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Mortality of COVID-19 patients with comorbidity of diabetes mellitus: a retrospective study

by Difran Nobel Bistara

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Mortality of COVID-19 patients with comorbidity of diabetes mellitus: a retrospective study

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ABSTRACT

Background: Chronic diseases such as diabetes mellitus (DM) are risk factors that cause COVID-19 patients to experience high morbidity and mortality rates. Diabetes becomes the most hazardous comorbid during the pandemic because it increases the likelihood of more serious effects when infected with the coronavirus. This study aims to provide an overview of mortality in patients with COVID-19 who have comorbid DM.

Methods: The research design used was a case-control study design with a retrospective approach. The population in this study were all COVID-19 patients with comorbid DM. The study criteria were COVID-19 patients with comorbid diabetes mellitus. Multivariate analysis using logistic regression analysis was performed to determine the parametric analysis of correlation tests.

Results: The results of a multivariate analysis of variables related to mortality rates in COVID-19 patients with comorbid diabetes mellitus, one of which is other comorbidities. Concomitant acute respiratory distress syndrome became the only variable with a p-value <0.05.

Conclusion: Acute respiratory distress syndrome is another comorbid disease that is the number one cause of COVID-19 patients dying during the treatment period, apart from the pure diabetes mellitus that they suffer.

Keywords: COVID-19; comorbid; diabetes mellitus; mortality.
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INTRODUCTION

Diabetes is a burden for Indonesia because it requires extensive resources to manage it.[1] The demographic shift, rising average life expectancy, and rising risk factors for non-communicable diseases can all contribute to an annual increase in people with non-communicable diseases. In Indonesia, diabetes mellitus (DM) is one of the chronic diseases, and its prevalence is rising.[2]

Diabetes prevalence increased by 6.2% in Indonesia during the pandemic, which suggests that by 2020, there will be more than 10.8 million diabetics living there. Indonesia is one of the top 10 countries, with 10.7 million DM sufferers, ranking seventh. The third place goes to Southeast Asia, which includes Indonesia, with a prevalence of diabetes patients of 11.3%.[3] Since Indonesia is the only country in Southeast Asia to be included, its impact on the region's diabetes prevalence can be estimated.[4] According to Riskesdas' findings from 2018, the prevalence of diabetes mellitus, based on a doctor's diagnosis in people of all ages, reached 2.02% in the East Java province and 4.43% in the Surabaya metropolitan region. The results of a preliminary study conducted at the Islamic Hospital A. Yani Surabaya showed that patients with COVID-19 always increased every month with the following description: in June 2021, there were 233 patients, then it increased significantly in July to 474 patients and in August decreased to 246 patients. As many as 80% of patients with comorbid diabetes mellitus.[5]

Severe Acute Respiratory Syndrome Coronavirus-2 (SARS CoV-2), which causes Coronavirus Disease 2019 (COVID-19), is a single-stranded RNA virus that began to spread worldwide since the end of 2019.[6] By August 2, 2021, it was estimated that the virus had infected more than 198 million people, caused more than 4 million fatalities worldwide, and was still growing.[7] Chronic diseases such as DM are risk factors that cause COVID-19 patients to experience high morbidity and mortality rates. Because diabetes raises the likelihood of more serious problems when infected with the coronavirus, it becomes the most hazardous comorbid during the pandemic.[8] One meta-analysis's findings revealed that 42 COVID-19 patients per 1000 cases had concomitant diabetes

mellitus, and their mortality rate was 10%.[9] According to another study, there is no relationship between DM and COVID-19 mortality. However, research and study into the connection between comorbid conditions like diabetes mellitus and COVID-19 are ongoing.[10] This study is expected to provide an overview of mortality in patients with COVID-19 who have comorbid DM.

METHODS

Study design

In this study, a case-control study using a retrospective approach was the chosen research method. The sample in this study were COVID-19 patients taken from the patient's medical records, and 151 respondents fulfilled the research criteria using the total sampling technique. The inclusion criteria in this study were all patients who arrived and were diagnosed with COVID-19 at RSI Surabaya A. Yani and patients with comorbid diabetes mellitus. The exclusion criteria in this study were patients diagnosed with Covid-19 who had incomplete medical record data. Research variables include the mortality of COVID-19 patients with comorbid diabetes mellitus as the dependent variable and comorbidities as the independent variable. This study was conducted in May 2022 with data on COVID-19 patients with comorbid DM from June to July 2021 at the Surabaya Islamic Hospital A. Yani.

