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The Association Between Patient Characteristics and Disease Outcomes of COVID-19 in Jember, Indonesia

Diana Chusna Mufida

Azham Purwandhono

Enny Suswati

Angga Mardro Raharjo

NIP. 197203182003122001

NIP. 198105182006041002

NIP. 197002141999032001

NIP. 198003052008121002

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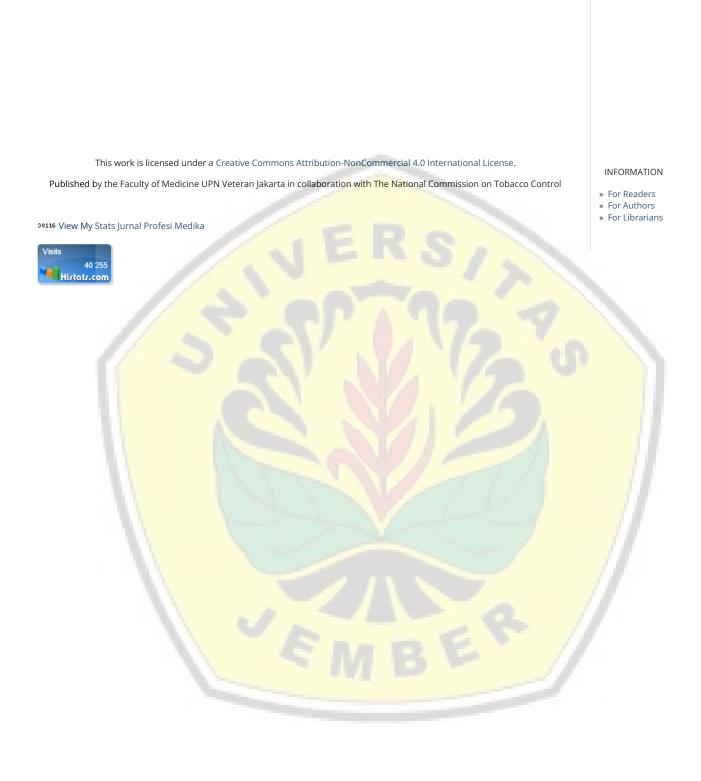


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THE ASSOCIATION BETWEEN PATIENT CHARACTERISTICS AND DISEASE **OUTCOMES OF COVID-19 IN JEMBER, INDONESIA**

Diana Chusna Mufida¹, Putu Ayu Laksmi Lestari², Azham Purwandhono³, Enny Suswati¹, Angga Mardro Raharjo⁴

¹Department of Microbiology, Faculty of Medicine, University of Jember, Jember, 68121 Indonesia

*Correspondence email: chusna.fk@unej.ac.id

ABSTRACT

COVID-19 can cause serious conditions in both comorbid and elderly patients; hence, they need to be given proper follow-up treatment. This study aimed to determine the association between patient characteristics and disease outcomes of COVID-19 in Jember, Indonesia. This research is an analytic observational study with a cross-sectional approach. The sample was 304 patients confirmed positive for COVID-19 at the COVID-19 referral hospitals in Jember. This study used medical record data analyzed using both univariate and bivariate tests. Patient characteristics related to the disease outcomes in patients who were positive for COVID-19 in Jember, are as follows: age (p = 0.000), clinical symptoms (p = 0.017), comorbidities (p = 0.000), and complications (p = 0.000). The unrelated variables were sex (p = 0.455), education level (p = 1.000), domicile (p = 1.000), occupation (p = 1.000) 0.322), and smoking history (p = 0.147). Patients most at risk of developing fatal outcomes are those with complications. Patient characteristics associated with the disease outcomes in patients positive for COVID-19 were age, clinical symptoms, comorbidities, and complications. While, those that were not related to the disease outcomes in patients were sex, education level, occupation, domicile, and smoking history.

