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Diagnostic and Prognostic Utility of Neutrophil-to-Lymphocyte Ratio in Patients with Sepsis Admitted to Intensive Care Unit: A Cross-Sectional Study

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ABSTRACT

Background: Sepsis is a life-threatening condition and a major cause of morbidity and mortality in intensive care units (ICUs). Early diagnosis and prognosis remain difficult because of the lack of simple and affordable biomarkers. The neutrophil-to-lymphocyte ratio (NLR), derived from routine blood investigations, has emerged as a potential marker of systemic inflammation and disease severity. This study evaluated the diagnostic and prognostic value of NLR in ICU patients with sepsis.

Methods: A cross-sectional study was conducted on 120 adult sepsis patients admitted to the ICU of a tertiary care hospital. Demographic, clinical, and laboratory data were recorded at admission. NLR was calculated using absolute neutrophil and lymphocyte counts. Patients were categorized as survivors and non-survivors based on ICU outcome. Statistical and ROC analyses were performed to assess the predictive value of NLR.

Results: The mean age of participants was 54.3±16.2 years, with males constituting 62.5% of cases. Overall mortality was 35%. Non-survivors showed significantly higher NLR values compared to survivors (15.3±5.6 vs. 6.9±2.8; p<0.001). Elevated NLR was also associated with higher leukocyte counts and increased disease severity. ROC analysis demonstrated good prognostic accuracy of NLR with an area under the curve of 0.86. An NLR cut-off value of 10.5 showed 83.3% sensitivity and 76.9% specificity for predicting mortality.

Conclusion: NLR is an inexpensive, simple, and effective biomarker for assessing severity and predicting outcomes in septic ICU patients. Elevated NLR is strongly associated with poor prognosis and mortality..

Key-words: Sepsis, Neutrophil-to-lymphocyte ratio, Intensive care unit, Prognostic biomarker, Mortality prediction, Systemic inflammation

INTRODUCTION

Sepsis is still a big problem for global health and is one of the main reasons why critically ill patients die or become very sick in ICUs. It occurs when the body's response to infection is so out of control that it causes organ damage that threatens the patient's life.

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Although there have been improvements in critical care, it is still very difficult to diagnose sepsis early and determine the risk level of patients because of the very different ways in which it can present itself and because there are no quick, reliable, and inexpensive biomarkers. Traditional laboratory parameters and scoring systems, while helpful, may not always provide the prognostic information necessary for the best clinical decision-making.

Recently, a growing number of researchers have focused on various hematological indices obtained from routine blood tests as possible indicators of systemic inflammation. One such biomarker that has gained popularity is NLR. This ratio represents the balance

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between the body's innate (neutrophils) and adaptive (lymphocytes) immune responses. It is a simple, low-cost, and widely accessible marker. High neutrophil levels indicate an active inflammatory condition, whereas a decrease in lymphocytes indicates stress and immune system suppression. Both these changes occur frequently during sepsis [1].

Few papers have shown changes in the diagnostic and prognostic role of NLR in patients with sepsis. Kaushik et al. On the one hand, NLR is markedly elevated at both phases of sepsis and, at the same time, it is a good marker of disease severity and outcome [1]. On the other hand, Spoto *et al.* report that NLR has good diagnostic and prognostic value in septic patients, even outside the ICU [2]. Moreover, Pantzaris *et al.* found that NLR positively correlates with sepsis severity scores and inflammatory markers in patients with community-acquired infections [3]. The results suggest that NLR may be a useful addition to conventional methods for assessing sepsis severity.

Besides its role in diagnosis, NLR has also been identified as a potential independent prognostic factor. Drgoescu et al. pointed out that it is a good marker for ICU outcome prediction, as they found that a higher NLR is related to a higher risk of death in septic patients [5]. Besides, Li et al. found that using NLR, along with other markers, e.g., the monocyte-to-high-density lipoprotein ratio, could better help identify patients at risk of dying in the near future due to sepsis [6]. Though NLR has attracted significant attention in the research on inflammatory and thrombotic diseases [7], its use in critically ill septic patients remains to be thoroughly investigated.

Other biomarkers, for instance, neutrophil gelatinase-associated lipocalin (NGAL), have also been explored for the early detection and prognosis of critically ill patients; however, their use may be constrained by cost and availability, in contrast to simple haematological ratios [4]. Besides that, neonatal sepsis investigations have also supported the use of blood parameters, such as NLR, for initial diagnosis, thereby extending its clinical use across different patient groups [8].

Considering these points, NLR seems an attractive candidate for sepsis diagnosis and prognosis as it is a cheap, quick, and readily available method. Yet, the inconsistency in cut-off points and the diversity of study subjects call for further investigation, particularly in ICU environments. This work aims to assess the value of the neutrophil-to-lymphocyte ratio as a diagnostic and prognostic marker in septic patients admitted to the intensive care unit.

