

ASSOCIATION OF NEUTROPHIL-TO-LYMPHOCYTE RATIO, C-REACTIVE PROTEIN, AND LACTATE DEHYDROGENASE WITH DISEASE SEVERITY IN COMMUNITY-ACQUIRED PNEUMONIA: A CROSS-SECTIONAL STUDY

Dr. Niel Rajesh Bhalani^{*1}, Dr. Elen Ann Abraham², Dr. Ramprasath³

¹*Third-Year Postgraduate, Department of Respiratory Medicine, Sree Balaji Medical College and Hospital, Bharath Institute of Higher Education and Research (BIHER), Chennai, Tamil Nadu, India.

²Associate Professor, Department of Respiratory Medicine, Sree Balaji Medical College and Hospital, Bharath Institute of Higher Education and Research (BIHER), Chennai, Tamil Nadu, India, ORCID: 0009-0007-1510-0935, Email: drelennan153@gmail.com

³Senior Resident, Department of Respiratory Medicine, Sree Balaji Medical College and Hospital, Bharath Institute of Higher Education and Research (BIHER), Chennai, Tamil Nadu, India, ORCID: 0009-0001-9167-6991, Email: ram07sridhar@gmail.com

ABSTRACT:

Background: Community-acquired pneumonia (CAP) remains a major cause of infectious morbidity and mortality worldwide despite advances in antimicrobial therapy and supportive care. Early identification of patients at risk of severe disease is essential for appropriate triage and timely management. Although clinical severity scores such as CURB-65 and the Pneumonia Severity Index (PSI) are widely used, readily available inflammatory biomarkers may further improve early risk stratification.

Methods: A hospital-based cross-sectional analytical study was conducted among 100 adult patients with community-acquired pneumonia admitted to a tertiary care hospital. Demographic characteristics, clinical presentation, laboratory investigations, and chest radiographic findings were recorded. Neutrophil-to-lymphocyte ratio (NLR), C-reactive protein (CRP), and lactate dehydrogenase (LDH) levels were measured at admission. Disease severity was assessed using CURB-65 and PSI scores. Correlation analysis, multivariate logistic regression, and receiver operating characteristic (ROC) curve analysis were performed to evaluate the association and predictive performance of the biomarkers.

Results: Among the 100 patients, 62% were males and the majority belonged to the 41–60-year age group (44%). Fever (92%), cough (88%), and dyspnoea (74%) were the predominant presenting symptoms. Mean NLR increased significantly from 4.2 ± 1.3 in mild CAP to 13.6 ± 3.1 in severe CAP ($p < 0.001$). Similarly, CRP increased from 32.8 ± 18.5 mg/L to 142.7 ± 44.8 mg/L, while LDH increased from 278 ± 71 U/L to 604 ± 102 U/L across increasing severity categories ($p < 0.001$ for both). NLR demonstrated the strongest correlation with CURB-65 ($r = 0.71$), whereas CRP showed the highest correlation with PSI ($r = 0.74$). Multivariate logistic regression identified NLR ≥ 10 (adjusted OR 4.82, $p < 0.001$), CRP ≥ 100 mg/L (adjusted OR 3.42, $p < 0.001$), LDH ≥ 450 U/L (adjusted OR 2.63, $p = 0.002$), age > 60 years, and diabetes mellitus as independent predictors of severe CAP. ROC analysis demonstrated excellent predictive performance for CRP (AUC 0.91), followed by NLR (AUC 0.89) and LDH (AUC 0.86).

Conclusion: NLR, CRP, and LDH are inexpensive and readily available inflammatory biomarkers that show significant associations with disease severity and adverse clinical outcomes in community-acquired pneumonia. Their integration with established clinical severity scores may improve early identification of high-risk patients, facilitate prompt clinical decision-making, and optimize patient management, particularly in resource-limited settings.

KEYWORDS: Community-acquired pneumonia; Neutrophil-to-lymphocyte ratio; C-reactive protein; Lactate dehydrogenase; CURB-65; Pneumonia Severity Index.

