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An overview of Covid-19 patients with and without comorbid Diabetes Mellitus at Surabaya Hajj general hospital

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ABSTRACT

Diabetes mellitus (DM) is one of the most common comorbidities found in patients infected with Covid-19 with severity and death. To obtain an overview of Covid-19 patients with and without comorbid DM. A retrospective cohort study, taking subjective data on Covid-19 patients with and without DM at Surabaya Hajj general hospital for the period of March 2020 to June 2021. Data analysis using the Chi-square test was to determine differences in both test variables. The death of Covid-19 patients with comorbid DM was found with the condition in which the average random blood glucose (RBG) increased by >150 mg/dl (286 mg/dl), as well as in recovered patients (197 mg/dl); meanwhile, patients without comorbid DM died with also an increase in the RBG value (166 mg/dl). Male patients were found to be more prone to get infected with Covid-19 than female patients. It can be concluded that there was no significant difference in the severity of cases in Covid-19 patients with comorbid DM and without comorbid DM. Deaths due to Covid-19 in patients with comorbid DM or without comorbid DM occurs due to the increasing blood glucose value by >150 mg/dl.

1. Introduction

Diabetes mellitus (DM) is a disease that becomes one of the health problems both in Indonesia and in various countries in the world (Purnomo, 2018). Since the outbreak caused by the severe acute respiratory syndrome (SARS-CoV-2) virus in December 2019, DM as become a special concern. DM can be a risk factor that can increase the severity leading to death in Covid-19 patients (Mahamat-Saleh et al., 2021; Varghese et al., 2021). Data from the Ministry of Health in January 2022 recorded the death rate in Indonesia as reaching 3.3% (Ministry of Health, 2022).

Corona Virus Disease (Covid-19) can affect the physiological system of patients with diabetes mellitus which can aggravate the condition which might lead to death. This was due to an increase in the expression of Angiotensin-Converting Enzyme 2 (ACE2) and an extension of the time for viral clearance (Rahayu et al., 2021). Pathophysiologically, DM patients infected with Covid-19 occur because of an increase in ACE2 expression, an increase in furin which can propel virus replication process, and disruption in T cells (Kumar et al., 2020). Excessive stress conditions can trigger high secretion of catecholamine and glucocorticoid hormones resulting in an increase blood glucose. This process causes insulin resistance and blood glucose to increase so as to encourage the production of oxidative stress which inhibits the production of glycolysis and proinflammatory cytokines (Verma et al., 2021).

Comorbid DM was a condition where the patient has experienced an increase in blood glucose levels before being infected with Covid-19. DM is one of the most common comorbidities found in patients who infected Covid-19 (Du et al., 2020). Covid-19 conditions with comorbid DM were able to increase the risk of severity and death (Gregg et al., 2021; Magdy Beshbishy et al., 2021; Norouzi et al., 2021). Recently researches suggest that Covid-19 can have an impact on increasing the risk of DM (Rathmann et al., 2022). DM is a condition characterized by an increase in laboratory values in the form of FPG (Fasting plasma glucose) level of 126 mg/dl (7.0 mmol/l) or an RBG of 200 mg/dl (11.1 mmol/l) (American Diabetes Association, 2010). This study was conducted to obtain an overview of Covid-19 patients with and without diabetes mellitus comorbid on the mortality of patients at Surabaya Hajj general hospital.

2. Materials and Methods

This study used 179 samples of Covid-19 patients that had been adjusted with the research criteria and who have completed treatment. A number of 73 samples were recovered patients and 106 other patients were Covid-19 patients who were died. Comorbid DM on Covid-19 patients were patients who had a history of DM before being infected with Covid-19. The rest of samples were Non-comorbid DM patients are Covid-19 patients who do not have comorbid DM after being infected with Covid-19.

2.1. Type of Research

This is an observational study with a retrospective cohort design that takes subjective data at Surabaya Hajj general hospital for the period of March 2020 to June 2021. Patients were observed in their final condition of being both dead and recovered. Recovered patient is defined as a patient who returns home with a negative PCR or a patient with an improved clinical condition with positive PCR but has completed the isolation period with the approval of the doctor in charge. The ethics of this research were obtained and issued by the hospital in June 2021 No.073/12/KOM.ETIK/2021.

