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Original Article

Medical comorbidities as predictors of COVID-19 short-term mortality: A historical cohort study in Indonesia

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Abstract

Objectives: In this study, we aimed to evaluate the relation of comorbidities to coronavirus disease 2019 (COVID-19) short-term mortality. **Materials and Methods:** This was a single-center observational study with a historical cohort method at Bethesda Hospital Yogyakarta, Indonesia. COVID-19 diagnosis was made using reverse transcriptase–polymerase chain reaction on nasopharyngeal swabs. Patient data were obtained from digital medical records and used for Charlson Comorbidity Index assessments. Inhospital mortality was monitored throughout their hospital stay. **Results:** This study enrolled 333 patients. According to the total number of comorbidities in Charlson, 11.7% (n = 39) of patients had no comorbidities; 30.9% (n = 103) of patients had one comorbidity; 20.1% (n = 67) of patients had two comorbidities; and 37.2% (n = 124) of patients had more than three comorbidities. In multivariate analysis, these variables were significantly related to short-term mortality in COVID-19 patients: older age (odds ratio [OR] per year: 1.64; 95% confidence interval [CI]: 1.23–2.19; P 0.001), myocardial infarction (OR: 3.57; 95% CI: 1.49–8.56; P: 0.004), diabetes mellitus (OR: 2.41; 95 CI: 1.17–4.97; P: 0.017), renal disease (OR: 5.18; 95% CI: 2.07–12.97; $P < 0.001$), and longer duration of stay (OR: 1.20; 95% CI: 1.08–1.32; $P < 0.001$). **Conclusion:** This study revealed multiple short-term mortality predictors in COVID-19 patients. The coexistence of cardiovascular disease, diabetes, and renal problem is a significant predictor of short-term mortality in COVID-19 patients.

Keywords: *Comorbidity, Coronavirus disease 2019, Mortality, Predictor, Prognosis*

Introduction

Coronavirus disease 2019 (COVID-19) is a worldwide pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Since the first incidence of SARS-CoV-2 infection was identified in Wuhan, Hubei Province, China, in December 2019, the disease has escalated at an alarming rate [1,2]. As of November 1, 2021, the World Health Organization had confirmed 246,357,468 cases of COVID-19 worldwide, including 4,995,412 casualties [3]. While the SARS-CoV-2 virus predominantly affects the respiratory system, cardiovascular, neurologic, and renal problems can also contribute to clinical fatality [4,5].

In a previous study in China, 344 patients with COVID-19 were transferred to the intensive care unit (ICU). On day 28, 133 people deceased, and the median survival time was 25 days. Numerous patients have a variety of comorbidities [6]. Another study in China found that 247 of 633 COVID-19 patients had at least one comorbidity [7].

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In Indonesia, data on medical comorbidities and COVID-19 prognosis are limited. In this study, we aimed to evaluate the relation of comorbidities to COVID-19 short-term mortality. In addition, we would like to investigate the relationship between specific comorbidities and COVID-19 short-term mortality.

Materials and Methods

Study design and clinical data

This study was cohort research conducted at Bethesda Hospital Yogyakarta, Indonesia. We enrolled people who tested positive for COVID-19 on nasopharyngeal swabs using reverse transcriptase–polymerase chain reaction. Patient data were retrieved from digital medical records. The dataset

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contains demographic information, including age, gender, length of stay, and information about the comorbidities.

Outcome

The primary outcome that was evaluated was short-term mortality. In this study, the term short-term mortality refers to inhospital mortality. Comorbidities' mortality burden was quantified in this study using the Charlson Comorbidity Index. The Charlson Comorbidity Index is a widely used tool for predicting mortality by identifying or weighing comorbidities. Health researchers widely use it to quantify disease burden and case mix [8]. The performance of the index was evaluated using the International Classification of Diseases, tenth revision (ICD-10). In this study, the mentioned ICD-10 codes were used to define the various comorbidities: diabetes (E10, E11), hypertension (I10-I15), cardiovascular disease (I25), chronic obstructive pulmonary disease (COPD) (J44), asthma (J45), acute kidney injury (AKI; N17), chronic kidney disease (N18), and dementia diagnoses (F00-04, F05.1, G30, G31, A81.0).

