Comorbid Diseases and Outcomes of Critically Ill COVID-19 Patients Admitted to an Indonesian Intensive Care Unit from May to October 2021

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ABSTRACT

Introduction: Coronavirus disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The spread of COVID-19 has become a worldwide health threat, with 583,038,110 cases and a death toll of 6,416,023. This study attempted to determine the relationship of age, sex, and comorbid diseases with the outcomes of critically ill COVID-19 patients at Prof. Dr. IGNG Ngoerah Central General Hospital, Denpasar, Indonesia.

Methods: This analytic study employed a retrospective approach, analyzing secondary data from medical records using a purposive sampling method. The research included univariate analysis, bivariate analysis using the chi-square test, and multivariate analysis using a general linear model performed with the assistance of IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, N.Y., USA). A statistical analysis result with a p-value of less than 0.05 was deemed significant.

Results: A total of 264 critically ill COVID-19 patients were hospitalized in the Intensive Care Unit of Prof. Dr. IGNG Ngoerah Central General Hospital from May to October 2021. Comorbid diseases were present in 215 patients. The comorbid diseases that had the greatest impact on increasing mortality were diabetes mellitus, hypertension, kidney disease, and cardiovascular disease (p=0.000–0.006, 95% CI).

Conclusion: Age and sex do not have any significant relationship with the outcomes of critically ill COVID-19 patients. Meanwhile, comorbid diseases, such as diabetes mellitus, hypertension, and renal and cardiovascular diseases, pose a significant impact on the mortality rate of critically ill COVID-19 patients.

Keywords: Coronavirus disease 2019 (COVID-19); critical illness; comorbid diseases; health risks

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Highlights:

1. This study investigated patients who were critically ill with COVID-19 to determine the relationship between age, sex, comorbidities, and patient outcomes.

2. The findings of this study may provide additional data on the impact of comorbidities on the severity of COVID-19, which can be valuable to prevent mortality due to the infection.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is an infectious disease that is caused by an infection by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). SARS-CoV-2, a novel type of coronavirus belonging to a group that typically causes respiratory infections, has not been previously found in humans. There are two kinds of coronavirus that can incur extreme health consequences: one is responsible for Middle East respiratory syndrome (MERS), and the other causes severe acute respiratory syndrome (SARS) (World Health Organization, 2020). The spread of the COVID-19 infection has emerged as the most catastrophic global health threat, rapidly disseminating across various countries. On March 11, 2020, the World Health Organization (2020) declared a worldwide pandemic of COVID-19 in response to the rapid spread of the coronavirus. Numerous countries have reported positive

cases of COVID-19 since then.

The World Health Organization (2022) reported on August 10, 2022, that the global incidence of COVID-19 had reached 583,038,110 cases, with a death toll of 6,416,023 cases. The United States has recorded the highest number of positive COVID-19 cases, totaling 78,809,456, along with a death toll of 945,242. Indonesia documented a total of 6,249,403 positive COVID-19 cases, resulting in a death toll that reached 157,113. The country ranked 17th in the world and 4th in Southeast Asia in terms of the highest number of positive COVID-19 cases (Center for Strategic and International Studies, 2021). According to the provided data, the Bali province of Indonesia recorded a high number of positive COVID-19 cases until July 2022, with as many as 162,499 cases and a death toll of 4,611. Moreover, Bali had the eighth-highest number of cases in Indonesia (World Health Organization, 2022).

A study conducted by Styawan (2021) in Indonesia found a higher prevalence rate of positive COVID-19 cases among young individuals aged 31–35 years, with a rate of 31%. The study further showed that the highest mortality rate was observed in the elderly population, namely individuals over 60 years old. In the analysis comparing the prevalence of positive COVID-19 cases in different sex categories, it was found that males were more susceptible to COVID-19 infection than females, with rates of 58.5% versus 41.4%. The analysis of comorbid diseases revealed that confirmed COVID-19 patients commonly exhibited hypertension, diabetes mellitus, heart disease, chronic obstructive pulmonary disease (COPD), cancer, tuberculosis, stroke, kidney disease, human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS), asthma, and hyperthyroidism.

