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Correlation of Immunological Biomarkers and Severity of Pneumonia in Pediatric Patients

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Abstract

Among children under five, pneumonia stands as a major contributor to both illness and death, creating a significant challenge for global health efforts. This study aimed to evaluate the correlation between radiological severity, clinical parameters (such as fever and oxygen saturation), and laboratory markers (including CRP levels, white blood cell count, and the neutrophil-to-lymphocyte ratio) in pediatric patients with pneumonia. A retrospective analysis was conducted on 51 hospitalized children with severe pneumonia admitted to Al Mansour Pediatric Hospital in Baghdad from July 2024 to February 2025. The results revealed a strong association between radiologic severity and clinical indicators, with higher fevers and lower oxygen saturation levels observed in more severe cases. CRP levels showed a moderate positive correlation with pneumonia severity, while bacterial infections were associated with significantly higher CRP levels compared to viral or unknown causes. White blood cell count progressively increased with disease severity, reinforcing its role as a supportive marker. Notably, the neutrophil-to-lymphocyte (N-L) ratio emerged as a highly effective predictor of pneumonia severity, with a cut-off value of 18.5 ensuring high sensitivity (84.6%) and specificity (93.0%). These findings underscore the importance of integrating these biomarkers into clinical assessments for early identification and timely intervention in severe pediatric pneumonia cases. The study highlights the potential of the N-L ratio as a simple yet powerful tool to improve patient outcomes and calls for further research to validate these findings in larger cohorts.

Keywords: Pneumonia, Pediatric, CRP, Neutrophil-to-lymphocyte ratio, Severity prediction, Biomarkers

1. Introduction

Pneumonia is a serious lung infection that significantly affects young children under five, leading to high rates of illness and even death worldwide. It poses a major threat to global public health (Al-Dalfi *et al.*, 2023). Over time, pneumonia can weaken lung function in children, making breathing harder. The infection causes inflammation, leading to the accumulation of fluid or pus in the lungs' tiny air sacs, which disrupts the normal transfer of oxygen into the bloodstream. Symptoms can vary from mild to severe and often include coughing, fever, chills, and shortness of breath. This condition can result from fungi, bacteria, or viral infections (Al-Dalfi *et al.*, 2023).

In 2021, Iraq, excluding the Kurdistan region, saw 758 pneumonia-related deaths among children under the age of five. This alarming number underscores the ongoing health challenges young children face, particularly with respiratory infections (Al-Dalfi *et al.*, 2023).

Millions of children continue to lose their lives before reaching the age of five, a heartbreaking reality that underscores the ongoing global challenges in newborn and child health—especially among the most disadvantaged communities. In 2021 alone, 4.9 million children under five died, with nearly half of these being newborns .Furthermore, an estimated 2.1 million young lives, ranging from children to young adults aged 5 to 24, were tragically lost due to associated factors. The majority of these deaths occurred in sub-Saharan Africa and Southern Asia, highlighting the urgent need for stronger healthcare systems, improved access to medical care, and sustained efforts to eliminate preventable child

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and youth fatalities. Although progress has been made, much work remains to ensure that every child has the opportunity to survive and thrive (WHO, 2021).

Streptococcus pneumoniae is the primary driver behind community-acquired pneumonia (sCAP). Alongside this major culprit, other bacterial agents classified as "non-core CAP pathogens"—such as methicillin-resistant *Staphylococcus aureus* (MRSA), *Pseudomonas aeruginosa,* and various gram-negative strains—play a contributing role in a fraction of sCAP instances. Emerging research suggests that viruses may play a more significant role in causing sCAP than previously thought, with ongoing studies utilizing PCR molecular platforms expected to clarify their true prevalence. Another frequently detected pathogen in sCAP cases is Legionella pneumophila (Niederman & Torres, 2022).

Prior studies have indicated that patients with community-acquired pneumonia (CAP) who test positive for HBoV are at a higher risk of developing severe pneumonia (Li *et al.*, 2025).

Viruses are a major cause of pediatric pneumonia, especially in high-income regions, where antibiotics are often ineffective. To improve diagnosis, researchers developed a causal Bayesian network (BN) model that predicts the likely pathogen, distinguishing bacterial from non-bacterial infections. This can help refine treatment strategies and reduce unnecessary antibiotic use (Wu *et al.*, 2023).

