Original Article

Association between Comorbidities and COVID-19 Mortality: a Cross-Sectional Study in a Community Health Center in Indonesia

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Abstract

Objective: To analyze the risk factors for mortality and comorbidity of COVID-19 patients in a public health center work area in Indonesia.

Methods: This was a cross-sectional observational analytic quantitative study using secondary data of 820 confirmed COVID-19 cases in Brebes Public Health Center work area during the period of June 2020–December 2021. Univariate and bivariate analyses were used to analyze the obtained data statistically with a p-value of <0.005 considered significant.

Results: Of the 820 confirmed COVID-19 patients, 85.1% recovered and 15.0% died. Analysis on the characteristics of these cases showed that 51.2% females and 48.8 % males were included in this study, with 77.6% of them were <60 years old. No history of comorbidities was identified in 92.1% of the cases. In remaining cases with comorbidities, Diabetes Mellitus was recognized as the most prevalent (n=39, 4.8%). Results of the Chi-Square test demonstrated that comorbidity status (p-value= 0.001), place of quarantine (p=0.000; p>0.05), and diabetes (p=0.000, OR =2.87, 95% CI 19 1.24–0280) were significantly associated with mortality.

Conclusion: Comorbidity status, diabetes, and the place quarantine are risk factors for mortality among COVID-19 confirmed cases, especially in Brebes Public Health Center work area. Thus, it is important to increase knowledge about COVID-19 prevention and risks to prevent transmission among those with higher risks for mortality. Further studies on factors related to sustainable supports for COVID-19 patients are also necessary.

Keywords: Characteristics, comorbidity, COVID-19, risk factors

Introduction

During the pandemic, the number of COVID-19 cases continued to increase, progressed very quickly, and spread globally. COVID-19 is a disease caused by the Severe Acute Respiratory Syndrome Coronavirus *2* (SARS-CoV-2) that is transmitted from human to human, with a potential aerosol transmission. Transmission becomes easier on a closed environment as this kind of environment can support a high concentration of virus that persist for a longer time.[1] With its highly transmissible characteristics, the virus had been able to maintain the COVID-19 pandemic for year and the number of cases continued to increase daily.[1] As of December 15, 2021, the WHO reported 318,648,834 confirmed cases with 518,343 deaths worldwide (CFR 1.7%). In the same period, Indonesia recorded 4,270,794 confirmed cases, 4,118,164 recovered cases (96.4%), 7,877 active cases (0.2%), and 144,167 deaths(CFR 3.4%).[2] The province with the highest number of cases was DKI Jakarta with COVID-19 positive patients of 870,363, 852,973 recovered, and 13,611 died. The second rank was occupied by West Java Province with 709,515 cases, 693,895 recovered, and 14,761 died, followed by Central Java in the third rank with 487,098 cases, 455,763 recovered (RR 93.56%), and 30,297 died (CFR 6.2%). Despite the fact that

Central Java ranked third in the daily cases as of December 15, 2021, it ranked first in terms of the cumulative deaths due to COVID-19.[3] In Brebes district, as of December 15, 2021, 14, 177 cases were confirmed, 12,405 recovered completely, and 1,607 died (CFR 8.8%). In the sampe period, in five community centers in Brebes District, it was recorded that in Brebes Community Health Center (Puskesmas), 1,775 confirmed cases was registered with 244 deaths. Meanwhile, in Puskesmas Buniayu, 1,587 confirmed cases were recorded with 127 deaths. In Puskesmas Banjarharjo and Puskesmas Bulakamba, 1,095 and 1,108 cases were confirmed with 100 and 177 deaths, respectively. In addition, Puskesmas Ketanggungan recorded 850 confirmed cases and 99 deaths.[4] Current studies on this disease have identified several groups as the most vulnerable group for COVID-19 including the elderly, health workers, smokers, vape users, men, and individuals with blood type A. Furthermore, SARS CoV-2 is also more easily transmitted to those who are immunocompromised and those with commorbidities.[5]

