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### **RESEARCH ARTICLE**

### THE ROLE OF NEUTROPHILS TO LYMPHOCYTES RATIO AS PREDICTIVE BIOMARKER IN ACUTE MYOCARDIAL INFARCTION PATIENTS AT AL-GAMHURIA MODERN GENERAL HOSPITAL – ADEN-YEMEN

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### Abstract

Inflammation plays a fundamental role in the development of atherosclerosis and in the pathogenesis of acute myocardial infarction (AMI). Neutrophils to lymphocytes ratio (NLR) was recognized as important inflammatory marker in predicting the severity and prognosis of AMI. The aim of this study is to determine the role of NLR as predictive biomarker in AMI patients at Al-Gamhuria Modern General Hospital. This study was considered a descriptive cross-sectional study, which was conducted in Al-Gamhuria Modern General Hospital from March through August 2022. The study includes 124 patients diagnosed as AMI and classified into two groups: 70 patients with low NLR and 54 patients with high NLR. Out of 124 patients, 56.5% of patients had low NLR and 43.5% had high NLR. Patients with high NLR were older ( $62.31 \pm 7.30$  vs. 57.80  $\pm$  5.17 years), had higher prevalence of D.M., hyperlipidemia, more smokers and Khat chewers compared to patients with low NLR. High NLR group had more elevated CK-MB and Troponin T, more reduced ejection fraction (EF) and fractional shortening (FS) compared to low NLR group (P < 0.001). High NLR group also had poorer Killip class (P < 0.001), and were more prone to death inside the hospital compared to low NLR group (11.1% vs. 1.4%), (P= 0.042). As conclusion, NLR is a strong predictor of myocardial damage, myocardial dysfunction as well as in-hospital mortality in patients with AMI. NLR as an inflammatory marker can also predict the consequences on the heart post-MI.

**Keywords:** Neutrophils to lymphocytes ratio, Acute myocardial infarction, Predictive biomarker.

### Introduction

Despite the advances in the diagnosis and management of coronary artery disease (CAD), it stills the most common cause of mortality in both developed and developing countries. Acute coronary syndrome (ACS) is among the common and severe presentations of CAD. It includes unstable angina, non-ST-segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI) [1].

Atherosclerosis is a chronic inflammatory process, so inflammation is a vital element in ACS [2].

Inflammation plays a critical role in the development of ventricular remodeling. Myocardial ischemia triggers an inflammatory response, mainly characterized by infiltration with neutrophils, followed by monocytes /macrophages and lymphocytes [3].

Small numbers of infiltrating lymphocytes also play a key role in remodeling, whereas monocytes cause proinflammatory, angiogenic and fibrotic response [4].

During post-MI inflammation resolution, proinflammatory macrophages are thought to undergo local conversion to resolution-mediating macrophages. Neutrophils seem to play crucial role in this process, as their granule content does not only contribute to ischemic damage and well-described ischemia-reperfusion injury, but also to the recruitment of monocytes and macrophage reprograming toward a resolving phenotype [5].

Neutrophil depletion in experimental MI results in impaired resolution of inflammation and uncoordinated

fibrotic scar formation, which translates into adverse remodeling and decreased cardiac function [6].

In support of this beneficial role for neutrophils during tissue repair, there is also evidence for anti-inflammatory and reparative properties of neutrophils in other, noncardiovascular inflammatory conditions, including bacterial infection and non-sterile injury. Phagocytic removal of bacteria and dead cells by neutrophils clears the wound for rebuilding and repair, and depletion of neutrophils from inflamed tissue has been shown to increase the pathology, e.g., in the setting of intestinal inflammation. This proposed "healing" role of neutrophils is novel and somewhat unexpected in the setting of myocardial ischemia, given that neutrophils have been mostly considered exclusively proinflammatory by contributing to myocardial tissue damage [7]. Nevertheless, the contribution of neutrophils in lethal reperfusion damage is controversially discussed in the literature, and attempts to develop anti-neutrophil therapies have been largely unsuccessful [8].

Unlike the neutrophils and monocytes, a lower lymphocyte count has been observed in acute myocardial infarction (AMI) [9]. T cells are a key component of the adaptive immune system and T cells can be divided into helper T cells (CD4: Th1, Th2, Th17, etc.), cytotoxic T cells (CD8), and regulatory T cells according to the role of immune response.

Previous studies demonstrated activation of peripheral T lymphocytes evidenced by increased expression of human leukocyte antigen (HLA-DR) and CD69 in AMI [10]. However, patients with AMI had lower CD4+ but higher CD8+ T lymphocytes in both the percentages and absolute numbers, leading to an inverted CD4/CD8 ratio. A prolonged depressed CD4/CD8 ratio was a poor prognostic factor [11]. CD4+ T lymphocytes are able to differentiate into Th1 and Th2 lineage in response to the local milieu of cytokines. The frequency of Interferon-(IFN-γ)-producing T-cells Gamma (Th1) was significantly increased in patients with AMI within 24 hours after the onset of symptom [12].

