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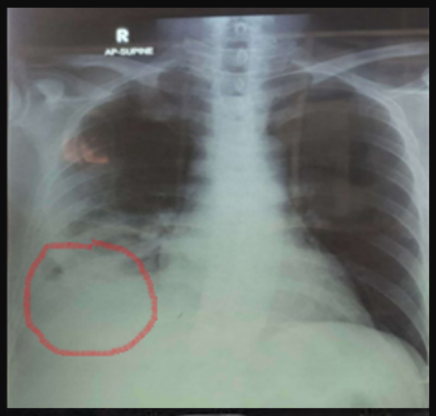

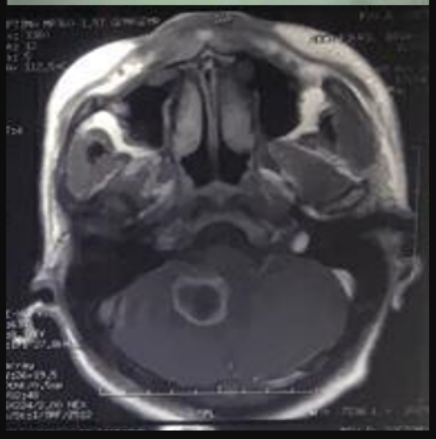

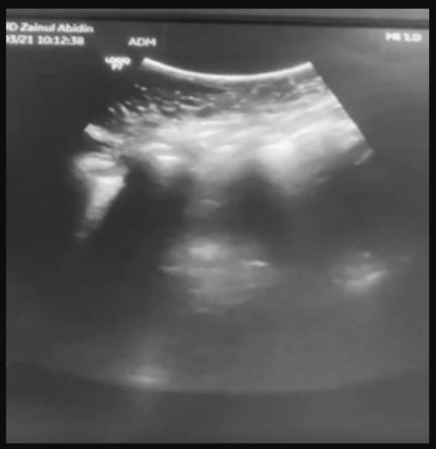

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INTRODUCTION

Jurnal Respirasi (JR) (p-ISSN: 2407-0831, e-ISSN: 2621-8372) was previously named Majalah Kedokteran Respirasi (MKR) which was established in 2010. The chief editor of MKR was Yusuf Wibisono, dr., Sp.P(K), FCCP. In 2015, MKR changed its name to **JR** with Winariani Koesoemoprodjo, dr., Sp.P(K), MARS, FCCP as its chief editor.

JR is a national journal published by Department of Pulmonology & Respiratory Medicine, Faculty of Medicine Universitas Airlangga/Dr. Soetomo General Hospital, Surabaya. **JR** is published three times a year, every January, May, & September, and contains 9 (nine) complete texts in English. **JR** provides a forum for original article, case reports, and literature reviews.

ACCREDITATION

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FOCUS AND SCOPE

This journal publishes various scientific works on the medical world, especially in the field of Pulmonology and Respiratory Medicine, such as:

- Tuberculosis
- Pneumonia
- Lung Cancer
- Asthma
- Chronic Obstructive Pulmonary Disease (COPD)
- Asthma-COPD Overlap Syndrome (ACOS)
- Mediastinal Tumor
- Pleural Effusion
- Pneumothorax
- Fluidopneumothorax
- Chemotherapy
- Radiotherapy
- Superior Vena Cava Syndrome (SVCS)
- Cor Pulmonale
- Atelectasis
- Hemoptysis
- Respiratory Distress
- Occupational Respiratory
- Pneumoconiosis
- Obstructive Sleep Apnea (OSA)
- Lung Mycosis
- Pneumocystis carinii
- Middle East Respiratory Syndrome Coronavirus (MERS CoV)
- Severe Acute Respiratory Syndrome (SARS)
- Immunology
- Endobronchial Ultrasound Bronchoscopy Procedure (EBUS)
- Pleurodesis
- Thoracoscopy
- Thoracocentesis
- Ventilator
- Non-Invasive Ventilation (NIV)
- Pulmonary Disease and Other Actions

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ORIGINAL ARTICLE

Correlation between FEV_1% Predicted and Blood Eosinophils in Patients with Exacerbations of Chronic Obstructive Pulmonary Disease (COPD)

