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Blood and sputum eosinophilia in COPD exacerbation

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Abstract

Background: Exacerbations in chronic obstructive pulmonary disease (COPD) are major contributors to worsening lung function, impaired quality of life, emergency healthcare use, and COPD-related mortality. COPD exacerbations are heterogeneous in terms of airway inflammation and etiology.

Objectives: To assess the relation between blood and sputum eosinophils and COPD exacerbation.

Subjects and methods: Prospective cohort study, conducted on 100 COPD patients presented in outpatient clinic. All patients were subjected to medical history including: occupational history, smoking history, comorbidity, number of exacerbations in last year and their degree, history of admission in the last year and treatment taken for COPD. Modified Medical Research Council scale of dyspnea, peak expiratory flow rate, oxygen saturation using pulse oximetry. Complete blood count with differential eosinophilic count. Sputum sample differential cell count was done.

Results: The eosinophil level in blood before and after treatment showed a significant positive correlation with the number of hospital admission in the last year ($r = 0.29$; $P = 0.003$ and $r = 0.3$; $P = 0.002$, respectively). Regarding the eosinophil level either in blood or in sputum, it showed significant statistical elevation in patients not using steroid treatment in comparison to patients who used systemic or inhaled steroid treatments ($P < 0.001$ and 0.004 , respectively).

Conclusion: Blood eosinophil count can be used as a severity marker of COPD exacerbations. The eosinophil levels, either in blood or sputum, were significantly correlated with the degree of exacerbation. Sputum eosinophilia can also predict the risk of hospitalization. In addition, blood eosinophil count can direct the use of oral corticosteroids in exacerbation.

Keywords: Exacerbations, Chronic obstructive pulmonary disease, Eosinophilic count

Introduction

Exacerbations in chronic obstructive pulmonary disease (COPD) are major contributors to worsening lung function, impaired quality of life, emergency healthcare use, and COPD-related mortality [1].

Even though COPD is habitually considered as inflammation mediated by neutrophils, eosinophils are present in the sputum and blood of some patients with COPD,

whether during stable disease or acute exacerbation of COPD (AECOPD) [2–4]. The phenotype of COPD, which is associated with elevated eosinophil counts, showed a severe exacerbation form with long stay time in hospital and a higher readmission rate [5].

The frequency of AECOPD seems to be related to blood eosinophil level and seems to worsen in patients not receiving ICS and was more marked for severe events [6].

Objectives

To assess the relation between blood and sputum eosinophils and COPD exacerbation.

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Methods

Study design and population

This is a prospective cohort study conducted on 100 COPD patients who admitted or presented in the outpatient clinic of Abbasia Chest Hospital from January 2018 to October 2018 for exacerbation of COPD.

Exclusion criteria

- History of conditions known to cause eosinophilia, e.g., drug allergies and parasitic infestations
- Other eosinophilic pulmonary diseases as asthma, allergic bronchopulmonary aspergillosis, and hyper-eosinophilic syndrome

Patient’s evaluation

- All patients were asked about their occupational history, smoking history and index [7], comorbidity, number of exacerbations in the last year and their degree, and history of hospital admission in the last year
- Complete clinical examination, including Modified Medical Research Council (mMRC) scale of dyspnea [8], peak expiratory flow rate, and oxygen saturation by pulse oximetry
- Laboratory investigation including complete blood count (CBC) with differential count (eosinophilic count), liver function test (SGOT and SGPT), kidney function test (urea and creatinine), and sodium and potassium levels
- Sputum and blood cytology: The sputum sample was collected at the time of presentation and after treatment, and the differential cell count was evaluated as Hastie et al. methods, 2017; hence, the patients were considered to be eosinophilic if the sputum level exceeds 2% and there is blood eosinophilia of 0.3×10^9 cells/L or greater [9].

Statistical methods

The data were collected and statistically analyzed by Minitab 17.1.0.0 for windows (*Minitab Inc., 2013, PA, USA*). Continuous data are presented as mean and SD and categorical data as number and percentage; the normality of data was examined using the Shapiro-Wilk test. Comparison between two continuous groups was done using an independent *t* test. A Pearson correlation coefficient was used to estimate the linear relationship between two or more numerical variables; the sign before the “r” represents the direction of the relationship. All

tests were two-sided, and *P* was considered significant if < 0.05 .

