



Original Research Article

To correlate the value of neutrophil to lymphocyte ratio with prognosis of ST-elevation myocardial infarction and non ST-elevation myocardial infarction patients at a tertiary care hospital

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ABSTRACT

Introduction : Myocardial infarction (MI) is one of the leading causes of death in India. Atherosclerosis is the major predisposing factor. Leucocytes play an important role in the formation of arterial thrombus, the healing process and the reperfusion injury in post-MI cases. Hence Neutrophil to Lymphocyte Ratio [NLR] is a potential marker to determine inflammation in cardiac disorders. It is inexpensive, easy to obtain and is widely available.

Material and Methods: A detailed medical history was obtained from the study population. Report of ECG changes, absolute neutrophil count and absolute lymphocyte count at the time of admission was noted down from the laboratory reports attached to the case sheets. The NLR was calculated.

The patients were classified into 2 groups based on ECG changes

1. STEMI group

2. NSTEMI group

Follow up was done for the duration of hospitalisation and complications, if any during this period were noted.

Discussion: The study included a total of 62 study subjects with 31 in STEMI group and 31 in NSTEMI group. Among MI cases with $NLR < 2.5$, 6/15 were referred to higher centre and 9/15 were discharged. Among MI cases with $NLR \geq 2.5$, 13/47 cases were referred to higher centre and 34/47 were discharged. In this study, NLR between 2 groups had no statistically significant difference in occurrence of complications

Conclusion: This study demonstrated that average NLR is not useful indicator of adverse-outcomes during hospitalization in patients presenting with STEMI and NSTEMI.

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1. Introduction

Myocardial infarction (MI) is one of the leading causes of death in India. In men aged 29-69 years, the incidence of MI in India is 64.37/1000 people.¹ The incidence of Major Acute Cardiovascular Events and death is linked to elevated total leukocyte count (TLC).² A potential marker to determine inflammation in cardiac and non-cardiac disorders is the Neutrophil to Lymphocyte Ratio (NLR).³ It is inexpensive, easy to obtain and is widely available.⁴

The reports of previous studies show that there is an increased risk of mortality, re-infarction, severity of Coronary Artery Disease (CAD), hospitalisation for heart failure and post MI complications in patients who had a higher NLR.⁵⁻⁷

The prognostic value of NLR in ST-elevation MI [STEMI] is well established. Higher the value of NLR, poorer is the prognosis of STEMI.⁶ Very few studies have been done to establish the prognostic value of NLR in non ST-elevation MI [NSTEMI].

The purpose of this study is to determine the NLR and to correlate NLR with prognosis of both NSTEMI and STEMI

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Ischemic heart disease can be divided into stable coronary artery syndrome (presenting as angina pectoris) and acute coronary syndrome (unstable angina or MI).

The primary cause of different manifestations of coronary artery disease (CAD) including acute coronary syndrome (ACS), myocardial infarction, and angina pectoris is atherosclerosis.⁸

Risk factors such as hypertension, smoking, diabetes mellitus and high plasma levels of low density lipoproteins, disturb the normal function of the endothelium which results in an impairment of maintenance of an anti-thrombotic surface and local control of vascular tone within the coronary vessel.⁹ The clinical consequences of the thrombus depend on the the composition of the plaque, depth of the injury, the extent of platelet activation, and the site of the thrombus.¹⁰

1.1. Consequences and complications of myocardial infarction⁸

Contractile dysfunction, papillary muscle dysfunction, right ventricular infarction, myocardial rupture, arrhythmias, pericarditis, chamber dilation, mural thrombus. ventricular aneurysm and progressive heart failure.

The risk for complications and the overall prognosis depends on infarct size, site, and type (subendocardial versus transmural infarct)

1.2. Myocardial damage is detected using

1. Cardiac biochemical markers like troponin, creatine kinase isoenzyme (CK-MB)
2. Electrocardiogram (ECG) ECG signs of myocardial ischaemia are defined as ST segment elevation or depression ≥ 0.2 mV in one lead or ≥ 0.1 mV in at least two adjacent leads.
3. Imaging techniques

Cardiac imaging techniques is a diagnostic criteria in line with symptoms and ECG changes; Echocardiography, computed tomography (CT) and magnetic resonance imaging (MRI) have been increasingly used in the setting of acute coronary syndrome (ACS) in recent years.¹¹

1.3. Haematological parameters in myocardial infarction

The non-specific reaction to myocardial injury is associated with polymorphonuclear leukocytosis, which appears within a few hours after the onset of pain and persists for 3–7 days; the white blood cell count often reaches levels of 12,000–15,000/cumm.¹¹

1.4. Atherogenesis and the Neutrophil/Lymphocyte Ratio

Atherosclerotic plaques are usually associated with neutrophilia together with lymphopenia as a result of endothelial dysfunctions.

