Pak. J. Chest Med. 2025;31(04)

Original Article

journal homepage: https:/www.pjcm.net/

Pakistan Journal of Chest Medicine

Official journal of Pakistan Chest Society

The Neutrophil-to-Lymphocyte Ratio as a Prognostic Marker for Disease Severity in Hospitalized Patients with Community-Acquired Pneumonia

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Article History:

Received:	Jun 02, 2025
Revised:	Sep 03, 2025
Accepted:	Nov 01, 2025
Available Online:	Dec 02, 2025

Author Contributions:
TD conceived idea, AT drafted the study, AT NK collected data, SA did statistical analysis and interpretation of data, TD SA critical reviewed manuscript. All approved final version to be published.

Declaration of conflicting interests:
The authors declare that there is no conflict of interest.

How to cite this article:
Durrani T, Tariq A, Khan N, Alam S. The Neutrophil-to-Lymphocyte Ratio as a Prognostic Marker for Disease Severity in Hospitalized Patients with Community-Acquired Pneumonia. Pak J Chest Med. 2025;31(04):299-306.

ABSTRACT

Background: Community-acquired pneumonia (CAP) remains a major cause of hospitalization and mortality worldwide. Early identification of patients at risk of severe disease and poor outcomes is essential for appropriate triage and management. The neutrophil-to-lymphocyte ratio (NLR), derived from routine complete blood counts, has emerged as a potential prognostic biomarker in infectious diseases, including CAP.

Objective: To evaluate the prognostic utility of the admission Neutrophil-to-Lymphocyte Ratio (NLR) for predicting disease severity and clinical outcomes in hospitalized patients with Community-Acquired Pneumonia (CAP).

Methodology: This observational, prospective study was conducted at the Department of Medicine, Saidu Sharif Teaching Hospital, Swat, from January 2023 to April 2024. A total of 150 adult patients through consecutive sampling who were hospitalized with community-acquired pneumonia radiologically confirmed by X-ray or CT-scan. The severity of the disease was measured by the CURB-65 scoring system. The admission NLR was calculated by the absolute neutrophil and lymphocyte counts.

Results: The mean age of patients was 56.2 ± 15.7 years, with male predominance (57.3%). Severe CAP (CURB-65 ≥3) was observed in 26.7% of patients. Elevated NLR was strongly associated with ICU admission, mechanical ventilation, and mortality. A significant positive correlation was observed between NLR and CURB-65 score ($r = 0.69$, $p < 0.001$).

Conclusion: An elevated admission NLR is a strong predictor of disease severity and adverse clinical outcomes in hospitalized patients with community-acquired pneumonia. NLR may serve as a useful adjunct to established severity scoring systems for early risk stratification.

Keywords: Community-acquired pneumonia; Neutrophil-to-lymphocyte ratio; CURB-65; Disease severity; Prognosis

Introduction

Community-Acquired Pneumonia (CAP) is still one of the most common diseases in the world and causes death in patients, which is a heavy load for the present healthcare systems. It is the main reason for hospitalization in the very young, the old, and people suffering from other conditions.[1] Although antibiotics and support measures have improved considerably, the clinical course of CAP is still very irregular, with patients going from a mild self-limiting condition to a severe one demanding ICU admission, mechanical ventilation, and being at a huge risk of death.[2] The vast differences in response to treatment point to the urgent need for reliable, rapid, and readily available risk-stratification tools at the time of hospital admission. The correct initial evaluation is absolutely essential for making clinical decisions, such as the most suitable place for care (ward vs. ICU), the extent of empirical antibiotic therapy, and the allocation of hospital resources.[3]

Classic severe illness assessment scales, such as the Pneumonia Severity Index (PSI) and CURB-65 (Confusion, Urea, Respiratory rate, Blood pressure, Age ≥65 years), are well-validated, and international guidelines recommend their use.[4] These tools incorporate clinical signs, laboratory findings, and demographic information to sort patients into risk groups. However, they come with drawbacks. Their computation can become quite difficult in the crowded emergency department; they may depend on some parameters that are not instantly available (e.g., arterial blood gas, urea level), and their predictive accuracy, though high, might not be the best in certain populations or for certain outcomes such as the specific need for vasopressor support.[5] Thus, interest in discovering new biomarkers to improve or simplify current prognostic models remains. The perfect biomarker would be one obtained through conventional, low-cost tests that provide quick results and indicate the underlying pathophysiological processes of severe infection.