INTRODUCTION

Community-acquired pneumonia (CAP) is an acute infection of the lung parenchyma acquired outside healthcare facilities and remains one of the leading causes of infectious morbidity and mortality worldwide.[1] Despite substantial advances in antimicrobial therapy, vaccination, and supportive care, CAP continues to account for considerable hospital admissions, intensive care unit (ICU) utilization, and healthcare expenditure globally.[2] The global burden is particularly high among older adults, individuals with chronic comorbid conditions, and populations in low- and middle-

income countries, where delayed diagnosis and limited healthcare resources contribute to poor clinical outcomes.[3] CAP continues to be a major public health concern because of its high incidence, significant mortality, and increasing socioeconomic burden.[4]

Patients with CAP frequently develop serious complications, including respiratory failure, sepsis, septic shock, acute respiratory distress syndrome (ARDS), and multiorgan dysfunction, all of which substantially increase mortality risk and prolong hospitalization.[5] Early recognition of patients at risk for severe disease is therefore essential to facilitate timely initiation of appropriate antimicrobial therapy, determine the need for hospitalization or ICU admission, and improve overall patient outcomes.[2]

Current international guidelines recommend objective severity assessment at the time of presentation using validated clinical prediction tools such as the Confusion, Urea, Respiratory Rate, Blood Pressure and Age ≥ 65 years (CURB-65) score and the Pneumonia Severity Index (PSI).[2] Although these scoring systems demonstrate good prognostic accuracy, their routine clinical use has several limitations. CURB-65 may underestimate severity in certain patient groups, whereas PSI requires multiple demographic, clinical, laboratory, and radiological variables, making bedside application relatively cumbersome, particularly in busy emergency departments.[4]

The severity of CAP depends not only on microbial virulence but also on the magnitude of the host inflammatory response.[5] Excessive neutrophilic inflammation, lymphocyte depletion, cytokine release, endothelial dysfunction, and pulmonary tissue injury contribute significantly to disease progression and adverse clinical outcomes.[5] Consequently, considerable attention has focused on identifying readily available inflammatory biomarkers that can complement conventional clinical severity scores.[6]

Among the routinely available inflammatory biomarkers, the neutrophil-to-lymphocyte ratio (NLR), C-reactive protein (CRP), and lactate dehydrogenase (LDH) have shown considerable promise. The NLR reflects the balance between innate inflammatory activation and adaptive immune response and can be calculated easily from a routine complete blood count.[6] CRP is a well-established acute-phase reactant that correlates with the intensity of systemic inflammation and bacterial infection.[8] LDH is released following cellular injury and has been recognized as an indirect marker of pulmonary tissue damage and disease severity.[9]

Recent studies have demonstrated that elevated NLR is independently associated with increased disease severity, ICU admission, treatment failure, and mortality among patients with CAP.[7] Similarly, CRP has been shown to correlate with disease severity and provides useful prognostic information during the early stages of hospitalization.[8] Comprehensive reviews further suggest that combining inflammatory biomarkers with established clinical severity scores may improve early risk stratification compared with clinical scoring systems alone.[9] Contemporary evidence also supports the integration of inflammatory biomarkers into routine clinical assessment to facilitate individualized management of patients with CAP.[10]

However, evidence regarding the combined usefulness of NLR, CRP, and LDH as adjuncts to both CURB-65 and PSI remains limited, particularly in resource-constrained healthcare settings. Therefore, the present study was undertaken to evaluate the association of neutrophil-to-lymphocyte ratio, C-reactive protein, and lactate dehydrogenase with disease severity among adult patients with community-acquired pneumonia and to determine their usefulness as adjuncts to established clinical severity scoring systems for predicting disease severity and clinical outcomes.

METHODOLOGY

Study Design and Setting

A hospital-based cross-sectional analytical study was conducted in the Department of Respiratory Medicine, Sree Balaji Medical College and Hospital, Chennai, Tamil Nadu, India, after obtaining approval from the Institutional Ethics Committee. The study included adult patients diagnosed with community-acquired pneumonia (CAP) during the study period.

Study Population

A total of 100 consecutive adult patients with a diagnosis of community-acquired pneumonia were enrolled.

Inclusion Criteria

- ☐ Patients aged 18 years or older.
- ☐ Clinical features suggestive of community-acquired pneumonia, including fever, cough, sputum production, dyspnoea, or pleuritic chest pain.
- ☐ Radiological confirmation of pneumonia on chest radiography.
- ☐ Patients admitted within 48 hours of symptom onset without prior hospitalization.