Infarcted patients have elevated cortisol levels. This increase induces the reduction of lymphocytes by apoptosis, and CD4+ and CD8+ cells become more sensitive to tumor necrosis factor-alpha (TNF- α). This is one of the most likely mechanisms to explain lymphopenia developed during cardiovascular disease evolution. However, the pathophysiological mechanism of this decrease has not yet been fully elucidated.^{12,13}

On the other hand, mechanisms related to neutrophilia in cardiovascular diseases are more clarified, especially in atherosclerosis. Neutrophils act through lipid mediation, necrosis and inflammation secreting chemokines and cytokines. This cell type regulates ICAM-1 and expresses MPO, a protein that contributes to the formation of free radicals, promoting greater LDL oxidation, exacerbating the pathological process.¹⁴

2. Objectives

1. To correlate NLR in with prognosis of STEMI and NSTEMI .
2. To correlate the NLR with the changes in ECG.

3. Materials and Methods

3.1. Study Population

Patients with Myocardial Infarction admitted to Department of General Medicine, Mandya Institute of Medical Sciences, Mandya who fulfil the inclusion and exclusion criteria.

3.2. Inclusion criteria

1. Patients who give consent to the study
2. Patients with Myocardial Infarction of both the sexes and above the age of 18 years.
3. Patients with Electrocardiography change suggestive of Myocardial Infarction (ST elevation or T wave inversion) and elevated cardiac enzymes (CK-MB, Troponin-I).

3.3. Exclusion criteria

1. Patients with history of any conditions which can alter total or differential leukocyte count such as trauma, surgery, neoplasm or infectious disease 30 days before admission.
2. Patients with history of haematological disorders, blood transfusion and those who had receiving immunosuppressant, steroid therapy or chemotherapy

3.4. Clinical methodology

A detailed medical history and a questionnaire on risk factors were obtained from each patient from their case sheets and by interacting with the patients.

Report of ECG changes, values of CK-MB, troponin, absolute neutrophil count [ANC] and absolute lymphocyte count [ALC] at the time of admission was noted down from the laboratory reports attached to the case sheets.

The patients were classified into 2 groups based on ECG changes

1. STEMI patients: It includes the patients whose ECG report shows ST segment with presence of elevated cardiac markers
2. NSTEMI patients: It includes the patients whose ECG report shows no raise in the ST segment with T wave inversion and presence of elevated cardiac markers

The Neutrophil to Lymphocyte ratio is obtained by dividing the absolute neutrophil count by the absolute lymphocyte count.

The MI patients were hospitalised for heparin therapy for 3-5 days. The patients were referred to higher centre if they developed any complications of MI and those without any complications during hospital stay were discharged with an advice for complete cardiovascular evaluation by cardiologists at higher centre.

Follow up was done for the duration of hospitalisation and complications if any during this period were noted.

3.5. Statistical methodology

Data was entered in Microsoft Excel software. Analysis was done using SPSS software to calculate descriptive statistics like proportion, mean, standard deviation, etc. Inferential statistical tests like ANOVA and Fisher’s Exact tests were used to find the association between qualitative data, Kruskal-Wallis rank sum test is used to determine the difference between means and standard deviation

4. Results

Abbreviations: HTN, hypertension; DM, diabetes mellitus; TLC, total leucocytic count; ANC, absolute neutrophilic count; ALC, absolute lymphocytic count; NLR, neutrophil-to-lymphocyte ratio; NSTEMI, non-ST elevation myocardial infarction; STEMI, ST elevation myocardial infarction.

5. Discussion

We have conducted this study to determine the NLR in patients presenting with MI and to assess the association between NLR at admission and occurrence of complications of MI during hospital stay in patients with NSTEMI or STEMI.

