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ORIGINAL ARTICLE

Association of Selected Biomarkers with Pneumonia Severity: A Retrospective Observational Study

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ABSTRACT

Introduction: *Pneumonia is associated with substantial morbidity and mortality, with disease severity varying considerably among patients. Early identification of severe pneumonia is essential for timely management and appropriate risk stratification. Selected inflammatory biomarkers may provide complementary information regarding disease severity.* ***Objective:*** *To assess the association of selected biomarkers with pneumonia severity and determine their independent association with severe pneumonia.* ***Methods & Materials:*** *This retrospective observational study included 151 patients with pneumonia treated at Uttara Adhunik Medical College Hospital, Dhaka, from January to December 2025. Clinical characteristics and biomarkers (WBC, NLR, CRP, and procalcitonin) were assessed. Pneumonia severity was classified using CURB-65, with scores <3 as non-severe and 3–5 as severe. Biomarkers were compared between groups, and multivariable logistic regression identified independent predictors of severe pneumonia.* ***Results:*** *Among 151 patients, 65.6% had non-severe and 34.4% severe pneumonia. WBC, NLR, CRP, and procalcitonin were significantly higher in severe cases (all p<0.001). Age >65 years, COPD, and SpO_2 <90% were independent predictors of severe pneumonia. Elevated WBC (>15 × 10^9/L), NLR (>10), CRP (>100 mg/L), and procalcitonin (>0.5 ng/mL) were also independently associated with severe disease.* ***Conclusion:*** *Elevated WBC count, NLR, CRP, and procalcitonin were significantly associated with severe pneumonia and remained independently associated after adjustment for relevant clinical factors. These selected biomarkers may provide useful complementary information for early identification and risk stratification of patients with severe pneumonia.*

Keywords: *Pneumonia; disease severity; biomarkers; neutrophil-to-lymphocyte ratio; C-reactive protein; procalcitonin; white blood cell count; CURB-65*

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INTRODUCTION

Pneumonia is a major infectious disease associated with substantial morbidity, mortality, and healthcare utilization worldwide. The clinical presentation and disease course are highly heterogeneous, ranging from mild illness that can be managed with routine treatment to severe disease requiring intensive care, mechanical ventilation, or resulting in death. Early recognition of patients at increased risk of severe outcomes is therefore essential for appropriate triage, timely treatment, and optimal allocation of healthcare resources [1,2]. Several validated clinical prediction tools have been developed to assess pneumonia severity and estimate the risk of adverse outcomes. The Pneumonia Severity Index (PSI) incorporates demographic characteristics, comorbidities, physical examination findings, and laboratory parameters to stratify patients according to mortality risk [3]. Similarly, the CURB-65 score, based on confusion, blood urea nitrogen, respiratory rate, blood pressure, and age, provides a simple approach to identifying patients at increased risk of mortality and guiding decisions regarding the site of care [4]. Although these scoring systems are clinically useful, their predictive performance may be influenced by the availability and accuracy of clinical information and may not fully reflect the dynamic inflammatory and physiological responses associated with pneumonia severity. Biomarkers may provide additional information regarding the host response to infection and the extent of systemic inflammation. C-reactive protein (CRP) is a widely available marker of inflammation and has been associated with adverse outcomes in patients with community-acquired pneumonia. In hospitalized patients, CRP and serum albumin have demonstrated independent associations with mortality, and incorporation of these biomarkers into established severity models may improve prognostic discrimination [5]. Procalcitonin (PCT), another extensively investigated biomarker, has also been associated with prognosis in pneumonia. A systematic review and meta-analysis involving more than 6,000 patients found that elevated PCT concentrations were associated with increased mortality, particularly among patients with community-acquired pneumonia [6]. However, PCT should not be interpreted as a stand-alone marker for differentiating bacterial from viral pneumonia because its diagnostic accuracy for this purpose