Results

The demographic characters of patients are summarized in Table 1, the mean (SD) age of patients was 59 (10) years, most of them were males (86%) and smoker (70%). The mean (SD) smoking index was 447 (234). More than half (51%) of patients showed compensated ABG. The dyspnea scale-mMRC mean was 3.17 ± 0.91 , the mean peak expiratory flow rate (PEFR) was 307.95 mL, (64%) of cases showed blood eosinophilia, and (51%) had sputum eosinophilia (Fig. 1). The mean (SD) level of eosinophils in blood and sputum was 5.21 ± 3.98 and $3.89 \pm 4.16 \times 10^3 \mu\text{L/mL}$, respectively, and ranged from (0.47–19.9) and (0–20) $\times 10^3 \mu\text{L/mL}$, respectively, as shown in Table 2.

Both eosinophil levels in blood and in sputum were significantly higher in groups with severe COPD exacerbation than in mild and moderate groups ($P < 0.001$), as in Table 3.

Repeated admission was significantly and positively correlated with sputum eosinophils ($r = 0.28$; $P = 0.004$ and $r = 0.26$; $P = 0.008$) respectively (Fig. 2).

Almost all (83%) of cases were treated by steroids, and only 17% refused steroid therapy in management as mentioned in Table 4; the group that was treated by steroid therapy either systemic or inhaler had a significantly lower level of eosinophils in blood and sputum than the other group, $P < 0.001$ and 0.004 , respectively.

Table 1 Demographic data of patients

Factors	Total (n = 100)	
Age	Mean	SD
	58.78	9.818
	Min	Max
Sex	42	88
	N	%
	Female	14
Smoking status	Male	86
	N	%
	Smoker	70
Smoking index	Ex-smoker	26
	Non-smoker	4
	Mean	SD
447.47	233.73	
Min	Max	
102.20	985.50	

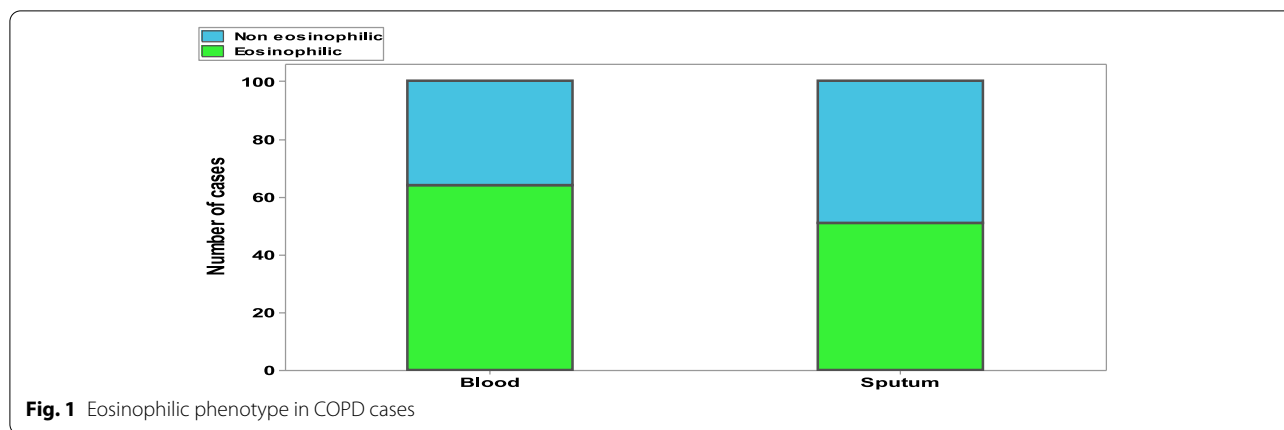


Fig. 1 Eosinophilic phenotype in COPD cases

Table 2 Eosinophilic count in blood and sputum and respiratory parameter assessment of patients

