

ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE WITH POLYMORPHIC PHAGOCYtic CELLS

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ABSTRACT

Chronic obstructive pulmonary disease is a progressive non-communicable disease due to the chronic inflammation response. An acute exacerbation is a weighting of the symptoms experienced by the patient before. Acute exacerbations of Chronic obstructive pulmonary disease are thought to be associated with acute inflammation involving pro-inflammatory cells. Bangil Hospital data in 2019, Chronic obstructive pulmonary disease patients reached 2928 and 388 exacerbation events. Study aims to analyze the correlation between acute exacerbation of chronic obstructive pulmonary disease with polymorphic phagocyte cells in the Emergency Department of Bangil Hospital, Indonesia.

This was a cross-sectional retrospective study. We collected the patient who came to the emergency room with acute exacerbation event and recorded the number of times the patient experiences an acute exacerbation event and the results of a complete blood lab polymorphic phagocyte cell, including basophils, neutrophils and eosinophils from the medical record. Data analysis in this study used the Spearman method to determine the correlation between Chronic obstructive pulmonary disease exacerbation and polymorphic phagocyte cells.

Chronic obstructive pulmonary disease exacerbations 1-5 times were obtained in 54 patients. The patients were 41 males (75.9%) and 13 females (24.1%). The chronic obstructive pulmonary disease patients were 46-65 years ($n=31$, 52.4%), >65 years ($n=21$, 38.9%), and 26-45 years ($n=2$, 3.7%). Patients who had moderate symptoms were 34 patients (61.1%), severe symptoms 7 patients (12.9%), and mild symptoms 13 patients (24.1%). Statistical test results showed an association of acute exacerbation of chronic obstructive pulmonary disease with basophils ($p=0.018$), neutrophils ($p=0.001$), and eosinophils ($p=0.0012$).

This study concludes there is a correlation between the incidence of acute exacerbation and chronic obstructive pulmonary disease with polymorphic phagocyte cells.

KEYWORDS: chronic obstructive pulmonary disease, acute exacerbations, neutrophil, basophil, eosinophil.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a non-communicable, preventable disease, and it is a public health problem in Indonesia [Rosyid A, Maranatha D, 2018]. Based on WHO data, in 2002, COPD ranks 5th as a cause of death globally, and it is estimated that in 2030 it will be third worldwide after cardiovascular disease and cancer. The Asian Pacific COPD Round Table Group estimates that moderate to severe COPD patients in

Asia Pacific countries in 2006 had reached 56.6 million people with a prevalence of 6.3%. Meanwhile, the number of COPD patients in Indonesia is estimated to be 4.8 million, with a majority of 5.6% [PDPI, 2016; Agusti A, Vogelmeier CF, 2018]. The significant risk of COPD is cigarette smoking which leads to the development of COPD [Kwon N et al., 2013].

Indonesia has the highest number of smokers and ranks first in Southeast Asia [Ismail I et al., 2020]. Smokers spanned through different social classes, status, gender, and age. The major causes of smoking behavior are the availability of cigarettes everywhere in the country [Pribadi E, Devy S, 2020]. The prevalence of smokers in Indonesia

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in 2010 was 34.7%, with the highest prevalence in Central Kalimantan province, Indonesia with 43.2% and the lowest in Southeast Sulawesi with 28.3% [PDPI, 2016]. There was a high smoking prevalence in the age group of 25-64 years with a range of 37-38.2%, and 18.6% in the population aged 15-24 years who smoked every day. The prevalence of male and female smokers was 16 times higher in men with a value of 65.9% compared to the value for women of 4.2%, showing that men dominated the number of smokers in Indonesia [Ummah F et al., 2020]. Elderly smokers have a 50% risk of developing COPD [Lundbäck B et al., 2003]. In addition to the dose of cigarettes, types of cigarettes also have a chance of increasing lung function abnormalities. Secondhand smoke also has the same risk level as active smokers for developing COPD. Based on RISKESDAS data in 2013, East Java, Indonesia, had a COPD prevalence of 3.6%. Based on Bangil Hospital, Indonesia, there were 2059 patients diagnosed with COPD and 282 patients with acute COPD exacerbation in 2018. In 2019, there was an increase in patients to 2928 patients diagnosed with COPD, but there was a decrease in COPD patients' acute exacerbation to 106 patients [Indonesia Ministry of Health, 2013].

Bacteria mostly are the cause of acute exacerbation of COPD patients at Arifin Rachmad Hospital in Riau, Indonesia. Gram-negative bacteria are the most common cause than gram-positive bacteria [Martantya R et al., 2014]. COPD is a preventable and treatable chronic lung disease characterized by persistent and usually progressive airway limitation [Hariyono R et al., 2019]. It is associated with an excessive chronic inflammatory response to the airways and lung parenchyma due to harmful gases or particles. Moreover, it can result in tissue damage to the airway. As a result of the inflammatory response, the body releases pro-inflammatory mediators such as TNF- α , IL-6, and IL-8, which will attract CD8 + Tc1 cells, macrophages, B lymphocytes, and polymorphic phagocyte cells consisting of neutrophils, eosinophils, and basophils. This inflammatory process will cause pathological changes that cause narrowing of the airways, leading to air trapping and limited airflow. Acute exacerbation of COPD is an acute event characterized by worsening of the patient's respiratory condition, such as shortness of breath and cough with or without sputum from day

to day compared to before. Exacerbations and comorbid play a role in the severity of COPD [Indonesia Ministry of Health, 2013; Martantya R et al., 2014].

