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ASSOCIATION OF NEUTROPHIL-LYMPHOCYTE RATIO AND C-REACTIVE PROTEIN LEVELS WITH DISEASE SEVERITY IN CHILDREN WITH BRONCHIOLITIS: A PROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

Background:

Bronchiolitis is a major cause of hospitalization in infants, particularly during the viral season. While clinical assessment remains the mainstay for diagnosis and management, the need for objective laboratory markers to predict disease severity is increasingly recognized. The Neutrophil-to-Lymphocyte Ratio (NLR) and C-Reactive Protein (CRP) are simple, cost-effective biomarkers that reflect systemic inflammation and immune response.

Objectives:

This study aimed to determine the association between NLR and CRP levels with clinical severity in infants diagnosed with bronchiolitis.

Methods:

A prospective observational study was conducted at a tertiary care hospital in India. A total of 120 children aged below 24 months diagnosed with bronchiolitis were enrolled. Based on the Bronchiolitis Severity Score (range: 7–21), patients were categorized into mild (n=46), moderate (n=52), and severe (n=22) groups. NLR was calculated from the differential leukocyte count, and serum CRP levels were measured. Statistical analysis included ANOVA and ROC curve analysis.

Results:

Mean NLR and CRP values increased progressively with disease severity (NLR: 1.9, 3.3, 5.7; CRP: 4.0, 8.8, 13.6 mg/L respectively; $p<0.001$). ROC analysis showed NLR >3.7 had 88.2% sensitivity and 81.3% specificity (AUC=0.84), while CRP >9.5 mg/L yielded 81.8% sensitivity and 72.0% specificity (AUC=0.79). Severe bronchiolitis correlated with feeding difficulty, oxygen desaturation, and prolonged hospital stay.

Conclusion:

Both NLR and CRP serve as valuable adjunctive markers for predicting bronchiolitis severity, aiding in early risk stratification and clinical decision-making.

Keywords: Bronchiolitis, Neutrophil-to-Lymphocyte Ratio, C-Reactive Protein, Inflammatory Biomarkers, Disease Severity

INTRODUCTION

Bronchiolitis is a leading cause of lower respiratory tract infections and hospital admissions in infants and young children under two years of age, particularly during the winter and early spring seasons [1,2]. It is most commonly caused by respiratory syncytial virus (RSV), although other viruses such as rhinovirus, parainfluenza, and human metapneumovirus may also be implicated [3]. The disease is characterized by inflammation, edema, and necrosis of epithelial cells lining the small airways, leading to mucus production and airway obstruction [4].

Diagnosis and assessment of bronchiolitis remain largely clinical, based on respiratory distress signs, auscultatory findings, and feeding difficulty. However, the subjective nature of these assessments often leads to variability in the evaluation of disease severity [5]. The Bronchiolitis Severity Score (BSS) is one standardized tool used to objectively grade disease severity based on clinical parameters such as respiratory rate, retractions, wheeze, and general condition [6].

In recent years, attention has turned toward identifying laboratory markers that may support clinical decision-making in bronchiolitis. C-Reactive Protein (CRP), an acute-phase reactant produced by the liver in response to interleukin-6 stimulation, has long been used to assess inflammation in pediatric infections [7]. However, CRP levels can also rise in bacterial co-infections, making its specificity for viral bronchiolitis somewhat limited.

The Neutrophil-to-Lymphocyte Ratio (NLR), calculated from a routine differential leukocyte count, has emerged as a potential biomarker reflecting the systemic balance between innate and adaptive immune responses [8]. Elevated NLR has been associated with poor outcomes in various pediatric infections, including sepsis, pneumonia, and bronchiolitis [9,10].

Studies from developed countries have begun exploring the role of NLR and CRP in bronchiolitis; however, there remains a paucity of data from resource-limited settings like India, where such simple and low-cost markers could significantly aid in early triage and treatment planning. Moreover, little is known about the combined predictive power of NLR and CRP in relation to bronchiolitis severity scores in infants.