A significant increase of IFN- $\gamma$  and TNF- $\alpha$  production (Th1) and a significant decrease of IL-10 production (Th2) in cultures of lymphocytes taken from patients with AMI were also observed, suggesting a predominance of proinflammatory Th1 cells and cytokines in AMI. In clinical setting, high numbers of Th2 cells were independently associated with decreased carotid intima-media thickness and a reduced risk of AMI, suggesting a protective role of Th2 cells in AMI [13]. Natural killer (NK) cells are a type of cytotoxic lymphocyte critical to the innate immune system. A reduction in both the absolute number and the cell fraction of NK cells was documented in patients with AMI [10]. A recent study reported that sustained NK cell deficit was associated with low-grade inflammation,

suggesting a protective role of NK cells in atherosclerosis and AMI [14].

The ratio between the absolute number of neutrophils and the absolute number of lymphocytes indicates the equilibrium between neutrophils and lymphocytes in circulation. It reflects the state of acute inflammation and ongoing stress response. In AMI, the equilibrium might swing to the extreme edge such that neutrophils to lymphocytes ratio (NLR) increases due to excessive acute inflammation and stress response [15].

NLR has recently emerged as a potential new biomarker predicting worse clinical conditions ranging from infectious diseases to cardiovascular diseases [16]. High NLR is an independent predictor of major adverse cardiac events and mortality in patients with AMI [17].

A previous study done by Gazi and Bayram, demonstrated that the NLR was higher in patients with complications in AMI [18]. NLR is also an indicator of systemic inflammation and a prognostic marker in patients undergoing percutaneous coronary intervention (PCI) [19]. Moreover, it has been shown to be associated with larger infarct size [20]. An increasing rate of in-stent thrombosis, non-fatal MI and cardiovascular mortality has been correlated with the NLR increase [21], as well as the frequency of ventricular tachyarrhythmias is associated with higher levels of NLR [22].

In NSTEMI patients, higher NLR has been associated with a greater prevalence of atrial fibrillation and heart failure, a lower left ventricular EF and greater rates of coronary artery bypass grafting (CABG) [23]. Lee, et al, have demonstrated that the NLR value at the admission is an independent predictor of 1-year re-infarction and mortality in diabetic patients with AMI [24].

### **Materials and Methods**

### Study area and period

This descriptive cross-sectional study was carried out among AMI patients at Al-Gamhuria Modern General Hospital in Aden, Yemen, from March to August, 2022.

### Study population

The study population consisted of all patients who had complained from suspected anginal symptoms with paraclinical evidence of MI by either ECG, cardiac enzymes or echocardiography and attended to the emergency department of the hospital, after fulfilling the exclusion criteria.

### Sample size

The study was conducted on 124 AMI patients who attended the emergency department of the hospital during the study period.

The AMI study population was divided into two main groups (the cut-off point for this division was taken as 3.61, which was the mean NLR in this study):

- Low NLR (n=70).
- High NLR (n=54).

#### Inclusion and exclusion criteria

All Patients who attended to emergency department of Al-Gamhuria Modern General Hospital, Aden, and diagnosed as AMI.

Patients with a history of trauma, surgery, neoplasm or infectious disease in the last 30 days prior to admission, patients with autoimmune disease and patients with current use of immunosuppressants (including corticosteroids) were excluded from the study.

### Data collection

The data was collected using a questionnaire designed for this study included demographic, clinical, and paraclinical variables as well as detailed history, physical examination, and medical records.

History was taken from the patients or their relatives, after obtaining informed consent, including basic demographics, comorbid diseases, cardiovascular risk factors (diabetes mellitus "D.M.", arterial hypertension "AHT", hyperlipidemia), drug history and special habits (smoking, Khat chewing). Physical examination was done, including measurement of blood pressure and heart rate (HR) with chest and cardiovascular examination.

Blood samples were drawn (3 ml in tube containing EDTA (ethylene diamine tetraacetic acid) and 2 ml in another tube not containing EDTA) for laboratory investigations, including complete blood count (CBC), fasting blood glucose (FBG), random blood glucose (RBG), serum creatinine, lipid profile and cardiac enzymes (creatine kinase-myocardial band "CK-MB" and troponin T).

Surface electrocardiography (ECG) including six limb leads and six chest leads was done, concentrating on Q waves, ST- segments and T waves, while transthoracic echocardiography was conducted by cardiologist, concentrating on ejection fraction (EF) and fractional shortening (FS). All patients were followed up to assess the in-hospital outcome.

### Ethical considerations

This study was conducted after getting approval from the department of internal medicine and the department of postgraduate studies in the faculty of medicine and health sciences of the University of Aden as well as the ethical committee in the faculty of medicine. Permission was also obtained from the general director of Al-Gamhuria modern general hospital. A verbal consent was obtained from each patient, seeking the benefits of the patients over the study.

### Statistical analysis

All analyses were performed using the computer software program of the Statistical Package for Social Sciences (SPSS version 23). Pearson's correlation test was performed, and p values was obtained to assess the strength of any association between variables. The descriptive statistics (on SPSS 23) were used for details on the overall data. Categorical variables were presented as frequency and percentage and continuous variables were expressed as means  $\pm$  standard deviation (SD). Chi square test or Fisher's exact test were used to compare categorical variables and student's t-test was used to compare continuous variables. p < 0.05 was considered statistically significant.

