



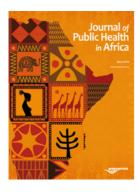


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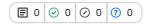
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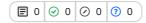
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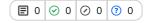
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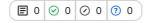
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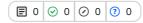
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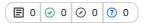
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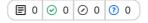
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#### KETERANGAN LAYAK ETIK

DESCRIPTION OF ETHICAL APPROVAL
"ETHICAL APPROVAL"

No: 16/EA/KEPK/2021

Protokol penelitian yang diusulkan oleh :

The research protocol proposed by

<u>Peneliti utama</u> : Santi Martini

Principal In Investigator

Nama Institusi : Fakultas Kesehatan Masyarakat Universitas Airlangga

Name of the Institution Faculty of Public Health Universitas Airlangga

Dengan judul:

Tittle

"Epidemiologi Covid 19: Faktor Risiko, Karakteristik Klinis, dan Outcome"

"Epidemiology of COVID-19: Risk Factors, Clinical Characteristics and Outcomes"

Dinyatakan layak etik sesuai 7 (tujuh) Standar WHO 2011, yaitu 1) Nilai Sosial, 2) Nilai Ilmiah,

- 3) Pemerataan Beban dan Manfaat, 4) Risiko, 5) Bujukan/Eksploitasi, 6) Kerahasiaan dan Privacy, dan
- 7) Persetujuan Setelah Penjelasan, yang merujuk pada Pedoman CIOMS 2016. Hal ini seperti yang ditunjukkan oleh terpenuhinya indikator setiap standar.

Declared to be ethically appropriate in accordance to 7 (seven) WHO 2011 Standards, 1) Social Values, 2) Scientific Values, 3) Equitable Assessment and Benefits, 4) Risks, 5) Persuasion/Exploitation, 6) Confidentiality and Privacy, and 7) Informed Concent, referring to the 2016 CIOMS Guidelines. This is as indicated by the fulfillment of the indicators of each standard.

Pernyataan Laik Etik ini berlaku selama kurun waktu tanggal 05 Juli 2021 sampai dengan tanggal 05 Julii 2022

This declaration of ethics applies during the period July 05, 2021 until July 05, 2022

Surabaya, 05 Juli 2021
Professor and Chairperson,

Dr. Rr. Soenarnatalina Melaniani, Ir., M.Kes. NIP. 19601225 199003 2 001



### Death risk among COVID-19 patients with diabetes mellitus

Dahlia Dahlia,<sup>1</sup> Kurnia Dwi Artanti,<sup>2</sup> Arief Hargono,<sup>2</sup> Santi Martini,<sup>2</sup> Nayla Mohamed Gomaa Nasr,<sup>3</sup> Chung-Yi Li,<sup>2,4</sup>

<sup>1</sup>Student of Bachelor Program of Public Health, Universitas Airlangga, Indonesia; <sup>2</sup>Division of Epidemiology, Faculty of Public Health, Universitas Airlangga, Indonesia; <sup>3</sup>Doctoral candidate at the University of Debrecen, Faculty of Medicine, Department of Public Health and Epidemiology, Debrecen, Hungary; <sup>4</sup>Department of Public Health, National Cheng Kung University, Taiwan

#### **Abstract**

Deaths from COVID-19 are increasing in patients with comorbidities. One of the most common comorbidities is diabetes mellitus. The researchers wanted to see how having diabetes affected the mortality rate COVID-19 participants. investigation is a case control observational analytical study. Different types of people, called "cases," and "controls," complete the research sample. Each group had 68 responders, for a grand total of 136. Medical records from COVID-19 patients treated at Airlangga University Hospital, Surabaya, between March 2020 and September 2021 serve as the study's secondary data source. The purpose of this study's data analysis is to calculate an odds ratio. Patients with COVID-19 with concomitant diabetes mellitus had an increased risk of death, and this risk increased with age, gender, and COVID-19 symptoms. In contrast, education, occupation, and laboratory results were not significantly related to mortality among COVID-19 individuals with concomitant diabetes mellitus (GDA status). The results of this study show that COVID-19 patients with concomitant diabetes mellitus are at a higher risk of death if they are over the age of 65, if they are male, and if they have severe symptoms.

