Original Article

To Compare Neutrophil Lymphocyte Ratio with Other Parameters in Acute Exacerbation of COPD and Stable COPD: A Hospital Based Study

Kailash Sharma[1], Gajendra Singh[2], Ummed Singh[3]

[1]Medical Officer, Department of Pulmonary Medicine, Government Medical College, Bharatpur, Rajasthan, India, [2]Senior Resident, Department of Medicine, Government Medical College, Bharatpur, Rajasthan, India, [3]Assistant Professor, Department of Medicine, Government Medical College, Bharatpur, Rajasthan, India.

Abstract

Background: White blood cell (WBC) count and its subtypes are also well known systemic inflammatory markers. The ratio of neutrophils to lymphocytes (NLR), which is calculated from complete blood count with differential, is an inexpensive widely available marker of inflammation. The aim of this study to compared the neutrophil lymphocyte ratio with other parameters in acute exacerbation of COPD and stable COPD. **Subjects and Methods:** A Hospital based comparative study done on 50 Patients with COPD (stable/ exacerbation) attending at Government Medical College, Bharatpur, Rajasthan. While the upper limit of neutrophils count for normal range was set at 8x109/l, the lower limit of lymphocyte count for the normal range was set at 0.9x109/l. NLR was calculated as the ratio of neutrophils to lymphocytes, both of which were obtained from the same automated blood samples for the study. **Results:** Our study showed that the comparison of mean value of age, BMI & pack years was statistically significant (P=0.0112, P<0.0001 & P=0.0141 respectively) in between groups. The comparison of mean value of NLR was statistical significant (P=0.0009) in between groups. NLR measurement demonstrated a sensitivity and specificity of 40%and 77.14%. PPV and NPV for NLR were 63.64%and 56.25%, and OR and RR were 2.250 and 1.455. A positive correlation was determined between NLR and CRP (r=0.482; p<0.05).**Conclusion:** NLR, like CRP, both readily available and simple parameters, could also be used as a cost-effective marker of inflammation in AECOPD.

Keywords: AECOPD, Stable COPD, NLR.

Corresponding Author: Dr. Gajendra Singh, Senior Resident, Department of Medicine, Government Medical College, Bharatpur, Rajasthan, India.

Introduction

Chronic obstructive pulmonary disease (COPD) is a heterogeneous disease, made up of a number of different syndromes which are defined as COPD through spirometry testing. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lung to noxious particles or gases".[1] This definition encompasses a wide variety of diseases, ranging from chronic bronchitis to emphysema.[2]

AECOPD is defined as the deterioration in clinical picture with increased dyspnoea, a decrease in daily performance, an increase in sputum production, increased cough, and high fever. Many studies show that there is an obvious increase in inflammation in airways during exacerbations among COPD patients who are generally categorized as mild, moderate and severe.[3,4] The more severe the attack, the more is the inflammation present. If we consider an infection as the underlying COPD attack, we often base it on C-reactive protein (CRP) level in daily practice. Generally, the more severe the attack is, the higher is the level of CRP present in the haemogram.[5]

White blood cell (WBC) count and its subtypes are also well known systemic inflammatory markers. The ratio of neutrophils to lymphocytes (NLR), which is calculated from complete blood count with differential, is an inexpensive widely available marker of inflammation. The availability of the NLR has been demonstrated in the risk stratification of patients with various cardiovascular diseases, many kinds of solid tumors, sepsis, and infectious conditions.[6-8]Gunay et al. reported that NLR values were significantly higher in patients with COPD than in age- and sex-matched healthy control subjects, and these values increased further during acute COPD exacerbations as compared with periods of stability.[9]

As infection, either bacterial or viral, is the main cause leading to clinical AECOPD, CRP is the common marker to show the existence of infection in patients with COPD. The aim of this study to compared the neutrophil lymphocyte ratio with other parameters in acute exacerbation of COPD and stable COPD.

Subjects and Methods

A Hospital based comparative study done on 50 Patients with COPD (stable/ exacerbation) attending at Government

Medical College, Bharatpur, Rajasthan.

Inclusion Criteria

- COPD patients (acc to GOLD-2017 criteria) when clinically stable at least for 3 months.
- Primary diagnosis of AECOPD, defined as an acute worsening of respiratory symptoms such as dyspnea, cough, or sputum purulence severe enough to warrant hospital admission.
- Patient's giving written consent.

Exclusion Criteria

- Any subjects who could not perform spirometry or who had been treated with systemic steroids within the previous 8 weeks.
- Patients with any respiratory disease mimicking COPD such as bronchiectasis, asthma, and tuberculosis destroyed lung.
- Myocardial infarction or cerebral infarction within the previous 3 month.
- Pregnant women.
- Hepatitis, thyroid diseases, autoimmune diseases, or any acute infection.
- Receiving systemic corticosteroids, antibiotics, or immunosuppressive treatment.

Methods

- All the patients who were enrolled prospectively from outpatient and emergency units according to Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2019 criteria; forced expiratory volume in 1 second (FEV1)/ forced vital capacity (FVC)<0.7. GOLD divides patients into four subgroups as A, B, C, and D (ABCD).10 Patients were considered to have AECOPD if they met Anthonisen's criteria.11 Patients with AECOPD were categorized according to the nature of expectoration either with mucoid or purulent sputum.
- All the patients to be subjected for the demographic details of the patients like age, sex, height, weight were collected and BMI was calculated. Risk factors of all the patients like smoking, diabetes, allergies etc. were noted.
- Clinical examination including blood pressure, chest x rays.
- Routine blood tests for CBC including differential counts of leukocytes, such as neutrophils and lymphocytes, C-reactive protein (CRP).

