Original Research Paper

Survival analysis of COVID-19 patients with comorbidities in Bekasi during 2020-2021

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Abstract

Coronavirus disease 2019 (COVID-19) is a respiratory infectious disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). COVID-19 in patients with comorbidities progresses more rapidly to severity and frequently leads to death. Therefore, the objective of this study is to determine the length of survival and estimation of the Hazard Ratio (HR) of COVID-19 patients with comorbidities. The study design used a retrospective cohort of 3,751 samples and was analyzed using Kaplan Meier and cox regression. The survival function description shows the difference in the mean survival of COVID-19 patients without comorbid and patients with comorbidities of 78 days and 23 days, respectively, with HR of 4.4. In conclusion, comorbid COVID-19 patients possess a lower survival and a higher risk of death.

Keywords: COVID-19; comorbid; survival function

Analisis survival pasien COVID-19 dengan komorbiditas di Bekasi tahun 2020-2021

Abstrak

Coronavirus disease 2019 (COVID-19) merupakan penyakit infeksi pernafasan yang disebabkan oleh *Severe Acute Respiratory Syndrome Coronavirus* 2 (SARS-CoV-2). COVID-19 pada pasien dengan komorbid lebih cepat berkembang menuju keparahan dan seringkali menyebabkan kematian. Oleh karena itu, penelitian ini bertujuan untuk mengetahui lama ketahanan hidup dan estimasi *Hazard Ratio* (HR) pasien COVID-19 dengan komorbid. Desain penelitian menggunakan kohort retrospektif pada 3,751 sampel dan dianalisis menggunakan Kaplan Meier dan *cox regression*. Gambaran *survival function* menunjukkan perbedaan rerata ketahanan hidup pasien COVID-19 tanpa komorbid dan pasien dengan komorbid masing-masing 78 hari dan 23 hari dengan HR 4.4. Sebagai kesimpulan, pasien COVID-19 dengan komorbid mempunyai survival lebih rendah serta risiko kematian lebih tinggi.

Kata Kunci: COVID-19; komorbid; *survival function*

1. Introduction

Coronavirus disease 2019 (COVID-19) is a new type of respiratory tract infection caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). COVID-19 was first discovered in December 2019, spreading rapidly causing a worldwide pandemic and becoming a major global health problem (Wang et al., 2020; World Health Organization, 2020). According to the World Health Organization (WHO), as of June 29, 2021, SARS-CoV-2 had infected more than 180 million people and resulted in nearly 4 million deaths (World Health Organization, 2021). Data from the task force for handling COVID-19, the number of positive cases of COVID-19 in Indonesia as of September 19, 2021 was confirmed as many as 4,190,763 cases with a death toll of 140,468 or the Case Fatality Rate (CFR) (3.35%) (Satgas COVID-19, 2021).

COVID-19 is a disease that spreads very quickly and can be life-threatening with a higher severity, especially if the patient has comorbidities and the patient is elderly (Bobdey et al., 2021; Djaharuddin et al., 2021). The results of a systematic review and meta-analysis showed that the most common comorbidities in COVID-19 patients were hypertension (28.3%), diabetes mellitus (14.29%), cardiovascular disease (12.3%) and chronic kidney disease (5.19%) (Fathi et al., 2021). Comorbid COVID-19 patients are a group that is vulnerable to experiencing worsening conditions when exposed to COVID-19. The risk of severity in COVID-19 patients with hypertension increased by 2.3 times, respiratory disease 2.46 times, cardiovascular disease 3.42 times (J. Yang et al., 2020).

The risk of death in COVID-19 patients with comorbidities is up to 2.4 times higher than in those without comorbidities (Espinosa et al., 2020). The prevalence of death cases is more in men than women (Biswas et al., 2021; Djaharuddin et al., 2021; Espinosa et al., 2020; Jin et al., 2020). Research by Chan et.al (2020) shows that almost 80% of cases occur in patients aged over 60 years who have comorbidities, where as many as 2/3 of cases of death due to COVID-19 are men, while 1/3 of cases are women (Chan et al., 2020). The average case mortality based on comorbidities was cardiovascular disease 10.5%, diabetes mellitus (DM) 7.3%, chronic lung disease 6.3%, hypertension 6.0%, cancer 5.6% while without comorbidities 0.9% (Zhonghua, 2020).

