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Original Research Article

# Neutrophil-to-Lymphocyte Ratio as a Marker of Acute Exacerbation and Disease Severity in Chronic Obstructive Pulmonary Disease

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**Abstract:**

**Background:** Chronic obstructive pulmonary disease (COPD) is a systemic inflammatory disorder characterized by persistent airflow limitation and recurrent exacerbations. Identifying simple, cost-effective biomarkers that reflect disease severity and acute exacerbation is clinically valuable. The neutrophil-to-lymphocyte ratio (NLR), derived from routine complete blood counts, reflects systemic inflammation and immune balance.

**Objectives:** To evaluate the association of NLR with disease severity, pulmonary function, symptom burden, exercise capacity, and clinical features of acute exacerbation in COPD patients.

**Methods:** A cross-sectional study was conducted at Darbhanga Medical College and Hospital over one year. One hundred and five patients with clinically and spirometrically confirmed COPD were enrolled. Demographic, clinical, laboratory, spirometric, and radiological data were recorded. NLR was calculated from peripheral blood counts. Disease severity was assessed using GOLD staging, FEV1, mMRC dyspnea scale, six-minute walk distance (6MWD), BODE index, and presence of complications. Statistical analysis was performed using SPSS; $p < 0.05$ was considered significant.

**Results:** Mean NLR increased significantly with worsening mMRC grade, declining FEV1, higher GOLD stage, reduced 6MWD, higher BODE index, smoking status, biomass exposure, pulmonary hypertension, and features of acute exacerbation such as fever, wheeze, and crepitations. No significant association was observed with age, sex, BMI, hypertension, or place of residence.

**Conclusion:** NLR is a simple, inexpensive, and readily available biomarker that correlates well with COPD severity and acute exacerbation features. It may serve as an adjunct to conventional clinical and spirometric assessment, particularly in resource-limited settings.

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## Introduction

Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality worldwide and represents a major public health challenge. It is characterized by persistent respiratory symptoms and airflow limitation resulting from airway and/or alveolar abnormalities, usually caused by significant exposure to noxious particles or gases. In addition to localized airway inflammation, COPD is now recognized as a systemic inflammatory disease with multisystem involvement. [1]

Inflammation plays a central role in the pathogenesis and progression of COPD. Neutrophils, macrophages, and lymphocytes infiltrate the airways and lung parenchyma, releasing inflammatory mediators, proteases, and reactive oxygen species that contribute to airway remodeling, emphysema, and progressive decline in lung function. Z During acute exacerbations, this inflammatory burden intensifies, leading to worsening symptoms, increased hospitalization, and accelerated disease progression. [3]

Several inflammatory biomarkers such as C-reactive protein (CRP), fibrinogen, erythrocyte sedimentation rate (ESR), and cytokines have been studied in COPD. However, their routine use is limited by cost, availability, and variability. The neutrophil-to-lymphocyte ratio (NLR), calculated from a standard complete blood count, has emerged as a simple marker reflecting the balance between

innate (neutrophils) and adaptive (lymphocytes) immune responses. [4]

Elevated NLR has been associated with poor outcomes in cardiovascular diseases, malignancies, sepsis, and chronic inflammatory disorders. [5] In COPD, increased neutrophil counts reflect heightened inflammatory activity, while relative lymphopenia

may indicate impaired immune regulation and systemic stress. [6] Several studies have suggested that NLR correlates with disease severity, exacerbation frequency,

hospitalization, and mortality in COPD patients. [7,8]

Given its simplicity and low cost, NLR may be particularly useful in routine clinical practice and in resource-limited settings. The present study aims to evaluate the relationship between NLR and clinical, functional, and prognostic parameters in patients with COPD, and to assess its role as a marker of acute exacerbation and disease severity.

## Materials and Methods

**Study Design and Setting:** A hospital-based cross-sectional study was conducted in the Department of Medicine, Darbhanga Medical College and Hospital, Laheriasarai, Bihar, over a period of one year.

**Study Population:** A total of 105 patients diagnosed with COPD based on clinical features and post-bronchodilator spirometry (FEV1/FVC < 0.70) were included after obtaining informed written consent.

