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COVID-19 and Diabetes Mellitus at RSU South Tangerang-Indonesia: Clinical Profile and Treatment Strategies

(*COVID-19 dan Diabetes Mellitus di RSU Tangerang Selatan-Indonesia: Profil Klinis dan Strategi Pengobatan*)

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ABSTRACT

Background: Diabetes Mellitus is one of the risk factors for COVID-19. This causes the morbidity and severity of COVID-19 patients to be higher in patients with diabetes. **Objectivity**: This study aimed to determine the effectiveness of treatment therapy for COVID-19 patients with comorbid diabetes at the South Tangerang City General Hospital. **Methods**: This study used a descriptive design with a quantitative approach and retrospective data collection. Sampling was done by Total Sampling with a total sample of 127 patients from 234 patients. **Result:** The characteristics of COVID-19 patients with comorbid diabetes were dominated by the male gender (55.1%), with an age range of 46-55 years (38.6%), high school education (43.3%), and have a private employee type of work (55.1%). The symptoms of COVID-19 patients with comorbid diabetes were cough (89.8%), with a length of stay for patients 7–14 days (72.4%).Treatment for COVID-19 with comorbid diabetes was antibiotics azithromycin (26.0%), antiviral remdesivir (62.2%), methylprednisolone (73.2%), acetylcysteine (85.0%), vitamin C (89.8%), and the antidiabetic group that is often used is insulin novorapid (41.7%). **Conclusion:** The results of laboratory examinations showed that COVID-19 treatment therapy is effective in reducing the amount of virus in the blood, which is indicated by an increase in the PCR value (p-value <0.001), lowering blood sugar levels (which is characterized by a decrease in blood sugar levels when (p-value <0.001)), and reduce hypercoagulation which is characterized by a reduction in the value of D-dimer (p-value < 0.005).

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INTRODUCTION

Diabetes Mellitus is a risk factor for the occurrence of COVID-19, this causes the morbidity and severity of COVID-19 patients to be higher in diabetic patients (Roeroe *et al.,* 2021). COVID-19 data on patients with diabetes mellitus have not been widely reported in Indonesia. Previous studies stated that patients with diabetes mellitus accounted for 9.6% of all COVID-19 cases, and the mortality rate reached 42.9% (Minuljo *et al.,* 2020).

Co-morbidities with diabetes mellitus are thought to increase the risk of COVID-19 infection (Jaya *et al.,* 2022), inappropriate treatment for COVID-19 patients with co-morbidities of diabetes mellitus can increase inflammation, weaken the immune response, and possibly increase ACE2 levels, along with vascular dysfunction and a prothrombotic state that causes lung tissue damage (Li *et al.,* 2021), administration of treatment with glucocorticoids can result in glucose disturbances in people with diabetes, thereby increasing the susceptibility to infection with COVID-19(Ugwueze *et al.,* 2020).

The potential effect of this class of glucose-lowering drugs is unclear (Pal & Bhadada, 2020). Over the past year, several retrospective clinical studies have reported that specific use in diabetic and obese patients infected with COVID-19 prior to hospital admission correlates with reduced severity and mortality (Ibrahim *et al.,* 2021). However, other lowering drugs used to control blood sugar levels do not appear to produce the same effect (Singh & Khunti, 2020). Thus, it is crucial to know the treatment strategy for the clinical outcome of T2DM patients during the COVID-19 outbreak.

Diabetes Mellitus Type 2 (DMT2) also causes an imbalance between coagulation and fibrinolysis with increased clotting factors so that it can support hypercoagulation. Therefore DMT2, together with COVID-19, can also worsen the patient's condition (Fitrian, 2020). So patients with T2DM are advised to increase the frequency of blood glucose measurements and adjust the dose if the target blood glucose level is not achieved (Edwar *et al.,* 2021). worsening, length of hospitalisation and patients undergoing intensive care (Bravi *et al.,* 2020).

Three types of antivirals used in the treatment of COVID-19: remdesivir 68% of 53 patients with severe symptoms were declared cured; favipiravir 71.43% of 98 patients were said cured, oseltamivir 31% of 99 patients were declared cured (Jomah *et al.,* 2020).

