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Diagnostic Accuracy of Elevated Neutrophil: Lymphocyte Ratio (NLR) and Platelet: Lymphocyte Ratio (PLR) for the Prediction of 28-Day Mortality in Patients Presenting with Acute Exacerbation of COPD at Tertiary Care Hospital, Karachi

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ABSTRACT

Chronic obstructive pulmonary disease (COPD) patients experiencing sudden flare-ups and immediate risk of death, and basic inflammatory indicators may assist in early risk assessment. **Objectives:** To assess the diagnostic performance of elevated neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio in predicting 28-day mortality among patients presenting with acute exacerbations of chronic obstructive pulmonary disease. **Methods:** The study was a prospective observational cohort study conducted at the Ojha Institute of Chest Diseases, Karachi (June 2025 to November 2025), following ethical approval. 88 AECOPD patients aged 20-70 years were recruited through consecutive sampling. Complete blood counts were used to calculate baseline NLR and PLR, which had predetermined cutoffs (>6.74 and >203.6). Mortality within 28 days was tracked among patients. Data analysis was done using SPSS version 25.0. Sensitivity, specificity, and ROC curves, along with multivariate logistic regression with confounder adjustments, were used to assess prognostic performance. **Results:** Among 88 AECOPD patients, the mean age was 61.16 ± 9.89 years, and 26 (29.5%) died within 28 days. Elevated NLR (84.1%) and PLR (78.4%) were common. The sensitivity of NLR was higher (80.77%), whereas its specificity (14.52%) and prognostic value (AUC 0.58) were lower, and the performance of PLR was poorer (AUC 0.52). Subgroup analysis indicated a better performance among older patients. In general, both biomarkers showed less than optimal prognostic value for 28-day mortality, with NLR being slightly better than PLR. **Conclusions:** While increased NLR and PLR were typical findings in acute COPD exacerbations, they showed poor diagnostic utility for forecasting 28-day mortality.

INTRODUCTION

Chronic obstructive lung disease (COPD) is the most common condition of health outcomes and fatality rates across the globe and is a progressive airflow limitation with frequent acute exacerbations. There exists a high mortality rate in acute exacerbations of COPD (AECOPD), especially in the initial 28 days of hospital-based care, and thus, there is a necessity to identify early and reliable prognostic indicators to inform clinical management [1]. Although treatment progress has been made, determining outcomes in AECOPD is difficult, particularly in limited healthcare environments. Systemic inflammation is a central component of AECOPD pathophysiology and leads to the further course of the disease, dysfunction of organs, and death. In this regard, inflammatory biomarkers based on routine complete blood counts have received attention because they are simple, available, and cost-effective. As part of inflammatory biomarkers, NLR and PLR have been suggested as useful predictors in acute COPD exacerbations [2]. There is an indication that patients who have high neutrophil-to-lymphocyte ratio (NLR) and

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platelet-to-lymphocyte ratio (PLR) are more likely to die in-hospital and early post-admission, which indicates that they may be used as cheap prognostic biomarkers in acute exacerbation of COPD [3]. There is evidence to indicate that the hematological ratios continue to be prognostic even in critically ill patients. NLR and PLR above normal have both been shown to predict ICU mortality risk in affected individuals during AECOPD and should therefore be used in severe cases of the disease [4]. Extensive database studies have also supported the role of inflammatory markers in disease severity and outcome prediction, such as NLR, in predicting in-hospital death in patients with AECOPD who have acute respiratory failure complications [5]. Additionally, Evidence synthesized from a previous study demonstrated that elevated NLR correlates strongly with all-cause mortality among patients with COPD, which justifies its usefulness as a strong prognostic biomarker [6]. This body of evidence has been extended by recent prospective cohort studies that have shown that inflammatory and nutritional markers such as NLR remain independently related to death from any cause in hypercapnic respiratory failure COPD patients [7]. Moreover, high NLR has been aligned with higher inflammatory load, represented by higher levels of C-reactive proteins in cases of acute exacerbation [8]. Moreover, the prognostic significance of a platelet-to-lymphocyte ratio (PLR) is supported by evidence showing that an elevated platelet-to-lymphocyte ratio (PLR) correlates with 90-day mortality in patients with acute exacerbation of COPD, which further supports its prognostic importance. [9]. The relevance of high levels of inflammatory biomarkers in poor clinical outcomes in AECOPD is further supported by studies based on long-term observation [10].

