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TANAFFOS

Can the Eosinophil-to-Platelet Ratio Predict Chronic Obstructive Pulmonary Disease Exacerbations and Length of Hospital Stay?

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Background: An acute exacerbation of chronic obstructive pulmonary disease is a severe condition that escalates the burden on patients and the healthcare system. This study aimed to evaluate the prognostic value of the eosinophil-to-platelet ratio (EPR) in predicting COPD exacerbations and hospital admissions, with these outcomes also assessed as secondary endpoints.

Materials and Methods: This cohort study was conducted from 2023 to 2025 at Masih Daneshvari Educational Hospital in Tehran, Iran, among patients with confirmed COPD exacerbation. Participants were assessed during the recovery phase after management of the acute exacerbation. Collected clinical data included the history and frequency of exacerbations in the preceding 12 months; blood test results at discharge; 90-day mortality; hospital readmission; ICU admission; and corticosteroid use within 12 months post-discharge. Data were analyzed using STATA version 17.

Results: This study evaluated 249 individuals with COPD exacerbation, with a mean age of 65.66±9.17 years. In individuals with EPR≤1, the risk of experiencing more COPD exacerbations was 17% higher than in those with EPR>1 (adjusted RR=1.17, 95% CI=0.92 –1.49, P=0.195). These results were not statistically significant. In addition, in patients with EPR≤1, the risk of having a higher number of hospitalization days was 16% lower compared to those with EPR>1 (adjusted RR=0.84, 95% CI=0.72–0.98, P=0.036). EPR was not associated with ICU admission and the need for systemic corticosteroids.

Conclusion: The association between lower EPR values and a higher number of exacerbations, as well as shorter hospital stays, suggests that EPR could reflect distinct exacerbation phenotypes or patterns of disease activity.

Keywords: Chronic Obstructive Pulmonary Disease; Eosinophil; Platelet; Prognosis

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a predominant cause of mortality and morbidity globally. It ranks as the fourth leading cause globally, with anticipated increases in both prevalence and mortality in the forthcoming decades. COPD is defined by ongoing respiratory symptoms and a progressive reduction in airflow, resulting from abnormalities in the airways and alveoli. The disease course is characterized by acute exacerbations, defined as episodes of symptom worsening necessitating further treatment. Exacerbations represent significant occurrences associated with accelerated decline in lung function, increased healthcare utilization, diminished health-related quality of life, and elevated mortality risk (1-4).

COPD exacerbation is characterized by an escalation of COPD symptoms beyond typical daily fluctuations, necessitating alterations to regular treatment regimens. Such exacerbations are frequently associated with deteriorating health, readmissions, elevated hospitalization rates, and disease advancement (5).

Research indicates that low blood eosinophil levels may predict a negative prognosis in people with COPD. An eosinophil count <50/μL may serve as a valuable biomarker for identifying sepsis and predicting mortality in critically unwell individuals. A diminished eosinophil count may forecast increased mortality in hospitalized patients with acute exacerbations of COPD. It was noted that blood eosinophilia correlates with an increased risk of exacerbations in COPD patients (6-9).

Platelet count may serve as a predictor of disease prognosis. Multiple studies indicate that thrombocytopenia serves as an independent predictor of mortality in the intensive care unit (ICU), with a relative risk between 1.9 and 4.2. Recent studies indicate that a decrease in platelet count correlates with respiratory diseases (10-12).

Current studies indicate that eosinophil and platelet counts may serve as predictors for outcomes in chronic obstructive pulmonary disease; however, research remains limited. Therefore, in this study, we aimed to investigate the prognostic value of the eosinophil-to-platelet ratio (EPR) for COPD exacerbations and hospital admissions. In addition, the predictive ability of the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) for the aforementioned outcomes was evaluated as a secondary objective.

MATERIALS AND METHODS

Study design and participants

This cohort study was conducted in 2023-2025 at Masih Daneshvari Educational Hospital in Tehran, Iran, involving patients with COPD exacerbation. The inclusion criteria were age over 40 years, involvement with chronic obstructive pulmonary disease, hospitalization in Masih Daneshvari Hospital in a stable disease condition (six months before exacerbation or six weeks after remission), and confirmed COPD by spirometry as FEV1<80% and FEV1/FVC < 70%. Therefore, participants were enrolled in the study at the time of discharge and at the disease control condition.