Keywords: COVID-19; Disease outcome; Patient characteristics

INTRODUCTION

COVID-19 is a new disease caused by Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection. The pathogen that causes COVID-19 is the Betacoronavirus which belongs to the Sarbecovirus subgenus. In December 2019, at Wuhan City, Hubei Province, China, this disease appeared for the first time with the discovery of cases of respiratory disease with distinctive findings on radiological images.¹

On March 11, 2020, WHO declared that the COVID-19 outbreak became a global pandemic.² One study suggested that male patients and those with anorexia may have worsening disease progression.³ Older patients (> 65 years) with comorbidity and ARDS have a high risk of death. 4 COVID-19

patients from the older age groups have much more severe disease and have a worse response to treatment than younger age groups⁵. Men with COVID-19 infection have > 50% higher risk of severe infection and death than women⁶. Symptoms of fever are most common in patients and strongly associated with the patient's clinical status⁷, besides that smokers are susceptible to respiratory viruses.⁸

This global pandemic has affected all levels of society, both in villages and cities. Health staff, social workers, and educators have a higher risk of severe SARS-CoV-2 infection.⁹ The government has made much effort. Almost the entire area of Jember regency was currently categorized into an orange zone with a medium risk level based

² Faculty of Medicine, University of Jember, Jember, 68121 Indonesia

³ Department of Anatomical Pathology, Faculty of Medicine, University of Jember, Jember, 68121 Indonesia

⁴ Department of Public Health, Faculty of Medicine, University of Jember, Jember, 68121 Indonesia

on data published by the Provincial Government of East Java. 10 COVID-19 cases in Jember were increasing, with 620 positive cases as of September 9, 2020, 513 recovered cases, and 43 deaths. The Case Fatality Rate (CFR) was 6.94%. 11 There is still no definite vaccine and drug to deal with COVID-19 cases, while the spread of COVID-19 is significantly high even though the mortality rate is low. COVID-19 can cause severe conditions in elderly patients and those with comorbidity; therefore, it is essential to know the association between the characteristics of a positive patient with COVID-19 and the disease outcomes so that the patient can be provided with proper diagnosed be management.

MATERIAL AND METHODS Study design and participants

This study was an observational analytic with a cross-sectional approach. This was conducted at three COVID-19 referral hospitals in Jember, namely Kaliwates Hospital, Jember Klinik Hospital, and Citra Husada Hospital, from August 2020 to February 2021. The population of this study was all patients who tested positive for COVID-19 at those COVID-19 Referral Hospitals from April to November 2020. The sampling technique used was total sampling with a number of samples of 304. This study utilized the patients' medical records as the instrument. The independent variables of this study were age, sex, level of education, occupation, domicile, clinical symptoms, history of comorbidity, history of smoking, and complications. In contrast, the dependent variable was the patient's disease outcomes. This study has received ethical approval from the Ethics Commission of the Faculty of Medicine, University of Jember.

Procedures

This research began with population determination, namely, patients tested positive for COVID-19 at the Referral Hospitals for COVID-19 in Jember. Sample collection was conducted by using a total sampling technique with the following

inclusion criteria: patients tested positive for COVID-19 with evidence of positive RT-PCR swabs and or Fast Molecular Test (TCM) and the exclusion criteria as follows: patients who were tested positive for COVID-19 with medical record data that did not meet the requirements set by the researchers. The medical record data was declared eligible if it contains at least 5 of the nine patient characteristics determined by the researchers. After collecting the sample, the patient's characteristics were recorded and grouped according to the disease outcome of the patients who tested positive for COVID-19 based on the medical record data.

Statistical analysis

This study utilized univariate and bivariate analyses. Univariate analysis was performed by calculating the distribution and percentage of each variable. Bivariate analysis was carried out to determine the association between age, sex, education level, occupation, domicile, clinical symptoms, comorbidity history, smoking history, and complications with patient's disease outcome who were tested positive for COVID-19 in Jember. The Chi-Square Test was the main statistical test with a p <0.05 or 95% confidence level. If the Chi-Square Test requirements were not fulfilled, then the alternative test applied was the Fisher's Exact Test

RESULT

Sociodemographic and clinical characteristics of patients who tested positive for COVID-19 are shown in Table 1. Patients who tested positive for COVID-19 in Jember were mostly aged \geq 45 years, with a total of 154 (50.7%) patients of different types. Male patients of 156 patients (51.3%). 245 (80.6%) patients had met the 9-year compulsory education level. Two hundred thirty-one patients were indoor workers (76%), and the majority of the patients lived in cities with as many as 189 (62.2%) patients. A total of 257 (84.5%) patients had clinical symptoms. A total of 272 (89.5%) patients had no smoking history, and 32 (10.5%) patients had a smoking history. A total of 105 (34.5%) patients had comorbidity. A total of 40 (13.2%) patients had complications. Disease outcomes in patients confirmed positive for COVID-19 in Jember are as follows: 270 (88.8%) patients recovered, and 34 (11.2%) patients died.

