

Neutrophil-To-Lymphocyte Ratio as a Prognostic Marker in Pediatric Intensive Care: A North Indian Cohort Study

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Abstract

Background and Aims: Acute infectious diseases continue to account for substantial morbidity and mortality among children admitted to pediatric intensive care units (PICUs). Early recognition of children at risk of deterioration is important for timely monitoring and escalation of care. The neutrophil-to-lymphocyte ratio (NLR), derived from a routine complete blood count, offers a simple measure of the inflammatory and immune response. The present observational cohort study assessed the prognostic value of admission NLR for mortality and organ dysfunction in children with acute infectious diseases admitted to a tertiary care PICU in North India.

Materials and methods: This 18-month observational cohort study was conducted in a tertiary care teaching hospital in North India. Consecutive eligible children aged 1 month to 18 years admitted with acute infectious diseases were enrolled and followed until PICU discharge, hospital discharge, or mortality. Admission NLR was calculated from the initial complete blood count. Organ dysfunction was evaluated with the PEdiatric Logistic Organ Dysfunction-2 (PELOD-2) score within 24 hours of admission. The primary outcome was PICU mortality. Secondary outcomes included the relationship of NLR with organ dysfunction scores and the duration of PICU and hospital stay.

Results: All 100 enrolled children were included in the analysis. Median NLR was higher among non-survivors [4.13 (1.89-5.46)] than survivors [1.31 (0.79-3.21); $p = 0.030$]. Receiver operating characteristic analysis showed an area under the curve of 0.759 (95% confidence interval 0.627-0.890; $p = 0.034$) for mortality prediction. Sensitivity, specificity, positive predictive value, and negative predictive value were 66.67%, 70.21%, 12.50%, and 97.06%, respectively. Admission NLR showed mild but statistically significant positive correlations with neurologic dysfunction ($r = 0.213$, $p = 0.033$) and cardiovascular dysfunction ($r = 0.307$, $p = 0.002$). No significant correlation was observed with PICU or total hospital stay.

Conclusion: Admission NLR is a low-cost, readily available marker associated with mortality and selected organ dysfunction in critically ill children with acute infectious diseases. It may support early risk stratification in resource-limited settings, provided it is interpreted alongside clinical assessment and validated severity scores.

Keywords: Neutrophil-to-lymphocyte ratio; Prognostic marker; Organ dysfunction; Pediatric intensive care.

Introduction

Acute infectious diseases are a frequent cause of critical illness in children and remain an important contributor to morbidity and mortality in pediatric intensive care, especially in resource-limited settings [1,2,3]. Early recognition of children likely to deteriorate is a central part of PICU care because timely escalation of monitoring and treatment may influence outcomes.

Severity scores such as PELOD-2, PRISM III, and PIM2 provide structured estimates of illness severity and organ dysfunction. However, these tools require several clinical and laboratory variables, which may limit their use for rapid bedside risk assessment in busy or resource-constrained units [4,5,6,7]. Simple markers obtained from routine investigations may therefore have more practical value.

The neutrophil-to-lymphocyte ratio (NLR) reflects the relationship between innate inflammatory activation and adaptive immune suppression. A higher NLR has been associated with greater disease severity and poorer outcomes in several infectious and inflammatory conditions [8,9]. Pediatric studies have also suggested its usefulness in sepsis and severe infections [10,11].

Despite growing interest in NLR, evidence from Indian PICUs is limited, particularly among children admitted with acute infectious diseases. This study evaluated whether NLR at admission predicts mortality and organ dysfunction in children admitted to a tertiary care PICU in North India.

Materials and methods

The study used an observational cohort design and was conducted over 18 months, from May 2023 to November 2024, in the PICU of a tertiary care teaching hospital in North India. Institutional Ethics Committee approval was obtained before commencement of the study and it was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from parents or legal guardians.

During the recruitment period, children aged 1 month to 18 years admitted with acute infectious diseases were screened for eligibility. Consecutive eligible patients were enrolled and followed until PICU discharge, hospital discharge, or mortality. After application of the inclusion and exclusion criteria, 100 children were included.

Children admitted for postoperative care were excluded. Additional exclusion criteria were chronic infectious diseases such as tuberculosis or human immunodeficiency virus infection, chronic organ dysfunction, malignancy, immunodeficiency, connective tissue disorders, and PICU stay of less than 2 hours.

Admission NLR was the primary predictive variable. It was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count. The primary outcome was PICU mortality. Secondary outcomes included neurologic, cardiovascular, respiratory, renal, and hematologic organ dysfunction assessed through PELOD-2 score, duration of PICU stay, and total hospital stay. Age, sex, and clinical diagnosis were recorded as baseline descriptive characteristics and potential confounders.

On PICU admission, clinical details were recorded through history taking, physical examination, and baseline investigations. Complete blood counts were measured with a Sysmex XN-1000 automated hematology analyzer (Sysmex Corporation, Kobe, Japan). NLR was calculated from the first admission sample obtained during initial PICU evaluation.