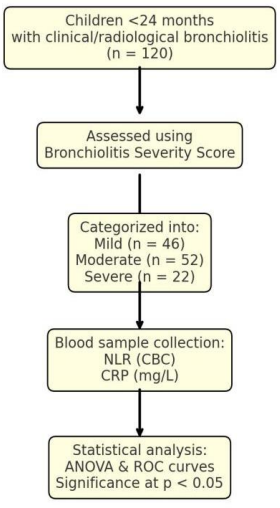
This prospective observational study was conducted to evaluate the association of NLR and CRP with disease severity in bronchiolitis using the standardized BSS score. Identifying such correlations may provide clinicians with objective tools to guide hospital admission decisions, monitor progression, and optimize resource allocation in pediatric respiratory illnesses.

METHODOLOGY

Study Design and Setting:

This was a prospective observational study conducted in the Department of Pediatrics at Saveetha medical college hospital in South India during june 2024- january 2025. The study was approved by the institutional ethics committee, and informed consent was obtained from the parents or legal guardians of all participants.

Figure 1. Study methodology flow diagram



Participants:
A total of 120 children aged below 24 months who were diagnosed clinically or radiologically with bronchiolitis were consecutively enrolled. Inclusion criteriainvolved children presenting with cough, tachypnea, chest retractions, wheeze, and crepitations consistent with viral bronchiolitis. Children were excluded if they had:

- Pre-existing chronic respiratory or cardiac illness,
- Known immunodeficiencies,
- Prior use of zinc supplements or corticosteroids,
- Clinical suspicion of bacterial superinfection.

Severity Assessment:
Each child was assessed at admission using the standardized Bronchiolitis Severity Score (BSS), which included:

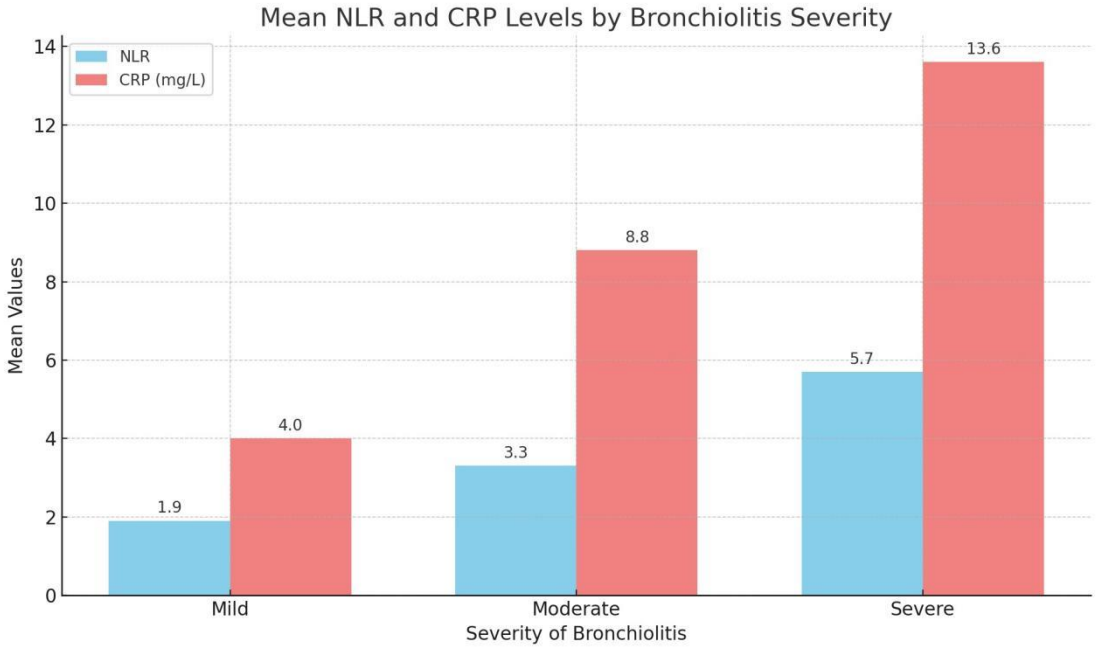
- Respiratory rate
- Wheezing intensity
- Accessory muscle usage
- Oxygen saturation (SpO2)
- General appearance
- Feeding ability
- Cyanosis

Each parameter was scored from 1 to 3, yielding a total score ranging from 7 (mild) to 21 (severe). Based on the total BSS:**Mild:** 7–10,**Moderate:** 11–14 and **Severe:** ≥15.
Data Collection and Investigations:
At the time of clinical evaluation, venous blood was drawn for:Complete Blood Count (CBC) to calculate NLR = Absolute Neutrophil Count / Absolute Lymphocyte Count and C-Reactive Protein (CRP) measured in mg/L using immunoturbidimetric assay.
Primary Outcome:
The primary outcome was the severity of bronchiolitis as determined by BSS. The study evaluated the correlation between disease severity and levels of NLR and CRP.
Statistical Analysis:
Data were analyzed using SPSS version 25.0. Mean values of NLR and CRP across severity groups were compared using Analysis of Variance (ANOVA). Receiver Operating Characteristic (ROC) curves were plotted to evaluate the diagnostic accuracy of NLR and CRP. A p-value < 0.05 was considered statistically significant.