The high number of COVID-19 cases with comorbid diabetes, as well as several combinations of treatment therapy given to COVID-19 patients with comorbid diabetes, so it is necessary to analyzeanalysefectiveness of COVID-19 treatment therapy in COVID-19 patients with comorbid diabetes at the hospital.

MATERIAL AND METHODS

Research Design

This type of research was descriptive with a quantitative approach and retrospective data collection using medical records of patients diagnosed with COVID-19 with comorbid diabetes at the South Tangerang City General Hospital.

Methods

The data collected was secondary data obtained from medical records. The data collection technique was carried out with permission to collect data from the authorities in the hospital and collect the required medical record room of the South Tangerang City General Hospital. The inclusion criteria for this study were patients with comorbid diabetes who were hospitalized in 2021, had complete medical record data, and had SARV-2 PCR results. Patients aged less than 26 years, having diabetes complications with other diseases (such as hypertension, heart disease, autoimmune and rheumatoid arthritis, gout were excluded) were excluded from this study.

RESULTS

a. Socio-Demographic Characteristics of COVID-19 Patients with Comorbid Diabetes

Table 1. Socio-Demographic Characteristics of COVID-19 Patients with Comorbid Diabetes

Variable	Parameter	n (%)
Age	26-35 Years	7 (5,5)
	36-45 Years	9 (7,1)
	46-55 Years	49 (38,6)
	56-65 Years	42 (33,1)
	>65 Years	20 (15,7)
Gender	Male	70 (55,1)
	Female	57 (44,9)
Level Education	Elementary School	20 (15,7)
	Junior high school	14 (11,0)
	Senior High School	55 (43,3)
	University	30 (30,7)
Occupation	Private employees	70 (55,1)
	Government employees	11 (8,7)
	Pension	6 (4,7)

	Housewife	40 (31,5)
Symptoms	Fever	51 (40,2)
	Cough	114 (89,8)
	Have a cold	19 (15,0)
	Out of breath	79 (62,2)
	Diarrhea	12 (9,4)
	Nauseous	94 (74,0)
	Vomit	28 (22,0)
Type of Treatment	ICU	6 (4,7)
	Isolation Room	121 (95,3)
length of treatment	< 7 Days	12 (9,4)
	7-14 Days	92 (72,4)
	15-21 Days	16 (12,6)
	22-28 Days	7 (5,5)
Patient Condition	Recovered	112 (88,2)
	Death	15 (11,8)

Based on the results of the study in Table 1, the characteristics of the patients were dominated by the male gender (55.1%) and aged 46-55 years (38.6%), graduated from high school (43.3%), and worked as a private employee (55.1%). The most common clinical symptom was cough (89.8%). The type of treatment was isolation room (95.3%), the longest and longest treatment was 7-14 days (72.4%), and patients who were declared cured were (88.2%) while patients died (11.8%).

b. Classes and types of drugs used by COVID-19 patients with comorbid diabetes

Table 2. Groups and types of drugs

Class of Drugs	Types of Drugs	n (%)
Antibiotics	Levofloxacin	23 (18,1)
	Azithromycin	33 (26,0)
	Ciprofloxacin	21 (16,5)
Antivirus	Remdesivir	79 (62,2)
	Favipiravir	47 (37,0)
	Oseltamivir	3 (2,4)
	Methisoprinol	13 (10,2)

Corticosteroids	Methylprednisolone	93 (73,2)
	Dexamethasone	5 (3,9)
Mucolytic	Acetylcysteine	108 (85,0)
	Erdosteine	7 (5,5)
	Ambroxol	3 (2,4)
Multivitamin	Vitamin C	114 (89,8)
	Vitamin D	108 (85,0)
	Curcuma	51 (40,2)
	Becom Zet	6 (4,7)
	Imboost	13 (10,2)
	Mecobalamin	5 (3,9)
	Zinc	113 (89,0%)
Antidiabetes	Lantus	42 (33,1)
	Novorapid	53 (41,7)
	Metformin	25 (19,7)
	Humalog	2 (1,6)
	Apidra	10 (7,9)