### **Results**

### Distribution of age and gender in patients with high NLR compared to patients with low NLR

Out of 124 AMI patients, 56.5% of AMI patients had low NLR, while 43.5% had high NLR. The study of age distribution in patients with low NLR compared to patients with high NLR showed that the mean age of patients in high NLR group was higher than the mean age of patients in low NLR group ( $62.31 \pm 7.30$  vs.  $57.80 \pm 5.17$  years), which was statistically significant (*P*-value= 0.000). The study of gender showed that male gender was 81.5% in high NLR group vs. 71.4% in low NLR group, which was statistically non-significant (*P*-value= 0.212) (Table 1).

Table (1): Distribution of age and gender in patients with high NLR compared to patients with low NLR.

Findings		Low NLR (n =70) = (56.5%)		High (n=54) =	NLR (43.5%)	Total (n =124)		<i>P</i> -value
		n	%	n	%	n	%	
Mean Age (years) (± SD)		$57.80\pm5.17$		62.31			<0.001 *	
Gender	Male	50	71.4	44	81.5	94	75.8	0.212
	Female	20	28.6	10	18.5	30	24.2	0.212
Note: % calculated from Total of Column n (number of patients). NLR (Neutrophils to Lymphocytes Ratio).								
* (Statistically significant).								

### Classical cardiovascular risk factors of patients with high compared to patients with low NLR

Patients with high NLR had higher prevalence of D.M. compared to patients with low NLR [41(75.9%) vs. 31(44.9%)], which was statistically significant (P-value= 0.001). In addition, patients with high NLR had statistically significant higher prevalence of Khat chewing [40 (74.1%) vs. 39 (55.7%), P-value= 0.035], and hyperlipidemia [34 (63.0%) vs. 22 (31.4%), P-value <0.001]. Patients with high NLR had also higher prevalence of smoking compared to patients with low NLR [32 (59.3% vs. 13 (18.6%)], which was statistically significant (P- value <0.001). AHT was found in 32 (59.3%) in high NLR group compared to 51 (72.9%) in low NLR group, which is statistically non-significant (P-value= 0.126) (Table 2).

## Clinical characteristics of patients with high and low NLR

The mean systolic blood pressure (SBP) in patients with high NLR was  $127.04 \pm 31.91$  vs.  $130.21 \pm 19.75$  in patients with low NLR, which was statistically nonsignificant (P- value= 0.497). Similarly, the mean diastolic blood pressure (DBP) was nearly the same,  $78.89 \pm 17.50$  vs.  $78.14 \pm 11.65$  in patients with high and low NLR respectively, which was statistically nonsignificant (P- value= 0.777). On the other hand, the mean HR was statistically significantly higher in high NLR group compared to low NLR group ( $104.02 \pm 18.68$  vs.  $86.54 \pm 11.15$ , P- value <0.001). Regarding the type of MI according to ECG findings, anterior MI was the most prevalent type in patients with high NLR compared to patients with low NLR [43 (79.6%) vs. 32 (45.7%), which was statistically significant (P- value < 0.001) (Table 3).

### Kidney function and parameters of myocardial damage and dysfunction among patients with high NLR compared to patients with low NLR

Patients with high NLR had more elevated serum creatinine compared to patients with low NLR (1.27  $\pm$  0.46 vs. 0.80  $\pm$  0.23), which was statistically significant (*P*- value < 0.001).

Similarly, high NLR group had higher CK-MB and Troponin T compared to low NLR group [(69.13 ± 39.46 vs. 31.79 ± 17.02), (2.19 ± 2.11 vs. 0.71 ± 1.52), respectively], which were considered statistically significant (*P*-value < 0.001 for both). On the other hand, EF and FS appeared more reduced in patients with high NLR compared to patients with low NLR [(44.15 ± 11.06 vs. 53.26 ± 7.60), (29.39 ± 8.14 vs. 35.97 ± 6.16), respectively], which were also statistically significant (*P*-value < 0.001 for both) (Table 4).

Table	(2).	Distribution	of classical	l risk factors	in natients	with low	and high NLR
abic	(4)•	Distribution	i or crassical	I HSK Idetors	in patients	with low	and ingli MLR.