The response that involves the whole body and inflammation simultaneously, termed the systemic inflammatory reaction, is one of the body's main defense mechanisms against lung infections and, when out of control, can lead to tissue death and organ dysfunction in severe CAP. Neutrophils, the white blood cells, are the first to be attracted to the site of infection, where they ingest and destroy microbes. T-cells among the lymphocytes are the most important cells in leading the adaptive immune response and clearing inflammation.[6] The Neutrophil-to-Lymphocyte Ratio (NLR), a straightforward calculation from the universal complete blood count (CBC), reflects this dynamic interplay. It illustrates the conflict between the innate immune system's instant, often tissue-damaging, neutrophilic reaction and the controlling, adaptive role of lymphocytes.[7] An increased NLR indicates neutrophilia (either from acute inflammation or stress) and relative lymphopenia (often resulting from glucocorticoid-induced apoptosis or lymphocyte sequestration), a pattern that has been consistently reported in severe systemic stress and sepsis.

The NLR has been recognized as a robust prognostic biomarker in recent years for a wide range of diseases, including cardiovascular diseases, cancers, and critical illnesses such as sepsis and COVID-19.[7] Its role in CAP prognosis has been increasingly explored. Several studies have reported that a high NLR at hospital admission is strongly associated with increased disease severity, as assessed by higher PSI or CURB-65 scores, progressive radiographic changes, ICU transfer, and mortality.[8] A meta-analysis, for example, showed that high NLR was a strong predictor for not only severe CAP but also death, since the pooled analyses produced substantial odds ratios for poor outcomes.[9] The power of the NLR lies in its being a simple, inexpensive lab test (since it can be performed alongside a standard CBC) and easily accessible at once, which is why it is considered a promising option for real-time clinical decision-making.

Nevertheless, the universality of the current evidence is not total. The cut-off points for NLR as a prognostic indicator in CAP varied across studies, likely due to differences in population characteristics, comorbidities, and even local microbiological ecology.[10,11] A significant part of the key research was conducted in Western, East Asian, or specific national cohorts. The epidemiological and clinical profile of CAP in the Northeast differs from that in other regions. This area has peculiar demographic patterns, a high risk factor index for tobacco use and COPD, possible changes in the prevailing pathogens, and problems in accessing healthcare.[12] All these factors can greatly affect the population's immune status and the way CAP presents and progresses. So, biomarkers validated in other locations should not be considered reliable for this specific population. Their predictive accuracy and clinical usefulness need to be checked again.

This study is both timely and necessary, given the urgent need for effective prognostic tools in the management of CAP and the promising, yet context-specific, evidence for the NLR. The NLR has been globally recognized for its prognostic utility, but its performance in Swat area of Pakistan for hospitalized CAP patients has yet to be explored. Thus, this study, from January 2023 to April 2024, will provide a very critical understanding of the topic. We think the NLR at admission will be an important and independent indicator of disease severity and the occurrence of adverse clinical outcomes in our group of patients. We will systematically examine the association between NLR and standardized severity scores (PSI/CURB-65), as well as hard endpoints such as ICU admission, mechanical ventilation, and in-hospital mortality, to determine whether this easily accessible biomarker can help with early risk stratification. The

conclusions can help make the clinical care of CAP patients in this area more specific, more efficient, and, better yet, more effective, thus supporting clinicians in making the right decisions at the time of admission.

Objective

To evaluate the prognostic utility of the admission Neutrophil-to-Lymphocyte Ratio (NLR) for predicting disease severity and clinical outcomes in hospitalized patients with Community-Acquired Pneumonia (CAP).