Based on the results of the study in **Table 2,** the most widely used types of antibiotics were azithromycin (26.0%), the most frequently used antiviral group was remdesivir (62.2%), the class of corticosteroid drugs used was methylprednisolone (73.2%), the most widely used mucolytic drug class is acetylcysteine (85.0%), the most commonly given multivitamin was vitamin C (89.8%). The most widely prescribed antidiabetic drug was novorapid (41.7%).

c. Laboratory test on COVID-19 patients with comorbid diabetes and bivariate analysis

Table 3 Laboratory test of COVID-19 patients with comorbid diabetes

Variable	Referral Value	n = 127				*p-value*
		Before treatment		After treatment		
		Means	Min - Max	Means	Min - Max	
PCR	>40	25,528	12,3-39,4	39,096	15,9-42,0	<0,001
Instantaneous Blood Glucose	< 200	225,47	63-516	186,3	91-452	<0,001
HbA_1C	<6,5	7,547	5,1-4,5	-	-	0,000

Oxygen Saturation	95-100	95,39	84-100	96,19	71-100	0,056
Creatinin	Male < 1,14 mg/dL, Female < 1,2 mg/dL	1,003	0,30-10,88	0,98	0,30-11,74	0,452
D-dimer	<500	2454,59	310-20000	1573,84	250-20000	0,005

Based on Table 3, the results of the statistical test showed that there was an effect of treatment therapy in COVID-19 patients on blood glucose (p-value 0.000). The HbA_1C value before treatment with an average patient value of 7.547%, while the HbA_1C value after treatment was not described in the patient's medical record data. The average oxygen saturation value before treatment was 95.39%, and after treatment was 96.19%. The patient's oxygen saturation value shows that the patient's general condition does not experience shortness of breath, which is marked by oxygen saturation in the normal range of 95-100. Statistical test results show no effect of treatment therapy in COVID-19 patients on oxygen saturation values (p-value > 0.05). Creatinine values before treatment obtained an average of 1.033 mg/dL and after treatment with an average value of 0.980 mg/d. The results of statistical tests showed that there was no effect of medication therapy on patients' creatinine values (p-value> 0.05). The D-dimer value was obtained before treatment, with an average yield value of 2454.59 g/mL, while the D-dimer after treatment obtained an average of 1573.84 g/mL. The results of the statistical test showed that (P-value: 0.005) or p-value <0.05, meaning that there was an effect of treatment therapy in COVID-19 patients with comorbid diabetes in the hospital on the patient's D-dimer.

DISCUSSION

Based on **Table 1,** the sample used in this study was 127 patients. This shows that the average age of COVID-19 patients with comorbid diabetes is 46-55 years, with a total of 49 people (38.6%). It belongs to the category of early elderly; at that age, there is a decrease in the immune system, so it is more at risk of experiencing mortality (Wu & McGoogan, 2020). Other research suggests that the risk of infection increases with age, this occurs because of changes in the physiological function of organ systems, causing adaptive immunity and innate immunity to decrease (Chakhtoura *et al.*, 2017), so there is a higher risk of being infected with COVID-19. Based on gender characteristics, male patients were more dominant than female patients, namely 70 people (55.1%). Men have more androgen hormones. Androgen signaling can increase the risk of COVID-19 infection (Stárka & Dušková, 2021). Men and women have differences in body physiology, so there are differences in immunity between men and women. Women have the hormone estrogen, which maintains more protective humoral and cellular immunity than men (Ortona & Elena, 2011).

Patients with COVID-19 with the highest comorbid diabetes in high school education were 55 people (43.3%). One's education is associated with one's knowledge of something (Wardani & Anggraini, 2014), person's knowledge is associated with receiving information, especially health information; when someone has sufficient information, it tends to be easier to avoid disease (Setyaningsih & Diyono, 2020). Based on the work characteristics of COVID-19 sufferers, private employees were dominated by 70 people (55.1%). This study found that private employees were more susceptible to the incidence of COVID-19 with comorbid diabetes. Someone who works is difficult to get information because he does not have free time to look for information (Garavand *et al.*, 2016). In addition, workers have low physical activity (Ryde *et al.*, 2020). Low activity is associated with low immunity (Nieman & Wentz, 2019). Workers are more susceptible to infections due to social contact with fellow workers because workers infected with COVID-19 without symptoms can still work, so they have a great potential to transmit the disease to others while working or when communicating.