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ABSTRACT

Introduction: Chronic obstructive pulmonary disease (COPD) exacerbations are still the leading causes of mortality. Eosinophil counts were recommended in assessing the risk of exacerbations. This additional examination was preferred rather than the pulmonary function test (PFT), which was considered less precise and had vast differences. Therefore, an analysis of the correlation between the FEV1% predicted and blood eosinophil counts were needed as a reference in the diagnosis of COPD exacerbation. This study aimed to determine the correlation between FEV1% predicted and blood eosinophils counts in patients with COPD exacerbations.
Methods: This was a retrospective cross-sectional study by analyzing medical records of patients with COPD exacerbations at Dr. Soetomo General Hospital, Surabaya, from 2017 to 2018.
Results: The characteristics of patients with exacerbations of COPD consisted of 91.7% male patients. Most of them were in the age group of 61-70 years old, 58.3% were in the private sector, 75% had a high school diploma, and 41.7% had normal body mass index (BMI). The percentage of the FEV1% predicted is directly proportional to the percentage of blood eosinophils with weak and statistically insignificant strength.
Conclusion: The FEV1% predicted and blood eosinophil counts had a very weak correlation and statistically insignificant strength. Thus, it could not be used as a reference for diagnosis using one of the variables. Further research is needed with sputum eosinophils and biopsy as consideration for more accurate results.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a persistent and progressive airflow obstruction due to increased inflammation in the airways.[1] Data published by World Health Organization (WHO) shows that the incidences of COPD cause 5% of deaths worldwide in 2015; it is estimated to constantly increasing to become the third-largest cause of deaths in the world by 2030. Furthermore, the irreversible nature of COPD will make it more likely to increase in the coming decades.[2]

The COPD diagnosis was conducted using anamnesis (medical history of patients) and physical examination, which was then confirmed through a pulmonary function test (PFT). This could be diagnosed when the pulmonary function had an FEV_1/FVC ratio below 70% after bronchodilator inhalation.[3] In the PFT, the amount and velocity of air entering and leaving the lungs, along with the quality of the lungs in delivering oxygen to the bloodstream, were measured using a spirometer.[4]

One of the essential parameters in the PFT is the forced expiratory volume in 1 second (FEV_1) examination, which was performed by measuring the volume of air exhaled during the first second of maximum expiration.[5] Through this examination, the severity of airflow obstruction in COPD could be deter- mined. The predictive value of FEV1% or normal

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predictive value of FEV_1 percentage can evaluate the severity of COPD based on mild, moderate, severe, and very severe categories.[6]

The increased severity in COPD patients is associated with the incidence of exacerbations that have a significant and prolonged impact on health status and lung function. A COPD exacerbation is a series of acute worsening of a COPD patient's condition beyond normal daily variations. Therefore, it requires changes in treatment or hospitalization.[7] In the exacerbation conditions, eosinophil counts were needed to assess the risk and success of each therapy.[6] It was chosen because the PFT results were considered less precise and varied greatly.[8] An analysis of the relationship between the FEV_1% predicted and blood eosinophils was needed as a reference in diagnosing COPD exacerbations.

METHODS

This retrospective analytic study used a cross-sectional design. The results were obtained by analyzing the medical record data of exacerbated COPD inpatients at Dr. Soetomo General Hospital, Surabaya, from January 2017 to December 2018.

The inclusion criteria in this study were the exacerbations of COPD patients and inpatients at Dr. Soetomo General Hospital, Surabaya. In contrast, those with a coincidence of other diseases that could affect the prediction of FEV_1% test values and blood eosinophils had been excluded. From the total of 138 study subjects, 110 of them had a secondary disease coincidence, and 16 subjects had incomplete medical record files. Thus, there were only 12 subjects who meet the inclusion criteria.

Data analysis of this study was conducted by performing a normality test and correlation analysis using IBM SPSS 24 program. The normality test was performed using a Kolmogorov-Smirnov (K-S) test, while the correlation assessment was performed using Spearman's correlation analysis.

RESULTS

The characteristics of the study subjects, including gender, age, occupation, education, and body mass index (BMI), can be seen in Table 1.

The study subjects comprised of 91.7% male and 8.3% female with an age range of 48-81 years old, and the mean age was 62.67 years old. About 58.3% of the subjects work in the private sector, and 75% have a high school diploma. Their BMI calculation results ranged from 17.63 to 29.67 with a mean of 22.73, thus most of them were in the normal category as much as 41.7%.