Statistical analysis

Data descriptive analysis was carried out using Microsoft Excel®, and the IBM SPSS Statistics, Version 25.0, IBM Corporation, (Armonk, New York) was used to conduct statistical analysis. We evaluated discrete variables to determine the risk factor for short-term mortality in COVID-19 patients with and without comorbidities. The *t*-test, Mann–Whitney test, and Chi-square test statistics were performed to determine differences in study variables between groups. We utilized Cox proportional hazard models to assess whether comorbidities predicted inhospital mortality. A proportional subdistribution hazard model analysis was utilized, representing mortality as a competing risk. The univariate models' significant predictors were then included in multivariate models, adjusting for possible confounding variables. The proportional hazard assumption was tested for all reported variables. We derived odds ratios (OR) with confidence intervals (CIs) of 95%. $P = 0.05$ was considered statistically significant.

Ethical considerations

This research was authorized by the Bethesda Hospital's Ethics Board and Clinical Research Division with the number 23/KEP-RSB/II/21 dated February 1, 2021. All study participants gave signed informed consent. Similarly, this study followed the ethical principles outlined in the 1964 Helsinki Declaration and its revisions.

Results

The median age of the 333 patients was 59 (19–91) years, with a proportion of patients aged <50 years being 23.4% ($n = 78$); 50–50 years being 28.5% ($n = 95$); 60–69 years being 27.3% ($n = 91$); 70–79 years being 15.3% ($n = 51$); and ≥80 years being 5.4% ($n = 18$). In total, 58.6% of patients ($n = 195$) were male and 41.4% were female ($n = 138$).

According to the total number of comorbidities enrolled in Charlson, 11.7% ($n = 39$) of patients had no comorbidities, 30.9% ($n = 103$) of patients had one comorbidity, 20.1% ($n = 67$) of patients had two comorbidities, and 37.2% ($n = 124$) of patients had more than three comorbidities. Diabetes mellitus (33.6%, $n = 112$) and cerebrovascular disease (25.2%, $n = 84$) were the two most common comorbidities in this study. Patients were hospitalized for an average of 8 (1–37) days throughout treatment. The median age of COVID-19 patients who died was 67 (26–91) years, whereas the median age of those who survived was 57 (19–86) years [Table 1].

The unadjusted analysis revealed that the following variables contribute to a greater likelihood of death in patients with COVID-19: older patient age, greater comorbidities, longer hospital stay, and several types of comorbidities in the patient. In multivariate analysis, these variables were significantly related to short-term mortality in COVID-19 patients: older age (OR per year: 1.64; 95% CI: 1.23–2.19; *P* 0.001), myocardial infarction (OR: 3.57; 95% CI: 1.49–8.56; *P*: 0.004), diabetes mellitus (OR: 2.41; 95 CI: 1.17–4.97; *P*: 0.017), renal disease (OR: 5.18; 95% CI: 2.07–12.97; $P < 0.001$), and longer duration of stay (OR: 1.20; 95% CI: 1.08–1.32; $P < 0.001$) [Table 2].

Discussion

Our findings showed that myocardial infarction (OR: 3.57; 95% CI: 1.49–8.56; *P*: 0.004), diabetes mellitus (OR: 2.41; 95% CI: 1.17–4.97; *P*: 0.017), and renal disease (OR: 5.18; 95% confidence CI: 2.07–12.97; $P < 0.001$) are significant prognostic factors for short-term mortality in COVID-19 patients. Multiple comorbidities are connected with the severity of the course of COVID-19. These findings support a prior systematic review that demonstrated that patients with COVID-19 who also have comorbid conditions such as hypertension or diabetes are more prone to developing a more severe disease course and progression. There is a greater chance of ICU admission and mortality for older patients, particularly those aged 65 and older with comorbidities and infections [9]. Age-related immune cell defects associated with a more vigorous inflammatory response have been proposed to explain the elderly's increased mortality [10].