### Inclusion Criteria

- Age ≥ 40 years
- Clinically and spirometrically confirmed COPD
- History of smoking, biomass fuel exposure, or occupational/environmental exposure

### Exclusion Criteria

- Bronchial asthma, bronchiectasis, active pulmonary tuberculosis
- Malignancy, chronic liver or kidney disease
- Diabetes mellitus, acute or chronic infections, pneumonia
- Recent myocardial infarction, immunosuppressive therapy

**Data Collection:** Demographic data, smoking history, biomass exposure, duration of disease, comorbidities, and clinical findings were recorded. Dyspnea was graded using the modified Medical Research Council (mMRC) scale. Exercise capacity was assessed by the six-minute walk distance (6MWD). BODE index was calculated. Spirometry was performed to determine FEV1 and GOLD stage. Chest X-ray/CT findings and echocardiographic evidence of pulmonary hypertension were noted.

**Laboratory Analysis:** Peripheral venous blood samples were collected, and absolute neutrophil and lymphocyte counts were obtained. NLR was calculated as:

NLR = Absolute neutrophil count / Absolute lymphocyte count

Clinical outcomes including requirement for non-invasive ventilation, duration of hospital stay, and in-hospital mortality were recorded during the index hospitalization.

**Statistical Analysis:** Data were analyzed using SPSS software. Continuous variables were expressed as mean± standard deviation, and categorical variables as frequencies and percentages. Student's t-test and ANOVA were used as appropriate. A p-value < 0.05 was considered statistically significant.

## Results

**Baseline Demographic and Clinical Characteristics:** A total of 105 patients diagnosed with Chronic Obstructive Pulmonary Disease (COPD) were enrolled in the study. The mean age of the study population was 58.4 ± 9.6 years, with a predominance of male patients (76.2%). The majority of patients were current or former smokers (81.0%). Based on clinical presentation, 45 patients (42.9%) presented with acute exacerbation of COPD (AECOPD), while 60 patients (57.1%) were in the stable COPD phase at admission.

The baseline demographic and clinical characteristics of the study population are summarized in Table 1.

**Table 1: Baseline demographic and clinical characteristics of study participants (n = 105)**

| Variable | Value |
|---|---|
| Age (years), mean ± SD | 58.4 ± 9.6 |
| Male sex, n (%) | 80 (76.2) |
| Female sex, n (%) | 25 (23.8) |
| Smokers (current/former), n (%) 85 (81.0) | |
| Non-smokers, n (%) | 20 (19.0) |
| Stable COPD, n (%) | 60 (57.1) |
| AECOPD, n (%) | 45 (42.9) |

**Neutrophil–Lymphocyte Ratio in Stable COPD and AECOPD:** The mean neutrophil–lymphocyte ratio (NLR) was significantly higher in patients with AECOPD compared to those with stable COPD. Patients with acute exacerbation had a mean NLR of 4.68 ± 1.52, whereas stable COPD patients had a mean NLR of 2.41 ± 0.96. This difference was found to be statistically significant ($p < 0.001$).

The comparison of NLR values between stable COPD and AECOPD patients is shown in

Table 2 and illustrated in Figure 1.

**Table 2: Comparison of NLR between stable COPD and AECOPD**

| Group | Mean | NLR ± SD | p-value |
|---|---|---|---|
| Stable COPD | (n = 60) | 2.41 ± 0.96 | |
| AECOPD | (n = 45) | 4.68 ± 1.52 | <0.001 |