The signs and symptoms of COVID-19 are generally similar to other respiratory infections, such as fever, cough, and shortness of breath. In severe cases, COVID-19 could cause pneumonia, respiratory failure, kidney disease, and even death.[6,7] Based on a study by Dessie *et al*., several risk factors influence the risk for mortality due to coronavirus, such as chronic comorbidities, complications, acute kidney injury, chronic obstructive pulmonary disease, hypertension, cardiovascular diseases (CVD), cancer, increased D-dimer level, male gender, older age, active smoking, and obesity.[8] In a previous study, Djaharuddin *et al*.[9] stated that most deaths linked to comorbidities occured in patients with hypertension, cardiovascular disease, and diabetes. These authors also stated that more than half of the patients (52.56%) who died due to COVID-19 had ≥2 comorbidities, with the remaining had one comorbidity.[9] This study aimed to analyze the relationship between risk factors for case fatality and comorbidities in COVID-19 cases in Brebes District, Central Java, Indonesia.

Methods

This was a quantitative study using a cross-sectional observational analytic approach on data collected from Puskesmas Brebes during the period June 2020–December 2021. A total of 820 cases was included and demographic data such as patient status, age, gender, comorbidities, treatment history, and symptoms were collected. Data were obtained from the patient medical record of confirmed COVID-19 patients of Puskesmas Brebes. The inclusion criteria were patients diagnosed with COVID-19 at Puskesmas Brebes during the period of June 2020 - December 2021, while the exclusion criterion was incomplete medical records. The scoring criteria used were: recovered (1) and died (2) for age; male (1) and female (2) for gender; >60 years (elderly) (1) 45–59 years (pre-elderly); and 19–44 years (adult) (2); 10–18 years (adolescent); 6–9 years (Child) (3), 1–5 years (under-five) (4), and 0 years (infant) (5) for age. In addition, a yes/no scoring was applied for comorbidities with Yes being 1 and No being 2. The comorbidities analyzed in this study were diabetes mellitus, hypertension, pneumonia/acute respiratory infection (ARI), cardiovascular disease, rheumatoid arthritis, and asthma. All data were then tested statistically using the Chi-square test. Microsoft Excel and SPSS v.24 were used to perform univariate and bivariate (Chi-square test) analyses.

Results

The characteristics of COVID-19 patients in this study were listed in Table 1. Of the 820 confirmed COVID-19 cases, 85.1% were

Table 1 Characteristic Distribution of Cases (n=820)

Variable	n=820	%
Patient Status		
Recovered	698	85.0
Died	122	15.0
Gender		
Male	400	48.8
Female	420	51.2
Age		
>60 years (Elderly)	183	22.5
45–59 years (Pre-elderly)	261	31.8
19–44 years (Adult)	321	39.3
10–18 years (Adolescent)	25	3.1
6–9 years (Child)	11	1.3
1–5 years (Under-Five)	14	1.7
0 years (Infant)	5	6

declared recovered, while 15.0% ended in fatality. The number of male and female cases was almost similar (51.2% vs. 48.8 %). The majority of cases was found in the <60 years old group (77.6%).

Table 2 presents that 92.1% of the patients in this study did not have any comorbidity, leaving only 7.9% of them suffered from comorbidities. The most prevalant comorbidity was diabetes mellitus, which was recognized in 39 patients (4.8%).

The history of hospitalization is presented in Table 3. Approximately two third of the patients (n=548, 66.8 %) had a history of hospitalization and the remaining one third underwent self-isolation (n=272, 33.2 %). Most patients referred for hospitalization were treated at Brebes District General Hospital (n=299, 36.5%).