Risk Factors	Low NLR (n =70)		High (n=	Total (n=124)		<i>P</i> -value	
	n	%	n	%	n	%	
AHT	51	72.9	32	59.3	83	66.9	0.126
D.M.	31	44.9	41	75.9	72	58.5	0.001*
Hyperlipidemia	22	31.4	34	63.0	56	45.2	< 0.001*
Khat Chewing	39	55.7	40	74.1	79	63.7	0.035*
Current Smoking	13	18.6	32	59.3	45	36.3	< 0.001*
Note: % calculated from Total of Column n (number of patients), NLR (Neutrophils to Lymphocytes Ratio), AHT (Arterial							
Hypertension) D.M. (Diabetes Mellitus) *(Statistically significant)							

Table (3): Distribution of clinical characteristics	in patients with	low and high NLR.
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Findings		Low NLR (n =70)		High NLR (n=54)		Total (n=124)		<i>P</i> -value
		n	%	n	%	n	%	
Mean SBP (± SD)		$130.21 \pm 19.75$			0.497			
Mean DBP (± SD)		$78.14 \pm 11.65$			0.777			
Mean H	R (± SD)	$86.54 \pm 11.15$		$104.02 \pm 18.68$				<0.001 *
	Anterior	32	45.7	43	79.6	75	60.5	
Type of MI Inferior Lateral		33	47.1	9	16.7	42	33.9	<0.001 *
		5	7.1	2	3.7	7	5.6	
Note: % calculated from Total of Column n (number of patients). NLR (Neutrophils to Lymphocytes Ratio), SBP (Systolic Blood Pressure) in mmHg, DBP (Diastolic Blood Pressure) in mmHg, HR (Heart Rate) in beats per minute, MI (Myocardial Infarction).								

\* (Statistically significant).

 Table (4): Distribution of kidney function and parameters of myocardial damage and dysfunction in patients with low and high NLR.

Findings	Low NLR (n =70)	High NLR (n=54)	<b>P-value</b>			
Mean Serum Creatinine (± SD)	$0.80\pm0.23$	$1.27\pm0.46$	<0.001 *			
Mean CK-MB (± SD)	$31.79 \pm 17.02$	$69.13\pm39.46$	<0.001 *			
Mean Troponin T (± SD)	$0.71\pm1.52$	$2.19\pm2.11$	<0.001 *			
Mean EF (± SD)	$53.26\pm7.60$	$44.15 \pm 11.06$	<0.001 *			
Mean FS (± SD)	$35.97 \pm 6.16$	$29.39\pm8.14$	<0.001 *			
Note: % calculated from Total of Column n (number of patients). NLR (Neutrophils to Lymphocytes Ratio), serum creatinine in mg/dl, CK-						

MB (Creatine Kinase Myocardial Band) in U/L, Troponin T in ng/dl, EF (Ejection Fraction) in %, FS (Fractional Shortening) in %. \* (Statistically significant).

Table (5): Distribution of Killip class and in-hospital death in patients with low and high NLR.

Findings		Low NLR (n =70)		High NLR (n=54)		Total (n = 124)		<i>P</i> -value
		n	%	n	%	n	%	
Killip Class	Class I	47	67.1	17	31.5	64	51.6	<0.001 *
	Class II	20	28.6	21	38.9	41	33.1	
	Class III	2	2.9	10	18.5	12	9.7	
	Class IV	1	1.4	6	11.1	7	5.6	
	Yes	1	1.4	6	11.1	7	5.6	0.042 *
m-nospital Death	No	69	98.6	48	88.9	117	94.4	
Note: % calculated from Total of Column n (number of patients). NLR (Neutrophils to Lymphocytes Ratio). * (Statistically significant).								

Table (6): Correlation between NLR and parameters of myocardial damage and dysfunction.

Downworkows	NLR						
rarameters	r	P- value					
СК-МВ	0.514	< 0.001 *					
Troponin T	0.455	< 0.001 *					
EF	- 0.442	< 0.001 *					
FS	- 0.422	< 0.001 *					
NLR (Neutrophils to Lymphocytes Ratio), r (Pearson's correlation coefficient), CK-MB (Creatine Kinase Myocardial Band), EF (Ejection							
Fraction), FS (Fractional Shortening). * (Statistically significant)							

# Killip classification and in-hospital mortality among patients with high NLR compared to patients with low NLR

Patients with high NLR had poorer Killip class (class III & IV) than those with low NLR [10 (18.5%) vs. 2 (2.9%) for class III, 6 (11.1%) vs. 1 (1.4%) for class IV], which was statistically significant (P- value < 0.001). Regarding the in-hospital death, six patients within high NLR group died inside the hospital before they had been discharged with percentage of 11.1%. On the other hand, only one patient within low NLR group died in the hospital before discharge with percentage of 1.4%, and this was statistically significant (P- value= 0.042) (Table 5).

## Correlation between NLR and parameters of myocardial damage and dysfunction

The correlation between NLR and parameters of myocardial damage (CK-MB, Troponin T) and myocardial dysfunction (EF, FS), was analyzed by calculating Pearson's correlation coefficient (r). In all patient groups, NLR positively correlates with CK-MB as well as Troponin T (r = 0.514 and 0.455 respectively) and negatively correlates with EF and FS (r = -0.442 and -0.422 respectively). These results suggest that the correlation between NLR and these parameters were statistically significant (P- value < 0.001) (Table 6).

### **Discussion**

Neutrophils to lymphocytes ratio is an established biomarker for systemic inflammation. In this descriptive cross-sectional study, the aim was to establish the role of NLR as predictive biomarkers in AMI patients. Of all 124 AMI patients included in the present study, 56.5% of patients had low NLR, while 43.5% had high NLR. Patients with high NLR were older than patients with low NLR [Mean age ( $62.31 \pm 7.30$  vs.  $57.80 \pm 5.17$  years)], which was statistically significant. Sawant, et al, 2014 in USA [25] and Yang-Chun Han, et al, 2013 in Korea [26], pointed out the same results.

