VOLUME - 12, ISSUE - 04, APRIL - 2023 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

General Medicine

CLINICAL SIGNIFICANCE OF NEUTROPHIL TO LYMPHOCYTE RATIO IN PREDICTING THE OUTCOME IN PATIENTS PRESENTING WITH ACUTE CORONARY SYNDROME : A DESCRIPTIVE LONGITUDINAL STUDY

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ABSTRACT

Introduction: Cardiovascular disease is the leading cause of death worldwide, which accounts to about 17.7 million deaths worldwide.This makes it a paramount importance in finding newer bio markers which adds to the better prognostication. Recently Neutrophil to Lymphocyte ratio has gained the clinical importance in predicting the mortality and morbidity in patients with acute coronary syndrome owing to the association of inflammatory reaction in pathogenesis of ACS. The present study was done to correlate the Neutrophil to Lymphocyte ratio in predicting the outcome in patients presenting with acute coronary syndrome. **Aim:** To determine the significance of Neutrophil to Lymphocyte ratio in prognostication and risk stratification in patients presenting with acute coronary syndrome. **Methodology:** This is a short term hospital based study conducted in 150 patients presenting to tertiary care hospital with ACS. The data obtained from the hemogram, biochemical and radiological investigations were correlated between those without complications and those who developed complications in the due course in the hospital.Neutrophil to lymphocyte ratio is calculated for all these patients and were grouped into three tertiles for analysis as low NLR<2.6, medium NLR 2.6-4.5 and high NLR >4.5. Later prognostic efficacy of NLR ratio in these patients was determined. **Results:** In our study it was found that high NLR was significantly associated with development of complications (P <0.001). It was also observed that all those patients who expired came under high NLR tertile. There was trend towards significance with high NLR being more common in smokers i.e (43.9% v/s low or medium NLR 28.8% (p=0.072).High NLR was associated with high HsCRP both at 0 and 48 hrs. There was a trend towards significance , with high NLR being more common in STEMI patients (49% v/s 32.7% in low /medium NLR group, P= 0.055) **Conclusion:** Assessment of NLR proves to be efficient in risk stratification and prognostication in patients with acute coronary syndrome. Higher incidence of mortality or increased length of stay was observed with high NLR values.

KEYWORDS :

INTRODUCTION

The neutrophil-to-lymphocyte ratio (NLR) is a simple and easily measurable marker of systemic inflammation that has been studied in various cardiovascular diseases. In acute coronary syndrome (ACS), which includes unstable angina, non-ST-segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI), NLR has been identified as a potential biomarker of disease severity and prognosis.

Studies have shown that elevated NLR levels are associated with worse clinical outcomes in ACS, including increased risk of major adverse cardiovascular events (MACE), such as recurrent myocardial infarction, stroke, and death. In addition, higher NLR levels have been associated with larger infarct sizes, increased incidence of heart failure, and poorer left ventricular function.

NLR has also been shown to be a useful tool for risk stratification in ACS patients. It can help identify patients who are at higher risk of adverse outcomes and may benefit from more aggressive management strategies. Moreover, NLR can be used as a prognostic marker to guide treatment decisions and monitor response to therapy.

The significance of NLR in ACS lies in its potential to improve risk stratification, prognostication, and clinical decision-making. By incorporating NLR into clinical practice, healthcare providers may be able to more accurately identify patients at higher risk of adverse outcomes and tailor their management accordingly. This could lead to improved patient outcomes and reduced healthcare costs. Thus our study aims to determine the efficacy of NLR in prognostication and risk stratification of ACS.

METHODOLOGY

In this study we included 150 cases of ACS admitted at MIMS Mandya hospital during 2021-2022 who satisfied inclusion and exclusion criteria

Inclusion Criteria

Chest pain
ECG satisfying the diagnostic criteria of ACS
CKMB levels double the normal limit

Exclusion Criteria

Recent infection
Haematological disease
Autoimmune disease
Severe renal disease (GFR<30ml/min/1.73m^2)
Severe liver disease
Ongoing treatment with immunosuppressive agents.