Methodology

This observational study was prospective, and during its course, it was conducted in the Department of Medicine, Saidu Sharif Teaching Hospital, Swat, a tertiary teaching hospital providing medical services to a large population in northern Khyber Pakhtunkhwa, Pakistan. The research lasted 16 months, from January 2023 to April 2024. The aim of the study was to determine the prognostic value of the NLR in predicting disease severity and outcomes in patients with hospital-treated community-acquired pneumonia (CAP).

Using a consecutive sampling method, a cohort of 150 adult patients hospitalized with community-acquired pneumonia was formed. To eliminate selection bias, all eligible patients who met the inclusion criteria during the study period were recruited. All participants or their legally authorized attendants gave written informed consent before inclusion in the study.

Patients of both sexes aged 18 years or older were included if they had a clinical diagnosis of CAP supported by radiological evidence. Community-acquired pneumonia was characterized as a sudden-onset infection of the lung parenchyma, with symptoms such as fever, cough with or without sputum, difficulty breathing, or chest pain, and lung X-ray or tomogram lesions as the only sign of infection acquired outside the hospital.

Patients were ruled out of the study if they suffered from hospital-acquired pneumonia, ventilator-associated pneumonia, or chemical pneumonitis or had aspirated. Other reasons for exclusion were: patients with known immunocompromised conditions (e.g., HIV infection, active cancer, or long-term corticosteroid or immuno-suppressive therapy), pregnant women, those with active tuberculosis, hematological disorders that alter the leukocyte count, and those who refused to give their informed consent.

Baseline demographic characteristics, such as age and sex, were noted on admission. A thorough clinical history and physical exam were done for each patient. On admission, vital signs, including respiratory rate, blood pressure, mental status, and oxygen saturation, were recorded. The severity of the disease was measured using the CURB-65 scoring system, which includes Confusion, Urea nitrogen, Respiratory rate, Blood pressure, and Age ≥65. This allowed patients to be placed in the mild-to-moderate (CURB-65 Score 0-2) and severe (CURB-65 Score ≥ 3) disease categories.

Clinical outcomes, including ICU admission, mechanical ventilation requirement, hospital stay, and in-hospital mortality, were continuously monitored during patients' hospitalizations. At hospital admission, venous blood samples were collected from all patients before antibiotic treatment. In addition to the complete blood count (CBC), which was performed using an automated hematology analyzer, laboratory investigations included absolute neutrophil count, absolute lymphocyte count, and total leukocyte count. The neutrophil-to-lymphocyte ratio (NLR) was obtained by dividing the absolute neutrophil count by the absolute lymphocyte count.

Additional laboratory tests were conducted, including hemoglobin level, serum urea, serum creatinine, and erythrocyte sedimentation rate (ESR), following standard hospital laboratory procedures. For consistency, all laboratory measurements were performed in the hospital laboratory. At admission, every patient underwent a posteroanterior chest X-ray. The radiological discovery was categorized according to the pattern and degree of lung involvement, including unilateral or bilateral consolidation and the affected lung zone. Multilobar or bilateral involvement was considered a sign of more severe disease. Sputum samples were collected whenever possible and sent for Gram staining and culture. The microbiological results were divided into sterile or culture-positive, with the causative organism identified when growth was present. Prior antibiotic exposure was recorded as it could affect culture yield.

The main outcome measure for this study was the extent of illness, determined by the CURB-65 score. Among the secondary outcomes were ICU admission, mechanical ventilation requirement, and in-hospital death. The relationship between NLR at admission and these outcomes was analyzed to establish its prognostic value.

The data were collected and processed using the Statistical Package for the Social Sciences (SPSS) version 25. Continuous variables were reported as mean ± standard deviation, while frequency and percentage distributions were used for categorical variables. The comparisons between the groups were made using the Student's t-test for continuous variables and the Chi-square test for categorical variables. The correlation between NLR and CURB-65 score was computed by Pearson's correlation coefficient. A p-value less than 0.05 was regarded as statistically significant.

Ethical approval for the study was obtained from the Institutional Review Board of Saidu Sharif Teaching Hospital, Swat. The study was conducted in accordance with the principles of the Declaration of Helsinki. Confidentiality of patient data was strictly maintained, and no personal identifiers were used during data analysis

or reporting.