Disease severity and organ dysfunction were assessed with the PEdiatric Logistic Organ Dysfunction-2 (PELOD-2) score calculated within the first 24 hours of PICU admission [12]. The PELOD-2 assessment included neurologic, cardiovascular, respiratory, renal, and hematologic systems. Outcome status and lengths of stay were recorded until PICU discharge, hospital discharge, or mortality.

Several steps were taken to reduce bias. Consecutive eligible admissions were enrolled, exposure and outcome definitions were specified before analysis, complete blood counts were performed on the same analyzer platform, and organ dysfunction was assessed using the standardized PELOD-2 score. Residual confounding from referral delay, prior antibiotic exposure, nutritional status, and coinfections could not be fully eliminated.

Data were entered in Microsoft Excel and analyzed using SPSS version 25 (IBM Corp., Armonk, NY, USA). Continuous variables were treated as continuous data and summarized as median with interquartile range (IQR). Categorical variables were summarized as frequency and percentage. Group comparisons were performed using the Mann-Whitney U test, Chi-square test, or Fisher exact test, as appropriate. Receiver operating characteristic (ROC) analysis was used to assess the ability of admission NLR to predict mortality. Spearman rank correlation was used to evaluate the association between NLR and organ dysfunction scores. A p-value ≤ 0.05 was considered statistically significant.

Results

A total of 100 children admitted with acute infectious diseases were included in the analysis, and all completed in-hospital follow-up for outcome assessment. Baseline demographic and clinical characteristics are shown in Table 1. Most patients were female (63%), and 38% were younger than 1 year. Lower respiratory tract infection was the most common diagnosis (40%). Overall mortality was 6%.

Table 1: Baseline demographic and clinical characteristics of study subjects (n = 100)

Variable	Number (%)
Gender	
Male	37 (37.0)

Variable	Number (%)
Female	63 (63.0)
Age group	
<1 year	38 (38.0)
1-5 years	30 (30.0)
6-10 years	17 (17.0)
>10 years	15 (15.0)
Etiology of acute infectious disease	
Lower respiratory tract infection	40 (40.0)
Acute gastroenteritis	12 (12.0)
Dengue	10 (10.0)
Sepsis	8 (8.0)
Pleural effusion	6 (6.0)
Meningitis	3 (3.0)
Meningoencephalitis	3 (3.0)
Multiple organ dysfunction syndrome	2 (2.0)
Dengue encephalitis	2 (2.0)
Enteric fever	1 (1.0)
Septic shock	1 (1.0)
Acute respiratory distress syndrome	1 (1.0)
Miscellaneous	11 (11.0)
Outcome	
Survived	94 (94.0)
Expired	6 (6.0)

Median NLR was significantly higher in non-survivors than survivors [4.13 (1.89-5.46) vs 1.31 (0.79-3.21), $p = 0.030$]. ROC analysis showed an area under the curve (AUC) of 0.759 (standard error 0.067; 95% confidence interval 0.627-0.890; $p = 0.034$), indicating acceptable discriminatory ability for mortality prediction (Figure 1 and Table 2).

Figure 1: ROC curve for NLR predicting mortality

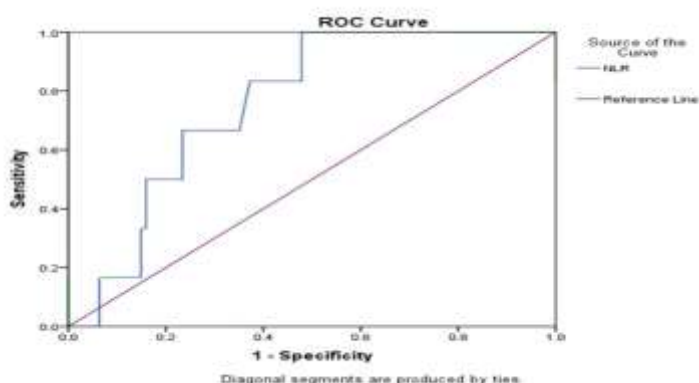


Table 2: Area under the ROC curve for admission NLR

Test result variable	Area under curve	Std. error	p-value	95% CI lower bound	95% CI upper bound
NLR	0.759	0.067	0.034	0.627	0.890

The diagnostic performance of admission NLR for mortality prediction at the ROC-derived threshold is shown in Table 3. Sensitivity and specificity were 66.67% and 70.21%, respectively. The negative predictive value was high at 97.06%, whereas the positive predictive value was 12.50%.

Table 3: Diagnostic performance of admission NLR for mortality prediction

Parameter	Value
Sensitivity	66.67%
Specificity	70.21%
Positive predictive value	12.50%
Negative predictive value	97.06%

Admission NLR had mild but statistically significant positive correlations with neurologic dysfunction ($r = 0.213$, $p = 0.033$) and cardiovascular dysfunction ($r = 0.307$, $p = 0.002$). Correlations with renal, respiratory, and hematologic dysfunction were not statistically significant (Table 4). No significant correlation was observed between NLR and duration of PICU stay ($r = 0.029$, $p = 0.774$) or total hospital stay ($r = 0.023$, $p = 0.820$). No subgroup, interaction, or sensitivity analyses were performed.

