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Predictive role of platelets to lymphocytes ratio and neutrophil to lymphocytes ratio in COPD exacerbation

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Abstract

Background The hallmark of COPD is the progressive destruction of the lung parenchyma, which is frequently brought on by the body's inflammatory reaction to external stimuli (such as smoking cigarettes or pollution). According to reports, the peripheral blood's essential immune-related cell populations' absolute counts and ratios can accurately represent chronic inflammatory diseases. Complex interactions between immune-related cells, such as lymphocytes and neutrophils, are involved in inflammation, which can cause irreversible damage and loss of respiratory tissue. The neutrophil-to-lymphocyte ratio (NLR) and the platelet-to-lymphocyte ratio (PLR), two hematological indicators of inflammation, have been studied in a variety of disease states, including solid tumors, systemic lupus erythematosus, coronary artery disease, retinal artery occlusion, chronic kidney disease, and stable COPD.

Aim Correlation between NLR and PLR and outcome of COPD exacerbation.

Materials and methods This cross-sectional study included 80 patients with COPD exacerbation who visited the outpatient clinic or were admitted to the Chest Department. CRP and calculation of NLR and PLR within 24 h from admission and 1 month after discharge were obtained to identify the prognostic value of NLR and PLR for the exacerbation, hospitalization, mechanical ventilation, and mortality in patients with COPD.

Results During COPD exacerbation PLR, NLR showed a statistically significant correlation with the need for hospitalization with a p value < 0.001. As regards correlation with mortality NLR was statistically significant with a p value of 0.006 while PLR showed a non-significant p value of 0.077. PLR and NLR were correlated with CRP as an inflammatory marker and both were statistically significant with p value 0.004 and < 0.001 respectively. During exacerbation, PLR and NLR were correlated with the need for mechanical ventilation and the results were statistically significant with p value < 0.001. PLR and NLR showed a significant increase during exacerbation compared to stable COPD patients 1 month after discharge with p value of < 0.001.

Conclusion PLR and NLR are simple tests that could be used to predict the severity of COPD exacerbation and the need for hospitalization, MV, and mortality prediction.

Keywords PLR, NLR, COPD

Introduction

More than 200 million people suffer from chronic obstructive pulmonary disease (COPD), which is ranked as the third most common cause of death globally [1]. COPD is a significant cause of healthcare expenses since it frequently requires hospitalization and causes disability [2]. A non-fully reversible airflow limitation is the

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hallmark of COPD, which is defined by the progressive destruction of the pulmonary parenchyma and frequently results from the inflammatory response to external stimuli (such as cigarette smoking and environmental pollution) [3]. Acute exacerbations of COPD (AECOPD) are characterized by a worsening of the patient's baseline dyspnea, cough, and/or sputum production. They are seen as a crucial part of the disease's normal course [4]. AECOPD is related to death, loss of lung function, poor performance status and physical activity, and exacerbation of preexisting pathological conditions [5]. A complex web of interactions between immune-related cells, including lymphocytes and neutrophils, is involved in inflammation, which can cause irreversible damage and loss of respiratory tissue [6]. According to reports, the ratios and absolute numbers of important immune-related cell groups in peripheral blood can accurately represent chronic inflammatory conditions [7]. The neutrophil-to-lymphocyte ratio (NLR) and the platelet-to-lymphocyte ratio (PLR), two hematological indicators of inflammation, have been studied in a variety of disease states, including solid tumors, systemic lupus erythematosus, coronary artery disease, retinal artery occlusion, chronic kidney disease, and stable COPD [8].

Aim of the work

Correlation between NLR and PLR and outcome of COPD exacerbation.

Materials and methods

Sample size

A previous study showed that the correlation coefficient between the neutrophil/lymphocyte ratio (NLR) and the CRP in AECOPD (acute exacerbation COPD) patients was 0.326 [9]. So, the sample size to study the results of the current study with a significant $P < 0.05$ and a power of 80%, is calculated according to this formula:

$$r = 0.326\beta = 0.2Z1 - \alpha/2 = 1.96Son = 72$$

And by adding 10% as a drop-out rate so at least 80 patients should be recruited for the study.