Exclusion criteria were a history of previous hospitalization under oral corticosteroid treatment and obstructive airway disease secondary to other causes such as interstitial lung disease and pneumonia.

The diagnosis of COPD was made in accordance with the Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2018 guidelines by a pulmonary disease specialist.

After obtaining informed consent from the patients to participate in the study, all demographic information, comorbidities, and clinical characteristics were recorded. All participants received standard medical care, which included bronchodilators, steroids, antibiotics, oxygen therapy, and other interventions based on clinical indications. This encompassed respiratory support (non-invasive ventilation, mechanical ventilation), fluid management (intravenous fluids, diuretics), treatment of comorbidities (such as heart failure management, anticoagulation), and pulmonary rehabilitation.

The study received approval from the review board of the Research Ethics Committees at the School of Medicine, Shahid Beheshti University of Medical Sciences (IR.SBMU.MSP.REC.1403.404).

Data gathering

Eligible patients were enrolled in the study at the time of hospital discharge, and follow-up was initiated according to the study protocol. Demographic and basic information, including age, gender, occupational exposures (such as farming or bread baking), body mass index (BMI), smoking status, comorbidities, medication history, and clinical data such as the history of disease exacerbation in the previous 12 months, were collected through face-to-face interviews and review of medical records at the time of discharge. In addition, information on blood cell counts, including absolute eosinophil, neutrophil, lymphocyte, and platelet counts, was obtained

from patients' electronic medical records at the time of initial hospital discharge, based on the most recent laboratory test results.

Follow-up and outcomes

All eligible patients were followed for 12 months post-discharge through telephone interviews to assess the occurrence of the predefined outcomes.

In this study, the primary outcomes included the number of COPD exacerbations, length of hospital stay during follow-up, and 90-day all-cause mortality. Secondary outcomes included ICU admission and the need for systemic corticosteroids.

In this phase of the study, all information was collected using a researcher-made checklist by an internist under the supervision of a pulmonary disease specialist. Data were gathered every 3 months through telephone interviews with patients or their relatives until the end of the follow-up period.

Clinical definitions

An acute exacerbation of chronic obstructive pulmonary disease was defined as an exacerbation of respiratory symptoms such as severe difficulty breathing, thicker mucus, wheezing, and cough, etc., leading to hospitalization, emergency department visit, and ICU admission (13).

Eosinophil-to-Platelet Ratio (EPR): EPR was calculated by dividing the absolute eosinophil count by the absolute platelet count, both expressed in $\times 10^9/L$.

Neutrophil-to-Lymphocyte Ratio (NLR): NLR was calculated by dividing the absolute neutrophil count ($\times 10^9/L$) by the absolute lymphocyte count ($\times 10^9/L$).

Platelet-to-Lymphocyte Ratio (PLR): PLR was calculated by dividing the absolute platelet count ($\times 10^9/L$) by the absolute lymphocyte count ($\times 10^9/L$).

Statistical analysis

Initially, the normal distribution of quantitative variables was assessed using histograms. Quantitative variables were reported as mean and standard deviation (SD) or median and interquartile range (Q1–Q3), and categorical variables were described using frequency and percentage (%). To compare the means of quantitative variables across the EPR quartiles, depending on the normality of distribution, either the one-way ANOVA (parametric) or Kruskal-Wallis (non-parametric) test was used. In addition, for normally distributed variables, the assumption of homogeneity of variances was assessed using Bartlett's test following one-way ANOVA. In addition, a post-hoc analysis was conducted using the Bonferroni test after one-way ANOVA. For comparisons of means between two groups where the variables did not follow a normal distribution, the non-parametric Mann-Whitney U test was used. To assess differences in the distribution of categorical variables, appropriate statistical tests such as the Chi-square test or Fisher's exact test were applied.