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remains limited [7]. Hematological indices derived from routinely available complete blood counts have also attracted increasing attention because of their low cost and accessibility. The neutrophil-to-lymphocyte ratio (NLR) reflects the interaction between innate inflammatory activation and lymphocyte-mediated immune response and has been investigated as a prognostic marker in pneumonia. A systematic review reported that elevated NLR was associated with adverse outcomes, including mortality and intensive care unit admission, in patients with community-acquired pneumonia [8]. More recently, studies evaluating combinations of inflammatory and cardiovascular biomarkers, including NLR, CRP, PCT, B-type natriuretic peptide, and D-dimer, have demonstrated significant associations with pneumonia severity, suggesting that a multimarker approach may provide complementary prognostic information [9]. Other biomarkers, such as midregional proadrenomedullin, have similarly shown potential for prognostic assessment in community-acquired pneumonia [10]. Despite these findings, the clinical value of individual biomarkers may vary according to patient characteristics, disease severity, comorbidities, and the clinical setting. Therefore, this study aimed to assess the association between selected biomarkers and pneumonia severity and to determine whether these biomarkers are independently associated with severe pneumonia after adjustment for relevant clinical and demographic factors.

METHODS & MATERIALS

This retrospective observational study was conducted in the Department of Respiratory Medicine, Uttara Adhunik Medical College Hospital, Dhaka, Bangladesh, from January 2025 to December 2025. A total of 151 patients with pneumonia who were admitted to or treated at the study hospital during the study period were included. Patients of both sexes and all age groups with a documented clinical diagnosis of pneumonia and adequate clinical and laboratory records were eligible for inclusion. Eligible patients were identified from hospital admission registers, emergency department records, laboratory reports, and medical records. Patients with incomplete records regarding clinical characteristics, pneumonia severity, or relevant biomarker measurements were excluded. Data were retrospectively collected using a structured data collection form. Sociodemographic characteristics included age, sex, and smoking status. Relevant comorbidities, including diabetes mellitus, hypertension, chronic obstructive pulmonary disease (COPD), and chronic kidney disease, were also recorded. Clinical variables recorded at admission included fever, cough, dyspnea, chest pain, altered mental status, respiratory rate, oxygen saturation (SpO_2), and systolic blood pressure. Pneumonia severity was assessed using the CURB-65 score, which incorporates confusion, blood urea nitrogen level, respiratory rate, blood pressure, and age ≥65 years. Patients were categorized as having non-severe pneumonia when the CURB-65 score was less than 3 and severe pneumonia when the score was 3–5. The primary outcome was pneumonia severity, categorized as non-severe or severe. Laboratory parameters obtained at or near the time of hospital presentation were recorded from the patients' medical and laboratory records. The selected biomarkers included total white blood cell (WBC) count, neutrophil count, lymphocyte count, neutrophil-to-lymphocyte ratio (NLR), C-reactive protein (CRP), and procalcitonin. NLR was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count. For multivariable analysis, biomarker values were categorized using clinically relevant cutoffs: WBC count >15 × 10^9/L, NLR >10, CRP >100 mg/L, and procalcitonin >0.5 ng/mL.Data were analyzed using Statistical Package for the Social Sciences (SPSS), version 27.0 (IBM Corp., Armonk, NY, USA). Categorical variables were presented as frequencies and percentages. Continuous variables were expressed as mean ± standard deviation (SD) for normally distributed data and median with interquartile range (IQR) for non-normally distributed data. Differences in biomarker levels between patients with non-severe and severe pneumonia were assessed using the independent-samples t test or Mann–Whitney U test, as appropriate. Variables considered clinically relevant and/or demonstrating an association with severe pneumonia in univariable analysis were entered into a multivariable logistic regression model to identify factors independently associated with severe pneumonia. Adjusted odds ratios (AORs) with 95% confidence intervals (CIs) were reported. A two-sided p-value <0.05 was considered statistically significant.

RESULTS

Table I shows total of 151 patients with pneumonia were included in the study. The largest proportion of patients were aged 41–60 years, comprising 55 (36.4%), followed by those aged 61–75 years, 49 (32.5%). Twenty-five (16.6%) patients were aged ≤40 years, while 22 (14.6%) were aged >75 years. Males constituted the majority of the study population, with 92 (60.9%) patients, compared with 59 (39.1%) females. Most patients were never smokers, 91 (60.3%), whereas 60 (39.7%) were current or former smokers. Diabetes mellitus was present in 43 (28.5%) patients, hypertension in 57 (37.7%), COPD in 31 (20.5%), and chronic kidney disease in 13 (8.6%).