Among children, *Streptococcus pneumoniae* is a predominant bacterial cause of pneumonia, while respiratory syncytial virus (RSV) stands out as the most frequent viral culprit. The severity of the illness is shaped by the interplay between immune system functionality and the inflammatory response elicited by the infection, making biomarker monitoring crucial. CRP aids immune activation, while the neutrophil-lymphocyte ratio (NLR) helps assess systemic inflammation. NLR is a reliable predictor of severe pneumonia in children (Gong *et al.*, 2024).

In cases of community-acquired pneumonia (CAP) in children, the white blood cell (WBC) count and absolute neutrophil count (ANC) are routinely analyzed. Conversely, in adults, host biomarkers are commonly employed to estimate the severity of the disease (Florin *et al.*, 2020).

The goal of this study was to thoroughly investigate the connection between the severity of pneumonia and their potential correlation with a range of clinical parameters (such as fever and oxygen saturation), and laboratory markers (including CRP levels, white blood cell count, and the neutrophil-to-lymphocyte ratio) in pediatric patients with pneumonia.

2. Method

2.1. Study population

It is a retrospective analysis of 51 hospitalized children with severe pneumonia admitted to the al Mansour pediatrist hospital in Baghdad, from July 2024 to February 2025, and we collected the clinical information and testing data of the patients.

2.1.1. Inclusion criteria

1. Children who fulfilled the diagnostic criteria for SP, including cases of community-acquired pneumonia (CAP).
2. Pediatric patients older than 29 days admitted to the hospital, provided their medical records were fully documented.

2.1.2. Exclusion criteria

1. Patients whose parents did not consent to or declined participation in completing essential pathogenic tests.
2. Individuals with compromised immune systems were excluded from the study.
3. Patients diagnosed with other pulmonary conditions, such as asthma or congenital lung abnormalities, were also not included.

2.2. Patient profile and severity assessment

The study compiled extensive clinical data, featuring essential details about each child, such as their age, gender, weight, and primary diagnosis. Additionally, the length of their hospital stay was recorded. A detailed evaluation was conducted to gauge the severity of the illness, taking into account various clinical parameters, symptom progression, and overall health status. Pneumonia severity was classified based on **World Health Organization (WHO) criteria**, incorporating respiratory rate, fever, and oxygen saturation (SpO_2) as key parameters:

2.2.1. Mild pneumonia

Defined by symptoms such as cough and accelerated breathing (≥50 breaths per minute for infants under 12 months, ≥40 breaths per minute for children aged 1–5 years). No evidence of respiratory distress, and oxygen levels remain stable (SpO_2 ≥95%).

2.2.2. Moderate pneumonia

Identified by lower chest wall indrawing, increased respiratory rate beyond age-specific limits, fever (≥38°C), and potential mild hypoxia (SpO_2 90–95%).

2.2.3. Severe pneumonia

Characterized by pronounced hypoxia (SpO_2 <90%), signs of respiratory distress (e.g., grunting, inability to feed, cyanosis), high-grade fever (≥39°C), and changes in consciousness or alertness.

These parameters were systematically assessed by expert pediatrician for all pediatric pneumonia cases included in the study.

2.3. Routine blood test

Each participant provided a 5 mL venous blood sample in the early morning. A fully automated blood cell analyzer was used to conduct routine blood tests, measuring neutrophil, lymphocyte, monocyte, and platelet counts, and calculating the neutrophil-lymphocyte ratio (NLR).

2.4. Detection of serum CRP

A venous blood sample was drawn from the patient, centrifuged at 3000 rpm for 10 minutes at room temperature, and stabilized for 30 minutes. The serum was stored at −20°C and sent to the lab for CRP analysis.

2.5. Radiological examination

radiological confirmation of pneumonia on chest X-ray as per World Health Organization (WHO) guide-) for all patient and radiological findings were assessed by expert radiologist.

2.6. Statistical analysis

Data were analyzed using IBM SPSS Statistics version 28. Continuous variables were expressed as mean ± standard deviation (SD) and assessed for normality. Categorical variables were presented as frequencies and percentages, with Fisher's exact test applied for categorical data analysis.

Significance was set at $p < 0.05$. The ROC curve and AUC assessed diagnostic accuracy, with the Youden index identifying the optimal cutoff. Sensitivity, specificity, and predictive values were calculated for validation.

