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# EARLY DIAGNOSTIC AND PROGNOSTIC ROLE OF NEUTROPHIL-LYMPHOCYTE RATIO IN NEONATAL SEPSIS: INSIGHTS FROM A PROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

**Background:** Neonatal sepsis poses a significant diagnostic challenge due to its nonspecific early signs and delayed culture results. The neutrophil-lymphocyte ratio (NLR), derived from routine hematological profiles, has gained attention as a potential early marker of systemic inflammation. This study aims to explore the utility of NLR in diagnosing neonatal sepsis and predicting associated clinical outcomes.

**Materials and Methods:** This prospective observational study was conducted in a tertiary care neonatal intensive care unit over 18 months. A total of 150 neonates with clinical suspicion of sepsis were included. Upon admission, blood samples were collected for complete blood count, C-reactive protein, and blood cultures. NLR was calculated from absolute neutrophil and lymphocyte counts. Sepsis was confirmed via culture positivity, and clinical outcomes such as mortality and NICU stay duration were tracked. Data were analyzed using SPSS v25.0, with ROC analysis applied to evaluate diagnostic performance.

**Results:** Among 150 neonates, 92 (61.3%) had positive blood cultures. The average NLR in septic neonates was significantly higher (3.91 ± 1.74) than in those without confirmed infection (1.88 ± 0.96, $p < 0.001$). An NLR threshold of ≥2.6 provided a sensitivity of 85.9% and specificity of 78.4% (AUC = 0.886; 95% CI: 0.822–0.939). Elevated NLR also correlated with greater mortality ($p = 0.02$) and extended NICU stays ($p < 0.01$).

**Conclusion:** NLR serves as a practical, cost-efficient biomarker for early identification and risk stratification in neonatal sepsis. Its incorporation into standard diagnostic protocols may enhance timely clinical decision-making.

**Keywords:** Neonatal sepsis, Neutrophil-lymphocyte ratio, Biomarkers, Inflammation, ROC curve, NICU outcomes.

## INTRODUCTION

Sepsis in the neonatal period remains one of the leading contributors to infant morbidity and mortality, especially in developing countries where early diagnosis and intervention are often delayed.[1] Defined as a systemic inflammatory response to infection occurring within the first 28 days of life, neonatal sepsis poses a considerable diagnostic dilemma due to its nonspecific early clinical signs and the time-intensive nature of definitive blood culture confirmation.[2,3]

Globally, neonatal sepsis is responsible for a substantial proportion of neonatal deaths, with incidence rates highest in low-resource settings. Clinical manifestations such as poor feeding, lethargy, temperature instability, and respiratory distress frequently overlap with other neonatal illnesses, complicating timely recognition.[4] Although blood cultures are considered the diagnostic gold standard, they often require 48–72 hours for results and may yield false negatives in low-grade bacteremia or prior antibiotic exposure.[5]

As a result, there is growing interest in the use of readily available hematological and biochemical

parameters that can support early diagnosis. Among these, the neutrophil-to-lymphocyte ratio (NLR), calculated from a standard complete blood count, has shown promise as a surrogate marker of systemic inflammation.[6] An increased NLR reflects a shift toward neutrophilic predominance with concurrent lymphopenia, commonly seen in acute infection and physiological stress.[7] These changes in leukocyte profile mirror underlying immune responses and may offer diagnostic and prognostic insight.

While NLR has been widely investigated in adult and pediatric populations with sepsis, its application in the neonatal context is less thoroughly studied. Preliminary findings suggest that NLR could be used not only to detect sepsis early but also to predict severity and adverse outcomes.[8] The ease of availability, low cost, and rapid turnaround of NLR measurement make it an attractive option, particularly in settings where advanced inflammatory markers like procalcitonin or interleukins may not be routinely accessible.[9]

This study was undertaken to evaluate the role of NLR as a diagnostic and prognostic indicator in neonatal sepsis. The primary objective was to assess its ability to differentiate culture-confirmed sepsis from non-infectious conditions in neonates presenting with clinical signs of infection. Secondary objectives included analyzing its association with short-term outcomes such as in-hospital mortality and length of stay in the neonatal intensive care unit (NICU). Through this investigation, we aim to validate the practical utility of NLR in guiding early clinical decision-making in neonatal sepsis.

## MATERIALS AND METHODS

**Study Design and Setting:** This prospective observational study was conducted over a period of 12 months (June 2024 to May 2025) in the Neonatal Intensive Care Unit (NICU).Shadan Medical College Hyderabad. The study was approved by the Institutional Ethics Committee, and informed consent was obtained from the parents or legal guardians of all enrolled neonates.

**Study Population:** Neonates admitted to the NICU with clinical suspicion of sepsis were consecutively enrolled. Inclusion criteria comprised neonates aged 0–28 days presenting with at least two of the following signs suggestive of sepsis: temperature instability, poor feeding, lethargy, apnea, respiratory distress, irritability, or abnormal cry. Exclusion criteria included neonates with congenital anomalies, known immunodeficiencies, or those who had received prior antibiotic treatment for more than 24 hours before admission.