Finally, to evaluate the correlation between EPR, NLR, and PLR with the number of COPD exacerbations and the length of hospitalization, Spearman's rank correlation test was used. According to interpretation guidelines, correlation strength was defined as strong (≥ 0.70), moderate ($0.40 - 0.70$), and weak (≤ 0.40), based on the correlation coefficient (rho).

In this study, Poisson regression was used for the outcome of COPD exacerbation number, and negative binomial regression was used for the outcome of the length of hospitalization, both at univariate and multivariable levels, to examine the association of EPR, NLR, and PLR with each outcome and to control for potential confounding variables. Optimal cutoff points for EPR, NLR, and PLR to predict COPD exacerbation number were determined based on the maximum value of the Youden index (sensitivity + specificity − 1). Finally, the association between each parameter and the outcome of interest was evaluated using the appropriate regression models. The assumption of equidispersion was assessed for Poisson regression; when evidence of overdispersion was present, negative binomial regression was used instead. Model goodness-of-fit was assessed using the lowest log-likelihood and Akaike Information Criterion (AIC) values. Results of the models were reported as relative risk (RR).

All statistical analyses were two-sided with a 95% confidence level and a significance level of less than 0.05. Data analysis was performed using STATA version 17(StataCorp LLC, College Station, TX 77845, USA).

RESULTS

Description of patients' information

The current study investigated 249 people diagnosed with COPD. The mean age of the patients was 65.66±9.17 years, with 83.94% (n=209) being male. The primary underlying disease in these patients was hypertension, present in 32.53% of cases. 89.56% of patients were current smokers, whereas 10.04% indicated occupational exposure linked to COPD, such as in bread baking or farming. Furthermore, 56.22% of the patients (n=140) had a history of COPD exacerbations in the last year (Table 1). The median EPR for all patients was 0.4, with an interquartile range of 0.95 to 0.09. When categorizing EPR in patients by quartiles, 63 patients (25.30%) were placed in quartile 1 (≤ 0.1), 122 patients (49%) were within the range of quartile 1 to quartile 3 (0.1 - 0.95), and 64 patients (25.70%) were categorized in quartile 3 (> 0.95) (Table 2).

After comparing demographic and baseline characteristics among the EPR groups, only the mean body mass index (BMI) and the prevalence of chronic kidney disease showed statistically significant differences (P<0.05). Specifically, individuals with an EPR > 0.95 had a higher mean BMI and a greater prevalence of chronic kidney disease compared to the other groups (Table 1).

Table 1. Demographic and clinical characteristics of COPD patients based on Eosinophil-to- platelets ratio (EPR) quartiles

Variables	EPR ≤ 0.1 (≤ Q1, n = 63)	EPR (0.1 – 0.95) (Q1 – Q3, n= 122)	EPR > 0.95 (> Q3, n=64)	Total (n =249)	P_value
Age (Years)	65.87 ± 9.35	64.91 ± 8.88	66.87 ± 9.53	65.66 ± 9.17	0.377
Gender					
Female	9 (14.29)	21 (17.21)	10 (15.63)	40 (16.06)	0.871
Male	54 (85.71)	101 (82.79)	54 (84.38)	209 (83.94)	
Body mass index (BMI, kg/m²)	23.39 ± 5.44	24.56 ± 5.43	**25.81 ± 5.55 ***	24.59 ± 5.51	**0.041***
Underlying disease (YES)					
Diabetes	9 (14.29)	12 (9.84)	7 (10.94)	28 (11.24)	0.660
Hypertension	27 (42.86)	35 (28.69)	19 (29.69)	81 (32.53)	0.128
Ischemic heart diseases	6 (9.52)	11 (9.02)	10 (15.63)	27 (10.84)	0.359
Congestive Heart Failure	2 (3.17)	2 (1.64)	0 (0.0)	4 (1.61)	0.278
Benign prostatic hyperplasia	2 (3.17)	2 (1.64)	2 (3.13)	6 (2.41)	0.648
Chronic kidney diseases	0 (0.0)	0 (0.0)	3 (4.69)	3 (1.20)	**0.032***
Others[1]	3 (4.76)	4 (3.28)	2 (3.13)	9 (3.61)	0.825
Exposures and history (Yes)					
Current smoker	58 (92.06)	107 (87.70)	58 (90.63)	223 (89.56)	0.622
Occupational exposures [2]	5 (7.94)	15 (12.30)	5 (7.81)	25 (10.04)	0.510
COPD exacerbations during the past year	39 (61.90)	69 (56.56)	32 (50.0)	140 (56.22)	0.399
Medication history (Yes)					
Bronchodilator	63 (100.0)	121 (99.18)	64 (100.0)	248 (99.60)	1.000
Antibiotic	62 (98.41)	122 (100.0)	64 (100.0)	248 (99.60)	0.253