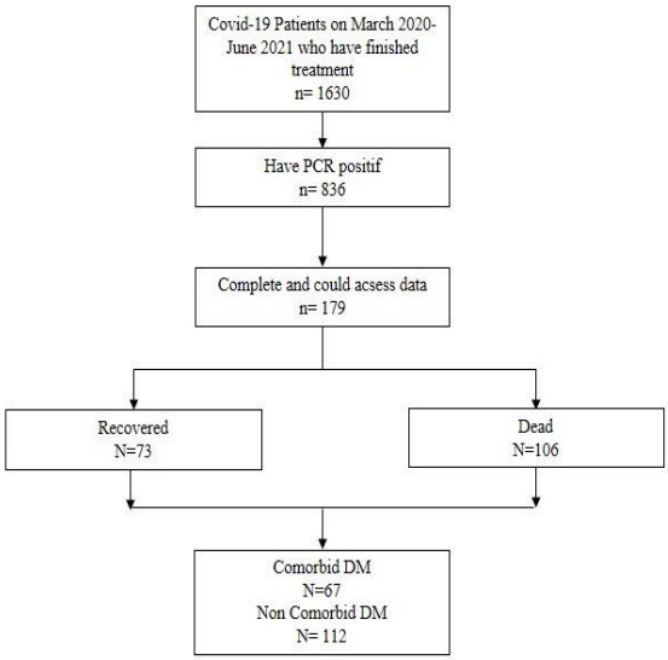

Fig .1. Flowchart sample patients collection

2.2. Research Sample

Research was based on the inclusion and exclusion criteria of the study: Inclusion criteria: Covid-19 patients with positive PCR detection who have undergone isolation, patients with comorbid diabetes mellitus and without diabetes mellitus, proven by their Random blood glucose values in their laboratory results and patients aged >18 years. Exclusion Criteria: patients who were referred to other hospitals before treatment was performed, patients' data were not accessible.

2.3. Data Analysis

To see the differences in the two studied groups (died and recovered), data analysis was carried out using the Chi-square test, with an error tolerance value of p-value <0.05 for each test variable using SPSS software version 20.0.

3. Results and Discussion

Based on the results of the study, there were 179 Covid-19 patients with the final condition of 106 patients dying and 73 patients recovering. There were 55 patients with comorbid DM and 112 patients without comorbid DM in the period of March 2020 to June 2021. Based on the description of the RBG value of Covid-19 patients with comorbid DM and without DM, it was found that Covid-19 patients without comorbid DM also experienced an increase in RBG value of 166 mg/dl in the final condition of dying, but in the recovered patients, the average RBG value was considered normal 110 mg/dl or <150 mg/dl. Meanwhile, Covid-19 patients with comorbid DM, both recovered and dead patients, both experienced an average increase in RBG values of 197 mg/dl and 286 mg/dl Table 1.

The average random blood glucose value in Covid-19 patients with comorbid of DM, both died and recovered, increased compared to the normal value of <150 mg/dl. It was also found that Covid-19 patients who did not have comorbid diabetes mellitus experienced an increase in random blood glucose values during treatment until they died with an average value of 166 mg/dl. The results of the study by Zhu et al., (2020) found that patients with type 2 diabetes mellitus required more medical intervention and had a significantly higher mortality rate (7.8%) and multi-organ injury compared to non-diabetic individuals (Zhu et al., 2020).

DM is a very important risk factor in clinical development and mortality in Covid-19 patients, in addition, well-controlled blood glucose can maintain glycemic variability which is associated with a significant reduction in the mortality effect. Blood glucose was an independent risk factor in the development of critical cases, death in non-critical cases, and in-hospital mortality in critical conditions (HR=1.30, 95% CI 1.03-1.63, p=0.026) (Wu et al., 2020). The results of the meta-analysis showed that each increase in fasting blood glucose (FBG) of 1 mmol/dL could increase the severity of up to 33% (Lazarus et al., 2020), poor prognostic results also occur in Covid-19 patients who have increased GDP values (Cai et al., 2020). DM is associated with an increase in blood glucose that occurs due to the body's lack of insulin or inability to regulate it. The results of Mahardhika's systematic review (2021) suggested that hyperglycemia that occur in both diabetic and non-diabetic Covid-19 patients experience severity to death (Mahardhika, 2021). The severity of Covid-19 is positively correlated with the incidence of hyperglycemia as well as increase in blood glucose (Xiao et al., 2021). A study by Shauly-Aharonov et al., (2021) found that elevated pre-infection blood glucose may be a risk factor for severe Covid-19 in non-diabetic patients (Shauly-Aharonov et al., 2021).

Table 1. Random blood glucose value in Covid-19 patients

Random Blood Glucose Value (RBG)	Average Value	
	Without Diabetes mellitus (mg/dl)	With Diabetes mellitus (mg/dl)
Dead	166	286
Recovered	110	197

Diabetic patients with both high and low pre-infection blood glucose are at a risk for severe Covid-19 infection. An increase in blood glucose is predicted to lead to the development of Covid-19 disease and death (Wang et al., 2021). Patients living with diabetes or uncontrolled blood glucose tend to experience disorders of the innate immune system due to the dysfunction of macrophages and lymphocytes which can lead to multiple organ failure. Increased glucose can directly increase the replication of SARS-CoV-2 and continuous glycolysis in which hyperglycemia might lead to viral proliferation. Patients with Covid-19 should be aware of adherence to prescribed drugs and also blood glucose levels should be checked more often than before (Lim et al., 2021).