Karyono & Wicaksana (2020) conducted an analysis on the characteristics of COVID-19 patients and found that the age group of 31–45 years had a higher prevalence rate (29.3%) compared to other age groups. According to the findings of the study, males accounted for 54.6% of the confirmed cases, while females accounted for 45.4%. In the study, the three most common comorbidities observed among COVID-19 patients were hypertension (52.1%), diabetes mellitus (33.6%), and cardiovascular disease (33.6%). The COVID-19 patients also had other comorbid diseases, such as chronic obstructive pulmonary disease, kidney disease, asthma, cancer, tuberculosis, liver disease, and immune disorders.

Research carried out by Kangdra (2021) concluded that the incidence of positive COVID-19 cases was higher in males, accounting for 59.1% of the total cases, compared to a 40.9% prevalence rate in females. In addition, the study found that individuals in the age group of 46–65 years had a higher prevalence rate (60.9%) in comparison to other groups. The study indicated that certain comorbid factors were associated with positive COVID-19 cases. These comorbidities included diabetes mellitus (20%), hypertension (16.4%), chronic obstructive pulmonary disease (1.3%), ischemic stroke (5.5%), and pulmonary tuberculosis (3.6%). Out of all the patients, 57.3% did not have any comorbidities.

In a study carried out by Cibro et al. (2022), they revealed that the prevalence rate of confirmed COVID-19 cases was higher in males (50.7%) than in females (47.9%). The age group of individuals above 50 years constituted the largest proportion of COVID-19 patients, with a prevalence rate of 60.7%. According to the comorbidity data, the most common diseases among the COVID-19 patients were diabetes mellitus (47%), kidney disease (40%), hypertension (26%), chronic obstructive pulmonary disease (23%), tuberculosis (7%), cardiovascular disease (5%), cancer (3%), asthma (3%), and stroke (3%). In order to build upon previous research on the prevalence of positive COVID-19 cases, this study aimed to determine the relationship between comorbidities and outcomes among critically ill COVID-19 patients hospitalized in the Intensive Care Unit of Prof. Dr. IGNG Ngoerah Central General Hospital, Denpasar, Indonesia, from May to October 2021.

METHODS

This research was conducted in the form of an analytic study using a retrospective approach, with the subjects selected by purposive sampling (Campbell et al., 2020; Talari & Goyal, 2020). In this study, we carried out analysis on secondary data obtained from medical records. The purpose was to map the characteristics of critically ill COVID-19 patients as well as determine the relationship between comorbid diseases and patient outcomes.

The population of this study comprised all patients who were critically ill with COVID-19 and admitted to the Intensive Care Unit (Mawar Room) of Prof. Dr. IGNG Ngoerah Central General Hospital, Denpasar, Indonesia, between May and October 2021. The research samples were collected from the medical records of these critically ill COVID-19 patients (Vassar & Matthew, 2013). The data included the age, sex, and comorbidities of the patients. The number of patients who were critically ill with COVID-19 in the Intensive Care Unit of Prof. Dr. IGNG Ngoerah Central General Hospital, Denpasar, Indonesia, throughout the specified period of time was 264 individuals. However, the number of patients with complete data for inclusion in the study was only 215 individuals (Andrade, 2021).

The dependent variable in this study was the incidence of critical COVID-19, while the independent variables were age, sex, and comorbid diseases. The statistical analyses performed in this study were univariate analysis, bivariate analysis utilizing the chi-square test, and multivariate analysis utilizing a general linear model. The bivariate analysis was carried out to ascertain the relationship between variables, whereas the multivariate analysis results simultaneously indicated which independent variable had the most significant influence on the dependent variable. The comorbidity with the most significant influence on mortality could be identified from the odds ratio (OR), as represented by the Exp(B). We used IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, NY, USA) to perform the statistical analyses. A p-value of less than 0.05 showed a statistically significant result (McHugh, 2013). The demographic data and analysis results were processed to be presented in tabular format, showing the distribution of frequency and percentage.

