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RELATIONSHIP OF COMMORBID DISEASE TO MORTALITY EVENTS IN COVID-19 PATIENTS

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ABSTRACT
Background: Covid-19 is a disease caused by acute respiratory syndrome due to corona virus 2. Patients with Covid-19 experience symptoms of severe shortness of breath resulting in death. The risk of death for Covid-19 sufferers will be greater if the patient has a history of comorbid diseases such as hypertension, diabetes mellitus, cardiovascular disease or kidney disease.Objective: The purpose of this study was to determine the relationship between comorbid diseases and the incidence of mortality in patients with Covid-19.Method: Research design using descriptive analytic. The research population was all Covid-19 sufferers who were treated at Mojowarno Christian Hospital (RSK) during 2021 totaling 450 sufferers. The research sample was 212 respondents with a sampling technique using systematic random sampling. The data was obtained from the medical records of Covid-19 patients who were treated at the Mojowarno Hospital. Statistical test using chi square and odds ratio with a significance level of P <0.05. Results: The results of the study found that comorbid diabetes mellitus showed a result of P: 0.000, meaning that there was a relationship between comorbid diabetes mellitus and the incidence of mortality in patients with Covid-19. Comorbid kidney disease shows a P value: 0.003, meaning that there is a relationship between comorbid kidney disease and the occurrence of mortality in Covid-19 sufferers. Comorbid heart disease results obtained P: 0.089, meaning that there is no relationship between comorbid heart disease and mortality in patients with Covid-19. Hypertensive comorbid disease on mortality with a P value: 0.134 meaning that there is no relationship between hypertension comorbid disease and the risk of mortality in patients with Covid-19. Conclusion:Covid-19 sufferers who have comorbid diabetes mellitus cause greater mortality. This is because diabetes mellitus can cause a cytokine storm which plays a role in increasing the severity of COVID-19 sufferers so that it often causes death.

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1. INTRODUCTION

Covid-19 (corona virus disease 2019) is a disease caused by typecorona virus Sars-CoV-2, which was first reported in Wuhan China on December 31 2019. Covid-19 is an infectious disease caused by acute respiratory syndromecorona virus 2 (severe acute respiratory syndrome corona virus 2 or SARS-CoV02) (Satria, et al 2020). Patients with Covid-19 are usually marked with mild to acute respiratory infections, pneumonia, weakness, muscle aches, and diarrhea. A person who is heavily infected with Covid-19 can result in acute respiratory syndrome, kidney failure and death (Ministry of Health, 2020). In patients with SARS-Cov or corona viruses, it usually causes the same symptoms as H7N9 which can easily experience respiratory failure until death occurs (Fang et al., 2020). This condition has been described as a pandemic by the Public Health Emergency of International Concern (PHEIC) and was declared by the World Health Organization on March 11, 2020 (Suganthan, 2019).

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Covid-19 sufferers who have comorbid diseases can increase the risk of infection until death occurs (Satria, et al 2020). The increased risk of death reached 1.95 times in patients with Covid-19, however, diabetes mellitus had a double death rate in patients with Covid-19 (Mentari, 2021). Comorbid diseases that are often encountered in patients with Covid-19 include hypertension, diabetes mellitus, heart disease, kidney disease and cancer. The prevalence of Covid-19 sufferers with diabetes mellitus reaches 41.7% and hypertension reaches 56.6% (Guan et al. al, 2020).

Covid-19 cases have been reported in 210 countries totaling 1.93 million and resulting in 120,000 deaths (Li et al., 2020). In Indonesia, the first Covid-19 case was recorded on March 2 2020. There were 1,191,990 confirmed cases of Covid-19 with 32,381 deaths spread across 34 provinces on February 11 2021 which was declared by the government's task force for handling Covid-19 . The number of confirmed cases in East Java Province as of December 31 2020 was 84,152 cases spread across all districts/cities. Based on medical record data for Covid-19 sufferers at Mojowarno Christian Hospital with comorbid diseases, there are 450 data from 2021 to 2022.

