

Analysis of NLR, HDL, and Hs-Troponin I as A Diagnostic Marker in STEMI and NSTEMI Patients

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ABSTRACT

The limitations of health facilities in diagnosing AMI, especially in remote areas require an easy and inexpensive examination such as Neutrophil Lymphocyte Ratio (NLR) and High-Density Lipoprotein (HDL), which have a positive correlation with hs-Troponin I. The purpose of this study was to analyze the value of NLR, HDL, and hs-Troponin I as diagnostic markers in STEMI and NSTEMI patients. This retrospective study used medical record data for 152 STEMI patients and 93 NSTEMI patients from January to December 2020 at Dr. Wahidin Sudirohusodo. The NLR value was based on the results of routine blood tests using Sysmex XN-10, the results of HDL examinations using the Bio Majesty JCA-BM9010/c instrument, and the results of the hs-Troponin I examination using the Vidas instrument. Statistical tests using the Mann-Whitney test, the diagnostic value of NLR, and hs-Troponin I was analyzed by ROC to obtain the cut-off. The test result is significant if $p < 0.05$. The sample consisted of 152 samples of STEMI patients and 93 NSTEMI patients. The NLR value in STEMI patients was significantly different from NSTEMI patients ($p < 0.001$), HDL levels were not significantly different in STEMI and NSTEMI patients ($p = 0.475$), while hs-Troponin I levels were significantly higher in STEMI patients than NSTEMI ($p < 0.001$). The ROC curve showed the sensitivity and specificity of NLR, namely 64% and 70% at the cut-off of 4.32, and the sensitivity and specificity of hs-Troponin I was 78% and 60% at the cut-off of 910.5 ng/L. The NLR and hs-Troponin I values were increased in STEMI patients compared to NSTEMI due to the increased inflammatory response and the higher risk of damage to the myocardium. The coordinates of the NLR ROC curve show a cut-off of 4.32 and hs-Troponin I 910.5 ng/L provides optimal sensitivity and specificity. The conclusion of this study is NLR and hs-Troponin I can be used as diagnostic markers in STEMI and NSTEMI patients with a cut-off value of NLR 4.32 and hs-Troponin I 910.5 ng/L.

Keywords: STEMI, NSTEMI, NLR, HDL, hs-Troponin I, diagnostic

INTRODUCTION

Acute Coronary Syndrome (ACS) is a group of symptoms described as an acute ischemic myocardial condition. Chest pain is the main symptom encountered and is used as the basis for initial diagnostic and therapeutic but is further classified based on electrocardiographic (ECG) examination. There are two classifications of ACS patients based on ECG namely myocardial infarct with an elevation of ST-segment (STEMI) and myocardial infarct without elevation of ST-segment (NSTEMI).^{1,2}

In STEMI, there is a total blockage in the coronary artery that causes a wide infarct to the myocardium that is marked by an elevation in the wave of the ST or Q-segment that is associated with early death. While in NSTEMI, the blockage is not complete and does not involve the entire myocardium, so there is no ST-segment elevation.³

World Health Organization (WHO) states that ACS is one of the causes of global death. There have been more than 17.3 million deaths a year since 2013, and this number is predicted to reach more than 23.6 million a year in 2030. While in Indonesia the number of deaths caused by ACS is high, reaching 1.25 million deaths from a population of 250 million people according to Riset Kesehatan Dasar (Riskedas) in 2018 with the highest prevalence in North Kalimantan (2.2%), D.I. Yogyakarta (2.0%), Gorontalo (2.0%) and South Sulawesi (1.5%).⁴⁻⁶

In acute myocardial infarction (AMI) patients, troponin levels increase rapidly. Usually in 1 hour with a highly sensitive test (hs-Tn) after the onset of symptoms and keeps increasing for a varied period. High sensitivity Troponin I (hs-TnI) examination, which is a diagnostic test to detect a cardiac abnormality with minimal lesions to the cardiac muscle. hs-TnI may enable the detection of circulating Troponin I in the cardiac muscle in low

concentrations. High levels of hs-TnI circulating have been related to the atherosclerosis prevalence in obstructive coronary disease.^{7,8}