Regarding the gender, patients with high NLR were more likely to be men, compared to patients with low NLR (81.5% vs. 71.4%), but was statistically non-significant. The same results were referred by Yang-Chun Han, et al, 2013 in Korea [26] in a study, which found that high NLR group were statistically non-significantly more likely to be men than low NLR group.

Arterial hypertension, which is one of the most important modifiable risk factors for AMI, was highly prevalent in both high and low NLR group (59.3% vs. 72.9%), This was statistically non-significant, similar to Sawant, et al, 2014 in USA [25] and Rheem Muhmmed Suliman, et al, 2010 in Oman [27]. Diabetes mellitus was statistically significantly more prevalent in patients with high NLR compared to patients with low NLR (75.9% vs. 44.9%). These results were mentioned in studies done by Ergelen, et al, 2014 in Turkey [28] and Rheem Muhmmed Suliman, et al, 2010 in Oman [27]. Hyperlipidemia, which is another important risk factor for AMI, was highly prevalent among high NLR group more than among low NLR group (63% vs. 31.4%), which was statistically significant, similar to a study done by Jingyu, et al, 2014 in China [29]. Smoking was also more prevalent in patients with high NLR compared to patients with low NLR (74.1% vs. 55.7%). These results were statistically significant. A study by Hartopo, et al, 2015 in Indonesia [15] revealed more or less similar results. Regarding the habit of Khat chewing, patients with high NLR were more Khat chewer than those with low NLR (59.3% vs. 18.6%) and this was statistically significant.

This study showed that the mean SBP as well as the mean DBP at presentation in high NLR group were not different when compared to low NLR group [( $127.04 \pm 31.91$  vs.  $130.21 \pm 19.75$ ), ( $78.89 \pm 17.50$  vs.  $78.14 \pm 11.65$ ) respectively] [29]. On the other hand, HR in patients with high NLR was higher when compared to low NLR patients ( $104.02 \pm 18.68$  vs.  $86.54 \pm 11.15$ ), which was statistically significant. The same results were pointed out by a study conducted by Jingyu He, et al, 2014 in China [29].

Regarding the type of MI according to ECG findings, the anterior wall MI was the most presented type in patients with high NLR (79.6%) and more prevalent when

compared to patients with low NLR (45.7%), in whom the inferior wall MI was the most presented type (47.1%). These results were statistically significant. A study done by Ergelen, et al, 2014 in Turkey [28], showed that the anterior wall MI was more prevalent in high NLR group compared to low NLR group, but was not significantly different.

Serum creatinine as marker of renal function, was more elevated at presentation in patients with high NLR than in those with low NLR ( $1.27 \pm 0.46$  vs.  $0.80 \pm 0.23$ ), which was statistically significant. These results were similar to studies done by Uzma Gul, et al, 2017 in Pakistan [30] and Ergelen, et al, 2014 in Turkey [28].

Regarding the parameters of myocardial damage, CK-MB was more elevated in patients with high NLR group than in those with low NLR (69.13  $\pm$  39.46 vs. 31.79  $\pm$ 17.02), which was considered statistically significant. Studied done by Yang-Chun Han, et al, 2013 in Korea [26], Hong, et al. 2019 also in Korea [31], Ergelen, et al, 2014 in Turkey [28] and Chen, et al, 2018 in China [32], stated that CK-MB was more raised in high NLR group compared to low NLR group, which were similar to the results of this study. This also applied to Troponin T, which was more elevated in patients with high NLR than in those with low NLR (2.19  $\pm$  2.11 vs. 0.71  $\pm$  1.52), similar to studies done by Yang-Chun Han, et al, 2013 in Korea, (130) Hong, et al. 2019 also in Korea [31]. Sawant, et al, 2014 in USA [25] also showed that Troponin T more raised in High NLR group compared to low NLR group, but with no significant difference.

Regarding the parameters of myocardial dysfunction, in this study, EF more reduced in patients with high NLR than in patients with low NLR (44.15  $\pm$  11.06 vs. 53.26  $\pm$  7.60). This was statistically significant similar to studies done by Yang-Chun Han, et al, 2013 in Korea [26] Hong, et al. 2019 also in Korea [31], Gul, et al, 2014 in Turkey [33] and Chen, et al, 2018 in China [32]. This was also true regarding FS, which also more reduced in high NLR group than in low NLR group (29.39  $\pm$  8.14 vs. 35.97  $\pm$  6.16), similar to a study conducted by Chen, et al, 2018 in China [32].

In both patients' groups, NLR positively correlates with CK-MB and Troponin T (r = 0.514 and 0.455 respectively), and negatively correlates with EF and FS (r = -0.442 and -0.422 respectively). According to these results, the correlations between NLR and the parameters of myocardial damage and dysfunction were considered statistically significant. This was similar to study conducted by Chen, et al, 2018 in China [32]. A study done by Shumilah, et al in Sana'a, Yemen [34], also revealed the significant positive correlation between NLR and CK-MB.