#### Introduction

COVID-19 or commonly called Coronavirus disease 2019 by the World Health Organization is a new viral disease that is currently making people around the world anxious and has a significant impact on human life, especially in the health sector. The corona virus is likely to evolve further, quicker, causing more severe infection organ failure and, ultimately, death. This state of emergency is observed even more frequently in patients with previous health problems or a history of illness.1 It was found that the mortality rate due to COVID-19 is increasing in patients with comorbidities. Based on a report from the Central of Disease Control (CDC), COVID-19 is twelve times more deadly for patients with comorbidities than patients without comorbid diseases. The mortality rate (CFR) for patients with cardiovascular disease is 10.5%, 7.3% for people with diabetes mellitus, 6.3% for patients with chronic respiratory disease, 6% for patients with hypertension, and 5.6% for cancer patients.2

Comorbidity is a risk factor for the severity of COVID-19. One of the comorbidities is diabetes mellitus. The problem with diabetes is primarily a poorer prognosis, not a greater chance of contracting the virus. Diabetes mellitus is characterized by high glucose levels. High glucose levels tend to worsen the disease a patient has, including COVID-19 itself. This is because high glucose levels can affect the ability of the virus to infect humans, increase the risk of inflammation and compromise the body's immune system. Therefore, the morbidity and mortality rates of COVID-19 in patients with diabetes mellitus are significantly higher than in non-diabetic patients. This study aimed to analyze the risk of death in COVID-19 patients with comorbid diabetes mellitus.

#### **Materials and Methods**

The research method used in this study was a cross-sectional analytical observational study. The time frame for this study was between October 2021 and April 2022. The study relied on secondary sources of information, specifically the medical records of inpatients at the Universitas Airlangga Hospital in Surabaya between March 2020 and September 2021. All 257 people enrolled in COVID-19 who also had diabetes mellitus were analyzed in this study. Patients with COVID-19 and concomitant diabetes mellitus who did not survive were considered the case population, while those who did survive were considered the control group. A sample was selected from the study population that met the inclusion criteria during the period March 2020 to September 2021 with a ratio of the case group to the control group 1:1. The total sample in this study was 136 people.

Data analysis was performed univari-

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Key words: Age, COVID-19, Death, Diabetes mellitus, Men

Contributions: Design the work: DD. Data collection: KDA. Data analysis: DD. Interpretation of data: DD, SM. Drafting: DD. Review & editing: DD, KDA, AH, SM, NMG, CYL.

Conflict of interest: The authors declare that there is no conflict of interest.

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ately and bivariately. In this study, univariate analysis was intended to identify the mortality rate in COVID-19 patients with comorbid diabetes mellitus based on patient characteristics including age, gender, education and occupation and the mortality rate in COVID-19 patients based on patient clinical characteristics which include symptoms of COVID-19 and laboratory results (RBS)





status). Bivariate analysis was conducted to determine the relationship between each independent variable in the form of risk factors including age, gender, education, occupation, COVID-19 symptoms and laboratory results (RBS status) with the dependent variable, namely death in COVID-19 patients.

#### Results

#### Respondent characteristics description

The description of respondent characteristics is presented in Table 1 which shows that the sample size studied was 136 people. As a percentage, the elderly made up 38.2% of the COVID-19 cohort with concomitant diabetes mellitus. Fifty-seven percent were male. With 41.2%, high school diploma or equivalent is the most prevalent degree of education. Of the COVID-19 patients who also have diabetes mellitus, 62.5% are employed. COVID-19 patients who also had diabetes mellitus had a 50% higher chance of having moderate symptoms. A majority (55.7%) of COVID-19 patients with concomitant diabetes mellitus had uncontrolled blood sugar levels as determined by a Random Blood Sugar Status (RBA).

## Risk factors for COVID-19 patient mortality with comorbid diabetes mellitus

Table 2 displays the causes of death among COVID-19 patients. If we look at the OR value, we see that respondents who are 65 and older have a 2.10 times higher mortality rate than those who are 20-35. The 95% CI ranged from (1.82 to OR 5.37) with a mean of 2.88. It means that COVID-19 patients with concomitant diabetes mellitus have a higher death rate as they get older. According to the OR value, men have a 2.16 times higher mortality rate than women. As a result, COVID-19 patients who also had diabetes mellitus died at a higher rate if they were male. The 95% CI for the correlation between education and likelihood of having a health problem was (0.72 to OR 8.59). This finding suggests that among COVID-19 patients who also had diabetes mellitus, there was no correlation between educational attainment and mortality. 95% confidence interval for the occupation was (0.68, OR, 2.74). Patients with COVID-19 and concomitant diabetes mellitus showed no statistically significant association between occupation and mortality. People with severe symptoms are 10.07 times more likely to die than those with no symptoms, as indicated by the OR value. The 95% CI ranged from (OR 2.21) to (OR

45.91). What this means is that COVID-19 individuals who also have diabetes mellitus have a far higher risk of dying from their condition. The odds ratio (95% CI) for the status of random blood sugar was (0.92–3.61). Patients with COVID-19 with concomitant diabetes mellitus showed no statistically significant correlation between Random Blood Sugar status and mortality.