Based on a study conducted in 30 hospitals in Mexico, the survival of COVID-19 patients with comorbid diabetes mellitus and kidney disorders, hypertension increased the risk of death with a hazard ratio of 1.91 (95% CI 1.70-2.15) where survival in the first 7 days was 0.822 and continued to decline on the 15th day, which was 0.482 (Murillo-Zamora & Hernandez-Suarez, 2021). Patient survival describes the cure rate and shows positive indicators that can be used by health workers for decision making and planning related to handling COVID-19. Public Hospital (RSUD) of dr. Chasbullah Abdul Madjid Bekasi City is the main referral hospital for COVID-19 patients in Bekasi City with an average number of COVID-19 patients every month of approximately 400 patients.

However, the results of research related to the risk of death for COVID-19 patients with comorbidities are mostly performed abroad. In addition, research on COVID-19 patients with comorbidities also discusses more about the risk of death compared to patient survival. Thus, this study aims to determine the length of survival of COVID-19 patients with comorbidities in Bekasi City in 2020-2021.

2. Research Method

The study used a retrospective cohort design by looking at survival in two groups of COVID-19 patients (comorbid COVID-19 patients and COVID-19 patients without comorbid). The population in this study were COVID-19 patients who were treated from September 1, 2020 to March 31, 2021. The minimum sample size was calculated using the survival test formula from Lwanga and Lemeshow with a significance degree of 95% (α=5%), 95% power. (β=5%), which refers to the hazard ratio of COVID-19 patients with a history of hypertension of 1.91 from the Murillo & Hernandez study, the minimum sample required was 63 cases (Murillo-Zamora & Hernandez-Suarez, 2021).

The sampling technique used was purposive sampling. Sample criteria include: patients with confirmed COVID-19 in the study period, both those with co-morbidities and those without as evidenced by positive PCR swab results; recorded the date of confirmed COVID-19 and the number of days of treatment. The sample of this study was 3751. The variables measured in this study were gender (women and men), comorbidities, discharge status (dead or alive), age (children and adolescents, early adulthood, middle adulthood, late adulthood). The analysis used is survival analysis using Kaplan-Meier with log rank and for the modeling using Cox regression with the assumption of proportional hazard. The use of the Kaplan-Meier test with log rank aims to identify the probability of survival, while the Cox regression is intended to obtain the HR (Heat Rate) value and determine the confidence interval

(Muhani & Sari, 2020; Sari & Muhani, 2020). This research has been through a process of ethical review by the ethics team of dr. Chasubullah Abdul Madjid Public Hospital Bekasi City with number: No.032/KEP/RSCAM/VI/2021.

3. Result and Discussion

Respondents in this study amounted to 3.751, the majority were female, as many as 1.907 (50.8%). Age was dominated by middle adults as much as 1.737 (46.3%). Patients died 630 (16.8%) and patients with comorbid 1.294 (34.5%), as presented in **Table 1**.

Table 1. Characteristics of respondents

Variable	Category	N (%)
Gender	Woman	1.907 (50.8)
	Man	1.844 (49.1)
Age	Children and teenagers	145 (3.9)
	Early adult	1.087 (29)
	Middle adult	1.737 (46.3)
	Late adult	783 (20.9)
Home status	Alive	3.122 (83.2)
	Die	630 (16.8)
Comorbid	No comorbid	2.458 (65.5)
	Comorbid	1.294 (34.5)

Based on **Table 2**, the most common comorbid types were diabetes mellitus as many as 251 respondents (19.4%), then hypertension 178 respondents (13.7%), heart disease 72 respondents (5.6%), lung disease 56 (4.3%), chronic kidney disease 21 (1.6%), and stroke, HIV, asthma, cancer 0.5%, 0.6%, and 0.3% respectively.