Procedure

For complete blood count (CBC), peripheral venous blood samples were obtained by using EDTA-containing blood collector tubes, and CBC assays were performed by fully-automated device.

To define NLR, CBC with automated differential counts, including neutrophils and lymphocytes, were made on admission. While the upper limit of neutrophils count for normal range was set at 8x109/l, the lower limit of lymphocyte count for the normal range was set at 0.9x109/l. NLR was calculated as the ratio of neutrophils to lymphocytes, both of which were obtained from the same automated blood samples for the study.

Statistical Analysis

All statistical analyses were performed using SPSS 16. Descriptive analyses were performed for all variables.

Results

Our study showed that the comparison of mean value of age, BMI & pack years was statistically significant (P=0.0112, P<0.0001 & P=0.0141 respectively) in between groups [Table 1]. The comparison of mean value of NLR was statistical significant (P=0.0009) in between groups [Table 2].

Mean NLR levels were significantly higher in AECOPD group compared to patients with stable COPD (p=0.0009). NLR measurement demonstrated a sensitivity and specificity of 40% and 77.14%. PPV and NPV for NLR were 63.64% and 56.25%, and OR and RR were 2.250 and 1.455. A positive correlation was determined between NLR and CRP (r=0.482; p<0.05) [Table 3].

Table 1: Comparison between Stable COPD & AECOPD regarding age

Parameters	Stable COPD (N=25)	AECOPD (N=25)	P-value
Age (yrs)	62.67±7.050	66.16±10.90	0.0112
BMI (kg/m2)	19.12±1.314	18.19±1.327	<0.0001
Smoking History (Pack years)	21.24±10.71	29.67±16.14	0.0141

Table 2: NLR in admitted patients with stable and exacerbated COPD.

Markers	Stable COPD (N=35)	AECOPD (N=35)	P-value
NLR	4.263±1.900	6.389±3.071	0.0009

Table 3: Statistical analysis of CRP, NLR & PLR

	Sensitivity	Specificity	PPV	NPV	Odd ratio	Relative ratio	P-value
NLR	40.0%	77.14%	63.64%	56.25%	2.250	1.455	<0.05

Discussion

AECOPD is among the most common diseases in clinical practice, especially in patients with infections. Inflammation encompasses a complex network of interactions involving various immune-related cells, including neutrophils and lymphocytes, which can lead to persistent respiratory tissue injury and damage.[12] It has been reported that the absolute counts of key immune-related cell populations in the peripheral blood, and their ratios, can adequately reflect chronic inflammatory conditions.[13]

ErcanKurtipek et al,[14] who reported that out of the 94 patients, 48(51%) had stable copd with a mean age of 66.65±10.17 years (range: 49-79 years), and 46(49%) patients having acute exacerbation with a mean age of 62.67±9.41 years (range: 48-92 years). Another study by RecaiErgün et al,[15] reported the mean age of the patients as 69.0±9.2 and 104 (78.2%) of patients were male, which was compatible with our results.

Our study showed that the mean value of BMI was 19.12±1.314 kg/m2 and patient with acute exacerbation a mean value of BMI was 18.19±1.327 kg/m2 comparison of mean was statistical significant (P<0.0001). The loss of weight is most likely multifactorial in origin. Established explanations for weight loss in COPD include increased basal metabolic rate due to the increased energy cost of breathing, as well as physical inactivity and malnutrition due to eating difficulties. Fletcher revealed that in susceptible smokers (comparable with the host factors),[16] tobacco smoking is strongly related to chronic bronchitis and airflow obstruction, and that these were two different diseases. Cigarette smoking is recognized as the cause of COPD in the vast majority of patients. Although not fully understood, it is widely accepted that an abnormal inflammatory response of the lungs to noxious particles and gases beyond the normal protective inflammatory response is involved in the development of COPD.

Mean NLR levels were significantly higher in AECOPD group compared to patients with stable COPD (p=0.0009). NLR measurement demonstrated a sensitivity and specificity of 40%and 77.14%. PPV and NPV for NLR were 63.64%and 56.25%, and OR and RR were 2.250 and 1.455.

LEE et al,[17] found NLR values were significantly higher in patients with COPD exacerbation when compared to those with stable disease and healthy controls (12.4±10.6, 2.4±0.7 and 1.4±0.5, respectively).

Three further studies, one prospective and two retrospective, were conducted in Turkey,[14,18,19] All these studies included patients with stable COPD and AECOPD, whereas healthy controls were only enrolled in the two retrospective studies by BILIR et al,[18] and IN et al.[19] These studies confirmed significantly higher NLR values in COPD patients when compared to healthy controls, whereas AECOPD patients had significantly higher NLR values when compared to patients with stable COPD.

XIONG et al,[20] observed ROC analysis (AUC 0.91) indicated that a NLR cut-off value of 3.3 predicted mortality with sensitivity of 85.8% and specificity of 89.7%. According to this cut-off point, COPD subjects were divided into a high NLR group and a low NLR group; exacerbations and mortality were significantly lower in the latter group.

Conclusion

NLR, like CRP, both readily available and simple parameters, could also be used as a cost-effective marker of inflammation in AECOPD.

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