High-Density Lipoprotein (HDL) is a type of cholesterol that have anti-atherosclerotic and functions as a cholesterol transport, decreasing the inflammation reaction and increasing the nitric oxide production from endothelial cells, obstructing LDL oxidation and endothelial cells apoptosis, thrombocyte activation and molecule adhesion expression. Low HDL levels are related to cardiovascular events risk, Scaffer *et al.* reported a significant relation between HDL and Coronary Heart Disease (CHD) risk. A study by Tok *et al.* reported that the number of leukocytes is higher in patients with lower HDL levels, and lymphocytes were significantly lower in patients with low HDL. Prajapati *et al.* also reported that there was a significant increase in NLR in CHD patients with low HDL.⁹⁻¹²

The atherogenesis process is an inflammatory process where neutrophils have a role in the formation of leukocyte and thrombocyte aggregates and reperfusion in STEMI/NSTEMI patients. Lymphocytes also have an important role in inflammation response modulation in the atherosclerosis process. Several research shows a correlation between the number of leukocytes in circulation with an increase in cardiovascular risk. Most reported a higher NLR in STEMI patients compared to NSTEMI or normal control. Ema *et al.* found NLR usually has a positive correlation with myocardial necrosis markers that showing the importance of NLR in evaluating how severe the myocardial lesion is in assessing the inflammatory intensity in ACS.^{9,13-18}

The diagnosis of AMI can be established through ECG or Troponin enzyme, but not all health facilities have them. An affordable examination that can be used in all health facility settings is needed, namely the Neutrophil Lymphocyte Ratio (NLR) and High-Density Lipoprotein (HDL). Based on that, this research aims to see how NLR, HDL, and hs-Troponin I levels are in patients with STEMI and NSTEMI in Wahidin Sudirohusodo General Hospital, Makassar.

METHODS

This is a retrospective cross-sectional study that is done by obtaining secondary data of patients diagnosed with STEMI and NSTEMI from medical records of Dr. Wahidin Sudirohusodo Hospital during January–December 2020.

This study's population is the medical records of patients above 18 years old, diagnosed with STEMI

and NSTEMI by a Cardiologist at Wahidin Sudirohusodo Hospital. The study sample is the population that fulfills the inclusion criteria, namely STEMI and NSTEMI patients that have Complete Blood Count (CBC) data by Sysmex XN-10, HDL results using Bio Majesty JCA-BM9010/c and hs-Troponin I result using Vidas.

Data analysis was carried out using SPSS ver 22, the statistical method used was the calculation of the frequency distribution and statistical tests. Data normality used Kolmogorov-Smirnov, while statistical test used the Mann-Whitney test. Diagnostic value of NLR, HDL, and hs-Troponin I, used Receiver Operating Characteristics (ROC) analysis to obtain the cut-off value. The test results were significant if the p-value <0.05.

Ethical Clearance was obtained from the Health Research Ethics Commission, Faculty of Medicine, Hasanuddin University/Hasanuddin University Hospital/Dr. Wahidin Sudirohusodo Hospital with article number 251/UN4.6.4.5.31/PP36/2021.

RESULTS AND DISCUSSIONS

This research was done at the Medical Records Installation of Dr. Wahidin Sudirohusodo Hospital in April 2021, and there was a total of 247 patients with STEMI and NSTEMI, but 2 were excluded due to the presence of lung carcinoma and sepsis, causing the total of the subject to be 245 subjects in which 152 patients had STEMI and 93 patients had NSTEMI.

Table 1 shows that the subjects were mostly male (78%), between the age of 33–88 years old, with an average age of 57.7 years old. NLR values vary between 0.60–58.44 with a mean of 6.59+6.83 and HDL levels vary from 70.84 mg/dL with a mean of 41.9+11.0. While hs-Troponin I varied from 10.7–40,000 ng/L with a mean of 12,600.6 000 ng/L with a mean of 12,600.6+15,582.5 ng/L.

Table 2 shows that a higher NLR was found in patients with STEMI with a median of 5.98 compared to NSTEMI patients with a median of 3.12. Statistical tests showed a significant difference, with $p < 0.001$. This can be interpreted that there is a significant relationship between NLR with STEMI and NSTEMI patients. This is in line with the results of research conducted by Bajari and Tak, where the mean NLR in STEMI patients was higher and showed a statistically significant difference compared to NSTEMI patients. This was caused by neutrophil activation that releases various proteolytic enzymes such as myeloperoxidase that is responsible for tissue injury while lower numbers of lymphocytes will cause an increase of cortisol that induces apoptosis.^{19,20} This can be seen in Figure 1.