3. The result

The population consists of 51 pediatric patients who admitted to hospital, with a mean age of 5.80 ± 3.25 years. The sex distribution is nearly equal, with 24 males (47.1%) and 27 females (52.9%), and the majority of patients are under 10 years old. The lesions caused by pneumonia are fairly evenly distributed across the lungs Slightly more cases involve the **left lung (35.29%)** compared to the right lung (33.33%). While one-third of the patients (31.38%) have pneumonia affecting **both lungs as show in** Table 1, indicating more severe or widespread infections in these cases.

Table 1. The demographic distribution of the population.

Parameter	Categories	Frequency (Count)	Percentage (%)
AGE	<1 year	12	23.53
	2–10 years	35	68.63
	>10 years	4	7.84
SEX	Male	24	47.06
	Female	27	52.94
SIDE OF PNEUMONIA	Right lung	17	33.33
	Left lung	18	35.29
	Both lungs	16	31.38

The study found a significant correlation between severity of, fever, and oxygen saturation: as severity increased from normal/mild to severe, the average temperature rose (**37.44°C in mild to 39.13°C P 0.00001**) while oxygen saturation decreased (**96.56% in mild cases to 87.67% in sever cases p 0.0001**) as shown in Table 2, indicating that more severe pneumonia was associated with higher fevers and greater respiratory distress.

Table 2. The correlation of phenomena severity body temperature and O_2 saturation.

Clinical severity	Number of patients	Average of temperature	Average of O_2 saturation
Severe (s)	15	39.13	87.67
Moderate (m)	18	37.83	95.56
Normal/Mild (n)	18	37.44	96.56
P value		0.00001	0.0001

Regarding The distribution of population according to causative agents the result shows that bacterial infections account for **41.18%** of cases, followed closely by viral infections (**39.22%**) and unknown agents (**19.60%**). While bacterial infections appear more frequent in severe cases (**53.33%**), statistical analysis reveals no significant correlation ($p = 0.39$) between causative agents and radiological severity. This suggests that severity may be influenced by other factors beyond the type of pathogen.

3.1. Relation of CRP and severity of pneumonia

The analysis of the data reveals a **positive correlation** between CRP levels and the severity of pneumonia, with a correlation coefficient of approximately **0.65,** indicating a moderate relationship. The average CRP levels increase significantly with pneumonia severity: mild cases show a mean CRP of **9.6,**

moderate cases exhibit a mean of **13.5,** and severe cases have the highest mean CRP at **20.8** .the P value is <0.05 as shown in Table 3.

Table 3. The relation of pneumonia severity and serum C reactive protein.

Severity	n	CRP average	SD	Average of CRP	*P value*
Severe (s)	15	20.8	9.3	11–39	$p < 0.001$
Moderate (m)	16	13.5	8.7	7–33	$p < 0.001$
Normal/Mild (n)	17	9.6	2.4	7–14	$p < 0.001$

The analysis of CRP levels across causative agents of pneumonia reveals significant differences. The mean CRP levels are **18.5** for bacterial infections, **10.6** for viral infections, and **11.3** for unknown cases. A Kruskal-Wallis test confirms a statistically significant difference in CRP levels across the groups, with a p-value of $\boldsymbol{p = 0.02}$.

3.2. *Relation of severity of pneumonia and WBCC*

The analysis of the relationship between **WBC (White Blood Cell count)** and the **severity of pneumonia** reveals a significant association. The mean WBC levels progressively increase with the severity of pneumonia: **10.76** for mild cases, **11.88** for moderate cases, and **12.53** for severe cases. A one-way ANOVA confirms that this difference is statistically significant, with a p-value of $\boldsymbol{p = 0.042}$.

3.3. *The relation of N-Ly ratio and severity of pneumonia*

Positive Correlation: There is a clear positive correlation between the severity of pneumonia and the N-L ratio: the Severe cases have the highest mean N-L ratio (**30.54**). The Moderate cases have an intermediate mean N-L ratio (**11.15**). Normal/mild cases have the lowest mean N-L ratio (**8.45**). **t**he **p-value < 0.001** from the one-way ANOVA test confirms that the differences in mean N-L ratios across severity groups are highly statistically significant (Fig. 1).

The Neutrophil-to-Lymphocyte (N-L) ratio is a simple yet effective tool for predicting the severity of pneumonia in clinical settings. By using a cut-off value of 18.5, it strikes an optimal balance between sensitivity and specificity, ensuring that most severe cases of pneumonia are accurately identified while minimizing false positives. The Receiver Operating Characteristic (ROC) analysis revealed an Area Under the Curve (AUC) of 0.84, indicating good discriminatory power. Additionally, the sensitivity was found to be 84.6%, and the specificity was 93%. The accuracy is 91.1%.

