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Predictive value of hematological indices in community acquired pneumonia in children: A prospective observational study

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ABSTRACT

Introduction: Community acquired pneumonia is an important cause of morbidity and mortality in the paediatric population, especially in the under-5 age group. It is essential to identify parameters for early diagnosis and prognostication. Conventionally used markers such as CRP and procalcitonin are expensive and often unavailable in low-resource settings. This mandate the use of novel and ubiquitous investigations such as complete hemogram. The present study aimed at evaluating the role of novel systemic inflammatory indices – Neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), platelet-to-lymphocyte ratio (PLR), systemic immune-inflammatory index (SII), and systemic inflammatory response index (SIRI) - in predicting disease severity in children with community acquired pneumonia.

Methods: This prospective observational study, conducted at a tertiary care centre of North India, included 130 children aged 1 month–14 years admitted to the Paediatrics ward with a diagnosis of community acquired pneumonia. The relevant clinical features and complete hemogram of the child were recorded and defined indices calculated. The role of these indices in predicting the need for ICU admission, vasopressor use, and development of complications including mortality was evaluated using ROC curves.

Results: NLR was found to have the highest sensitivity in predicting disease severity. It could predict the need for ICU admission with a sensitivity of 78.5% and specificity of 50% (p=0.0174). It might be an important marker in predicting mortality in children with community acquired pneumonia. MLR also demonstrated high specificity in predicting complications.

Conclusion: NLR derived from routine hemogram can be used as a simple and non-expensive screening tool for predicting the development of severe illness and complications in children hospitalized with community acquired pneumonia.

KEY WORDS: *Community-Acquired Pneumonia; Lymphocytes; Neutrophils; Prognosis*

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INTRODUCTION

Pneumonia is an acute infection of the lung parenchyma caused by bacteria, viruses, or atypical pathogens. [1, 2] Community-acquired pneumonia (CAP) is defined as an acute infection of the pulmonary tissue in an immunocompetent child who has not been recently hospitalized, or has been hospitalized for less than 48 hours, and has acquired the infection from the community. [3] Pneumonia is an important cause of hospitalization in children. [2] Although it is a major cause of morbidity and mortality in all age groups, mortality rates are higher at the extremes of age, particularly in children and the elderly.

Biomarkers such as procalcitonin and C-reactive protein (CRP) have been used to assess disease severity in children with pneumonia. However, they are often unavailable in low-resource settings and may lack specificity. [3] This highlights the need for readily available, reliable, and relatively inexpensive parameters for assessment of disease severity and prognostication in children with pneumonia. As leukocytes play a major role in the immune and inflammatory responses of the body, leukocyte-derived ratios have been studied and shown potential in predicting prognosis and treatment response in adults with several diseases, including CAP. [4,5,6] Neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), platelet-to-lymphocyte ratio (PLR), systemic immune-inflammatory index (SII), and systemic inflammatory response index (SIRI) are novel inflammatory biomarkers that have shown promising results in predicting outcomes in pneumonia. NLR, in particular, has demonstrated predictive value for hospitalization, intensive care unit (ICU) admission, and mortality in children with severe pneumonia. [7] However, evidence regarding the utility of these parameters in the pediatric population remains limited.

This study aimed to assess the utility of hematologic parameters, including NLR, MLR, PLR, SII, and SIRI, in predicting the course of community-acquired pneumonia in children in terms of duration of hospitalization, need for ICU admission, development of complications such as parapneumonic effusion or empyema, and mortality.

METHODS

This prospective observational study was conducted at a tertiary care center of North India. The study protocol was approved by the Institutional Ethics Committee (IEC approval no. BREC/25/378). Children aged 1 month – 14 years admitted to the Paediatrics ward of the hospital between 1st November, 2025 and 31st January, 2026 with a diagnosis of community acquired pneumonia were included in the study. A written informed consent was obtained from the parents/guardians of the participants. Patients with hospital acquired pneumonia, acute bronchiolitis and tuberculosis were excluded from the study. Children with nephrotic syndrome and on steroid therapy were also excluded.

Sample Size Calculation

This prospective observational study was aimed to investigate the predictive value of systemic inflammatory indices—namely neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), platelet-to-lymphocyte ratio (PLR), systemic immune-inflammation index (SII), and systemic inflammation response index (SIRI)—for estimating disease severity in children with community-acquired pneumonia (CAP), using duration of hospital stay as the primary outcome.