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Table I: Sociodemographic and baseline characteristics of patients with pneumonia (*n*=151)

Variables	Frequency	Percent
Age (years)		
≤40	25	16.6
41–60	55	36.4
61–75	49	32.5
>75	22	14.6
Smoking status		
Never smoker	91	60.3
Current/former smoker	60	39.7
Diabetes mellitus		
Yes	43	28.5
No	108	71.5
Hypertension		
Yes	57	37.7
No	94	62.3
COPD		
Yes	31	20.5
No	120	79.5
Chronic kidney disease		
Yes	13	8.6
No	138	91.4

Figure 1 show male patients constituted the majority (60.9%), while females accounted for 39.1% of the participants.

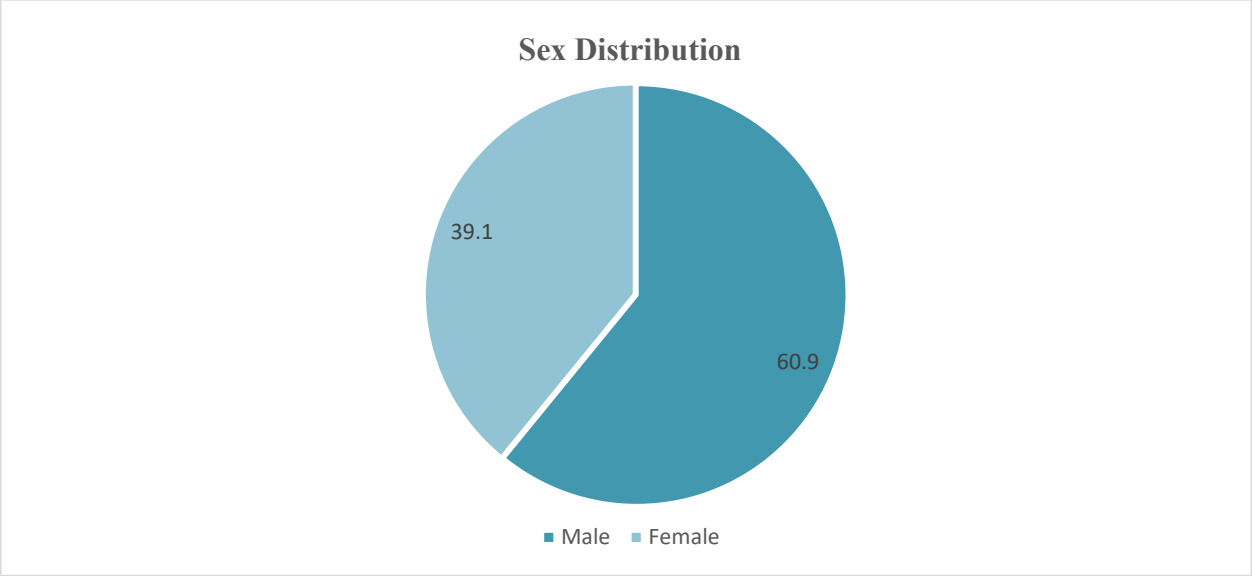


Figure 1: Distribution of the study patients by sex (*n*=151)

Table II shows fever was the most frequently reported clinical feature, present in 136 (90.1%) patients, followed by cough in 128 (84.8%) and dyspnea in 104 (68.9%). Chest pain was reported by 47 (31.1%) patients, while altered mental status was present in 19 (12.6%). A respiratory rate of <30/min was observed in 102 (67.5%) patients, whereas 49 (32.5%) had a respiratory rate of ≥30/min. On admission, SpO_2 was ≥90% in 108 (71.5%) patients and <90% in 43 (28.5%). Systolic blood pressure was ≥90 mmHg in 143 (94.7%) patients and <90 mmHg in 8 (5.3%).