**Sample Size Calculation:** Based on an anticipated sensitivity of NLR of 80%, a confidence level of 95%, and a margin of error of 8%, the minimum sample size required was calculated to be 138. To account for potential dropouts or incomplete data, 150 neonates were enrolled.

**Data Collection:** On admission, detailed demographic data including age, sex, gestational age, birth weight, and mode of delivery were recorded. Venous blood samples were collected before initiation of antibiotic therapy for complete blood count, C-reactive protein (CRP), and blood culture. NLR was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count.

Blood cultures were processed using standard microbiological techniques. Neonates were categorized into two groups based on blood culture results: culture-positive and culture-negative. Clinical outcomes such as duration of NICU stay and in-hospital mortality were also recorded.

**Outcome Measures:** The primary outcome was to determine the diagnostic accuracy of NLR in predicting culture-positive neonatal sepsis. Secondary outcomes included correlation of NLR with mortality and duration of NICU stay.

**Statistical Analysis:** All statistical analyses were performed using IBM SPSS Statistics version 25.0. Descriptive statistics were expressed as mean ± standard deviation (SD) or median (interquartile range) for continuous variables, and as frequencies and percentages for categorical variables. Comparisons between groups were made using independent sample t-tests or Mann–Whitney U tests for continuous variables, and Chi-square or Fisher's exact tests for categorical variables.

Receiver Operating Characteristic (ROC) curve analysis was used to evaluate the diagnostic performance of NLR. The area under the curve (AUC), sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated. A p-value of <0.05 was considered statistically significant.

## RESULTS

**Table 1: Demographic Characteristics of the Study Population (n = 150)**

| Variable | Value |
|---|---|
| Total Neonates (n) | 150 |
| Male | 86 (57.3%) |
| Female | 64 (42.7%) |
| Mean Birth Weight (g) | 2620 ± 410 |
| Gestational Age (weeks) | 37.8 ± 1.6 |
| Vaginal Delivery | 88 (58.7%) |
| Cesarean Section | 62 (41.3%) |

**Table 2: Comparison of NLR in Culture-Positive and Culture-Negative Neonates**

| Group | Mean NLR ± SD | p-value |
|---|---|---|
| Culture-Positive (n = 92) | 3.91 ± 1.74 | <0.001 |
| Culture-Negative (n = 58) | 1.88 ± 0.96 | — |

**Table 3: Diagnostic Performance of NLR (Cut-off ≥2.6)**

| Parameter | Value |
|---|---|
| Sensitivity | 85.9% |
| Specificity | 78.4% |
| Positive Predictive Value | 88.1% |
| Negative Predictive Value | 74.5% |
| AUC (95% CI) | 0.886 (0.822–0.939) |

**Table 4: Association between NLR and Mortality**

| Outcome | Mean NLR ± SD | p-value |
|---|---|---|
| Survived (n = 135) | 2.72 ± 1.41 | 0.02 |
| Expired (n = 15) | 4.12 ± 1.66 | — |

**Table 5: Association between NLR and NICU Stay Duration**

| NLR Group | Mean NICU Stay (days) | p-value |
|---|---|---|
| <2.6 (n = 68) | 5.1 ± 1.9 | <0.01 |
| ≥2.6 (n = 82) | 8.6 ± 2.7 | — |

**Table 6: Microbiological Profile of Culture-Positive Neonatal Sepsis (n = 92)**

| Isolated Organism | Number of Cases (n) | Percentage (%) |
|---|---|---|
| Klebsiella pneumoniae | 28 | 30.4% |
| Escherichia coli | 21 | 22.8% |
| Staphylococcus aureus | 16 | 17.4% |
| Pseudomonas aeruginosa | 11 | 12.0% |
| Acinetobacter baumannii | 9 | 9.8% |
| Others | 7 | 7.6% |

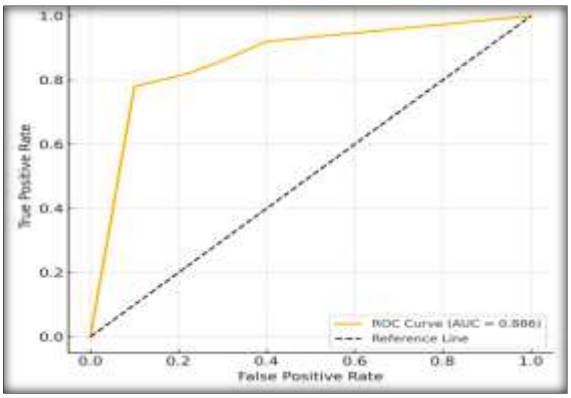


**Figure 1: ROC curve in predicting neonatal sepsis**

This prospective study evaluated the diagnostic and prognostic role of the neutrophil-lymphocyte ratio (NLR) in neonates with suspected sepsis. Out of 150 neonates enrolled, 92 (61.3%) were culture-positive, indicating a substantial burden of confirmed sepsis within the study cohort. Demographic characteristics such as mean birth weight (2620 ± 410 grams) and average gestational age (37.8 ± 1.6 weeks) were representative of term and late-preterm populations, with a slight male predominance (57.3%).

