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# A Study of Clinical Correlation with Inflammatory Markers in Patients of COPD with Acute Exacerbation

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**Abstract:** ***Introduction: The sudden worsening of COPD symptoms, such as shortness of breath, increased sputum volume and color, and systemic inflammation, is known as an acute exacerbation of chronic obstructive pulmonary disease (AECOPD), and it significantly lowers survival rates. Procalcitonin and high-sensitivity C-reactive protein (hsCRP) have been studied as predictive biomarkers in individuals with AECOPD. Two novel inflammatory markers, the neutrophil-to-lymphocyte ratio (NLR) and the platelet-to-lymphocyte ratio (PLR), are important predictors of outcome in AECOPD patients. Hospitalized AECOPD patients may benefit from the use of NLR and PLR, which are readily available, and affordable markers. Aim: Study of inflammatory markers in COPD and their correlation with clinical outcome. Methods: A prospective observational comparative study was conducted on 100 patients of COPD at the Department of General Medicine, Saraswathi Institute of Medical Sciences, Hapur, and all necessary investigations were done. Results: A total of 100 individuals with COPD were included; fifty of them were in a stable state (controls), while the remaining fifty patients were experiencing an acute exacerbation (cases). While PLR levels in patients and controls were similar with no discernible difference, mean levels of NLR, hsCRP, and procalcitonin in cases were considerably higher than in controls. Procalcitonin and hsCRP levels were favorably connected with the levels of these two inflammatory indicators, NLR and PLR. Of the fifty patients, 21 required mechanical ventilation, and 9 required inotropic assistance. Out of 50 patients, only 6 (12.00%) died . The length of hospital stay was significantly correlated with NLR and PLR levels. While PLR was significantly higher in patients who needed mechanical ventilation, NLR and PLR levels were not significantly correlated with either need for inotropic support or mortality. Neither was NLR significantly correlated with the requirement for mechanical ventilation. Conclusion: Compared to individuals with stable state COPD (controls), patients with AECOPD (cases) had higher levels of NLR. Therefore, NLR levels can be used as a marker to predict acute exacerbation, and procalcitonin and hsCRP levels were positively correlated with NLR and PLR levels.***

**Keywords:** COPD, NLR, PLR, Procalcitonin

## 1. Introduction

Chronic obstructive pulmonary disease is characterized by persistent airflow limitation which is progressive and associated with chronic inflammation in the airway and alveoli to noxious particles or gases.(1) COPD is among the four leading causes of death.(2)

Chronic obstructive pulmonary disease is a chronic inflammatory disease of the airway, primarily associated with smoke exposure. (3,4) Exposure to inhaled pollutants, mainly cigarette smoke is thought to cause chronic inflammation seen in COPD via the activation of structural and inflammatory cells within the lungs. These cells release chemotactic mediators which recruit more inflammatory cells into the lung parenchyma triggering a state of chronic inflammation, which causes structural changes in the airway, airway obstruction, and symptoms related to breathing. There are pieces of evidence that COPD is a systemic inflammatory disease, in which there is systemic inflammation and extra pulmonary manifestations are commonly present.

Systemic inflammation may also worsen comorbid diseases, such as coronary artery disease, cardiac failure, osteopenia and bone mineralization disorders, anemia, lung malignancies, depressed mood, and hyperglycemia.

Acute exacerbation of chronic obstructive pulmonary disease is a sudden deterioration of symptoms of COPD like shortness of breath, quantity andcolor of sputum, and increased systemic inflammation, and has a significant impact on survival. It may be triggered by an infection with bacteria or viruses or by environmental pollutants. (9)

Procalcitonin and hsCRP are two examples of biomarkers that have been studied as prognostic indicators in AECOPD patients. Two novel inflammatory indicators, NLR and PLR, play an important role in determining the prognosis of several illnesses, such as AECOPD, pneumonia, ischemic heart disease, and acute pulmonary embolism. NLR and PLR are easily accessible and affordable indicators that may be useful in hospitalized AECOPD patients' risk categorization, particularly in settings with limited resources. When comparing individuals with AECOPD to those with stable-state COPD, NLR and PLR are significantly greater, and NLR is more sensitive than PLR in predicting an acute exacerbation. (10)

## 2. Methods

This was a prospective observationalcomparative study in which we recruited100 patients with COPD, from the Departmentof General Medicine at Saraswathi Medical College, Hapur. Every patient was subjected todetailed history and clinical examination and relevant investigations including CBC, kidney function test, liver function test, hsCRP, procalcitonin, electrocardiogram, chest X-ray, and pulmonary function test. NLR, PLR, hsCRP, and procalcitonin levels were measured patients admitted with AECOPD within24 hours of admission and in patients with astable state on an outpatient basis.

**Inclusion Criteria**

- Patients of COPD diagnosed on the basis of GOLD guidelines.
- Adult >40 years of age, both male and female.

**Exclusion Criteria**

- Patients with bronchiectasis, pulmonary tuberculosis, and bronchial asthma.
- Myocardial infarction or stroke in the last 3 months.
- Malignancies.
- Patients with a history of treatments withsteroids in the last 3 months.
- All the patients of AECOPD admitted to the hospital were followed up for the clinical outcome, which was assessed by duration of hospitalization, need for mechanical ventilation, need for ionotropic support and mortality.