Patients were interviewed at admission for history and thorough physical examination was done. Venous sample was taken for hemogram, biochemical investigations were done including cardiac enzymes . ECHO was done for all these patients. The patients were grouped into three tertiles for analysis as low NLR<2.6, medium NLR 2.6-4.5 and high NLR >4.5. All these patients were followed up for the length of their stay in hospital and their mortality and morbidity status was assessed. Later prognostic efficacy of NLR ratio in these patients was determined.

Statistical Analysis

The data was entered using Microsoft Excel software. Data was analysed using SPSS. Analysis was tested using chi square test, Fischer exact test, independent sample t test. Continuous data were expressed as percentage. A P value of <0.05 was considered as statistically significant.

RESULTS

For the present study we included all the consenting patients with Acute Coronary Syndrome admitted to the intensive care unit of a tertiary care hospital MIMS, Mandya.A total of 150 patients who satisfy inclusion and exclusion criteria were included in the study. We grouped the patients into three tertiles for NLR assessment low NLR <2.6, medium NLR 2.6-4.5 and high NLR >4.5. Since only 2 patients came under low NLR we have clubbed low and medium NLR and assessment of the

same was done against high NLR.

NLR and Complication

Table 1: NLR and Complications

Complication	NLR			P-value
	Low or Medium NLR	High NLR	Total	
With complications	0 (0%)	31 (31.6%)	31 (20.7%)	<0.001
Without complications	52 (100%)	67 (68.4%)	119 (79.3%)	
Total	52	98	150	

P-value is based on chi-squared test.

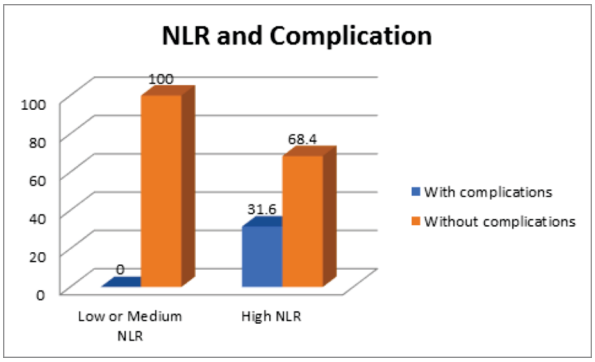

Fig 1: NLR and Complications

Based on the above table it appears that NLR (neutrophil lymphocyte ratio) is associated with occurrence of complications in acute coronary syndrome. The table shows the number and percentage of patients with low/medium NLR and high NLR in two groups – with and without complications

Among the patients with complications non had low/ medium NLR, while 31(31.6%) had high NLR. Among the patients without complications, 52(43.7%) had low / medium NLR and 67(56.3%) had high NLR

The chi-squared test result suggests that there is significant association between NLR and occurrence of complications (P<0.001). i.e, patients with high NLR are more likely to experience complications compared to those with low/ medium NLR

NLR and Mortality

Table 2: NLR and Mortality

Mortality	NLR			P-value
	Low or Medium NLR	High NLR	Total	
Yes	0 (0%)	4 (4.1%)	4 (2.7%)	0.299
No	52 (100%)	94 (95.9%)	146 (97.3%)	
Total	52	98	150	

P-value is based on Fisher Exact test.

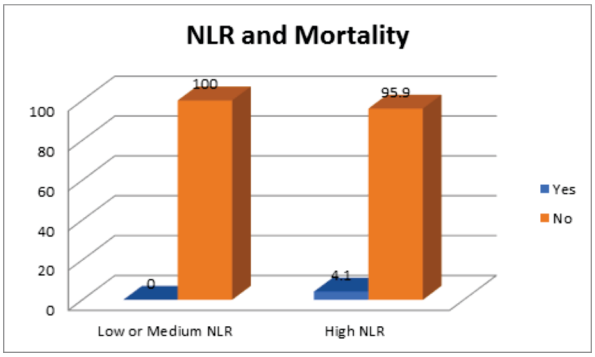

Fig 2: NLR and Mortality

Based on the above given table, it appears that there is no significant association between NLR(Neutrophil to Lymphocyte Ratio) and mortality. The table shows the number and percentage of patients with low / medium NLR and high NLR in two groups – those who died(yes) and those who did not die (no).

Among the patients who died, none had low/ medium NLR. Among the patients who did not die, 52 (35.6%) had low/ medium NLR and 94 (64.4%) had high NLR.

