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ORIGINAL RESEARCH

Evaluation of role of Neutrophil to lymphocyte ratio in patients with Chronic obstructive pulmonary disease

Dr. Kothapalli Jayanth[1], Dr. Nitin Gupta[2], Dr. Savita Kapila[3], Dr. Sumegha Singh[4], Dr. Parmjeet Singh[5], Dr. Vikram Rajput[6]

[1]Junior Resident, [2]Associate Professor, [3]Professor, [4,5]Senior Resident, [6]Assistant Professor, Department of General Medicine, MMIMSR, Mullana, India

Corresponding author
Dr. Kothapalli Jayanth
Junior Resident, Department of General Medicine, MMIMSR, Mullana, India

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ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality across the globe. The neutrophil to lymphocyte ratio, which represents the innate and adaptive immune systems, respectively, is known as the neutrophil to lymphocyte ratio (NLR). Hence; the present study was conducted for evaluating the potential role of Neutrophil to lymphocyte ratio (NLR) in patients with Chronic obstructive pulmonary disease (COPD). **Materials & methods:** 50 patients with Chronic obstructive pulmonary disease (COPD) and 50 patients with acute exacerbation of COPD, who are admitted in MMIMSR, Mullana. Detailed demographic (age, sex, weight), clinical (comorbidities, duration of treatment, days of stay in the hospital, mortality, concomitant antibiotic therapy), laboratory investigations (CBC, Peripheral smear study, Renal function tests, Liver function tests, FBS, PPBS, Serum Vitamin B12 assay) data from each patient was recorded.**Results:** There was a significant increase in absolute neutrophil count and decrease in absolute lymphocyte count in AECOPD patients in comparison to COPD patients. Mean neutrophil to lymphocyte ratio among the COPD patients was found to be significantly lower in comparison to patients with AECOPD. An NLR of 3.1 was considered the optimal cut-off value with maximal sensitivity and specificity for respiratory hospitalization following ROC curve analysis. The sensitivity and specificity were 68.3 % and 66.4%, respectively. **Conclusion:** Elevated NLR can be used as a marker in the determination of increased inflammation in acutely exacerbated COPD. NLR could be beneficial for the early detection of potential acute exacerbations in patients with COPD who have normal levels of traditional markers.

Key words: Neutrophil, Lymphocyte, Chronic obstructive pulmonary disease

INTRODUCTION

Across the globe, the illness regarding the respiratory system is the major factors responsible for the death rate. These factors may be acute or chronic in nature. Across the worldwide, four percent of the illness is due to the respiratory problems. But around 8.3 percent of this severe illness is affecting the life of the patient affected by it. It Around the year, the 3rd reason, i.e, approximately 5.5 percent responsible for death is COPD globally. The meticulous data of India regarding the incidence of COPD has remained misunderstood. This is due to the proportions and heterogeneity among the people of India.[1, 2]AECOPD is elucidated as worsening of threshold of dyspnea of an individual, croup and sputum. AECOPDs are highly related to increased potential for frequent exacerbations, damaging the coexisting pathological diseases, representing bad status along with lack of physical exercise. This leads to lowered functioning of respiratory system and finally resulting to mortality. Etiology of AECOPD includes microorganisms such as bacteria or any virus in about 50 percent cases.[3, 4]

NLR has been used as a clinical outcome predictor in a number of tumour types and ischemic stroke. Variations in immune system and inflammation response are reflected in the fluctuation of NLR. In order to quickly, cheaply, and simply measure the degree of inflammation in COPD patients, Gunay et al. originally employed the NLR. Later research revealed that NLR has been a reliable indicator for death and for aggravation of COPD.[5, 6]Hence; the present study was conducted for evaluating role of Neutrophil to lymphocyte ratio in patients with Chronic obstructive pulmonary disease

MATERIALS & METHODS

The present study included 50 patients with COPD and 50 patients with AECOPD, who are admitted in MMIMSR, Mullana. The Institutional Human Ethical

