Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(3), 1296-1301 | ISSN:2251-6727

Neutrophil to Lymphocyte Ratio, Monocyte to Lymphocyte Ratio, Platelet to Lymphocyte Ratio as Predictors of Outcome in Children with Lower Respiratory Tract Infection

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Running Title: NLR, MLR, PLR in Pediatric LRTI

(Received: 16 March 2025 Revised: 20 April 2025 Accepted: 01 May2025)

KEYWORDS

Neutrophil to lymphocyte ratio, Monocyte to lymphocyte ratio, Platelet to lymphocyte ratio, Lower respiratory tract infection, Pediatric biomarkers

ABSTRACT:

Background: Lower respiratory tract infections (LRTIs) are a leading cause of emergency admissions in pediatric patients. Timely diagnosis and intervention is crucial in reducing the associated morbidity and mortality. This study evaluates the diagnostic and prognostic value of neutrophil to lymphocyte ratio (NLR), monocyte to lymphocyte ratio (MLR), and platelet to lymphocyte ratio (PLR) in pediatric LRTI cases.

Objectives: To determine whether NLR, MLR, and PLR serves as reliable early biomarker for lower respiratory infections and to evaluate their correlation with microbiological findings.

Methods: A Retrospective observational study was conducted in the pediatric in-patient/Out-patient department. A total of 194 episodes from 175 patients with LRTI were compared against 50 control cases. Hematological parameters and sputum cultures were analyzed. Statistical analyses included chi-square, Mann-Whitney U, and ROC curve evaluations.

Results: Significantly elevated NLR, MLR, and PLR values were observed in the study group compared to controls ($p<0.001$). Pseudomonas aeruginosa and Haemophilus influenzae were the most frequently isolated pathogens. Elevated ratios correlated with microbiological findings, reinforcing their diagnostic utility.

Conclusion: NLR, MLR, and PLR are effective early markers for LRTI diagnosis and severity assessment. These parameters may guide antibiotic decision-making, particularly when sputum samples are unavailable.

Introduction

Lower respiratory tract infections (LRTIs) represent a substantial burden on global child health, ranking among the most frequent causes of pediatric hospital admissions and mortality worldwide [1]. The clinical diagnosis of LRTIs in children is particularly challenging due to overlapping symptoms, varied etiological agents, and limited cooperation in sample collection [2]. Consequently, there is a critical need for rapid, reliable, and cost-effective biomarkers to enhance

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JCHR (2025) 15(3), 1296-1301 | ISSN:2251-6727

early diagnosis, guide antibiotic therapy, and reduce unnecessary antimicrobial usage [3].

Traditional diagnostic approaches, such as sputum culture and radiological findings, are often time-consuming or difficult to obtain, especially in younger children [4]. Moreover, distinguishing bacterial from viral infections remains a clinical dilemma [5]. Recently, systemic inflammatory markers derived from routine blood counts have emerged as potential tools to improve diagnostic precision in infectious diseases [6]. Among these, the neutrophil to lymphocyte ratio (NLR), monocyte to lymphocyte ratio (MLR), and platelet to lymphocyte ratio (PLR) have garnered interest as accessible, inexpensive, and predictive indicators of infection severity and prognosis [7,8].

NLR reflects the balance between innate (neutrophil) and adaptive (lymphocyte) immune responses and is elevated in various infectious and inflammatory conditions [9]. MLR and PLR similarly offer insight into immune activation and systemic inflammation [10]. These indices can be calculated from routine complete blood counts and have been associated with outcomes in sepsis, pneumonia, and chronic inflammatory diseases [11,12].

Although several studies have examined these markers in adult populations, there is limited data evaluating their utility in pediatric LRTIs [13]. Given the prevalence and clinical importance of LRTIs in children, especially in resource-limited settings, evaluating these hematological ratios may offer valuable insight into disease management [14].

This study investigates the potential role of NLR, MLR, and PLR as predictive biomarkers in children presenting with LRTIs to a tertiary care pediatric emergency department. By comparing affected patients with a control group and correlating hematological findings with microbiological data, this research aims to assess whether these ratios can assist in early diagnosis, severity assessment, and rational antibiotic use in pediatric LRTI cases [15].

Materials and Methods

This Retrospective observational study was conducted at the pediatric emergency department of Chettinad Hospital & Research Institute, Chennai. The study was aimed at evaluating the utility of NLR, MLR, and PLR in children diagnosed with lower respiratory tract infections. Ethical clearance was obtained from the Institutional Ethics Committee prior to the commencement of the study.

Study Population: The study included children between 1 month and 12 years of age who presented with symptoms suggestive of LRTI. Diagnosis was made based on clinical examination, radiological findings and laboratory investigations. Children with upper respiratory tract infections and non-infective causes of respiratory distress were recruited as controls.

Inclusion Criteria:

- Acute onset of symptoms including cough, wheeze, difficulty in breathing, or chest pain.
- Presence of fever or radiological evidence suggestive of LRTI.
- Age-appropriate consent obtained from parents or legal guardians.