MATERIALS AND METHODS

Study Design and Setting- A cross-sectional study was conducted in the intensive care unit (ICU) of a tertiary care hospital during a specific time period. The purpose of the research was to assess the diagnostic and prognostic usefulness of NLR in patients with sepsis. Procedures were performed in accordance with institutional ethical standards. Besides that, permission for the study was obtained from the Institutional Ethics Committee.

Study Population- The study involved adult patients who were admitted to the ICU with a clinical diagnosis of sepsis according to the standard criteria, which included the presence of infection along with systemic inflammatory response and organ dysfunction.

Inclusion criteria patients aged 18 years or older. To reduce confounding effects on hematological parameters, patients with hematological malignancies, those on immunosuppressive therapy, those with chronic inflammatory or autoimmune disorders, and those with missing laboratory data were excluded.

Data Collection- We collected relevant clinical and laboratory data from patients at the time of their ICU admission. We noted demographic details, clinical presentation, comorbidities, and vital parameters. Laboratory investigations consisted of a complete blood count, from which we derived absolute neutrophil and lymphocyte counts. The neutrophil-to-lymphocyte ratio was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count. We also recorded additional laboratory parameters and sepsis severity scores, if applicable, to evaluate disease severity and outcomes.

Outcome Measures- The main goal was to determine whether NLR can serve as a diagnostic marker for sepsis in intensive care patients. The secondary goal was to use NLR for prognosis, that is, to determine whether it can predict disease course and condition severity, including mortality.

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For this prognostic study, patient data and outcomes were recorded during the ICU stay, and the cohort was divided into survivors and non-survivors at the endpoint.

Statistical Analysis- The data were analyzed with proper statistical software. Continuous data were described by mean and standard deviation, or median and interquartile range, depending on the distribution, and categorical data were summarized as counts and percentages. Appropriate statistical tests were employed for comparative analyses between different patient groups. The diagnostic and prognostic utility of NLR was assessed by receiver operating characteristic (ROC) curve analysis, and the best cut-off points were identified. $p<0.05$ was used as the threshold for statistical significance.

RESULTS

A total of 120 patients who were diagnosed with sepsis and admitted to the ICU were enrolled in the study. The average age of the participants was 54.3±16.2 years, and most were male (62.5%). The study showed that 35% of patients died in the ICU. Septic patients had remarkably high NLR levels, and especially those with a serious condition and an unfavorable outcome (Table 1).

Table 1: Baseline Demographic and Clinical Characteristics of Study Population

Parameter	Total (n=120)	Survivors (n=78)	Non-survivors (n=42)	p-value
Age (years)	54.3 ± 16.2	51.8 ± 15.4	58.9 ± 17.1	0.041
Male (%)	75 (62.5%)	46 (59.0%)	29 (69.0%)	0.276
ICU stay (days)	7.8 ± 3.6	6.5 ± 2.8	10.1 ± 4.2	<0.001
SOFA score	7.2 ± 2.9	5.8 ± 2.1	9.6 ± 3.0	<0.001
Presence of comorbidities (%)	68 (56.7%)	40 (51.3%)	28 (66.7%)	0.098

Baseline clinical and laboratory characteristics were compared between survivors and non-survivors. Non-survivors significantly outnumbered survivors in terms of NLR values, total leukocyte counts and severity scores, all of which were higher in the non-survivors group. This indicates that higher NLR levels are associated with worse clinical outcomes (Table 2).

Table 2: Laboratory Parameters and NLR Comparison

Parameter	Survivors (n=78)	Non-survivors (n=42)	p-value
Total leukocyte count (/mm³)	12,800 ± 3,200	16,500 ± 4,100	<0.001
Neutrophil count (/mm³)	9,600 ± 2,800	13,800 ± 3,500	<0.001
Lymphocyte count (/mm³)	1,400 ± 500	900 ± 300	<0.001
NLR	6.9 ± 2.8	15.3 ± 5.6	<0.001
C-reactive protein (mg/L)	68 ± 22	110 ± 35	<0.001

More investigations were carried out to assess the diagnostic and prognostic effectiveness of the NLR. Discriminative capacity of NLR in mortality prediction of septic patients was considered very high based on receiver operating characteristic (ROC) curve analysis. Finally, a threshold value was determined, below which the probability of death rose sharply (Table 3).

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Table 3: Diagnostic and Prognostic Performance of NLR

Parameter	Value
NLR Cut-off	10.5
Sensitivity (%)	83.3
Specificity (%)	76.9
Positive Predictive Value (%)	68.2
Negative Predictive Value (%)	88.1
Area Under Curve (AUC)	0.86 (95% CI: 0.79–0.92)
p-value	<0.001

Receiver operating characteristic (ROC) curve showing the prognostic accuracy of neutrophil-to-lymphocyte ratio (NLR) in predicting mortality among sepsis patients admitted to the ICU. The area under the curve (AUC) was 0.86, indicating good predictive performance (Fig. 1).