This study was conducted by performing a polymorphic phagocyte cell count test in COPD patients who came to the emergency department during acute exacerbations. Acute exacerbation of COPD was chosen because it has characteristic symptoms compared to stable COPD. In previous research journals on COPD, an increase in neutrophils and no increase in eosinophils or basophils [Martantya R et al., 2014], whereas, in previous research journals on COPD exacerbations, there was an increase in neutrophils, but not eosinophils [Juwariyah J et al., 2017]. There was no significant and statistically significant correlation between acute exacerbation of COPD with basophils, eosinophils, and neutrophils in both research journals [Martantya R et al., 2014; Juwariyah J et al., 2017]. This study aims to determine the correlation between the incidence of acute exacerbation of COPD with polymorphic phagocyte cells consisting of basophils, neutrophils, and eosinophils.

MATERIAL AND METHODS

This was a quantitative research using a retrospective cross-sectional design. This study aims to determine and analyze the correlation between the incidence of acute exacerbation of COPD and polymorphic phagocyte cells. It is hoped that the correlation between acute exacerbation of COPD and polymorphic phagocyte cells consists of 3 types, namely basophils, eosinophils, and neutrophils. In this study, the population to be studied was an acute exacerbation of COPD patients who came to the Bangil Hospital Emergency Department, Indonesia, from 2018 to 2019. The research sample was taken according to inclusion using the simple random sampling method and obtained a sample of 54 patients. Data collection was carried out from December 2019 to



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January 2020. The independent variable in this study was COPD patients with acute exacerbations, and the measurement results were the number of times they experienced exacerbations with an ordinal data scale. In contrast, the dependent variable was the phagocyte cells present in the complete blood cell examination, namely basophils, neutrophils and eosinophils, with measurement results in the form of percentages and interval scales.

In this study, the data collection procedure was carried out after obtaining ethical permission from the Faculty of Medicine ethics team, Muhammadiyah University of Surabaya, Indonesia and internal ethics permission from the ethics team of the Bangil Hospital, Indonesia. The medical record data that has been obtained is then analyzed using the univariant correlation test to see the value of the frequency distribution of each variable and the spearman bivariate correlation to determine and assess the correlation between COPD exacerbations and polymorphism phagocyte cells. The correlation level criteria were assessed from a sig >0.05 , and the levels ranged from almost no correlation to perfect correlation. Processing and data analysis were carried out using the 25th edition of the Statistical Package for the Social Sciences application to obtain the results and conclusions of this study.

RESULTS

Based on table 1, among the 54 patients in the study, there were 41 males (75.9%) and 13 females (24.1%). The majority of COPD patients in this study were 46-65 years old. The majority of patients had moderate symptoms (61.1).

Table 2 reveals that the correlation value between the exacerbation of COPD and basophil polymorphic phagocyte cells is 0.321. This shows a positive correlation between the incidence of exacerbation of COPD and basophil polymorphic phagocytic cells. The higher the incidence of exacerbation of COPD, the higher the basophil cell levels. There was a significant correlation between the exacerbation of COPD and polymorphic basophil phagocyte cells ($p=0.018$).

The correlation value between the exacerbation of COPD and the neutrophil polymorphic phagocyte cells was -0.433, as shown in Table 2. This

TABLE 1.

Characteristics of respondents

Variable	n	%
Sex		
Man	41	75.9%
Woman	13	24.1%
Age		
26-45 years	2	3.7%
46-65 years	31	57.4%
> 65 years	21	38.9%
Symptoms of exacerbation		
Mild Symptoms (1 Symptom)	13	24.1%
Moderate Symptoms (2 Symptoms)	34	63.0%
Severe Symptoms (3 Symptoms)	7	12.9%
Total	54	100.0%

TABLE 2.

Correlation between chronic obstructive pulmonary disease exacerbation and basophil, neutrophil and eosinophil cell levels

Exacerbation Incident	Cell Levels (%)	Correlation	P
basophil cell levels			
1	0.67	0.321	0.018
2	0.95		
3	0.40		
4	1.25		
5	1.10		
neutrophil cell levels			
1	81.70	-0.433	0.001
2	71.44		
3	73.60		
4	58.95		
5	70.20		
eosinophil cell levels			
1	1.04	0.339	0.012
2	2.12		
3	4.30		
4	9.60		
5	8.10		

indicates a negative correlation between the incidence of exacerbation of COPD with polymorphous neutrophil phagocyte cells. The higher the incidence of exacerbation of COPD, the lower the levels of neutrophil cells. There was a significant correlation between the exacerbation of COPD and neutrophil polymorphic phagocyte cells ($p=0.001$).