Basis for Sample Size Estimation

As the outcome of interest was a continuous variable (duration of stay), and the study intended to evaluate multiple inflammatory biomarkers as predictors, sample size estimation was performed using the framework of multiple linear regression. Using findings from a previous study, the required sample size was calculated using the formula for multiple linear regression:

$$n = \frac{(Z_{1-\alpha/2} + Z_{1-\beta})^2 + k + 1}{f^2}$$

Where:

- $Z_{1-\alpha/2} = 1.96$
- $Z_{1-\beta} = 0.84$
- $k = 6$
- $f2 = 0.15$

$$n = \frac{(1.96 + 0.84)^2 + 6 + 1}{0.15} \approx 98$$

Final Sample Size

A minimum of 98 sample size was calculated. However, a total number of 130 participants were obtained and recruited during the three month study period, which provided sufficient statistical power for the primary objective and supported the secondary analyses

Data collection: Demographic characteristics, clinical examination findings, and investigations including Chest X-ray findings, and complete hemogram were recorded. Treatment was given as per standard protocols. Children with an FiO2 requirement ≥50%, acidosis on blood gas analysis (pH≤7.25), early signs of shock and need for vasopressors or invasive ventilation were admitted to pediatric ICU. Requirement of oxygen support, if any, including invasive ventilation and high-frequency ventilation, vasopressor use, and complications, if any, were documented.

Following indices were calculated using the complete hemogram:

- NLR = $\frac{Neutophils}{Lymphocytes}$
- MLR = $\frac{Monocytes}{Lymphocytes}$
- PLR = $\frac{Platelets}{Lymphocytes}$
- SII = $\frac{Platelets\ x\ Neutrophils}{Lymphocytes}$
- SIRI = $\frac{Neutrophils\ x\ Monocytes}{Lymphocytes}$

Statistical Analysis:

The presentation of the Categorical variables was done in the form of number and percentage (%). On the other hand, the quantitative data were presented as the means ± SD and as median with 25th and 75th percentiles (interquartile range). The data normality was checked by using Shapiro-Wilk test. The cases in which the data was not normal, non-parametric tests were used. The association of the quantitative, non-normally distributed variables was analyzed using Mann-Whitney Test. The association of the qualitative variables were analyzed using Chi-Square test. If any cell had an expected value of less than 5 then Fisher's exact test was used. Spearman rank correlation coefficient was used for correlation of length of hospital stay with NLR, MLR, PLR, SII

and SIRI. Multivariate logistic regression was used to find out independent significant risk factors of ICU admission, mortality, complications, and requirement of inotropes. Receiver operating characteristic curve was used to assess cut off point, sensitivity, specificity, positive predictive value and negative predictive value of NLR, MLR, PLR, SII and SIRI for predicting ICU admission, mortality, complications, and requirement of inotropes. Univariate and multivariate linear regression was used to assess significant factors affecting duration of hospital stay. The data entry was done in the Microsoft EXCEL spreadsheet and the final analysis was done with the use of Statistical Package for Social Sciences (SPSS) software, IBM manufacturer, Chicago, USA, version 25.0. For statistical significance, p value of less than 0.05 was considered statistically significant.

RESULTS

A total of 130 patients were enrolled during the 3-month period with a median age of 1.0 (0.5-3) years. The baseline characteristics of participants have been summarized in Table-1 and clinical outcomes have been summarized in Table-2.

Table 1: Baseline Characteristics (n=130)

Variable		**Frequency**	**Percentage**
Age	<1 year	64	49.23%
	1-5 years	48	36.92%
	6-10 years	11	8.46%
	11-14 years	7	5.38%
Sex	Male	78	60%
	Female	52	40%
Danger signs		16	12.3%
Past history of Pneumonia		24	18.46%
Immunization	Complete	96	73.85%
	Incomplete	9	6.92%
	Not Known	25	19.23%
Comorbidities		29	22.3%
Variable		**Mean (days)**	**Median (25^{th}-75^{th} centile)**
Symptoms	Duration of cough	5.48 ± 6.19	3(2-7)
	Duration of Fever	4.97 ± 5.5	4(2-7)

Table 2: Outcome Variables (n=130)

Variable			
Length of Hospital Stay		6.72 ± 4.55	5(3-7)
Oxygen support	Invasive ventilation	14	10.76%
	HHHFNC	17	13.08%
	CPAP	1	0.77%
	NP	47	36.15%
	FM	5	3.85%
	NRM	7	5.38%
	Total	91	70%
Vasopressor use		10	7.69%
ICU Admission		28	21.54%
	Empyema	3	2.31%

Complications	Hydropneumothorax	1	0.77%
	Pleural effusion	8	6.15%
	Respiratory failure	13	10.00%
	Total Complications	25	19.23%
Mortality		8	6.15%

