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Risk Factors for Mortality of Patients with COVID-19 in RSJPD Harapan Kita, Jakarta

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Abstract

Background: *The COVID-19 disease has caused significant morbidity and mortality worldwide since COVID-19 was first reported in December 2019. The more severe types of disorders leading to mortality occured more frequently in the elderly and in patients with more than one comorbidity. This study aimed to determine the risk factors associated with mortality in COVID-19 patients at RSJPD Harapan Kita.*

Methods: *In this cross-sectional study, 500 adult inpatients (≥18 years old) with laboratory-confirmed COVID-19 from RSJPD Harapan Kita between March 2020 until April 2021 were enrolled. The Demographic, clinical, and outcome data were extracted from the hospital medical record system. To explore the risk factors associated with mortality, univariate, bivariate and multivariate analysis using logistic regression were used.*

Results: *Of the 500 patients included in this study, 110 (22%) died in the hospital. The logistic regression multivariate analysis pointed out that age ≥65 years (adjusted odds ratio (aOR)=2.624; 95% CI=1.552–4.435), chronic lung disease (aOR=8.173; 95% CI=3.834–17.422), chronic kidney disease (aOR=2.523; 95% CI=1.358–4.689), and cardiovascular disease (aOR=3.149; 95% CI: 1.763–5.624) had been recognized as risk factors of mortality among COVID-19 patients.*

Conclusion: *Age ≥65 years, chronic lung disease, chronic kidney disease patients, and cardiovascular disease had been recognized as risk factors for mortality of COVID-19 patients at RSJPD Harapan Kita. Further research on the risk factors associated with COVID-19-related deaths need to be conducted to manage disease progression and to improve the treatment. (**J Respirol Indones 2022; 42 (2): 115–20)***

Keywords: *COVID-19, Risk Factors, Mortality, Comorbidities.*

Faktor Risiko Kematian pada Pasien COVID-19 di RSJPD Harapan Kita, Jakarta

Abstrak

Latar Belakang: *Penyakit COVID-19 telah menyebabkan morbiditas dan mortalitas yang bermakna di seluruh dunia sejak laporan pertama COVID-19 pada Desember 2019. Jenis gangguan yang lebih parah yang menyebabkan kematian, muncul lebih sering pada pasien usia lanjut dan pasien yang memiliki lebih dari satu penyakit penyerta. Penelitian ini bertujuan untuk mengetahui faktor risiko yang berhubungan dengan kematian pada pasien COVID-19 di RSJPD Harapan Kita.*

Metode: *Dalam uji potong lintang ini, 500 pasien rawat inap dewasa (≥18 tahun) dengan COVID-19 terkonfirmasi laboratorium dalam rentang Maret 2020 hingga April 2021 dari RSJPD Harapan Kita dimasukkan ke dalam penelitian. Data demografi karakteristik klinis dan luaran diekstraksi dari sistem rekam medis rumah sakit. Untuk mengeksplorasi faktor risiko yang terkait dengan mortalitas, analisis univariat, bivariat dan multivariat dengan regresi logistik digunakan dalam penelitian ini.*

Hasil: *Dari 500 pasien yang termasuk dalam penelitian ini, 110 subjek (22%) meninggal di rumah sakit. Analisis multivariat regresi logistik menunjukkan bahwa usia ≥65 tahun (adjusted odds ratio (aOR)=2,624; 95% CI=1,552–4,435), penyakit paru kronik (aOR=8,173; 95% CI=3,834–17,422), penyakit ginjal kronik (aOR=2,523; 95% CI=1,358–4,689), dan penyakit kardiovaskular (aOR=3,149; 95% CI=1,763–5,624) diidentifikasi sebagai faktor risiko kematian pada pasien COVID-19.*

Kesimpulan: *Usia ≥65 tahun, penyakit paru kronik, penyakit ginjal kronik, dan penyakit kardiovaskular diidentifikasi sebagai faktor risiko kematian pada pasien COVID-19 di RSJPD Harapan Kita. Penelitian lebih lanjut tentang faktor risiko terkait kematian pada COVID-19 diperlukan untuk mengendalikan perkembangan penyakit dan meningkatkan pengobatannya. (**J Respirol Indones 2022; 42 (2): 115–20)***

Kata Kunci: *COVID-19, Faktor Risiko, Mortalitas, Komorbiditas.*

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INTRODUCTION

In March 2020, the World Health Organization (WHO) officially declared COVID-19 a pandemic. COVID-19 is a disease caused by a new type of virus from one of the largest virus family, namely Coronavirus. The WHO named this virus as 2019-novel coronavirus (2019-nCoV) and finally it was named Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2).[1] As of 9th March 2022, 450 million confirmed cases of COVID-19, including 6.01 million deaths, had been reported to WHO.[2]