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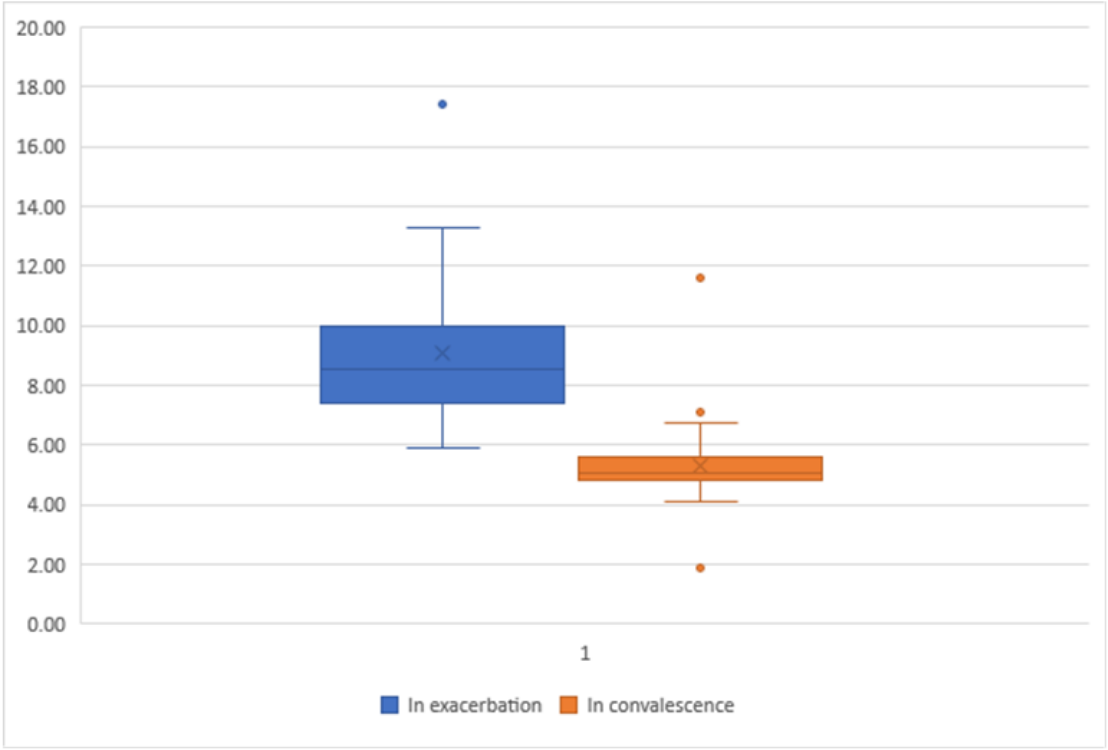
Committee provided ethical clearance prior to the study's start. The chosen patients were informed about the study's purpose and asked to provide written, informed permission in their native tongue. Thorough history was gathered from the present, as well as a thorough physical examination. Individual patient data was recorded, including full demographic (age, sex, weight), clinical (comorbidities, length of treatment, hospital days, mortality, concurrent antibiotic therapy), and laboratory (CBC, peripheral smear study, RFT, LFT, FBS, PPBS, serum vitamin B12 assay) data. All the results were evaluated using SPSS software. Chi-square test and student t test was used for analysis of level of significance. P-value of less than 0.05 was taken as significant.

RESULTS

Both the study groups were comparable in terms of age and gender-wise distribution of patients. Mean Absolute neutrophil count among the patients of the COPD group and AECOPD group was 5.55 (x 10^3/µL) and 13.81 (x 10^3/µL) respectively while mean absolute lymphocyte count among the patients of the COPD group and AECOPD group was 2.21 (x 10^3/µL) and 1.40 (x 10^3/µL) respectively. While comparing the results statistically, significant results were obtained. Hence; there was a significant increase in absolute neutrophil count and decrease in absolute lymphocyte count in AECOPD patients in comparison to COPD patients. Mean neutrophil to lymphocyte ratio among the COPD patients was 2.697 and was found to be significantly lower in comparison to patients with AECOPD (Neutrophil to lymphocyte ratio: 10.252). Among the 50 patients with AECOPD, patients in the convalescent period (Neutrophil to lymphocyte ratio: 5.286) had a significantly decreased Neutrophil to lymphocyte ratio: value compared with those in the exacerbation period (Neutrophil to lymphocyte ratio: 9.056). An NLR of 3.1 was considered the optimal cut-off value with maximal sensitivity and specificity for respiratory hospitalization following ROC curve analysis. The sensitivity and specificity were 68.3 % and 66.4%, respectively. In other words, if the neutrophil to lymphocyte ratio exceeds the cut-off value, there is a high probability of respiratory hospitalization. Moreover, the area under the ROC curve is 0.718, which is a statistically significant result indicating that the neutrophil lymphocyte ratio is a reliable predictor of respiratory hospitalization.

