

## NEUTROPHIL-LYMPHOCYTE AND PLATELET-LYMPHOCYTE RATIOS AS MARKERS OF SEVERITY IN ACUTE COPD EXACERBATIONS—A STUDY FROM A TERTIARY CARE TEACHING CENTER

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### Abstract

**Background:** Chronic obstructive pulmonary disease (COPD) is considered one of the most significant public health problems, affecting over 200 million individuals and ranking among the leading causes of death worldwide. The neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) are simple and easily obtainable markers derived from a complete blood count, even in peripheral hospitals. This study evaluated the association between rising NLR and PLR levels and the severity of acute COPD exacerbations. **Materials and Methods:** A cross-sectional study was conducted from January 2020 to June 2021. A total of 106 cases of acute exacerbation of COPD were admitted. Patient history was recorded, and clinical examinations were performed. NLR and PLR ratios were assessed, and their association with age groups and COPD severity was analyzed. **Result:** The mean age of the study population was 68.6 years (SD = 9.25). The distribution of COPD severity classes was as follows: Class I (51.87%), Class II (20.75%), Class III (22.64%), and Class IV (4.71%). PLR showed a statistically significant association with age group ( $p = 0.001$ ), whereas NLR did not ( $p = 0.216$ ). Both NLR and PLR were significantly associated with COPD severity ( $p = 0.001$ ). **Conclusion:** NLR and PLR are simple, accessible markers that rise with COPD exacerbation severity, indicating worse prognosis and survival. Identifying high-risk patients using these biomarkers enables timely intervention and rehabilitation, reducing morbidity and mortality while improving quality of life.

## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a significant global health concern, characterized by persistent respiratory symptoms and airflow limitation.<sup>[1]</sup> Acute exacerbations, marked by worsened dyspnea and increased sputum, are critical events in COPD progression, an inflammatory response leading to pulmonary tissue destruction. Clinically, this manifests as chronic bronchitis and emphysema, potentially culminating in respiratory failure.<sup>[2]</sup>

Recent research has explored novel inflammatory biomarkers, such as the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR), as indicators of systemic inflammation in COPD. These easily accessible laboratory biomarkers reflect innate and acquired immune responses,

which are crucial in systemic inflammatory responses to infection.<sup>[3-5]</sup>

This study aims to categorize patients with acute COPD exacerbations by severity, measure NLR and PLR, and assess the association of these ratios with exacerbation severity, providing insights into their potential as clinical markers.

## MATERIALS AND METHODS

This cross-sectional study was conducted at Justice K.S. Hegde Charitable Hospital, a tertiary care teaching center in Mangalore, India, between January 2020 and June 2021. The study aimed to assess the association of neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) with the severity of acute exacerbations of chronic obstructive pulmonary disease (COPD).

A total of 106 patients, aged 35 years and above, diagnosed with COPD and admitted with an acute exacerbation, were included. Patients with chronic infections or chronic systemic rheumatological diseases were excluded. Following informed consent, participants underwent detailed clinical examination, complete blood count (CBC), platelet count, and spirometry to determine the severity of COPD exacerbation, which was categorized into mild, moderate, severe, and very severe based on post-bronchodilator FEV1 values according to GOLD criteria.<sup>[6]</sup>

Heparinized blood samples were collected at admission to calculate NLR (neutrophil count divided by lymphocyte count) and PLR (platelet count divided by absolute lymphocyte count). The primary outcomes measured were the number of ventilator days, hospital stay duration, and the need for antibiotics, reflecting the severity of the exacerbation. Statistical analysis was performed using Epi info version 7 to determine the association

between NLR and PLR values and the categorized severity of COPD exacerbations.

## RESULTS

The study population's demographic and clinical profiles are detailed in [Table 1A and 1B]. The mean age of participants was 68.6 years (SD = 9.25). The study included 59 males (55.67%) and 47 females (44.33%). COPD class distribution was as follows: Class I (51.87%), Class II (20.75%), Class III (22.64%), and Class IV (4.71%). Other hematological and pulmonary function test results are depicted [Table 1A and 1B].

[Table 2] shows the association of various parameters with age group. PLR showed statistically significant association with age group (p=0.001), while NLR did not (p=0.216). COPD class also showed statistically significant association with age group (p=0.03).

