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Comorbidity and Fatality Among Covid Patients: A Hospital Based-Retrospective Cohort Study

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Abstract

People with comorbid diseases have a high risk of contracting COVID-19, because the immune system has decreased, thus increasing the risk of transmission of COVID-19 and even potentially increasing the risk of fatality. This study aimed to determine the comorbidity and mortality among COVID-19 confirmed cases during May to September, 2021. The study was a retrospective cohort with secondary data from the COVID-19 with in Hospital report from May to September, 2021, with a total sample of 178. We extracted demographic and clinical data, including hospital outcomes (discharge or death). The result of the research showed that the respondents separated in to two groups, half of them are patients with comorbidity (89 patients) and the rest are patients non comorbidity. From 89 patients with comorbidity, 62 % were died and 38 % were discharged. The most comorbidites were 67,4% diabetes mellitus, 33% hypertension. The fatality rate of COVID-19 patients was 34% devided to 61,8% were comorbidity patients and 5,5% were non comorbidity. The comorbidity related to fatality rate of COVID-19 patient's (p=0.000). It is important for society to avoid and control comorbid factors of COVID-19.

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INTRODUCTION

WHO declared Coronavirus disease (COVID-19) a pandemic in March 2020. The increase in the number of COVID-19 cases occurred quickly and spread between countries. Indonesia is one of country in Southeast Asia that has contracted COVID-19. Whitch announced cases of COVID-19 on March 2, 2020, where 2 Indonesians were confirmed to COVID-19 (Kemenkes, 2020). COVID-19 is an infectious disease caused by severe acute respiratory syndrome Coronavirus-2 (SARS-CoV-2). This virus can infect anyone and cause symptoms of varying degrees of severity. The elderly and people with comorbid diseases have a higher risk of contracting COVID-19. Because the immune system in the elderly and people with comorbid diseases has decreased, thus increasing the risk of transmission of COVID-19 and even potentially increasing the risk of death (Kemenkes, 2020).

Comorbids that often accompany COVID-19 patients are immunocompromised, heart disease, liver disease, diabetes, asthma, hypertension, Chronic Obstructive Pulmonary Disease (COPD), Tuberculosis (TB), Human Immunodeficiency Virus (HIV), kidney disease, post-stroke, cancer, and other chronic diseases (Kemenkes, 2020). Research in China shows the mortality rate for patients with confirmed COVID-19 who have comorbidities, namely hypertension 9.5%, diabetes 7.4%, chronic obstructive pulmonary disease (COPD) 7%, cardiovascular disease 7.3%, liver disease 2.4%, obesity 13%, kidney disease 0.7%, and malignancy 2%. Other data from Italy shows the death rate of COVID-19 infection with hypertension 73.8%, diabetes 35.5%, COPD 13.7%, cardiovascular disease 42.5%, liver disease 3.7%, obesity 8.5%, kidney disease 20.2%, and malignancy 5%, (Ejaz et al., 2020).

Diabetes is one of the main causes of morbidity and mortality worldwide (Hussain et al., 2020). Patients with diabetes mellitus tend to be susceptible to infection because of the impaired ability of phagocytic cells. Diabetic patients experience increased ACE-2 receptors so they can increase the risk or exacerbate COVID-19 infection (Karya et al., 2021a). SARS-CoV-2 uses ACE-2 as a receptor to enter cells. ACE-2 is expressed not only in type I and II alveolar epithelial cells in the lung and upper respiratory tract, but also in several other locations such as the heart, endothelium, renal tubular epithelium, intestinal epithelium, and pancreas. The S-glycoprotein on the surface of SARS-CoV-2 binds to ACE-2 and causes formation changes. This allows proteolysis by host cell proteases (TMPRSS2 and Furin) resulting in virion internalization (Singh et al., 2020).

