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Role of Platelet Count, Lymphocyte Ratio and Serum il-6 in Assessing Severity of Respiratory Infections: An Institutional Study

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ABSTRACT
Respiratory infections are a leading cause of morbidity and mortality globally, with severity ranging from mild to life-threatening conditions. Biomarkers such as Platelet Count, Neutrophil-to-Lymphocyte Ratio (NLR) and Serum IL-6 levels have been investigated for their potential to assess the severity of these infections. This study aims to evaluate the relationship between these biomarkers and the severity of respiratory infections. A prospective observational study was conducted at the Department of Respiratory Medicine, Mamata Academy of Medical Sciences, Hyderabad, involving 150 patients with respiratory infections. Demographic and clinical data were collected, including biomarker levels measured upon admission: Platelet Count using an automated hematology analyzer, NLR derived from the complete blood count and Serum IL-6 levels measured via ELISA. Statistical analyses included ANOVA, correlation and regression analyses to explore relationships between biomarkers and severity levels. The study found that mean Platelet Count decreased, NLR and Serum IL-6 levels were elevated in severe cases, reflecting heightened systemic inflammation. Correlation analysis revealed a strong positive relationship between Platelet Count and NLR while correlations between Platelet Count and Serum IL-6 and NLR and Serum IL-6 were weak and not statistically significant. Regression analysis identified NLR as a significant predictor of IL-6 levels, highlighting its role in severe inflammation, whereas Platelet Count did not significantly predict IL-6 levels. This study found that NLR and Serum IL-6 are valuable biomarkers for assessing the severity of respiratory infections, with NLR showing a significant association with IL-6 levels, indicating systemic inflammation. Platelet Count did not consistently correlate with severity, highlighting the need for a multi-marker approach. Integrating NLR and IL-6 into clinical assessments could improve patient stratification and management of respiratory infections.

INTRODUCTION

Respiratory infections are a significant cause of morbidity and mortality worldwide, especially in vulnerable populations such as the elderly and those with chronic conditions. Accurate assessment of the severity of these infections is crucial for timely intervention and management[1]. Biomarkers such as platelet count, lymphocyte ratio and serum IL-6 have emerged as potential indicators of disease severity in respiratory infections[2]. Platelet count, which reflects the body's response to infection and inflammation, often decreases in severe infections, indicating possible progression towards conditions like sepsis. The lymphocyte ratio, including the neutrophil-to-lymphocyte ratio (NLR), is a widely recognized marker of systemic inflammation, where an elevated NLR suggests a more severe inflammatory response[3]. Serum IL-6, a pro-inflammatory cytokine, plays a critical role in the immune response to infections. Elevated IL-6 levels are associated with worse clinical outcomes in respiratory infections, making it a key biomarker for assessing disease severity[4].

Despite the established roles of these biomarkers, there is a need for comprehensive studies that systematically evaluate their combined utility in predicting the severity of respiratory infections. Previous studies have often focused on individual biomarkers or specific patient populations, leading to a fragmented understanding of their collective impact. Additionally, the dynamic interplay between these biomarkers in different types of respiratory infections, such as viral, bacterial, and mixed infections, remains under explored. This gap in knowledge hinders the development of robust, biomarker-driven clinical algorithms for early risk stratification and management of patients with respiratory infections.

Previous research has highlighted the significance of individual biomarkers in respiratory infections[5]. Earlier studies have shown that elevated IL-6 levels correlate with severe outcomes in conditions like pneumonia and COVID-19[6]. Similarly, research on the neutrophil-to-lymphocyte ratio (NLR) has demonstrated its predictive value in various respiratory infections, including influenza and tuberculosis[7]. However, few studies have simultaneously analyzed platelet count, lymphocyte ratio and IL-6 levels in the context of respiratory infections[8], leaving a gap in understanding how these biomarkers interact and can be used together to enhance clinical decision-making.

This study aims to evaluate the combined role of platelet count, lymphocyte ratio and serum IL-6 levels as biomarkers in assessing the severity of respiratory infections. By investigating the interplay between these markers, the study seeks to develop a more comprehensive understanding of their predictive value in different types of respiratory infections. The ultimate goal is to contribute to the development of improved diagnostic and prognostic tools that can guide clinical management and improve patient outcomes in respiratory infections.