Table 1. Sociodemographic and clinical characteristics of patients confirmed positive for COVID-19

Characteristics	Total (N)	Percentage (%)	
Age			
< 45 Years	150	49.3	
≥ 45 Years	154	50.7	
Sex			
Male	156	51.3	
Female	148	48.7	
Level of education Finished the 9-year			
compulsory education Unfinished the 9-year	245	80.6	
compulsory education	59	19.4	
Occupation			
Indoor	231	76	
Outdoor	73	24	
Domicile			
City	189	62.2	
Village	115	37.8	
Clinical symptoms Have clinical			
symptoms	257	84.5	
Have no clinical			
symptoms	47	15.5	
Comorbidity history			
With comorbidity	105	34.5	
Without comorbidity	199	65.5	
Smoking history			
Smoking	32	10.5	
Not Smoking	272	89.5	
Complications			
With complication	40	13.2	
Without complication	264	86	
Disease outcome			
Death	34	11.2	
Recovery	270	88.8	

The clinical symptoms, comorbidity, and complications were experienced by patients who tested positive for COVID-19 in this study. The most frequently occurring clinical symptom was cough in 167 (54.9%) patients, and the least frequently occurring was chest pain in 6 (2%) patients. The most common comorbidity among the patients hypertension - cardiovascular disease in 46 (15.1%) patients, and the least common was COPD in 1 (0.3%) patients. The most frequent complication experienced patients was ARDS in 25 (8.22%) patients (Table 2).

The association between patient characteristics and disease outcomes in patients tested positive for COVID-19 in Jember, as follows: age (p-value = 0.000), clinical symptoms (p-value = 0.017), history of comorbidity (p-value = 0.000), and complications (p-value = 0.000). Meanwhile, the unrelated variables were sex (p = 0.455), education level (p = 1.000), domicile (p =1.000), occupation (p = 0.322), and smoking history (p = 0.147). Patients aged \geq 45 years had a greater risk of 7.142 to experience a fatal outcome than those aged <45 years. Patients with clinical symptoms were 14.664 times more likely to experience a fatal outcome than those who did not have clinical symptoms. Patients with a history of comorbidity had a 9.495 times greater risk of experiencing a fatal outcome than those who did not have comorbidity. Patients with complications had a 25.667 times greater risk of experiencing a fatal outcome than those without complications (Table 3).

Table 2 Clinical symptoms, comorbidities, and complications experienced by patients confirmed positive for COVID-19

Percentage Patient characteristic Total (N) (%) Clinical symptoms 47 15.5 Asymptomatic 38.2 116 Fever 167 54.9 Cough 35 11.5 Headache Abdominal 43 14.1 pain Nausea 21 64 vomiting Shortness of 101 33.2 breath Chest pain 6 2 Weak limb-8.9 stroke Kidney disorders 10 3.28 Others **Comorbidity** Without 199 comorbidity 65.5 Diabetes 41 mellitus 13.5 Hypertension 46 Cardiovascular Disease 15.1 Asthma 11 3.6 **COPD** 0.3 TBC 2 0.6 Obesity 0 2 Stroke 0.6 2 Malignancy 0.6 Pregnancy 4 1.3 Other 12 Complications Without 264 86.84 complication **ARDS** 25 8.22 Dyspnea 8 2.63 Sepsis 5 1.64 Cardiac arrest 2 0.65 Others 0.33

Table 3. Association between patient characteristics and disease outcomes of patients confirmed positive for COVID-19