Data described as mean ± standard deviation or frequency and percentage

[1] Such as any type of cancer, rheumatoid arthritis, and thyroid dysfunction; [2] such as farming or bread baking

Comparing the EPR, NLR, and PLR values between outcomes

Table 2 presents the median values of the studied indices (EPR, NLR, and PLR), along with the distribution of clinical outcomes. The median number of COPD exacerbations among all patients was 2, with an interquartile range (IQR) of 1 to 3. During the 90-day follow-up period, the mortality rate was 2.81% (n=7). The median length of hospital stay due to COPD exacerbations was 12 days, with an IQR of 7 to 16 days. During follow-up, 98.39% of patients required corticosteroid therapy, and 3.21% were admitted to the ICU. Comparison of the distribution of each clinical outcome across EPR groups showed no statistically significant differences (P>0.05) (Table 2).

Table 3 presents a comparison of the median values of EPR, NLR, and PLR, as well as their categorized distributions based on Youden's index, across clinical outcomes. Regarding 90-day mortality, only the median NLR was statistically different between deceased and alive patients (P=0.023). The median NLR in deceased patients was higher than in surviving patients. Moreover, all deceased individuals had an elevated NLR (>2.5).

In terms of corticosteroid requirement, the median values of EPR and PLR were higher in patients who required corticosteroids compared to those who did not. However, this difference was not statistically significant (P>0.05), unlike NLR (Table 3).

Table 2. Comparison of laboratory factors and clinical outcomes based on Eosinophil-to- platelets ratio (EPR) quartiles

Variables	EPR ≤ 0.1 (≤ Q1, n = 63)	EPR (0.1 – 0.95) (Q1 – Q3, n= 122)	EPR > 0.95 (> Q3, n=64)	Total (n =249)	P_value
Laboratory's finding					
Neutrophil (count/ µL)	6320 (4760 – 8700)	6060 (4440 – 8217)	5218.5 (3880 – 6906)	5964 (4346 – 7839)	**0.049***
Lymphocyte (count/ µL)	1080 (643 – 1564)	1767.50 (1200 – 2480)	1870.50 (1450 – 2525)	1590 (1038 – 2240)	**<0.001***
Eosinophil (count/ µL)	8.40 (0 – 12.6)	91.50 (46.8 – 128)	274.45 (207.8 – 398)	92 (19.6 – 194)	**<0.001***
Platelets (count/µL)	201000 (166000 – 247000)	224000 (169000 – 268000)	194500 (153500 – 234500)	206000 (166000 – 255000)	**0.032***
Eosinophil-to-platelets ratio (EPR)	0.04 (0 – 0.06)	0.40 (0.25 – 0.54)	1.32 (1.02 – 1.97)	0.40 (0.09 – 0.95)	**<0.001***
Neutrophil-to-lymphocyte ratio (NLR)	6.67 (3.61 – 8.76)	3.36 (2.21 – 5.40)	2.63 (1.78 – 3.86)	3.52 (2.33 – 6.42)	**<0.001***
Platelets-to-lymphocyte ratio (PLR)	198.84 (139.92 – 303.86)	129.36 (94.25 – 184.40)	101.66 (78.26 – 133.82)	131.74 (93.37 – 196.76)	**<0.001***
Outcomes					
COPD exacerbation number	2 (1 – 3)	2 (1 – 3)	1 (1 – 2)	2 (1 – 3)	0.133
90-days mortality					
No	61 (96.83)	119 (97.54)	62 (96.88)	242 (97.19)	1.000
Yes	2 (3.17)	3 (2.46)	2 (3.13)	7 (2.81)	
Length of hospital stay (LOS, days)	12 (6 – 17)	11 (7 – 16)	13 (10 – 16)	12 (7 – 16)	0.113
Need to systemic corticosteroids					
No	1 (1.59)	2 (1.64)	1 (1.56)	4 (1.61)	1.000
Yes	62 (98.41)	120 (98.36)	63 (98.44)	245 (98.39)	
ICU admission					
No	61 (96.83)	118 (96.72)	62 (96.88)	241 (96.79)	1.000
Yes	2 (3.17)	4 (3.28)	2 (3.13)	8 (3.21)	