Numerous poor outcomes associated with COVID-19 have been associated with cardiovascular disease. Nonetheless, this may be a direct result of cardiovascular disease or a consequence of other comorbidities occurring concurrently with the cardiovascular disease [11]. Uncertainty surrounds the mechanism behind COVID-19 and cardiovascular disease, although the mechanism may involve ischemia linked with infection that develops into myocardial injury or a virally generated inflammatory storm that causes shock and is followed by ischemic injury. In addition, a recent study discovered evidence of myocardial infection caused directly by the virus [12].

Type 2 diabetes patients were also more prone to develop a more severe COVID-19 infection. A prior cohort analysis of 7337 COVID-19 patients with type 2 diabetes and those without type 2 diabetes revealed that individuals with type 2 diabetes needed more hospital treatments than those without type 2 diabetes [11]. Patients with poor blood glucose control showed a significantly higher overall

Table 1: Baseline characteristics of patients with coronavirus disease 2019

Characteristics	All participants (*n*=333), % (*n*)	Deceased (*n*=83), % (*n*)	Alive (*n*=250), % (*n*)
Age (years), median	59 (19-91)	67 (26-91)	57 (19-86)
<50	23.4 (78)	10.8 (9)	27.6 (69)
50-59	28.5 (95)	19.3 (16)	31.6 (79)
60-69	27.3 (91)	33.7 (28)	25.2 (63)
70-79	15.3 (51)	22.9 (19)	12.8 (32)
≥80	5.4 (18)	13.3 (11)	2.8 (7)
Sex			
Male	58.6 (195)	66.3 (55)	56 (140)
Female	41.4 (138)	33.7 (28)	44 (110)
Weighted Charlson Comorbidity Index			
0	11.7 (39)	2.4 (2)	14.8 (37)
1	30.9 (103)	18.1 (15)	35.2 (88)
2	20.1 (67)	15.7 (13)	21.6 (54)
≥3	37.2 (124)	63.9 (53)	28.4 (71)
Comorbidities within the Charlson Comorbidity Index			
Myocardial infarction	11.4 (38)	24.1 (20)	7.2 (18)
Congestive heart failure	15.3 (51)	24.1 (20)	12.4 (31)
Cerebrovascular disease	25.2 (84)	31.3 (26)	23.2 (58)
Chronic pulmonary disease	3.6 (12)	4.8 (4)	3.2 (8)
Ulcer disease	0.6 (2)	0	0.8 (2)
Mild liver disease	0.3 (1)	1.2 (1)	0
Diabetes mellitus	33.6 (112)	49.4 (41)	28.4 (71)
Hemiplegia	1.2 (4)	0	1.6 (4)
Renal disease	11.4 (38)	27.7 (23)	6 (15)
Diabetes with end-organ damage	0.6 (2)	0	0.8 (2)
Any malignancy	0.9 (3)	0	1.2 (3)
AIDS	0.9 (3)	2.4 (2)	0.4 (1)
Length of stay (days), median	8 (1-37)	7 (1-26)	8 (1-37)

AIDS: Acquired immune deficiency syndrome

death rate than those with proper glucose control [13]. Numerous mechanisms have been proposed to link diabetes and COVID-19, including immune system impairment, preexisting proinflammatory conditions, direct pancreatic injury, and disruption of angiotensin-converting enzyme 2 (ACE2) signaling [14,15].

A previous study indicated that COVID-19 patients with renal disease had a higher death rate, with stage 2 and stage 3 AKI patients having 3.5- and 4.7-fold greater mortality, respectively, than individuals with normal kidney function [16]. The specific pathophysiologic relationship between COVID19 and kidney disease is unclear. However, ACE2 appears to have a role. ACE2 has been recognized as the receptor for SARS-CoV-1, and its role as a cell entrance receptor for SARS-CoV-2 was verified earlier [17,18]. ACE2s are expressed in various organs, most notably the gastrointestinal tract and kidney. Human tissue RNA sequencing reveals that ACE2 expression is approximately one hundred times more in the kidneys than in the lungs; consequently, kidneys with substantial ACE2 expression may be the main target of infection by SARS-CoV-2 [19]. Previous research examining the renal histopathological features in COVID-19 supports the hypothesis that SARS-CoV infection occurs directly in the kidney [20,21].