Table 2. Comorbid type

Variable	F	%
Diabetes mellitus	251	19.4
Hypertension	178	13.7
Lung disease	56	4.3
Heart disease	72	5.6
Chronic kidney disease	21	1.6
Stroke	11	0.9
HIV	6	0.5
Asthma	8	0.6
Cancer	4	0.3
More than one comorbid	687	53.1

Kaplan-Meier results in **Table 3** showed that COVID-19 patients without comorbidities, on average, could survive for 78 days. Meanwhile, COVID-19 patients with comorbidities are only able to survive on average for 23 days. In the Kaplan-Meier analysis, the results of the survival function show that there is an intersection as displayed in **Figure 1**, thus, it is continued for cox regression analysis. The results of the Cox regression test show that the hazard ratio is 4.4. Based on these results, it can be concluded that COVID-19 patients with comorbidities are at risk of 4 times greater risk of dying compared to COVID-19 patients without comorbidities, as illustrated in **Table 4**.

Table 3. Kaplan-Meier analysis

Comorbid	Estimated
No Comorbid	78.140
Comorbid	23.254
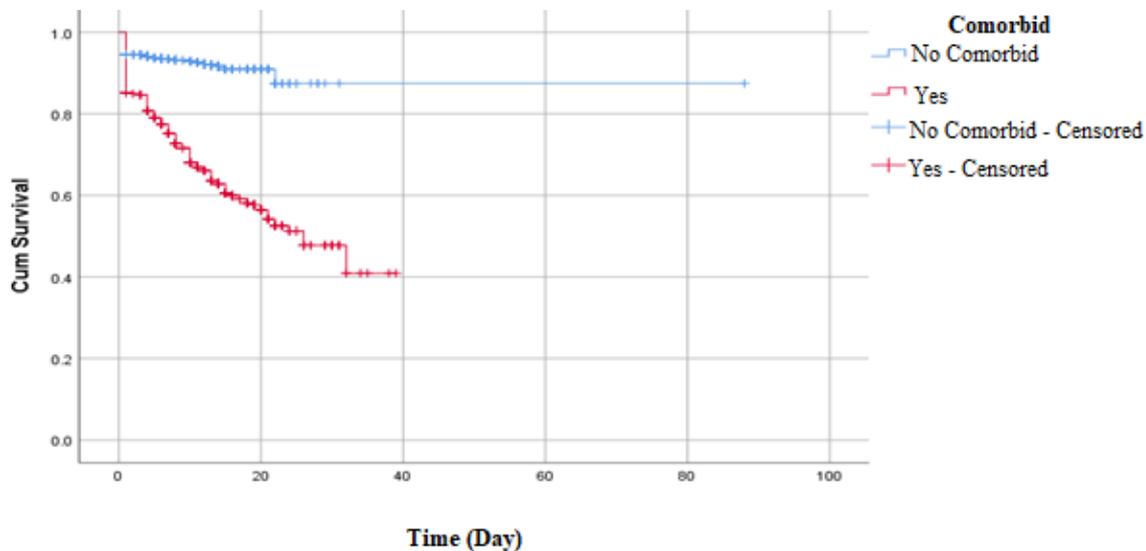
Figure 1. COVID-19 patient survival function

Table 4. Cox regression test results

Variable	β	p	HR	Confident Interval	
				Lower	Upper
Comorbid	1.481	0.000	4.39	3.676	5.263

The results of this study indicate that there are more female COVID-19 patients than males, as many as 1907 (50.8%) and 1844 (49.1%), respectively. This result is slightly different from the results of several previous studies which found that more cases of COVID-19 occurred in men than women (Docherty et al., 2020; Fathi et al., 2021; Mahumud et al., 2020; Ramírez-Soto et al., 2021; Sieber et al., 2021). It is possible due to the increasing number of cases of COVID-19 so that its spread is becoming more even in men and women. The age of the respondents in this study was dominated by middle adults as many as 1737 (46.3%) with 630 patients (16.8%) passing away. The number of deaths from COVID-19 in this study was lower than in the UK, which was 26% and higher than in India and America, by 5.8% and 13.1%, respectively (Altonen et al., 2020; Bobdey et al., 2021; Docherty et al., 2020). Comorbid COVID-19 patients in this study amounted to 1,294 (34.4%). This number is higher than the comorbidities in Jakarta as much as 31% but lower than in Oman, which is 51% (Khamis et al., 2020; Surendra et al., 2021). The results of this study indicate that 53.1% of patients who have more than one comorbid are at risk for death. Meanwhile, the results of another study revealed that 76% of deaths due to COVID-19 occurred in patients with more than one comorbidity (Bobdey et al., 2021).