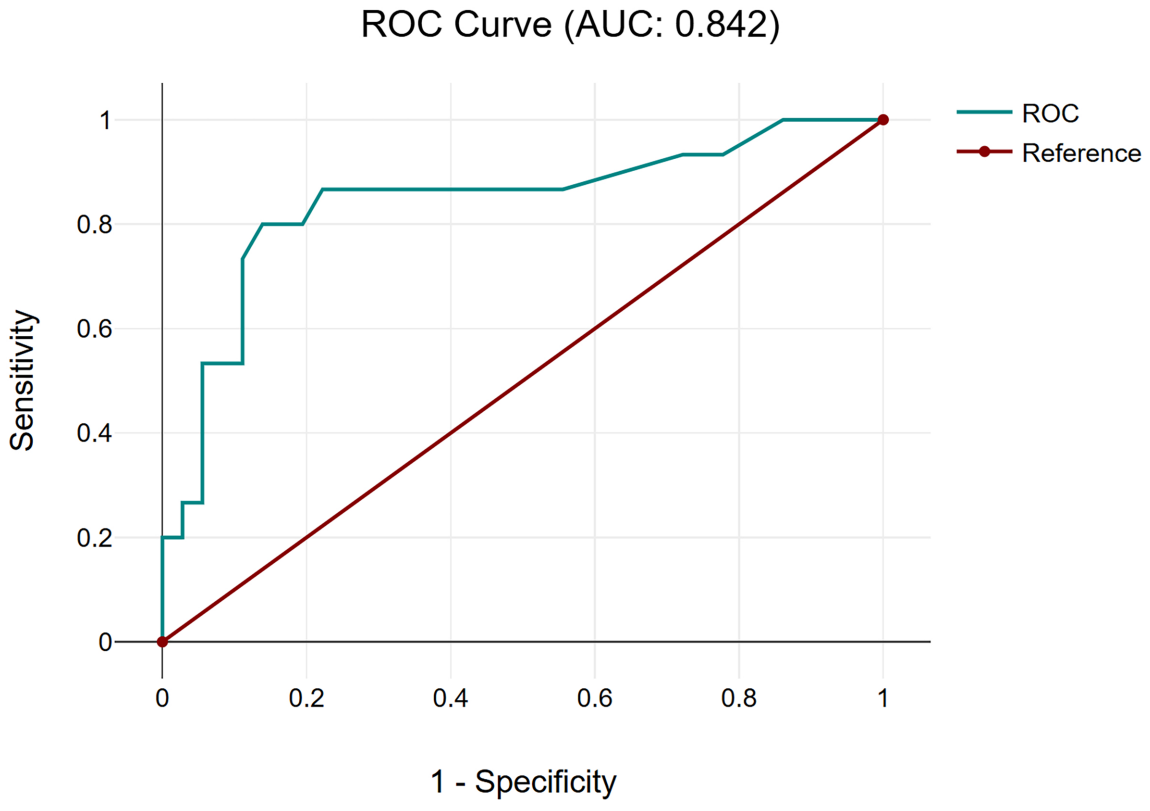

Fig. 1. ROC curve the sensitivity and specificity of N-L ratio.

Table 4. The sensitivity and specificity of N-L ration in predicting severity of pneumonia.

Metric	Value
Sensitivity	84.6%
Specificity	93.0%
Positive Predictive Value (PPV)	78.6%
Negative Predictive Value (NPV)	95.2%
Accuracy	91.1%

4. Discussion

The causative agent of pneumonia in the study was very closely Regarding The distribution of population according to causative agents the result shows that bacterial infections account for **41.18%** of cases, followed closely by viral infections (**39.22%) this result was close to the result of** Sam M Janes in study about the community acquired pneumonia in pediatrics age group the study identified viral pathogens as the leading cause of pneumonia, with *S. pneumoniae* being the most frequently observed typical bacterial pathogen (Popovsky & Florin, 2020).

The current study result was disagree to the result of Ki Wook Yun, in study about Well-crafted epidemiological studies from developed countries have demonstrated that respiratory viruses account for 30% to 70% of cases in children hospitalized with community-acquired pneumonia (CAP). Meanwhile, atypical bacteria are observed in 7% to 17% of cases, and pyogenic bacteria are implicated in just 2% to 8% of instances. These statistics underscore the diverse roles of pathogens in pediatric CAP (Ki Wook, 2023).