Table 1. Characteristics of the study subjects

Characteristics	N	Minimum	Maximum	Mean	SD
Gender	12 (100%)				
Men	11 (91.7%)				
Women	1 (8.3%)				
Age (Years Old)	12 (100%)	48	81	62.67	± 11,097
41-50	2 (16.7%)				
51-60	3 (25%)				
61-70	4 (33.3%)				
71-80	2 (16.7%)				
81-90	1 (8.3%)				
Occupation	12 (100%)				
Civil Servant	3 (25%)				
Private Employee	7 (58.3%)				
Farmer	2 (16.7%)				
Education	12 (100%)				
Elementary School	2 (16.7%)				
Middle School	1 (8.3%)				
High School	9 (75%)				
Body Mass Index (BMI)	12 (100%)	17.63	29.67	22.73	± 4,521
Severe Underweight	0 (0%)				
Underweight	3 (25%)				
Normal	5 (41.7%)				
Overweight	1 (8.3%)				
Obese	3 (25%)				

The mean percentage of the FEV1% predicted test results of the study subjects was 53.83%, with a score range from 13% to 119%. The results of the FEV_1 %predicted of the subjects indicated that there were 8.3% mild COPD, 41.7% moderate COPD, 33.3% severe COPD, and very severe COPD, as much as 16.7% (Table 2).

The mean percentage of the blood eosinophils of the study subjects was 4.45%, with a range from 0.2% to 23.1%. Thus, the samples that did not experience eosinophilic inflammation were 66.7%, while those who experienced eosinophilic inflammation were 33.3%, characterized by eosinophilic blood levels ≥ 2% (Table 3).

The Kolmogorov-Smirnov (K-S) normality test found that the FEV1% predicted data had a normal distribution. Still, at the same time, the results of the blood eosinophils had an abnormal distribution. The mean of the FEV_1% predicted values were 53.83, whilst the mean percentage of the blood eosinophils was 4.45 (Table 4).

Based on Spearman's correlation test, the correlation coefficient (r_s) obtained between the FEV_1% predicted and the blood eosinophils had a value of 0.14, which indicates a very weak direct proportionality. Furthermore, the p-value of 0.665 (greater than 0.05) indicates that the relationship between the two variables is statistically insignificant (Table 5).

Table 2. FEV_1% predicted test results of the study subjects

Variables	N	Minimum	Maximum	Mean	SD
FEV_1% Predicted (%)	12 (100%)	13	119	53.83	± 28,415
Mild (FEV_1% ≥ 80%)	1 (8.3%)				
Moderate (50% ≤ FEV_1% < 80%)	5 (41.7%)				
Severe (30% ≤ FEV_1% < 50%)	4 (33.3%)				
Very Severe (FEV_1% < 30%)	2 (16.7%)				

Table 3. Percentage of blood eosinophils of the study Subjects

Variables	N	Minimum	Maximum	Mean	SD
Eosinophils (%)	12 (100%)	0.2	23.1	4.45	± 7,080
Non-Eosinophilic (< 2%)	8 (66.7%)				
Eosinophilic (≥ 2%)	4 (33.3%)				

Table 4. Kolmogorov-Smirnov (K-S) normality test results

Variables	N	Mean	SD	P
Predicted FEV_1%	12	53.83	28.415	0.2
Blood Eosinophils	12	4.45	7.080	0.0

Table 5. Spearman's Correlation Test Results

Pulmonary Physiological Variables	N	r_s	P
Predicted FEV1%	12	0.14	0.665

DISCUSSION

Characteristics of the Subjects

The patients with COPD exacerbations were predominantly male, which can be attributed to the smoking habit, which is more common in male. Smoking behaviour can reduce the immune system of the respiratory tract. Furthermore, it also causes a series of inflammatory processes that cause remodelling, resulting in narrowing the airways. With this, respiratory distress symptoms, a decline of FEV_1, and mortality were more remarkable in smokers.[9] Thus, significant changes in the epidemiology of COPD cases occurred due to changes in smoking patterns, which is one of the most critical risk factors for COPD.[10]

The study subjects who experienced COPD exacerbations were between 48-81 years old with a mean of 62.67 years old, and most were between 61-70 years old. Obstruction of the respiratory tract structures and parenchyma get worse as COPD patients aged.[6] In elderly patients, a more rapid and progressive decrease in FEV_1 was found.[11] The effects of smoking, pollutant

exposure, history of acute exacerbations, and BMI may generally worsen in patients with exacerbations of COPD as they aged.

The occupation of study subjects was dominated by the private sector as much as 58.3%. Long-term occupational exposure to air pollutants in the form of vapour, gas, dust, or even smoke can cause obstructive pulmonary dysfunction and affect 15% of the progression of COPD incidences.[12] However, the risk factors could not be identified with certainty due to the limited data, and the group categories were too broad.