Furin is a type 1 membrane-bound protease which has high expression in diabetic patients. Entry of the virus into the cell triggers an inflammatory response by recruiting helper T cells that produce interferon-G. Disorganized immune response with increased ACE-2 receptors and furin expression leads to higher levels of pulmonary inflammation and can lower insulin levels. This causes recruitment of other inflammatory cells leading to a cytokine storm that can lead to organ damage and multi-organ failure (Singh et al., 2020). Viral load, dysregulated immune response, cytokine storm, alveolar dysfunction, endothelial dysfunction and coagulopathy are specific factors responsible for the increased risk and severity of SARS CoV-2 infection in diabetes (Erener, 2020).

Individuals with hypertension have a high number of ACE-2 receptors, which makes it easier for the corona virus to spread in the body (Drew and Adisasmita, 2020). ACE-2 was identified as a target receptor for SARS-CoV-2. ACE-2 is a multifunctional protein that is a specific functional receptor for SARS-CoV-2 and is the start of COVID-19 infection (Rahayu et al., 2021). Its main physiological role includes the enzymatic conversion of angiotensin (Ang) II to Ang-(1-7) and Ang 1 to Ang (1-9), which is a cardiovascular protective peptide (Nabila, 2021). The vascular system, electrolyte balance and blood pressure are regulated by ACE-2 (Wulandari et al., 2021). ACE-2 binds to the S-protein of SARS CoV-2 so that the virus can enter cells and replicate. ACE-2 receptors are abundant in the cardiovascular system, nasopharynx, and lungs. In cases of comorbid hypertension there is increased expression of ACE-2 receptors making them more susceptible to COVID-19 infection, especially treatment with angiotensin II receptor blockers (ARBs) and angiotensin-converting enzyme inhibitors (ACEi) (Shi et al., 2020).

The binding of SARS-CoV-2 to ACE-2 results in reduced expression of ACE-2 on the cell surface, thus blocking the ability of cells to degrade angiotensin II to become angiotensin. Disruption of angiotensin production causes the vasodilator effect to not be maximized so that it disrupts blood pressure homeostasis, causes vasoconstriction of blood

vessels which will worsen the condition of COVID-19 patients with comorbid hypertension (Alfad et al., 2020). Patients with comorbid hypertension will experience dysregulation of the body's immune system, namely high lymphocyte count, CD8+ T dysfunction so that the body's response to viral infection is ineffective. This situation will increase the production of cytokines causing storms, microcirculatory ischemia which eventually results in organ failure (Kamyshnyi et al., 2020).

METHODS

The study was a retrospective cohort using secondary data from the COVID-19's in Hospital report from May to September, 2021. The population in this study was 178 Covid-19 patients, both accompanied by comorbidities and not. Meanwhile, the sample in this study was all 178 the entire population. The instrument used in this study was an assessment sheet to summarize data taken from patient's medical records. The data was collected by taking the necessary data from the patient's medical record were age, gender, obesity, family history, and fatality records of Covid-19 patients. We extracted demographic and clinical data, including hospital outcomes (discharge or death).

RESULTS

Table 1: The characteristic of Respondents.

	Died		**Discharged**	
	F	**%**	**F**	**%**
Comorbidity	55	61,8	34	38,2
Non comorbidity	5	5,6	84	94,4
Total	60	33,7	118	66,3
P value	.000			
	Comorbidity		**Non comorbidity**	
	F	**%**	**F**	**%**
D Dimer				
Normal	20	22.5	42	47.2
Abnormal	69	77.5	47	52.8
Weight				
Obese	5	5.6	1	1.2
Non obese	84	94.4	88	98.8
Gender				
Male	43	48.3	48	53.9
Female	46	51.7	41	46.1
Age				
16-25	-	-	5	5.6
26-35	1	1.1	13	14.6
36-45	6	6.7	15	16.9
46-55	28	31.5	23	25.8
56-65	29	32.6	20	22.5
>65	25	28.1	13	14.6

The result showed that from 89 patients with comorbidity, 62 % were died and 38 % were discharged. The most comorbidites were 67,4% diabetes mellitus, 33% hypertension. The comorbidity related to fatality rate of COVID-19 patient's (p=0.000). 62% of patients with comorbidities died. The high fatality rate in this study was related to age, body weight, and D-Dimer (p=0,000). 38% respondents in this study had a younger age and normal d-dimer levels.