RESULTS

The results of the univariate analysis showed the frequency and percentage of the independent variables observed among patients who were critically ill with COVID-19 in the Intensive Care Unit of Prof. Dr. IGNG Ngoerah Central General Hospital, Denpasar, Indonesia. As shown in Table 1, the analysis results included the distribution of age, sex, and comorbid diseases among the critically ill patients.

It was found that the largest proportion of the patients, specifically 155 individuals (71.1%), were 50 years old or older. A total of 60 patients (28.9%) were under the age of

50. The majority of patients who were critically ill with COVID-19 were male, accounting for 127 individuals (59.0%), in comparison with only 88 female patients (41.0%). Out of the total number of COVID-19 patients who were critically ill, 215 (81.4%) had comorbidities. Those that did not have any comorbidities were much fewer, with as many as 49 patients (18.6%). From May to October 2021, there were a total of 264 COVID-19 patients who were in a critical condition. Among the 264 patients, comorbidities were present in 215 individuals (81.4%). The predominant comorbid diseases found among the critically ill COVID-19 patients were diabetes mellitus with 83 patients (28.5%), hypertension with 72 patients (24.7%), and kidney disease with 64 patients (21.9%). The most prevalent outcome observed in the patients with comorbid diseases was mortality due to critical COVID-19, with as many as 246 cases (87.9%). Only 35 patients, accounting for 12.1%, survived the COVID-19 infections.

Table 1. Characteristics of patients who were critically ill with COVID-19

Variables	n	%
Age (y.o.)		
<50	60	28.9
≥50	155	71.1
Total	215	100.0
Sex		
Male	127	59.0
Female	88	41.0
Total	215	100.0
Comorbidity		
Present	215	81.4
Absent	49	18.6
Total	264	100.0
Comorbid diseases		
Diabetes mellitus	83	28,5
Hypertension	72	24.7
Kidney disease	64	15.8
Cardiovascular disease	46	2.74
Stroke	8	2.74
Cancer	8	1.03
Hyperthyroidism	3	0.68
Autoimmune disease	2	0.68
Liver disease	2	0.34
COPD	1	0.34
Asthma	1	0.34
Pulmonary TB	1	0.34
Total	291	100.0
Outcomes		
Mortality	256	87.9
Survival	35	12.1
Total	291	100.0

Note: COPD = chronic obstructive pulmonary disease; TB = tuberculosis; y.o. = years old.

In this study, bivariate analysis was performed to investigate whether age, sex, and comorbid diseases were related to the outcomes of patients who were critically ill with COVID-19 in the Intensive Care Unit of Prof. Dr. IGNG Ngoerah Central General Hospital, Denpasar, Indonesia. Specifically, the chi-square was employed for the bivariate analysis of two variables. Table 2 presents the results of the analysis of age and patient outcome variables. No statistically significant relationship was observed between the age variable and the outcomes of critically ill COVID-19 patients. The analysis yielded a p-value of 0.372 for both age groups, namely those under 50 years old and those 50 years old or older.

Table 2. Relationship between age and outcomes in the patients who were critically ill with COVID-19

Age (y.o.)	Mortality		Survival		p
	n	%	n	%	
<50	58	96.6	2	3.4	0.372
≥50	145	93.5	10	6.5	0.372
Total	203	100.0	12	100.0	

Note: The chi-square test was employed in the analysis. y.o. = years old.

Table 3 displays the results of the bivariate analysis examining the relationship between sex and outcomes of critically ill COVID-19 patients in the Intensive Care Unit of Prof. Dr. IGNG Ngoerah Central General Hospital, Denpasar, Indonesia. According to the data, there was no statistically significant relationship between age and outcomes, as indicated by a p-value of 0.854.

Table 3. Relationship between sex and outcomes among the critically ill COVID-19 patients

Sex	Mortality		Survival		p
	n	%	n	%	
Male	116	91.3	11	8.7	0.854
Female	81	8.7	7	91.3	0.854
Total	197	100.0	18	100.0	

Note: The chi-square test was employed in the analysis

The results of the bivariate analysis examining the relationship between comorbidities and outcomes among the patients who were critically ill with COVID-19 in the Intensive Care Unit of Prof. Dr. IGNG Ngoerah Central General Hospital, Denpasar, Indonesia, are presented in Table 4. The data displayed in the table revealed that there was a statistically significant relationship between comorbidities and patient outcomes. Specifically, comorbidities were related to increased mortality among the critically ill COVID-19 patients throughout May–October 2021. This was indicated by a p-value of 0.000 for each comorbid disease.