Data described as median and interquartile range or frequency and percentage

[1] Such as any type of cancer, rheumatoid arthritis, and thyroid dysfunction

Table 3. Comparison of EPR, NLR and PLR based on clinical outcomes

Factors	Outcomes		
	90-days mortality		P_value
	No (n = 242)	Yes (n = 7)	
Eosinophil-to-platelets ratio (EPR)	0.40 (0.09 – 0.95)	0.42 (0.05 – 0.96)	0.784
EPR ≤ 1	187 (77.27)	7 (100.0)	0.353
EPR >1	55 (22.73)	0 (0.0)	
Neutrophil-to-lymphocyte ratio (NLR)	**3.45 (2.30 – 6.10)**	**7.71 (3.55 – 18.40)**	**0.023***
NLR ≤ 2.5	72 (29.75)	0 (0.0)	0.198
NLR >2.5	170 (70.25)	7 (100.0)	
Platelets-to-lymphocyte ratio (PLR)	132.62 (92.10 – 197.05)	115.22 (96.61 – 145.68)	0.523
PLR ≤ 196	178 (73.55)	6 (85.71)	0.680
PLR > 196	64 (26.45)	1 (14.29)	
	Need systemic corticosteroids		P_value
	No (n = 4)	Yes (n = 245)	
Eosinophil-to-platelets ratio (EPR)	0.32 (0.09 – 0.73)	0.40 (0.09 – 0.95)	0.636
EPR ≤ 1	3 (75.0)	191 (77.96)	1.000
EPR >1	1 (25.0)	54 (22.04)	
Neutrophil-to-lymphocyte ratio (NLR)	4.06 (3.49 – 5.57)	3.48 (2.30 – 6.41)	0.568
NLR ≤ 2.5	0 (0.0)	72 (29.39)	0.327
NLR >2.5	4 (100.0)	173 (70.61)	
Platelets-to-lymphocyte ratio (PLR)	124.23 (59.60 – 189.63)	131.74 (93.70 – 196.76)	0.454
PLR ≤ 196	3 (75.0)	181 (73.88)	1.000
PLR > 196	1 (25.0)	64 (26.12)	
	ICU admission		P_value
	No (n = 241)	Yes (n = 8)	
Eosinophil-to-platelets ratio (EPR)	0.40 (0.09 – 0.95)	0.38 (0.17 – 0.76)	0.770
EPR ≤ 1	186 (77.18)	8 (100.0)	0.206
EPR >1	55 (22.82)	0 (0.0)	
Neutrophil-to-lymphocyte ratio (NLR)	3.47 (2.30 – 6.10)	7.44 (3.03 – 13.40)	0.106
NLR ≤ 2.5	71 (29.46)	1 (12.50)	0.444
NLR >2.5	170 (70.54)	7 (87.50)	
Platelets-to-lymphocyte ratio (PLR)	132.77 (92.10 – 197.05)	117.09 (105.32 – 137.64)	0.539
PLR ≤ 196	177 (73.44)	7 (87.50)	0.684
PLR > 196	64 (26.56)	1 (12.50)	

Data described as median and interquartile range (Q1 – Q3) or frequency and percentage

*Statistically significant, P<0.05

Correlation of clinical indices with outcomes

After assessing the correlation between EPR, NLR, and PLR values with the number of severe COPD exacerbations and the number of hospitalization days, only a significant positive and weak correlation was observed between EPR and the number of hospitalization days (rho=0.13, P=0.038). This indicates that higher EPR values were associated with a longer duration of hospitalization. Details of the correlation analysis between these indices and the clinical outcomes are illustrated in Figure 1.