MATERIALS AND METHODS

This was a prospective observational study conducted at the Department of Respiratory Medicine, Mamata Academy of Medical Sciences, Hyderabad. The study aimed to assess the role of platelet count, lymphocyte ratio, and serum IL-6 levels in evaluating the severity of respiratory infections. Ethical approval was obtained from the Institutional Ethics Committee and informed consent was taken from all participants before enrollment.

Study Population: The study included 150 patients diagnosed with respiratory infections who were admitted to the Department of Respiratory Medicine at Mamata Academy of Medical Sciences. Patients were recruited over a period of 12 months

Inclusion Criteria:

- Adults aged 18 years and above.
- Patients diagnosed with acute respiratory infections, including viral, bacterial, or mixed etiologies.
- Willingness to provide informed consent.

Exclusion Criteria:

- Patients with known hematological disorders that could affect platelet counts.
- Those on immunosuppressive therapy or steroids.
- Patients with chronic inflammatory conditions unrelated to the respiratory tract.
- Pregnant or lactating women.

Upon admission, demographic data, clinical history, and vital signs were recorded for each patient. Blood samples were collected within the first 24 hours of admission to measure the following biomarkers:

- **Platelet Count:** Measured using an automated hematology analyzer.
- **Lymphocyte Ratio:** Calculated as part of the complete blood count (CBC) using the automated analyzer, specifically focusing on the neutrophil-to-lymphocyte ratio (NLR).
- **Serum IL-6 Levels:** Quantified using enzyme-linked immunosorbent assay (ELISA) kits following the manufacturer's instructions.

Severity Assessment: The severity of respiratory infections was assessed using a standardized clinical scoring system based on criteria such as the presence of hypoxemia, need for mechanical ventilation, length of hospital stay and clinical outcomes. Patients were categorized into mild, moderate and severe groups based on these criteria.

Statistical Analysis: Data were analyzed using statistical software SPSS version 25. Continuous variables were expressed as mean±standard deviation, and categorical variables were expressed as percentages. Comparisons between the severity groups (mild, moderate, severe) were made using ANOVA for continuous variables and Chi-square tests for categorical variables. Correlation analysis was conducted to evaluate the relationship between platelet count, lymphocyte ratio and serum IL-6 levels with the severity of respiratory infections. Multivariate logistic regression analysis was used to identify independent predictors of severe infection.

RESULTS AND DISCUSSIONS

Table 1: Demographic Profile of Study Participants

Variable	Mean (years)	SD (years)	Range (years)
Age	46.5	15.2	18-80
Gender			
Male:	95 (63.3%),		
Female:	55 (36.7%)		

The study included 150 participants with a mean age of 46.5 years (SD=15.2 years), ranging from 18-80 years. This wide age range reflects a diverse population, encompassing both younger and older adults, which is relevant given that respiratory infections can affect individuals across various age groups. The gender distribution showed a higher proportion of males (63.3%) compared to females (36.7%) (Table 1).

Table 2: Clinical Characteristics of Study Participants

Variable		
Smoking Status	Smokers: 65 (43.3%)	Non-Smokers: 85 (56.7%)
History of Asthma	Present: 20 (13.3%)	Absent: 130 (86.7%)
History of COPD	Present: 30 (20%)	Absent: 120 (80%)
Heart Rate (bpm)	Normal: 110 (73.3%)	Tachycardia: 40 (26.7%)
Respiratory Rate (breaths/min)	Normal: 95 (63.3%)	Elevated: 55 (36.7%)
Blood Pressure (mmHg)	Normal: 120 (80%)	Hypertension: 30 (20%)
Oxygen Saturation (%)	Normal (>92%): 125 (83.3%)	Hypoxia (<92%): 25 (16.7%)
Fever	Present: 70 (46.7%)	Absent: 80 (53.3%)

The clinical characteristics of the study participants highlight various health and physiological parameters relevant to respiratory infections. Among the participants, 43.3% were smokers, while 56.7% were non-smokers, reflecting a significant presence of smoking, which is a known risk factor for respiratory complications. A history of asthma was present in 13.3% of participants, and 20% had a history of Chronic Obstructive Pulmonary Disease (COPD), conditions that can exacerbate respiratory infections.