Table 4. Relationship between the critically ill COVID-19 patients' comorbidities and outcomes

Comorbid diseases	Mortality		Survival		p
	n	%	n	%	
Diabetes mellitus	81	97.5	2	2.5	0.000
Hypertension	62	86.1	10	13.9	0.000
Kidney disease	60	93.7	4	6.3	0.000
Cardiovascular disease	35	76	11	24	0.000
Stroke	6	75	2	25	0.000
Cancer	4	50	4	50	0.000
Hyperthyroidism	3	100	0	0	0.000
Autoimmune disease	2	100	0	0	0.000
Liver disease	1	50	1	50	0.000
COPD	0	0	1	100	0.000
Asthma	1	100	0	0	0.000
Pulmonary TB	1	100	0	0	0.000
Total	256	100	35	0	

Note: The chi-square test was employed in the analysis. COPD = chronic obstructive pulmonary disease; TB = tuberculosis.

Table 5. Results of the multivariate analysis examining comorbidities and mortality among the critically ill COVID-19 patients

Comorbid diseases	Mortality		Exp(B)	95% CI	p
	n	%			
Diabetes mellitus	81	97.5	1.629-1.738	95%	0.001
Hypertension	62	86.1	1.667-1.771	95%	0.000
Kidney disease	60	93.7	1.700-1.800	95%	0.001
Cardiovascular disease	35	76	1.776-1.865	95%	0.006
Stroke	6	75	1.949-1.989	95%	0.291
Cancer	4	50	1.949-1.989	95%	0.291
Hyperthyroidism	3	100	1.976-2.001	95%	0.521
Autoimmune disease	2	100	1.982-2.001	95%	0.601
Liver disease	1	50	1.989-2.003	95%	0.712
COPD	0	0	1.989-2.003	95%	0.712
Asthma	1	100	1.989-2.003	95%	0.712
Pulmonary TB	1	100	1.989-2.003	95%	0.712
Total	256	100			

Note: The multivariate analysis was performed using general linear model. COPD = chronic obstructive pulmonary disease; TB = tuberculosis; Exp(B) = odds ratio; CI = confidence interval.

Table 5 exhibits the results of the multivariate analysis, which determined the comorbidity with the most significant influence on the outcomes of critically ill COVID-19 patients. Diabetes mellitus and hypertension were identified as the comorbidities with the most significant impact on mortality, according to the multivariate analysis.

The data from the multivariate analysis revealed that the yielded p-values varied for the relationship between mortality and different comorbidities, i.e., diabetes mellitus (p=0.001), hypertension (p=0.000), kidney disease (p=0.001), and cardiovascular disease (p=0.06). The results indicated that these four comorbidities exerted the most significant influence on the incidence of mortality among patients who were critically ill with COVID-19 in the Intensive Care Unit of Prof. Dr. IGNG Ngoerah Central General Hospital, Denpasar, Indonesia, from May to October 2021.

DISCUSSION

This study presented the distribution of patients who were critically ill with COVID-19 and hospitalized in the Intensive Care Unit of Prof. Dr. IGNG Ngoerah Central General Hospital, Denpasar, Indonesia, from May to October 2021. It was found that the majority of the patients, amounting to 155 individuals (71.7%), were 50 years old or older. The results of this study align with previous research conducted by Cibro et al. (2022), which revealed that individuals aged 50 years or older were more susceptible to suffering from COVID-19. The study reported that 133 patients (60.7%) fell within this age group. This susceptibility is attributed to a gradual reduction in the homeostasis function (body balance) of the body that diminishes with advancing age. Homeostasis is a primary principle of physiology that reflects the ability of the body to autonomously regulate and uphold stability against suboptimal internal and external environments in order to ensure survival. The SARS-CoV-2 virus enters the body by binding to the angiotensin-converting enzyme 2 (ACE2) receptor, which then triggers a series of homeostatic response processes. The renin-angiotensin-aldosterone system (RAAS) is the main homeostatic system in the body that involves the brain, lungs, kidneys, and liver to regulate electrolyte balance, blood pressure, and fluid volume. The entry of the SARS-CoV-2 virus into the body causes dysregulation of RAAS, which plays a crucial role in causing lung damage. Therefore, increasing age causes the elderly to be in an unfavorable condition to fight aggressive infections (Siswanto, 2020).