RESULTS

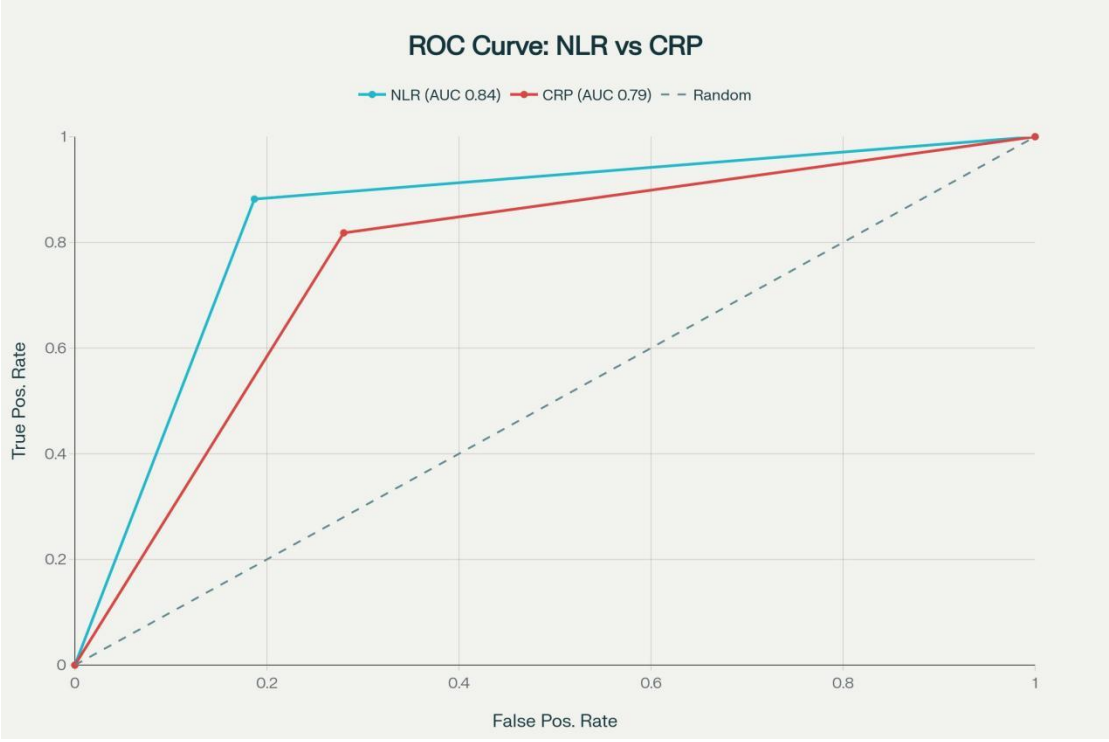
A total of 120 children under the age of 24 months, clinically diagnosed with bronchiolitis, were included in the study. Based on the Bronchiolitis Severity Score (BSS), the cohort was stratified into three groups: mild (n = 46, 38.3%), moderate (n = 52, 43.3%), and severe (n = 22, 18.3%). The mean age of participants was 7.8 ± 3.1 months, with a slight male predominance (55.8%). Demographic characteristics were comparable across all severity groups with no statistically significant differences in age or gender.
The primary objective was to evaluate whether inflammatory markers—specifically Neutrophil-to-Lymphocyte Ratio (NLR) and C-Reactive Protein (CRP)—correlated with disease severity. Mean values of both NLR and CRP showed a progressive and statistically significant increase from mild to severe groups ($p < 0.001$ by ANOVA). As presented in Table 1, the mean NLR was 1.9 in mild, 3.3 in moderate, and 5.7 in severe bronchiolitis cases. Similarly, mean CRP levels were 4.0 mg/L, 8.8 mg/L, and 13.6 mg/L in mild, moderate, and severe cases, respectively.