DISCUSSION

The results showed that from the 89 COVID-19 patients with comorbidities, 61,8% were died and 38,2% discharged. The commorbidities seperated in to two groups are 67% were diabetic, and 33% were hypertension. Diabetes occupies the most common comorbid found in COVID-19 patients ini Madura and the second position as the most common comorbidity in COVID-19 patients in Indonesia, (Karyono and Wicaksana, 2020). Even the non

comorbidity patient from this research, 5,6% of them was died, and the rest are discharged (94,4%). It was found that the age of COVID-19 patients with the most comorbidities was in the 56-65 year age group of 32.6% (29 respondents). Age more than 45 years is one of the risks of developing diabetes, (Perkeni, 2021). As age increases, glucose intolerance will increase (Masruroh, 2018). So risk of developing type II Diabetes Mellitus will increase from the age of 45 and over. As people get older, they will experience progressive shrinkage of pancreatic β cells. When the hormone is so little to produced its causes glucose levels to rise.

The World Health Organization also states that after a person reaches the age of 40, blood glucose levels rise 1-2 mg% per year during fasting and will increase by around 5.6 - 13 mg% 2 hours after eating. It can be concluded that age is the main factor in the increase in the prevalence of type II diabetes and impaired glucose tolerance (Fanani, 2020). Age is a factor that cannot be avoided or modified. A person aged 40 years begins to experience physiological and metabolic decline, including a decrease in the body's metabolic processes in the pancreas organ, which triggers insulin resistance which can affect blood glucose levels.

The research showed that COVID-19 patients with comorbidities (94.4% /84 respondents) were not obese. In diabetics there is a problem in the working effect of insulin in the metabolism of sugar into imperfect cells so that blood sugar remains high. This situation can be toxic and cause a feeling of weakness and unwell as well as cause complications and other metabolic disorders. If the body is unable to get enough energy from sugar, the body will process other substances to be converted into energy such as fat. The use or destruction of fat and protein causes weight loss (Rias, 2017). The mortality of COVID-19 patients with comorbidities was 61.8% (55 respondents). Comorbid is a condition where the patient already has a pre-existing disease, is chronic in nature and will aggravate the course of the COVID-19 disease. Immune factors in comorbid patients diseases have decreased. This condition could increases the risk of transmission of COVID-19 and has the potential to experience clinical deterioration, thereby increasing the risk of death (Kemenkes, 2020). COVID-19 patients with comorbidities have a higher death rate compared to patients without comorbidities (Ejaz et al., 2020). Comorbid diabetes and heart disease in COVID-19 patients can be a risk factor for death in this study because $P < 0.05$. Diabetic patients have a 2 times greater risk of developing a more severe or critical illness that requires treatment in an intensive care unit. On hospitalization, patients with diabetes are three times at risk of dying from COVID-19 (Longato et al., 2020; Wang, 2020).