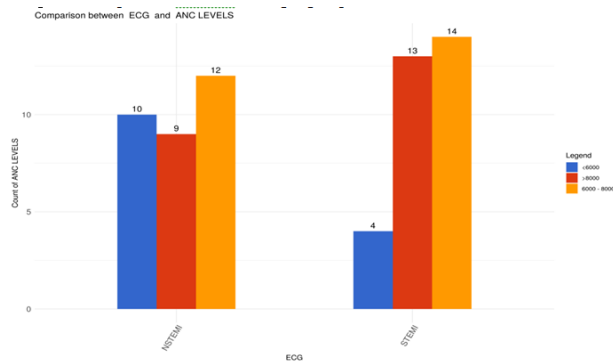


Fig. 1: Comparison of ANC among 2 groups

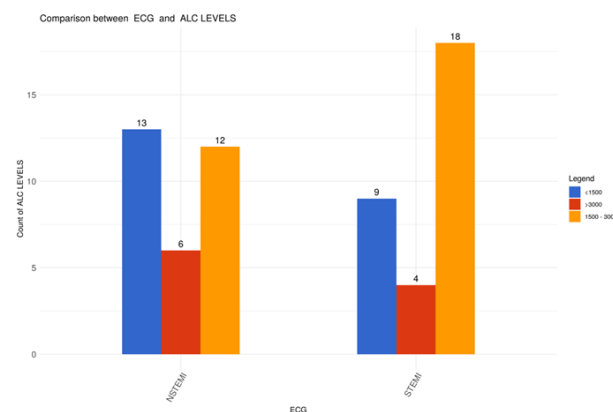


Fig. 2: Comparison of ALC among 2 groups

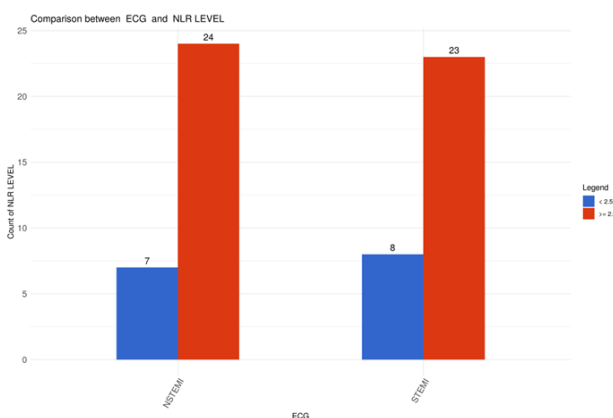
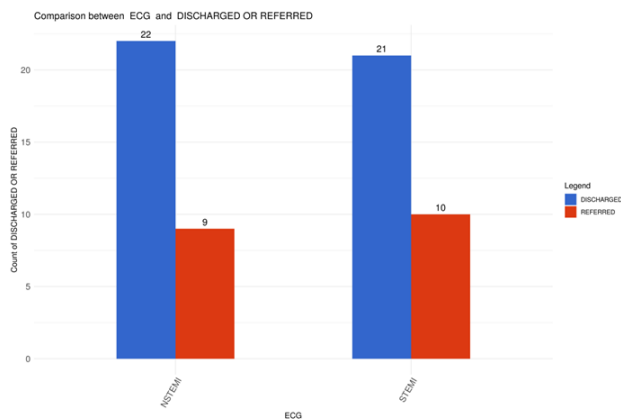


Fig. 3: Comparison of NLR among 2 groups

Table 1: Distribution of NLR among study population

Variables	NLR <2.5	NLR ≥2.5	p value	
Age (years <i>average</i>)	65	60	0.218486	ANOVA
Male gender(n)	9	31	0.760111	
HTN(n)	8	17	0.364903	
DM(n)	5	21	0.553158	Fisher's Exact Test
Alcohol(n)	6	19	1	
Smoking(n)	6	24	0.558173	
TLC (average) cells/cumm	11701.33	10225.02	0.136768	Kruskal-Wallis rank sum test
ANC (average) cells/cumm	6487.47	8342.51	0.034667	
ALC(average) cells/cumm	4432	1537.62	0	
STEMI(n)	8	23	1	Fisher's Exact Test
NSTEMI(n)	7	24		
Discharged(n)	9	34	0.520814	
Referred(n)	6	13		

**Fig. 4:** Comparison of outcome among two groups

The study included a total of 62 study subjects with MI. Thirty one among them showed ST elevation on ECG (STEMI), other 31 did not show ST elevation on ECG (NSTEMI).

Forty(64.6%) of them were males with average age of 60 years with mean TLC of 10340cells/cumm, mean ANC of 7700cells/cumm, mean ALC of 2160cells/cumm and average NRL of 5.59

Twenty two(35.4%) of them were females with average age of 63years with mean TLC of 11020cells/cumm. mean ANC of 8240cells/cumm, mean ALC of 2377 cells/cumm and average NRL of 5.65

Among 62 cases studied, 25(40.3%) had hypertension, 26(41.9%) had diabetes mellitus, 30(48.4%) were smokers and 25(40.3%) were chronic alcoholics.

5.1. Absolute Neutrophil count

The average ANC of patients who were discharged was 8286 cells/cumm whereas the average ANC of those referred to higher centre was 7006 cells/cumm

In the present study, neutrophil counts were divided into 3 groups. And of which 22 patients had neutrophil count of >8000cells/cumm, 14 had neutrophil count <6000cells/cumm and 26 with neutrophil count between 6000-8000cells/cumm. Comparing between groups, 9 cases of NSTEMI and 4 cases of STEMI had ANC >8000cells/cumm Figure 1 .