Exclusion Criteria

- ☐ Hospital-acquired or ventilator-associated pneumonia.
- ☐ Active pulmonary tuberculosis.
- ☐ Human immunodeficiency virus (HIV) infection or other severe immunocompromised states.
- ☐ Patients receiving chemotherapy or long-term immunosuppressive therapy.
- ☐ Hematological malignancies or disorders affecting leukocyte counts.
- ☐ Patients with incomplete clinical or laboratory data.

Data Collection

After obtaining informed consent, demographic characteristics, smoking history, comorbid illnesses, presenting symptoms, and physical examination findings were recorded using a predesigned case record proforma. Vital parameters, including respiratory rate, pulse rate, oxygen saturation (SpO₂), blood pressure, and body temperature, were documented at admission.

Routine laboratory investigations included complete blood count, serum urea, serum creatinine, C-reactive protein (CRP), and lactate dehydrogenase (LDH). The neutrophil-to-lymphocyte ratio (NLR) was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count obtained from the admission complete blood count. Chest radiography was performed in all patients to confirm the diagnosis and determine radiological involvement.

Severity Assessment

Disease severity was assessed using the Confusion, Urea, Respiratory Rate, Blood Pressure, Age ≥ 65 years (CURB-65) score and the Pneumonia Severity Index (PSI) at the time of admission. Patients were categorized into severity groups based on these validated scoring systems.

Outcome Measures

The primary outcome was the association of NLR, CRP, and LDH with CAP severity. Secondary outcomes included the relationship of these biomarkers with ICU admission, in-hospital mortality, and their diagnostic performance in predicting severe community-acquired pneumonia.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using the Statistical Package for the Social Sciences (SPSS) software. Continuous variables were expressed as mean $\pm$ standard deviation (SD), whereas categorical variables were summarized as frequencies and percentages. Comparisons between groups were performed using analysis of variance (ANOVA) for continuous variables and the Chi-square test for categorical variables. Pearson's correlation coefficient was used to evaluate the relationship between biomarker levels and severity scores. Multivariate logistic regression analysis was performed to identify independent predictors of severe CAP. Receiver operating characteristic (ROC) curve analysis was used to determine the diagnostic performance of NLR, CRP, and LDH, and the area under the curve (AUC), sensitivity, specificity, and optimal cut-off values were calculated. A p-value of <0.05 was considered statistically significant.

RESULTS

Table 1. Demographic Characteristics of the Study Population (n = 100)

Variable	Category	n	%
Age group (years)	18–40	18	18.0
	41–60	44	44.0
	>60	38	38.0
Gender	Male	62	62.0
	Female	38	38.0
Smoking status	Current	35	35.0
	Former	13	13.0
	Never	52	52.0
Comorbidities	Diabetes mellitus	32	32.0
	Hypertension	27	27.0
	COPD	15	15.0
	No comorbidity	26	26.0

Table 2. Clinical Profile of Patients with Community-Acquired Pneumonia (n = 100)

Parameter	Value
Fever	92 (92.0%)
Cough	88 (88.0%)
Sputum production	61 (61.0%)
Dyspnoea	74 (74.0%)
Pleuritic chest pain	38 (38.0%)
Respiratory rate (breaths/min)	28.4 ± 6.7
Pulse rate (beats/min)	101.8 ± 13.9
SpO ₂ (%)	89.6 ± 5.2
SpO ₂ <90%	40 (40.0%)
Temperature (°C)	38.2 ± 0.9

Table 3. Radiological and Baseline Laboratory Findings**A. Chest X-ray Findings**

Pattern	n (%)
Right lower lobe	36 (36.0%)
Left lower lobe	21 (21.0%)
Bilateral multilobar	29 (29.0%)
Others (upper lobe/interstitial)	14 (14.0%)

Baseline Laboratory Parameters

Parameter	Mean ± SD
Haemoglobin (g/dL)	12.3 ± 1.9
Total leukocyte count (cells/mm ³)	13,760 ± 3,410
Platelet count (×10 ⁵ /mm ³)	2.54 ± 0.72
Serum urea (mg/dL)	38.2 ± 12.6
Serum creatinine (mg/dL)	1.09 ± 0.34

Table 4. Distribution of Community-Acquired Pneumonia Severity According to CURB-65 and PSI

