

ORIGINAL RESEARCH

To study the correlation between the neutrophil-lymphocyte ratio (NLR) and COPD patients

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ABSTRACT

Aim: To examine the correlation between the neutrophil lymphocyte ratio (NLR) and patients diagnosed with chronic obstructive pulmonary disease (COPD). **Materials and methods:** A cohort of 100 patients with COPD was split into two groups, each consisting of 50 individuals. COPD group (n=50): This group consisted of individuals with stable COPD, meaning they had not had any major changes in symptoms and had not required any further treatment for the last three months. AECOPD group (n=50): This group consisted of 50 patients who had Acute Exacerbation of COPD (AECOPD), which is described as a sudden worsening of symptoms in individuals with COPD that need further treatment. Participants (n=50): Individuals who are in good health, have never smoked or been exposed to biomass, do not have any other medical conditions, and do not exhibit any clinical symptoms. Participants' blood samples were obtained and analyzed for total and differential leukocyte count, as well as absolute eosinophil and neutrophil counts. **Results:** The mean neutrophil-to-lymphocyte ratio (NLR) was substantially greater in the acute exacerbation of chronic obstructive pulmonary disease (AECOPD) group (4.21±0.11) compared to the stable COPD group (3.15±0.08). Nevertheless, there was no substantial disparity in the amounts of haemoglobin or the proportion of eosinophils between the two groups. ROC analysis shown that the Neutrophil-to-Lymphocyte Ratio (NLR) had a strong predictive value for exacerbations of Chronic Obstructive Pulmonary Disease (COPD). With a threshold of 3.56, the sensitivity, specificity, and Area Under Curve (AUC) were 76.45%, 71.78%, and 0.56, respectively. **Conclusion:** Regular and intense flare-ups of COPD have a negative impact on the patient's health and can contribute to the advancement of the illness and increased risk of death. Early identification and treatment of exacerbations may be facilitated by predicting them in advance. Recent research indicates that the Neutrophil-to-Lymphocyte Ratio (NLR) serves as an inflammatory biomarker that experiences a substantial increase during exacerbations of Chronic Obstructive Pulmonary Disease (COPD).

Keywords: COPD, Neutrophil-to-Lymphocyte Ratio, AECOPD

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a prevalent and highly consequential illness that poses a significant risk to human well-being. Typically, it is a gradual condition that is linked to an atypical inflammatory reaction in the lungs caused by harmful particles or gases[1]. The most recent epidemiological assessment of Chronic Obstructive Pulmonary Disease (COPD) in China reveals that the occurrence of COPD among Chinese individuals aged 40 and above has risen from 8.2% in 2008 to 13.7% in 2015[2]. COPD, being a systemic illness, may lead to many unfavorable effects outside the lungs. Muscle dysfunction is a prevalent symptom of COPD at a

systemic level. Muscle dysfunction in patients with COPD can be caused by several mechanisms, including abnormalities in deoxygenated type I muscle fibers and mitochondrial contents in the muscle system. There is also an imbalance of oxidative stress that promotes muscle protein degradation. Additionally, hypoxemia and hypercapnia impair the muscles' ability to use oxygen and affect the synthesis and breakdown of contractile proteins. The systemic inflammatory response in individuals with chronic obstructive pulmonary disease (COPD) is strongly linked to their ability to tolerate exercise. This response may trigger a range of reactions by activating transcription factors and the

mechanism of apoptosis[7,8]. This systemic adverse response significantly impacts the quality of life of patients with chronic obstructive pulmonary disease (COPD), as seen by a reduction in their capacity to exercise and engage in physical activity. This, in turn, leads to an increase in the incidence and death rate associated with COPD. Hence, precise evaluation and logical correction of patients' muscle functional state is a crucial component of COPD care.