Table 1: Assessment of hematological profile

Hematological profile	COPD group		AECOPD group		p-value
	Mean	SD	Mean	SD	
Absolute neutrophil count (x 10^3/µL)	5.55	0.67	13.81	2.08	0.001 (Significant)
Absolute lymphocyte count (x 10^3/µL)	2.21	0.65	1.40	0.26	0.003 (Significant)
NLR	2.697	0.735	10.252	2.657	0.000 (Significant)



Graph 1: Change in neutrophil to lymphocyte ratio between the exacerbation and convalescence periods among the patients of the AECOPD group

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Table 2: Neutrophil to lymphocyte ratio as a predictor for respiratory hospitalization

Area under ROC curve	Std. Error[a]	Asymptotic Sig[b] (p-value)	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.718	0.052	0.000	0.513	0.886
Cut-off variables				
Cutt-off for Neutrophil to lymphocyte ratio	3.1			
Sensitivity	68.3 %			
Specificity	66.4 %			

DISCUSSION

Among COPD subjects, literature demonstrates enhanced levels of activated neutrophils in the sputum samples. However; lessen quantity of neutrophil in pulmonary parenchyma tissue might be because of active transition of these cells in between airways along with pulmonary parenchyma. Neutrophils have capability to produce serum proteinases which might contribute to destruction of alveolar region.Still lot of debate exist in the literature in relation to the part played by neutrophils in pathophysiology of COPD. Associations exists among circulating neutrophils and decline in FEV_1. Likewise; quantity of neutrophils among bronchial biopsies are strongly associate with severity.[7- 10]

In the present study, mean Absolute neutrophil count among the patients of the COPD group and AECOPD group was 5.55 (x 10^3/µL) and 13.81 (x 10^3/µL) respectively while mean absolute lymphocyte count among the patients of the COPD group and AECOPD group was 2.21 (x 10^3/µL) and 1.40 (x 10^3/µL) respectively. While comparing the results statistically, significant results were obtained. Hence; there was a significant increase in absolute neutrophil count and decrease in absolute lymphocyte count in AECOPD patients in comparison to COPD patients. In a previous study conducted by Ardestani ME et al, mean neutrophil count and mean lymphocyte count was 7.51 (x 10^3/µL) and 1.61 (x 10^3/µL).[11] Bilir B et al, in another previous study reported that Mean Absolute neutrophil count among the patients of the COPD group and AECOPD group was 4.7 (x 10^3/µL) and 5.7 (x 10^3/µL) respectively while mean absolute lymphocyte count among the patients of the COPD group and AECOPD group was 1.9 (x 10^3/µL) and 1.4 (x 10^3/µL) respectively.[12] In another similar study conducted by Günay E et al, Mean Absolute neutrophil count among the patients of the COPD group and AECOPD group was 5.3 (x 10^3/µL) and 6.7 (x 10^3/µL) respectively while mean absolute lymphocyte count among the patients of the COPD group and AECOPD group was 2 (x 10^3/µL) and 1.5 (x 10^3/µL) respectively.[13] Taylan M et al, in another similar study reported that Mean Absolute neutrophil count among the patients of the COPD group and AECOPD group was 4.85 (x 10^3/µL) and 7.74 (x 10^3/µL) respectively while mean absolute lymphocyte count among the patients of the COPD group and AECOPD group was 1.93 (x 10^3/µL) and 1.43 (x 10^3/µL) respectively.[14]