Severity Index	Category	n	%
CURB-65	Mild (0–1)	44	44.0
	Moderate (2)	36	36.0
	Severe (≥3)	20	20.0
PSI	Class I–II	14	14.0
	Class III	46	46.0
	Class IV	28	28.0
	Class V	12	12.0

Table 5. Comparison of Biomarker Levels Across CAP Severity Groups

Severity	NLR (Mean ± SD)	CRP (mg/L) (Mean ± SD)	LDH (U/L) (Mean ± SD)
Mild (n=44)	4.2 ± 1.3	32.8 ± 18.5	278 ± 71
Moderate (n=36)	7.8 ± 2.5	86.5 ± 37.2	422 ± 89
Severe (n=20)	13.6 ± 3.1	142.7 ± 44.8	604 ± 102
ANOVA p-value	<0.001	<0.001	<0.001

Table 6. Correlation of Biomarkers with CAP Severity Scores**A. CURB-65**

Biomarker	Pearson's r	p-value
NLR	0.71	<0.001
CRP	0.65	<0.001
LDH	0.59	<0.001

B. PSI

Biomarker	Pearson's r	p-value
NLR	0.68	<0.001
CRP	0.74	<0.001
LDH	0.63	<0.001

Table 7. Association of Biomarkers with Clinical Outcomes and Predictive Performance

Outcome	Frequency	Mean NLR $\pm$ SD	Mean CRP $\pm$ SD	Mean LDH $\pm$ SD
Discharged without ICU	72 (72.0%)	5.9 $\pm$ 2.8	58.4 $\pm$ 33.7	345 $\pm$ 84
ICU admission	18 (18.0%)	10.7 $\pm$ 3.4	121.2 $\pm$ 42.5	528 $\pm$ 96
Death	10 (10.0%)	14.2 $\pm$ 3.7	156.8 $\pm$ 49.2	662 $\pm$ 108
ANOVA p-value	—	0.002	0.001	0.004

Independent Predictors of Severe CAP

Variable	Adjusted OR (95% CI)	p-value
Age >60 years	1.89 (1.02–3.49)	0.043
Smoking	1.79 (0.98–3.28)	0.061
Diabetes mellitus	2.03 (1.10–3.73)	0.025
NLR $\geq$ 10	4.82 (2.03–11.40)	<0.001
CRP $\geq$ 100 mg/L	3.42 (1.78–6.55)	<0.001
LDH $\geq$ 450 U/L	2.63 (1.43–4.85)	0.002

ROC Analysis

Biomarker	AUC (95% CI)	Cut-off	Sensitivity (%)	Specificity (%)	p-value
NLR	0.89 (0.83–0.95)	>9.2	85.0	81.8	<0.001
CRP	0.91 (0.86–0.96)	>95 mg/L	88.0	83.0	<0.001
LDH	0.86 (0.79–0.93)	>470 U/L	82.0	78.5	<0.001

Figure 1. Smoking Status Distribution Among Patients with Community-Acquired Pneumonia (n = 100)

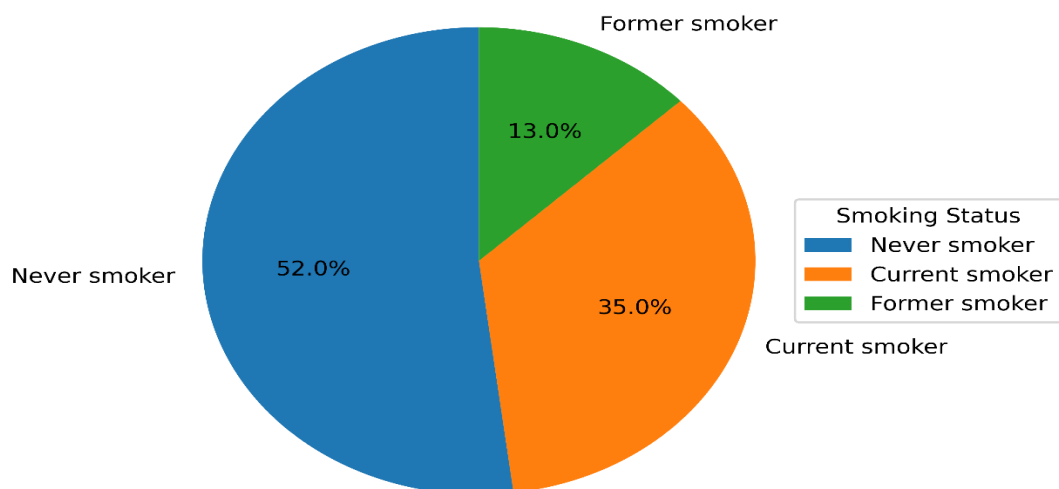


Figure 2. Distribution of Community-Acquired Pneumonia Severity According to CURB-65 Score (n = 100)