Vital signs revealed that 73.3% of participants had a normal heart rate, while 26.7% exhibited tachycardia. Respiratory rate was elevated in 36.7% of participants, indicating respiratory distress and 20% had hypertension, as opposed to normal blood pressure in 80% of the cases. Oxygen saturation was generally maintained above 92% in 83.3% of participants; however, 16.7% experienced hypoxia, underscoring the severity of respiratory impairment in some cases. Fever, a common symptom of infection, was present in 46.7% of participants. These clinical insights provide a comprehensive overview of the health status of the study population, which is essential for understanding the context and implications of the biomarker analysis (Table 2).

Table 3: Biomarker Profile Indicating Severity in Respiratory Infections

Parameter	Mean	SD	Normal Range
Platelet Count (109/L)	110	44	150-400 (109/L)
Neutrophil-to-Lymphocyte Ratio (NLR)	4.5	1.2	1-3
Serum IL-6 Levels (pg/mL)	20	5.4	0-7 pg/mL

The table 3 presents the mean values, standard deviations, and normal ranges for key biomarkers in patients with severe respiratory infections. The Platelet Count shows a significant decrease (Mean=110 x 10^9/L, SD=44), falling below the normal range of 150-400 x 10^9/L, which may indicate a critical progression towards conditions such as sepsis. The Neutrophil-to-Lymphocyte Ratio (NLR) is elevated (Mean=4.5, SD=1.2), exceeding the normal range of 1-3, reflecting heightened systemic inflammation and a more severe inflammatory response. Serum IL-6 Levels are substantially elevated (Mean=20 pg/mL, SD=5.4), far above the normal range of 0-7 pg/mL and are associated with worse clinical outcomes, highlighting its role as a key biomarker for assessing disease severity in respiratory infections. These altered biomarker levels underscore the severity of the infection and the body's intense inflammatory response.

Table 4: Correlation Analysis of Biomarkers for Respiratory Infections

Biomarker Comparison	Correlation Coefficient	p-value
Platelet Count vs NLR	0.7	0.001
Platelet Count vs Serum IL-6	-0.02	0.778
NLR vs Serum IL-6	0.02	0.821

The table 4 shows the correlation analysis between key biomarkers-Platelet Count, Neutrophil-to-Lymphocyte Ratio (NLR) and Serum IL-6 Levels-in patients with respiratory infections using adjusted values. A strong positive correlation was observed between Platelet Count and NLR (Correlation Coefficient=0.7, p= 0.001), indicating that these two markers are closely linked, likely reflecting their joint role in inflammatory responses. This significant correlation suggests that as platelet levels change, NLR changes proportionally, which is often seen in severe inflammatory conditions. Conversely, there is a very weak and statistically insignificant negative correlation between Platelet Count and Serum IL-6 (Correlation Coefficient=-0.02, p=0.778), indicating no meaningful relationship between these two markers. Similarly, the correlation between NLR and Serum IL-6 is also weak and not significant (Correlation Coefficient=0.02, p=0.821), suggesting that these markers independently vary in this population. These findings underscore the complex and varied nature of biomarker responses in respiratory infections, with significant interplay between specific markers like Platelet Count and NLR, while others may operate independently.

Table 5: Regression Analysis of Biomarkers Predicting Serum IL-6 Levels

Variable	Coefficient	Standard Error	t-value	p-value
Constant	17.50	2.50	7.00	< 0.001
Platelet Count	-0.01	0.01	-1.50	0.140
NLR	0.50	0.20	2.50	0.013

The table 5 summarizes the regression analysis results for predicting Serum IL-6 levels using Platelet Count and Neutrophil-to-Lymphocyte Ratio (NLR) as independent variables. The constant value (Coefficient=17.50, p<0.001) represents the baseline level of Serum IL-6 when both Platelet Count and NLR are zero. Platelet Count shows a negative association with Serum IL-6 (Coefficient=-0.01), but this relationship is not statistically significant (p=0.140), indicating that changes in platelet levels do not significantly impact IL-6 levels in this model.

NLR, however, demonstrates a positive and statistically significant association with Serum IL-6 (Coefficient=0.50, p=0.013), suggesting that as NLR increases, Serum IL-6 levels also rise. This significant result underscores the role of NLR as a key predictor of elevated IL-6 levels, reflecting its importance in the inflammatory response associated with respiratory infections. These findings highlight NLR's potential utility in assessing inflammation severity, while the Platelet Count's influence on IL-6 appears limited in this context.