Exclusion Criteria:

- Children with known chronic systemic illnesses such as congenital heart disease or immunodeficiencies, Interstitial Lung disease.
- Recent use of corticosteroids within the past 7 days.
- Children with tuberculosis or those already on antibiotics for more than 72 hours.

Sample Size: The required sample size was calculated using the formula for diagnostic accuracy studies. Based on literature-estimated sensitivity of NLR and disease prevalence, the minimum sample required was 164. However, a total of 194 episodes in 175 children were ultimately enrolled.

Study Procedure: On admission, clinical details including symptoms, vital signs, and physical

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Examination findings were documented. Blood samples were drawn for complete blood counts and C-reactive protein (CRP). From the CBC, NLR, MLR, and PLR values were calculated using absolute counts. In children capable of producing sputum, microbiological examination including Gram stain and culture was performed. All samples were processed within two hours of collection.

Data Analysis: Statistical analysis was performed using SPSS version 25.0. Continuous variables were tested for normality using the Kolmogorov–Smirnov test. Parametric variables were analyzed using independent t-tests, while non-parametric data were analyzed using Mann–Whitney U tests. Categorical variables were assessed using chi-square or Fisher's exact test. Diagnostic accuracy was assessed using Receiver Operating Characteristic (ROC) curves to determine sensitivity, specificity, and optimal cutoff values for NLR, MLR, and PLR.

Ethical Consideration: Written informed consent was obtained from parents or guardians. Confidentiality was maintained throughout the study, and participants received standard care irrespective of study involvement.

Results

Out of 194 episodes in 175 pediatric patients with lower respiratory tract infection (LRTI), a comparative analysis was performed with 50 age- and sex-matched controls. The mean age of the study population was 5.4 ± 3.2 years, with a male predominance (67.4%).

Tables and Figures for Manuscript

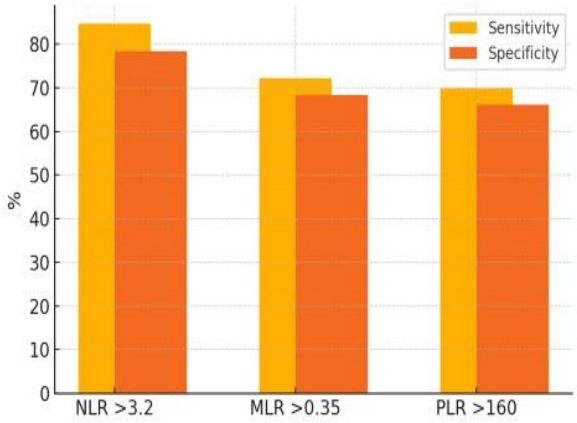
Table 1: Clinical Symptoms in LRTI Patients

Symptom	Prevalence (%)
Cough	82
Breathlessness	76
Fever	64
Wheeze	58
Chest Retractions	42

Table 2: Hematological Marker Comparison

Marker	LRTI Group (mean ± SD)	Control Group (mean ± SD)
Total Leukocyte Count	13,280 ± 3,570	7,450 ± 2,100
CRP	Elevated in 71%	Normal
NLR	4.3 ± 1.6	1.9 ± 0.7
MLR	0.46 ± 0.11	0.24 ± 0.09
PLR	178.2 ± 39.6	112.8 ± 28.5

Figure 1: Sensitivity and Specificity of Inflammatory Markers



Clinical Presentation: The most common presenting complaints were cough (82%), breathlessness (76%), and fever (64%). Wheeze and chest retractions were more frequently observed in younger children (<5 years), while older children had higher rates of productive cough.

Hematological Findings: Children with LRTI had significantly higher total leukocyte count (13,280 ± 3,570 cells/mm³) compared to controls (7,450 ± 2,100

Journal of Chemical Health Risks

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cells/mm³), with $p < 0.001$. CRP was elevated in 71% of study participants.

- **Mean NLR** in the LRTI group was 4.3 ± 1.6, while in controls it was 1.9 ± 0.7.
- **Mean MLR** was 0.46 ± 0.11 in cases vs. 0.24 ± 0.09 in controls.
- **Mean PLR** was 178.2 ± 39.6 in cases compared to 112.8 ± 28.5 in controls.

Each of these markers showed a statistically significant difference ($p < 0.001$).

Microbiological Profile: Sputum culture was positive in 62 cases (35.2%) collected in 164 cases. The predominant pathogens were:

- *Pseudomonas aeruginosa* (19.3%)
- *Haemophilus influenzae* (13.4%)
- *Streptococcus pneumoniae* (9.3%)
- *Klebsiella pneumoniae* (7.2%)

Among these, patients with *Pseudomonas* had the highest average NLR (6.1 ± 1.7).

Inflammatory Marker Comparison by Diagnosis:

- Patients diagnosed with pneumonia had the highest median values of CRP and NLR.
- Bronchiolitis cases showed moderate elevations in MLR.