COVID-19 is a health problem that is currently a priority in various countries in the world, including Indonesia. In Indonesia, as of March 9, 2022, COVID-19 cases have reached 5.8 million cases with around 30,000 new cases reported every day.[3] The COVID-19 problem in Indonesia that has become a concern, apart from the increasing number of new cases, is the death rate of COVID-19 patients which is also increasingly concerning. The Indonesian COVID-19 Task Force reported that the COVID-19 case fatality rate in Indonesia has touched 2.6%, higher than the global mean mortality rate of 1.3%. Until March 9, 2022, the number of patients who died from COVID-19 in Indonesia had reached more than 150,000 people with an average of 300 people dying every day.[3]

The COVID-19 disease has caused significant morbidity and mortality worldwide since COVID-19 was first reported in December 2019.[1] Based on previous studies, the more severe types of disorder that caused loss of life occured more frequently in elderly, especially the older adult population group and those with more than one comorbidity.[4]

RSJPD Harapan Kita is one of the COVID-19 referral hospitals in Jakarta area especially for COVID-19 patients with cardiovascular disease. Currently, there is no study to determine the risk factors associated with mortality in COVID-19 patients at RSJPD Harapan Kita. In addition, there was a suspicion regarding the number of deaths in certain age groups. The purpose of this study was to identify risk factors associated with mortality of COVID-19 patients at RSJPD Harapan Kita, Jakarta.

METHODS

This was a cross-sectional observational study with a quantitative approach. The population in this study were all COVID-19 patients at RSJPD Harapan Kita, Jakarta. The sample used in this study was 500 patients who met the inclusion criteria obtained using random sampling technique. This study was conducted on 500 adults patients (≥18 years old) hospitalized with confirmed COVID-19 infection at RSJPD Harapan Kita, Jakarta who were admitted to COVID-19 Isolation Room or COVID-19 ICU between March 2020 to April 2021. Confirmed cases of COVID-19 were determined by a positive result in the polymerase chain reaction (PCR) test. This study was approved by the Institutional Review Board of RSJPD Harapan Kita (No: LB.02.01/VII/578/KEP 054/202).

The demographic characteristics examined were age and sex. Clinical features included primary comorbidities such as hypertension, diabetes, chronic lung disease, chronic kidney disease, and cardiovascular disease. Demographic, clinical, and outcome data were extracted from the hospital medical record system.

Death following COVID-19 infection was considered as the main outcome in this study. The study population was categorized into two groups: death (described as patients with an outcome labeled death) and survived (described as patients with an outcome labeled cured or discharged).

Statistical analysis was performed using SPSS (version 24). The normality of continuous variables was assessed using the Kolmogorov–Smirnov test. In this study, continuous variables with and without normal distribution were mentioned as mean (with standard deviation) and median (with interquartile range/IQR), while categorical data were presented as frequency (percentage with 95% CI). Statistical analysis was accomplished in univariate analysis, bivariate analysis using chi-square test for categorical variables and Mann Whitney U test for continuous variables (OR with 95% CI), and multivariate analysis using logistic regression (OR with 95% CI).

RESULTS

The demographic and clinical characteristics of the patients are shown in Table 1. In terms of outcomes, 390 patients (78%) were discharged or survived and 110 (22%) died during hospitalization. The median age (IQR) was 54 (40-63), and 307 patients (61.4%) were male. The most common comorbidities were cardiovascular disease of 293 (58.6%), hypertension of 186 (37.2%), and diabetes mellitus of 146 (29.2%).

Table 1. Demographics and Clinical Characteristics of Patients with COVID-19

Variable	n	%
Mortality		
Death	110	22
Survived	390	78
Age		
≥65	102	20,.4
<65	398	79.6
Sex		
Male	307	61.4
Female	193	38.6
Comorbidities		
Hypertension	186	37.2
Diabetes Mellitus	146	29.2
Chronic Lung Disease	41	8.2
Chronic Kidney Disease	63	12.6
Cardiovascular Disease	293	58.6

Bivariate analysis was carried out to determine the variables to be included in the multivariate analysis (*P*<0.25). Based on the bivariate analysis in Table 2, the variables included in the multivariate analysis were age ≥65 years (OR=4.04; 95% CI:=2.52–6.48; *P* <0.001), hypertension (OR=1.48; 95% CI=0.96–2.28; *P*=0.090), diabetes mellitus (OR=2.30; 95% CI=1.48–3.58; *P*<0.001), chronic lung disease (OR=9.90; 95% CI=4.91–19.93; *P*<0.001), chronic kidney disease (OR=4.39; 95% CI=2.53–7.61; *P*<0.001), and cardiovascular disease (OR=4.45; 95% CI=2.61–7.59; *P*<0.001). The sex variable had *P*>0.25 so it was not included in the multivariate analysis.