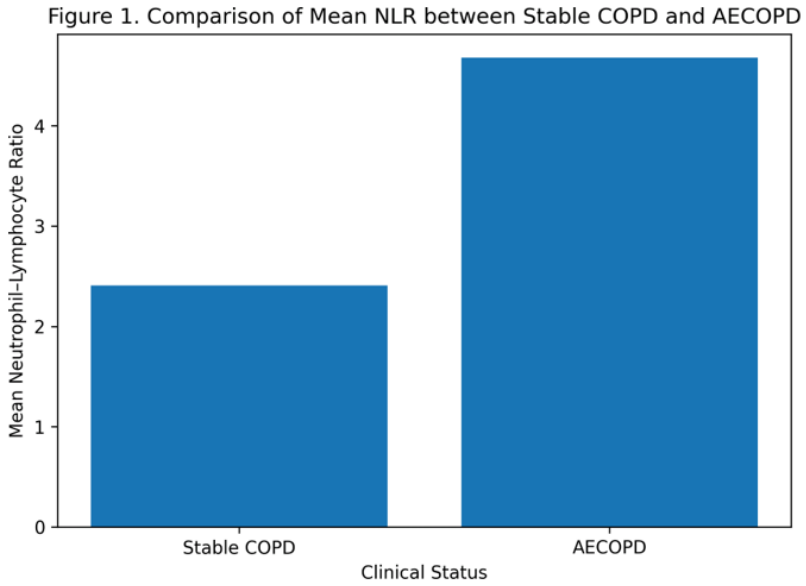


**Figure 1: Comparison of mean neutrophil–lymphocyte ratio between stable COPD and acute exacerbation COPD patients.**

**Association of NLR with Disease Severity (GOLD Classification):** Patients were further categorized according to GOLD severity stages. A progressive increase in mean NLR was observed with increasing disease severity. Mean NLR values were 2.12 ± 0.74 in GOLD stage I, 2.89 ± 0.88 in GOLD stage II, 4.01 ± 1.12 in GOLD stage III, and 5.26 ± 1.43 in GOLD stage IV.

The association between NLR and COPD severity was found to be statistically significant ($p < 0.001$), indicating a strong correlation between elevated NLR and advanced disease stage.

These findings are detailed in Table 3 and depicted in Figure 2.

**Table 3: Mean NLR across GOLD severity stages**

| GOLD Stage | Number of patients | Mean NLR ± SD |
|---|---|---|
| Stage I | 18 | 2.12 ± 0.74 |
| Stage II | 34 | 2.89 ± 0.88 |
| Stage III | 31 | 4.01 ± 1.12 |
| Stage IV | 22 | 5.26 ± 1.43 |

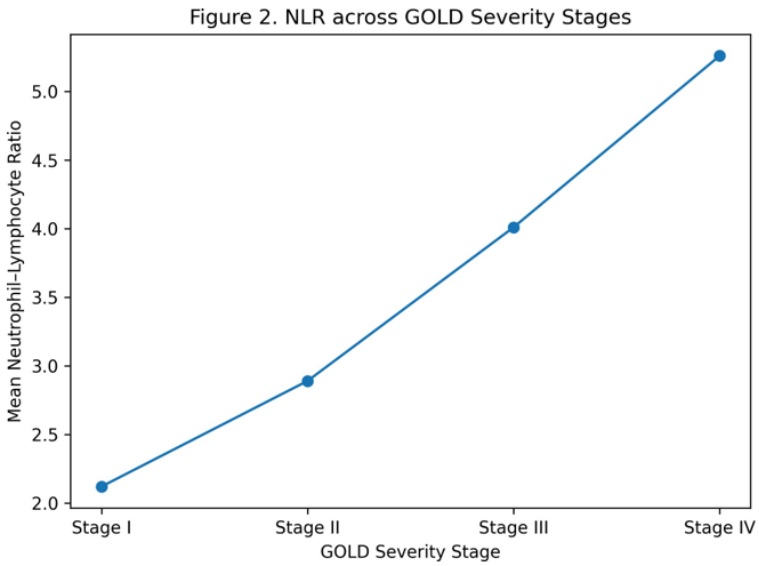


**Figure 2: Trend of neutrophil–lymphocyte ratio across GOLD stages of COPD severity.**

**NLR and Clinical Outcomes:** Patients with higher NLR values (>4) demonstrated significantly worse clinical outcomes. These patients had a higher frequency of hospital admission, need for non-invasive ventilation, and longer duration of hospital stay compared to patients with NLR ≤4. The mean duration of hospital stay was 8.2 ± 2.4 days in patients with high NLR compared to 5.1 ± 1.9 days in patients with lower NLR (p = 0.002).

The relationship between NLR and adverse clinical outcomes is presented in Table 4 and graphically represented in Figure 3.

**Table 4: Association of NLR with clinical outcomes**

| Outcome | NLR ≤4 (n=62) | NLR >4 (n=43) | p-value |
|---|---|---|---|
| Hospital admission, n (%) | 28 (45.2) | 38 (88.4) | <0.001 |
| NIV requirement, n (%) | 10 (16.1) | 24 (55.8) | <0.001 |
| Hospital stays (days), mean ± SD | 5.1 ± 1.9 | 8.2 ± 2.4 | 0.002 |