Table 3: Cutoff values, sensitivity, specificity for NLR, MLR (n=130)

	Variable (Cut-off values)	Sensitivity % (95% CI)	Specificity % (95% CI)
Neutrophil-to-Lymphocyte Ratio (NLR)	Vasopressor use 1.1905	90% (55.5 - 99.7%)	48.33% (39.1 - 57.6%)
	ICU Admission 1.1556	78.5% (59.0 - 91.7)	50% (39.9 - 60.1)
	Complications 1.1905	88% (68.8 - 97.5%)	53.33% (43.3 - 63.1%)
	Mortality 1.1905	100% (63.1 - 100.0%)	48.36% (39.2 - 57.6%)
Monocyte-to-Lymphocyte Ratio (MLR)	Vasopressor use 0.3061	40% (12.2 - 73.8%)	91.67% (85.2 - 95.9%)
	ICU Admission 0.0571	42.86% (24.5 – 62.8%)	74.51 (64.9 – 82.6)
	Complications 0.2093	48% (27.8 - 68.7%)	84.76% (76.4 - 91.0%)
	Mortality 0.3061	37.5% (8.5 - 75.5%)	90.98% (84.4 - 95.4%)

Table 4: PPV and NPV for NLR, MLR (n=130)

	PPV % (95% CI)	NPV % (95% CI)	p value
Neutrophil-to-Lymphocyte Ratio (NLR)	12.7% (6.0-22.7%)	98.3% (90.9-100.0%)	0.0042
	30.1% (19.9-42.0%)	89.5% (78.5-96.0)	0.0174
	31% (20.5-43.1%)	94.9% (85.9-98.9%)	<0.0001
	11.3% (5.0-21.0%)	100% (93.9-100.0%)	0.002
Monocyte-to-Lymphocyte Ratio (MLR)	28.6% (8.4-58.1%)	94.8% (89.1-98.1%)	0.3057
	31.6% (17.5-48.7%)	82.6% (73.3-89.7)	0.3773
	42.9% (24.5-62.8%)	87.3% (79.2-93.0%)	0.0057
	21.4% (4.7-50.8%)	95.7% (90.2-98.6%)	0.51

Table-3,4 depicts the sensitivity, specificity, Positive predictive value (PPV) and Negative predictive value (NPV) of Neutrophil-to-lymphocyte ratio (NLR), Monocyte-to-lymphocyte ratio (MLR) in predicting disease severity in terms of vasopressor use, ICU admission, complications including pleural effusion and empyema, and mortality. Of all the parameters, NLR has the highest sensitivity and moderate specificity in predicting disease severity in children hospitalized with community acquired pneumonia. It can predict the need for

ICU admission with a sensitivity of 78.5% and specificity of 50% at a cut-off of 1.1556 (p=0.0174). NLR demonstrated a high sensitivity compared to other markers. Figure 1 depicts ROC curves and Table IV depicts Area under the ROC curves with 95% Confidence intervals. It might be an important marker in predicting mortality in children with community acquired pneumonia at a cut-off value of 1.1905. Monocyte-to-lymphocyte ratio (MLR) offers a higher specificity, but lower sensitivity in predicting development of complications such as pleural effusion, empyema and respiratory failure at a cut-off 0.2093 (sensitivity-48%, specificity-84.76%, p=0.0057). Univariate linear regression analysis showed that NLR significantly reduced the duration of hospital stay (beta coefficient-0.304, standard error-0.119, p value-0.012), however it was not found to be an independent risk factor in multivariate regression analysis. Multivariate poisson regression analysis found platelet count to be a significant independent predictor of mortality, though it was not found to significantly predict variations in ICU stay, inotrope use or development of complications.

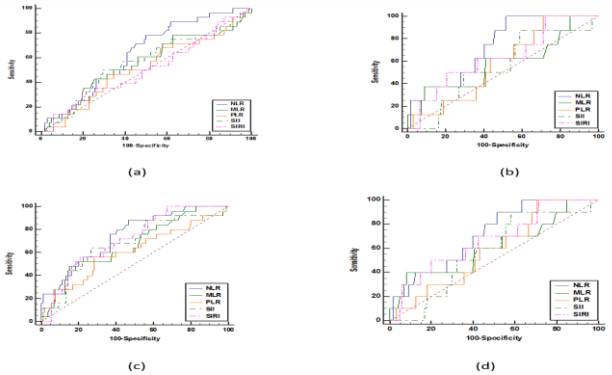

Figure 1: ROC curves displaying predictive abilities of NLR, MLR, PLR, SII and SIRI for: (a) ICU admission (b) Mortality (c) Complications (d) Vasopressor Use

DISCUSSION

Recent studies have identified hematological indices such as NLR, MLR and PLR as potential biomarkers for prognostication in a variety of disorders ranging from infectious pathologies including sepsis and necrotizing pneumonia to non-communicable diseases such as coronary artery diseases and rheumatological disorders. Owing to the easy-availability and low cost, these markers have gained interest especially in the resource-limited settings such as ours.