Table 4: Correlation of admission NLR with organ dysfunction scores

Organ system	Correlation (r)	p-value
Neurologic	0.213	0.033
Cardiovascular	0.307	0.002
Renal	-0.170	0.070
Respiratory	0.137	0.174
Hematologic	-0.110	0.277

Discussion

The main finding of this cohort study was that admission NLR was significantly higher among non-survivors than survivors in children admitted to the PICU with acute infectious diseases. The ROC-derived AUC of 0.759 indicates acceptable discrimination for mortality prediction. The high negative predictive value suggests that a lower admission NLR may help identify children at relatively lower risk of death, whereas the low positive predictive value highlights that NLR should not be used as a stand-alone rule-in test.

The clinical appeal of NLR lies in its availability and simplicity. Severe infectious diseases remain a major driver of pediatric critical illness, particularly in settings where delayed presentation and limited resources may worsen outcomes [1,2,3]. Established severity scores such as PELOD-2, PRISM III, and PIM2 provide valuable prognostic information but are more complex than a single laboratory-derived marker [4,5,6,7]. Because NLR is calculated from a routine complete blood count, it can be incorporated into early bedside assessment without additional cost or specialized testing.

From a pathophysiological perspective, NLR is biologically plausible as a marker of severe infection. Systemic inflammation is often accompanied by neutrophil mobilization driven by cytokines such as interleukin-1, interleukin-6, and tumor necrosis factor-alpha. At the same time, stress responses and immune dysregulation may contribute to lymphocyte apoptosis and lymphopenia [13,14,15]. A higher NLR may therefore reflect both heightened innate immune activation and relative suppression of adaptive immunity.

The direction of association observed in this cohort is consistent with previous literature. Kolaczowska and Kubes described the central role of neutrophil recruitment in inflammation [16], while Naess et al. reported that neutrophil-to-lymphocyte and monocyte-to-lymphocyte ratios may help diagnose bacterial infection in febrile patients [17]. Liu et al. found that NLR and plasma lactate predicted 28-day mortality in sepsis [18]. Similarly, de Jager et al. reported that lymphocytopenia and NLR predicted bacteremia better than conventional infection markers in an emergency care setting [19].

Comparable pediatric data also support the potential utility of NLR in sepsis. Dursun et al. reported that NLR and mean platelet volume may help predict pediatric sepsis [10], and Zhong et al. described NLR as a predictive marker for severe pediatric sepsis [11]. The present study contributes data from a North Indian PICU cohort and specifically examines children admitted with acute infectious diseases.

The observed correlations between admission NLR and neurologic and cardiovascular dysfunction were mild but statistically significant. These associations suggest that systemic inflammatory burden may be linked with selected organ dysfunction domains. In contrast, NLR did not correlate with PICU or hospital length of stay. Length of stay is shaped by many clinical and nonclinical factors, including nutritional status, nosocomial infection, response to therapy, discharge planning, and availability of intensive care resources.

Strengths of this study include the cohort design, use of a routinely available laboratory marker, standardized assessment of organ dysfunction through PELOD-2, and inclusion of a clinically relevant group of children with acute infectious diseases. These features make the findings especially relevant to resource-constrained settings where advanced biomarkers may not be readily available.

Several limitations merit consideration. The study was conducted at a single center and included a relatively small sample, with only six deaths. This limited statistical power and may have widened confidence intervals around performance estimates. The low number of events also prevented reliable multivariable adjustment; therefore, residual confounding by age, diagnosis, referral delay, prior antibiotic exposure, nutritional status, and coinfections may have influenced the observed associations. NLR was measured only at admission, so subsequent inflammatory changes were not captured. Selection from a tertiary care PICU may also over-represent severe or referred cases, limiting external validity.

Interpretation of the findings should therefore remain cautious. Admission NLR appears to be a useful low-cost adjunct for early risk stratification, particularly for identifying children at lower mortality risk when the value is low. It should not replace clinical assessment or validated severity scores. Larger multicenter studies with serial NLR measurements, prespecified cutoffs, and adjustment for important confounders are needed to validate its prognostic utility.

Generalisability is likely greatest for similar tertiary care PICUs in resource-constrained settings that manage children with acute infectious diseases. Application to postoperative patients, chronic infections, immunocompromised children, high-income settings, or units with substantially different case-mix should be undertaken carefully.

Conclusion

Among children admitted to the PICU with acute infectious diseases, admission NLR was associated with mortality and selected organ dysfunction. As an inexpensive and rapidly available marker derived from routine complete blood counts, NLR may be used as an adjunct to early risk assessment in resource-constrained settings. It should complement clinical judgment and validated severity scoring systems rather than replace them.

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