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Original Article

Evaluation of Neutrophil-to-Lymphocyte Ratio and Monocyte-to-Lymphocyte Ratio in Newly Diagnosed Patients with Myocardial Infarction

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ABSTRACT

Background: Myocardial infarction (MI) remains a leading cause of mortality worldwide, with India contributing significantly to global cardiovascular deaths. Inflammatory biomarkers accessible through routine complete blood counts offer potential as cost-effective prognostic tools.
Objectives: To evaluate the association of Neutrophil-to-Lymphocyte Ratio (NLR) and Monocyte-to-Lymphocyte Ratio (MLR) with in-hospital mortality in newly diagnosed MI patients.
Methods: Across-sectional study was conducted at Geetanjali Medical College and Hospital, Udaipur, from July 2023 to February 2024, involving 150 newly diagnosed MI patients. NLR and MLR were calculated from admission complete blood counts. Demographic data, cardiac biomarkers, and outcomes were recorded. Statistical analysis included Chi-square tests, ROC curve analysis, and calculation of sensitivity, specificity, and AUC.
Results: Among 150 patients, 88.67% were male and 50.67% were aged <40 years. NLR was significantly elevated in deceased patients (11.16 ± 10.87) compared to survivors (4.61 ± 5.01; p=0.049). MLR was significantly lower in deceased patients (2.00 ± 1.20 vs. 3.12 ± 1.57; p=0.004). NLR >2.3 demonstrated high sensitivity (90.1%) and good diagnostic accuracy (AUC=0.766, 95% CI: 0.619-0.888) for identifying mortality risk. Mortality increased with age, with the >60 years group showing the highest mortality rate (25%).
Conclusion: NLR is a highly sensitive prognostic marker for in-hospital mortality in MI patients, while MLR shows a paradoxical association requiring further investigation. These parameters offer accessible, cost-effective tools for early risk stratification.

Keywords: *Myocardial infarction, Neutrophil-to-Lymphocyte Ratio, Monocyte-to-Lymphocyte Ratio, inflammatory markers, prognosis, mortality.*

INTRODUCTION

Myocardial infarction (MI) remains one of the foremost causes of mortality and long-term disability globally, resulting from reduced blood flow to the heart muscle due to plaque buildup in coronary arteries [1]. The World Health Organization reports that India contributes to one-fifth of global cardiovascular deaths, with a particularly high incidence among younger populations. The Global Burden of Disease study highlights an age-standardized death rate for cardiovascular diseases in India of 272 per 100,000 people, significantly higher than the global average of 235 [2].

Cardiac markers such as CK-MB and Troponins are recognized as specific biomarkers for MI. However, these markers typically take 4-6 hours to become detectable following chest pain. Consequently, hematological parameters accessible through routine complete blood counts hold promise as diagnostic and prognostic indicators for acute coronary syndrome, being readily available, cost-effective, and simple to perform [3].

Myocardial infarction involves two primary phases of inflammation: the inflammatory phase and the proliferative phase. Neutrophils are the first leukocytes to appear in the damaged area, producing significant amounts of inflammatory mediators that regulate the response to tissue injury. In contrast, lymphocytes are crucial for myocardial remodeling after the inflammatory phase, with CD4+ T regulatory cells playing a key role in recruiting proangiogenic macrophages and facilitating collateral artery formation [4,5].

The neutrophil-to-lymphocyte ratio (NLR), a measure of systemic inflammation, has been linked to poor clinical outcomes in cardiovascular disorders including acute coronary syndrome. Recent data indicate a substantial and independent correlation between elevated NLR and increased risk of complications and death after acute myocardial infarction [6].

Similarly, the monocyte-to-lymphocyte ratio (MLR) reflects the balance between monocyte-mediated inflammatory responses and lymphocyte-mediated immune regulation, potentially offering additional prognostic information in cardiovascular disease.

This study aims to evaluate the association of NLR and MLR with in-hospital mortality in newly diagnosed patients with myocardial infarction.

MATERIALS AND METHODS

Study Design and Setting

This cross-sectional study was conducted at Geetanjali Medical College and Hospital (GMCH), Udaipur, after obtaining approval from the Institutional Research Ethics Board. The study period extended from July 2023 to February 2024.

Study Population

All newly diagnosed patients with myocardial infarction admitted to the Cardiac ICU were included in the study.

Inclusion Criteria:

- All newly diagnosed patients of myocardial infarction

Exclusion Criteria:

- Known case of myocardial infarction
- Patients with hematological disorders
- Malignancy
- Autoimmune disorders
- Infections
- Patients whose outcome data was not available or who left against medical advice (LAMA)

Sample Size

A total of 150 patients meeting the inclusion criteria were enrolled in the study.

Data Collection

After obtaining informed consent, demographic data including age, gender, clinical signs and symptoms, and source of drinking water were recorded. Biochemical and hematological investigations, ECG, angiography, and echocardiography reports were collected.

