RESEARCH PAPER

TO ASSESS THE ROLE OF INFLAMMATORY MARKERS IN OUTCOME OF NON-COVID PNEUMONIA AT TERTIARY CARE HOSPITAL

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Abstract

Non-COVID pneumonia remains a leading cause of hospitalization and mortality, particularly among older adults and individuals with underlying comorbidities. Early identification of patients at risk of adverse outcomes is essential for timely intervention. This prospective observational study evaluated the prognostic value of inflammatory biomarkers in 140 adults with clinically and radiologically confirmed non-COVID pneumonia admitted to a tertiary care teaching hospital. Serum interleukin-6 (IL-6), C-reactive protein (CRP), D-dimer, and ferritin were measured within 24 hours of admission, and their relationship with disease severity, assessed using the Pneumonia Severity Index (PSI) and in-hospital outcomes was analyzed. Most patients had moderate-to-severe disease, with 72.9% recovering without intensive care, 17.1% requiring ICU admission, and 10.0% experiencing in-hospital mortality. Concentrations of IL-6, CRP, D-dimer, and ferritin increased significantly with worsening PSI class (all $p<0.001$), with IL-6 demonstrating the strongest correlation with disease severity ($r=0.71$). Multivariable logistic regression identified PSI score, IL-6, CRP, D-dimer, ferritin, diabetes mellitus, chronic obstructive pulmonary disease, and chronic kidney disease as independent predictors of poor outcome. Receiver operating characteristic analysis demonstrated excellent predictive performance for PSI (AUC=0.91), while IL-6 showed the highest diagnostic accuracy among the biomarkers. These findings indicate that inflammatory biomarkers, particularly IL-6, provide important prognostic information and if combined with established clinical severity scores, may improve early risk stratification and guide clinical decision-making in patients with non-COVID pneumonia.

Keywords: Non-COVID pneumonia; Interleukin-6; C-reactive protein; D-dimer; Ferritin; Pneumonia Severity Index.

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Introduction

Pneumonia remains a major cause of hospitalization, morbidity, and mortality worldwide despite advances in antimicrobial therapy and critical care support.[1,2] Non-COVID pneumonia, including bacterial and mixed lower respiratory tract infections, continues to impose a substantial healthcare burden, particularly among elderly, immunocompromised individuals and patients with chronic comorbidities.[3,4] Severe pneumonia is characterized by an exaggerated inflammatory response that may lead to acute lung injury, sepsis, multiorgan dysfunction, and increased mortality.[5]

Inflammatory biomarkers have gained increasing importance in assessing disease severity and predicting outcomes in pneumonia.[6] Traditional markers such as C-reactive protein (CRP) are widely used in routine clinical practice; however, newer

biomarkers including Interleukin-6 (IL-6), D-dimer, and serum ferritin may provide better insight into the underlying inflammatory and coagulation disturbances associated with severe infection.[7,8] IL-6 is a key pro-inflammatory cytokine involved in the acute-phase response, while D-dimer reflects activation of coagulation and fibrinolysis.[9] Serum ferritin, an acute-phase reactant, is associated with macrophage activation and systemic inflammation.[10]

Previous studies have demonstrated the prognostic significance of these biomarkers in sepsis and COVID-19 pneumonia, but evidence regarding their comparative role in non-COVID pneumonia remains limited, particularly in the Indian population.[11,12] Clinical scoring systems such as CURB-65 and PSI are useful for severity assessment but may not fully reflect the intensity of the inflammatory response.[13] Therefore, integrating inflammatory biomarkers into clinical evaluation may improve risk stratification, early identification of severe disease, and prediction of hospitalization outcomes.[14]

The present study was undertaken to assess the role of inflammatory markers—IL-6, CRP, D-dimer, and serum ferritin—in determining severity and outcome among patients admitted with non-COVID pneumonia at a tertiary care hospital.