Table 1. Research sample characteristics (n=245)

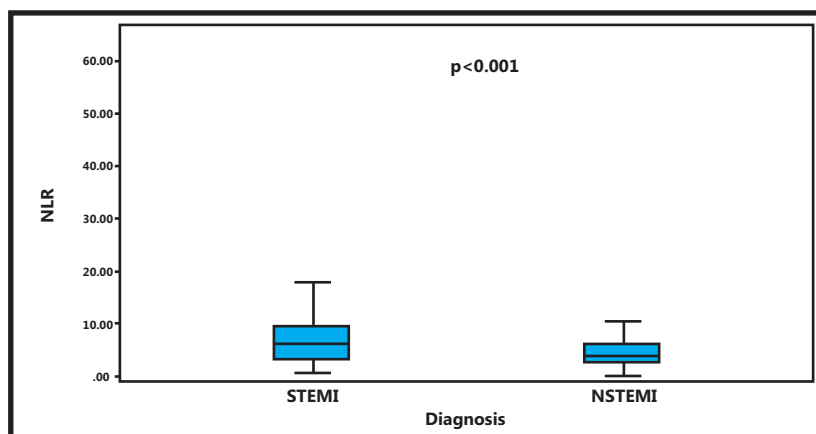
Characteristics	Mean±SD	Median(min-max)	n(%)
Age (y.o.)	57.7±10.3	58 (30-88)	
Gender			
Male			191 (78)
Female			54 (22)
Diagnosis			
STEMI			152 (62)
NSTEMI			93 (38)
Neutrophil (%)	72.2±13.9	74.4 (13.3-94.7)	
Lymphocyte (%)	18.0±10.1	16.5 (1.6-53.8)	
NLR	6.59±6.83	4.52 (0.60-58.44)	
HDL (mg/dL)	41.9±11.0	41 (7-84)	
hs-Troponin I (ng/L)	12,600.6±15,585.2	2598.1 (10.7-40,000)	

Source: Secondary data

Explanation: STEMI= ST-segment Elevation Myocardial Infarction; NSTEMI= Non-ST-segment Elevation Myocardial Infarction; NLR=Neutrophil Lymphocyte Ratio; HDL=High Density Lipoprotein; hs-Troponin I=high-sensitivity Troponin I

Table 2. The comparison of NLR, HDL levels and hs-Troponin I in STEMI and NSTEMI patients

Parameter	Median (min-max)		p*
	STEMI (n=152)	NSTEMI (n=93)	
NLR	5.98 (0.62-58.44)	3.12 (0.60-36.16)	<0.001
HDL (mg/dL)	42 (19-84)	41 (7-62)	0.475
hs-Troponin I (ng/L)	11,123.8 (18.5-40,000)	644(10,7-40,000)	<0.001

**Figure 1.** NLR values in STEMI and NSTEMI patients

High-density lipoprotein levels were not significantly different between STEMI and NSTEMI patients ($p=0.475$). This can be seen in Figure 2. These results are not in-line with a study by Avei *et al.*, who found a significant difference and correlation between the severity of CHD and a patient's HDL levels. A study by Kosmas *et al.*, also found that CHD patients had lower levels of HDL compared to the normal range, several prospective epidemiological studies have shown that there is an inverse relationship between low serum HDL levels and the

risk of CHD. High-density lipoprotein is proven to have anti-atherogenic properties, is protective towards the endothelium and increases the number and function of progenitor cell that play role in the endothelium healing process.^{21,22}

Hs-Troponin I levels were found to be higher in STEMI patients with a median of 11,123.8 ng/L compared to NSTEMI patient with a median of 644 ng/L. Statistical test results show a significant difference with $p < 0.001$. These are in line with a study by Marino *et al.* where the mean hs-Troponin I

