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# Determinants of exacerbations in patients with chronic obstructive pulmonary disease: retrospective cohort study

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## Abstract

**Purpose:** Exacerbations in patients with chronic obstructive pulmonary disease (COPD) are a significant cause of morbidity and mortality because of the increased progression of COPD, which is getting worse due to frequent recurrences. This study aimed to determine the factors associated with the incidence of exacerbations in patients with COPD at the Bandung Community Lung Health Center (BCLHC). **Methods:** This study is a secondary data analysis of patient medical records for 2015-2020 with a retrospective cohort study design. The sample in this study amounted to 122 COPD patients who were taken using a purposive sampling technique. The variables studied were age, sex, employment status, marital status, and smoking history. The bivariate data analysis used the chi-square test, and the multivariate data analysis used the multiple Cox regression test with $\alpha = 0.05$. **Results:** The results of the multivariate analysis showed an increased risk of exacerbations in the group with a history of smoking (RR = 7.6, 95% CI = 2.9-19.6) compared to the group with no history of tobacco and non-married status (RR = 1.9, 95% CI = 1.1-3.4) compared with the currently married group. **Conclusion:** It is hoped that COPD sufferers can stop smoking to reduce the risk of exacerbations and the need for support from families for COPD sufferers who are not married.

**Keywords:** COPD; exacerbations; factors

## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a disease that can be prevented and treated, which has now become a significant public health problem in the world, including in Indonesia [1]. Chronic obstructive pulmonary disease is characterized by persistent airflow limitation that is usually progressive and is associated with an increased chronic inflammatory response in the airways [2]. Chronic obstructive pulmonary disease was ranked 8th out of 315 causes of the global disease burden in 2015 [3]. Patients with COPD usually have no complaints or symptoms, so this can make the disease progressive if the risk factors are not avoided. The symptoms that can arise in chronic obstructive pulmonary disease are shortness of

breath, chronic cough for 2 weeks, and productive sputum [4].

As the condition of a COPD sufferer gets worse, the symptoms will get worse. This condition is called an exacerbation. Exacerbations are complex events in which a person's COPD symptoms worsen, usually associated with increased airway inflammation, mucosal production, and gas trapping in the airways (5). From January 1, 2010, to December 31, 2012, 70.7% of COPD cases were exacerbated from 184 patients at RSCM, while 29.3% were stable (6). As many as 61 pilgrims who suffered from COPD, 57.4% experienced exacerbations [7].

Exacerbations are a significant determinant of health status in patients with COPD, and it is known that exacerbations also promote the development of COPD, with approximately 25% of decreased lung function associated with exacerbations [8]. COPD exacerbations are an essential driver of death in people with COPD and are also associated with cardiovascular events. Any exacerbation requiring hospitalization increases the risk of subsequent exacerbations, and each severe exacerbation increases the risk of death [9].

Exacerbations can result in hospital admission or death and are closely related to the patient's quality of life. Assessment of the risk of exacerbations and prevention of future exacerbations is critical. The increased risk of exacerbation and death between different spirometric levels was due to exacerbations, which decreased lung function, worsened health status, and increased the risk of death [2].

Respiratory viral infections, primarily rhinovirus, trigger Most COPD exacerbations. Using molecular techniques, respiration so that viruses can be identified accounts for up to 60% of the incidence of exacerbations [8]. Exacerbations in COPD become more severe and are triggered by cardiovascular disease and various other factors. This study aims to analyze the factors associated with the incidence of exacerbations in patients with chronic obstructive pulmonary disease (COPD) at the Bandung Community Lung Health Center from 2015 to 2020.

## METHODS

This study used an analytic observational method with a retrospective cohort study design. The data used in this study is secondary data in the form of medical records of COPD patients receiving treatment at the Bandung Community Lung Health Center. This research was conducted at the Center for Community Lung Health in Bandung, especially in Asthma-COPD and Medical Records poly. This research was conducted in October 2020 - February 2021. This research has passed the ethical review test conducted by the Health Research Ethics Committee of UPN Veteran Jakarta with number 147/II/2021/KEPK.

The population in this study was all COPD patients who received treatment at BBKPM Bandung from 2015 to 2020. With a total sample size of 122 samples and the Lemeshow formula calculation, the hypothesis test for relative risk, 10%, was added to overcome the random error. The sample was divided into two groups: 61 exposed groups and 61 unexposed groups. The sample was selected using the purposive sampling technique based on inclusion and exclusion criteria. The exposed group comprised COPD patients in the risk category for each independent variable to be studied who met the inclusion criteria based on the medical record. In contrast, the unexposed group was COPD patients in the no-risk category for each independent variable to be studied that met the inclusion criteria based on medical records.