#### Discussion

# COVID-19 patients with concurrent diabetes mellitus: does older age increase the risk of death

Old age may worsen an individual's health problem due to the risk factors that influence it. In the aging process, the body undergoes physiological changes, resulting in the body being more susceptible to disease. Therefore, the elderly often develops health problems. This happens due to body cell degradation, thus, the body's resistance and functions decrease and the risk factors for disease increase.3 Age can also affect the severity of disease and death in patients. This also applies to COVID-19 patients. Patients with diabetes mellitus are at an increased risk of dying. A combination of advanced age and diabetes mellitus predicts a lower chance of success.4 Individuals older than 65 years old accounted for 80% of COVID-19 fatalities. Therefore, old age

might be viewed as a risk factor for mortality caused by COVID-19.<sup>5</sup> This study's findings are consistent with those of Raden (2020), who found that patients older than 64 faced a 2.097-fold increased probability of dying.<sup>6</sup> It was also found in the study by Clement Drew (2021) that COVID-19 patients older than 60 had a 6.71-fold increased risk of mortality.<sup>7</sup> Research by Zhang (2020) using the logistic regression method shows that age affects patient mortality, and these findings are important to our investigation.<sup>8</sup>

# Comparative analysis of gender and mortality in COVID-19 patients with concurrent diabetes mellitus

One of the risk factors for dving from COVID-19 is one's gender. This occurs because men and women's immune systems are fundamentally different, as are their lifestyles. Hormonal differences contribute to the higher mortality rate in men. Through immunological effects, the hormone estrogen on the female immune system will have a positive effect on fighting infection. In addition, Sexual hormones like progesterone, which is only found in females, play a significant impact in both the innate and adaptive immune systems.<sup>10</sup> Similar findings were found by Clement Drew (2021), who found that males had a mortality rate 2.65 times that of females.<sup>7</sup> Biswas's study also found that men had a 1.86 times higher mortality rate than women.11 Also, Siagian's (2020) research revealed that

Table 1. Respondent characteristics description.

Variables	Frequency (n)	Percentage (%)		
Age  20-35 36-55 56-65 >65	6 50 52 28	4.4 36.8 38.2 20.6		
Gender Male Female	69 67	50.7 49.3		
Education Elementary Junior High Senior/Vocational High College	18 28 56 34	13.2 20.6 41.2 25.0		
Occupation Employed Unemployed	85 51	62.5 37.5		
COVID-19 Symptoms Asymptomatic Mild Moderate Severe	11 14 68 43	8.1 10.3 50.0 31.6		
RBS Status Uncontrolled Controlled	76 60	55.9 44.1		





male COVID-19 patients had a much greater mortality rate than female COVID-19 patients. 12

## Death in COVID-19 patients with concurrent diabetes mellitus and low levels of education

The results of the study showed that among COVID-19 patients who also had diabetes mellitus, higher levels of education were not associated with a lower risk of death. In keeping with the findings of Margareth's (2020) study, which found no association between educational attainment and COVID-19 mortality, we find the following.<sup>13</sup> In addition, Linda's (2021) research found no correlation between patients' levels of education and their risk of dying from COVID-19.14 A person's motivation to take preventative measures against COVID-19 may be influenced by their degree of education.<sup>15</sup> However, education is not a risk factor for COVID-19 individuals who also have type 2 diabetes mellitus. Comorbid diabetes mellitus is a major contributor to mortality in COVID-19 patients, as these patients have a poor prognosis overall.

## Death in COVID-19 patients with concurrent diabetes mellitus and their occupation

COVID-19 patients with concomitant diabetes mellitus did not have a different

death rate based on their career, according to the study's findings. This finding is consistent with the findings of Shahir's (2020) study, which found no correlation between patients' occupations and their risk of dying from COVID-19.17 However, a different study found a correlation between patients' occupations and their risk of dying from COVID-19. The researchers noted that the workplace is a key setting for the spread of COVID-19. The type of one's work greatly alters the likelihood that one will be exposed to COVID-19. 18 The occupations mentioned in the study were those with a high potential for exposure to COVID-19, such as those in the medical field. 19 In addition, occupations that are included in high risk and comorbid diseases groups are more likely to cause COVID-19-related deaths.4