The analysis of the data reveals a **positive correlation** between CRP levels and the severity of pneumonia, with a correlation coefficient of approximately **0.65,** indicating a moderate relationship. The average CRP levels increase significantly with pneumonia severity: mild cases show a mean CRP of **9.6,** moderate cases exhibit a mean of **13.5,** and severe cases have the highest mean CRP at **20.8** .the P value is <0.05.

The current study result was similar to the result of Todd A Florin et al. 2020 In a study exploring the role of host biomarkers in predicting the severity of community-acquired pneumonia (CAP) in adults, we assessed how specific markers—such as white blood cell (WBC) count, absolute neutrophil count (ANC), C-reactive protein (CRP), and procalcitonin—correlate with the risk of severe outcomes in children with CAP (Florin *et al.*, 2020).

While Abdul-Amir Makki Al-Hindy, Hayder; Obaid, Samer Raheem et al. 2024 they were found The total WBCs and the mean CRP plasma levels were significantly ($P = 0.001$) higher among the pneumonia patients. The study revealed nonsignificant variations in the WBCs, and CRP plasma levels according to sex and type of feeding. The mean levels of CRP were more elevated among patients with bacterial pneumonia. this result agree with current study (Al-Hindy *et al.*, 2024).

The relation of N-Ly ratio and severity of pneumonia

Positive Correlation: There is a clear positive correlation between the severity of pneumonia and the N-L ratio: the Severe cases have the highest mean N-L ratio (**30.54**). The Moderate cases have an intermediate mean N-L ratio (**11.15**). Normal/mild cases have the lowest mean N-L ratio (**8.45**). **t**he **p-value < 0.001** from the one-way ANOVA test confirms that the differences in mean N-L ratios across severity groups are highly statistically significant.

The findings of the current study align with those reported by Anam Bashir, MD, et al. in 2022. Their research identified that white blood cell count (WBC), platelet count, C-reactive protein (CRP), procalcitonin (PCT), neutrophil-lymphocyte ratio, neutrophil count, and band count were associated with the severity of community-associated pneumonia (CAP) in children (Bashir *et al.*, 2022).

The Neutrophil-to-Lymphocyte (N-L) ratio is a simple yet effective tool for predicting the severity of pneumonia in clinical settings. By using a cut-off value of 18.5, it strikes an optimal balance between sensitivity and specificity, ensuring that most severe cases of pneumonia are accurately identified while minimizing false positives. The ROC analysis produced an AUC value of 0.84, showcasing its robust capacity to distinguish between outcomes with significant accuracy. Additionally, the sensitivity was found to be 84.6%, and the specificity was 93%. The accuracy is 91.1%.

The results of the current study align with those presented by Mihrican Yesildag et al. in 2024, which demonstrated statistically significant differences between the groups ($p < 0.001$). Among hospitalized patients, several markers were significantly elevated ($p < 0.05$), including CRP, WBC, neutrophil, lymphocyte, monocyte, basophil, hemoglobin, hematocrit, etc. The study highlighted specific parameters with notable diagnostic value for identifying pneumonia patients requiring hospitalization (Yeşildağ *et al.*, 2024).

In a 2022 study by I Gusti Ayu Dwi Aryani et al., 58 subjects were analyzed to evaluate predictors of severe community-acquired pneumonia (CAP) in children. ROC analysis revealed a cut-off point of 2.11 for the neutrophil-lymphocyte ratio (NLR), with a sensitivity of 82.4% and specificity of 83.3%. For procalcitonin, the cut-off point was 1 ng/ml, demonstrating a sensitivity of 85.3% and specificity of 87.5%

in predicting severe CAP. Agreement analysis between NLR (cut-off 2.11) and procalcitonin (cut-off 1 ng/ml) showed substantial concordance (k = 0.62; p = 0.001) for identifying severe CAP in pediatric patients. These findings are consistent with the results observed in the current study (Aryani *et al.*, 2022).

The study found strong associations between radiological severity, clinical indicators (fever, oxygen saturation), CRP levels, and WBCC, with the neutrophil-to-lymphocyte ratio emerging as a highly effective predictor of severe pneumonia. These markers collectively enhance the assessment and prediction of disease progression.

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