Most of the patients had been graduated from high school as much as 75%. Therefore, adequate knowledge could reduce the rate of hospital visits in COPD patients.[13] Meanwhile, a lack of knowledge and understanding had increased consultation and treatment costs in COPD patients.[14] However, the relationship between educational history and the incidences of COPD exacerbations has not been proven because of the limited data on medical records that did not include knowledge, understanding, and lifestyle habits in COPD patients.

Most of the BMI of study subjects were in the normal category. The BMI values that were low or below normal caused chronic obstruction, which worsened the prognosis of patients with exacerbations of COPD. The increased incidences of exacerbations accelerated FEV_1 decline, impaired quality of life (QoL), along with a high mortality rate were frequently found in exacerbated COPD patients with low BMI.[15] On the other hand, the risk of mortality was progressively decreased in COPD patients with a high BMI.[16] Furthermore, COPD patients with low BMI were associated with poor nutritional status, thus their immunity tended to decrease. In contrast, those with normal BMI and high immunity status were better at preventing exacerbations. Meanwhile, a relative increase towards normal BMI affected the reduction of clinical symptoms in COPD exacerbations but did not have a significant effect.[17]

FEV_1% Predicted Test Results of the Study Subjects

The results of the predicted FEV_1% were in the moderate COPD category (41.7%). In another study, the incidences of exacerbations that occurred more than once a year were mostly found in COPD patients with predicted FEV_1% classification of moderate COPD category.[18] The lower the FEV_1% predicted values, the more frequent exacerbations occurred, thus increasing the need for treatment.

Percentage of Blood Eosinophils of the Study Subjects

Most of the complete blood counts (CBCs) were in the non-eosinophilic category (blood eosinophils < 2%) as much as 66.7%. A total of 40% of COPD patients had eosinophilic inflammation,[19] and the cysteinyl leukotriene receptors on the mucosal walls of the airways would have continued to increase during exacerbations.[20] This was characterized by sputum eosinophils > 3% or blood eosinophils ≥ 2%.[21] The increased blood eosinophils in COPD had a one-way relationship with sputum eosinophils. In COPD exacerbations, the percentage of peripheral blood eosinophils ≥ 2% can be used as a sensitive biomarker to determine sputum eosinophils > 3%.[22]

Correlation of FEV_1% Predicted with Blood Eosinophils in COPD Exacerbations

Spearman's correlation coefficient (r_s) of the predicted FEV_1% of PFT and blood eosinophils in patients with COPD exacerbations had a value of 0.14, which indicated a very weak unidirectional correlation. The greater the FEV_1% predicted value, the higher the blood eosinophil levels. The relationship between both variables was not statistically significant, as proven by the p-value of 0.665 (more than 0.05).

Another study showed a significant negative correlation between the increase of FEV_1 and sputum eosinophils in COPD patients.[23] The differences in the study results and this study may occur because of the differences in the study materials studied, namely using blood and sputum eosinophils. Biomarkers of sputum eosinophils were considered to be able to assess lung function better than blood eosinophils. However, systemic blood eosinophils count could not be used to measure the severity of COPD. COPD patients with blood eosinophils ≥ 2% showed no clinical characteristics of symptoms, pulmonary function, exacerbations, and prognosis of COPD.[24] The increased number of peripheral blood eosinophils could identify the decreased lung function but could not indicate the severity of COPD, especially in the cases of exacerbations.[25]

This study was limited to the test of peripheral blood eosinophils without considering other methods such as sputum eosinophils. However, the assessment of sputum eosinophils from blood eosinophils still had limitations with a false discovery rate (FDR) of 72%-74% and a false negative rate (FNR) of 50%.[25] Nevertheless, there was a significant difference in the decrease of blood and sputum eosinophile values in COPD cases with infection.[26] Therefore, further research is needed by considering the type of eosinophil test in patients; moreover, it is also necessary to consider the incidence of infection as a comorbid disease that can affect the value of the study variables.

CONCLUSION

Characteristics of patients with COPD exacerbations in this research was comprised of 91.7% male, most were in the age group of 61-70 years old, 58.3% were working in the private sector, 75% had a high school diploma, and 41.7% had a normal BMI. In addition, the pulmonary function test (PFT) results of the FEV_1% predicted were mainly in the moderate COPD category of 41.7%. On the other hand, the results of the highest percentage of blood eosinophils were in the non-eosinophilic category, as much as 66.7%. Thus, the FEV_1 predicted test results and the percentage of blood eosinophils had a direct proportionality with fragile and statistically insignificant strength.

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