Methodology

This hospital-based observational study was conducted in the Departments of Medicine and Respiratory Medicine at a tertiary care teaching hospital. Adult patients (≥18 years) admitted with clinically and radiologically confirmed non-COVID pneumonia were enrolled consecutively after obtaining written informed consent. Patients presenting with symptoms such as fever, cough, sputum production, dyspnea, or pleuritic chest pain along with radiological evidence of pneumonia on chest X-ray or CT scan were included. COVID-19 infection was excluded by RT-PCR or rapid antigen testing at admission. Pregnant women, postpartum females, and patients receiving immunosuppressive therapy were excluded from the study.

Sample size was calculated using G*Power software (version 3.1) considering a medium effect size (Cohen's d = 0.5), 80% power, and 5% level of significance. After accounting for attrition, a total of 140 patients were included.

Data were collected using a structured predesigned case-record form. Demographic details, clinical history, comorbidities, vital parameters, radiological findings, and severity scores including CURB-65, PSI, and qSOFA were recorded. Baseline laboratory investigations included complete blood count, renal and liver function tests, ESR, blood glucose, arterial blood gas analysis, and microbiological investigations whenever indicated.

Blood samples were collected within 24 hours of admission for estimation of inflammatory markers including Interleukin-6 (IL-6), C-reactive protein (CRP), D-dimer, serum ferritin, and procalcitonin. CRP and D-dimer were measured using immunoturbidimetric methods, IL-6 by ELISA, ferritin by chemiluminescent immunoassay, and procalcitonin by electrochemiluminescence immunoassay. All analyses were performed in the central laboratory following standardized protocols and quality control measures.

Patients were monitored throughout hospitalization for clinical progression, oxygen requirement, ICU admission, ventilatory support, complications, duration of stay, and in-hospital outcome. Outcomes were categorized as recovery without ICU admission, recovery with ICU admission, or death.

Data were entered into a secure database and analyzed using SPSS software. Continuous variables were expressed as mean ± standard deviation or median with interquartile range, while categorical variables were presented as frequencies and percentages. Comparisons between groups were performed using Student's t-test, Mann–Whitney U test, Chi-square test, or ANOVA as appropriate. Correlation analysis and multivariable logistic regression were used to evaluate the association between inflammatory markers and disease severity or clinical outcomes. A p-value <0.05 was considered statistically significant.

Results

A total of 140 patients with non-COVID pneumonia were included in the study. The majority of participants belonged to the 40–60 years age group (44.3%), followed by patients aged >60 years (35.7%). Male predominance was observed, with 61.4% males and 38.6% females. Smoking history was present in 34.3% of patients, while 55.7% had one or more comorbidities.

Hypertension (34.3%) and diabetes mellitus (30.0%) were the most common comorbid conditions, followed by COPD (22.9%), CHF (20.0%), CKD (18.6%), CVA (15.7%), and CLD (10.0%). Nearly 44.3% of patients had no comorbidity, whereas 10.0% had three or more comorbid conditions.

The mean respiratory rate was 28.6 ± 6.8 breaths/min, pulse rate was 108.2 ± 18.6 beats/min, and oxygen

saturation (SpO_2) was 89.6 ± 6.8%, indicating significant respiratory compromise at presentation. Hypoxemia (45.0%) and elevated BUN (42.1%) were the most common severity-related abnormalities.

According to PSI classification, 28.6% of patients belonged to PSI Class III, while 35.7% were categorized into the high-risk group (PSI IV–V). Overall, 64.3% of patients had moderate-to-severe pneumonia.

Inflammatory markers demonstrated a significant stepwise increase with increasing PSI severity. Mean CRP levels increased from 72 ± 3.1 mg/L in low severity cases to 265 ± 11.5 mg/L in high severity cases ($p<0.001$). Similarly, IL-6 increased from 20 ± 0.9 pg/mL to 110 ± 15 pg/mL, D-dimer from 380 ± 15 ng/mL to 1600 ± 60 ng/mL, and ferritin from 200 ± 8 ng/mL to 820 ± 30 ng/mL across severity groups (all $p<0.001$).

Correlation analysis revealed significant positive correlations between inflammatory markers and PSI score. IL-6 showed the strongest correlation ($r=0.71$, $p<0.001$), followed by CRP ($r=0.65$), D-dimer ($r=0.60$), and ferritin ($r=0.58$).