The neutrophil-to-lymphocyte ratio (NLR), derived from a complete blood count with differential, is a cost-effective and readily accessible indicator of inflammation. It may provide insights into immune function and the presence of long-term systemic inflammation. The Neutrophil-to-Lymphocyte Ratio (NLR) serves as an indicator of widespread inflammation throughout the body. It is a reliable predictor of several types of cancer and is linked to the likelihood of illness recurrence and mortality in cases of severe malnutrition caused by chronic disorders such as cardiovascular diseases, sepsis, and infectious diseases[9–11]. Increasingly, research has shown that NLR plays a role in the progression of COPD. According to Lee et al, the NLR (neutrophil-to-lymphocyte ratio) was shown to be greater in COPD patients during acute episodes compared to the stable period and the healthy control group. However, the NLR dramatically reduced during the recovery phase of patients experiencing acute exacerbation[11]. Taylan et al. discovered that the Neutrophil-to-Lymphocyte Ratio (NLR) of patients with Chronic Obstructive Pulmonary illness (COPD) progressively rose as the illness worsened. This suggests that NLR might serve as an early indicator of acute episodes in COPD patients[12]. These studies validate that the Neutrophil-to-Lymphocyte Ratio (NLR) is a valuable diagnostic tool for evaluating the severity and acute exacerbations of Chronic Obstructive Pulmonary Disease (COPD). Nevertheless, the correlation between the neutrophil-to-lymphocyte ratio (NLR) and the ability to tolerate physical activity in patients with chronic obstructive pulmonary disease (COPD) has not been well investigated.

MATERIALS AND METHODS

This research was done at the Department of

Medicine as an observational study with a cross-sectional design. All individuals diagnosed with COPD according to the criteria outlined in the GOLD 2018 report [13] were included in the research. The research excluded pregnant and lactating females, as well as individuals with bronchiectasis, active TB, malignancy, or other inflammatory illnesses such as arthritis, inflammatory bowel diseases, or connective tissue disorders. A group of 100 COPD patients was split into two categories, each with 50 individuals. The COPD group (n=50) included patients with stable COPD, meaning their symptoms hadn't changed significantly, and they hadn't required additional treatment for three months. The AECOPD group (n=50) consisted of patients who had experienced Acute Exacerbation of COPD (AECOPD), marked by sudden symptom worsening needing extra treatment. Additionally, 50 healthy participants (controls) were included, without a history of smoking, exposure to biomass, medical conditions, or clinical symptoms. Demographic details and medical history were collected initially. Blood samples were analyzed for total and differential leukocyte count, absolute eosinophil, and neutrophil counts. The neutrophil-lymphocyte ratio was calculated by dividing neutrophil count by lymphocyte count.

STATISTICAL ANALYSIS

The categorical variables were summarized using proportions. The continuous variables were summarized using the mean and standard deviation (SD), then compared across groups using an unpaired t-test. A p-value less than 0.05 was deemed to be statistically significant.

RESULTS

The average age in the AECOPD group was 60.98±4.64 years, in the stable COPD group was 62.78±4.94 years, and in the control group was 63.45±3.87 years. There were a higher number of males in all three groups that were examined. The average BMI of participants was considerably lower in stable COPD patients, in comparison to AECOPD and controls. The prevalence of current smokers was considerably greater in the AECOPD group compared to the stable COPD group, as seen in Table 1.

Table 1 Basic parameter

Parameter	AECOPD(n=50)		Stable COPD(n=50)		Controls(n=50)		P-value
Gender							0.21
Female	10	20	13	26	12	24	
Male	40	80	37	74	38	76	
Age years							0.14
Below 30	2	4	3	6	3	6	
30-40	10	20	12	24	12	24	
40-50	12	24	13	26	11	22	
50-60	18	36	17	34	20	40	
Above 60	8	16	5	10	4	8	
Mean Age	60.98	4.64	62.78	4.94	63.45	3.87	

Body Mass Index (kg/m ²)	22.54	2.34	22.87	2.37	21.57	2.73	0.04
Smoking history							0.14
Current	20	40	7	14	0	0	
Ex-smoker	30	60	43	86	0	0	