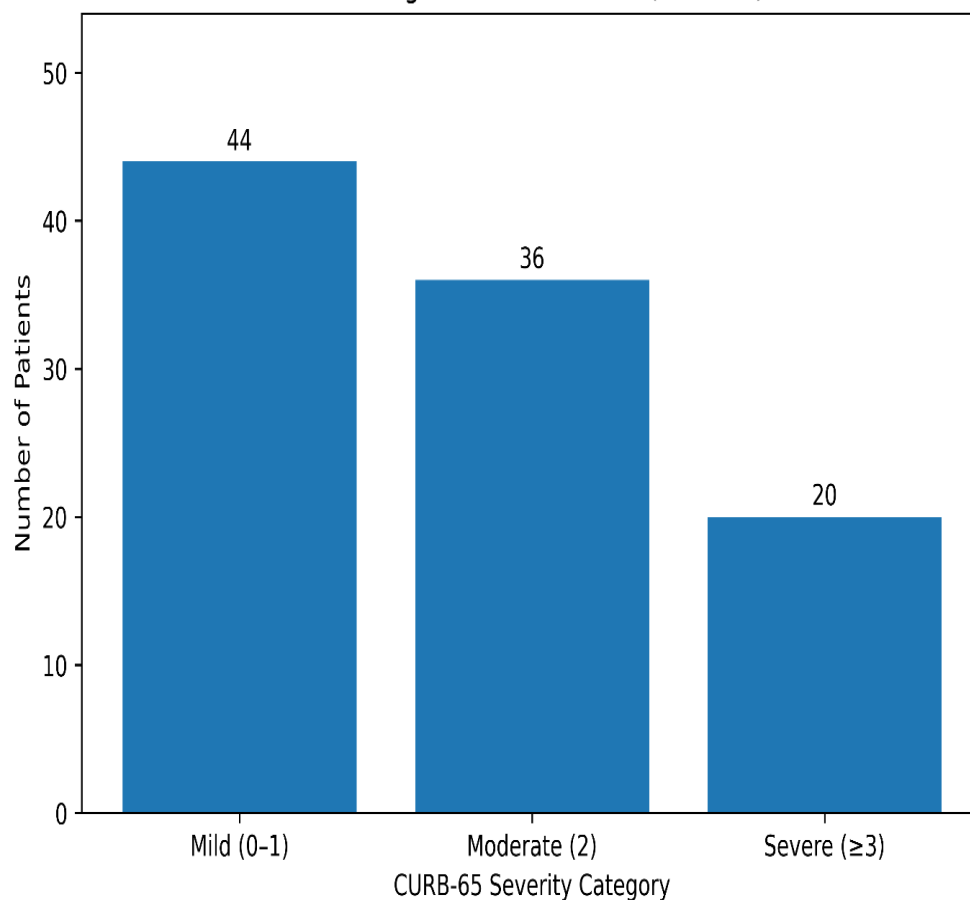
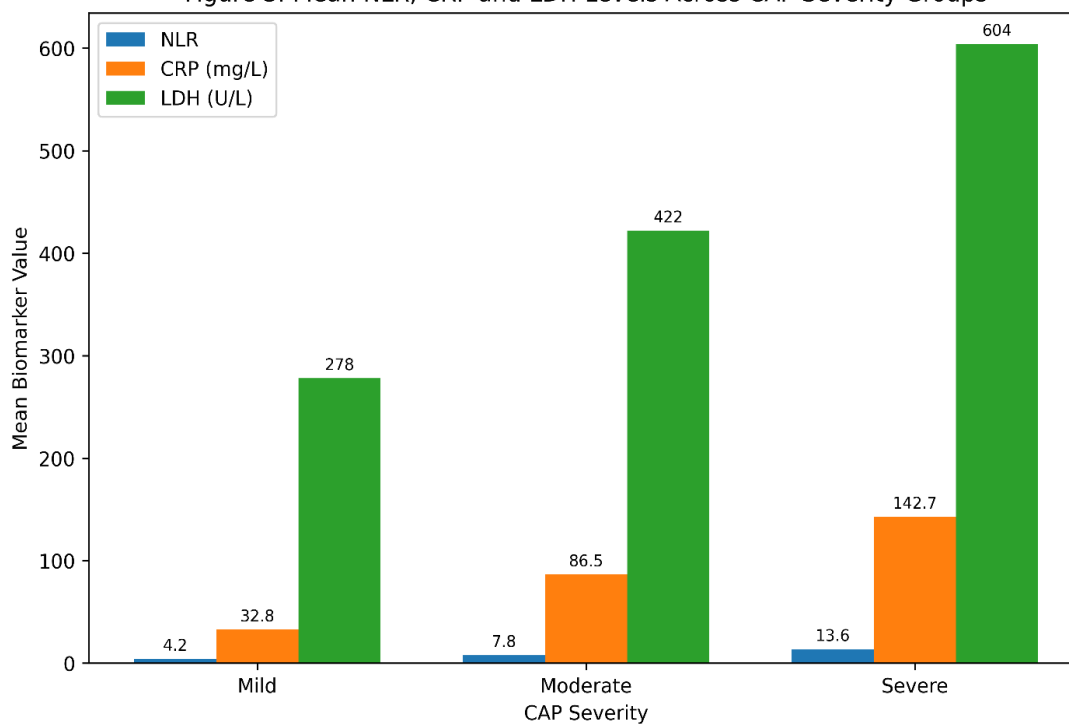