Data analysis was performed: univariate analysis, bivariate analysis with chi-square test, and multivariate analysis with multiple Cox regression test, which has a 95% degree of confidence or $\alpha = 0.05$. The operational definition of the variables studied is a risk if the age is> 65 years when the researcher conducts the research, is male, has a history of smoking, has unmarried marital status, and has unemployment status, which is obtained from medical record data and is not at risk if ≤65 years old when the researchers conducted the study, female, had no history of smoking, had a married marital status and had a working status obtained from medical record data.

## RESULTS

The univariate analysis conducted regarding the frequency distribution of exacerbations showed that the majority of COPD patients did not experience exacerbations: 69 patients or as many (5.6%), and based on the results of exacerbations in COPD patients, among 55 COPD patients who experienced exacerbations, the majority of COPD sufferers experienced exacerbations. The first exacerbation in 2019 was 18 patients with COPD, or 14.8%. Furthermore, Table 1 shows the results of the univariate analysis on the frequency distribution of the independent variables: age, gender, employment status, marital status, and smoking history.

The majority of COPD patients had an age of ≤65 years, which was 64.8%. Based on gender variables, the majority of COPD sufferers were male, 86.9%. In the variable of work status, it is known that the majority of COPD sufferers have a working status, which is 58.2%

of the group of COPD sufferers who have a working status, the majority of which are self-employed (23.8%). In the last variable, marital status, it is known that the majority of COPD sufferers are married, 68.0%. In the previous variable, smoking history, there were 61 COPD patients with a smoking history as the exposed group and 61 COPD patients without a smoking history as the non-exposed group.

**Table 1. Independent variable frequency distribution (n=122)**

| Variables | n | % |
|---|---|---|
| **Age** | | |
| ≤65 years | 79 | 64.8 |
| >65 years | 43 | 35.2 |
| **Gender** | | |
| Woman | 16 | 13.1 |
| Man | 106 | 86.9 |
| **Job-status** | | |
| Does not work | 51 | 41.8 |
| Work | 71 | 58.2 |
| **Marital status** | | |
| Yes | 83 | 68.0 |
| No | 39 | 32.0 |
| **Smoking history** | | |
| No | 61 | 50.0 |
| Yes | 61 | 50.0 |

Table 2 shows the results of the bivariate analysis with the chi-square test. Based on the results of the bivariate analysis, it was found that the variables age and sex had no statistical relationship with the incidence of exacerbations. Furthermore, patients with COPD who have a work status have a risk of 1.8 times higher than those who do not work experience exacerbations. Then, patients with COPD who have unmarried status have a 3.2 times higher risk compared to the group of patients with COPD who have married status to experience the incidence of exacerbations. Also, COPD patients who have a history of smoking have a 9.6 times higher risk than the group of COPD patients who do not have a history of smoking to experience exacerbations.

Three variables (p-value<0.25) at the bivariate analysis stage, employment status, marital status, and smoking history, are included in the multivariate analysis. Age and sex variables substantially affect the incidence of exacerbations; the researchers included age and sex in the multivariate analysis.

Furthermore, the variables are issued in stages based on the greatest p-value until the final modeling is obtained, where the p-value is <0.05. The final multivariate model consisted of marital status and smoking history. After that, the confounding test was conducted by comparing the RR before and after the variables were excluded. If when the variable is released, there is a change in RR> 10%, then the variable released is a confounding variable. The result obtained is that there is no confounding variable in this study.

**Table 2. The relationship between independent variables and exacerbations**

| Variable | Exacerbations (n, %) | | p-value | RR (95% CI) |
|---|---|---|---|---|
| | Yes | No | | |
| **Age (years)** | | | | |
| ≤65 | 15 (34.9) | 28 (65.1) | 0.292 | 0.7 (0.3-1.3) |
| >65 | 38 (48.1) | 41 (51.9) | | 1 |
| **Gender** | | | | |
| Man | 47 (44.3) | 59 (55.7) | 0.699 | 1.1 (0.5-2.7) |
| Woman | 6 (37.5) | 10 (62.5) | | 1 |
| **Job-status** | | | | |
| Work | 38 (53.5) | 33 (46.5) | 0.050 | 1.8 (1.0-3.3) |
| Does not work | 15 (29.4) | 36 (70.6) | | 1 |
| **Marital status** | | | | |
| No | 32(82.1) | 7 (17.9) | 0.000 | 3.2 (1.8-5.6) |
| Yes | 21 (25.3) | 62 (74.7) | | 1 |
| **Smoking history** | | | | |
| Yes | 48 (78.7) | 13 (21.3) | 0.000 | 9.6 (3.8-24.1) |
| No | 5 (8.2) | 56 (91.8) | | 1 |

**Table 3. The final model of multivariate analysis**

| Variable | p-value | RR | 95% CI | |
|---|---|---|---|---|
| | | | Lower | Upper |
| Marital status | 0.021 | 1.94 | 1.10 | 3.41 |
| Smoking history | 0.000 | 7.65 | 2.97 | 19.65 |

The variable that has the most significant influence on the incidence of exacerbations can be seen from the RR value of the analyzed variables. The variable with the highest RR means that it has the most significant influence on the incidence of exacerbations. Based on the results of the final modeling of multivariate analysis with Cox regression in Table 3, the variable that had the most significant influence on the incidence of exacerbations was smoking history (RR=7.6; 95% CI=2.9–19.6, p-value= 0.000). It can be concluded that in this study, COPD patients with a history of smoking had a 7.6 times higher risk of experiencing exacerbations than COPD patients who had no smoking history after being controlled by the marital status variable.