Regarding outcomes, 72.9% of patients recovered without ICU admission, 17.1% recovered after ICU admission, and 10.0% died during hospitalization. Poor outcomes were significantly more common among patients with high PSI severity. Mortality in the high-risk PSI group was 26.0%, compared to no mortality in the low-risk group.

Elevated inflammatory markers were strongly associated with adverse outcomes. Patients with CRP ≥90 mg/L, IL-6 ≥60 pg/mL, D-dimer ≥1000 ng/mL, and ferritin ≥500 ng/mL had significantly higher ICU admission and mortality rates compared to patients with lower marker levels.

Patients with multiple comorbidities showed progressively worse outcomes. Mortality increased from 3.2% in patients without comorbidities to 35.7% in those with three or more comorbid conditions.

Multivariate logistic regression identified PSI score, IL-6, CRP, D-dimer, ferritin, diabetes mellitus, COPD, and CKD as independent predictors of poor outcome (ICU admission or death). IL-6 showed the strongest independent biomarker association with adverse outcomes (AOR 1.02, $p<0.001$).

ROC curve analysis demonstrated excellent predictive performance of PSI score (AUC=0.91), followed by IL-6 (AUC=0.89), D-dimer (AUC=0.86), CRP (AUC=0.84), and ferritin (AUC=0.81) for predicting poor outcomes. IL-6 showed high sensitivity (85.2%) and specificity (80.4%) at a cut-off value of ≥65 pg/mL.

Table 1. Baseline Demographic and Clinical Characteristics

Characteristic	Value
Age 40–60 years	62 (44.3%)
Age >60 years	50 (35.7%)
Male	86 (61.4%)
Smoking History	48 (34.3%)
Comorbidities Present	78 (55.7%)
Respiratory Rate	28.6 ± 6.8
Pulse Rate	108.2 ± 18.6
SpO_2	89.6 ± 6.8

Table 2. Comparison of Inflammatory Markers Across PSI Severity Groups

Marker	Low	Moderate	High	p-value
CRP	72 ± 3.1	148 ± 6.2	265 ± 11.5	<0.001
IL-6	20 ± 0.9	50 ± 12	110 ± 15	<0.001
D-Dimer	380 ± 15	850 ± 30	1600 ± 60	<0.001
Ferritin	200 ± 8	420 ± 15	820 ± 30	<0.001

Figure 3. ROC Curve Analysis for Predicting Poor Outcome

Variable	Adjusted OR	95% CI	p-value	AUC
PSI Score	1.08	1.04–1.12	<0.001	0.91
IL-6	1.02	1.01–1.04	<0.001	0.89
CRP	1.01	1.003–1.02	0.002	0.84

D-Dimer	1.001	1.000–1.002	0.005	0.86
Ferritin	1.002	1.000–1.004	0.01	0.81

Figure 1. Distribution of PSI Severity Groups and Clinical Outcomes

Figure 2. Comparison of Inflammatory Markers Across PSI Severity Groups

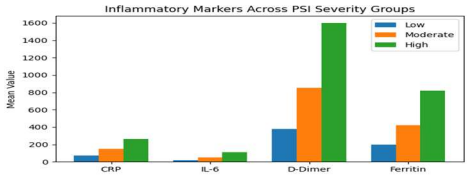
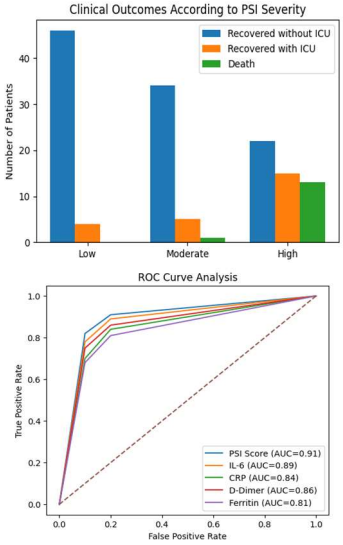


Figure 3. ROC Curve Analysis



Discussion

The present study evaluated the role of inflammatory biomarkers in determining disease severity and clinical outcomes among patients with non-COVID pneumonia admitted to a tertiary care hospital. The findings demonstrated that inflammatory markers, particularly IL-6, CRP, D-dimer, and ferritin, were significantly associated with pneumonia severity, ICU admission, and mortality.