When comparing the haematological characteristics of individuals with acute exacerbation of chronic obstructive pulmonary disease (AECOPD) with those with stable COPD, it was shown that the AECOPD group had considerably greater levels of total leucocyte count, neutrophil percentage, absolute neutrophil count, and absolute eosinophil count compared to the stable COPD group. The mean neutrophil-to-lymphocyte ratio (NLR) was substantially greater in the acute exacerbation of chronic obstructive pulmonary disease (AECOPD) group (4.21 ± 0.11) compared to the stable COPD group (3.15 ± 0.08). Nevertheless, there was no substantial disparity in the amounts of haemoglobin or the proportion of eosinophils between the two groups. A comparative analysis of hematological parameters

between stable COPD patients and controls revealed that the total leukocyte count, percentage of neutrophils and eosinophils, as well as the absolute counts of eosinophils and neutrophils, were considerably lower in the control group compared to the stable COPD group. The average NLR was substantially greater in the stable COPD group compared to the control group. The analysis of haematological parameters between AECOPD patients and controls shown that the total leucocyte count, neutrophil and eosinophil percentage, absolute eosinophil count, and absolute neutrophil count were notably elevated in the AECOPD patients, in comparison to the controls group. The NLR was markedly elevated in the AECOPD group in comparison to the control group [Table -2].

Table 2 Haematological parameter

Haematological parameter	AECOPD group (mean \pm SD)		COPD group (mean \pm SD)		Controls group (mean \pm SD)		p-value
Haemoglobin(g/dL)	10.78	1.74	10.98	1.85	10.54	1.45	0.14* 0.15# 0.33^
Total leucocyte count(per μ L)	12985.54	473.85	10213.78	553.67	90847.34	536.77	<0.001
Neutrophils (%)	74.98	6.84	70.12	5.73	62.43	5.43	<0.001
Lymphocytes(%)	21.34	2.18	25.79	2.11	35.65	2.17	<0.001
Eosinophils(%)	3.54	0.67	3.54	0.35	2.33	0.26	0.54* <0.001
Absolute eosinophil count (per μ L)	453.89	11.19	337.78	10.85	195.67	10.36	<0.001
Absolute neutrophil count (per μ L)	9915.74	28.96	7084.49	33.19	5499.83	37.17	<0.001
NLR	4.21	0.11	3.15	0.08	1.98	0.07	<0.001

ROC analysis shown that the Neutrophil-to-Lymphocyte Ratio (NLR) had a strong predictive value for exacerbations of Chronic Obstructive Pulmonary Disease (COPD). With a threshold of 3.56, the sensitivity, specificity, and Area Under Curve (AUC) were 76.45%, 71.78%, and 0.56, respectively. The study participants were categorized into two groups based on their blood eosinophil percentage: those with blood eosinophils below 2% and those with

blood eosinophils over 2%. In patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD), the neutrophil-to-lymphocyte ratio (NLR) was seen to be considerably elevated in both the non-eosinophilic group (with blood eosinophils <2%) and in those with blood eosinophils >2%. The NLR was comparable across the two groups, consisting of patients with stable COPD and controls, as shown in Table 3.

Table 3 NLR in non eosinophilic (blood eosinophils <2%) and eosinophilic (blood eosinophils >2%) groups among study participants

Parameter	Eosinophil<2%	Eosinophil>2%	p-value
Normal subjects	20	30	
NLR	1.97 \pm 0.23	1.97 \pm 0.23	0.28
Acute exacerbation patients	2	48	
NLR	7.89 \pm 1.22	4.23 \pm 1.09	<0.001
Stable COPD patients	3	47	
NLR	2.56 \pm 0.43	3.23 \pm 0.65	0.21

DISCUSSION

In this investigation, it was shown that the Total Leucocyte Counts (TLC) in patients with stable COPD were considerably elevated compared to the control group. This conclusion is similar with earlier studies [14-19]. COPD is defined by an abnormal inflammatory reaction to substances that irritate the airways, resulting in damage to the lung tissue and airways. This damage leads to ongoing symptoms and restricted airflow. In addition to airway inflammation, individuals with COPD also experience aberrant systemic inflammation, which is primarily responsible for the many systemic symptoms of the illness. Various processes have been suggested to explain the occurrence of systemic inflammation in COPD, such as the dissemination of inflammatory mediators from the pulmonary region, an inflammatory reaction to tissue hypoxia or bacterial elements, inflammation generated by smoking, and lung hyperinflation [20]. In addition, the worsening of COPD is marked by heightened inflammation caused by infection in most instances. This results in greater TLC as seen in this study and earlier research [13,14], as compared to both control subjects and stable COPD patients.