COVID-19 is a disease caused by SARS-CoV2 infection, which attacks the respiratory system so that several symptoms are obtained, such as shortness of breath, fever, vomiting, and diarrhea. Based on Table 1, the clinical symptoms of COVID-19 patients with comorbid diabetes experienced the most coughing as many as 114 people (89.8%), nausea as many as 94 people (74.0%), and shortness of breath as many as 79 people (62.2%), fever as many as 51 people. People (40.2%), vomiting as many as 28 people (22.0%), colds as many as 19 people (15.0%), and diarrhea as many as 12 people (9.4%). Several mechanisms can cause shortness of breath in COVID-19 patients, namely inflammation in the alveoli and lung tissue, thrombosis, micro clots, and neuroinvasion (Hentsch *et al.*, 2021). Fever occurs due to infection by a virus. When the virus infects the body, there will be tissue injury, so the body's defence system will respond in the form of fever by inducing the release of IL-1, Tumor necrosis factor (TNF), interferon- and IL-5), which will increase the set point in the hypothalamus, this causes an increase in body temperature (Walter *et al.*, 2016).

The mechanism of nausea/vomiting and diarrhea in COVID-19 occurs because the SARS-CoV virus uses angiotensin-converting enzyme 2 (ACE2) and serine protease TMPRSS2 (Transmembrane Protease Serine 2) for priming protein S. ACE2 and TMPRSS2 are not only expressed in the lungs but also the epithelium of the small intestine causing diarrhea (Megyeri *et al.*, 2021). Diarrhea is a symptom that often appears in patients infected with SARS-CoV-2, so this is a suspicion of the possibility of transmission through feces, thus the need for rapid and effective screening and diagnostic algorithms modification.

Based on **Table 2**, the type of patient care received more treatment in the isolation room compared to the ICU room (95.3%) and the type of ICU care (4.7%). ICU is an intensive care unit that treats patients

intensively. COVID-19 patients admitted to the ICU are in critical condition This study found that only a few COVID-19 patients were critically ill, with an average oxygen saturation value of >95. Hospital isolation rooms are used for patients who experience severe symptoms but do not require intensive care (Khaerunnisa *et al.*, 2022). The results showed that most of the patients were COVID-19 patients with severe symptoms but did not require intensive care. The length of patient care is generally 7-14 days for as many as 92 people (72.4%). Length of hospitalization is influenced by symptoms of fever that appear and abnormal CT scan values (Wu S *et al.*, 2020) (Baihaqi & Rumaropen, 2022). Treatment is generally 7-14 days (Widjaja *et al.*, 2021), and the recovery rate of patients is higher than those who die (Maharianingsih *et al.*, 2022). The average time for COVID-19 patients to recover is 11 days, but most COVID-19 patients recover between 7-14 days (Dessie *et al.*, 2022). The recovery time of COVID-19 patients is strongly influenced by age, and the elderly generally take longer to recover.

The management of the COVID-19 infectious disease is targeted at the symptomatic symptoms felt by the patient. Antibiotics do not directly act on SARS-CoV-2. Antibiotics are used in COVID-19 patients, but viral respiratory infections often cause bacterial pneumonia (Reardon, 2020). Based on **Table 2**, the most frequently used antibiotic was azithromycin (26.0%). Azithromycin is a macrolide antibiotic used for bacteria in the respiratory tract (Vitiello & Ferrara, 2022)

The results showed that the most commonly used antivirus was remdesivir (62.2%) **(Table 2).** Remdesivir is a nucleoside analog that inhibits RNA-dependent RNA polymerase (RdRp) from coronaviruses, including SARS-CoV-2 (Kokic *et al.*, 2021). What is inhibited is the viral RNA replication process. Remdesivir was confirmed as a non-obligate RdRp chain terminator of SARS-CoV-2.