Heart failure is one of the most complications of AMI, which assessed in this study by Killip classification. This study showed that patients with high NLR had poorer

Killip class than those patients with low NLR (class III-IV), representing (29.6%) and (4.3%) respectively. This was statistically significant and similar to studies done by Yang-Chun Han, et al, 2013 in Korea [26], Jingyu He, et al, 2014 in China [29], Ergelen, et al, 2014 in Turkey [28] and Gul, et al, 2014 also in Turkey [33].

Mortality is major concern for patients diagnosed with AMI. This study revealed that the in-hospital mortality was more prevalent in patients with high NLR compared to patients with low NLR (11.1% vs. 1.4%), which was statistically significant. Similar results were mentioned in studies conducted by Rheem Muhmmed Suliman, et al, 2010 in Oman [27], Yang-Chun Han, et al, 2013 in Korea [32], Gazi, et al, 2014 in Turkey [35] and Ergelen, et al, 2014 also in Turkey [28].

### **Limitations of the Study**

The present study must be interpreted within the context of its potential limitations: the sample size was relatively small and may not be representative. Hence, the conclusions deduced from this study cannot be generalized to the general population. This study also was a single-center designed study and further comparative multicenter studies will be needed.

### Conclusion

Patients with high NLR were approximately 43.5%, older and generally had higher prevalence of D.M. and hyperlipidemia than those patients with low NLR. Patients with high NLR were more smokers and Khat chewers than patients with low NLR.

Anterior wall MI was the most dominant type of MI in patients with high NLR compared to patients with low NLR, in whom the inferior wall MI was the most presented type. High NLR group had more elevated CK-MB and Troponin T, more reduced EF and FS compared to low NLR group. The NLR positively correlates with parameters of myocardial damage (CK-MB and Troponin T) and negatively correlates with parameters of myocardial dysfunction (EF and FS).

Patients with high NLR had poorer Killip class than those with low NLR, indicating the significant relation of NLR to the severity of heart failure post-MI. The NLR appeared to be a significant predictor of in-hospital mortality in AMI patients.

### **Conflict of Interest**

The author declares that he has no competing interests.

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### **References**

- [1] C.P. Cannon, A. Battler, R.G. Brindis, et al., American College of Cardiology key data elements and definitions for measuring the clinical management and outcomes of patients with acute coronary syndromes: A report of the American College of Cardiology Task Force on Clinical Data Standards (Acute Coronary Syndromes Writing Committee) J Am Coll Cardiol, 38: 2114-2130, 2013.
- [2] G.K. Hansson, Inflammation, atherosclerosis, and coronary artery disease, N Engl J Med, 352: 1685-1695, 2012.
- [3] I.M. Seropian, S. Toldo, B.W. Van Tassell, et al., Anti-inflammatory strategies for ventricular remodeling following ST-segment elevation acute myocardial infarction, J Am Coll Cardiol, 63: 1593-1603, 2014.
- [4] M. Nahrendorf, F.K. Swirski, Monocyte and macrophage heterogeneity in the heart, Circ Res, 112: 1624-1633, 2013.
- [5] J.E. Alard, A. Ortega-Gomez, K. Wichapong, et al., Recruitment of classical monocytes can be inhibited by disturbing heteromers of neutrophil HNP1 and platelet CCL5, Sci Transl Med, 7: 317ra196, 2015.
- [6] M. Horckmans, I. Ring, J. Duchene, et al., Neutrophils orchestrate post-myocardial infarction healing by polarizing macrophages towards a reparative phenotype, Eur Heart J, 38: 187-197, 2017.
- [7] B.M. Fournie, C.A. Parkos, The role of neutrophils during intestinal inflammation, Mucosal Immunol, 5: 354-366, 2012.
- [8] N.G. Frangogiannis, Regulation of the inflammatory response in cardiac repair, Circ Res, 110: 159-173, 2012.
- [9] J. Nunez, E. Nunez, V. Bodi, et al., Usefulness of neutrophil to lymphocyte ratio in predicting longterm mortality in ST segment elevation myocardial infarction, Am J Cardio, 101: 747-752, 2008.
- [10] B.A. Steppich, P. Moog, C. Matissek, et al., Cytokine profiles and T cell function in acute coronary syndromes, Atherosclerosis, 190: 443-451, 2007.
- [11] L.L. Liu, J.L. Lu, P.L. Chao, et al., Lower prevalence of circulating invariant natural killer T (iNKT) cells in patients with acute myocardial infarction undergoing primary coronary stenting, Int Immunophrmacol, 11: 480-484, 2011.