Statistically, the relationship between

Table 2 Characteristic Distribution Patient Confirmed COVID-19 based on Comorbidities

Variable	n=820	%
Comorbidity Status		
Yes	65	7.9
No	755	92.1
Diabetes Mellitus (DM)		
Yes	39	4.8
No	781	95.2
Hypertension		
Yes	20	2.4
No	800	97.6
Pneumonia/ARI		
Yes	9	1.1
No	811	98.9
Heart Failure		
Yes	3	0.4
No	817	99.6
Rheumatoid Arthritis		
Yes	1	0.1
No	819	99.9
Asthma		
Yes	1	0.1
No	819	99.9

Table 3 Distribution of COVID-19 Confirmed Case by Place of Quarantine

Place of Quarantine	n=820	%
Self-Isolation at Home or Puskesmas	272	33.2
Hospitalized	548	66.8
Dr. Kariadi National General Hospital	6	0.7
Brebes District General Hospital	299	36.5
Bhakti Asih General Hospital	109	13.3
Harapan Anda Islamic General Hospital	58	7.1
Mitra Keluarga General Hospital	17	2.1
Hermina Panandaran General Hospital	2	0.2
Kardinah City General Hospital Tegal	20	2.4
Dr. Soeselo District General Hospital Tegal	11	1.3
Mutiara Bunda Islamic General Hospital	3	0.4
Mitra Siaga Tegal Hospital	4	0.5
RS Bhakti Asih Kec. Jatibarang	6	0.7
RSUD Dedy Jaya Brebes	11	1.3
RSUD Surodadi Tegal	1	0.1
RS Harapan Sehat Bumiayu	1	0.1

variables in this study was considered to be significant if the p-value was less than <0.05. The results of the Chi-square test on the relationship between COVID-19 confirmed case and studied variables showed that confirmed COVID-19 cases was significantly associated with comorbidity status (p-value=0.001, OR 0.383, 95% CI (19) 0.216–0.680), meaning that patients with comorbidity had a risk probability that was 0.383 times higher to be declared as confirmed COVID-19 cases (Table 4); Diabetes (p-value=0.000, OR 2.87, 95% CI 19 1.24-0280) showing that patients with a history of diabetes had a 2.87 times higher risk to die due to COVID-19 (Table 4); and the place of quarantine (p-value =0.000. In addition, place of quarantine was also found to be

Table 4 Correlation Between Death and Comorbidities

Variable	Status Recovered n	Status Recovered %	Status Died n	Status Died %	p	OR	95% CI Lower	95% CI Upper
Comorbidity						0.383	0.216	0.679
Yes	46	6.6	19	15.7	0.001			
No	652	93.4	103	84.3				
Diabetes						2.87	0.144	0.569
Yes	25	3.6	14	11.5	0. 000			
No	673	96.4	108	88.5				
Hypertension						0.514	0.183	1.441
Yes	15	2.1	5	4.1	0.198			
No	683	97.9	117	95.9				
ARI						0.608	0.125	2.961
Yes	7	1	2	1.6	0.534			
No	691	99	120	98.4				
Heart Failure						1.176	1.142	1.210
Yes	3	0.4	0	0	0.468			
No	695	99.6	122	100				
RD Arthritis						1.175	1.142	1.209
Yes	1	0.1	0	0	0.676			
No	697	99.9	122	100				
Asthma						1.175	1.142	1.209
Yes	1	0.1	0	0	0.676			
No	697	99.9	122	100				

significantly linked to the death of confirmed COVID-19 cases with (p-value=0.000) (Table 5).

Discussion

The presence of comorbidities was shown to be linked to mortality in this present study. This result supports the finding of a study in Ternate City, North Maluku, which reported that comorbidities like hypertension, diabetes mellitus type 2, and asthma have a significant relationship (p-value≤0.05) with the severity of COVID-19 disease.[6] The same finding is also presented by a meta-analysis study showing that the existence of comorbidities