Study design

This cross-sectional study included 80 patients with COPD exacerbation who visited the outpatient clinic or were admitted to the Chest Department, Faculty of Medicine.

Inclusion criteria

Patients with COPD seeking medical advice at the Chest Department.

Exclusion criteria

1. Patient refuse.
2. Pneumonia.

Assessments

Complete blood counts, serum lactate dehydrogenase, liver enzyme tests (alanine aminotransferase, aspartate aminotransferase), kidney function tests (urea, creatinine), arterial blood gases were done to identify patients in hypercapnic respiratory failure needing non-invasive ventilation, electrocardiography was done to exclude ischemic heart diseases or myocardial infarction, chest X-ray, high-resolution CT chest without contrast to detect complications such as bronchogenic carcinoma, pneumonia or pneumothorax as a cause of COPD exacerbation, CRP, and calculations of NLR and PLR were performed on all patients within 24 h of admission and again 1 month after discharge following condition stabilization.

Statistical methods

In this work, we used the statistical program for the social sciences (SPSS) version 28 (IBM Corp., Armonk, NY, USA). The serial measurement comparison was done using the non-parametric Wilcoxon signed rank test [10]. To compare categorical data, the chi-square (α2) test was employed. *P* value less than 0.05 was deemed statistically significant.

Results

The study was carried out in the chest department and included 80 patients with COPD exacerbation who were seeking medical treatment at the chest department and

Table 1 Descriptive data of the basic clinical characteristics of the COPD patients, sex, comorbidities, hospitalization, MV, and outcome

		Count	%
Sex	Male	79	98.8%
	Female	1	1.3%
Hospitalization	Yes	38	47.5%
	No	42	52.5%
MV	Yes	27	33.8%
	No	53	66.3%
MV details	IMV	6	7.5%
	NIV	21	26.3%
	No	53	66.3%
Outcome	Died	5	6.3%
	Survive	75	93.8%

DM diabetes mellitus, *IHD* ischemic heart disease, *PHT* pulmonary hypertension, *IMV* invasive mechanical ventilation, *NIV* non-invasive mechanical ventilation

Table 2 NLR and PLR during exacerbation and after 1 month of discharge of patients with COPD exacerbation

	Mean	Standard deviation	Median	Minimum	Maximum
PLR during exacerbation	223.59	97.14	191.95	87.85	497.22
NLR during exacerbation	12.24	6.31	12.59	3.11	26.51
PLR after month	105.63	18.77	102.00	70.00	153.00
NLR after month	3.50	1.26	3.19	1.10	6.90

Table 3 Mean neutrophil to lymphocyte and platelet to lymphocyte ratio during exacerbation and its correlation to hospitalization in COPD patients

	Hospitalization										*P* value
	Yes					No					
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
PLR	264.24	99.99	247.09	106.66	489.74	186.80	79.00	171.00	87.85	497.22	< 0.001
NLR	17.02	5.12	16.77	5.25	26.51	7.92	3.55	7.45	3.11	15.57	< 0.001

Table 4 Mean neutrophil to lymphocyte and platelet to lymphocyte ratio during exacerbation and its correlation to mortality in COPD patients

	Outcome										*P* value
	Died					Survive					
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
PLR	273.48	53.50	312.50	211.25	312.50	220.26	98.69	190.69	87.85	497.22	0.077
NLR	18.89	1.76	18.75	16.95	20.75	11.80	6.25	11.18	3.11	26.51	0.006