Sample Collection and Laboratory Methods

Blood samples were collected from the venipuncture site under complete aseptic precautions. Complete blood count (CBC) was performed using the HORIBA-YUMIZEN H1500 automated cell counter, which works on the LMNE detection principle based on Double Hydrodynamic Sequential System (DHSS) flow cytometry.

Calculation of Ratios:

1. **NLR (Neutrophil-to-Lymphocyte Ratio)** = Absolute Neutrophil Count (ANC) / Absolute Lymphocyte Count (ALC)
   - Normal range: 2-2.3 [Reference 9]
2. **MLR (Monocyte-to-Lymphocyte Ratio)** = Absolute Monocyte Count (AMC) / Absolute Lymphocyte Count (ALC)
   - Normal range: 0.2-0.3 [Reference 9]

Statistical Analysis

Data were entered and cleaned using Microsoft Excel and analyzed using SPSS version 21 (IBM Corporation).

Statistical methods employed:

- Descriptive statistics (mean, standard deviation, frequencies, percentages)
- Chi-square test for categorical variable associations
- One-way ANOVA for comparing means across groups
- Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV)
- Receiver Operating Characteristic (ROC) curves with Area Under the Curve (AUC) calculation

A p-value < 0.05 was considered statistically significant.

RESULTS

Demographic Characteristics

Among 150 myocardial infarction patients, 76 (50.67%) were aged <40 years, while 74 (49.33%) were aged ≥40 years. The youngest patient was 21 years old. Male predominance was evident, with 133 (88.67%) male patients and 17 (11.33%) female patients (Table 1).

Table 1: Age and Sex Distribution of MI Patients (n=150)

Characteristic	Number	Percentage
Age <40 years	76	50.67%
Age ≥40 years	74	49.33%
Male	133	88.67%
Female	17	11.33%

Age-wise Mortality Outcomes

Mortality analysis revealed that individuals over 60 years, though forming only 10.7% of the cohort, contributed to 25% of deaths (4 out of 11 deaths). The 30-40 years age group had the highest number of MI cases (64 patients, 42.7%) with only 2 deaths, indicating favorable prognosis in younger patients (Table 2).

Table 2: Age-wise Distribution of MI Patients with Outcome

Age Group	Deceased (n=11)	Discharged (n=139)	Total	Mortality Rate
<30 yrs	1	19	20	5.0%
30-40 yrs	2	62	64	3.1%
41-50 yrs	2	24	26	7.7%
51-60 yrs	2	22	24	8.3%
>60 yrs	4	12	16	25.0%

Association of NLR with Outcome

NLR was significantly elevated in deceased patients (11.16 ± 10.87) compared to survivors (4.61 ± 5.01; p=0.049) (Table 3). This finding indicates that a heightened inflammatory response, as reflected by elevated NLR, is associated with increased mortality in MI patients.

Table 3: Comparison of NLR and MLR between Deceased and Alive Patients

Parameter	Deceased (n=11) Mean ± SD	Alive (n=139) Mean ± SD	P value
NLR	11.16 ± 10.87	4.61 ± 5.01	0.049*
MLR	2.00 ± 1.20	3.12 ± 1.57	0.004*

*Statistically significant ($p<0.05$)

Association of MLR with Outcome

MLR showed a paradoxical association, being significantly lower in deceased patients (2.00 ± 1.20) compared to survivors (3.12 ± 1.57; p=0.004). This finding may suggest reduced adaptive immune modulation or a dysregulated monocyte response in non-survivors.

NLR Association with Other Blood Parameters

Analysis across NLR categories revealed significant associations with white blood cell parameters:

Table 4: Association of NLR with Blood Parameters

Parameter	NLR <2 (n=48)	NLR 2-2.3 (n=18)	NLR >2.3 (n=84)	P value
TLC ($x10^3/mm^3$)	7.74	7.97	11.57	0.011*
ANC ($x10^3/mm^3$)	3.64	4.84	9.08	0.001*
ALC ($x10^3/mm^3$)	2.58	2.27	1.53	0.002*
AMC ($x10^3/mm^3$)	0.63	0.66	0.77	0.398

*Statistically significant

NLR elevation was driven by both neutrophilia (increased ANC) and lymphopenia (decreased ALC), reflecting systemic stress and poor immune regulation.

Diagnostic Performance of NLR

ROC curve analysis was performed to evaluate the diagnostic accuracy of NLR in identifying MI patients at risk of mortality:

Table 8: Diagnostic Performance of NLR in MI

Test	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUC (95% CI)
NLR >2.3	90.1	46.76	11.9	98.48	0.766 (0.619-0.888)

Key findings:

- **High Sensitivity (90.1%)**: NLR >2.3 detects most true positive cases
- **High NPV (98.48%)**: A negative result reliably rules out mortality risk
- **Good AUC (0.766)**: Indicates good diagnostic accuracy
- **Low PPV (11.9%)**: Indicates many false positives, suggesting use as screening rather than confirmatory test

DISCUSSION

Age and Gender Distribution

Our study revealed that over half (50.67%) of MI patients were aged below 40 years, highlighting a concerning trend toward younger onset of cardiovascular disease in India. This finding aligns with Lu et al. (2015) and Kumar et al. (2020), who emphasized the shift in cardiovascular disease burden towards younger age groups in developing regions [1,2]. The youngest patient in our cohort was 21 years old, reaffirming the need for early cardiovascular risk assessment.