The results of the multivariable analysis are summarized in Table 3. Age ≥65 years (aOR 2.624; 95% CI: 1.552–4.435), chronic lung disease patients (aOR 8.173; 95% CI: 3.834–17.422), chronic kidney disease (aOR 2.523; 95% CI: 1.358–4.689), and cardiovascular disease (aOR 3.149; 95% CI: 1.763–5.624) were identified as multicausal risk factors for mortality among COVID-19 patients.

Table 3. Final Model of Multivariate Analysis

Variables	Adjusted OR	95% CI	*P*
Age ≥65 years	2.624	1.552–4.435	<0.001
Comorbidities			
Chronic Lung Disease	8.173	3.834–17.422	<0.001
Chronic Kidney Disease	2.523	1.358–4.689	0.003
Cardiovascular Disease	3.149	1.763–5.624	<0.001

Table 2. Result of Bivariate Analysis

Variable	Death (n = 110)	Survived (n = 390)	Total (n = 500)	OR (95% CI)	*P*
Age					
≥65	45 (44.1%)	57 (55.9%)	102 (20.4%)	4.04 (2.52 – 6.48)	<0.001*
<65	65 (16.3%)	333 (83.7%)	398 (79.6%)		
Sex					
Male	63 (20.5%)	244 (79.5%)	307 (61.4%)	0.80 (0.52 – 1.23)	0.370
Female	47 (24.4%)	146 (75.6%)	193 (38.6%)		
Comorbidities					
Hypertension	49 (26.3%)	137 (73.7%)	186 (37.2%)	1.48 (0.96 – 2.28)	0.090
Non-Hypertension	61 (19.4%)	253 (80.6%)	314 (62.8)		
Diabetes Mellitus	48 (32.9%)	98 (67.1%)	146 (29,2%)	2.30 (1.48 – 3.58)	<0.001*
Non-Diabetes Mellitus	62 (17.5%)	292 (82.5%)	354 (70.8%)		
Chronic Lung Disease	28 (68.3%)	13 (31.7%)	41 (8.2%)	9.90 (4.91 – 19,93)	<0.001*
Non-Chronic Lung Disease	82 (17.9%)	377 (82.1%)	459 (91.8%)		
Chronic Kidney Disease	31 (49.2%)	32 (50.8%)	63 (12.6%)	4.39 (2.53 – 7.61)	<0.001*
Non-Chronic Kidney Disease	79 (18.1%)	358 (81.9%)	437 (87.4%)		
Cardiovascular Disease	91 (31.1%)	202 (68.9%)	293 (58.6%)	4.45 (2.61 – 7.59)	<0.001*
Non-Cardiovascular Disease	19 (9.2%)	188 (90.8%)	207 (41.4%)		

Note=*Significant (*P*<0.05)

DISCUSSION

This study identified several risk factors for mortality of COVID-19 patients in RSJPD Harapan Kita. Multivariate analysis showed that older age, chronic lung disease, chronic kidney disease, and cardiovascular disease were associated with higher odds of in-hospital death.

There was a statistically significant correlation (*P*<0.001) between older age and mortality of COVID-19 patients in RSJPD Harapan Kita. The risk analysis obtained an adjusted OR of 2.624 (95% CI=1.552–4.435), meaning that patients aged ≥65 years had a 2.624 times risk of dying compared to patients aged <65 years or in other words, patients aged ≥65 years had twice the risk of death compared to patients aged <65 years. The results of this study were in line with a study from Albitar, et al which stated that 80% of deaths associated with COVID-19 were observed in adults aged ≥65 years.[5] A proper explanation was that most of the older patients had numerous chronic diseases and poor health conditions to fight viral infections.[6]

Moreover, elderly patients were more likely to have weaker immune response; therefore, they were at greater risk to develop acute respiration distress syndrome (ARDS) and mortality.[7] Antibody production and response to viruses decrease with age, this occurs because of the reduced number of plasma cells contained in the bone marrow on the elderly population. This condition weakens the immune system so that the infection is not controlled and causes multi-organ failure, especially in organs or systems that have a lot of ACE-2 receptors such as the respiratory, cardiovascular, hepatic, and renal system.[8]

From several studies, it was mentioned that COVID-19 patients with chronic comorbidities have been associated with excessive COVID-19 situations including mortality. Multivariate analysis in this study obtained that comorbidities which had significant association with high risk of mortality were chronic lung disease, chronic kidney disease, and cardiovascular disease.