Table 5 Relationship Between Place of Quarantine and Mortality in COVID-19

Variable	Status Recovered n	Status Recovered %	Status Died n	Status Died %	p	OR	95% CI Lower	95% CI Upper
Place of Quarantine and Treatment						0.777	0.743	0.813
Hospital	426	61	122	100	0.00			
Self-isolation	272	39	0	0				

in COVID-19 patients increases the severity of the disease approximately three times higher (OR=2.85, 95% CI 2.09-3.89).[7] This is caused by the changes in the pathophysiology-related mechanism where chronic comorbidity causes dysregulation of the main physiological systems, including hypothalamus-pituitary-adrenal axis, sympathetic nervous system, and immune system.[8] COVID-19 virus can also induce or worsen the condition by binding to the Angiotensin-Converting Enzyme 2 (ACE2) receptors, which are widely distributed in various organs. This will lead to disturbances in the organ, such as causing the dysregulation of the renin-angiotensin-aldosterone system (RAAS) that leads to hemostatic, nervous, and main physiological system disturbances, making the patient more prone to organ failure that will eventually increase COVID-19 complications and eventually result in mortality.[9] This study found that the type of comorbidity also influence the the relationship betwee comorbidity and confirmed case, with diabetes mellitus having a significant relationship with confirmed COVID-19 cases (p-value=0.000). This is similar to the results of a previous study by Lee *et al.* that diabetes mellitus type 2 can increase the severity of COVID-19 patients by 1.55 times when compared to COVID-19 patients without DM.[10] COVID-19 patients with diabetes mellitus will have increased secretion of hyperglycemic hormones such as catecholamines and glucocorticoids, leading to elevated blood glucose variability, abnormal glucose level, and diabetes complications.[11] Diabetes is one of the main risk factors for COVID-19. This may be due to the fact that diabetic people are more susceptible to infection because of their hyperglycemia status, immune function disorders, vascular diseases such as hypertension, dyslipidemia, and cardiovascular disease. The disease severity and mortality of COVID-19 patients are higher in diabetic patients compared to non-diabetic patients.[12]

People suffering from diabetes mellitus with COVID-19 are observed to have increased secretions of hyperglycemic hormones, such as catecholamines and glucocorticoids, that will, in turn, produce elevated blood glucose, abnormal glucose variability, and diabetes complications.[12] Two previous studies in Indonesia also found a similar result where diabetes mellitus is identified as a comorbidity that can increase the severity of COVID-19 by 3.4 times and increase the risk for mortality 4.4 times compared to non-diabetic patients.[13,10]

In contrast, hypertension was not proven to have a significant relationship with the incidence of COVID-19 (p-value=0.119). This supports the finding of a study in 2020 that also used Chi-square test that hypertension is found to have no significant relationship with confirmed COVID-19 case (p-value=0.414) .[17]

Contrary those findings, Li *et al.*[18] found that 17.1% of patients with a history of infectious diseases experience comorbidities, including hypertension after they studied 1,527 patients treated in ICU and non-ICU. Therefore, hypertension is considered to be a comorbid of COVID-19. Several other studies also show that the presence of hypertension as a comorbid could worsen the prognosis of COVID-19 caused by the consumption of ACE inhibitors and ARBs as hypertension drugs, which could exacerbate COVID-19.[18] Theoretically, the underlying mechanism of the link betwen hypertension and COVID-19 is still unknown. However, considering the important role of RAS (Renin Angiotensin System)/ACE-2 in the pathophysiology of hypertension, a dysregulation of the system may be the important link for this mechanism. A suggestion has also been given regarding the possiblity that hypertension therapy using the SRA inhibitors can affect the binding process of SARS-CoV-2 to ACE-2 to support the infection process. Suggestions based on experimental findings also stated that RAS inhibitors that cause ACE-2 expression enhancement as compensation for ACE blockers can be detrimental in patients exposed to SARS-CoV-2.[19]

There is also no significant relationship found between ARI and confirmed COVID-19 cases in this study (p=0.535), which is in line with a study by Komang that demonstrated no connection between ARI and the incidence of COVID-19 (p>0.05).[20] Another study performed on community health center in 2020 also confirmed that based on the bivariate analysis, pneumonia is not significantly correlated with the incidence of COVID-19.[6]