pulmonary intensive care unit, 79 male (98,8%) and 1 female patient (1.3%). Out of 80 patients with COPD exacerbation, 38 were admitted to the chest department. Among them, 27 required mechanical ventilation, 6 patients required invasive ventilation, 21 ventilated non-invasively and 5 patients (6.3%) died as shown in Table 1. The mean age of the patients was 61.26 years. NLR, PLR, and CRP levels were measured for each patient upon admission and 1 month after discharge. The mean NLR was 12.24 during exacerbation and 3.5 after 1 month. The mean PLR was 223.59 during exacerbation and 105.63 after 1 month, as shown in Table 2. During COPD exacerbation PLR and NLR showed a statistically significant correlation with the need for hospitalization with p value < 0.001 (Table 3). As regards correlation with mortality NLR was statistically significant with a p value of 0.006 while PLR showed a non-significant p value of 0.077 (Table 4). PLR and NLR were correlated with CRP as an inflammatory marker and both were statistically significant with p value 0.004 and < 0.001 respectively (Table 5). During an exacerbation, PLR and NLR were correlated with the need for mechanical ventilation and the results were statistically significant with *a* p value of < 0.001 (Table 6). PLR and NLR showed a significant increase during exacerbation compared to stable COPD patients 1 month after discharge with p value < 0.001 (Table 7). NLR cut-off value 12.585 had specificity and sensitivity of 85.7% and 89.5% respectively and PLR cut-off value 193.325 had specificity and sensitivity of 71.4% and 68.4% respectively for hospitalization as shown in (Table 8) (Fig. 1). NLR cut-off value 14.89 had specificity and sensitivity of 96.2% and 100% respectively and PLR cut-off value 209.375 had specificity and sensitivity of 73.6% and 74.1% respectively for mechanical ventilation as shown in (Table 8) (Fig. 1).

Table 5 Mean neutrophil to lymphocyte and platelet to lymphocyte ratio during exacerbation and its correlation to CRP in COPD patients

		PLR	NLR
CRP	Correlation coefficient	0.320	0.733
	P value	0.004	< 0.001
	N	80	80

Discussion

For patients with chronic obstructive pulmonary disease (COPD), acute exacerbation of the illness is the leading cause of hospitalization and mortality. For prognostic

Table 6 Mean neutrophil to lymphocyte and platelet to lymphocyte ratio during exacerbation and its correlation to MV in COPD patients

	MV										*P* value
	Yes					No					
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
PLR	281.04	101.17	267.24	129.59	489.74	194.32	81.42	178.94	87.85	497.22	< 0.001
NLR	19.38	3.54	18.75	14.96	26.51	8.61	3.77	7.90	3.11	15.57	< 0.001

Table 7 Comparison between the mean ratio of NLR and PLR during exacerbation and after 1 month in all patients with COPD exacerbation

	During exacerbation					After 1 month					*P* value
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
PLR	223.59	97.14	191.95	87.85	497.22	105.63	18.77	102.00	70.00	153.00	< 0.001
NLR	12.24	6.31	12.59	3.11	26.51	3.50	1.26	3.19	1.10	6.90	< 0.001

Table 8 Prediction of hospitalization using PLR, NLR in COPD patients

	Area under the curve	*P* value	95% confidence interval		Cut-off	Sensitivity %	Specificity %
			Lower bound	Upper bound			
PLR	0.749	< 0.001	0.643	0.856	193.325	68.4	71.4
NLR	0.923	< 0.001	0.863	0.983	12.585	89.5	85.7

