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

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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.2 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).4

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.5 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
Sudirohusodo 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>
<thead>
<tr>
<th>Table 1. Characteristic distribution of study sample</th>
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<tr>
<td>Variable</td>
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<td>Gender</td>
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<td>Male</td>
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<td>Female</td>
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<td>Total</td>
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<td>Age</td>
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<td>&lt;50 y.o.</td>
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<td>50-59 y.o.</td>
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<td>&gt;=70 y.o.</td>
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<td>Min-max</td>
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<td>Mean±SD</td>
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<td>AMI diagnosis</td>
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<td>NSTEMI</td>
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<td>STEMI</td>
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<td>Total</td>
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![Figure 1. PLR and HDL ROC graph](image)

![Source of the Curve](image)

**Figure 1.** PLR and HDL ROC graph

<table>
<thead>
<tr>
<th>Table 2. Comparison of PLR and HDL in NSTEMI and STEMI patients</th>
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<td>Variable</td>
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<td>PLR</td>
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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 22.2%, 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. 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. 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.

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. 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.

Previous studies state that NSTEMI patients with lower HDL levels are linked to higher mortality risk during hospital admission. 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.

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 function.

| Table 3. Distribution of AMI patients according to HDL category |
|---------------------------------|----------------|----------------|----------------|
| **Cut-off HDL (mg/dL)**        | AMI            |                |                |
|                                | NSTEMI         | STEMI          | Total          |
| < 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. 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-economic factors, and cardiovascular risks) remain. 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.

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. 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

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