**Table 1A: Demographic and Clinical Profiles of the study subjects**

Variables	Mean (SD)
Age in years	68.6 (9.25)
Neutrophil count	82.12 (12.57)
Lymphocyte count	15.70 (11.70)
ALC	2029 (3823)
Platelet count	280571.69 (279987.87)
NLR	10.3 (10.1)
PLR	267.5 (335.1)
FVC	2.27 (0.53)
FEV1	1.55 (0.466)
FEV1/FVC	65.70 (16.75)

SD: Standard deviation, N: Numbers, ALC: Absolute Lymphocyte Count, NLR: Neutrophil Lymphocyte Ratio, PLR: Platelet Lymphocyte Ratio FVC: Forced Vital Capacity, FEV: Forced Expiratory Volume

**Table 1B: Demographic and Clinical Profiles of the study subjects**

Sex	N (%)
Male	59 (55.67)
Female	47 (44.33)
COPD class	
I	55 (51.87)
II	22 (20.75)
III	24 (22.64)
IV	5 (4.71)
Age group	
41-50	3(2.83)
51-60	19(17.92)
61-70	34(32.07)
71-80	42(39.62)
81-90	8(7.56)

N-Number; COPD-Chronic Obstructive Pulmonary Disease

**Table 2: Association of various parameters with age group**

Variable	Age group					p-value
	41-50	51-60	61-70	71-80	81-90	
NLR ; Mean(SD)	7.2(10.23)	183.41(130.15)	274.28(389.58)	332.31(379.35)	159.83(91.97)	0.216
PLR ;Mean (SD)	104.6(125.97)	8.82(7.34)	8.73(7.20)	12.78(12.84)	8.93(9.92)	0.001
COPD Class						0.03
Mild; N (%)	2(3.64)	9(16.37)	15(27.27)	24(43.64)	5(9.09)	
Moderate; N (%)	0	5(22.73)	11(50)	4(18.18)	2(9.09)	
Severe; N (%)	1(4.17)	5(20.83)	8(33.33)	10(41.67)	0	
Very severe; N (%)	0	0	0	4(80)	1(20)	

SD: Standard deviation, NLR: Neutrophil Lymphocyte Ratio, PLR: Platelet Lymphocyte Ratio

**Table 3: Association of severity of COPD with NLR and PLR**

Variable	Severity of COPD				p-value
	Mild	Moderate	Severe	Very severe	
NLR; Mean(SD)	3.98(3.15)	9.1(2.15)	19.44(5.37)	41.7(8.85)	0.001
PLR; Mean(SD)	172.19(208.46)	276.35(462.23)	438.32(373.67)	458(300.61)	0.001

SD: Standard deviation, NLR: Neutrophil Lymphocyte Ratio, PLR: Platelet Lymphocyte Ratio

[Table 3] shows the association of severity of COPD with NLR and PLR. NLR and PLR were significantly associated with the severity of COPD ( $p=0.001$ ). The mean NLR values for Mild, Moderate, Severe, and Very severe COPD were 3.98, 9.1, 19.44, and 41.7, respectively. The mean PLR values for Mild, Moderate, Severe, and Very severe COPD were 172.19, 276.35, 438.32, and 458, respectively.

## DISCUSSION

The majority of the study population consisted of males, as reported by McKay AJ et al. This trend likely reflects the lasting impact of higher smoking rates among men, combined with potential genetic predispositions and socio-environmental factors such as age, socioeconomic status, and pollution exposure.<sup>[1,2]</sup> Notably, our cohort exhibited a higher prevalence of COPD in the 71–80 age group, with a smaller yet significant proportion in the 81–90 age range, deviating slightly from global COPD demographics.<sup>[1]</sup>

Consistent with findings from other researchers, including a study on Asian COPD patients that linked increased NLR to reduced FEV<sub>1</sub>, our results demonstrated a statistically significant rise in NLR with increasing COPD severity. This aligns with prior studies establishing NLR as a reliable marker of systemic inflammation and exacerbation risk in COPD.<sup>[3,4]</sup> Physiologically, elevated NLR reflects an imbalance characterized by neutrophilia and relative lymphopenia.<sup>[4]</sup> Increased neutrophils drive cytokine release, contributing to lung tissue damage and impaired function. Given NLR's established role as a biomarker in various diseases, our findings further support its utility as a simple and efficient tool for assessing COPD exacerbation severity and predicting respiratory hospitalizations.<sup>[5,6]</sup> Additionally, our study observed a statistically significant increase in PLR with worsening COPD severity, mirroring trends seen in coronary artery disease and malignancies, where PLR has demonstrated prognostic value.<sup>[5]</sup> Maclay et al. have reported increased platelet activation in COPD, and our data support the notion that PLR may serve as a valuable biomarker for identifying high-risk COPD patients, particularly those with severe airway obstruction.<sup>[7]</sup> The observed increase in PLR with disease severity suggests that, like NLR, PLR reflects the heightened systemic inflammatory response associated with worsening COPD. Therefore, our results indicate that both NLR and PLR are valuable biomarkers for assessing the severity of COPD exacerbations.<sup>[8-10]</sup>

The current study, along with previous research, reinforces the notion that NLR and PLR are elevated in COPD patients and correlate with disease severity and exacerbations.<sup>[8-12]</sup> These biomarkers, derived from routine blood tests, provide a convenient and accessible tool for assessing systemic inflammation in COPD. Our findings align with prior studies, demonstrating that NLR and PLR levels are significantly higher in COPD patients and increase further during acute exacerbations.

## CONCLUSION

In conclusion, this study confirms that NLR and PLR are elevated in stable COPD and increase further during exacerbations, indicating their potential as markers of disease severity. Further research is needed to understand their role in COPD management better.

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