Table 2 shows that the correlation value between the exacerbation of COPD and eosinophil polymorphic phagocyte cells is 0.339. This shows a positive correlation between the incidence of exacerbation of COPD with eosinophil polymorphic phagocyte cells. The higher the incidence of exacerbation of COPD, the higher the levels of eosinophil cells. There was a significant correlation between the incidence of COPD exacerbations and the polymorphic eosinophil phagocyte cells ($p=0.012$).

DISCUSSION

This study analyzed the correlation between acute exacerbation of COPD and polymorphic phagocyte cells consisting of 3 types: basophils, eosinophils, and neutrophils. The results showed that there was a correlation between the incidence of exacerbation of COPD with polymorphic phagocyte cells, both basophils, neutrophils, and eosinophils. Basophil cell levels tend to increase along with the increasing incidence of exacerbation. In previous studies, it was found that the average count of basophils in patients with COPD did not increase, but the theory states that in people who have a bacterial infection, the count of basophils can increase [Martantya R et al., 2014]. Another study shows that decreased levels of eosinophils and basophils affect COPD patients' prognosis [Xiong W et al., 2017]. Basophils are circulating granulocytes that respond to allergic stimuli by migration and accumulation at sites of inflammation. Basophils act as phagocytosis, effector cells, and memory cells against allergens by producing lipid mediators and cytokines that can affect blood vessel extravasation and stimulate effector cluster of differentiation 4 (CD4) T cells directly to play a role in tissue remodelling. Cross-linking of FcεRI with the immunoglobulin E (IgE) -antigen complex will cause basophil degranulation and mediators' release, especially histamine [Bain B, 2014; Murray J et al., 2016].

Neutrophil cell levels tend to decrease with an

increasing incidence of exacerbation. The study results found that the neutrophil levels in the incidence of exacerbation were 1 to 5 times. The theory of Lockwood states that segmented neutrophils increase in response to inflammation and bacterial infection [Lockwood W, 2020]. In previous studies [Martantya R et al., 2014; Juwariyah J et al., 2017], it was found that there was an increase in neutrophil levels in acute exacerbation of COPD and COPD patients. However, there are differences with other studies' results [Palange P et al., 2006; Rumora L et al., 2008; Shivanand K et al., 2012] which found that COPD patients had a normal basophil, eosinophil, neutrophil, lymphocyte, and monocyte count. Increased neutrophil counts in COPD patients with comorbid infections may result from a response to airway inflammation, systemic inflammation, and also due to co-infectious diseases in the patient [Furutate R et al., 2016]. A study conducted by Kurtipek E. and co-authors explained that examination by looking at the levels of neutrophils and lymphocytes in acute exacerbated COPD patients tend to increase and is positively correlated with C-reactive protein testing, addition neutrophil, and lymphocyte examinations are parameters that are easy to measure, and economic costs but with a relatively high diagnostic accuracy [Kurtipek E et al., 2015]. When neutrophilia occurs in response to inflammation, it is sometimes accompanied by morphological changes such as toxic granulation, Döhle bodies, and vacuolization. Also, neutrophils may be associated with the presence of mucous hypersecretion [Xiong W et al., 2017; Agusti A, Vogelmeier CF., 2018].

The level of eosinophil cells tends to increase along with the increasing incidence of exacerbation. there is an increase in eosinophils in acute exacerbation of COPD [Papi A et al., 2006; Bafadhel M et al., 2011]. Besides, administration of corticosteroids can reduce the exacerbation of patients and improve clinical symptoms [Woods J et al., 2014]. Previous study stated that the average eosinophil level was $>2\%$, an increase in eosinophil levels was associated with a response to corticosteroid therapy in patients [Singh D et al., 2014]. The correlation between eosinophils and corticosteroid therapy was also found in the study of Wei X. and colleagues, which stated that there was a high number of eosinophils in stable COPD pa-

tients who responded to oral and inhaled corticosteroid administration [Wei X et al., 201]. There is an informative correlation between pre-therapy blood eosinophil levels and the frequency of COPD exacerbations [Pavord I et al., 2016]. In another study it was found that there was a decrease in eosinophil activity after being hospitalized, but it was not statistically significant [Juwariyah J et al., 2017]. Increased number of eosinophils in the airways is a pathological feature of asthma. In COPD, it is suspected that eosinophils play a role in the incidence of acute exacerbations and are often associated with poor lung function measurement results, including airway hyperresponsiveness. Drugs that suppress airway eosinophils, including corticosteroids, anti-IgE, and anti-IL-5, are generally effective at lower exacerbation levels [Murray

J et al., 2016].

This study has limitations. First, it only used medical record instruments in which the researcher is not directly involved in the patient's diagnosis. Second, the sampling did not match one of the exclusion criteria because the field conditions were different. Third, the lack of sample size is also a limitation of this study.

CONCLUSION

There is a correlation between the incidence of exacerbation of COPD with polymorphic phagocyte cells, both basophils, neutrophils, and eosinophils. Basophil and eosinophil cell levels tend to increase along with the increasing incidence of exacerbation. However, neutrophil cell levels tend to decrease with an increasing incidence of exacerbation.

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