Covid-19 sufferers who have comorbid hypertension result in greater death than Covid-19 sufferers who do not have comorbid diseases. People with high blood pressure tend to have a higher number of ACE-2 receptors, so that the corona virus spreads more easily throughout the body (Drew & Adisasmita, 2020). Whereas Covid-19 sufferers with comorbid diabetes mellitus will cause severe pro-inflammation or a cytokine storm which is stimulated by the Covid-19 virus when it enters the human body. The entry of the virus into the cell triggers an inflammatory response through helper T cells which will produce interferon γ which leads to a cytokine storm. Having impaired T-cell function and increased levels of interleukin-6 (IL-6) also play an important role in increasing the severity of Covid-19 disease in diabetics (Parveen. 2020). Covid-19 sufferers with comorbid heart disease complications that arise including cardiovascular arrhythmias, acute coronary syndrome, venous embolism, cardiogenic shock to heart failure (Hidayaniet al., 2020).

One in five people with Covid-19 will experience more serious and severe symptoms, including having difficulty breathing, but most will also

sufferers of Covid-19 can recover without being given special treatment. Among comorbid diseases, people with Covid-19 with comorbid hypertension or diabetes mellitus have a greater chance of dying with more serious symptoms (WHO, 2020b). Other sources state that not only diabetes mellitus or hypertension have a higher risk of death, but cardiovascular disease, kidney disease, also have a higher death rate than sufferers of Covid-19 who do not have comorbid diseases (Hidayani et al., 2020) .

Currently, Covid-19 is the biggest problem and is the center of attention in the world, as well as in Indonesia. One of the efforts made by the Indonesian government to prevent the spread of Covid-19, as recommended by WHO, includes cleaning hands with alcohol or washing hands thoroughly with soap and running water, maintaining a distance of at least one meter between individuals, avoiding crowded places, avoiding touching eyes, nose and mouth. In addition, the government is also holding a Covid-19 vaccination program to suppress the development of the spread of Covid

19 (WHO, 2020a). The purpose of this research is to find out the relationship between comorbid diseases and the incidence of mortality in patients with Covid-19 at Mojowarno Christian Hospital.

2. METHOD

Research design

The type of research being conducted is using a descriptive analytic research design, in which an analysis of each comorbid disease will be carried out in sufferers of Covid-19.

Study Participant

The research population was all Covid-19 sufferers at Mojowarno Christian Hospital (RSK) during 2021 totaling 450 sufferers. Based on the results of calculating the sample size, it was found that the number of samples to be taken was 212 respondents with a sampling technique using a systematic random sampling technique. This research was conducted at Mojowarno Christian Hospital, Jombang Regency, East Java in April 2022.

Instruments and data collection

The research instrument used note sheets to record data obtained from the medical records of Covid-19 sufferers who were treated at Mojowarno Christian Hospital from 1 January 2021 to 30 December 2021.

Data analysis

Data analysis was performed using the chi square statistical test with a significance level of $P < 0.05$ and an Odd Ratio.

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3. RESULTS

The following below are the results of the research obtained

Table 1. Characteristics of respondents based on demographic data of Covid-19 sufferers at Mojowarno Christian Hospital in 2021

	Karakteristik Responden	f	%
1	**Usia**		
	<20 Years	3	1.4
	20-30 Years	14	6.6
	31-40 Years	20	9.4
	> 40 Years	175	82.5
	Total	212	100
2	**Gender**		
	Man	171	80.7
	Women	14	19.3
	Total	212	100
3	**Work**		
	Doesn't work	88	41.5
	Farmer	12	5.7
	Self-employed	72	34
	civil servant	10	4.7
	Private	30	14.2
	Total	212	100
5	**Length of Hospitalization**		
	<10 Days	89	42
	>10 Days	123	58
	Total	212	100

Source: Secondary data, 2021

Based on table 1, it shows that most of the respondents were aged more than 40 years, 175 (82.5%) respondents, while a small number of respondents were less than 20 years old (1.47%). While the sex of the respondents was mostly male, 171 (80.7%) respondents, and a small proportion of respondents were female, 41 (19.3%) respondents. Based on the characteristics of the work of the respondents, the majority did not work as many as 88 (41.5%) of respondents, and a small proportion worked as farmers, amounting to 12 (5.7%) of respondents. while the characteristics of the respondents based on the length of stay were mostly more than 10 days 123 (58.0%) respondents, and a small proportion less than 10 days as many as 89 (42%) respondents.

Table 2 Characteristics of Respondents Based on Comorbid Diseases of Covid-19 Sufferers at Mojowarno Christian Hospital in 2021.

Comorbid disease	f	%
Do not have	98	46.2
Diabetes mellitus	53	25
Kidney	32	15
Heart	14	6.6
Hipertensi	15	7.2
Total	212	100

Source: Secondary Data, 2021

Based on table 2, it shows that the comorbid diseases of Covid-19 sufferers are mostly Diabetes Mellitus as many as 53 (25.0%) respondents, and the least comorbid disease is heart disease as many as 14 (6.6%) respondents.

