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Analysis of Factors Associated with the Risk of Mortality of Covid-19 Patients

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ABSTRACT

Corona disease (Covid-19) has become a global pandemic. In Indonesia, on 2020 there were 3,512 positive cases, with 306 people dying, the mortality rate is 9.1%. East Java has the highest Covid-19 death rate in Indonesia. The aim of this study was to identify the factors associate with the mortality of Covid-19 patients. The present study was conducted based on a retrospective analysis of the medical records of patients hospitalised at Ngudi Waluyo Hospital between March 2020 to September 2021. The study included all cases of patients with a complete medical records data. A total of 1.494 cases were included. The bivariate analysis using Chi-Square Test and univariate by Binary Logistic Regression analysis to evaluate the association between risk factors and mortality. The results showed a relationship between age, gender comobid and comobid classification. The main risk factor of mortality was the presence of comorbidities (p = 0.005; OR = 1,494; 95% CI = 1.132-1.071). The second factor was age (p=0.000; OR=1.419; 95% CI=1.308 – 1.540). Risk factors associated with mortality for patients with Covid-19 in the hospital included advanced age, presence of comorbid and gender. Risk factors of mortality were the presence of comorbidities and age.

Keywords: age; gender; comobid; mortality; Covid-19

INTRODUCTION

At the beginning of 2020, the world was shocked by the new virus outbreak, namely the new type of coronavirus Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), and the disease is called coronavirus disease 2019 (COVID-19). Currently, the spread of SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) from human to human is the primary transmission source so that the spread becomes aggressive. Transmission of SARS-CoV-2 can be through the air or contact form of droplets if the particles released by sick people are 5µm in diameter [(1)]. Infected people spread virus particles every time they talk, breathe, cough, or sneeze. Such viral particles in clumps of mucus, saliva, and water, and the behavior of the clot in the environment depends on the size of the lump. Larger globules fall faster than they evaporate, so they splash nearby in the form of droplets [(2)]. Our simulation results show that after coughing for ten seconds. However, most of the vaporized particles are more extensive than 5µm; 59.5% of the virus's original particles can still survive in the air [(3)]. Until now, the pathogenesis of Covid-19 is still not fully understood.

SARS-CoV-2 can only replicate inside the host cell. The process of developing the virus consists of several processes. The beginning process was the viral attachment to the host cell surface. Protein S on the surface of SARS-CoV-2 binds to the angiotensin-converting enzyme 2 (ACE-2) receptor on the cell surface. We can find the receptors in the nasopharynx mucosa, oropharynx, alveolar epithelial cells, arteries, heart, kidneys, and intestines-2. Second, the penetration of the virus into the host cell and subsequent fusion of the viral envelope with the cell membrane (endocytosis) mediated by the Transmembrane Serine Protease-2 (TMPRSS2) receptor. Third, the release of RNA, translation, transcription, and replication, then maturation, then the release process, where the virus recognizes innate immune receptors such as RNA sensors (TLR7/8; RIG-I/MDA-) is released and then enters the host cell. 5) and inflammasome sensor (NLRP3), then NF-KB, IRF3/7 activation will occur with pro-inflammatory cytokine products (IL1, IL6, IL8, TNF alpha, and Interferon). Viral antigen APC will stimulate the cellular and humoral immune response. The release of excessive cytokines will cause clinical reactions such as coughing, shortness of breath until a decrease in oxygen saturation, a reduction of lymphocytes, or positive ARDS. Proteins wrap RNA that make up the body of the virus. The glycoproteins in the newly formed viral envelope enter the membrane of the endoplasmic reticulum or Golgi cell. RNA genome and a nucleocapsid protein composed of a nucleocapsid. Viral antigen (Ag) will be presented to APC, stimulating the cellular and humoral immune response. Excessive cytokine release will

cause clinical reactions such as coughing, shortness of breath, decreased oxygen saturation, decreased lymphocytes, or ARDS. ARDS is what causes the high mortality of Covid-191 patients [(1)].