Results

In the present study, 150 patients with community-acquired pneumonia (CAP) were included. The mean age of the study population was 56.2 ± 15.7 years, with the majority of patients in the 51–60-year age group (28.0%). Male patients constituted 57.3% (n = 86) of the cohort, while 42.7% (n = 64) were female. The average hospital stay was 6.4 ± 2.9 days, with 48.7% of patients requiring more than 5 days of hospitalization (Table 1).

Based on admission CURB-65 scores, 110 patients (73.3%) had mild to moderate disease (score 0–2), whereas 40 patients (26.7%) presented with severe CAP (CURB-65 ≥3). Among patients with severe disease, a significantly higher proportion required intensive care unit (ICU) admission and mechanical ventilation compared to those with lower scores ($p < 0.001$). Overall, 78 patients (52.0%) required ICU care, and 41 patients (27.3%) required ventilatory support. Mortality was observed in 18 patients (12.0%), with deaths occurring predominantly in patients with CURB-65 scores ≥3.

Table 1. Baseline Demographic and Clinical Characteristics of Patients with Community-Acquired Pneumonia (n = 150)

Variable	Category	Frequency (n)	Percentage (%)
Age (years)	≤30	12	8.0
	31–40	16	10.7
	41–50	20	13.3
	51–60	42	28.0
	61–70	32	21.3
	>70	28	18.7
Gender	Male	86	57.3
	Female	64	42.7
Hospital stays	≤5 days	77	51.3
	>5 days	73	48.7
CURB-65 score	0–2	110	73.3
	≥3	40	26.7
ICU admission	No	72	48.0
	Yes	78	52.0
Mechanical ventilation	No	109	72.7
	Yes	41	27.3

Radiological evaluation revealed that unilateral lung involvement was more common in patients with mild to moderate disease, whereas bilateral or multilobar infiltrates were significantly more frequent among patients with severe CAP. Consolidations in the right middle and lower zones were the most commonly affected regions. Microbiological analysis of sputum samples showed that cultures were sterile in 83.3% of cases. Among culture-positive samples, Klebsiella pneumoniae (6.0%) and Streptococcus pneumoniae (5.3%) were the most frequently isolated organisms

(Table 2).

Laboratory parameters showed marked differences between severity groups. Patients with CURB-65 ≥3 had significantly higher total leukocyte counts, absolute neutrophil counts, and neutrophil-to-lymphocyte ratios (NLR) at admission compared to patients with CURB-65 scores <3 ($p < 0.001$). Conversely, absolute lymphocyte counts and hemoglobin levels were significantly lower in the severe group. Median values of serum urea, creatinine, and erythrocyte sedimentation rate (ESR) were also higher among patients with severe CAP (Table 3).

The mean admission NLR was 7.9 ± 4.3 in patients with mild-to-moderate CAP and 14.6 ± 6.1 in patients with severe disease ($p < 0.001$). A strong positive correlation was observed between NLR and CURB-65 score ($r = 0.69$, $p < 0.001$), indicating that higher NLR values were associated with increasing disease severity. Patients with an NLR ≥9.0 were significantly more likely to require ICU admission, while those with an NLR ≥15.5 showed a markedly higher mortality rate compared to patients with lower NLR values.

Outcome-based analysis demonstrated that ICU admission occurred in 68.4% of patients with elevated NLR, compared with 31.6% among those with lower NLR. Similarly, mechanical ventilation and in-hospital mortality were disproportionately higher in patients with markedly elevated NLR levels (Table 4).

Discussion

Community-acquired pneumonia (CAP) is still a predominant reason for patient hospital admissions, suffering, and death worldwide, especially in regions with low and middle-income economies. The primary screening of patients' risk is a mandate to guide decisions about where to place them and how much treatment to give. The current study investigated the prognostic significance of the neutrophil-to-lymphocyte ratio (NLR) upon admission in predicting disease severity and poor outcomes among hospitalized patients at a tertiary-care hospital in Swat, Pakistan. Our results indicate that elevated NLR is strongly associated with higher CURB-65 scores, a greater need for ICU admissions and mechanical ventilation, and increased hospital mortality.