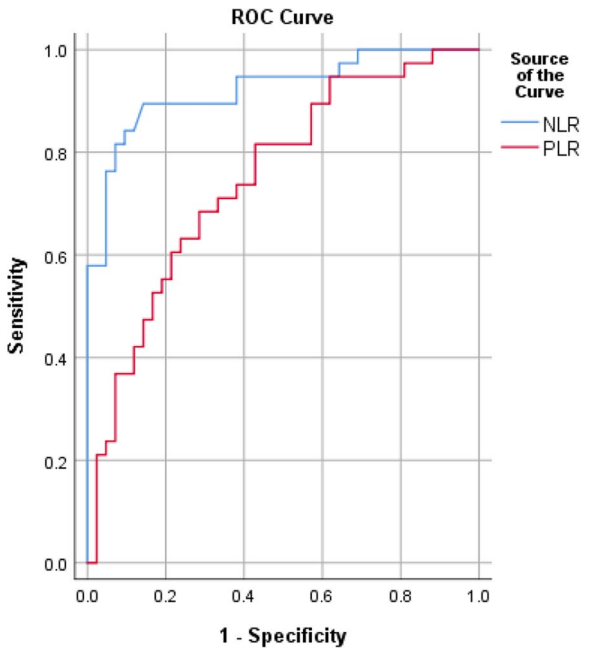

Fig. 1 ROC curve for prediction of hospitalization using PLR, NLR

assessment, clinicians are looking for straightforward, easily obtainable, and affordable biomarkers. The goal of the current study was to determine the predictive significance of NLR and PLR for COPD patient mortality, hospitalization, exacerbation, and mechanical ventilation. Systemic inflammation and enhanced airway inflammation were the causes of COPD and the NLR and PLR are inflammatory indicators for clinical outcomes in these patients [11]. Reduced lymphocytes and an increase in neutrophils and platelets were indicative of higher NLR and PLR [12] and a reduction in FEV1 [13] were the outcomes of activated neutrophils releasing proteolytic enzymes (such as matrix metalloproteinase, calprotectin, and elastase) and inflammatory cytokines. The immune system relies heavily on lymphocytes, and lymphopenia has been linked to increased infection and mortality rates [14, 15]. In COPD patients, platelet activation increases even more after an acute exacerbation. Hence, the correlation between decreased immune function (lymphocytes) and increased inflammatory response (platelets and neutrophils) in COPD patients may account for the higher NLR and PLR values. For each patient, NLR, PLR, and CRP were obtained on admission and 1 month after

Table 9 Prediction of MV using PLR, NLR in COPD patients

	Area under the curve	*P* value	95% confidence interval		Cut-off	Sensitivity %	Specificity %
			Lower bound	Upper bound			
PLR	0.763	< 0.001	0.655	0.871	209.375	74.1	73.6
NLR	0.993	< 0.001	0.981	1.005	14.89	100	96.2

discharge. PLR and NLR showed a significant increase during exacerbation compared to stable COPD patients after 1 month of discharge. During COPD exacerbation, NLR and PLR showed a statistically significant correlation with the need for hospitalization with cut-off values of 12.585 and 193.325 respectively, and were correlated with CRP during exacerbation and this agrees with Günay et al. [16]. When a patient is hospitalized for AECOPD, noninvasive mechanical ventilation (NIV) is the first mode of ventilation used to treat acute respiratory failure since it is believed to be the most successful in lowering the risk of intubation and mortality. Invasive ventilation is a rescue therapy after failing NIV. PLR and NLR were correlated with the need for mechanical ventilation and the results were statistically significant with a cut-off value of 209.375 and 14.89 respectively and this agrees with Teng et al. [17]. As regards correlation with mortality NLR was statistically significant while PLR was statistically non-significant and this agrees with Yao et al. [18] (Table 9).

In conclusion, both PLR and NLR levels significantly increased during exacerbation compared to stable COPD patients 1 month after discharge. Both PLR and NLR were found to have a statistically significant correlation with the need for hospitalization and mechanical ventilation. NLR showed a statistically significant correlation with mortality, while PLR did not. These simple tests can be used to predict the severity of COPD exacerbation and the need for hospitalization, mechanical ventilation, and mortality.

Abbreviations

NLR	Neutrophil to lymphocyte ratio
PLR	Platelet to lymphocyte ratio
COPD	Chronic obstructive pulmonary disease
CRP	C-reactive protein
AECOPD	Acute exacerbations of COPD
FEV1	Forced expiratory volume in 1st second
NIV	Non-invasive ventilation
DM	Diabetes mellitus
IHD	Ischemic heart disease
PHT	Pulmonary hypertension
IMV	Invasive mechanical ventilation

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Authors' contributions
HF contributed to the conception and design of the work, drafted the work, and revised it. AA shared in the acquisition and analysis of data, shared in writing the manuscript, drafted the work, and revised it. All authors read and approved the final manuscript.

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Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
The ethics committee of the faculty of medicine approved the study protocol (N-207–2023). The written informed consent was obtained from all the participants.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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