Even though there is growing evidence that inflammatory biomarkers like neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are linked to disease severity and mortality during acute exacerbation of COPD (AECOPD), the majority of existing studies have been retrospective, used heterogeneous populations, or assessed only short-term Furthermore, there are only a few studies by local populations which examine their independent prognostic performance based on standardized cut-off values and multivariate adjustment to predict short-term mortality. Regardless of the accumulating evidence of global data, local information assessing the diagnostic power of NLR and PLR as clarifying indicators of 28-day mortality in patients who present with AECOPD in Pakistan is insufficient. This study aimed to assess the diagnostic performance of NLR and PLR in predicting 28-day mortality in patients with acute exacerbation of COPD at a tertiary care center in Karachi. These easily obtainable biomarkers can be easily established as prognostic to enable the risk stratification of individuals during an early stage and to enable better clinical decision-making in a resource-constrained environment.

METHODS

It was a prospective observational cohort trial that was to be carried out at the Ojha Institute of Chest Diseases, Karachi, for six months (June 2025 to November 2025) following the approval of the research synopsis. The Institutional Review Board of Dow University of Health Sciences (IRB-3805/DUHS/Approval/2025/213; dated 29th May 2025) provided ethical approval. All participants were informed to sign informed consent before enrolment. The participants were informed of the purpose and procedures of the study, possible risks and benefits, and their confidentiality was assured, and they were even given the right to discontinue participation at any time without it impacting their medical care. Non-probability consecutive sampling was used to sample patients who presented with acute exacerbation of chronic obstructive pulmonary disease (AECOPD). Both male and female patients aged 20-70 years who met the operational definition of AECOPD were included. Acute exacerbation was considered a known case of COPD with acute (less than 14 days) worsening of respiratory symptoms, which included increased dyspnea, cough, or production of sputum, and at least two clinical characteristics: tachypnea, tachycardia, fever, hypoxemia, respiratory acidosis, or supportive radiographic evidence. Patients with predispositions to influence inflammatory markers were eliminated, such as vasculitis, connective tissue disorders, seropositive or seronegative arthritis, pregnancy, tuberculosis, asthma, pneumonia, idiopathic pulmonary fibrosis, lung carcinoma, or malignancies. The sample size was computed using a previously reported sensitivity (82.54%) and specificity (71.38%) of the neutrophil-to-lymphocyte ratio (NLR) to predict 28-day mortality under the assumption that the prevalence is 9, the confidence level is 95, and the margin of error is 10 to get the required sample size of 88 patients. Nevertheless, the mortality of the study group was more than expected, and this could affect the accuracy and extrapolation of the estimates. Baseline demographic information, such as gender and age, was taken at the time of admission. Complete blood count was taken, and NLR and platelet-to-lymphocyte ratio (PLR) were determined. NLR above 6.74 and PLR above 203.6 were taken as high, based on earlier defined thresholds. The patients were monitored over 28 days since the time of admission, and deaths within the 28 days were noted.

SPSS version 25.0 was used to perform statistical analysis. Mean + SD or median + interquartile range were used to represent continuous variables based on the distribution

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of data, which were evaluated by the Kolmogorov-Smirnov test. Frequencies and percentages were used to show categorical variables. The predictive ability of elevated NLR and PLR as prognostic factors to predict 28-day mortality was first assessed using 2 x 2 contingency tables, and sensitivity, specificity, positive predictive value, and negative predictive value were calculated. The analysis of the Receiver Operating Characteristic (ROC) curves was carried out to evaluate the accuracy of prediction, and the area under the curve (AUC) was determined. The Youden Index was used to find the optimal cutoff values. To determine the independent relation between elevated NLR and PLR and 28-day mortality, multivariable logistic regression analysis was performed that adjusted the results for the possible confounders such as age, gender, severity of exacerbation, and comorbidities. Adjusted odds ratios, as well as confidence intervals of 95 percent, were provided.