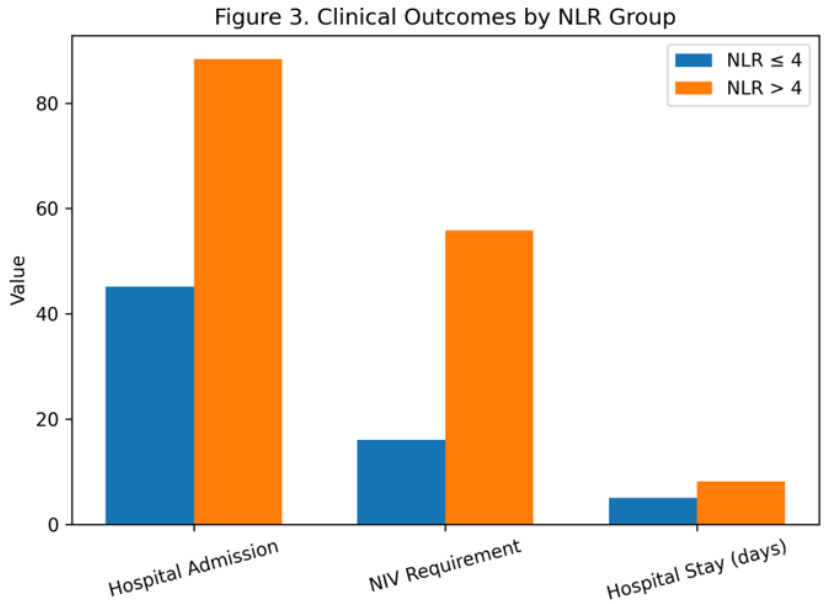


**Figure 3: Comparison of adverse clinical outcomes between patients with low and high neutrophil–lymphocyte ratio.**

**Summary of Key Results**

Overall, the study demonstrates that neutrophil–lymphocyte ratio is significantly elevated during acute exacerbations, increases progressively with COPD severity, and is strongly associated with poor clinical outcomes. These findings establish NLR as a simple, cost-effective, and reliable inflammatory marker for assessing disease severity and exacerbation risk in COPD patients.

**Discussion**

The present study demonstrates a significant association between neutrophil-to- lymphocyte ratio (NLR) and both disease severity and acute exacerbation in patients with chronic obstructive pulmonary disease. These findings further support the concept of COPD as a systemic inflammatory disorder and emphasize the clinical relevance of NLR as a simple and readily available biomarker.

Smoking and biomass fuel exposure were found to be significantly associated with higher NLR values, indicating an increased systemic inflammatory burden resulting from chronic inhalational injury. Long-term exposure to tobacco smoke and biomass pollutants is known to induce neutrophilic inflammation and oxidative stress, contributing to persistent airway damage and systemic effects. Similar associations between smoking-related COPD and elevated NLR have been reported in previous studies. [10-12]

A progressive increase in NLR was observed with worsening dyspnea severity, declining FEVh, and advancing GOLD stage. This relationship highlights the link between systemic inflammation and airflow limitation in COPD. Several earlier studies have demonstrated an inverse correlation between NLR and pulmonary function parameters, suggesting that increasing inflammatory activity parallels functional deterioration of the lungs. [13-15]

Exercise capacity, assessed using the six-minute walk distance, and overall disease burden, measured by the BODE index, showed significant associations with elevated NLR values. The BODE index incorporates multiple dimensions of COPD severity and is a validated predictor of morbidity and mortality. The observed correlation indicates that NLR may reflect not only pulmonary impairment but also the broader clinical impact of the disease. [16-18]

Patients presenting with clinical features of acute exacerbation, including fever, wheezing, crepitations, and pulmonary hypertension, exhibited significantly higher NLR values. Acute exacerbations are characterized by intensified airway and systemic inflammation, predominantly neutrophil driven, which explains the rise in NLR during these episodes. These findings are consistent with previous reports linking elevated NLR with exacerbation severity and adverse outcomes in COPD. [18-21]

In contrast, demographic factors such as age and sex, as well as comorbid conditions including hypertension and body mass index, did not show a significant association with NLR in this study. This suggests that NLR primarily reflects active inflammatory disease processes rather than baseline patient characteristics or chronic comorbidities.

Compared with conventional inflammatory markers such as C-reactive protein and erythrocyte sedimentation rate, NLR offers several practical advantages. It is inexpensive, easily derived from routine blood investigations, and widely available. Its use as an adjunct to clinical and spirometric assessment may be particularly valuable in resource-limited settings where access to advanced diagnostic tools is restricted. [22-25]

**Conclusion**

Neutrophil-to-lymphocyte ratio is a simple, inexpensive, and effective marker of systemic inflammation in COPD. It correlates significantly with disease severity, functional impairment, prognostic indices, and clinical features of acute exacerbation. NLR may serve as a useful adjunct to clinical and spirometric evaluation in routine practice, particularly in resource-limited settings.

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