Association of clinical indices with COPD exacerbation number

The results of the univariable (Model 1) and multivariable (Models 2 and 3) analyses for predicting the number of severe COPD exacerbations based on the EPR, NLR, and PLR indices are presented in Table 4. In the univariable analysis, only EPR was significantly associated with the number of COPD exacerbations (P=0.018). A similar association was observed in Model 2, after adjusting for age and sex. In this model, individuals with

EPR≤1 had a 31% higher risk of experiencing a greater number of exacerbations compared to those with EPR > 1 (RR=1.31, 95% CI:1.04–1.65, P=0.018). After further adjustment for additional confounding variables in Model 3, the association remained in the same direction, although it was no longer statistically significant (RR=1.17, 95% CI: 0.92–1.49, P=0.195) (Table 4).

Association of clinical indices with number of hospitalization days

In the univariable analysis, none of the three indices showed a statistically significant association with the number of hospitalization days (P > 0.05). However, after adjusting for potential confounding variables in Model 3, it was observed that individuals with EPR ≤ 1 had a 16% lower risk of prolonged hospitalization compared to those with EPR> 1 (RR=0.84, 95% CI:0.72–0.98, P=0.036). Details of these analyses are presented in Table 5.

Finally, although having NLR > 2.5 appeared to act as a risk factor and PLR > 196 appeared to have a protective effect regarding the number of severe respiratory exacerbations and days of hospitalization, neither of these associations reached statistical significance (P>0.05).

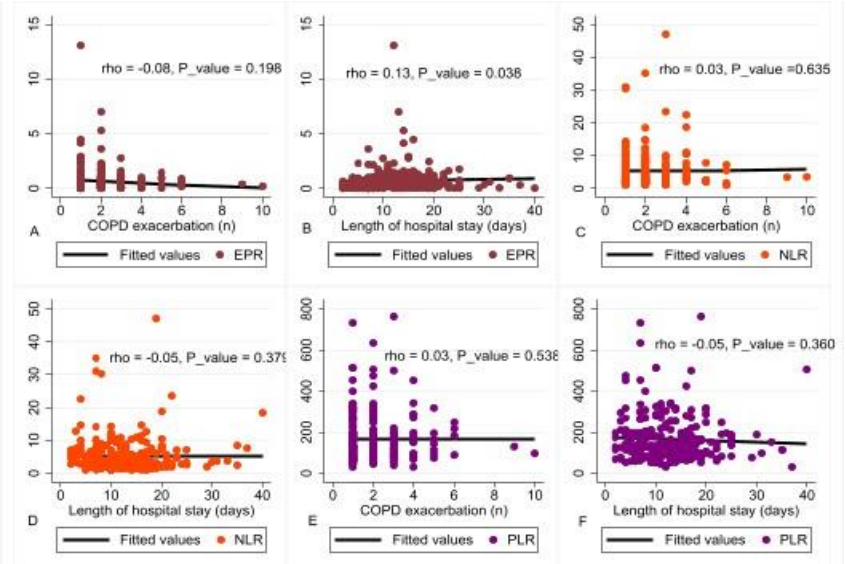

Figure 1. Correlation of EPR (A, B), NLR (C, D) , PLR (E,F) with COPD exacerbation number and length of hospital stay

Table 4. Results of univariate and multivariable Poisson regression on the association of EPR, NLR and PLR with COPD exacerbation number