## DISCUSSIONS

Exacerbations in patients with COPD are a complex event usually associated with increased airway inflammation, increased mucosal production, and gas trapping characterized by increased dyspnea, which are the main symptoms of exacerbations [5]. Therefore,

COPD sufferers who experience an exacerbation at BBKPM will immediately be rushed to the Emergency Room (IGD) for immediate treatment. Exacerbations are a significant determinant of health status in patients with COPD, and it is known that exacerbations also promote the development of COPD, with approximately 25% of decreased lung function associated with exacerbations [8]. Any exacerbation requiring hospitalization increases the risk of subsequent exacerbations, and each severe exacerbation increases the risk of death [9].

The majority of COPD patients who were sampled in this study were male; this is due to the theory, which states that the prevalence and mortality of COPD are higher among men than women [5]. The actual gender risk factor is not yet known with certainty about COPD. Gender in COPD is associated with cigarette consumption, which is more common in men than women smokers. Smoking habit is the single most important cause of COPD and the incidence of exacerbations than any other contributing factor. Smokers have the highest prevalence of respiratory disorders and decreased pulmonary function [10].

The study's results with bivariate analysis showed no relationship between age and sex on the incidence of exacerbations. This result is not in line with previous research; there was a decrease in the rate of exacerbations by 10% for each increasing decade of age and an increase in mortality by 66% for each increase in the age decade. In this study, the majority of COPD patients were less than 65 years old, so the results showed that there was no relationship between the age of COPD sufferers and the incidence of exacerbations. This is because, in theory and previous research, it is known that the incidence of exacerbations will be more common in COPD sufferers over the age of 65, and the results of this study are not in line with previous research, which states that exacerbations are more frequent. Men with COPD are often at greater risk or higher than women with COPD.

In this study, the majority of COPD patients were male, so the characteristics of the patients were homogeneous, thus affecting the study results. The results of the survey with bivariate analysis showed that there was a relationship between employment status, marital status, and smoking history. Occupational status can be related to the smoking history or habits of a COPD sufferer because smoking history is a significant factor in exacerbations. Data from the Riskesdas 2018 report shows that according to occupation, smoking prevalence is highest among fishermen/farmers/laborers, followed by entrepreneurs and employees [12]. There has been no previous research examining the effect of work status on the incidence of exacerbations in patients with COPD. The majority of COPD sufferers have heavy types of work: entrepreneurs, traders, and laborers. It can also affect the results of this study, as job status influences the incidence of exacerbations. In addition, no previous research has examined the effect of work status on the incidence of exacerbations in patients with COPD.

The relationship between health and marital status may not be constant over time, reflecting differences in the life histories of men and women from different birth cohorts [13]. When two people are bound in a marriage bond, they begin to prepare for life together by adjusting to their partner's routine, including when their partner is sick, to remind them to take medication and routinely re-control in health services [14].

Based on the results of multivariate analysis, it is known that the variables of marital status and smoking history have a relationship with the incidence of exacerbations. This result aligns with other research, which shows a significant relationship between marital status and quality of life in the elderly [15]. The multivariate test results showed that the smoking history variable had a relationship with the incidence of exacerbations. COPD patients with a smoking history had a 7.6 times greater risk of experiencing exacerbations when compared to COPD patients who did not have a smoking history after controlling for marital status variables. This is consistent with the results of previous research [6] that active smoking is an independent risk factor for the incidence of COPD exacerbations with OR 5.11. Compared to previous ones, the higher RR value in this study is due to combining the smoking history variable with the comorbidity history variable. The study included 61 COPD patients with both smoking and comorbidity histories and 61 COPD patients with no smoking history but with comorbidity histories.

This study has several limitations. First, the design of this study is a retrospective cohort so that information bias can occur. Second, this study may have residual confounding of variables that were not studied or considered because of adjusting for available data in medical records.

## CONCLUSIONS

An overview of the frequency distribution of the incidence of exacerbations in patients with chronic obstructive pulmonary disease (COPD shows that the majority of exacerbations experienced by COPD patients occurred in 2019. Based on the results of the bivariate analysis, it is known that there is a relationship between employment status, marital status, smoking history, and the incidence of

exacerbations in patients with COPD. Age, sex, and occupational status did not correlate with the incidence of exacerbations in COPD patients after controlling for confounding variables. Marital status and smoking history have a significant relationship with the incidence of exacerbations in COPD patients. Smoking history after controlling for marital status variables.

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