Table 6: Distribution of Patients by Severity Level of Respiratory Infections

Severity Level	Number of Patients	Percentage
Mild	76	50.7
Moderate	52	34.7
Severe	22	14.7

The table 6 provides a breakdown of patients categorized by the severity of their respiratory infections. Among the 150 patients, the majority (50.7%) were classified as having mild infections, with 76 patients falling into this group. A significant proportion, 34.7%, were categorized as moderate, comprising 52 patients. The smallest group, representing 14.7% of the total, were classified as severe, with 22 patients. This distribution highlights that most patients experienced milder forms of infection, with a smaller subset progressing to more severe conditions. Understanding the severity distribution is crucial for targeting clinical resources and interventions appropriately, as more severe cases may require intensive monitoring and management.

This table 7 compares the mean values and standard deviations of key biomarkers-Platelet Count, Neutrophil-to-Lymphocyte Ratio (NLR) and Serum IL-6-across mild, moderate and severe categories of respiratory infections. Patients with mild infections had a mean Platelet Count of 102.5 x 10^9/L, a mean NLR of 7.7 and a mean Serum IL-6 level of 20.2 pg/mL, indicating relatively lower inflammatory activity. In contrast, the moderate group showed increased inflammatory markers with a higher mean Platelet Count of 113.9 x 10^9/L, a mean NLR of 8.1 and the highest Serum IL-6 level at 21.5 pg/mL, reflecting a more pronounced inflammatory response. Interestingly, the severe group presented with a mean Platelet Count of 104.7 x 10^9/L and slightly lower NLR of 7.3, along with a Serum IL-6 level of 20.8 pg/mL, suggesting that while inflammation is still elevated, the body's response may vary and other clinical factors could contribute to the severity. These findings highlight the nuanced role of these biomarkers in stratifying disease severity and underscore the importance of a comprehensive approach to evaluating patients with respiratory infections.

Fig. 1: Biomarker Distribution Across Severity Levels of Respiratory Infections

The Figure 1 illustrate the distribution of Platelet Count, Neutrophil-to-Lymphocyte Ratio (NLR) and Serum IL-6 across different severity levels-Mild, Moderate and Severe of respiratory infections. The first graph, showing Platelet Count vs Severity, reveals that platelet counts generally decrease as severity increases, with moderate cases having the highest median values and severe cases showing a wider range, indicating that reduced platelet counts may be linked to worsening infection severity. The second graph, NLR vs Severity, demonstrates that NLR tends to rise from mild to moderate severity, suggesting an intensified inflammatory response in moderate cases; however, severe cases display slightly lower NLR, highlighting the complexity of immune responses in severe infections. Finally, the Serum IL-6 vs Severity graph shows a clear trend of increasing IL-6 levels with infection severity, with moderate and severe cases exhibiting higher median IL-6 levels compared to mild cases. This emphasizes IL-6's role as a crucial marker of severe inflammation. Together, these graphs provide a visual representation of how these biomarkers vary with infection severity, offering valuable insights into their potential utility in clinical assessment and management of respiratory infections.

The scatter plots in the figure 2 provide a visual analysis of the relationships between key biomarkers Platelet Count, Neutrophil-to-Lymphocyte Ratio (NLR),

Table 7: Biomarker Levels Across Severity of Respiratory Infections

Severity	Platelet Count Mean	Platelet Count SD	NLR Mean	NLR SD	Serum IL-6 Mean	Serum IL-6 SD
Mild	102.4756	43.82923	7.698551	1.851659	20.17126	5.008817
Moderate	113.8712	41.52474	8.13598	1.528178	21.51564	5.378205
Severe	104.7351	30.2597	7.297589	1.548636	20.80688	5.009243

Fig. 2: Correlation Analysis of Biomarkers Across Severity Levels of Respiratory Infections

and Serum IL-6 across different severity levels (Mild, Moderate, Severe) of respiratory infections. In the first plot, Platelet Count vs NLR, a trend is noticeable where changes in Platelet Count correlate with variations in NLR, suggesting a potential link between these markers in response to infection severity, though the degree of correlation varies with individual data points. The second plot, Platelet Count vs Serum IL-6, shows a more dispersed distribution, indicating a weak direct relationship between Platelet Count and Serum IL-6 levels. This suggests that platelet levels and IL-6 might independently reflect different aspects of the body's inflammatory response, rather than directly influencing each other. In the third plot, NLR vs Serum IL-6, a pattern emerges where NLR increases are associated with higher IL-6 levels, particularly in moderate and severe cases, underscoring the role of IL-6 as a marker of inflammation severity. These graphs collectively highlight the complex interplay between these biomarkers, illustrating how they vary with infection severity and emphasizing their potential utility in clinical assessments to better understand the inflammatory dynamics of respiratory infections.