Factor		Model 1 Crude RR[1], 95% CI	P_value	Model 2 Adjusted RR, 95% CI	P_value	Model 3 Adjusted RR, 95% CI	P_value
EPR	**>1**	Reference	**0.018***	Reference	**0.018***	Reference	0.195
	≤ 1	**1.31**		**1.31**		1.17	
		(1.04 – 1.65)		**(1.04 – 1.65)**		(0.92 – 1.49)	
NLR	**≤ 2.5**	Reference	0.490	Reference	0.371	Reference	0.907
	> 2.5	1.22		1.30		1.01	
		(0.69 – 2.14)		(0.73 – 2.31)		(0.82 – 1.24)	
PLR	**≤ 196**	Reference	0.871	Reference	0.966	Reference	0.478
	>196	0.98		1.004		0.92	
		(0.80 – 1.19)		(0.82 – 1.22)		(0.75 – 1.13)	

** Statistically significant, P_value < 0.05*

[1]Relative risk: 95% Confidence Interval

*Model 1: **EPR or NLR or PLR***

*Model 2: gender, age, **EPR or NLR or PLR***

*Model3: gender, age, **EPR or NLR or PLR**, body mass index, history of diabetes, hypertension, ischemic heart diseases, chronic kidney diseases, smoking, job-related exposures, COPD exacerbations during the past year*

Table 5. Results of univariate and multivariable negative binomial regression on the association of EPR, NLR and PLR with length of hospital stay

Factor		Model 1 Crude RR[1] , 95% CI	P_value	Model 2 Adjusted RR, 95% CI	P_value	Model 3 Adjusted RR, 95% CI	P_value
EPR	**>1**	Reference	0.367	Reference	0.298	Reference	**0.036***
	≤ 1	0.93		0.92		**0.84**	
		(0.79 – 1.08)		(0.78 – 1.07)		**(0.72 – 0.98)**	
NLR	**≤ 2.5**	Reference	0.395	Reference	0.201	Reference	0.261
	> 2.5	1.06		1.09		1.08	
		(0.92 – 1.23)		(0.95 – 1.26)		(0.94 – 1.25)	
PLR	**≤ 196**	Reference	0.100	Reference	0.127	Reference	0.071
	>196	0.88		0.89		0.87	
		(0.76 – 1.02)		(0.76 – 1.03)		(0.75 – 1.01)	

** Statistically significant, P < 0.05*

[1]Relative risk 95% Confidence Interval

*Model 1: **EPR or NLR or PLR***

*Model 2: gender, age, **EPR or NLR or PLR***

*Model3: gender, age, **EPR or NLR or PLR**, body mass index, history of diabetes, hypertension, ischemic heart diseases, chronic kidney diseases, smoking, job-related exposures, COPD exacerbations during the past year*

DISCUSSION

In this cohort study of 249 patients with COPD exacerbation, we investigated the predictive ability of three hematological indices such as eosinophil-to-platelet ratio (EPR), neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR) in relation to short-term clinical outcomes, including the number of exacerbations, hospitalization duration, 90-day mortality, ICU admission, and corticosteroid use. Our findings suggest that EPR may serve as a potential marker for both the frequency of COPD exacerbations and the length of hospital stay, although the strength of these associations varied across statistical models. Notably, a lower EPR (≤1) was independently associated with an increased number of exacerbations and shorter hospitalization, even after adjustment for confounders. In contrast, while PLR and NLR showed trends in relation to outcomes, their associations were not statistically significant in most models. These findings contribute to the growing body of evidence suggesting that simple, readily available blood indices may hold clinical utility in risk stratification and outcome prediction in patients with COPD exacerbations.

In line with the results of our study, Hu et al. evaluated the prognostic role of EPR in 508 patients with COPD exacerbation and found that an EPR < 0.755 was significantly associated with higher mortality, particularly among those presenting to the emergency department. There was no difference in COPD exacerbations and hospital readmission based on EPR groups (14). We observed that EPR ≤1 was independently associated with an increased number of COPD exacerbations and shorter hospitalization, even after adjustment for confounders. Although we were unable to further investigate the association between EPR and mortality due to the low number of deaths, we observed that all deceased patients had an EPR less than 1. Also, Yogesh et al. mentioned that EPR is a useful prognostic marker of clinically significant in-hospital outcomes during COPD exacerbations. EPR <0.755 was a significant predictor of adverse events (15).