COPD was not found to be a significant predictive factor in our study. This is in contrast to earlier studies. In addition to other comorbidities, COPD is associated with a bad prognosis. A meta-analysis of numerous China-based studies indicated that patients with preexisting COPD identified with COVID-19 had a four-fold increase in death. This study evaluated neither the smoking status nor the severity of COVID-19. Only one previous study discovered a link between smoking and a COVID-19 severe infection [22].

When age and sex were adjusted, a greater Charlson Comorbidity Index score was related to a higher likelihood of COVID-19 severity and short-term mortality. This study suggests that individual comorbidities are independent predictors for poor COVID-19 clinical outcomes [23,24]. These findings may aid in developing COVID-19 pandemic management models, public health policies, and therapeutic judgments. As a result, individuals with comorbidities ought to take appropriate actions to prevent catching SARS CoV-2 since they often have a poor prognosis.

Numerous limitations apply to this study. First, it was based on the findings of a retrospective study of medical records, which could have lacked details about symptoms and previous conditions. Second, this study focused only on a short-term prognosis. Third, this study did not include vaccination history. Additional study is required to investigate the impact of comorbidities on COVID-19 outcomes and whether additional validated comorbidity indexes may effectively predict poor COVID-19 outcomes.

Table 2: Unadjusted and multivariate study of factors relating with short-term mortality among coronavirus disease 2019-infected patients (*n*=333)

Characteristics	Unadjusted results		Multivariate results	
	Death with COVID-19, OR (95% CI)	*P*	Death with COVID-19, OR (95% CI)	*P*
Age (years), median	1.06 (1.04-1.08)	<0.001	1.64 (1.23-2.19)	0.001*
Sex				
Male	1.54 (0.92-2.59)	0.101	1.54 (0.81-2.93)	0.189
Female	Reference		Reference	
Weighted Charlson Comorbidity Index				
0	Reference		Reference	
1	3.15 (0.69-14.48)	0.140	1.78 (0.36-8.76)	0.476
2	4.45 (0.95-20.91)	0.058	1.67 (0.31-8.98)	0.548
≥3	13.81 (3.19-59.86)	<0.001*	5.20 (0.93-29.18)	0.061
Comorbidities within the Charlson Comorbidity Index				
Myocardial infarction	4.09 (2.04-8.20)	<0.001*	3.57 (1.49-8.56)	0.004*
Congestive heart failure	2.24 (1.20-4.20)	0.012*	0.85 (0.35-2.11)	0.733
Cerebrovascular disease	1.51 (0.87-2.62)	0.141	1.05 (0.50-2.21)	0.898
Chronic pulmonary disease	1.532 (0.449-5.223)	0.496	1.26 (0.22-7.09)	0.796
Ulcer disease	4,986,033,534	0.999		
Mild liver disease	4,925,228,246	1.000		
Diabetes mellitus	2.46 (1.48-4.10)	0.001*	2.41 (1.17-4.97)	0.017*
Hemiplegia	0.000	0.999		
Renal disease	6.01 (2.95-12.21)	<0.001*	5.18 (2.07-12.97)	<0.001*
Diabetes with end-organ damage	0.000	0.999		
Any malignancy	0.000	0.999		
AIDS	6.15 (0.55-68.69)	0.140	13.41 (0.85-210.70)	0.065
Length of stay (days), median	1.10 (1.03-1.18)	0.004*	1.20 (1.08-1.32)	<0.001*

**P*-value is statistically significant. AIDS: Acquired immune deficiency syndrome, CI: Confidence interval, OR: Odds ratio, COVID-19: Coronavirus disease 2019

Conclusion

This study revealed multiple short-term mortality predictors in COVID-19 patients. The coexistence of cardiovascular disease, diabetes, and renal problem is a significant predictor of short-term mortality in COVID-19 patients.

Data availability

The data generated for this study are available upon request to the first author, Rizaldy Taslim Pinzon.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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