In the present study, pneumonia predominantly affected middle-aged and elderly individuals, with the majority of patients belonging to the 40–60 years and >60 years age groups. This finding is consistent with previous studies showing that increasing age is associated with higher susceptibility to pneumonia due to declining immune function and greater prevalence of comorbidities.[1,3] Male predominance observed in the study may be related to higher exposure to smoking and other environmental risk factors.[4]

More than half of the patients had associated comorbidities, with hypertension, diabetes mellitus, COPD, and CKD being the most common. Patients with multiple comorbidities demonstrated significantly poorer outcomes, including higher ICU admission and mortality rates. These findings support previous evidence that chronic systemic diseases impair host defense mechanisms and increase vulnerability to severe respiratory infections.[5,15]

The study also demonstrated significant abnormalities in physiological parameters at admission, including tachypnea, tachycardia, hypotension, elevated BUN, and hypoxemia, all of which increased progressively with disease severity. A substantial proportion of patients belonged to moderate-to-high PSI severity groups, indicating significant disease burden.[13]

A major finding of the study was the strong association between inflammatory biomarkers and PSI severity. CRP, IL-6, D-dimer, and ferritin showed a significant stepwise increase across PSI severity groups ($p<0.001$). Among all biomarkers, IL-6 demonstrated the strongest positive correlation with PSI score ($r=0.71$), highlighting its central role in systemic inflammatory response.[7,8] Elevated IL-6 levels may reflect cytokine-mediated inflammation and progression toward severe disease.[9]

Similarly, elevated CRP levels were associated with increased disease severity and adverse outcomes, supporting its role as a reliable acute-phase marker in pneumonia.[6] Increased D-dimer levels indicated activation of coagulation pathways and endothelial injury, while elevated ferritin reflected hyperinflammatory response and immune dysregulation.[10,11]

Clinical outcomes in the present study showed that most patients recovered without ICU admission; however, mortality was significantly higher among patients with high PSI severity and elevated inflammatory markers. Patients with IL-6 ≥60 pg/mL, CRP ≥90 mg/L, D-dimer ≥1000 ng/mL, and ferritin ≥500 ng/mL demonstrated markedly increased ICU admission and mortality rates.

Multivariate logistic regression analysis identified PSI score, IL-6, CRP, D-dimer, ferritin, diabetes mellitus, COPD, and CKD as independent predictors of poor outcome. Among these, IL-6 emerged as the strongest biomarker predictor. ROC curve analysis further demonstrated excellent predictive performance of PSI score and IL-6 for predicting ICU admission and

mortality, suggesting that IL-6 may serve as a valuable adjunctive prognostic marker in routine clinical practice.[12,14]

Despite these important findings, the study has certain limitations. Being a single-center observational study with a relatively small sample size, the generalizability of results may be limited. Additionally, long-term follow-up and evaluation of other emerging inflammatory biomarkers were not performed. However, the study provides important real-world evidence regarding the prognostic utility of inflammatory markers in non-COVID pneumonia.

Conclusion

The present study demonstrates that inflammatory biomarkers play a significant role in assessing disease severity and predicting clinical outcomes in patients with non-COVID pneumonia. IL-6, CRP, D-dimer, and ferritin levels increased significantly with increasing PSI severity and were strongly associated with ICU admission and mortality.

Among all biomarkers, IL-6 emerged as the strongest independent predictor of poor outcome and showed excellent diagnostic accuracy for predicting severe disease. In addition, comorbidities such as diabetes mellitus, COPD, and CKD significantly contributed to adverse outcomes.

The findings suggest that incorporation of inflammatory biomarkers, particularly IL-6, along with PSI scoring may improve early risk stratification, prognostic assessment, and clinical decision-making in non-COVID pneumonia patients. Early identification of high-risk patients using biomarker-based assessment may facilitate timely intensive management and improve patient outcomes.

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