Mean neutrophil to lymphocyte ratio among the COPD patients was 2.697 and was found to be significantly lower in comparison to patients with AECOPD (Neutrophil to lymphocyte ratio: 10.252). Our results were in concordance with the results obtained by previous authors who also reported similar findings. In the study conducted by Lee SJ et al, mean neutrophil to lymphocyte ratio among the patients with AECOPD was 12.4 and was significantly higher in comparison to COPD patients (neutrophil to lymphocyte ratio: 2.4).[15] In another previous study conducted by Ardestani ME et al, mean NLR among patients of the COPD group and AECOPD group was 2.41 and 4.1 respectively (p-value < 0.001).[11] In another similar study conducted by Günay E et al, mean NLR among the patients of the COPD group and AECOPD group was 2.59 and 4.28 respectively (p-value < 0.001).[13] Taylan M et al, in another similar study reported that Mean NLR among the patients of the COPD group and AECOPD group was 3.1 and 7.1 respectively; on comparing statistically, significant results were obtained.[16]

Among the 50 patients with AECOPD, patients in the convalescent period (Neutrophil to lymphocyte ratio: 5.286) had a significantly decreased Neutrophil to lymphocyte ratio: value compared with those in the exacerbation period (Neutrophil to lymphocyte ratio: 9.056). In a similar study conducted by Lee SJ et al, among the 50 patients with AECOPD, patients in the convalescent period had a significantly decreased NLR value compared with those in the exacerbation period.[15]

COPD consists of broadly two phases; stable period and other one being acute exacerbation period. Stable period has lower systemic inflammatory period which includes activation and enhancement of circulating inflammatory cells, and inflammatory proteins. However; exacerbation phase is associated with worsening and enhancement of inflammatory proteins. Early documentation and treatment of AE-COPD is a crucial subject in routine medical practice. Also; the incidence along severity of exacerbation periods correlates with significant enhanced mortality rate. Early identification of immune status to clinical profile among AECOPD subjects. Hence; early identification of inflammatory markers in AECOPD is

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needed for assessing degree of inflammation (Taylon M et al). Furutate R et al, reported that during exacerbation period, there was significant enhancement of NLR while comparing to stable period.[14, 16]

An NLR of 3.1 was considered the optimal cut-off value with maximal sensitivity and specificity for respiratory hospitalization following ROC curve analysis. The sensitivity and specificity were 68.3 % and 66.4%, respectively. In other words, if the neutrophil to lymphocyte ratio exceeds the cut-off value, there is a high probability of respiratory hospitalization. Moreover, the area under the ROC curve is 0.718, which is a statistically significant result indicating that the neutrophil lymphocyte ratio is a reliable predictor of respiratory hospitalization. In a similar study conducted by Lee SJ et al, authors reported cut-off for NLR to be 2.8 for predicting respiratory hospitalization with sensitivity and specificity of 60 percent and 60.9 percent respectively.[15] The NLR assessment reflects the body's overall inflammatory condition and simultaneously gives information on two distinct immune pathways. It gives information about the neutrophils that cause inflammation to persist in the first place, as well as information about the lymphocyte route that plays a regulatory function.[17]Kurtipek et al, showed that NLR marker had good positive prognostic value in predicting AECOPD; however, the accuracy of NLR marker was higher, as a result of which it has been recommended to be used in the treatment of patients.[18]In a previous study conducted by El-Gazzar AG et al, authors assessed NLR in COPD patients. They evaluated 100 COPD patients and 60 healthy subjects. NLR was increased significantly in COPD patients (2.24) compared to control group (1.31). During exacerbation NLR was elevated significantly compared to stable condition. NLR showed a significant positive correlation with smoking index, COPD stage, and dyspnea severity. They concluded that NLR increased in stable COPD patients and further increased during exacerbation that can predict in hospital mortality.[19]

CONCLUSION

There is abundantly evident that NLR may serve as a biomarker for COPD and its aggravation. Further validation, however, will come from larger-scale investigations in the future. When COPD is acutely worsened, elevated NLR can be utilized as a marker to determine increased inflammation. NLR may be helpful in the early identification of possible acute exacerbations in COPD subjects with physiological levels of conventional markers.

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