Characteristics	Disease outcomes of COVID-19 positive patients in Jember			P-Value	OR	
	De	Deaths		very		
	n	%	n	%		
Age						
≥ 45 Years	29	85.3	121	44.8	0.000	7.142
< 45 Years	5	14.7	149	55.2		
Sex						
Male	20	58,8	136	50.4	0.455	
Female	14	41.2	134	49.6		
Level of education Finished the 9th year						
compulsory education Unfinished the 9th year	27	79.4	218	80.7	1.000	
compulsory education	7	20.6	52	19.3		
Occupation		20.0	02	17.0		
Indoor	26	76.5	205	75.9	1.000	
Outdoor	8	23.5	65	24.1	1.000	
Domicile	J	23.3	05	27.1		
City	18	52.8	171	63.3	0.322	
Village	16	47.1	99	36.7	0.322	
Clinical symptoms	10	4/.1	77	30.7		
With clinical symptoms Without clinical	34	100	223	82.6	0.017	14.66
symptoms Smoking history	0	0	47	17.4		
Smoking	6	17.6	26	9.6	0.147	
Not Smoking Comorbidity history	28	82.4	244	90.4		
With comorbidity Without	27	79.4	78	28.9	0.000	9.495
comorbidity Complications	7	20.6	192	71.1		
With complication Without	22	64.7	18	6.7	0.000	25.66
complication	12	35.3	252	93.3		

DISCUSSION

The Association between age and disease

The age group ≥ 45 years had the highest percentage of deaths, namely 85.3%. The results of this study are in line with a study proposing that old age is the strongest risk factor associated with fatal outcomes. 12 COVID-19 patients aged ≥50 years had a 15.4-fold higher risk of death than those aged <50 years. Increased mortality in elderly patients is due to decreased immune function. 13 The induction of pro-inflammatory cytokines after infection is not sufficiently controlled by anti-inflammatory mechanisms in the elderly so that it has the potential to cause a poor prognosis. 14

Association between sex and disease outcome

The percentage of male patients who died was 58.8%, while women were 41.2%. This suggests that there was no association between sex and hospital mortality in COVD-19 patients because the mechanisms underlying sex were not strong enough to significantly influence hospital mortality due to a complex variety of causes. 15

The Association between education level and disease outcome

The Chi-Square Test results prove that there is no association between education level and disease outcome in patients who were tested positive for COVID-19 in Jember. Previous research related to this has yet to be found. The level of education with the outcomes of the disease in patients was not significantly related because the disease outcome was related to the patient's condition and the severity of the disease and closely related to the treatment undertaken during hospitalization.

The Association between occupation and disease outcome

Chi-Square Test result proves no association between occupation and disease outcomes in patients who were tested positive for COVID-19 in Jember. The absence of an

association between occupation and disease outcomes in patients may be due to differences in patient immunity when infected with COVID-19 and differences in their medical history. This study shows that more patients infected with COVID-19 work indoors than outdoors. This may be caused by environmental influences and the person's immunity. Patients who work in indoor areas, such as office workers, tend to work in closed areas, have low exposure to direct sunlight, and sometimes have less supportive air circulation.

Meanwhile, for patients who work in outdoor areas, such as farmers – the majority occupation in Jember, it is possible to get sufficient sun exposure and good air circulation. This may provide benefits to strengthen the immune system. Sun exposure can trigger the formation of vitamin D naturally, which plays a role in supporting increased body immunity. Vitamin D has a direct antiviral effect, especially against coronavirus. Vitamin D can modulate and regulate the immune and oxidative responses to COVID-19 infection¹⁶.

The association between domicile and disease outcome

Based on the results of this study, it was found that there was no significant difference between the number of patient deaths due to COVID-19 in villages and cities. This may be caused by the fact that more rural residents did not follow the strict measure of COVIDprevention behaviour than residents¹⁷. This study also shows that more patients infected with COVID-19 live in cities than in villages. One of the factors that cause the spread of COVID-19 is population density. Cities are places with a high population density. This allows the level of interaction between residents to be higher, causing any infectious disease to spread rapidly.¹⁸