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Table II: Distribution of the study patients by clinical characteristics (*n*=151)

Variables	Frequency	Percent
Fever		
Yes	136	90.1
No	15	9.9
Cough		
Yes	128	84.8
No	23	15.2
Dyspnea		
Yes	104	68.9
No	47	31.1
Chest pain		
Yes	47	31.1
No	104	68.9
Altered mental status		
Yes	19	12.6
No	132	87.4
Respiratory rate		
<30/min	102	67.5
≥30/min	49	32.5
SpO_2 on admission		
≥90%	108	71.5
<90%	43	28.5
Systolic blood pressure		
≥90 mmHg	143	94.7
<90 mmHg	8	5.3

Figure 2 shows regarding pneumonia severity, 99 (65.6%) patients had non-severe pneumonia, whereas 52 (34.4%) had severe pneumonia.

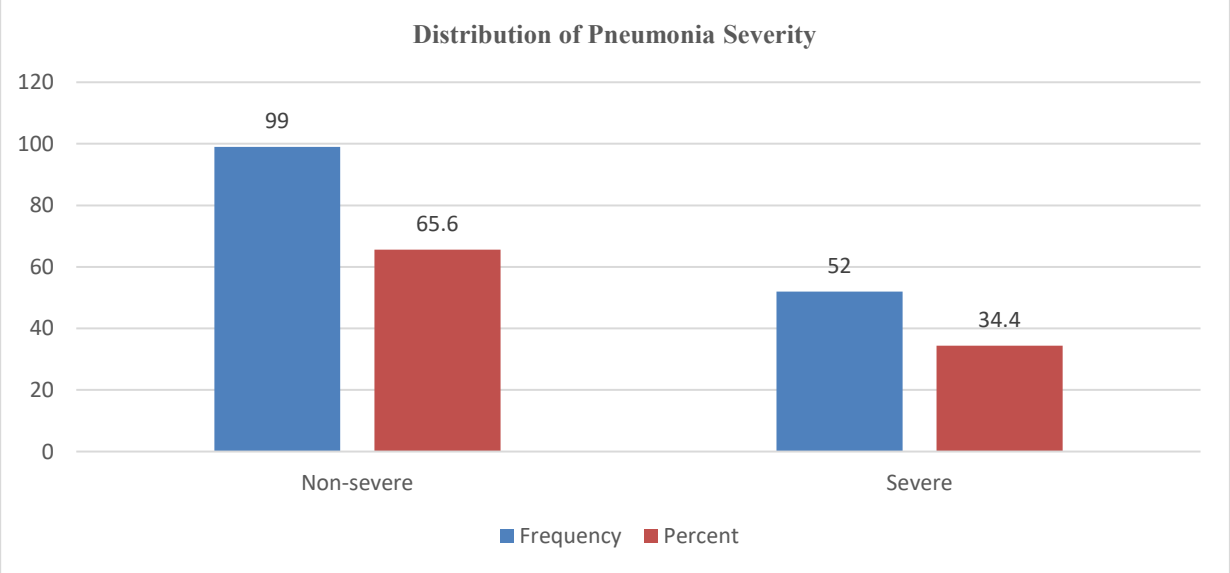


Figure 2: Distribution of the study patients by pneumonia severity (*n*=151)

Table III shows the mean WBC count was 12.4 ± 5.1 ×10^9/L, the mean neutrophil count was 9.8 ± 4.7 ×10^9/L, and the mean lymphocyte count was 1.4 ± 0.7 ×10^9/L. The mean NLR was 8.1 ± 5.9. The median CRP level was 86.5 mg/L (IQR, 48.0–154.0), while the median procalcitonin level was 0.42 ng/mL (IQR, 0.16–1.24).