5.2. Absolute Lymphocyte count

The average ALC of patients who were discharged was 2278 cells/cumm whereas the average ALC of those referred to higher centre was 2147 cells/cumm

Lymphocyte counts in the study groups were divided into 3 groups. Of the total patients 22 had counts of <1500cells/cumm, 30 had counts between 1500-3000cells/cumm and 10 had counts of more than 3000cells/cumm. Figure 2

5.3. Neutrophil to lymphocyte ratio

The mean NRL among male is 5.59 and the mean NRL among female is 5.65

Mean NRL of those who were discharged without any complications at the time of admission was 5.44 and 6.02 for those who were referred to higher centre

In this study, patients were divided into 2 groups on the basis neutrophil to lymphocyte ratio.

- 1 Patients with neutrophil to lymphocyte ratio < 2.5 and
- 2 Patients with neutrophil to lymphocyte ratio ≥2.5.

Of the total sample of 62, 15 patients had NRL of <2.5. Dividing between groups patients with NSTEMI had more number of patients (8 cases) with NRL of ≥2.5 than patients with STEMI (7 cases). Figure 3

Among MI cases with NRL < 2.5, 6/15 were referred to higher centre and 9/15 were discharged

Among MI cases with NRL ≥ 2.5, 13/47 cases were referred to higher centre and 34/47 were discharged.

NLR as previous studies have shown would be influenced by both increase in neutrophils and decrease in lymphocytes. Low NLR may result from both increased migration of neutrophils from blood vessels to peripheral tissues, and increased lymphocyte counts in the acute phase of STEMI. As NLR takes into account both variables simultaneously, it would be better than looking into single variable.

In this study, NLR between 2 groups had no statistically significant difference on occurrence of complications as the patients who were discharged had higher value of NLR ratio than patients who were referred to higher centres

Not many studies have been conducted to correlate NLR ratio at admission with complication occurring in the first 5 days of admission following MI.

Three studies have been previously published concerning the predictive capacity of NLR in STEMI or NSTEMI^{13,15,16} in different time. Park et al. reported that when patients were stratified by NLR measured 24 hours after admission for STEMI, NLR predicted mortality more accurately than when NLR at admission was used¹⁵. However, Azab et al. employed average NLR, calculated as an average of the NLR during hospitalization, was a better predictor of outcome than other max NLR, or NLR at admission or discharge in patients presenting with NSTEMI¹³. And Núñez et al. reported that the maximum NLR recorded during the first 96 hours after STEMI predicted mortality better than the maximum value of leucocyte¹⁶

One major obstacle in implementing NLR-based predictive prognostic matrices is determining an appropriate cut-off value. The appropriate NLR cut-off is likely to change with laboratory techniques employed, the stage of illness, concomitant infection and patient demographic characteristics¹⁷

Therefore, a large multicentre study employing a clinically significant NLR cut off rather than NLR interval grouping will be required to develop an appropriate cut-off for NLR

6. Conclusion

In our study there was no significant correlation of NLR on outcome of patients both in STEMI and NSTEMI. This is probably due to

1. NLR, Only at admission was considered.
2. The duration of follow up was very less to accurately predict the prognostic value of NLR. A longer-term (more than one month) of follow up may be needed for more comprehensive assessment of relationship between NLR and long-term mortality outcome.
3. Alternative concomitant etiologies for elevated NLR may have been present and not accounted for e.g. occult infection or malignancy.

4. Duration of MI symptoms may have an important impact on NLR levels but was not addressed in current study.
5. We did not compare the prognostic value of NLR with other inflammatory markers such as: C-reactive protein, fibrinogen, myeloperoxidase, tumor necrosis factor α or interleukin (IL)-6 etc.
6. This was a non-randomized single centre study that included a relatively small number of patients was subject to selective bias and possibly restricted us from identifying and analyzing all potential confounding factors.
7. NLR might be a useful marker in risk scoring, while the cut-off points and normal ranges should be furthermore determined by randomized multicenter trials.

While a single baseline admission complete blood count sampling has the benefit of being readily available, serial sampling may potentially yield a better analytical time point. However, since the exact time to peak inflammatory response after STEMI remains unknown, it is difficult to determine the most efficient collection time.

A larger multi-centre study with larger population size and diversity is warranted to best determine the future prognostic role of NLR, its best predictive cut off value, and sampling time.

7. Source of Funding

None.

8. Conflict of Interest

None.

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