**Statistical Analysis**

The presentation of the categoricalvariables was done in the form of numberand percentage. On the contrary, the quantitative data were presented as means ±standard deviation (SD) and as median with 25th and 75th percentiles (interquartilerange). The data entry was done in the Microsoft Excel spreadsheet and the final analysis was done with the help of SPSS software.

## 3. Results and Observations

Of the one hundred patients, fifty were in a stable state while the other fifty were experiencing an acute exacerbation. Based on statistical analysis, there was no significant difference seen in the age and sex distribution between the cases and controls.

A significant difference was seen between anthropometric parameters weight (kg), height, and body mass index (BMI), whichwere considerably higher in the controlgroup as compared to patients with acute exacerbation and spirometry parameters FEV1(%), FVC (%), FEV1/FVC were also considerably higher in controls than cases.

In our research, there was no discernible difference in the mean levels of PLR between cases and controls, but mean levels of NLR, hsCRP (mg/L), and procalcitonin (ng/mL) were significantly greater in patients than in controls.

In our study, mean levels of NLR and PLRwere positively correlated with hsCRP (mg/L) and with procalcitonin (ng/mL); however, this correlation was statistically not significant,

A non-significant positive correlation was seen between the duration of hospitalization (days) and NLR whereas PLR was significantly correlated with the duration of hospitalization.

Comparing patients who required mechanical ventilation to those who did not, the mean level of PLR in the former group was noticeably higher. In addition, patients requiring mechanical ventilation had a mean level of NLR that was higher than that of patients not requiring it, while the difference was not statistically significant. While the difference was statistically not significant, the mean levels of NLR and PLR were higher in patients who required inotropic support or died than in patients who did not or who survived.

In our study, we observed that the value ofAUC for ROC of NLR was higher as compared toPLR but lower than procalcitonin and hsCRP to anticipate acute exacerbation in a patient withCOPD. Procalcitonin (ng/mL) had the highestdiscriminatory power to anticipate acuteexacerbation in patients with COPD followed by hsCRP and NLR and the discriminatorypower of PLR is non-significant.

| VARIABLES | hsCRP | PROCALCITONIN |
|---|---|---|
| NLR | | |
| Correlation coefficient | 0.047 | 0.187 |
| p- value | 0.745 | 0.193 |
| PLR | | |
| Correlation coefficient | 0.201 | 0.097 |
| p- value | 0.162 | 0.500 |

| VARIABLES | NLR | PLR |
|---|---|---|
| Duration of stay | | |
| Correlation coefficient | 0.254 | 0.377 |
| p- value | 0.076 | 0.007 |

## 4. Discussion

In our study, 50 patientseither male or female of COPD admitted with acute exacerbation, and 50 cases of age>40 years, either male or female of stable COPD were included in the study.

The mean age (years) in caseswas 60.1 ± 9.23 and in controls was 57.34± 8.74 with no significant difference between them on statistical analysis and the distribution of gender was also comparable between cases and controls.

The mean levels of weight (kg), height(cm), and BMI (kg/m²) in controls wereconsiderably higher as compared to cases.Mean levels of FEV1 (%), FVC (%), and FEV1/FVC in controls were considerably higher as compared to cases.

In our study, the mean value of NLR was significantly higher in cases than in controls whereas no remarkable difference was seen in PLR between cases and controls. The mean of hsCRP and procalcitonin in cases was significantly higher as compared to controls with a positive correlation between NLR and PLR and hsCRP and procalcitonin; however it was statistically not significant. We assessed clinical outcome by four parameters: duration of stay, need for mechanical ventilation, need of inotropes and moratlity. There was no association between NLR and the need of mechanical ventilation, need for inotropes and mortality. We also noticed that the value of AUC for ROC to predict acute exacerbation in patients was highest for procalcitonin followed by hsCRP, NLR, and least for PLR. So, procalcitonin had the highest power to predict AECOPD.

## 5. Limitations of Study

Due to the small number of COPD cases in our study, the study's statistical power was low. The severity of COPD was not taken into account in our study as we did not compare

different stages of the disease. We included stable-state COPD patients as controls rather than healthy individuals. The relationships between NLR and PLR and other inflammatory markers such as tumor necrosis factor-alpha, interleukin 6, and erythrocyte sedimentation rate were not studied.

## 6. Conclusion

Thus we concluded that the levels of NLRwere raised in patients with AECOPD than instable-state COPD patients. So levels of NLR can be used as a marker of acute exacerbation.Levels of NLR and PLR positively correlated with hsCRP and procalcitonin levels. Procalcitonin had the highest discriminatorypower to predict AECOPD followed by hsCRP, NLR, and PLR. Levels of both of these inflammatory markers (NLR and PLR) were positively correlated with the duration of hospitalization in patients with AECOPD. Levels of NLR and PLR were not significantly associated with the need for inotropic supportand mortality, levels of NLR were also not significantly associated with the need formechanical ventilation whereas levels of PLR were significantly higher in patients who required mechanical ventilation

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