In Indonesia, on April 10, 2020, there were 3,512 positive cases, 282 people recovered, and 306 people died, with a mortality rate of 9.1%. The presence of comorbidities owned by positive patients with the coronavirus, vulnerable age, and inadequate health facilities lead high mortality rate in Indonesia. At the beginning of June 2021, COVID-19 patients in Indonesia experienced a remarkable increase until their peak in early August 2021. After that, they experienced a significant decline starting from the 2nd week of August until September 2021 [(4,5)].

A few months ago, East Java was the province that contributed the highest number of COVID-19 deaths nationwide. The latest data for September, East Java contributed a total of 29,035 COVID-19 patients who died. Blitar is the second contributor to the Covid-19 death rate after Mojokerto. The death of male COVID-19 patients, older age, and several diseases can worsen the condition of Covid-19 patients, such as diabetes, asthma, and other illnesses that aggravate the condition of Covid-19 patients [(6,7)]. So the researchers wanted to identify the factors associated with the mortalityof COVID-19 patients.

The aim of this study was to identify the factors associate with the mortality of Covid-19 patients.

METHODS

The present study was conducted based on a retrospective analysis of the medical records of patients hospitalised at Ngudi Waluyo Hospital between March 2020 to September 2021. This hospital is one of the hospital that treats the most Covid-19 patients the period from September 2020 to September 2021, because the only provincial covid-19 referral hospital in East Java in Blitar Regency.

This study included all cases of patients with a complete medical records data. A total of 1.494 cases were included in the final analysis. The independent variables of this study were age, gender, comorbid disease. The dependent variable in this study was mortality. Descritive analysis used a frequency distribution, namely age, gender, comorbidities, and patients who died. Bivariate analysis using Chi-square test. Multivariate analysis using Binary Logistic Regression.

RESULTS

Data of this study included age, gender, presence of comorbidities, types of comorbid diseases. The table 1 shows that most of the respondents were 51-60 years old by 20.3%. A total of 52.5% were female, then 10.6% with comorbid of cerebrovarcular disease. Respondents without comorbidities were 49.4%.

Table 1. Distribution of respondents' demographic data at Ngudi Waluyo Hospital Blitar

Demographic	Frequency	Percentage
Age		
1-10 years	79	5.3
11-20 years	31	2.1
21-30 years	193	12.9
31-40 years	223	14.9
41-50 years	264	17.7
51-60 years	304	20.3
61-70 years	278	18.6
71-80 years	99	6.6
91-100 years	23	1.5
Gender		
Men	710	47.5
Women	784	52.5
Comorbid		
Yes	272	18.2
No	1222	81.8
Kind of comorbid		
No comorbid	738	49.4
Cerebrovarcular disease	158	10.6
Respiratory disease	143	9.6
Renal disease	92	6.2
Inpartu	92	6.2
Cardiovarcular disease	75	5.0
Diabetes Mellitus	68	4.6
GIT disease	39	2.6
Newborn	29	1.9
HIV	22	1.5
Neoplasma disease	21	1.4
Septic	7	0.5
Hipertension	7	0.5
Hematology disease	3	0.2

Table 2. Distribution of mortality among respondents at Ngudi Waluyo Wlingi Hospital Blitar

Mortality	Frequency	Persentase
Yes	272	18.2
No	1222	81.8

Table 2 shows that the respondents who did not die were 81.8% (1222 people). Based on table 3, it shows that there was a relationship between gender and mortality (p-value = 0.025). Based on table 4, it shows that there was a relationship between age and mortality (p-value = 0.000). Based on table 5, it shows a relationship between the presence of comorbidities and mortality (p-value = 0.000). Based on table 6, it shows a relationship between the type of comorbidity and mortality (p-value = 0.000).