- [12] X. Cheng, Y.H. Liao, H. Ge, et al., TH1/TH2 functional imbalance after acute myocardial infarction: coronary arterial inflammation or myocardial inflammation, J Clin Immunol, 25: 246-253, 2005.
- [13] D. Engelbersten, L. Andersson, I. Ljungcrantz, et al., T-helper 2 immunity is associated with reduced risk of myocardial infarction and stroke, Arterioscler Thromb Vasc Biol, 33: 637-644, 2013.
- [14] K. Backteman, J. Ernerudh, L. Jonasson, Natural killer (NK) cell deficit in coronary artery disease: no aberration in phenotype but sustained reduction of NK cells is associated with low-grade inflammation, Clin Exp Immunol, 175: 104-112, 2014.
- [15] A.B. Hartopo, I. Puspitawati, B.Y. Setianto, Onadmission High Neutrophil to Lymphocyte Ratio as Predictor of In-hospital Adverse Cardiac Event in ST-elevation Myocardial Infarction, Acta Med Indones-Indones J Intern Med, 47(1): 3-10, 2015.
- [16] J.A.L. Meeuwsen, M. Wesseling, I.E. Hoefer, et al., Prognostic value of circulating inflammatory cells in patients with stable and acute coronary artery disease, Front Cardiovasc Med, 4: 44, 2017.
- [17] M. Akpek, M.G. Kaya, Y.Y. Lam, et al., Relation of neutrophil/lymphocyte ratio to coronary flow to inhospital major adverse cardiac events in patients with ST-elevated myocardial infarction undergoing primary coronary intervention, Am J Cardiol, 110: 621-627, 2012.
- [18] E. Gazi, B. Bayram, Relationship between neutrophil/lymphocyte ratio and complications in patients with acute myocardial infarction, Anatol J Clin Investig, 6(1): 217-220, 2012.
- [19] B. Sarli, A.O. Baktir, H. Saglam, et al., Neutrophilto-lymphocyte ratio is associated with severity of coronary artery ectasia, Angiology, 65: 147-151, 2014.
- [20] S. Chia, J.T. Nagurney, D.F. Brown, et al., Association of leukocyte and neutrophil counts with infarct size, left ventricular function and outcomes after percutaneous coronary intervention for STelevation myocardial infarction, Am J Cardiol, 103: 333-337, 2009.
- [21] M.G. Kaya, M. Akpek, Y.Y. Lam, et al., Prognostic value of neutrophil/lymphocyte ratio in patients with ST-elevated myocardial infarction undergoing primary coronary intervention: A prospective, multicenter study, Int J Cardiol, 168: 1154-1159, 2013.

- [22] S. Ghaffari, M. Nadiri, L. Pourafkari, et al., The predictive value of total neutrophil count and neutrophil/lymphocyte ratio in predicting In-Hospital mortality and complications after STEMI, J Cardiovasc Thorac Res, 6: 35-41, 2014.
- [23] B. Azab, M. Zaher, K.F. Weiserbs, et al., Usefulness of neutrophil to lymphocyte ratio in predicting short- and long-term mortality after non-STelevation myocardial infarction, Am J Cardiol, 106: 470-476, 2010.
- [24] G.K. Lee, L.C. Lee, E. Chong, et al., The long-term predictive value of the neutrophil-to-lymphocyte ratio in type 2 diabetic patients presenting with acute myocardial infarction, QJM, 105: 1075-1082, 2012.
- [25] A.C. Sawant, P. Adhikari, S.R. Narra, et al., Neutrophil to lymphocyte ratio predicts short- and long-term mortality following revascularization therapy for ST elevation myocardial infarction, Cardiology Journal, 21(5): 500-508, 2014.
- [26] Yang-Chun Han, Tae-Hyun Yang, Doo-Il Kim, et al., Neutrophil to Lymphocyte Ratio Predicts Long-Term Clinical Outcomes in Patients with ST-Segment Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention, Korean Circ J, 43: 93-99, 2013.
- [27] Rheem Muhmmed Suliman, Bahnacy Juma, Ali Almadhani, et al., Predictive Value of Neutrophil to Lymphocyte Ratio in Outcomes of Patients with Acute Coronary Syndrome, Archives of Medical Research, 41: 618-622, 2010.
- [28] M. Ergelen, H. Uyarel, S. Altay, et al., Predictive value of elevated neutrophil to lymphocyte ratio in patients undergoing primary angioplasty for STsegment elevation myocardial infarction, Clin Appl Thromb Hemost, 20: 427-432, 2014.
- [29] Jingyu He, Jing Li, Yunfei Wang, et al., Neutrophilto-lymphocyte ratio (NLR) predicts mortality and adverse-outcomes after ST-segment elevation myocardial infarction in Chinese people, Int J Clin Exp Pathol, 7(7): 4045-4056, 2014.
- [30] Uzma Gul, Sajjad Hussain, Rubab Munir, et al., Neutrophil Lymphocyte Ratio: A Prognostic Marker in Acute ST Elevation Myocardial Infarction, Journal of the College of Physicians and Surgeons Pakistan, 27(1): 4-7, 2017.
- [31] D. Hong, K.H. Choi, Y.B. Song, et al., Prognostic implications of post-percutaneous coronary intervention neutrophil-to lymphocyte ratio on infarct size and clinical outcomes in patients with acute myocardial infarction, Scientific Reports, 9: 9646, 2019.