In severe cases, COVID-19 can exacerbate into acute respiratory distress syndrome, sepsis, septic shock, as well as multi-organ failures, including kidney or heart failure.[21] No significant relationship was found between heart failure and confirmed COVID-19 cases (p-value=0.468). This finding is in line with a similar study by Steven *et al.*, which presented no significant relationship between history of hearth disease and vulnerability for COVID-19 (p-value =0.828).[19] In contrast, Zheng et al. in their study found that patients with

cardiovascular hypertension and coronary heart disease (CHD) have a higher risk of experiencing more severe manifestations when infected by SARS-CoV-2, which then contribute to a significant part of mortality caused by COVID-19. This is probably because of the higher ACE2 expression in patients with cardiovascular disease.[18] Patients who are >60 years old infected by SARS-CoV-2 can experience more systemic and critical pneumonia manifestations when compared to younger patients, and their condition may be aggravated by cardiovascular disease.[22] Patients with a history of cardiovascular disease could become unstable during the course of SARS-CoV-2. Patients with Acute Coronary Infection Syndrome (ACS) who are infected with SARS-CoV-2 often have a poor prognosis. In these patients, the reduced heart function will lead to ischemia or mycardial necrosis which will stop the heart. Some COVID-19 patients in Wuhan who had a history of ACS experienced a more severe disease and the mortality rate for this group of patients is higher.[20, 21] The difference between the result of this study in terms of cardiovascular disease as a comorbid of COVID-19 may stem from the fact that only a a small number of subjects in the sample that take ACEIs or ARBs routinely.

Asthma is also shown as having no significant relationship with confirmed COVID-19 cases (p=0.676 >0.05). Coronavirus is a virus that attacks the respiratory system and produces similar symptoms as other respiratory viruses. Respiratory viruses may lead to asthma symptoms that can be life-threatening. The World Health Organization also lists tasthma, diabetes, and heart diseases as conditions that make an individual more susceptible to coronavirus infection. Coronavirus attacks the lungs, and then damages the heart. Individuals with cardiovascular disease and hypertension have a higher risk of getting infected and experiencing fatality due to coronavirus infection. The infection caused by the coronavirus seems to be more critical than other viruses because it can cause damages to the heart muscle and trigger heart injuries like pericarditis and myocarditis.

According to a study by Winogroho *et al*.,[23] the place of quarantine has a significant influence on the healing process and shortens the exposure period to COVID-19 among nurses. This study showed that the place quarantine contributes positively to the length of quarantine time. Individual will feel more comfortable if they are quarantined in a comfortable and supportive environment for the healing process. This is in line with a study by Wang *et al*. that stated nosocomial infection is hazardous for the patient, other patients, and healthy people.[24] Zhongnan Hospital reported a case where a patient was admitted due to stomach ache to the same hospital for COVID-19 patients and eventually suffered from COVID-19. Furthermore, more than ten hospital workers were infected with this disease in the same hospital. This is in line with the risk factors stated by the US Centers for Disease Control and Prevention (CDC) that include close contact, living in the same house with a COVID-19 patient, and a history of traveling to areas affected by COVID-19. The risk is considered low when there is no close contact (in a radius of 2 meters).[25] Currently, SARS-CoV-2 is transmitted from human to human, leading to aggressive transmission of the disease. This virus is transmitted from symptomatic patients through droplets that are propelled during coughing or sneezing.[22,26] The virus can also be transmitted through aerosols that could penetrate the body, especially the lungs, through inhalation through the nose or mouth. The coronavirus also shows a higher level of transmission than SARS due to the genetic recombination that increases transmission ability.[27]

In this study, only COVID-19 cases recorded at the Brebes Community Health Center were analyzed. For this reason, further comprehensive studies are needed to determine the risk factors that influence COVID-19 comorbidity and mortality.

In conclusion, the risk factors that are significantly associated to confirmed COVID-19 cases and deaths in the work area of Brebes Community Health Center are comorbidity status, especially diabetes, and the place of quarantine, with diabetes mellitus as the factor that is linked to the highest mortality. It is suggested that community should increase their knowledge on COVID-19 prevention and that follow up studies are needed for this isssue.

Acknowledgements

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