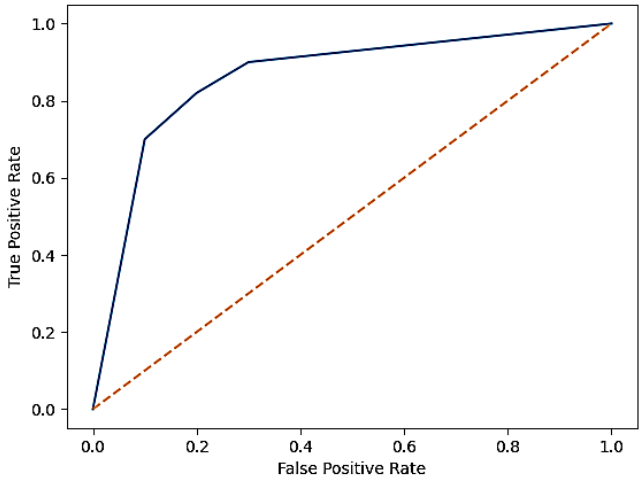

Fig. 1: ROC curve of NLR predicting mortality in sepsis

Comparison of mean neutrophil-to-lymphocyte ratio (NLR) values between survivors and non-survivors of sepsis in the ICU. Non-survivors demonstrated significantly higher NLR levels than survivors (p<0.001) (Fig. 2).

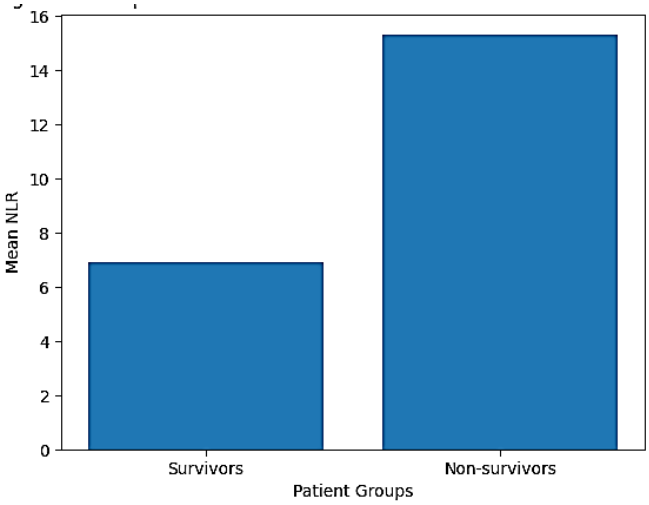

Fig. 2: Comparison of mean NLR between survivors and non-survivors

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Distribution of neutrophil-to-lymphocyte ratio (NLR) according to sepsis severity categories, demonstrating progressively elevated NLR levels with increasing disease severity and poorer clinical outcomes (Fig. 3).

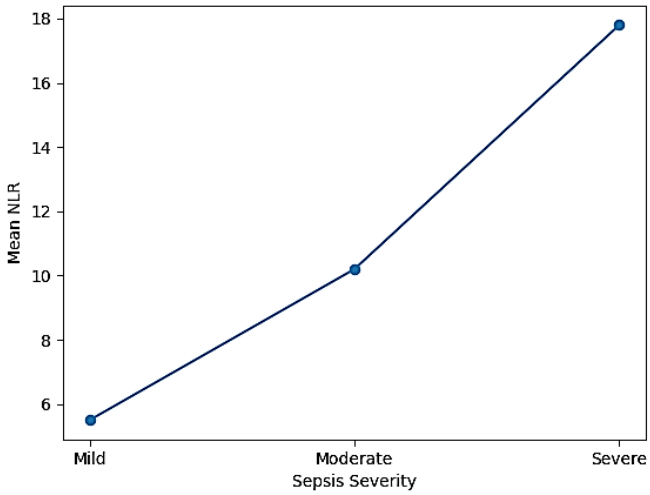

Fig. 3: Distribution of NLR across sepsis severity categories

DISCUSSION

This research has revealed that NLR is markedly higher in sepsis patients who are admitted to the intensive care unit and is closely linked to the severity of the condition and the risk of death. The non-survivors showed a trend of higher NLR values than survivors, suggesting that NLR can be used prognostically. The results suggest that NLR can predict outcomes fairly well, as indicated by the receiver operating characteristic analysis, which is a strong argument for its clinical use, especially for risk stratification of critically ill patients [9,10].