- [32] C. Chen, B.L. Cong, M. Wang, et al., Neutrophil to lymphocyte ratio as a predictor of myocardial damage and cardiac dysfunction in acute coronary syndrome patients, Integr Med Res, 7(2): 192-199, 2018.
- [33] M. Gul, H. Uyarel, M. Ergelen, et al., Predictive Value of Neutrophil to Lymphocyte Ratio in Clinical Outcomes of Non-ST Elevation Myocardial Infarction and Unstable Angina Pectoris: A 3-Year Follow-Up, Clinical and Applied Thrombosis/Hemostasis, 20(4): 378-384, 2014.
- [34] A.M. Shumilah, A.M. Othman, A.K. Al-Madhagi, Accuracy of neutrophil to lymphocyte and monocyte to lymphocyte ratios as new inflammatory markers in acute coronary syndrome, BMC Cardiovasc Disord, 21: 422, 2021.
- [35] E. Gazi, B. Bayram, S. Gazi, et al., Prognostic Value of the Neutrophil– Lymphocyte Ratio in Patients with ST-Elevated Acute Myocardial Infarction, Clinical and Applied Thrombosis/Hemostasis, 21(2): 155-159, 2015.

مقالة بحثية

دور نسبة العدلات إلى اللمفاويات كمؤشر حيوي تنبؤي لدى مرضى احتشاء عضلة القلب الحاد في مستشفى الجمهورية العام النموذجي – عدن – اليمن

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### المُلخّص

يلعب الالتهاب دوراً أساسياً في نشوء تصلب الشرايين وفي تكون مرض احتشاء عضلة القلب الحاد. تُعرف نسبة العدلات إلى اللمفاويات بأنها علامة التهابية للتنبؤ بحدة احتشاء عضلة القلب الحاد. هدف البحث هو تحديد دور نسبة العدلات إلى اللمفاويات كمؤشر حيوي تنبؤي لدى مرضى احتشاء عضلة القلب الحاد في مستشفى الجمهورية العام النموذجي – عدن، حيث أجريت در اسة وصفية مستعرضة في مستشفى محتى مرضى احتشاء عضلة القلب الحاد في مستشفى الجمهورية العام النموذجي – عدن، حيث أجريت در اسة وصفية مستعرضة في مستشفى الجمهورية العام النموذجي خلال الفترة من مارس حتى أغسطس 2022م. وتضمنت الدر اسة 124 مريضاً شُخصوا باحتشاء عضلة القلب الحاد في مستشفى الجمهورية العام النموذجي – عدن، حيث أجريت در اسة وصفية مستعرضة في مستشفى حيث تم تصنيفهم إلى مجمو عتين: 70 مريضاً لديهم نسبة عدلات إلى ليمفاويات منخفضة، و 34 مريضاً لديهم نسبة عدلات إلى لمفاويات مرتفعة. وكات النتائج كما يلي: من بين 124 مريضاً لديهم نسبة عدلات إلى ليمفاويات مرتفعة أو 2.5 سببة عدلات إلى لمفاويات مرتفعة. وكانت النتائج كما يلي: من بين 124 مريضاً لديهم نسبة عدلات إلى لمفاويات مرتفعة أو 2.5 سببة عدلات إلى لمفاويات مرتفعة أو 2.5 سببة العدلات إلى لمفاويات مرتفعة. وكانت النتائج كما يلي: من بين 124 مريضاً دق.5 من المرضى كان لديهم نسبة عدلات إلى لمفاويات منغضة، و 2.5 سببة عدلات إلى لمفاويات مرتفعة أكبر عمراً (2.3 ± 2.5 مريضاً لديم نسبة عدلات إلى ليمفاويات منغضة. و 2.5 سببة الدين لديمم نسبة عدلات إلى ليمفاويات منغطي أو كثر مضعاً للقات موانة بألمارضي الذين لديمم نسبة عدلات إلى ليمفاويات منغضة. إلى مستويات التروبونين 1 (Troponin 1) وكانت مرقعة أكبر عمراً (2.5 ± 2.5 سببة العدلات إلى ليمفاويات منغة أعلى، ونسبة المدان العرضي القدافي (الموادي القدائي أو ملع ملون العارمين القدين 10 (Troponin 2) وكانت العار العاد إلى المفاويات منغوضية، وكان لدي معمو عة نسبة العدلات إلى ليمفاويات المنغفية إلى ونسبة العدلات إلى لمفاويات المزيفي ألدى مجمو عة نسبة العدلات إلى لمفاويات المرتفعة أعلى، وعسبة العدلات إلى المفاويات المرتفعة أو 2.5 سببة العدلات إلى المفاويات المرتفعة فأ والنة مجمو عة نسبة العدلات إلى المفاويات المرتفعة فئة والنا المناويات المز تعبو ألى 1.6 ((20.0 حوالي المان العنا أوى كرضي ألدي مرص الونة داخل المستشفى موار

الكلمات المفتاحية: نسبة العدلات إلى اللمفاويات، احتشاء عضلة القلب الحاد، مؤشر حيوي تنبؤي.

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