RESULTS

The study included 88 patients who had an acute exacerbation of chronic obstructive pulmonary disease (AECOPD). The study gives a summary of the baseline demographic and clinical characteristics of the study population. The average age of the participants was 61.16/9.89 years, and the majority of the participants were males (84.1%). The acute exacerbation period in the median was 10.00 days (IQR: 9.00). The majority of patients were jobless (88.6%), and earned less than 75,000 PKR per month per family (92.0%). The neutrophil-to-lymphocyte ratio (NLR) was 9.00 (IQR: 3.00), and the platelet-to-lymphocyte ratio (PLR) had a mean value of 300.71 ± 188.14. The patients had a high NLR (>6.74) and high PLR (>203.6) in 84.1% and 78.4% of cases, respectively. After a total of 28 days, the mortality rate was 29.5% (Table 1).

Table 1: Demographic and Clinical Characteristics of the Study Population (n=88)

Variables	Mean ± SD / n (%)
Age (Years)	61.16 ± 9.89
Gender	
Male	74 (84.1%)
Female	14 (15.9%)
Duration of Acute Exacerbation	
Duration (Days)	10.00 (9.00)*
Occupational Status	
Employed	10 (11.4%)
Unemployed	78 (88.6%)
Family Monthly Income	
>75,000 PKR	7 (8.0%)
≤75,000 PKR	81 (92.0%)
Others	
Neutrophil-to-Lymphocyte Ratio	9.00 (3.00)*
Platelet-to-Lymphocyte Ratio	300.71 ± 188.14
Elevated NLR	74 (84.1%)
Elevated PLR	69 (78.4%)
28-Day Mortality	26 (29.5%)

*Continuous variables expressed as median (IQR) or mean ± SD; categorical variables as n (%)

The diagnostic performance of elevated neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) to predict 28-day mortality was assessed using 2 × 2 contingency tables. Elevated NLR had a high sensitivity (80.77%) but low specificity (14.52%) with a positive predictive value (PPV) of 28.38% and a negative predictive value (NPV) of 64.29%. NLR was less sensitive (65.38%) and also lacked specificity (16.13%). Both ratios had low diagnostic accuracy (Table 2).

Table 2: Prognostic Performance of Elevated NLR and PLR for Prediction of 28-Day Mortality (n=88)

Biomarkers	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Diagnostic Accuracy (%)
Elevated NLR	80.77	14.52	28.38	64.29	34.09
Elevated PLR	65.38	16.13	24.64	52.63	30.68

This study used Receiver Operating Characteristic (ROC) curve analysis to evaluate the predictive ability of NLR and PLR for 28-day mortality. The NLR had moderate predictive performance with a larger area under the curve (AUC) than PLR (Table 3).

Table 3: ROC Curve Analysis of NLR and PLR for Prediction of 28-Day Mortality

Biomarkers	AUC (95% CI)	Optimal Cutoff	Sensitivity (%)	Specificity (%)
NLR	0.58 (0.45–0.70)	>6.74	80.77	14.52
PLR	0.52 (0.39–0.65)	>203.6	65.38	16.13

Post-stratification analysis of elevated NLR was done to examine its diagnostic capabilities in various subgroups. The sensitivity was higher in males (82.61%) than in females (66.67%), and the specificity was low in each group. The diagnostic accuracy of patients with age ≥65 years was higher (44.74%) than in younger patients. In all stratified variables, high NLR sensitivity and low specificity were observed (Table 4).

Table 4: Post-Stratification Diagnostic Performance of Elevated NLR for 28-Day Mortality (n=88)

Stratification Variables	Category	Sensitivity (%)	Specificity (%)	Diagnostic Accuracy (%)
Gender	Male	82.61	17.65	37.84
	Female	66.67	0.00	14.29
Age (years)	<65	76.92	8.11	26.00
	≥65	84.62	24.00	44.74
Duration of Exacerbation	<10 Days	75.00	9.09	32.35
	≥10 Days	85.71	17.50	35.19

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Monthly Income	≤75,000	78.26	15.52	33.33
	>75,000	100.00	0.00	42.86
Occupational Status	Employed	100.00	14.29	40.00
	Unemployed	78.26	14.55	33.33

