ratio of triglycerides to HDL cholesterol. Lipids Health Dis, 2019; 18(156): 1-10.
16. Bougarne N, Weyers B, Desmet SJ, Deckers J, Ray DW,

et al. Molecular actions of PPAR? in lipid metabolism and inflammation. Endocr Rev, 2018; 39(5): 760-802.
17. Erwinanto, Santoso A, Putranto JNE, Tedjasukmana P, Sukmawan R, *et al*. Panduan tatalaksana dislipidemia 2017. Jakarta, Perhimpunan Dokter Spesialis Kardiovaskular Indonesia (PERKI), 2017; 15-16.
18. Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, *et al*. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: Executive summary association task force on clinical practice guidelines. Circulation, 2019; 140: 563-95.