Figure 3. Mean NLR, CRP and LDH Levels Across CAP Severity Groups



DISCUSSION

The present study demonstrated that inflammatory biomarkers were closely associated with disease severity and clinical outcomes in patients with community-acquired pneumonia. Mean NLR, CRP, and LDH increased significantly from

mild to severe CAP ($p < 0.001$). All three biomarkers showed significant positive correlations with both CURB-65 and Pneumonia Severity Index (PSI) scores. Patients requiring ICU admission and those who died had substantially higher biomarker levels than patients discharged without ICU care. Furthermore, multivariate logistic regression identified age > 60 years, diabetes mellitus, $\text{NLR} \geq 10$, $\text{CRP} \geq 100$ mg/L, and $\text{LDH} \geq 450$ U/L as independent predictors of severe CAP. ROC analysis demonstrated excellent diagnostic performance, with CRP showing the highest area under the curve (AUC 0.91), followed by NLR (AUC 0.89) and LDH (AUC 0.86). These findings collectively indicate that routinely available inflammatory biomarkers provide valuable adjunctive information for early risk stratification in CAP.

One of the principal findings of the present study was the progressive increase in neutrophil-to-lymphocyte ratio with increasing disease severity. Mean NLR increased from 4.2 in mild CAP to 13.6 in severe CAP and demonstrated the strongest correlation with CURB-65 score ($r = 0.71$). Similar observations were reported by Sharma et al., who demonstrated that elevated NLR independently predicted adverse clinical outcomes and remained a significant prognostic marker among hospitalized CAP patients even after adjustment for conventional risk factors.[15] Likewise, Ghosh et al. evaluated hospitalized Indian patients with CAP and observed that higher NLR values were significantly associated with increasing CURB-65 scores, ICU admission, and mortality, supporting the usefulness of NLR in routine clinical practice within Indian healthcare settings.[16]

The present study also demonstrated a marked rise in CRP concentrations with increasing disease severity and found that CRP showed the strongest correlation with PSI score ($r = 0.74$). Elevated CRP levels were also independently associated with severe CAP on multivariate analysis. Although our study evaluated CRP as an individual biomarker, Miao et al. demonstrated that inflammatory indices incorporating CRP, particularly the albumin-to-CRP ratio, accurately predicted short-term mortality among elderly patients with CAP, emphasizing the importance of CRP-based inflammatory assessment in prognostic evaluation.[17] Similarly, Han et al. reported that CRP-based inflammatory indices were significantly associated with disease severity in pneumonia, further supporting the biological relevance of CRP as an indicator of systemic inflammatory burden.[18]