In the present study, role of systemic inflammatory indices including NLR, MLR, PLR, SII, SIRI and D-dimers was assessed in predicting need for ICU admission, vasopressor use and risk of complications such as effusions and empyema and in-hospital mortality in children with community acquired pneumonia. NLR was found to be a sensitive marker of disease severity in children with community acquired pneumonia. However, the specificity was low. This implies that NLR can be used as a potential screening tool for predicting the development of severe illness and complications, including pleural effusions, empyema and respiratory failure. These findings align with previous literature. [8] A large, multicenter, retrospective study in adults with CAP found an NLR value of 12 at admission was associated with a more severe disease, reflected in increased length of hospital stay and higher likelihood of ICU admission and in-hospital mortality. [9]

In the present study, value of NLR above 1.1556 predicted severe disease and need for ICU admission, whereas a slightly higher cut-off of 1.1905 was needed to reliably predict development of complications and mortality. In another study by Lakshmanan M et al, NLR has been described as a sensitive point-of-care marker for identifying bacterial etiology in pediatric community acquired pneumonia with a sensitivity of 87.6% and a specificity of 62.8% at a cut-off of 1.74. [8]. This is in contrast to the adult literature where a cut-off as high as 12 has been proposed. [9.10] Huang et al proposed an optimal NLR cut-off of 6.5 for predicting 30-day mortality in elderly population with CAP. [11]

Studies in adult population have established association between hematological indices such as NLR and SII with severe illness and mortality. Although, few studies in children have found association of these novel indices with Mycoplasma pneumoniae pneumonia and Necrotizing pneumonia, scarce literature is available on role of these parameters in prognostication of community acquired pneumonia in pediatric population. [12] Moreover, the available literature on utility of SII is predominantly about patients with Mycoplasma pneumoniae pneumonia rather than CAP. SIRI and MLR have also been found to

predict Mycoplasma pneumoniae pneumonia with high sensitivity and specificity. [13] However, in our study, PLR, SII and SIRI were not found to have a statistically significant correlation with pneumonia severity in children.

In a similar study by Shao L et al, values of NLR, MLR, PLR, SII and SIRI were significantly higher in children with Mycoplasma pneumoniae pneumonia as compared to control group, suggesting a role of these parameters in diagnosis [13]. In contrast to these findings, Aliye Gamze Calis et al found that NLR, MLR, and PLR have a poorer predictive performance compared to conventional scores such as CURB-65 and PSI. however, they might be used as adjuncts to these scores. [14] Wincy wing sze ng et al have identified NLR as a useful marker in prognostication of hospitalized patients with community acquired pneumonia. They observed higher NLR values in non-survivors than survivors. Also, it was seen that a persistent elevation was associated with treatment failure and suggestive of poor prognosis. [15]

In the present study, MLR had higher specificity and low sensitivity in predicting ICU admission and mortality, but this was not found to be statistically significant. However, at a cut-off of 0.2093, it can predict the risk of development of complications i.e. effusions, empyema and respiratory failure with a high specificity of 84.76% which was statistically significant (p=0.0057). This data corroborates the results reported in previous literature suggesting a role of MLR in predicting disease severity in CAP. [6] However, to the best of our knowledge, no literature is available in assessing the role of MLR in predicting complications in children with community acquired pneumonia.

Heock Lee et al assessed role of incremental change in NLR and CRP in prognostication of children hospitalized with community acquired pneumonia. They found that NLR on D4 of admission and its incremental change were strong predictors of ICU admission and 30-day mortality. [16]

Since only the initial values of the inflammatory indices were taken, temporal trends and the prognostic significance of changes in these indices over the course of time could not be assessed. This remains a major limitation of the

present study. Another limitation was the relatively small sample size of the study, thus limiting the generalizability of the results to broader population. Distinction of viral and bacterial pneumonia and identification of causative organism using nasopharyngeal swab could not be done.

CONCLUSION

NLR derived from routine hemogram can be used as a simple and non-expensive screening tool for predicting the development of severe illness and complications in children hospitalized with community acquired pneumonia.

CONFLICT OF INTEREST

None

SOURCES OF FUNDING

None

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