The association between clinical symptoms and disease outcome

The Chi-Square Test results prove that there is an association between clinical ISSN 0216-3438 (Print). ISSN 2621-1122 (Online)

symptoms and disease outcomes in patients who are tested positive for COVID-19 in The clinical symptoms frequently experienced by patients were cough (54.9%), fever (38.2%), and shortness of breath (33.2%). Patients with clinical symptoms were more likely to experience a fatal outcome than those who did not. Several factors are associated with the worsening clinical status in adults with COVID-19: fever, cough, and dyspnea.⁷

The association between history of smoking and disease outcome

Fisher's Exact Test results prove no association between smoking history and disease outcomes in patients who tested positive for COVID-19 in Jember. 6 (17.6%) patients with a history of smoking died. This study contradicts a study that stated that smoking status was associated with the severity of disease and mortality in COVID-19 patients¹⁹.

The association between comorbidity and disease outcome

Patients with comorbidity have the highest mortality percentage at 27 (79.4%). Comorbidity most commonly found in patients were hypertension - a cardiovascular disease with as many as 46 (15.1%) patients, 41 (13.5%) diabetes mellitus patients and 11 (3.6%) asthma patients. Patients with more than one comorbidity are strongly associated with poor disease outcomes. This proves that the comorbidity history of more than one patient contributes to the complexity of the disease and often causes patients to have poor outcomes.²⁰ The common comorbidity experienced by the COVID-19 patients were hypertension, diabetes mellitus. cardiovascular disease, cerebrovascular disease and chronic kidney disease.8 ACE2 receptor expression is increased in several comorbid conditions such as hypertension and diabetes. SARS-CoV-2 attacks cells via the ACE2 receptor. Therefore, a history of comorbidity increases the severity of COVID-19 cases.²¹

The association between complications and disease outcome

Patients with complications had a greater percentage (64.7%) of death than those without complications. Complications that often occurred in patients in this study were ARDS (acute respiratory distress syndrome) in 25 (8.22%) patients, dyspnea in 8 (2.63%) patients, and sepsis in 5 (1.64%) patients. ARDS was the most frequent complication of patients in this study. ARDS is a condition associated with various disease processes resulting in decreased lung growth and severe hypoxemia. Cytokine storms are one of the main features of ARDS in COVID-19 patients. Pathological evidence of ARDS COVID-19 cases shows clear desquamation of pneumocytes, formation of hyaline membranes, and pulmonary edema.²² Sepsis is a life-threatening organ dysfunction caused by dysregulation of the immune system against infection.²³ The pathophysiology of sepsis is related to an immune response initiated by pathogens that attack the host. Then the immune system fails to return to a homeostatic state. culminating pathological syndrome characterized continued excessive inflammation suppressed immunity.²⁴ COVID-19 patients who suffer from sepsis show changes such as those found in septic shock, including changes in mental condition, dyspnea, reduced urine output, faster heart rate, weak pulse, and cold extremities.²⁵ Dyspnea was statistically and significantly higher in the critical or deceased group.²⁶ Dyspnea indicates poor lung function and a lack of oxygen. Therefore, COVID-19 patients with dyspnea may be more likely to develop the severe and critical disease.²⁷

Limitations

There several limitations are implementing this research, including using medical record data as the data source. There may be incompleteness in implementing medical record data, which prevents the researchers from getting many more samples. This study used a cross-sectional approach; hence, it has not explained the course of the

disease in detail. In this study, not all patient characteristics related to disease outcomes were studied, so further research needs to be carried out in this regard.

CONCLUSION

Most of the patients who tested positive for COVID-19 in Jember aged \geq 45 years were male. Patients were dominantly indoor workers, and the majority lived in cities. Patients who were most at risk of experiencing the outcome of death were patients who experienced complications. Patient characteristics related to the disease outcomes in patients who tested positive for COVID-19 in Jember were age, clinical symptoms, comorbidity history, complications. Meanwhile, patients' unrelated disease outcomes were sex. education level, occupation, domicile, and smoking history. Related institutions are advised to be more careful in handling patients who are elderly, have a comorbidity, and experience complications to avoid more severe disease and death rates. People with advanced age and a history of comorbidity are always expected to be aware of the condition if they experience illness. Therefore, if they feel the symptoms of COVID-19, they are advised to examine the nearest health facility.

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