The most common comorbid types in this study were diabetes mellitus as many as 251 respondents (19.4%), then hypertension 178 respondents (13.7%), heart disease 72 respondents (5.6%), lung disease 56 (4.3%), chronic kidney disease 21 (1.6%) followed by stroke, HIV, asthma, cancer 0.5%, 0.6%, and 0.3%, respectively. This is in accordance with several systematic reviews and meta-analyses which discovered that DM and hypertension were the two most common comorbidities in COVID-19 patients (Altonen et al., 2020; Fathi et al., 2021; J. Yang et al., 2020).

The results presented that there was a difference in the average length of life of COVID-19 patients. COVID-19 patients without comorbidities, on average, can survive for 78 days. Meanwhile, COVID-19 patients with comorbidities are only able to survive on average for 23 days. The results of the Cox regression test displayed that the hazard ratio value was 4.4. Comorbid COVID-19 patients are 4 times more likely to die than patients without comorbidities. The results of the study in Mexico displayed the same thing where the survival of COVID-19 patients with comorbid DM, hypertension and kidney disorders, hypertension increased the risk of death by (hazard ratio = 1.91, 95%, CI 1.70-2.15) where survival in the first 7 days was 0.822 and continued to decline on the 15th day at 0.482 (Murillo-Zamora & Hernandez-Suarez, 2021).

Indications for hospitalization in COVID-19 patients vary. It is definitely based on clear and accurate examinations. Most of the patients were treated with severe acute respiratory infection or severe acute respiratory syndrome. Criteria for intensive care also vary in each country, the need for care in the ICU ranges from 17%-38% (Docherty et al., 2020; Khamis et al., 2020; Machado-Alba et al., 2021). Old age, chronic disease, and male sex are consistently associated with increased risk of severity and mortality (Docherty et al., 2020).

The results of the study by Satria et.al, (2020) showed diabetes and cardiovascular disease to be the main risk factors for death in COVID-19 at 30.3% (OR 4,348, P 0.000) and 10.6% (OR 4,319, P 0.016) (Satria et al., 2020). The results of this study were strengthened by the results of a meta-analysis which showed an increase in severity and mortality 2-fold and 3-fold in DM, 3 and 4-fold in hypertension, and cardiovascular disease with the highest increase, which are 4-fold and 6-fold (De Almeida-Pititto et al., 2020). This study also presented similar results where DM was the most comorbid in COVID-19 patients. Diabetes mellitus is a disease of carbohydrate metabolism disorders caused by the failure of the pancreas gland to produce the hormone insulin. This condition causes high blood sugar levels and if it lasts chronically or for a long time it can cause a decrease in the function of white blood cells or leukocytes. As a result, the immune system will decrease so that individuals will be more susceptible to infection due to the entry of microorganisms including viruses (Smeltzer, S.C. & Bare, 2017). Recent findings suggest that higher levels of circulating cytokines such as interleukin-6 suggest a proinflammatory environment and have been associated with severity in COVID-19 patients with DM (Aggarwal et al., 2020; Sardu et al., 2020; Zheng et al., 2021). COVID-19 patients with DM possess a threefold increased risk of developing pneumonia, a twofold increased risk of severity/chronicity, and a threefold increased risk of in-hospital death (Leon-Abarca et al., 2021; Mantovani et al., 2020).

Cardiovascular disease and hypertension are associated with smoking, hypertension, and diabetes mellitus, which are thought to be at risk of increasing the excretion of ACE2 receptors or angiotensin converting enzyme 2 (Susilo et al., 2020). Indeed, there are no research results that confirm the definite link between hypertension and the severity of COVID-19, but in general, the severity of COVID-19 will be easier for people with hypertension related to old age and complications of other health problems (Q. Yang et al., 2020).

4. Conclusion

The results unveiled that there were differences in the average survival of patients infected with COVID-19. Comorbid COVID-19 patients have a lower survival (23 days) compared to COVID-19 patients without comorbidities (78 days) with a 4-times risk of death in patients with comorbidities. This research can be used as the basis for implications for further research related to the survival of COVID-19 patients in each different comorbid.

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