Table III: Distribution of Selected Biomarkers Among Patients with Pneumonia (*n*=151)

Biomarker	Mean ± SD / Median (IQR)
WBC count (×10^9/L)	12.4 ± 5.1
Neutrophil count (×10^9/L)	9.8 ± 4.7
Lymphocyte count (×10^9/L)	1.4 ± 0.7
NLR	8.1 ± 5.9
CRP (mg/L)	86.5 (48.0–154.0)
Procalcitonin (ng/mL)	0.42 (0.16–1.24)

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Table IV shows comparison of biomarker levels between non-severe and severe pneumonia showed significantly higher values in the severe group. The mean WBC count was 15.2 ± 5.7 $\times 10^9$/L among patients with severe pneumonia compared with 10.9 ± 4.1 $\times 10^9$/L among those with non-severe pneumonia (p<0.001). Similarly, the mean NLR was higher in the severe group than in the non-severe group, 11.9 ± 7.0 versus 6.1 ± 3.7, respectively (p<0.001). The median CRP level was 137.5 mg/L (IQR, 83.0–211.0) in the severe group compared with 65.2 mg/L (IQR, 38.0–108.0) in the non-severe group (p<0.001). Median procalcitonin was also significantly higher among patients with severe pneumonia, 0.86 ng/mL (IQR, 0.31–2.14) versus 0.25 ng/mL (IQR, 0.10–0.62), respectively (p<0.001).

Table IV: Comparison of Selected Biomarkers Between Non-Severe and Severe Pneumonia (*n*=151)

Biomarker	Non-severe (n=99)	Severe (n=52)	p-value
WBC count ($\times 10^9$/L)	10.9 ± 4.1	15.2 ± 5.7	<0.001
NLR	6.1 ± 3.7	11.9 ± 7.0	<0.001
CRP (mg/L)	65.2 (38.0–108.0)	137.5 (83.0–211.0)	<0.001
Procalcitonin (ng/mL)	0.25 (0.10–0.62)	0.86 (0.31–2.14)	<0.001

Table V shows multivariable logistic regression analysis identified several independent predictors of severe pneumonia. Age >65 years was independently associated with severe pneumonia (AOR, 2.31; 95% CI, 1.15–4.65; p=0.019), as was COPD (AOR, 2.47; 95% CI, 1.08–5.66; p=0.033). Patients with an admission SpO_2 <90% had significantly higher odds of severe pneumonia (AOR, 3.86; 95% CI, 1.72–8.66; p=0.001). Among the biomarkers, WBC >15 $\times 10^9$/L (AOR, 2.42; 95% CI, 1.12–5.23; p=0.024), NLR >10 (AOR, 3.18; 95% CI, 1.47–6.88; p=0.003), CRP >100 mg/L (AOR, 3.54; 95% CI, 1.65–7.59; p=0.001), and procalcitonin >0.5 ng/mL (AOR, 2.76; 95% CI, 1.29–5.91; p=0.009) were independently associated with severe pneumonia.

Table V: Independent Predictors of Severe Pneumonia

Variable	AOR	95% CI	p-value
Age >65 years	2.31	1.15–4.65	0.019
COPD	2.47	1.08–5.66	0.033
SpO_2 <90%	3.86	1.72–8.66	0.001
WBC >15 $\times 10^9$/L	2.42	1.12–5.23	0.024
NLR >10	3.18	1.47–6.88	0.003
CRP >100 mg/L	3.54	1.65–7.59	0.001
Procalcitonin >0.5 ng/mL	2.76	1.29–5.91	0.009

Multivariable logistic regression was performed to identify factors independently associated with severe pneumonia. (AORs) with 95% CI were reported. A p-value <0.05 was considered statistically significant.