The mean NLR value among neonates with culture-positive sepsis was markedly elevated (3.91 ± 1.74) in comparison to those without confirmed infection (1.88 ± 0.96), with a statistically significant difference ($p < 0.001$), suggesting that NLR may serve as a useful early marker of infection. This difference underscores the inflammatory response that is more pronounced in systemic infections.

The receiver operating characteristic (ROC) analysis provided an area under the curve (AUC) of 0.886 (95% CI: 0.822–0.939), indicating excellent discriminatory capacity of NLR in identifying neonatal sepsis. Using a threshold of ≥2.6 for NLR yielded a sensitivity of 85.9%, specificity of 78.4%, positive predictive value of 88.1%, and negative predictive value of 74.5% . These metrics support the use of NLR as a clinically reliable screening parameter.

Further evaluation revealed that neonates who did not survive during hospitalization had higher NLR values (4.12 ± 1.66) compared to those who survived (2.72 ± 1.41), with a statistically significant difference ($p = 0.02$), indicating a potential correlation between elevated NLR and disease severity (Table 4). Similarly, neonates with NLR values ≥2.6 had longer NICU stays (8.6 ± 2.7 days) compared to those with NLR <2.6 (5.1 ± 1.9 days), with this association also reaching statistical significance ($p < 0.01$).

Microbiological profiling revealed Klebsiella pneumoniae (30.4%) as the most frequently isolated organism, followed by Escherichia coli (22.8%) and Staphylococcus aureus (17.4%), consistent with known regional trends in neonatal bloodstream infections.

## DISCUSSION

Neonatal sepsis is a critical clinical condition requiring prompt diagnosis and intervention due to its association with high morbidity and mortality. However, conventional diagnostic methods such as blood cultures are time-consuming and often delayed, prompting the need for faster, adjunctive tools. In this context, our study explored the role of the neutrophil-lymphocyte ratio (NLR) as an accessible biomarker for early identification and risk prediction in neonates with suspected sepsis.

The NLR, derived from routine hematological parameters, has emerged as a marker reflecting the balance between innate immune activation and adaptive immune suppression.[10] An increase in NLR suggests an exaggerated inflammatory response, a hallmark of systemic infection. Our analysis demonstrated that neonates with culture-confirmed sepsis exhibited significantly elevated NLR values ($3.91 \pm 1.74$) compared to those without sepsis ($1.88 \pm 0.96$, $p < 0.001$), underscoring its diagnostic relevance.

These findings are in line with reports by Yuan et al., who noted that NLR values tend to be substantially higher in infected neonates than in non-infected controls.[11] Additionally, the diagnostic performance of NLR in our cohort, as indicated by an area under the ROC curve (AUC) of 0.886, confirms its strong discriminatory capacity. Comparable AUC values have been observed in similar neonatal studies, further supporting its diagnostic utility.[12]

By establishing an NLR cutoff of 2.6, the sensitivity and specificity achieved were 85.9% and 78.4% respectively. These metrics are consistent with prior literature that has identified similar thresholds as clinically useful.[13,14] Such a high predictive accuracy implies that NLR can be incorporated as part of early screening protocols for sepsis, especially in settings with limited access to advanced diagnostics.

Beyond diagnostic value, our study also observed significant associations between elevated NLR and adverse outcomes. Neonates who did not survive had a mean NLR of $4.12 \pm 1.66$, which was notably higher than the $2.72 \pm 1.41$ observed among survivors ($p = 0.02$). This trend suggests that NLR not only reflects infection but may also correlate with disease severity and prognosis. Comparable results were documented by Ozdemir et al., who linked increased NLR values to poor neonatal outcomes.[15]

We also identified a correlation between higher NLR values ($\geq 2.6$) and prolonged NICU stay durations ($8.6 \pm 2.7$ days vs. $5.1 \pm 1.9$ days, $p < 0.01$), indicating greater clinical burden and potentially more complicated courses. Given that the predominant organisms isolated were gram-negative bacilli, notably Klebsiella pneumoniae and Escherichia coli, our microbiological profile aligns with established regional patterns.[16]

## CONCLUSION

The findings of this prospective study establish the neutrophil-lymphocyte ratio (NLR) as a valuable, cost-effective biomarker for early detection and prognostication of neonatal sepsis. A significantly elevated NLR was observed in neonates with culture-proven sepsis, with a threshold value of $\geq 2.6$ demonstrating high sensitivity (85.9%) and specificity (78.4%). Moreover, increased NLR values were positively associated with higher mortality and prolonged NICU stay. Given its availability through routine hematological tests, NLR offers a pragmatic advantage in resource-limited settings where rapid diagnostic tools may not be accessible. Incorporating NLR into the initial sepsis screening panel can facilitate timely intervention and improve neonatal outcomes. Further multicentric validation is recommended to generalize its clinical applicability.

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**Conflicts of Interest**

The authors declare no conflicts of interest related to this study.

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