The current research revealed that the Neutrophil-to-Lymphocyte Ratio (NLR) was notably elevated in individuals with stable Chronic Obstructive Pulmonary Disease (COPD) compared to both healthy controls and much more so in those with Acute Exacerbation of COPD (AECOPD) as compared to those with stable COPD and healthy controls. Several research have

shown similar conclusions. NLR, which stands for Neutrophil-to-Lymphocyte Ratio, is a well-recognized indicator of inflammation and has been seen to rise in several inflammatory disorders [21,22,23]. Exacerbations in COPD are characterized by an intensification of the chronic inflammatory process of COPD in both the lungs and the body as a whole. Exacerbations may be caused by bacteria, viruses, or non-infectious factors, which all result in heightened inflammation in the airways and the production of proinflammatory cytokines and chemokines. The indicators of inflammation are often elevated in acute exacerbations of chronic obstructive pulmonary disease (AECOPD), resulting in an intensified systemic inflammatory response characterized by the recruitment and activation of neutrophils. These findings indicate a greater NLR (neutrophil-to-lymphocyte ratio) in patients with acute exacerbations of chronic obstructive pulmonary disease (AECOPD), as compared to those with stable COPD and control subjects.

Given that NLR is notably elevated in patients experiencing acute exacerbations of chronic obstructive pulmonary disease (AECOPD), it might serve as a biomarker for exacerbation in individuals with COPD. In this investigation, using a cut-off value of 3.56, the sensitivity, specificity, and Area Under Curve (AUC) for predicting an exacerbation were 76.45%, 71.78%, and 0.56, respectively. Prior research has consistently shown the strong predictive ability of NLR in forecasting a worsening of COPD symptoms [15-19,24].

Table 4 comparison of our study with others study

Studies	AECOPD	Stable COPD	Controls	p-value
NLR				
Current study	4.21±0.11	3.15±0.08	1.98±0.07	<0.001
Şahin Fet al.,[15]	8.51±8.70	2.79±1.65	1.31±0.46	<0.001
Prasannan G et al.,[16]	5.523	4.226	-	0.008
Sharma Ketal.,[17]	6.389±3.071	4.263±1.900	-	0.0009
El-Gazzar AG et al.,[18]	2.65±0.41	2.24±0.56	-	<0.0001
Mohamed-Hussein AA et al., [19]	3.7±0.3	1.2±0.7	-	<0.05
NLRcut-off for predicting exacerbations	Cut-off	Sensitivity	Specificity	AUC(95%CI)
Current study	3.56	76.45%	71.78%	0.56
Acartürk Tunçay Eet al.,[23]	3.54	78%	69%	-

Patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD) who had a blood eosinophil percentage of less than 2% had a substantially larger neutrophil-to-lymphocyte ratio (NLR) compared to those with eosinophil levels over 2%. However, there was no significant difference in NLR when comparing controls and stable COPD patients in these groups. In addition, there were relatively few AECOPD patients that exhibited this pattern, hence no definitive conclusion could be made based on this observation. The NLR was not assessed in relation to other factors such as the severity of underlying COPD, the severity of exacerbations, or the frequency of prior exacerbations. Due to the study's cross-sectional design and lack of follow-up,

the predictive significance of NLR was not investigated.

CONCLUSION

Regular and intense flare-ups of COPD have a negative impact on the patient's health and can contribute to the advancement of the illness and increased risk of death. Early identification and treatment of exacerbations may be facilitated by predicting them in advance. Recent research indicates that the Neutrophil-to-Lymphocyte Ratio (NLR) serves as an inflammatory biomarker that experiences a substantial increase during exacerbations of Chronic Obstructive Pulmonary Disease (COPD). This biomarker may be used to forecast COPD

exacerbations and aid in the early detection of such exacerbations.

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