DISCUSSION

This study demonstrated that severe pneumonia was associated with significantly higher WBC count, NLR, CRP, and procalcitonin levels. Age >65 years, COPD, admission SpO_2 <90%, WBC >15 $\times 10^9$/L, NLR >10, CRP >100 mg/L, and procalcitonin >0.5 ng/mL were independently associated with severe pneumonia, supporting the potential role of routinely available biomarkers as adjuncts to clinical severity assessment. Most patients were aged 41–75 years, and 60.9% were male. The predominance of middle-aged and older adults is consistent with the epidemiology of hospitalized community-acquired pneumonia, which occurs more frequently among older adults. [11] In the present study, age >65 years was independently associated with severe pneumonia, consistent with evidence linking advanced age and comorbidity with poorer outcomes. [12] COPD was present in 20.5% of patients and was independently associated with severe pneumonia (AOR, 2.47), possibly reflecting reduced pulmonary reserve and chronic airway inflammation. [13] Hypoxemia was also an important predictor; admission SpO_2 <90% was strongly associated with severe disease (AOR, 3.86), supporting previous evidence that oxygenation provides important prognostic information in pneumonia. [14] The most prominent finding was the marked elevation of inflammatory biomarkers in severe pneumonia. WBC count was significantly higher in severe than non-severe disease (15.2 ± 5.7 vs 10.9 ± 4.1 $\times 10^9$/L), and WBC >15 $\times 10^9$/L remained independently associated with severity. These findings support the value of leukocytosis and inflammatory markers in assessing pneumonia severity. [17] NLR showed a particularly strong association, with mean values of 11.9 ± 7.0 in severe versus 6.1 ± 3.7 in non-severe pneumonia; NLR >10 was independently associated with severe disease (AOR, 3.18). Previous evidence similarly supports NLR as a simple and inexpensive marker of adverse outcomes in community-acquired pneumonia. [18] Higher NLR has also been associated with poorer outcomes among hospitalized patients. [19] CRP and procalcitonin demonstrated similar patterns. Median CRP was 137.5 mg/L in severe versus 65.2 mg/L in non-severe pneumonia, while CRP >100 mg/L independently predicted severe disease (AOR, 3.54), consistent with evidence supporting CRP as a marker of pneumonia severity. [15] Procalcitonin was also higher in severe pneumonia (0.86 vs 0.25 ng/mL), and levels >0.5 ng/mL were independently associated with severity (AOR, 2.76), supporting its prognostic value in hospitalized pneumonia. [16] The concurrent elevation of WBC, NLR, CRP, and procalcitonin suggests a greater systemic inflammatory response in severe pneumonia. These biomarkers may complement clinical assessment, although their predictive performance varies according to population and threshold, and no single biomarker should replace established clinical assessment. [20,21] Their combined use with established pneumonia severity scores may provide additional prognostic information and facilitate early identification of patients requiring closer monitoring. [22]. Overall, the findings support an integrated clinical and biomarker-based approach to pneumonia severity assessment. In particular, the independent associations of hypoxemia,

elevated NLR, CRP, and procalcitonin indicate that these readily available parameters may help identify patients at increased risk of severe disease and guide early clinical monitoring. However, this study observed, severe pneumonia was associated with significantly higher WBC, NLR, CRP, and procalcitonin levels. Older age, COPD, hypoxemia, and elevated inflammatory biomarkers were independent predictors of severe disease. These readily available biomarkers may therefore serve as useful adjuncts to clinical assessment for early identification of patients at increased risk of severe pneumonia.

CONCLUSION

Severe pneumonia was significantly associated with elevated WBC count, NLR, CRP, and procalcitonin levels. Older age, COPD, admission hypoxemia, and elevated inflammatory biomarkers were independently associated with severe disease. These findings suggest that routinely available biomarkers, particularly NLR, CRP, and procalcitonin, may provide useful complementary information for early identification and risk stratification of patients with severe pneumonia. Biomarker assessment alongside clinical evaluation may therefore support timely monitoring and management of patients at increased risk of severe pneumonia.

LIMITATIONS

This study was limited by its relatively small sample size, single-center design, and retrospective observational nature, which may restrict generalizability and preclude causal inference. The selected biomarker levels may have been affected by sampling timing, prior treatment, comorbidities, and underlying etiology. Longitudinal biomarker changes and their incremental value beyond established severity scores were not assessed.

RECOMMENDATIONS

Based on the findings of this study, prospective multicenter studies are recommended to validate the association of the selected biomarkers with pneumonia severity. Serial biomarker measurements may help determine their value in monitoring disease progression and response to treatment. Further studies should also assess whether combining these biomarkers with established pneumonia severity scores improves risk stratification and clinical decision-making.

CONFLICT OF INTEREST

None declared

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Self

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