Data collection

Researchers examined all COVID-19 patients treated at the Surabaya A. Yani Islamic Hospital with concomitant diabetes mellitus on the Epidemiological Surveillance (ES) form. The ES form is filled out by doctors treating COVID-19 patients from all units in the hospital. The ES form asked about the patient's clinical and demographic parameters, such as age, gender, length of stay, symptoms, comorbidities, D-Dimer results, and death outcome. Patients are classified as having DM if there is a history of DM and receiving antidiabetic drugs before the diagnosis of COVID-19. All patients who did not meet these criteria were excluded from the study data. Other comorbidities, such as Pneumonia, ARDS, CKD, hypertension, stroke, dyspepsia, and heart disease, were diagnosed based on the history profile and treatment for each disease given before the COVID-19 diagnosis.

Data analysis

After the data is collected, then the data is planned to be processed with the following stages: Editing, Coding, Tabulating, and Scoring. The statistical test used by the researcher is Logistic Regression which is a test to find the relationship between two data factors. Then use this relationship to predict the value of one of these factors based on other factors to compare observations before and after treatment.

RESULTS

Results of this study show no differences in the characteristics of respondents, including age, gender, length of treatment, symptoms, comorbidities, and D-dimer values in patients with COVID-19 with comorbid diabetes mellitus (Table 1). As a result of the COVID-19 disease with comorbid diabetes mellitus, from a total of 151 respondents, most of them could be cured, namely 102 respondents and 49 respondents who died from COVID-19. The respondent's age range is 57 years, with a mean value (57.15 years). Most of the respondents were female, as many as 77 respondents (51%). The length of treatment was mostly with a mean value (9.97 days). Symptoms that appear in most respondents sequentially are

Table 1. Characteristics of respondents at Islamic Hospital Surabaya

Characteristics	(All = 151)	Living (102)	Died (49)	P-Value
Age (mean, years)	57.15	56.37	58.78	0.350
Gender				
Male (n, %)	74 (49%)	49 (32.5%)	25 (16.6%)	0.986
Female (n, %)	77 (51%)	53 (35.1%)	24 (15.9%)	
Length of treatment (mean, days)	9.97	10.64	8.59	0.007*
Shortness of breath (n, %)	80 (53%)	50 (33.1%)	30 (19.9%)	0.169
Fever (n, %)	78 (51.7%)	50 (33.1%)	28 (18.5%)	0.388
Cough (n, %)	98 (64.9%)	62 (41.1%)	36 (23.8%)	0.147
Nausea (n, %)	70 (46.4%)	41 (27.2%)	29 (19.2%)	0.037*
Dizziness (n, %)	10 (6.6%)	5 (3.3%)	5 (3.3 %)	0.295
Diarrhea (n, %)	15 (9.9%)	6 (4%)	9 (6%)	0.022*
Pain (n, %)	27 (17.9%)	21 (13.9%)	6 (4 %)	0.261
Concomitant disease				
Pneumonia (n, %)	134 (88.7%)	90 (59.6%)	44 (29.1%)	1.000
ARDS (n, %)	31 (20.5%)	12 (7, 9%)	19 (12.6%)	0.000*
Chronic kidney disease (n, %)	7 (4.6%)	5 (3.3%)	2 (1.3%)	1.000
Hypertension (n, %)	24 (15.9 %)	15 (9.9%)	9 (6%)	0.636
Stroke (n, %)	3 (2%)	3 (2%)	0 (0%)	0.551
Dyspepsia (n, %)	13 (8.6%)	11 (7.3%)	2 (1.3%)	0.224
Chronic heart failure (n, %)	35 (23.2%)	23 (15.2%)	12 (7.9%)	0.838
D-Dimer (mean, ng/ml)	1533.61	1251.55	1991.95	0.243

Note: *p<0.05

Table 2. The effect of DM on the mortality of COVID-19 patients was adjusted and compared with other comorbidities

Variable	SE	P-Value
Pneumonia	0.606	0.826
ARDS	0.443	0.001*
CKD	0.909	0.824
Hypertension	0.505	0.399
Stroke	2.320	0.999
Dyspepsia	0.818	0.285
CHF	0.442	0.907

Note: *p<0.05

cough, shortness of breath, fever, nausea, and diarrhea. Then the comorbidities in most patients were pneumonia as many as 134 respondents (88.7%) with an average D-dimer value of 1533.61. This retrospective study analyzed medical records based on the p-value of the Fisher's exact test or Chi-Square (X^2) results; it was found that mortality in COVID-19 patients with comorbid diabetes mellitus was associated with length of stay, symptoms that appeared were nausea and diarrhea, as well as other comorbidities, is acute respiratory distress syndrome (ARDS). These three variables have a p-value <0.05, which reveals that the length of treatment and symptoms of nausea and diarrhea and comorbidities ARDS are risk factors associated with death in hospital and can help identify a higher risk of death in COVID-19 patients with comorbid diabetes mellitus.