Table 3. Cross-tabulation between Comorbid Diseases of Covid-19 Patients and Events Mortality at Mojowarno Christian Hospital in 2021.

Comorbid disease	Mortalitas						Statistic Test	
	Yes		No		Total			
	f	%	f	%	f	%	Chi Square	Odd Ratio
Do not have	27	27.5	71	72.5	98	46.2		
Diabetes mellitus	33	62.3	20	37.7	53	25	0.000	0.64

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Kidney	18	56.3	14	43.7	32	15	0.003	0.52
Heart	7	50	7	50	14	6.6	0.089	0.44
Hipertensi	7	46.7	8	53.3	15	7.2	0.134	0.43
Total	92	43.4	120	56.6	212	100		

Source: Secondary Data, 2021

Based on table 3 it shows that most of the comorbid diseases that have died were Covi-19 sufferers with comorbid diabetes mellitus as many as 33 (62.3%) respondents. Meanwhile, comorbid diseases with the least risk of death were Covid-19 sufferers with comorbid hypertension with 7 (46.7%) respondents. Statistic testwho squaresindicates comorbid diabetes mellitus results P: 0.000, meaning that there is a relationship between comorbid diabetes mellitus and mortality in patients with Covid-19. Comorbid disease with kidney disorders shows a P value: 0.003, meaning that there is a relationship between comorbid kidney disease and the occurrence of mortality in Covid-19 sufferers. Comorbid heart disease results obtained P: 0.089, meaning that there is no relationship between comorbid heart disease and mortality in patients with Covid-19. Hypertensive comorbid disease on mortality with a P value: 0.134 meaning that there is no relationship between hypertension comorbid disease and the risk of mortality in patients with Covid-19. The odds ratio of 0.64 means that the chance of dying for a Covid-19 patient who has comorbid diabetes mellitus is 0.4 times greater than not dying. The odds ratio of 0.52 means that the chance of dying for a Covid-19 patient who has comorbid kidney disease is 0.5 times greater than not dying. The odds ratio is 0.44, which means that the chance of dying for a Covid-19 patient who has comorbid heart disease is 0.4 times greater than not dying. The odds ratio of 0.43 means that the chance of dying for a Covid-19 patient who has comorbid hypertension is 0.4 times greater than not dying.

4. DISCUSSION

Based on the results of the study, most of the respondents who had comorbidities were respondents with diabetes comorbidities. Diabetes mellitus often occurs between the ages of 35-80 years (Indonesian Ministry of Health, 2018). According to the results of the study, respondents with comorbid diabetes mellitus were mostly over 40 years old. Herra (2014) said that a person enters an age prone to developing diabetes mellitus, namely after the age of 40 years. The results of the study also found that the average gender of Covid-19 sufferers who had comorbid diabetes mellitus was female. In line with the 2018 Riskesdas that the prevalence of diabetes mellitus in women is higher than in men with a prevalence of 1.78% (Ministry of Health RI, 2018) Female sex tends to be more at risk of developing diabetes mellitus associated with a greater body mass index and menstrual cycle syndrome and during menopause it is easy to accumulate fat which results in delays in the transport of glucose into cells (Trisnawati & Setyorogo, 2013). Diabetes mellitus is also suffered by many

non-working respondents. This is in line with the research results put forward by Araina et al (2021) that activity and work are factors that influence the incidence of diabetes mellitus. Statistical test resultswho squaresindicates comorbid diabetes mellitus results P: 0.000, meaning that there is a significant relationship between comorbid diabetes mellitus and mortality in patients with Covid-19. The odds ratio of 0.64 means that the chance of dying for a Covid-19 patient who has comorbid diabetes mellitus is 0.4 times greater than not dying.

Comorbid disease with kidney disorders shows a P value: 0.003, meaning that there is a relationship between comorbid kidney disease and the occurrence of mortality in Covid-19 sufferers. In a study by Gansevoort et al (2020), states that patients with severe chronic kidney disease have a very high risk of mortality from Covid-19 in fact, the risk of chronic kidney disease is higher than other risk factors including hypertension, diabetes, cardiovascular disease , and lung disease. This is caused by changes in the immune system including persistent systemic inflammation and immunosuppression. Apart from respiratory cells, other organs will also be affected by SARS-Cov-2 including the kidneys, ileum and heart, especially in conditions of viremia. Therefore, proximal renal tubular epithelial cells, glomerular mesangial cells, and podocytes will express ACE2 on their surface which is a target for Covid-19 (Gansevoort & Hilbrands, 2020). The odds ratio of 0.52 means that the chance of dying for a Covid-19 patient who has comorbid kidney disease is 0.5 times greater than not dying.