DISCUSSION

The paper compared NLR and PLR as predictors of 28-day mortality in patients with AECOPD. The ratios of inflammation were frequently elevated, and their diagnostic ability varied across subgroups of patients. According to Fu *et al.* systemic inflammatory indices, including NLR, PLR, and others, tend to be elevated in AECOPD, which implies the heightened degree of inflammatory processes [11]. It aligns with the current research, where a high percentage of patients were identified with high NLR (84.1%) and PLR (78.4%). Yu *et al.* developed a risk prediction model of in-hospital mortality in AECOPD and discovered that inflammatory markers were potential [12], but not independent, predictors of mortality, which is consistent with the low overall diagnostic quality of NLR and PLR in this study. The GOLD 2023 report also indicates that the change of systemic inflammatory response during exacerbations depends upon the severity of the disease and the peculiarities of the patient [13], which is consistent with the heterogeneous diagnostic performance, which is present in stratified patient groups in the current study. Liu *et al.* found that use of NLR along with other clinical measures enhanced the prognostic capacity in critically ill COPD patients, suggesting that the use of NLR individually has poor predictive capacity [14]. Similarly, Fayiad and Amer demonstrated that values of NLR and PLR predictors yield varying results [15], which are in line with the sensitivity, specificity, and the variation in the predictive value in the present study. The same authors noted that the predictor of higher mortality in this study is higher NLR, not just in the short term as reported by Liu *et al.* [16], but also in this study, higher NLR is a relatively high sensitivity but low specificity predictor of 28-day mortality. In COPD, El-Gazzar *et al.* have concluded that the discriminatory ability of poor outcome of NLR and PLR is weak, which is parallel to the low values of diagnostic accuracy in this analysis [17]. Paliogiannis et al. concluded that even though NLR in COPD is always higher, it varies in prognostic value, and the heterogeneity of the results among stratified subgroups has the same consistency [18]. Ye *et al.* found that in their study, the NLR prognostic value is dependent on the severity of disease and clinical outcomes, and in line with the fluctuation in age and length of exacerbation [19]. The baseline considerations and comorbidities mentioned by Sørensen et al. influence the relationship between NLR and mortality, which is in line with the differences in the stratified outcomes of the diagnostic findings in the study [20]. Overall, these findings indicate that high values of NLR and PLR can be expected in AECOPD, but they do not have a high degree of diagnostic utility in terms of the 28-day mortality, and they require patient-specific factors and heterogeneity of the disease.

The present study has several limitations due to its single-center design and relatively small sample size (n = 88), which can influence the extent of generalizability. It is also observational, and its causal inference is not possible; the possible confounders (comorbidities and severity of infection) had not been completely controlled. Baseline NLR and PLR have also been evaluated only and not serially, and other inflammatory (e.g., CRP, procalcitonin) and long-term outcomes beyond 28 days were not evaluated, which limited a more comprehensive assessment of prognostic value. To enhance the external validity, future studies must use larger and multicenter cohorts. Serial biomarker measurements and other inflammatory and clinical parameters would be valuable to increase the prognostic models. Integration of NLR and PLR with the existing clinical scoring systems can enhance risk stratification, and follow-up studies should be conducted over a long period to enhance risk evaluation, including readmission and prolonged mortality.

CONCLUSIONS

The present study showed that the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are both common in patients with acute exacerbation of COPD and indicate an increase in the systemic inflammatory response. Nonetheless, both biomarkers exhibited poor prognostic performance as they were associated with 28-day mortality, but are less specific and have a moderate overall predictive ability, with NLR being marginally better than PLR. In general, NLR and PLR can be used as simple and inexpensive indicators of inflammation in AECOPD, but not as independent prognostic factors. They are probably more useful in combination with other clinical parameters and known risk assessment models.

Authors' Contribution

Conceptualization: AA
Methodology: AA, FA, NS, RN
Formal analysis: AA, RN, MA
Writing and Drafting: AA, NS, KS, MA
Review and Editing: AA, FA, NS, RN, KS, MA

All authors approved the final manuscript and take responsibility for the integrity of the work

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Conflicts of Interest

All the authors declare no conflict of interest.

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