Therefore, the potential role of EPR in predicting COPD complications such as mortality and hospitalization warrants further investigation in future studies.

Albuaini et al. found that COPD patients with eosinophil counts ≤300 cells/μL had worse clinical outcomes, including longer hospital stays, higher ICU admission and mechanical ventilation rates, and greater mortality, compared to those with higher eosinophil counts (>300 cells/μL) (16). The results of Albuaini et al. are

partially inconsistent with ours, likely due to methodological differences, particularly the direct assessment of eosinophil count in relation to outcomes in their study, which was not performed in ours.

Studies evaluating the prognostic role of eosinophil count in COPD exacerbation have shown inconsistent findings. In a systematic review, Chen et al. reported a significant association between high blood eosinophil counts (especially >300 cells/μL) and increased risk of COPD exacerbation, particularly among patients from Europe and Asia, regardless of baseline status or follow-up duration (17). In contrast, Martínez-Gestoso et al. found no significant association between eosinophil levels and clinical outcomes such as hospital stay, readmission, ICU admission, or mortality, either during the stable or acute phase of the disease (18). In our study, we assessed the EPR rather than the absolute eosinophil count alone. This difference in approach may partially explain the discrepancies between our findings and those of previous studies that focused solely on eosinophil counts. Unlike absolute eosinophil levels, EPR incorporates platelet count, which may reflect additional inflammatory or thrombotic processes (19). Therefore, EPR could provide a more comprehensive marker of systemic inflammation in COPD exacerbation (19). However, it may also dilute or alter the direct association observed in studies evaluating eosinophils independently. This methodological difference emphasizes the importance of considering the choice of biomarker and composite indices when comparing findings across studies.

One possible explanation for the observed association between lower EPR values and a higher number of COPD exacerbations, yet fewer days of hospitalization, could lie in the nature and severity of the exacerbations. Patients with lower EPR may experience frequent but milder exacerbations that do not require prolonged inpatient care (20). These exacerbations might be managed more rapidly with outpatient or short-term treatments, leading to a higher exacerbation count but shorter hospital stays on average.

Additionally, since EPR reflects a balance between eosinophilic and platelet-related inflammatory activity, a lower EPR may indicate reduced eosinophilic inflammation or increased platelet levels, which could be associated with different exacerbation phenotypes, such as non-eosinophilic COPD, which tends to be more frequent but less responsive to steroids and possibly less severe in terms of hospitalization needs (14,21).

Furthermore, patients with lower EPR may receive earlier interventions (such as frequent corticosteroid use), resulting in shorter hospital stays despite repeated exacerbations (21). However, this interpretation requires careful consideration, and further research is needed to clarify the biological mechanisms linking EPR to exacerbation frequency and hospitalization duration.

Limitations

As the study was conducted in a single tertiary care hospital and with a small sample size, the generalizability of the findings to broader populations, different healthcare settings, or geographic regions may be limited. Furthermore, outcome data such as hospital readmissions, corticosteroid use, and exacerbation frequency were collected through telephone interviews, which may be subject to recall bias or underreporting, particularly among elderly participants or their caregivers.

CONCLUSION

Based on our findings, EPR may serve as a potential predictor of certain clinical outcomes in patients with COPD exacerbation. Specifically, the association between lower EPR values and a higher number of exacerbations, as well as shorter hospital stays, suggests that EPR could reflect distinct exacerbation phenotypes or patterns of disease activity. However, further prospective studies are needed to validate EPR as a reliable prognostic biomarker in this population.

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Ethical approval and consent for publication

Participation in this study was voluntary. This means patients did not have to participate if they did not want to. Informed consent was obtained from all participant or their guardian. This study was approved by the ethics committee and review board of the Faculty of Medicine, Shahid Beheshti University of Medical Sciences, with the number IR.SBMU.MSP.REC.1403.404.

Conflict of interest

The authors declare no conflict of interest.

Availability of data and materials

The individual data are confidential and cannot be shared according to the ethics committee decision. But the datasets used during the current study are available from the corresponding author upon reasonable request.

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