The Fisher Exact test result suggests that there is no significant association between NLR and mortality (P=0.299). This means that patients with high NLR are not more likely to die compared to those with low/ medium NLR.

NLR and HsCRP

Table 3: NLR and HsCRP

	Low or Medium NLR Mean ± SD	High NLR Mean ± SD	P -Value
HsCRP at 0 hour	1.9 ± 3.1	3.3 ± 5.5	0.046
HsCRP at 48 hour	1.2 ± 2.3	4.4 ± 7.2	<0.001

P-values are based on two independent samples t-test.

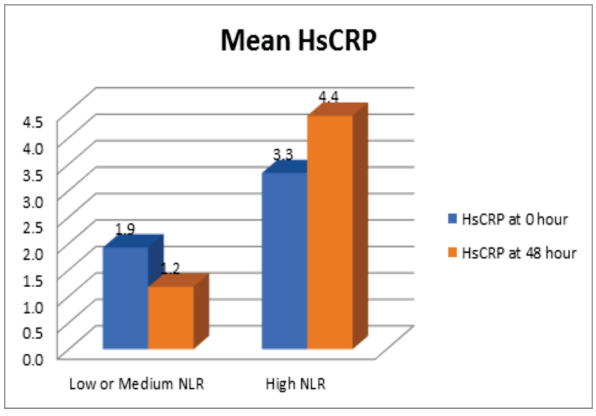

Fig 3: NLR and HsCRP

Based on the above given table , it appears that NLR is associated with levels of hsCRP (high sensitivity C Reactive Protein), a marker of inflammation. The table shows the mean and standard deviation (SD) of hsCRP level at 0 hr and 48 hr in two groups – low / medium NLR and high NLR.

Among the patients with low / medium NLR , mean hsCRP level at 0hr was 1.9±3.1mg/L, while among those with high NLR, it was 3.3±5.5mg/L, The difference was statistically significant with. p value of 0.046.

Similarly among the patients with low/ medium NLR, the mean hsCRP level at 48hr was 1.2±2.3mg/L, While amomg those with high NLR, it was 4.4±7.2mg/L, The difference was highly significant with a p value of <0.001.

These results suggest that patients with high NLR have higher level of hsCRP, indicating a greater degree of inflammation compared to those with low / medium NLR.

NLR and Diagnosis

Table 4: NLR and Diagnosis

Diagnosis	NLR			P-value
	Low or Medium NLR	High NLR	Total	
STEMI	17 (32.7%)	48 (49%)	65 (43.3%)	0.055
NSTEMI/UA	35 (67.3%)	50 (51%)	85 (56.7%)	
Total	52	98	150	

P-value is based on chi-squared test.

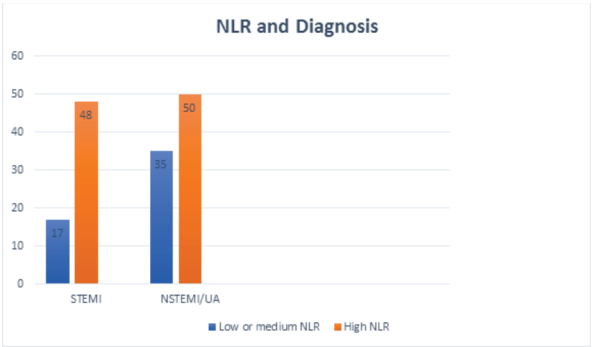

Fig 4: NLR and Diagnosis

Based on the given above table, it appears t there is marginally significant association between NLR and the diagnosis of types of acute coronary syndromes, STEMI and NSTEMI/UA

The above table shows the number and percentage of patients with low/ medium NLR and high NLR in two groups STEMI and NSTEMI/UA. Among the patients with STEMI, 17(32.7%) had low / medium NLR and 48(49%) had high NLR. Among the patients with NSTEMI/UA, 35 (67.3%) had. Low/medium NLR and 50 (51%) had high NLR.

The chi-squared test result suggests a marginally significant association between NLR and diagnosis ($p = 0.055$), indicating that patients with STEMI may have higher likelihood of having high NLR compared to those with NSTEMI/UA. However, the association is not strong enough to reach statistical significance.

