

**RELATIONSHIP BETWEEN NEUTROPHYL-TO-LYMPHOCYTE RATIO WITH CORONARY ARTERY LESION IN ACUTE CORONARY SYNDROME PATIENTS****Zanurul Rifhan, Rahmad Isnanta, Zainal Safri****DOI: 10.5281/zenodo.3624377****Abstract**

Acute Coronary Syndrome (ACS) is the leading cause of death from cardiovascular disease. ACS is an abnormal condition caused by cardiac dysfunction and narrowing of the coronary arteries. Narrowing of the coronary arteries in the pathophysiology of ACS involves the process of atherosclerosis. It is important to assess early whether there are coronary artery lesions or not. Neutrophyl-to-lymphocyte Ratio (NLR) is a simple ratio between neutrophils and lymphocytes that can be obtained from routine blood tests and is known to be related to the severity of coronary artery lesions. This research is a retrospective research on 61 samples obtained through consecutive sampling between January-December 2018 at H. Adam Malik General Hospital, Medan. Data obtained from medical records of patients where NLR levels were found from routine blood results and the number of coronary artery lesions found from the results of the patient's coronary angiography. All data were collected and analyzed using SPSS version 22. Based on data analysis, we found that there's a significant relationship between NLR levels and the number of coronary artery lesions in ACS patients with $p = 0.002$

Keywords: Neutrophyl-to-lymphocyte ratio, Coronary Artery Lesions, Acute Coronary Syndrome.**Introduction**

Acute coronary syndrome (ACS) is a collection of clinical symptoms of myocardial ischemia that occurs suddenly due to lack of blood flow to the heart myocardial (1). These complaints are known as typical chest pain (or angina pectoris) characterized by changes in ST segments of the electrocardiography (ECG) and elevated levels of cardiac enzymes. ACS can be divided into unstable angina pectoris (UAP), non ST-segment Elevation Myocardial Infarction (NSTEMI) and ST-segment elevation Myocardial Infarction (STEMI) (2). In 2016, ACS caused 7 million deaths out of 17.3 million deaths from cardiovascular disease globally (3,4). This disease is associated with the process of atherosclerotic plaque formation in the endothelial lining of coronary arteries. The process of plaque formation involves impaired endothelial function of blood vessels, foam cell formation, fatty streak formation, and fibrous cap formation (5). Rupture of the affected plaque releases thrombus which can block blood flow in the coronary arteries so that blood supply to the myocardial decreases and causes ACS (6). This process involves an inflammatory process so that white blood cells such as neutrophils and lymphocytes are involved. Neutrophyl-to-lymphocyte ratio (NLR) is an inflammation marker obtained from routine blood test and is known to be associated with the progression of atherosclerotic plaque in ACS patients (7,8). Research by Ahmadi et al (2018) found a significant increase in NLR levels (> 3) in patients suffering from ACS and had undergone coronary angiography (9). The purpose of this study was to determine the relationship between NLR values and the number of coronary artery lesions in ACS patients.

Research Methods**Sampling method**

This research is a retrospective analytic study using cross sectional method. The research was conducted at the H. Adam Malik General Hospital Medan throughout January - December 2018. The sample collection was carried out using the consecutive sampling method with a total sample of 61 people. Criteria for inclusion of samples were patients with acute coronary syndrome which were established based on history taking, physical examination, ECG and cardiac enzyme markers, aged > 18 years, and had undergone coronary angiography. The use of data is based on patient consent both verbally and in writing by signing an informed consent sheet. This study was approved by the Health Research Ethics Committee at the Faculty of Medicine, University of North Sumatra (KNEPK FK USU).



Data Analysis

The sample data is taken from medical records, and the data taken are laboratory results and the results of the patient's coronary angiography. Examination of blood samples using the automatic cell counting method with Sysmex XN 1000 and coronary angiography performed by cardiology specialists using the Innova 2100 IQ. The NLR value is obtained by dividing the absolute neutrophil value from the absolute lymphocyte value from the patient's routine blood results. The results of coronary angiography which are interpreted as vessel disease scores will be categorized as simple lesions or multiple lesions. The collected data will be analyzed using the chi-square method using SPSS 22.0. A p value of <0.05 (95%) was considered statistically significant.

Results

Demographic characteristics of the samples can be seen in Table 1. There were 55 male patients (90.2%) and 6 female patients (9.8%) with an average age of 54.69 years. Based on the disease, we found 45 people (73.8%) had STEMI, 10 people (16.4%) had NSTEMI, and 6 people (9.8%) had unstable angina pectoris.