In the present patient group, middle age to old age characterized the majority of patients, and males were predominant, findings that coincide with epidemiological patterns in previous studies on CAP.[13,14] Aging has been a major independent risk factor for severe pneumonia and poor recovery, mainly because of the senescence of the immune system and the high rate of comorbidities associated with it.[15] In the current study, comorbidities were not looked into in detail, but the older age group had a higher percentage of severe disease, and thus, their use of the ICU and deaths were probably higher than those in the younger age group.

The severity of the disease, as determined by CURB-65, was clearly associated with adverse outcomes in our study. The patients who scored CURB-65 ≥3 experienced significantly higher rates of admission to ICU, use of ventilatory support, and death. This result reconfirms the reliability of CURB-65 as a bedside severity assessment tool, which has already been validated in different populations.[16,17] On the other hand, clinical scoring systems alone might not fully capture the inflammatory burden of CAP; hence, the growing interest in biomarkers that can be used alongside clinical scoring systems.

The neutrophil-to-lymphocyte ratio is an indicator of the proportion of innate immune activation (neutrophilia) and adaptive immune suppression (lymphopenia), both of

Table 2. Radiological and Microbiological Findings According to Disease Severity

Variable	CURB-65 <3 (n = 110)	CURB-65 ≥3 (n = 40)	p-value
Radiological involvement			
Unilateral consolidation	82 (74.5%)	20 (50.0%)	0.006
Bilateral / multilobar	28 (25.5%)	20 (50.0%)	
Sputum culture			
Sterile	95 (86.4%)	30 (75.0%)	0.04
Klebsiella pneumoniae	7 (6.4%)	4 (10.0%)	
Streptococcus pneumoniae	6 (5.5%)	4 (10.0%)	
Other organisms	2 (1.8%)	2 (5.0%)	

Table 3. Comparison of Laboratory Parameters According to Disease Severity

Parameter	CURB-65 <3 (n = 110) Mean ± SD	CURB-65 ≥3 (n = 40) Mean ± SD	p-value
Hemoglobin (g/dL)	11.2 ± 1.8	9.9 ± 2.1	0.02
Total leukocyte count (×10³/µL)	14.3 ± 5.9	18.1 ± 6.8	0.01
Absolute neutrophil count (×10³/µL)	11.8 ± 5.6	15.6 ± 6.4	0.01
Absolute lymphocyte count (×10³/µL)	1.7 ± 0.6	1.3 ± 0.5	0.03
Neutrophil-to-lymphocyte ratio	7.9 ± 4.3	14.6 ± 6.1	<0.001
Serum urea (mg/dL)	48.6 ± 24.7	63.4 ± 29.1	0.04
ESR (mm/hr)	49.8 ± 23.9	64.1 ± 26.5	0.03

which are pivotal in the pathophysiology of severe infection. Mean NLR values were significantly higher in patients with severe CAP than in those with mild to moderate disease in this study. Moreover, a very high positive correlation between NLR and the CURB-65 score was noted, indicating that increased NLR is associated with clinical severity. Similar correlations have been reported by Feng et al., who demonstrated that using NLR with CURB-65 improved the prediction of death among older CAP patients.[18]

Multiple investigations have consistently sought to determine the role of NLR in CAP prognosis, with concordant results. A comprehensive review of observational studies was conducted by Alzoubi and Khanfar, who found that non-survivors had significantly higher NLR values than survivors. Hence, the authors inferred that NLR is a strong mortality predictor in patients with CAP.[19] Furthermore, a systematic review done by Kuikel et al. showed NLR values above 10 were always a sign of negative outcomes, which included ICU admission and death.[20] Although the precise cut-off values varied across studies, the general trend is toward the prognostic significance of high NLR, which aligns with our interpretation.