# The relationship between COVID-19 symptoms and the mortality of COVID-19 patients with comorbid diabetes mellitus

Based on the severity of the symptoms, COVID-19 is classified as asymptomatic, mild, moderate, severe, or critical. When the body is infected with COVID-19, it reacts by displaying symptoms. The body's defenses, in response to the cell death brought on by the virus's replication process, will set off an inflammatory cascade, giving birth to a wide range of symptoms. The development of symptoms is evi-

dence that the virus has successfully infected cells and is actively replicating and spreading to new targets. Accordingly, symptoms may increase a patient's likelihood of dying from COVID-19. Similar findings were found by Du (2020), who found that individuals with severe symptoms have a 7.35-fold higher probability of death.21 This finding is consistent with that of Zheng and Santos (2020) in Brazil, who found that COVID-19 patients with severe symptoms had a higher mortality rate.<sup>22,23</sup> Patients with COVID-19 who also have diabetes mellitus are at increased risk for both severe COVID-19 symptoms and death, as reported by Khumar (2020).24

#### The association between retinolbased sympathetic neurotransmitters and death in COVID-19 patients with concurrent diabetes mellitus

The study found no association between Random Blood Sugar (RBS) status and mortality among COVID-19 participants with concomitant diabetes mellitus. It is in line with the study by Linda (2021) stating that there was no relationship between Random Blood Sugar (RBS) status and the mortality of COVID-19 patients.<sup>5</sup> Blood sugar level is a clinical indicator for diagnosing diabetes mellitus. High blood sugar levels that interact with other factors such as old age, unhealthy diet, low physical

Table 2. Mortality risk factors for COVID-19 patients with comorbid diabetes mellitus.

Variables	Died		Reco	Recovered		Total		CI 95%	
	n	%	n	%	n	%		Lower	Upper
Age									
20-35	3	4.4	3	4.4	6	4.4	1.36	0.25	7.40
36-55 56-65	$\begin{array}{c} 26 \\ 22 \end{array}$	38.3 32.3	24 30	35.3 44.1	50 53	36.8 38.2	1.47	0.67	3.22
>65	17	25.0	11	16.2	28	20.6	2.10	1.82	5.37
Gender									
Male	41	60.3	28	41.1	69	50.7	2.16	1.09	4.30
Female	27	39.7	40	58.9	69	49.3			
Education	9	13.2	9	13.2	18	13.2	2.50	0.72	8.59
Elementary Junior High	8	13.2	20	29.5	28	20.6	2.50 1	0.72	0.39
Senior/Vocational High	30	44.1	26	38.2	56	41.2	2.88	1.08	7.63
College	21	31.0	13	19.1	34	25.0	4.03	1.38	11.80
Occupation									
Employed	45 23	66.2	40 28	58.9	85 51	62.5	1.37	0.68	2.74
Unemployed	23	33.8	20	41.1	91	37.5			
COVID-19 Symptoms Asymptomatic	3	4.4	8	11.8	11	8.1	1		
Mild	2	3.0	12	17.7	14	10.3	0.44	0.60	3.28
Moderate	29	42.6	39	57.3	68	50.0	1.98	0.48	8.13
Severe	34	50.0	9	13.2	43	31.6	10.07	2.21	45.91
RBS Status	49	00.0	00	40.0	<b>E</b> 0	FF 0	1.00	0.00	0.01
Uncontrolled Controlled	43 25	63.2 36.8	33 35	48.6 51.4	76 60	55.9 44.1	1.82	0.92	3.61
Controlled	20	90.0	99	91.4	00	77.1			



activity can modulate immune and inflammatory responses. Thus, patients with diabetes mellitus are susceptible to diseases including exposure to COVID-19.6 In contrast to the HbAIC test, patients with high HbAIC showed higher inflammatory parameters, increased renal function and blood viscosity. Increased HbAIC will be associated with clinical COVID-19 patients. Elevated HbAIC can serve as an indicator of long-term glycemic status. This is because COVID-19 is associated with worse outcomes in patients with poorly controlled diabetes mellitus and higher mortality in those who already have the disease. Improper glycemic management contributes to poor clinical outcomes and an increased risk of death in COVID-19 patients.26

#### **Conclusions**

This study found that COVID-19 patients with severe symptoms, those who were male, and those who were older than 65 and who had diabetes mellitus had the highest mortality rates. Patients who are >65 years old, male and have severe COVID-19 symptoms are included in the high-risk group. High risk groups should receive appropriate treatment, supervision and care.

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