Tabel 3. The relationship between gender and mortality in respondents at Ngudi Waluyo Hospital Blitar

Gender	Mortality	
	Yes	No
Women	126	658
Man	146	564
	272	1222
Chi Square p=0.025		

Tabel 4. The relationship between age and mortality in respondents at Ngudi Waluyo Hospital Blitar

Age	Mortality	
	Yes	No
1-10 years	4	75
11-20 years	2	29
21-30 years	6	187
31-40 years	28	195
41-50 years	44	220
51-60 years	70	234
61-70 years	74	204
71-80 years	34	65
91-100 years	10	13
Chi Square p=0.000		

Tabel 5. The relationship between the presence of comorbidities and mortality

Presence comorbidities	Mortality	
	Yes	No
No	107	631
Yes	165	591
	272	1222
Chi Square p=0.000		

Tabel 6. The analysis of the relationship between type comorbidities and mortality

Type comorbid	Mortality	
	Yes	No
Cerebrovascular	51	107
Renal disease	19	73
Cardiovarcular disease	18	57
Resiratory disease	36	107
Diabetes Melitus	17	51
Hipertension	0	7
Neoplasma disease	2	19
Septic	7	0
Inpartu/ obgyn	2	90
HIV	7	15
GIT disease	6	33
Newborn	0	29
Hematology disease	0	3
Without komorbid	107	631
Chi Square p=0.000		

Tabel 7. The analysis on age factors that increase the risk of mortality

No	Age	p-value	Exp (B)	95% C.I. for EXP(B)	
				Lower	Upper
1	61 – 70 years	0.033	0.389	0.163	0.925
2	51 – 60 years	0.003	0.260	0.107	0.630
3	41 – 50 years	0.000	0.187	0.075	0.466

The age group 61-70 years has the highest risk of death compared to other age groups (table 7). Comorbid cardiovascular disease has the highest risk of death compared to other comorbid types (table 8).

Table 8. The analysis of the type of comorbid factors that increase the risk of mortality

No	Type of comorbid	p-value	Exp (B)	95% C.I. for EXP(B)	
				Lower	Upper
1	Cerebrovascular disease	0.000	2.811	1.900	4.157
2	HIV	0.031	2.752	1.096	6.907
3	Respiratory disease	0.002	1.984	1.291	3.287
4	Diabetes mellitus	0.024	1.966	1.094	3.532
5	Cardiovascular disease	0.032	1.862	1.055	3.287

Tabel 9. The most influential factor on the risk of mortality from Covid-19

No	Factors	p-value	Exp (B)	95% C.I. for EXP(B)	
				Lower	Upper
1	Komorbid	0.005	1.494	1.132	1.971
2	Usia	0.000	1.419	1.308	1.540

The main factor that most influences the risk of death of Covid-19 patients is the presence of comorbidities with a value (p = 0.005; OR = 1,494; 95% CI = 1.132-1.071). The presence of comorbidities in Covid-19 patients increases the risk of death by 1.494 times compared to patients who do not have comorbidities. The second influential factor was age with a value (p=0.000; OR=1.419; 95% CI=1.308 – 1.540). the older the age, the risk of death increases by 1,419 times compared to the younger age group.

DISCUSSION

Covid-19 is a health problem that affects all aspects of people's lives. Since being declared a pandemic by the WHO in May 2020, cases of COVID-19 have been increasing. Previous literature identified advanced age, higher disease severity, elevated inflammatory biomarkers, acute organ dysfunction, comorbidities, and presentation from long-term care facilities as risk factors for mortality in inpatients from Wuhan, China, and the United States [8]. This study of 1494 COVID-19 patients treated at Ngudi Waluyo Hospital Blitar in March 2020 - September 2021. The results showed that the highest percentage of Covid-19 patients aged 51-60 years was 304 people (20.3%). Most of the genderes are women by 784 people (52.5%). More than half had comorbid, namely 756 (50.6%), with the highest percentage being Cerebrovascular disease, namely 158 people (10.6%). The results of this study are in line with Satria's research (2020) which shows that from the gender, the most covid-19 sufferers are women, aged between 51-60 years, but the most comorbid in this study is diabetes [9].