It was found that there was a statistically significant correlation (*P*<0.001) between chronic lung disease and mortality of COVID-19 patients in RSJPD Harapan Kita. The risk analysis obtained aOR value of 8.173, meaning that patients with chronic lung disease such as asthma, emphysema, bronchitis, chronic obstructive pulmonary disease (COPD), and pulmonary hypertension had eight times greater risk of death compared to patients without chronic lung disease.

Intuitively, since COVID-19 mainly affects the respiratory system, patients with chronic lung disease may be susceptible to worse outcomes from COVID-19 than patients without chronic lung disease. According to recent findings, COVID-19-related lung disease in ARDS remains the leading cause of mortality worldwide.[9] Patients with lung disease may be at greater risk for Covid-19 morbidity, over and above risks conferred by metabolic conditions alone. This was supported by evidence that patients in such situations sustained damage to their lung tissue.[10] Furthermore, patients with lung disease including COPD also have impaired innate and adaptative immune responses and express inappropriate respiratory viral clearance.[11]

There was a statistically significant correlation (*P*=0.003) between chronic kidney disease and mortality of COVID-19 patients in RSJPD Harapan Kita. The risk analysis showed aOR 2.523, meaning that patients with chronic kidney disease such as acute kidney injury (AKI), severe electrolyte imbalances, and glomerular disease had the possibility of 2.523 times greater risk of death compared to patients without chronic kidney disease. This result was consistent with study from Surendra, et al who discovered a significant correlation (*P*<0.001) between chronic kidney disease and mortality in patients with an aOR of 2.60 (95% CI=1.64–4.13).[12]

Chronic kidney disease is the most common risk factor for mortality in patients with COVID-19 worldwide, and the risk increases with higher stages of chronic kidney disease, with the highest risk occurring in those with kidney failure receiving replacement therapy and kidney transplant

recipients.[13] This might be due to the fact that in patients with chronic kidney disease, the inflammatory immune response occurs because of continuous oxidative stress, due to the presence of prolonged levels of pro-inflammatory cytokines. As a result, a compromised immune system can increase the susceptibility to bacterial and viral infections, and this may be the main reason for the extended hazard of pulmonary inflammation.[14]

It was determined that there was a significant correlation (*P*<0.001) between cardiovascular disease and mortality of COVID-19 patients in RSJPD Harapan Kita. Risk analysis received an aOR of 3.149, meaning that patients with cardiovascular disease have a three times risk of death compared to patients without cardiovascular disease. This result was in accordance to a study from Du, et al which pointed out that there was a statistically significant correlation (*P*=0,007) between cardiovascular disease and mortality in COVID-19 patients (aOR=2.464, 95% CI=1.279–4.747).

COVID-19 patients with cardiovascular disease tend to be at high risk, possibly because of the presence of ACE-2 receptors on cardiac muscle cells. Patients with cardiovascular disease have a higher risk of developing acute coronary syndromes in acute infections, which sooner or later lead to myocardial damage or infarction.[15]

This study had several limitations. First, this study used cross-sectional design in which effect sizes were reported using odds ratios even though the percentage of outcome was low, so the results were likely to be overestimated. Second, pre-existing comorbidities were retrieved from the medical record database which was obtained not only from the assessment in the treatment room and laboratory measurement but also from the patient's acknowledgment at that time.

Therefore, the severity of the comorbidities and patient adherence to medical prescriptions could not be evaluated. In addition, this study was only conducted at RSJPD Harapan Kita, which was a COVID-19 plus cardiovascular referral hospital so that the characteristics of patients treated at this hospital were very different from patients admitted to other hospitals which were non-referral for cardiovascular and COVID-19. Therefore, the results of this study might not reflect the mortality rate and risk factors for COVID-19-related mortality in the general population.

CONCLUSION

In conclusion, about 22% of hospitalized patients with COVID-19 in our study died. Age ≥65 years, chronic lung disease, chronic kidney disease patients, and cardiovascular disease were recognized as risk factors for mortality of COVID-19 patients at RSJPD Harapan Kita. Further research on the risk factors associated with COVID-19-related deaths need to be conducted to manage disease progression and to improve the treatment.

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