COVID-19 patients with comorbid diabetes mellitus, one of which is comorbid. ARDS comorbidities are the only variables with a p-value < 0.05 (Table 2). This variable proves that ARDS is another comorbid disease that is the number one cause of COVID-19 patients dying during the treatment period, apart from the pure diabetes mellitus that they suffer.

DISCUSSION

In order to understand how COVID-19 spreads, epidemiology must consider three factors: agent, environment, and host. The agent in COVID-19 is SARS-CoV-2, which encompasses the pathogenicity and virulence of several strains.[11] Environment refers to extraneous components that affect the agent and the possibility of exposure, such as breathing droplets and contaminated surfaces. Any uninfected person with the susceptibility traits of age, sex, and comorbidities is considered the host.[12] The spread of COVID-19 will be inhibited if the interactions between these components are minimal.[13] COVID-19 has come to the attention of the world and is spreading globally with a huge impact on some countries.[14]

With a 33.6% prevalence, diabetes mellitus is the second-highest comorbidity among COVID-19 patients in Indonesia.[15] According to a different meta-analysis, diabetes mellitus accounts for 9.7% of COVID-19 patients' comorbidities, placing it second.[16] In nations like China, South Korea, and the United States, diabetes ranks as the second most prevalent comorbid condition. It is still exceedingly difficult to treat COVID-19 patients with concomitant diabetes mellitus. Patients with confirmed COVID-19 have a worsening of their illness due to the concomitant disease of DM.[17] Metformin is one of the treatments that is kept up in patients with diabetes mellitus who are proven COVID-19 positive since it has been found to affect lowering mortality in type 2 diabetes mellitus patients who are hospitalized.[18]

When the SARS-CoV-2 virus enters the human body, it triggers a severe proinflammatory response, also known as a cytokine storm, which is the main pathophysiology of the virus in humans.[19] SARS-CoV 2 binds to the S-glycoprotein on its surface to employ the ACE-2 receptor as a portal into human cells. When the virus enters cells, helper T cells that produce interferon create an inflammatory response that results in a cytokine storm.[20] Research on mice revealed that the expression of the ACE-2 receptor increased under diabetes circumstances. The discovery that patients with type 1 and type 2 DM had higher levels of ACE-2 expression further supported this investigation.[21] Furin, a type 1 membrane protease that contributed to the entry of SARS-CoV-2 into body cells and facilitated viral replication, was also found to be increased in diabetes settings. Increased levels of interleukin-6 (IL-6) and impaired T-cell function also significantly contribute to the progression of COVID-19 illness in people with diabetes.[22] Due to the extended removal of the virus from the body, diabetes can worsen COVID-19 infection and even raise the risk of mortality. The lengthening may be brought on by the anti-diabetic medication's inhibition of the Dipeptidyl Peptidase IV (DPP4) enzyme's activity. While DPP4 is an aminopeptidase found in cell membranes and involved in several physiological processes, including immunological responses, these medications have target activity on DPP4, increasing insulin production and lowering blood sugar levels.[23] Patients with diabetes mellitus also experience an increase in the severity of COVID-19 due to decreased macrophage function. Chronic hyperglycemia and inflammation cause aberrant and ineffective immune responses because they reduce polymorphonuclear leukocyte mobility, chemotaxis, phagocytic activity, decreased cytokine production, and suppression of Tumor Necrosis Alpha (TNF) activity on T cells.[24] Numerous pathophysiological mechanisms increase the risk of death in COVID-19 patients with type 2 diabetes.[25]

The likelihood of inadequate data since the risk factor data is finalized after the disease arises and frequency variations are limitations of this study. Due to the data being collected a year after it was recorded in the medical record, there is a population selection bias.

CONCLUSION

Acute respiratory distress syndrome is another comorbid disease that is the number one cause of COVID-19 patients dying during the treatment period, apart from the pure diabetes mellitus that they suffer.

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AUTHOR CONTRIBUTION

DNB: Conceptualize research and develop the methodology, collect research data, analyze data, prepare original manuscripts, perform editing, and review. **S**: Conceptualizing research, collecting research data, compiling original manuscripts. **AHS**: Conceptualizing research, collecting research data, compiling original manuscripts. **UH**: Conceptualizing research, collecting research data, compiling original manuscripts. **TAW**: develop the methodology, analyze data, prepare original manuscripts, edit, and review. **NS**: developing methodology, analyzing data, compiling original manuscripts, editing, and reviewing. **SP**: develop the methodology, analyze data, prepare original manuscripts, edit, and review.

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CONFLICT OF INTEREST

All researchers confirm that this study has no personal or financial conflicts of interest.

ETHICAL CLEARANCE

The Health Research Ethics Committee of the Universitas Nahdlatul Ulama Surabaya declared this research ethically worthy with letter No. 67/EC/KEPK/UNUSA/2022. Data collection begins with the respondent's consent, and all respondents' names are anonymized.

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