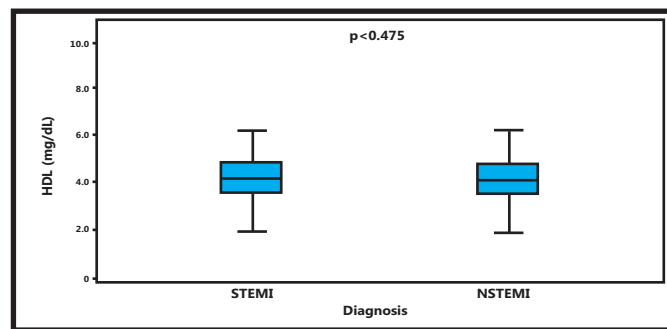


Figure 2. HDL levels in STEMI and NSTEMI patients

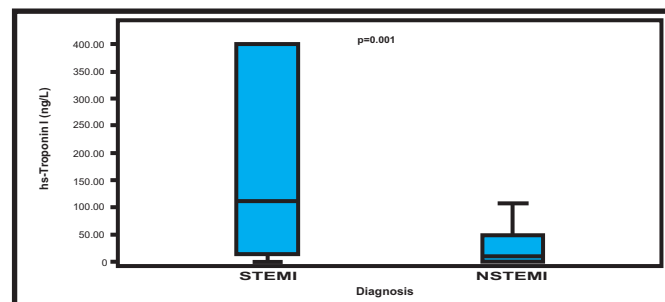


Figure 3. hs-Troponin levels in STEMI and NSTEMI patients

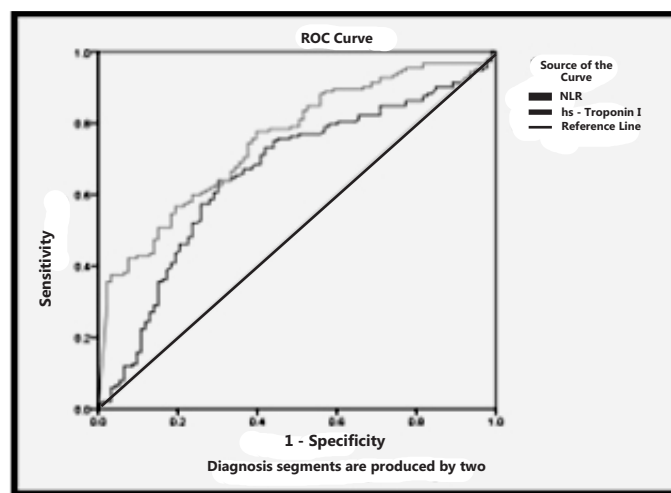


Figure 4. ROC curve NLR and hs-Troponin I as diagnostic markers

in STEMI patients (101,55 ng/L) was higher than in NSTEMI patients (76.8 ng/L). The increase of hs-Troponin I was in line with the extent of myocardial damage.²³ Thus it can be interpreted that there is a significant relationship between hs-Troponin I with STEMI and NSTEMI patients, as can be seen Figure 3.

Based on Figure 4, an NLR with a cut-off at 4.32 was deemed to have an optimal sensitivity and specificity based on the Youden index with a sensitivity of 64% and 70% specificity. Based on a prospective study done by Zazula *et al.* an NLR cut-off of 4.51 had a 23%

sensitivity and specificity of 91% was used as a predictor of ACS incidence. A retrospective study by Altun *et al.* also found an NLR cut-off of 4.84 with 58.6% sensitivity and 78.9% specificity could predict a high Syntax score in STEMI patients.^{15,20}

While the levels of hs-Troponin I with the cut-off point of 910.5 ng/L had a 78% sensitivity and 60% specificity that is in line with a prospective observational study by Marino *et al.* that found a hs-Troponin I cut-off of 23.02 had a 55% sensitivity and 77.7% specificity that can be an ACS diagnostic marker.²³

CONCLUSIONS AND SUGGESTIONS

Neutrophil lymphocyte ratio values in patients with STEMI are higher than in NSTEMI patients at the cut-off of 4.32 can be a diagnostic sign with a sensitivity of 64% and 70% specificity. For HDL levels there was no significant difference in STEMI and NSTEMI patients, while hs-Troponin I levels were higher in STEMI and NSTEMI patients with a cut-off of 910.5 ng/L can be a diagnostic sign with 78% sensitivity and 60% specificity.

The limitations of this study are the use of secondary data causing the information to be limited to what is recorded in the medical record and there was no analysis of various lipoproteins, causing the need for further studies regarding lipoprotein levels in STEMI and NSTEMI patients.

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