DISCUSSION

NLR stand for neutrophil to lymphocyte ratio, which is a ratio of the number of neutrophils to the number of lymphocytes. ACS stands for acute coronary syndrome, which is a clinical syndrome that includes STEMI,NSTEMI and unstable angina (UA).

There is a growing evidence that suggests that neutrophil to lymphocyte ratio (NLR) is associated with the pathogenesis of acute coronary syndrome (ACS). Elevated levels of NLR have been found to be associated with increased risk of poor prognosis in patients with ACS.

In 2018, A meta analysis of 17 studies involving a total of over 8988 patients found that higher NLR levels were significantly associated with an increased risk of ACS. Another meta-analysis by Chao-Hui Dong et al published in 2018 found that elevated NLR levels were associated with a higher risk of adverse cardiovascular events in patients with ACS[2].

Several studies have shown that NLR levels are significantly higher in patients with ACS compared to healthy individuals. This suggest that NLR may play a role in the pathogenesis of ACS. Neutrophils are known to play a crucial role in the pathogenesis of ACS by promoting inflammation, oxidative stress and thrombosis[3]. On the other hand, lymphocytes play a protective role by limiting inflammation and promoting tissue repair[4].

It has been proposed that high NLR is indicative of an imbalance between neutrophils and lymphocytes, which leads to pro- inflammatory state and impaired tissue repair mechanisms. This imbalance can promote the progression of atherosclerosis, plaque rupture, and subsequent thrombosis , leading to ACS.

In our study it was observed that there was significant association between NLR and occurrence of complications ($p < 0.001$), which is in conjunction with the previous studies which showed significant association between the NLR and complications in ACS.One study published in 2017 examined the association between NLR and in- hospital mortality in patients with ACS. This study found that patients with higher NLR levels were likely to develop complications such as cardiogenic shock, heart failure and arrhythmias[5]. Another study published in 2018 examined the association between NLR and long term outcomes in patients with ACS. The study found that elevated NLR levels were associated with higher risk of all- cause mortality, major adverse cardiovascular events, and stent thrombosis[6]. Though the previous studies showed significant association between high levels of NLR with mortality, It was observed in our study that there was no significant association between NLR and mortality ($p = 0.299$).

In our study it was observed that there was significant association between high NLR and higher hsCRP levels thus provides the evidence that NLR can be a useful indicator of the degree of inflammation in acute coronary syndrome which is in conjunction with the study published in 2017 in international journal of inflammation which showed significant association between higher NLR levels with higher hsCRP levels in patients with ACS[7]. Another study examined the association between NLR, hsCRP, and the severity of ACS. The study found that both NLR and hsCRP levels were significantly higher in patients with more severe ACS. The researchers also found a positive correlation betweenNLR and hsCRP levels in these patients[8]. Thus both bio markers may be useful in predicting the severity and prognosis in ACS

In our study it was observed that there was marginally significant association between NLR and diagnosis ($p = 0.055$) , indicating that patients with STEMI to have higher inflammatory burden as compared to NSTEMI and UA, A study published in 2016 in American Journal of cardiology found that NLR levels were significantly higher in patients with STEMI compared to those with NSTEMI[9]. Another study published in the scientific reports in 2021 found that elevated NLR levels were an independent predictor of STEMI in patients with ACS[10]. In addition to predicting the risk of STEMI, there is also evidence to suggest that NLR may be useful in assessing the severity and prognosis of the condition. A 2021study published in journal Angiology found that higher NLR levels were associated with larger infarct size in patients with STEMI[11]. Another study published in 2018 in International Journal of Cardiology found that elevated NLR levels were associated with a higher risk of adverse cardiovascular events in patients with STEMI[6].

Limitations

In the present study we have included only 150 patients. Our study determines the association between NLR and in-hospital mortality and the complications. The association between the NLR and survival and other adverse events post discharge could not be assessed.

CONCLUSION

In our study there was positive correlation between the higher NLR levels and occurrence of complications. It was also observed that there was association between higher NLR levels with STEMI as compared to NSTEMI and UA owing to the increased inflammatory burden in STEMI. Thus, NLR is a promising bio marker that could potentially aid in the diagnosis, risk stratification, and management of patients with ACS.

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