Another important finding of our study was the significant increase in LDH concentrations with increasing disease severity, reflecting progressive pulmonary tissue injury. Patients with severe CAP, ICU admission, and mortality exhibited markedly elevated LDH values. Since inflammatory biomarkers represent dynamic changes during hospitalization, serial assessment may further improve prognostic accuracy. Lee et al. demonstrated that serial NLR measurements closely paralleled clinical improvement or deterioration in hospitalized CAP patients and suggested that repeated biomarker estimation provides greater prognostic value than a single baseline measurement.[19]

The correlation analysis performed in the present study showed significant positive relationships between NLR, CRP, LDH and both CURB-65 and PSI scores. These observations suggest that inflammatory biomarkers complement established severity scoring systems by reflecting ongoing host inflammatory response and tissue injury that may not be completely represented by clinical variables alone. Supporting these findings, the systematic review by Kuikel et al. concluded that NLR consistently predicts severe disease, ICU admission, and mortality across multiple CAP studies and recommended its incorporation into routine clinical assessment because of its low cost, simplicity, and reproducibility.[20]

In our study, LDH independently predicted severe CAP with an adjusted odds ratio of 2.63 and demonstrated good diagnostic accuracy (AUC 0.86). These findings are comparable with those of García Clemente et al., who reported that elevated LDH levels were significantly associated with extensive pulmonary involvement, respiratory failure, and poor prognosis among patients with community-acquired pneumonia.[21] Likewise, Wu et al. demonstrated that LDH reflects pulmonary tissue injury and independently predicts severe pneumonia and adverse clinical outcomes, reinforcing its value as an objective biomarker of disease severity.[22]

Multivariate logistic regression in the present study identified $\text{NLR} \geq 10$ as the strongest independent biomarker predictor of severe CAP (adjusted OR 4.82). This finding is consistent with the landmark study by de Jager et al., who first demonstrated that elevated NLR independently predicts disease severity and mortality in community-acquired pneumonia and performs better than conventional leukocyte count alone for prognostic assessment.[23] Similar observations were reported by Cataudella et al., who found significantly higher NLR values among elderly CAP patients with adverse clinical outcomes and concluded that NLR is a reliable predictor of mortality in hospitalized patients.[24]

Receiver operating characteristic analysis in the present study showed excellent discriminative ability for all three biomarkers, with CRP achieving the highest AUC followed by NLR and LDH. These findings suggest that inflammatory biomarkers can substantially improve early identification of patients at risk of severe disease when interpreted alongside validated clinical severity scores. Comparable observations were reported by Menéndez et al., who demonstrated that inflammatory markers accurately identify patients at risk of clinical instability, delayed recovery, and poor outcomes and recommended their integration with conventional severity assessment tools for routine management of community-acquired pneumonia.[25]

Overall, the present study demonstrates that NLR, CRP, and LDH are inexpensive, widely available, and clinically valuable biomarkers that closely reflect disease severity, correlate with established prognostic scoring systems, and independently predict adverse outcomes. Integration of these biomarkers with CURB-65 and PSI may facilitate earlier recognition of high-risk patients, improve triage decisions, optimize ICU utilization, and enhance clinical management, particularly in resource-limited healthcare settings.

CONCLUSION

The present study demonstrated that the neutrophil-to-lymphocyte ratio (NLR), C-reactive protein (CRP), and lactate dehydrogenase (LDH) were significantly associated with the severity of community-acquired pneumonia. All three biomarkers increased progressively with increasing disease severity and showed significant positive correlations with both the CURB-65 score and Pneumonia Severity Index. Elevated biomarker levels were also associated with intensive care unit admission, in-hospital mortality, and independently predicted severe disease.

Among the evaluated biomarkers, CRP demonstrated the highest diagnostic accuracy, while NLR emerged as the strongest independent predictor of severe community-acquired pneumonia. These biomarkers are inexpensive, rapidly available, and routinely measured laboratory parameters that can effectively complement established clinical severity scoring systems.

Incorporating NLR, CRP, and LDH into the initial assessment of patients with community-acquired pneumonia may facilitate early identification of high-risk patients, improve clinical risk stratification, support timely therapeutic interventions, and optimize resource utilization, particularly in resource-limited healthcare settings. Larger multicentric prospective studies are warranted to validate these findings and establish standardized biomarker cut-off values for routine clinical practice.

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