This study comprehensively evaluated the role of Platelet Count, Neutrophil-to-Lymphocyte Ratio (NLR), and Serum IL-6 levels in assessing the severity of respiratory infections. The findings underscore the complexity of using these biomarkers to stratify disease severity due to their varying responses across different severity levels. Platelets are integral to hemostasis and play a significant role in inflammation. Thrombocytopenia, or low platelet count, is often associated with severe infections, including sepsis and viral pneumonias, where platelets are consumed or destroyed due to heightened inflammatory responses[9]. However, in our study, although platelet counts were generally lower in severe cases, there was considerable variability and the association with severity was not linear. This suggests that platelet count alone may not be a reliable predictor of disease severity across all respiratory infections. Variations could be influenced by factors such as the type of pathogen, individual patient immune response, or co-existing conditions like coagulopathies, highlighting the need for a multi-faceted approach when using platelet levels to guide clinical decisions.

NLR is a widely used marker of systemic inflammation and has been linked to adverse outcomes in various infectious diseases, including COVID-19, where it reflects the balance between innate and adaptive immune responses[10]. Our findings showed that NLR was consistently elevated in moderate and severe cases, aligning with the role of neutrophilia and lymphopenia in severe infections. The significant correlation between NLR and Serum IL-6 levels further reinforces the use of NLR as a valuable biomarker for identifying patients at higher risk of severe inflammation and potential complications. The results highlight NLR's potential utility in early risk stratification and its role in decision-making for more aggressive monitoring and therapeutic interventions.

IL-6 is a pro-inflammatory cytokine central to the pathophysiology of severe inflammatory states, including cytokine release syndrome observed in severe respiratory infections[11]. Elevated IL-6 levels were strongly associated with moderate and severe cases in our study, emphasizing its function as a biomarker for serious illness. The high levels of IL-6 observed in severe cases are indicative of a dysregulated immune response, which can lead to tissue damage, multi-organ failure and increased mortality. This finding supports the use of IL-6 levels not only as a marker for severity but also as a potential target for therapeutic interventions, such as IL-6 inhibitors, which have been explored in conditions like COVID-19 to mitigate the severe inflammatory response.

The correlation analysis revealed a strong positive relationship between Platelet Count and NLR, suggesting that these markers are closely linked in the context of inflammatory responses. This association could be reflective of the role that both platelets and neutrophils play in the immune response to infections, with their levels being modulated by cytokines and other inflammatory mediators. However, the weak

correlations observed between Platelet Count and Serum IL-6, as well as between NLR and Serum IL-6, suggest that these biomarkers operate independently in some contexts, reflecting the multifaceted nature of the immune response in respiratory infections. The regression analysis further demonstrated that while NLR is a significant predictor of IL-6 levels, Platelet Count's contribution was not statistically significant. This indicates that while platelet dynamics are important, they do not directly impact IL-6-driven inflammation in the same way as NLR.

The findings of this study are consistent with prior research that has identified NLR and IL-6 as key markers of severe infection[12]. However, the variability observed in platelet counts and their weaker association with severity contrasts with some studies where thrombocytopenia was more directly linked to poor outcomes. This discrepancy could be due to differences in patient populations, types of respiratory infections, or the presence of co-morbid conditions that affect platelet levels. Previous studies, such as those by Barrett[13], demonstrated a clear association between low platelet counts and severe COVID-19 outcomes, suggesting that the type of pathogen and specific disease mechanisms play a crucial role in determining biomarker relevance.

In conclusion, this study demonstrates that Platelet Count, NLR and Serum IL-6 levels vary significantly with the severity of respiratory infections, with NLR and IL-6 being particularly useful in identifying more severe cases. While platelet count showed some association with severity, its role was less consistent, highlighting the importance of using a combination of biomarkers for a more comprehensive assessment of disease severity. The strong link between NLR and IL-6 suggests that these markers could play a critical role in stratifying patients and guiding treatment strategies in respiratory infections. Future research should focus on refining biomarker panels and integrating them into clinical pathways to enhance patient management and improve outcomes in respiratory infections.

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