Comorbid heart disease results obtained P: 0.089, meaning that there is no relationship between comorbid heart disease and mortality in patients with Covid-19. This is not in line with the theory put forward by Herick, et al., 2020 that Covid-19 sufferers who have comorbid cardiovascular diseases become unstable when infected with SARS-CoV-2 as a consequence of an imbalance between increased metabolic needs due to infection and reduced heart reserve. Patients infected with SARS-CoV-2 with acute coronary syndrome (ACS) often have a poor prognosis. In ACS sufferers, reduced cardiac functional reserve occurs due to myocardial ischemia or necrosis, so that when infected with SARS CoV-2, cardiac insufficiency can occur, which can result in a sudden worsening of conditions (Willim et al., 2020). The odds ratio is 0.44, which means that the chance of dying for a Covid-19 patient who has comorbid heart disease is 0.4 times greater than not dying.

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The results of the statistical test between comorbid hypertension and mortality with a P value: 0.134 means that there is no relationship between comorbid hypertension and the risk of mortality in patients with Covid-19. The odds ratio of 0.43 means that the chance of dying for Covid-19 sufferers who have comorbid hypertension is 0.4 times greater than those who don't die. It can be said that Covid-19 sufferers who have comorbid hypertension have a chance of dying almost the same as the chance of staying alive or recovering. . This is not in line with the theoretical concept which says that comorbid hypertension in patients with Covid-19 results in increased expression of ACE-2 which results in high susceptibility to SARS-CoV-2 infection, especially treatment with angiotensin II receptor blockers (ARB) and angiotensin converting enzyme. inhibitors (ACEi). This can lead to worsening and severity of SARS-CoV-2 infection due to increased binding of the virus to target cells that utilize ACE-2. ACE-2 receptors are expressed by endothelial cells, so that dysfunction in vascular endothelial cells which often occurs in hypertensive patients can increase the increase in

ACE-2 receptor expression. So that in hypertensive patients who are infected with Covid-19 there is an increase in the severity of the infection causing mortality (Parveen, et al, 2020). Based on the results of the study, respondents with comorbid hypertension were mostly aged over 40 years, this was due to arterial pressure increasing with age, aortic regurgitation and degenerative processes more common in old age.. Corona virus disease control is exacerbated by the presence of comorbid hypertension which can increase morbidity and mortality in Covid-19 patients (Clerkin et al., 2020). Individuals with comorbid hypertension infected with SARS-CoV-2 may experience more severe clinical manifestations (Zhang et al., 2020). There are other factors that can cause Covid-19 sufferers with comorbid hypertension to have almost the same chance of mortality, which can be caused by the age of the respondents, a small percentage of whom are less than 40 years old, which means that the body's resistance to the severity of infection can be suppressed.

5. CONCLUSION

Based on the research results, the following conclusions can be drawn:

1. The most common comorbid disease in Covid-19 sufferers is Diabetes Mellitus.
2. Most cases of mortality in Covid-19 sufferers are experienced by Covid-19 sufferers with comorbid Diabetes Mellitus
3. There is a relationship between the comorbid disease Diabetes Mellitus and the incidence of mortality in patients with Covid-19.

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Writer Contribution

Chairman: Conceptualization of research, accompanying the implementation of each research implementation process
Member 1: Conceptualization of research, Perform data collection, perform data cleaning, prepare research budget
Member 2: Collect data, clean data, review and edit reports
Member 3: Perform data imputation and data analysis
Member 4: Writes, reviews and edits research reports
Member 5: Prepare research publications

Availability of Data and Materials

Data and materials that support the implementation of research are available according to needs. The research data is secondary data taken from the medical records of Covid-19 sufferers who were hospitalized at Mojowarno Christian Hospital from early January 2021 to the end of December 2021.

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Statement of Ethical Considerations

This research has been subjected to an ethical review by a team of reviewers from the Research Ethics Commission of the Faculty of Health Sciences, Unipdu Jombang and has been declared ethically feasible to proceed to the next research process as evidence that it has obtained an ethical clearance certificate.

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Conflict of Interest

The authors declare that they have no competing interests. There are no specific interests related to individuals or institutions.

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