While the majority of critically ill COVID-19 patients were 50 years of age or older, there was no statistically significant relationship between age and patient outcomes, as evidenced by a p-value of 0.372. This finding is consistent with previous research conducted by Daud et al. (2022), which demonstrated that there was no statistically significant relationship between age and the incidence of COVID-19. This was confirmed by the results of the analysis, which produced a p-value of 1.000. Age is considered an unmodifiable factor that influences the likelihood of developing a disease. Certain age groups may have reduced immunity, leaving them more vulnerable to COVID-19 infections (Hasnidar et al., 2020). A study undertaken by Ruapertiwi (2021) at Putri Hijau Level II Hospital, Kesdam I/Bukit Barisan, Medan, Indonesia, revealed that there was no statistically significant relationship between patient determinants, such as age, and the incidence of COVID-19. This was demonstrated by the results of the research, which yielded a p-value of 0.097.

Among all of the patients who were critically ill with COVID-19 in the Intensive Care Unit of Prof. Dr. IGNG Ngoerah Central General Hospital, Denpasar, Indonesia, there were 127 male patients (59.0%), which outnumbered their female counterparts. This finding aligns with a prior study performed by Wenham et al. (2020), which concluded that male patients were the predominant group, comprising 111 individuals (50.7%). The potential cause of this phenomenon could be attributed to differences in the immunological system of men, which exhibits higher sensitivity compared to women. Additionally, variations in lifestyle choices, such as smoking, might also contribute to this discrepancy. According to the Novel Coronavirus Pneumonia Emergency Response Epidemiology Team (2020), the Chinese Center for Disease Control and Prevention (China CDC) observed a higher prevalence of COVID-19 among male patients in comparison to female patients.

Although this study showed a higher prevalence of positive COVID-19 cases in male patients than in female patients, the statistical analysis did not indicate any significant relationship between sex and patient outcomes. This was demonstrated by the results of the statistical analysis, which yielded a non-significant p-value of 0.854. The results of a study conducted by Daud et al. (2022) corroborate this study by confirming that there was no statistically significant correlation between sex and COVID-19 cases, as evidenced by a p-value of 0.924. A separate study, which was carried out by Putri et al. (2021) in West Sumatra, Indonesia, provided similar findings. The study demonstrated that males and females have the same risk of being infected with COVID-19, as indicated by a p-value of 0.485.

This study also provided an analysis of the distribution of comorbid diseases among patients who were critically ill with COVID-19. The most common comorbidity among the patients was diabetes mellitus, affecting 83 individuals (28.5%). Subsequently, 72 patients (24.7%) had comorbid hypertension, 64 patients (21.9%) suffered from kidney disease, and 46 patients (15.8%) had been diagnosed with heart disease. The statistical analysis revealed a significant relationship between comorbidities and the outcomes of critically ill COVID-19 patients, as indicated by a

p-value of 0.000. In the multivariate analysis, it was also discovered that comorbidities, including diabetes mellitus, hypertension, kidney disease, and cardiovascular diseases, had the greatest impact on patient outcome compared to other comorbidities. Specifically, these comorbidities were linked to the mortality rate of critically ill COVID-19 patients, as evidenced by a p-value of 0.000–0.006. The results of this study are comparable to those of a study conducted by Alkautsar (2021), which involved comprehensive analyses of national and international journal articles related to COVID-19 patients. In addition, the bivariate data obtained from a study conducted by Drew & Adisasmita (2021) revealed a significant relationship between comorbid hypertension and the mortality of COVID-19 patients, as evidenced by a p-value of 0.000. Comorbid diabetes mellitus was discovered to be associated with a 1.55-fold increase in the severity of COVID-19 and a 1.65-fold increase in the risk of mortality, with a statistically significant p-value of 0.00001.