The male predominance (88.67%) is consistent with Singh et al. (2022), who reported 82% male prevalence in MI patients. This gender disparity is attributed to higher rates of tobacco use, occupational stress, and lower awareness of preventive care in men, along with cardioprotective effects of estrogen in premenopausal women.

Mortality and Age Association

Patients over 60 years, though forming only 10.7% of the cohort, contributed to 25% of deaths. This reinforces the established vulnerability of elderly patients to ischemic insults and complications. Firani et al. (2022) similarly observed significantly worse outcomes in older MI patients due to compromised cardiac reserve, multiple comorbidities, and delayed presentations [3]. Younger patients (<40 years) had better survival, supporting findings by Tang et al. (2013) regarding favorable outcomes in this subgroup [5].

NLR as a Prognostic Marker

The significantly elevated NLR in deceased patients (11.16 vs. 4.61; p=0.049) reinforces its standing as a sensitive prognostic marker in MI. This finding is consistent with Chen et al. (2018), who established a link between heightened neutrophil responses and adverse ventricular remodeling, and Firani et al. (2022), who demonstrated NLR's prognostic value [3,4].

NLR elevation reflects a combination of neutrophilia and lymphopenia, both hallmarks of systemic stress and poor immune regulation. Neutrophils are the first leukocytes to appear in damaged myocardium, producing inflammatory mediators that regulate tissue injury response. Lymphopenia, conversely, reflects stress-induced apoptosis and redistribution of lymphocytes.

The diagnostic performance analysis revealed that NLR >2.3 has high sensitivity (90.1%) and a good AUC (0.766), making it a valuable prognostic tool. However, the low PPV (11.9%) indicates that elevated NLR should be interpreted alongside other clinical parameters rather than as a standalone predictor.

MLR: A Paradoxical Finding

The significantly lower MLR in deceased patients (2.00 vs. 3.12; p=0.004) was unexpected. This paradoxical association may reflect several underlying mechanisms:

1. **Lymphocyte predominance in MLR calculation**: As MLR = AMC/ALC, a lower MLR could result from elevated lymphocyte counts rather than decreased monocytes
2. **Lymphocyte elevation in critical illness**: Severe inflammatory states may trigger compensatory lymphocyte responses
3. **Timing of sample collection**: MLR may vary significantly based on the time from symptom onset to blood collection

Further research is needed to elucidate the biological basis of this association and determine whether MLR has utility as a prognostic marker in MI.

Clinical Implications

The high sensitivity and NPV of NLR >2.3 suggest that this marker can effectively "rule out" mortality risk when negative. This has practical implications for early triage in resource-limited settings:

- **Low NLR (<2.3)** : Low risk of mortality, may be suitable for standard ward care
- **Elevated NLR (>2.3)** : Higher risk, warrants closer monitoring and aggressive management

The cost-effectiveness and accessibility of NLR calculation from routine complete blood counts make it particularly valuable in settings where advanced cardiac biomarker testing may be limited.

Comparison with Previous Studies

Our findings align with the meta-analysis by Chen et al. (2018), who demonstrated NLR's strong diagnostic utility in acute coronary syndrome patients with an AUC of approximately 0.72 and sensitivity of approximately 85% [4]. Similarly, Karaca et al. (2024) reported that higher NLR readings were linked to higher in-hospital mortality and major adverse cardiac events in STEMI patients [7].

The association of MLR with outcomes is less well-established in literature, and our paradoxical finding underscores the need for further investigation with larger sample sizes and serial measurements.

Study Limitations

This was a single-centre study, which may limit the generalizability of our findings to broader populations, and the modest sample size, particularly the small number of deceased patients (n=11), may have reduced the statistical power of our analysis. Furthermore, only short-term, in-hospital outcomes were assessed, while long-term prognostic implications were not evaluated, and a single time-point measurement was used, whereas serial NLR measurements might have provided additional prognostic information. Additionally, potential confounding factors, including pre-existing inflammatory conditions and medications that affect white blood cell counts, were not fully controlled.

CONCLUSION

This study demonstrates that the neutrophil-to-lymphocyte ratio (NLR) is a valuable prognostic marker for in-hospital mortality in patients with acute myocardial infarction. NLR >2.3 demonstrated high sensitivity (90.1%) and good diagnostic accuracy (AUC=0.766) for identifying patients at risk of mortality. The high negative predictive value (98.48%) suggests that a negative result effectively rules out mortality risk, making NLR a useful screening tool.

The paradoxical finding of lower MLR in deceased patients requires further investigation to elucidate the underlying biological mechanisms and determine its clinical utility.

The high proportion of young MI patients (50.67% aged <40 years) underscores the need for targeted preventive programs addressing modifiable risk factors in this vulnerable population. The increasing mortality with age (>60 years group: 25% mortality) emphasizes the need for closer monitoring and aggressive management in elderly MI patients.

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