The 33% of comorbidities are hypertention patients and 77,5% are having D-dimer abnormality. Hypertension increases the risk 2.2 and even 3,17 times for COVID-19 death (Lippi et al., 2020); (Shi et al., 2020). D-dimer is a product of fibrin degradation that occurs due to the conversion of fibrinogen to fibrin mediated by thrombin, fibrin reticulation mediated by factor XIII and fibrin degradation by plasmin. D-dimer levels depend on the process of coagulation and activation of fibrinolysis. D-dimer levels have a high sensitivity for thromboembolic disease, but have a low specificity because D-dimer is also found to be elevated in other conditions such as sepsis and ARDS. Changes in coagulation in the form of increased D-Dimer levels were found in patients with COVID 19 infection (Long et al., 2020). Patients with diabetes and hypertension comorbidities are vulnerable to SARS-CoV-2 infection due to decreased immune factors in co-morbid patients, which has the potential to experience clinical deterioration and increase the risk of death. In addition, in patients infected with COVID-19 there is hypercoagulability characterized by increased D-dimer levels and is often found in COVID-19 patients who experience clinical deterioration. Hypercoagulable occurs in COVID-19 patients with severe symptoms due to a hyperinflammatory response (Bastug et al., 2020). Increased D-dimer in COVID-19 patients is associated with abnormal immune mechanisms, increased disease severity and increased mortality. D-dimer measurement can be performed as an early marker of disease worsening and an increased risk of death (Li et al., 2020). The D-dimer in patients who died from COVID-19 was up to 9 times higher than in patients who recovered (Zhou et al., 2020)

Data were analyzed using Chi Square with a p value of .000 (<0.005), means that there is a relationship between comorbidities and the death of COVID-19 patients. This data is supported by research which shows that 88% of deaths in SARS-CoV-2 positive patients are caused by a history of comorbidities. Patients with diabetes mellitus tend to

be susceptible to infection because of the impaired ability of phagocytic cells. Diabetes mellitus patients experience an increase in ACE-2 receptors so that this situation can exacerbate COVID-19 infection. COVID-19 patients with comorbid diabetes in conditions of uncontrolled hyperglycemia have a higher risk of death because chronic hyperglycemia causes impaired immune response due to decreased mobilization of polymorphonuclear leukocytes, chemotaxis, cytokine secretion, and inhibition of TNF alpha on T cells (Karya et al., 2021b).

The vascular system, electrolyte balance and blood pressure are regulated by ACE-2 (Wulandari, 2020). Angiotensin-Converting Enzyme-2 (ACE-2) binds to the S-protein of SARS CoV-2 so that the virus can enter cells and replicate. ACE-2 receptors are abundant in the cardiovascular system, nasopharynx, and lungs. In cases of comorbid hypertension there is increased expression of ACE-2 receptors making them more susceptible to COVID-19 infection, especially treatment with angiotensin II receptor blockers (ARBs) and angiotensin-converting enzyme inhibitors (ACEi) (Shi et al., 2020)

COVID-19 patients with diabetes and hypertension comorbidities experience an increase in Angiotensin-Converting Enzyme 2 (ACE2) receptors. SARS-CoV-2 enters human cells through binding to the ACE-2 receptor. This situation makes COVID-19 patients with comorbidities more susceptible to further organ failure which will increase complications and death. The binding of SARS-CoV-2 to ACE-2 results in reduced expression of ACE-2 on the cell surface, thus blocking the ability of cells to degrade angiotensin II to become angiotensin. Disruption of angiotensin production causes the vasodilator effect to not be maximized so that it disrupts blood pressure homeostasis, causes vasoconstriction of blood vessels which will worsen the condition of COVID-19 patients with comorbid hypertension (Alfad et al., 2020). Patients with comorbid hypertension will experience dysregulation of the body's immune system, namely high lymphocyte count, CD8+ T dysfunction so that the body's response to viral infection is ineffective. This situation will increase the production of cytokines causing storms, microcirculatory ischemia which eventually results in organ failure (Kamyshnyi et al., 2020).

CONCLUSION

We found that mortality was associated with comorbidity (pre-existing hypertention and diabetes), higher age, heavier weight and abnormal D-Dimer.

SUGGESTION

Comorbidity in Covid-19 patients must be controlled as much as possible to prevent severity and fatality.

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CONFLICTS OF INTEREST

All authors stated that there was no conflict of interest during the research and publication.

AUTHOR CONTRIBUTIONS

Yeni Kartika Sari: Corresponding Author, research analysis, references. Thatit Nurmawati: Research ideas, research proposal, research instruments, references. Joko Ivnu Susanto: Research ideas, research proposal, research instruments, references.

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