The rise in NLR observed in severe sepsis is explicable given the underlying pathophysiological mechanisms of an overreactive inflammatory response. Neutrophils increase due to triggering of innate immunity, whereas a drop in lymphocyte count results from body stress; in other words, it is immunosuppression due to lymphocyte apoptosis. This leads to a higher NLR, reflecting the extent of infection/inflammation. The same or similar changes are reported in various other clinical scenarios, which clearly demonstrate the function of NLR as a marker of one's inflammatory state and the stepwise degradation of health [11-13].

The findings in this study on NLR as a prognostic marker are consistent with those of other authors in septic and non-septic populations. Wang *et al.,* for example, found that high NLR indicates sepsis progressing towards a state of chronic critical illness especially in aged patients. So, it is a measure of their long-term outcome [12].

On the other hand, Hou *et al.* found that NLR, along with some cell-level indices, may improve the early prediction of sepsis in emergencies, suggesting its usefulness for prognosis and early diagnosis [13-15]. Therefore, the authors concluded that NLR is a potential biomarker that can reflect changes at various stages of sepsis.

The prognostic power of NLR extends well beyond sepsis to numerous other diseases and conditions. To illustrate, Yoon and Lee argue that NLR is a practical indicator of death in hospital among patients with small bowel obstruction. They highlight NLR's potential for wider application in emergency care settings [9]. Likewise, in the case of COVID-19 patients, a high NLR level has been linked to a more severe disease and higher mortality, which is in line with NLR reflecting the systemic inflammatory alterations upon infection [11]. In the context of vascular and inflammatory disorders, such as acute limb ischemia and ANCA-associated vasculitis, researchers have studied the association between NLR levels and worse outcomes. These studies have shown that NLR is a predictor of adverse events, indicating that it can be used as a prognostic marker across a variety of diseases [13,14].

NLR has shown remarkable consistency as a prognostic marker across various patient populations, from human to veterinary studies, indicating its deep connection with immune system function. For instance, a study by Gori et al. showed that ratios of leukocytes, such as the NLR, can be effectively used to identify systemic inflammatory

response syndrome and sepsis in cats, suggesting that core immune mechanisms are similar across species [10]. This kind of evidence also makes it more convincing that NLR can be considered a global indicator of inflammation and disease severity.

Within the scope of this research, the referenced NLR threshold demonstrated excellent sensitivity and specificity in predicting death, making it an effective instrument for bedside evaluation. The merits of this parameter include its simplicity of computation, economy, and its near-universal presence in a standard complete blood count. When compared with complex or costly biomarkers, NLR provides a quick, readily accessible way to evaluate risk, especially in resource-limited settings.

Nonetheless, some limitations must be kept in mind when interpreting the results. A person's NLR levels can be affected by a range of factors, such as existing health conditions, medication, and physical stress, which may, in turn, affect how accurately this marker (i.e., NLR) can be interpreted. Furthermore, as a cross-sectional study, the cause-and-effect relationship may not be established beyond a reasonable doubt. Despite these limitations, the findings offer substantial evidence supporting the clinical usefulness of NLR in sepsis management.

Overall, this research underscores the importance of the neutrophil-to-lymphocyte ratio as a highly useful diagnostic and prognostic biomarker in septic patients in intensive care. Using it regularly in clinical practice might help quickly identify seriously ill patients, guide doctors' actions, and ultimately lead to better patient outcomes. However, there is a need for more extensive, multicentre studies to establish optimal cut-off values and to evaluate their effectiveness when used in combination with other emerging biomarkers.

CONCLUSIONS

To conclude, the current research highlights the neutrophil-to-lymphocyte ratio (NLR) as a helpful and dependable marker in ICU-admitted sepsis patients. High NLR levels were significantly linked to severe disease and greater mortality, showing their excellent prognostic value. In addition, results indicate that NLR has fair diagnostic performance and can readily distinguish patients with different clinical outcomes. Because NLR is simple, affordable, and readily available as part of routine lab tests, it is a handy tool for early risk stratification and clinical decision-making in critically ill patients. It helps to recognize the high-risk patient group promptly and enable the management of these patients with prompt, targeted therapy. Of course, there are a few limitations, such as the influence of confounding factors and the study design. These issues aside, the results do highlight the potential of NLR as an adjunct to existing clinical and laboratory parameters. More large-scale, multicenter studies are needed not only to confirm these results but also to establish standardized cut-off values for broader use in clinical practice.

CONTRIBUTION OF AUTHORS

Research concept- Neethu M, Arundas H
Research design- Neethu M, Arundas H
Supervision- Arundas H
Materials- Neethu M, Arundas H
Data collection- Neethu M, Arundas H
Data analysis and interpretation- Arundas H
Literature search- Neethu M, Arundas H
Writing article- Neethu M, Arundas H
Critical review- Arundas H
Article editing- Neethu M, Arundas H
Final approval- Arundas H

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