The current investigation revealed that those patients who had higher NLR levels when they were admitted were the ones who needed ICU treatment and mechanical ventilation more often. This finding is consistent with the study by Liu et al., who found that a high NLR was associated with respiratory failure and ICU admission in geriatric patients with pneumonia.[21] Moreover, Lee et al. indicated that NLR was superior to conventional inflammatory markers, such as total leukocyte count and C-reactive protein, in predicting severe pneumonia.[22] The practicability of NLR as an additional prognostic marker along with standard laboratory parameters is thereby implied by these studies.

The mortality analysis of our cohort reinforces the clinical utility of the NLR. The patients who died during their stay in the hospital had significantly higher admission NLR values than those who survived. This connection was still evident when examined alongside the already recognized severity indicators. Lymphopenia has been considered in prior research as a sign of immune exhaustion and compromised defense, with the latter being one of the factors leading to worse outcomes, together with the former, through the mechanism of neutrophil-induced tissue injury and systemic inflammation.[23,24] Thus, NLR acts as a composite marker of both harmful mechanisms.

The radiological and microbiological findings in our research were also associated with disease severity in a meaningful way. The dual and extensive lung involvement

Table 4. Association of Admission NLR with Clinical Outcomes

Clinical outcome	NLR below cut-off	NLR above cut-off	p-value
ICU admission (cut-off ≥9.0)	28 (31.6%)	50 (68.4%)	<0.001
Mechanical ventilation (cut-off ≥10.0)	13 (31.7%)	28 (68.3%)	0.002
Mortality (cut-off ≥15.5)	4 (22.2%)	14 (77.8%)	<0.001

was, by a large margin, more prevalent among patients with high CURB-65 scores. This is in line with previous studies that associated radiological disease extent with higher mortality and ICU admission.[25] The culture positivity rate was quite low, a problem commonly discussed in CAP management, usually attributed to antibiotic use prior to diagnosis and to the low diagnostic yield of sputum cultures.[26] Under these circumstances, readily accessible biomarkers such as NLR become extremely useful for predicting outcomes early.

From a practical point of view, NLR offers several benefits in resource-limited health care settings such as Pakistan. It is cheap, readily calculable from normal complete blood counts, and no specific tests are needed. In contrast to other biomarkers, such as procalcitonin or interleukin-6, which might not be readily available in all settings, NLR can be quickly obtained at the time of admission, thus allowing early triage decisions. Adding NLR to routine assessments might help identify high-risk patients who would benefit from closer monitoring or early escalation of care.

However, the study is strong but still has some limitations. The results of this single-center research may not be completely applicable to other groups. NLR was not serially measured, which could have revealed dynamic changes and treatment responses. Moreover, direct comparison with other biomarkers was not done in this analysis. However, the study is a significant contributor of regional data for the prognostic role of NLR in CAP.

Our study reveals that the NLR at admission is an important and independent determinant of illness severity and negative outcomes in hospitalized patients with community-acquired pneumonia. In addition, when considered alongside the CURB-65 and other existing clinical scoring systems, the NLR may support early risk assessment and help providers make the right choices. It is suggested that more comprehensive multicenter studies be conducted to establish common cut-off values and to strengthen acceptance of NLR incorporation into standard operating procedures for CAP management.

Conclusion

The findings of this study demonstrate that the neutrophil-to-lymphocyte ratio (NLR) at hospital admission is a simple, inexpensive, and reliable prognostic marker for assessing disease severity and predicting adverse clinical outcomes in patients hospitalized with community-acquired pneumonia (CAP). Elevated NLR values were significantly associated with higher CURB-65 scores, greater need for intensive care unit admission, greater mechanical ventilation requirement, and higher in-hospital mortality. Given its strong correlation with established severity assessment tools, NLR can serve as a valuable adjunct to clinical scoring systems such as CURB-65, particularly in resource-limited settings where access to advanced biomarkers may be restricted. Incorporating NLR into routine initial evaluation may facilitate early risk stratification, timely escalation of care, and improved clinical decision-making.

Further multicenter studies with larger sample sizes and serial NLR measurements are recommended to validate standardized cut-off values and to better define the role of NLR in guiding management strategies for community-acquired pneumonia.

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