Demographic characteristics of age and gender and the presence of comorbidities in this study were included as risk factors for COVID-19 death with a p-value of <0.005. In this study, the age group 61-70 years had the highest risk of death compared to other age groups. Age is one of the risk factors for COVID-19. This study is in line with the results of other studies, which show that the risk factor for death increases with the increasing age of Covid-19 patients [8,9]. The increased fatality rate in the elderly population is related to immunology and decreased immune response due to the aging process. Another study found that male patients aged >50 years or had comorbid conditions (e.g., kidney disease, cerebrovascular disease, cardiovascular disease, respiratory disease, diabetes, hypertension, and cancer) were significantly associated with an increased risk of death covid-19. 19. Age group >50 years had a 3.45-fold chance of confirmation of SARS-CoV-2 compared to age <50 years (RR 3.45: 95% CI 1.67–7.14; p = 0.0008), while age 50 years confirmed SARS-CoV-2 infection had a 15.4-fold risk of death compared with patients <50 years of age (RR 15.44: 95% CI 13.02–18.31; p < 0.00001) [10]. Based on the results of other studies, the predictive factors for the survival of geriatric patients with Covid-19, besides age, were also the level of weakness assessed based on the CFS (Clinical Frailty Scale). Frailty is an age-related clinical condition characterized by decreased physiological capacity in several organ systems. Changes in the immune system in the elderly with covid-19 contribute to increased susceptibility to infection, including a less immune solid response [11]. Based on the results of this study, from 278 respondents aged 61-70 years, 156 had comorbid. This comorbidity may cause weakness at the age of 61-70 years, causing a high risk of mortalities at that age.

The results of the cross-tabulation show that men have a higher mortality rate than women. Gender is associated with mortality, but with binary logistic regression testing, gender is not a factor that affects mortality. This study is not in line with previous research. Men have a higher risk of death than women. Gender differences have different in the response of the innate immune system, namely cytokines and chemocytokines. Men have a higher natural immune response than women, which can aggravate someone with covid-19. In addition, T cell activation in women increases but not in men [12].

Based on the type of comorbidity suffered sequentially, the most influential death are cerebrovascular disease, HIV, respiratory disease, diabetes mellitus, and cardiovascular disease. Patients with a history of the cerebrovascular disease have a high risk of death compared to other comorbidities. Other studies show that severity increases in patients with a history of cerebrovascular disease, with OR=4.85 (95% CI=3.11-7.57), indicating that nervous system disease is associated with the pathogenesis Covid-19 [13]. SARS -CoV-2 infects cells through the binding of the viral spike protein to the ACE2 receptor. ACE2 receptors are found not only in pulmonary alveolar epithelial cells but also in vascular endothelium. Therefore, cerebrovascular disease exacerbates covid-19 due to biochemical hypercoagulation that results in cerebral thrombogenesis and ischemic and direct vascular endothelial damage. Other studies have shown that respiratory system diseases, namely COPD, are also associated with worsening progression and prognoses of covid-19 [14].

Other studies have shown that respiratory system diseases, namely COPD, are also associated with worsening progression and prognoses of Covid-19 [15]. Damage to the pulmonary alveolar epithelial cells will aggravate the condition of COVID-19 patients who have comorbid Respiratory Disease. In addition, patients with comorbid diabetes also increase the severity of COVID-19. Diabetic uncontrol has higher mortality compared to

the controlled diabetic. Poor blood glucose control increases the risk of complications and death [16]. In another study, the meta-analysis results showed factors that increased the severity of COVID-19 (OR 2.61, 95% CI: 2.02–3.39) diabetes and hypertension (OR 2.37, 95% CI: 1.80–3.13) [13]. Meanwhile, in this study, hypertension was not a risk factor.

CONCLUSION

There is a relationship between age, gender, the presence of comorbidities, the type of comorbidity with the death of Covid-19 patients. The main risk factors for death were the presence of comorbidities and age. Comorbid risk factors that increase the risk of death for COVID-19 patients are cerebrovascular disease, HIV, respiratory disease, diabetes mellitus, and cardiovascular disease. Age factors that increase the risk of death are 61-70 years, 51-60 years, and 41-50 years.

Based on the results of this study, further researchers can research by analyzing factors related to the death of COVID-19 patients more specifically, such as the clinical character of Covid-19 patients.

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