Huang et al. (2020) provided a theoretical explanation stating that diabetes mellitus was the most predominant comorbid disease among COVID-19 patients, with a prevalence rate of 20%. This was followed by hypertension and other comorbidities. Diabetes mellitus is a condition that significantly poses an impact on morbidity and mortality worldwide. The condition is associated with a number of macrovascular and microvascular complications, which ultimately affect the overall survival of patients. Individuals with diabetes mellitus are more susceptible to infections, which can lead to more severe diseases (Pearson-Stuttard et al., 2016). However, further investigation is required to determine the effect of diabetes mellitus on the severity and mortality of COVID-19, either as an independent factor or in conjunction with other comorbidities (Zhou et al., 2020).

COVID-19 patients with multiple comorbidities are at a higher risk of experiencing an elevated degree of severity, which leads to mortality due to increased damage to many organs. This explanation is supported by the theory that ACE2, a SARS-Cov 2 receptor, can be found in multiple organs, such as the pancreas, heart, kidneys, lungs, intestines, stomach, bladder, and testicles. COVID-19 patients who have comorbid diabetes mellitus with uncontrolled hyperglycemia are at a higher risk of mortality compared to those with diabetes mellitus and controlled sugar levels (Rajpal et al., 2020). Comorbid diabetes mellitus has been believed to contribute to increased severity due to patients' heightened susceptibility to infection. The vulnerability of patients with diabetes mellitus to COVID-19 infection arises from an upregulation of ACE2, which allows enhanced viral attachment and replication. The development of immune dysfunction in diabetes mellitus can lead to a cytokine storm, which in turn contributes to the severity and mortality of COVID-19 (Muniyappa & Gubbi, 2020).

A study conducted in Guangzhou, China, that successfully isolated SARS-CoV-2 from urine samples of infected patients showed that the kidney is a potential target for SARS-CoV-2 infection. The incidence of acute kidney injury (AKI) was observed in 3–9% of the COVID-19 cases, with a mortality rate of 60–90% (Hassanein et al., 2020). The data from Indonesia, as reported by the COVID-19 Task Force (2021), revealed that the most prevalent comorbidity among 5,989 confirmed COVID-19 patients was hypertension (49.9%). Hypertension causes pathophysiological changes in the cardiovascular system, such as left ventricular hypertrophy and fibrosis. As a result, the heart of a hypertensive patient may be particularly vulnerable to SARS-CoV-2 infection (Fang et al., 2020).

This study offers valuable insights into the relationship between age, sex, comorbidities, and the outcomes of patients who were critically ill with COVID-19. The data obtained from this study have the potential to be relevant for formulating strategies and treatments aimed at minimizing unfavorable outcomes for COVID-19 patients with comorbidities. However, this study might be limited as it was conducted at a single center. Future studies with a larger sample size are necessary to broaden the extent of this study.

CONCLUSION

This study confirms that age and sex are not significantly related to the outcomes of patients who are critically ill with COVID-19. In contrast, there is a significant relationship between comorbidities and patient outcomes. Diabetes mellitus, hypertension, kidney disease, and cardiovascular disease notably contribute to the incidence of mortality among critically ill COVID-19 patients. Men and individuals that are 50 years of age or older, particularly those who have comorbid diseases, are recommended to strictly adhere to health protocols in order to prevent COVID-19 infection, considering the multiple risk factors that can heighten the likelihood of infection.

CONFLICT OF INTEREST

The authors declare no conflict of interest in conducting this study.

ETHICS CONSIDERATION

This study received an ethical exemption from the Research Ethics Committee of the Faculty of Medicine, Universitas Udayana, Denpasar, Indonesia, with registration No.2247/UN14.2.2.VII.14/LT/2024.

AUTHOR CONTRIBUTION

All authors contributed to the conception and design, analysis and interpretation of the data, drafting of the article, critical revision of the article for important intellectual content, final approval of the article, provision of study materials or patients, statistical expertise, provision of administrative, technical, or logistic support, as well as collection and assembly of data.

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