Factors	Total (n = 100)			
	Mean	SD	Min	Max
Respiratory parameters				
mMRC	3.17	0.91	2	4
PEFR (mL)	307.95	91.17	160	500
O2 saturation%	89.61	3.14	80	94
Arterial blood gas assessment				
	N	%		
Compensated	51	51		
Not compensated (RF type 2)	49	49		
Eosinophilic count in blood (cells/L)	5.21	3.98	0.47	19.50
Eosinophilic count in sputum	3.86	4.16	0	20

Table 3 Correlation between the “E” level in blood and sputum with exacerbation severity

Factors	Mild and moderate (n = 63)		Severe (n = 37)		P [§]
	Mean	SD	Mean	SD	
Eosinophilic count in blood	3.41	2.33	8.27	4.36	< 0.001
Eosinophilic count in sputum	2.05	1.95	6.95	5.04	< 0.001

[§] Independent t test, P is considered significant if < 0.05

Discussion

COPD is a mixed condition that involved many clinical and pathophysiological mechanisms, which showed a degree of variation in its severity in between the patients [10]. This mixture induced much variability in the responses to pharmacological treatments. Biomarkers that predict treatment responses to anti-inflammatory drugs may be useful for augmenting the benefit versus hazard ratio [11].

In COPD patients, sputum eosinophil counts predict the clinical outcome of corticosteroids [12]. On the other hand, using sputum eosinophils as a marker needs a time for induction; besides, some patients were incapable of giving adequate samples. For these reasons, measuring blood eosinophils is more convenient and appears to be a surrogate biomarker for sputum eosinophils as these measurements show a degree of correlation within the same individual, both in stable COPD patients and during exacerbations [13, 14].

In the current study, the level of eosinophils in blood at examination time was $0.521 \text{ cells} \times 10^9/\text{L}$, which was slightly higher than Couillard et al’s study [15], as the estimated level of blood eosinophils was $0.1 \text{ cells} \times 10^9/\text{L}$ in total cases and $0.3 \text{ cells} \times 10^9/\text{L}$ in eosinophilic groups. Another study [16] found that 17.9% of patients had a relative blood eosinophil level $> 0.3 \text{ cells} \times 10^9/\text{L}$, while the rest of the patients were below that level.

In correlating the blood and sputum eosinophils with exacerbation severity, the data showed significant statistical elevation in severe exacerbation groups than in mild to moderate groups, $P < 0.001$ for all. In addition, the level of eosinophils in sputum was significantly correlated positively with the number of admission to hospital in the last year ($r = 0.28$; $P = 0.004$ and $r = 0.26$; $P = 0.008$), respectively, which came in harmony with Couillard et al’s results [15], who recorded that 55 of 167 COPD cases had higher blood eosinophils; besides, the higher eosinophil level was associated with increasing the risk of readmission three times more than the other patients with lower eosinophils and gave a conclusion that blood eosinophils could be used as a marker of severe COPD exacerbation with higher readmission rate. Yun et al. [17] agreed and concluded that blood eosinophils $\geq 0.3 \text{ cells} \times 10^9/\text{L}$ were associated with increased exacerbation frequency.