Figure 2. Mean NLR and CRP values across bronchiolitis severity groups



To assess the diagnostic utility of these markers in identifying severe bronchiolitis, Receiver Operating Characteristic (ROC) curves were constructed. As shown in Figure 1, the ROC for NLR had an Area Under the Curve (AUC) of 0.84, with a sensitivity of 88.2% and specificity of 81.3% at a cut-off >3.7. In comparison, the CRP ROC curve yielded an AUC of 0.79, sensitivity of 81.8%, and specificity of 72.0% at a cut-off >9.5 mg/L, as summarized in Table 2.

Figure 3. ROC curves demonstrating the diagnostic accuracy of NLR and CRP for predicting severe bronchiolitis. NLR shows a higher AUC and better discriminative power.



In addition to biomarker elevations, clinical features such as oxygen desaturation (<90%), feeding difficulty, and prolonged hospital stay were significantly more common in the severe group. The trend of increasing inflammation with disease severity is further illustrated in the bar chart below (Figure 2), which clearly shows the stepwise rise in both NLR and CRP levels across the three groups.

These results suggest that both NLR and CRP are reliable adjunctive markers in assessing bronchiolitis severity, with NLR showing superior diagnostic performance. Their routine availability makes them particularly useful in emergency settings and peripheral hospitals where advanced diagnostic tools may be limited.

DISCUSSION

This study demonstrates a significant correlation between elevated Neutrophil-to-Lymphocyte Ratio (NLR) and C-Reactive Protein (CRP) levels with increasing severity of bronchiolitis in infants. These findings suggest that both NLR and CRP may serve as reliable, easily accessible inflammatory biomarkers to complement clinical assessment in bronchiolitis.

The clinical diagnosis of bronchiolitis remains subjective, often leading to variability in severity grading and treatment decisions [1]. In this context, objective markers like NLR and CRP can aid in triage, particularly in resource-limited settings. Our study found that infants with severe bronchiolitis had significantly higher mean NLR (5.7) and CRP levels (13.6 mg/L), with NLR showing higher diagnostic accuracy (AUC = 0.84) compared to CRP (AUC = 0.79). These findings are consistent with previous research by Can et al., who also noted elevated NLR levels in infants with more severe disease [2].

NLR reflects the balance between neutrophilic inflammation and lymphocytic response, making it a sensitive marker of systemic inflammation [3]. It has gained attention across various pediatric conditions, including pneumonia, sepsis, and appendicitis [4–6]. In bronchiolitis, inflammation is characterized by epithelial damage, airway edema, and neutrophil infiltration of the lower respiratory tract [7,8]. This immune activation may explain the rising NLR levels seen with increasing severity.

Our findings align with those of Kose et al., who demonstrated that NLR was significantly elevated in children with bronchiolitis compared to healthy controls [9]. Similarly, Demir et al. emphasized the role of NLR in predicting hospitalization needs in respiratory tract infections [10]. While CRP is a well-established acute-phase reactant, it is less specific in viral infections and may also rise in bacterial coinfections, limiting its utility.

This study's strengths include its prospective design, uniform application of a validated bronchiolitis severity score, and analysis of two inexpensive and widely available biomarkers. However, limitations should be acknowledged. Being a single-center study, the results may not be generalizable. We also did not account for viral subtype identification or monitor longitudinal trends of the biomarkers during hospitalization.

Despite these limitations, the evidence supports incorporating NLR as a risk stratification tool in pediatric bronchiolitis protocols. Its superior sensitivity and specificity over CRP suggest that it can be used even at peripheral centers without advanced diagnostics. Further multi-center studies are needed to validate these findings across different populations and healthcare settings.

CONCLUSION

This prospective observational study highlights the utility of Neutrophil-to-Lymphocyte Ratio (NLR) and C-Reactive Protein (CRP) as adjunctive biomarkers in assessing disease severity in bronchiolitis among infants. A significant association was found between elevated NLR and CRP levels with increasing severity scores, with NLR demonstrating superior diagnostic accuracy. These readily available, low-cost inflammatory markers may support early risk stratification and guide clinical decision-making, especially in resource-constrained settings. Integrating NLR into standard assessment protocols could improve triage efficiency and optimize inpatient care. Further research is warranted to validate these findings across broader pediatric populations and care levels.

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