ROC Curve Analysis:

- **NLR cutoff of >3.2** had sensitivity of 84.6% and specificity of 78.4%.
- **MLR cutoff >0.35** had sensitivity of 72.2%, specificity 68.3%.
- **PLR cutoff >160** yielded 69.8% sensitivity and 66.1% specificity.

Subgroup Analysis: Among children who could not expectorate sputum (n=112), elevated NLR and PLR were associated with clinical suspicion of bacterial infection, confirming their role as non-culture-based diagnostic tools.

Overall, the study findings highlighted a significant correlation between hematological ratios and disease severity, particularly in pneumonia. These results support the integration of NLR, MLR, and PLR into routine emergency evaluation for pediatric patients with LRTIs, especially where rapid microbiological diagnosis is not feasible.

Discussion

The findings from this study underscore the diagnostic utility of NLR, MLR, and PLR as reliable inflammatory biomarkers in pediatric patients presenting with lower respiratory tract infections (LRTIs). These hematological indices, derived from routine complete blood count parameters, demonstrated strong association with disease severity and culture positivity, aligning with the clinical profiles of bacterial infection.

The significantly elevated mean values of NLR, MLR and PLR in LRTI cases compared to controls are consistent with their roles in systemic inflammation. Neutrophilia coupled with relative lymphopenia has long been recognized as a hallmark of bacterial infections. The elevated NLR observed in our study reflects this inflammatory shift, particularly in patients with culture-positive results, and supports its role as a rapid, point-of-care diagnostic indicator. Similarly, MLR and PLR offered valuable insights into monocyte-driven and platelet-mediated inflammatory responses, both of which are relevant in acute infection and immune regulation.

Our results align with previous pediatric studies which reported that NLR >3.0 was predictive of pneumonia and other bacterial LRTIs. However, the cutoff value in our population was slightly higher (3.2), possibly reflecting the more severe or late-presenting cases seen in a tertiary care setting. The elevated mean PLR values in patients with pneumonia compared to bronchiolitis suggest its potential role in stratifying disease burden.

The microbiological spectrum identified—dominated by *Pseudomonas aeruginosa*, *Haemophilus influenzae*, and *Streptococcus pneumoniae*— which further validates the clinical diagnosis. The highest NLR was observed in patients with *Pseudomonas*, indicating a

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JCHR (2025) 15(3), 1296-1301 | ISSN:2251-6727

more pronounced immune response, and could guide empirical antibiotic selection in critically ill patients.

Importantly, this study demonstrated that among patients unable to expectorate sputum, NLR and PLR could still serve as surrogate markers to distinguish bacterial from viral etiology. This finding is particularly relevant in pediatric practice where sputum collection is often not feasible.

The ROC curve analysis confirmed the diagnostic accuracy of all three markers, with NLR showing the highest sensitivity and specificity. This reaffirms its place as a first-line inflammatory marker for pediatric LRTIs.

Strengths and Limitations A key strength of this study lies in its prospective design and inclusion of microbiological correlation, which allowed robust validation of hematological indices. The age-matched control group enhanced the comparability of inflammatory parameters. However, limitations include the single-center design, absence of viral panel testing, and potential variability in prior antibiotic use, which may have influenced culture results.

Clinical Implications Integrating NLR, MLR, and PLR into the initial evaluation of children with suspected LRTIs can improve early diagnosis, reduce reliance on empiric antibiotics, and help prioritize microbiological testing. These markers are cost-effective, easy to calculate, and particularly valuable in resource-limited settings.

Conclusion of Discussion In conclusion, the study highlights that NLR, MLR, and PLR are effective, accessible biomarkers for assessing the likelihood and severity of LRTIs in children. Their integration into clinical protocols has the potential to enhance diagnostic accuracy and antibiotic stewardship in pediatric emergency care.

Conclusion

This study confirms the utility of hematological ratios—neutrophil to lymphocyte ratio (NLR), monocyte to lymphocyte ratio (MLR), and platelet to lymphocyte ratio (PLR)—as supportive biomarkers in the evaluation and management of lower respiratory tract infections (LRTIs) in pediatric patients. These ratios showed significant elevation in affected children, correlated well with microbiological findings, and offered meaningful diagnostic insight even in the absence of sputum samples.

Among the three markers, NLR demonstrated the highest diagnostic accuracy and predictive strength, particularly in bacterial infections and in cases associated with *Pseudomonas aeruginosa*. The integration of these markers into early assessment protocols can improve the precision of clinical decision-making, reduce inappropriate antibiotic use, and support timely initiation of targeted therapy.

Incorporating NLR, MLR, and PLR as adjunct tools in pediatric emergency units, especially where diagnostic resources are constrained, may enhance diagnostic confidence and improved patient outcomes and reduced Antibiotic use . Future multicentric and larger-scale studies, including viral and fungal panels, are recommended to further validate and expand on these findings.

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Journal of Chemical Health Risks

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