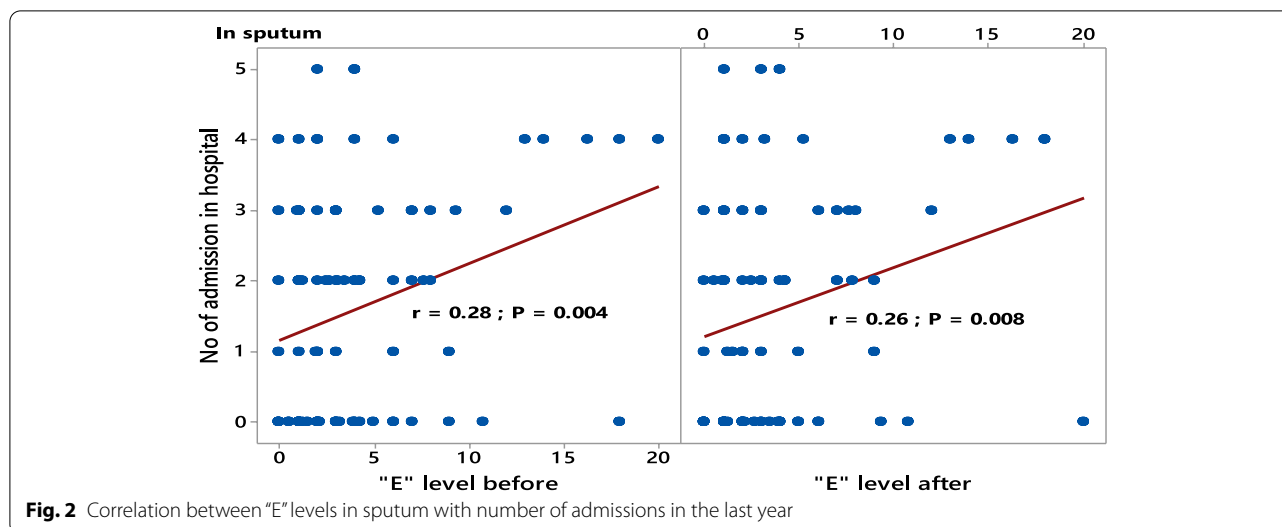


Table 4 Correlation between the “E” level in blood and sputum with steroid treatment

Steroid source	N	E in blood		E in sputum	
		Mean	SD	Mean	SD
Refused treatment	17	6.54	2.96	7.02	4.61
Steroid use	83	3.22	2.97	3.09	3.8
<i>p</i> ^s		< 0.001		0.004	

^sIndependent t test, *P* considered significant if < 0.05

The value of high blood eosinophils in predicting the exacerbation risk in COPD has also been examined in a recent large population study, which showed that the risk of both moderate and severe exacerbations was increased with higher eosinophil counts, but the effect was more pronounced in the severe exacerbation group. This might indicate that these patients may have a distinct inflammatory profile, making them more susceptible to developing severe events [18, 19].

The current study reported that blood and sputum eosinophils were significantly higher in patients who did not receive systemic or inhaled steroids rather than patients who received systemic or inhaled steroids, *P* < 0.001 and 0.004, respectively. A recent post hoc analysis [20] confirmed the use of the peripheral blood eosinophil counts as a predictor of exacerbation risk and ICS treatment response in patients with COPD. Another contrary study [16] included 32,693 COPD patients to evaluate the correlation between the blood eosinophil level and the related risk of hospitalization and mortality, besides examining the impact of ICS in admission rate or mortality. The results revealed that there were insignificant impacts of both high blood eosinophil

level and ICS use, on both readmission and mortality rate. A recent study [21] included 493 cases with COPD reporting that patients with lower eosinophil counts experienced poorer clinical outcomes, and eosinophil levels may be a helpful marker to predict outcomes in AECOPD. The better outcome may be related to a better response to systemic steroids in the eosinophilic group [22].

Cai and Wang [21] concluded that eosinophils as a blood marker of COPD remain controversial and more basic and systematic experiments are needed to clarify the pathogenesis of blood eosinophils in patients with COPD to better serve the clinic in the future.

The limitation of the study includes the study was unicentric and was conducted on a limited number of patients. Another limitation is that patients were not classified regarding their airflow limitation and were not followed throughout the exacerbation to trace the outcome.

Conclusion

Blood eosinophil count can be used as a severity marker of COPD exacerbations. The eosinophil levels, either in blood or sputum, were significantly correlated with the degree of exacerbation. Sputum eosinophilia can also predict the risk of hospitalization. In addition, blood eosinophil count can direct the use of oral corticosteroids in exacerbation.

Abbreviations

AECOPD: Acute exacerbation of COPD; CBC: Complete blood picture; COPD: Chronic obstructive pulmonary disease; ICS: Inhaled corticosteroids; mMRC: Modified Medical Research Council; SGOT: Serum glutamic-oxaloacetic transaminase; SGPT: Serum glutamic pyruvic transaminase.

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Authors' contributions

LAH Choosing the research subject, Revising the manuscript. EBA Choosing the research subject, Writing the manuscript, Follow up the patient data collection. HMA Follow up the patient data collection, Practical part of the research. All authors have read and approved the final manuscript.

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Availability of data and materials

Tables are included.

Declarations**Ethics approval and consent to participate**

The study protocol was reviewed and accepted by the institution ethical committee of scientific research, Faculty of Medicine, Ain Shams University (FMASU MSO 01/2022). Data were collected anonymously from patients' records.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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