Mortality in diabetic patients is not affected by anti-diabetic treatment but is thought to be caused by an increase of blood glucose values (Li et al., 2021). Patients with previous comorbid diabetes were found to have a significantly higher mortality rate with hyperglycemia than with normoglycemia ($p<0.001$). In addition, hyperglycemia was also associated with the need for mechanical ventilation and intensive care unit (ICU) admission (Carrasco-Sánchez et al., 2021). These results can explain the findings in this study, that diabetes mellitus comorbid conditions more commonly led to death than recovery and the severity would increase with the presence of diabetes mellitus, although it had no significant effect (p-value = 0.130). Table 2.

Based on gender, it was found that men were more affected by Covid-19 than women. Female patients with comorbid were at higher number compared to male; furthermore, male patients without comorbid DM are more common than women as shown in Fig.2 and Table 2.

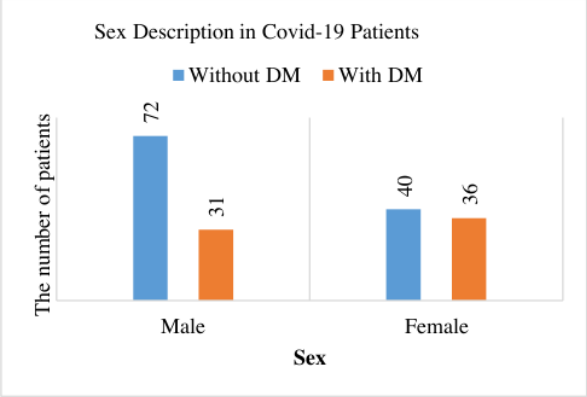

Fig.2. Sex Description In Covid-19 Patients

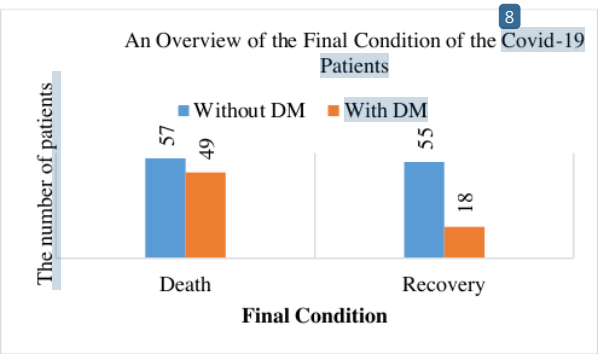

Fig.3. Overview of the Final Condition of Covid-19 Patients

Table 2. An Overview of Covid-19 Patients with and without Comorbid DM

Variables	Covid-19 Patients		P-values
	Without Diabetes mellitus	With Diabetes mellitus	
Sex			
Male	72 (69.9%)	31 (30.1%)	0.018
Female	40 (52.6%)	36 (47.4%)	
Final Condition			
Dead	57 (53.8%)	49 (46.3%)	0.003
Recovery	55 (75.3%)	18 (24.7%)	
Case Severity			
Mild	39 (73.6%)	14 (26.4%)	0.130
Severe	13 (54.2%)	42 (41.2%)	
Critical	60 (62.6%)	67 (37.4%)	

The results showed that death could also occur in Covid-19 patients without comorbid DM which can be seen in Fig. 2 and Table 2. Multivariate analysis in the study of Myers et al., (2021) found that the condition of patients with hyperglycemia, male sex, and older age could increase the risk of intubation to death but not HbA1c value (Myers et al., 2021). Patients with male gender should be more aware of a worse risk of death than female patients (Belice & Demir, 2020). Another finding in the study of Osi et al., (2020) and Nguyen et al., (2021) male patients were found to be more prone to get infected with Covid-19, although there was no significant difference between the two p-values 0.502 (Osi et al., 2020). Another result found that the number of male patients 2.4 times more likely to die than female patients (70.3% vs 29.7%) (Jin et al., 2020). Biological differences such as gender are playing a central role in genetic and hormonal regulation of the immune response in both the innate and adaptive immune systems. Most males with diabetes mellitus are more likely to be hospitalized; in addition, it was found that male patients are at a higher risk of severity and death due to Covid-19 (Kautzky-Willer, 2021). The increase in mortality occurred in male Covid-19 patients 1.89 times higher than in female (Biswas et al., 2021). The results of the study by Goodman et al., (2021), stated that the risk of death was 30% higher in male Covid-19 patients at all ages (Goodman et al., 2021). In general, women have a stronger immune response than men, this is associated with immune-related genes located on the X chromosome or there is an effect of sex hormones on immune cells (Jun et al., 2021). Males have higher plasma levels of pro-inflammatory cytokines and chemokines that can be correlated with non-classical monocytes, whereas females have a stronger T-cell response than males (Takahashi et al., 2020). This makes men be more at risk of infection and death from Covid-19.

4. Conclusion

Death can occur in patients either with or without comorbid diabetes mellitus due to a random increase in blood glucose >150 mg/dl. Hence, an increase in blood glucose in patients infected with Covid-19 should raise a special concern.

Author Contributions: UH data processing, collection, and performing experiments; UH, ED, and SG data analysis and draft manuscript.

Competing Interests

No potential conflict of interest relevant to this article was reported.

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