Based on the results of coronary angiography, we found 14 patients with simple lesions (no coronary artery lesions and CAD1VD) and 47 people with multiple lesions (CAD2VD and CAD3VD). Our neutrophil-to-lymphocyte ratio found a value of " <3 " of 10 people and a value of " > 3 " of 51 people (83.6%). Next, we performed a data analysis test using the chi square method between NLR levels and the number of coronary artery lesions and we found a significant result with a p value of 0.002 (table 2)

Table 1. Demographical characteristics of the research samples

Characteristics	n = 61
Gender	
Male	55 (90.2%)
Female	6 (9.8%)
Age (mean)	54.69
Smoking	26 (42.6%)
Hypertension	15 (24.6%)
Type 2 Diabetes Mellitus	10 (16.4%)
Dyslipidemia	15 (24.6%)
Obesity	15 (24.6%)
Acute Coronary Syndrome	
STEMI	45 (73.8%)
NSTEMI	10 (16.4%)
UAP	6 (9.8%)
Coronary Artery Lesions	
<i>Simple Lesion</i>	14 (23%)
<i>Multiple Lesion</i>	47 (77%)
Neutrophyl-to-lymphocyte ratio	
<3	10 (16.4%)
>3	51 (83.6%)

Discussion

Based on the results of the study, 55 people (90.2%) were male. This is consistent with research from Russell (2013) where ACS sufferers are mostly male (10). We found the average age of patients was 54.6 with the most age found at the age of 55 years (6 people). These results are consistent with studies from GRACE where as



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many as 2.5% of ACS patients are found in the 55-64 years age group (4). The prevalence of ACS tends to increase with age. The study from Joakimsem et al (1999) involving 3016 men and 3404 women aged 24-84 years found atherosclerotic plaque in 55.4% of men and 45.8% of women (11). Risk factors in this study were obesity (24.6%), Type 2 DM (16.4%), hypertension (24.6%), dyslipidemia (24.6%), and smoking (42.6%). This result was in line with research from Russell (2013) involving ACS patients and found 65.5% were hypertensive patients, 55.5% were smokers, and 43.2% were Type 2 DM patients (10). We found ACS patients that had been diagnosed with STEMI were 45 people (73.8%), patients with multiple lesions were 47 people (77%) and STEMI patients who had multiple lesions were 34 people. This result is in line with Rasoul's study (2010) where most patients suffering from ACS have been diagnosed with STEMI, and 70% of them have multiple lesions based on the results of their coronary angiography (12). ACS is a disease caused by the inflammatory process, and NLR is a simple marker of inflammation. We found NLR levels > 3 in 51 patients (83.6%). Both neutrophils and lymphocytes are known to be associated with the progression of atherosclerotic plaque (13). Absolute neutrophil levels have increased and absolute lymphocyte levels have decreased in the process of atherosclerosis (14). Neutrophils actively release myeloperoxidase which facilitates the formation of free radicals resulting in endothelial dysfunction, while lymphocytes are protective against the atherosclerosis process by facilitating the proliferation of smooth muscle cells in blood vessels (15,16). We analyzed data between NLR levels and the type of coronary artery lesions of patients and found a significant relationship between NLR levels and the number of coronary artery lesions with a p value of 0.002 ($p < 0.05$). These results are in line with previous studies from Balta where the higher the NLR level, the higher the progression of atherosclerotic plaque in the coronary arteries (8). Research from Ahmadi, et al (2018) found an increase in NLR levels was significantly related to the number of coronary artery lesions. The number of lesions in the coronary arteries is categorized by the vessel disease system, where if stenosis is found in 1 coronary artery it is categorized as CAD1VD, 2 blood vessels are categorized as CAD2VD, and 3 blood vessels are categorized as CAD3VD. They subdivided NLR values into 3 categories, namely low NLR levels (<2), moderate NLR levels (2-3), and high NLR levels (> 3). The results of his study were in the CAD1VD category found 41 patients with moderate NLR, in CAD2VD found 8 patients with high NLR, and in CAD3VD found 15 patients with high NLR (8).

Tabel 2. Relationship between NLR with Coronary Artery Lesions

Variables	NLR		Total	P (<0.05)
	<3	>3		
Coronary Artery Lesions				
<i>Simple Lesion</i>	6 (42.9%)	8 (57.1%)	14 (100%)	0.002*
<i>Multiple Lesion</i>	4 (8.5%)	43 (91.5%)	47 (100%)	

Conclusion

There is a significant relationship between NLR levels and the number of coronary artery lesions in patients with acute coronary syndrome where the higher the NLR level, the more number of coronary artery lesions found in ACS patients.

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