Vitamin C in COVID-19 patients is an immunomodulator that can improve immune function and reduce inflammation and oxidative stress (Suryati & Juliadi, 2021). Vitamin C was more often used in COVID-19 patients because a crucial antioxidant component used for critical care; oral and intravenous Vitamin C can reduce the increase in complications, reduce the severity and improve symptoms of COVID-19 patients (Maharianingsih *et al.*, 2022). Methylprednisolone has the most widely used class of corticosteroid drugs (73.2%). The use of methylprednisolone in COVID-19 patients functions as an anti-inflammatory (Xu *et al.*, 2020). The most widely used mucolytic drug group is acetylcysteine (85.0%). Symptoms that appear in COVID-19 patients are very diverse; some are asymptomatic (mild symptoms), but there are also severe symptoms marked by immunological complications such as macrophage activation syndrome, which causes cytokine storm syndrome and acute respiratory distress syndrome. Immunosuppression that results in cytokine storm syndrome, anti-viral treatment alone is not enough

but needs to be combined with appropriate anti-inflammatory treatment to reduce morbidity and mortality due to COVID-19 infection (Datta & Bhattacharjee, 2020).

Based on **Table 2**, the most widely used mucolytic drug group was acetylcysteine (85.0%). Acetylcysteine is an antioxidant and glutathione inducer indicated for mucolytic therapy (Slattery *et al.*, 2014). Acetylcysteine as a mucolytic drug, is most often given to COVID-19 patients because the drug is used to thin phlegm (Maharianingsih *et al.*, 2022)

Novorapid contains insulin aspart, rapidly lowering the patient's blood sugar; insulin aspart regulates glucose metabolism, thereby increasing peripheral glucose uptake, especially in skeletal muscle and fat (Evans *et al.*, 2019).

Based on **Table 3**, the first patient showed an average PCR of 25,525. PCR examination detects Coronavirus RNA. The mean value, less than the reference value, described a very high amount of viral RNA in the patient. After receiving COVID-19 therapy, the average value was 39,096, with the highest CT value > 40 with the number of recovered patients (88.2%) increasing the PCR value as a parameter for the reduced amount of viral RNA detected. The statistical test results showed a p-value of 0.000 (<0.05), meaning there was a significant difference between the amount of COVID-19 virus RNA before and after treatment. These results described that antiviral therapy as a treatment for COVID-19 effectively reduces the number of COVID-19 viruses that infect the body. Statistical tests show a significant difference between GDS before COVID-19 therapy and after COVID-19 therapy (p-value <0.05). GDS is a blood sugar measurement parameter as an objective sign of diabetes. The statistical test results showed that the average GDS of patients before treatment was 225.47 mg/dL, exceeding the standard threshold. However, after treatment, the patient's mean GDS value of 186.3mg/dL was within the standard threshold. COVID-19 infection can increase high blood sugar levels (Chen *et al.*, 2020); this is because the SARS-CoV virus damages the endocrine part of the pancreas so that the patient's insulin amount decreases which causes the patient's blood sugar to increase. At the same time, HbA1C is a laboratory parameter that measures the amount of hemoglobin bound to blood sugar during the last three months (Owora, 2018). HbA1C is used to measure the success of diabetes therapy (Bozkaya *et al.*, 2019)). In patients with COVID-19 infection, hypercoagulability occurs due to activation of the coagulation cascade through the expression of tissue factors and cessation of fibrinolysis, so it is necessary to examine D-dimer. This protein helps the clotting process or blood clotting (Kichloo *et al.*, 2020). This study showed a significant difference in the value of D-dimer before and after COVID-19 treatment ($p < 0.005$), which indicated that treatment therapy for COVID-19 patients in the hospital effectively reduced hypercoagulation caused by COVID-19. The kidney organ has an angiotensinogen II receptor which can be a target for SARS-CoV-2, which causes the entry of COVID-19, so kidney

function tests are carried out, namely creatinine (Xia *et al.,* 2021). The results of this study showed that there was no significant difference in creatinine values before and after COVID-19 treatment. This means that the treatment received by COVID-19 patients does not affect creatinine. In addition, oxygen saturation checks are also carried out because COVID-19 patients have lung infections, so the cross-sectional area of the oxygen exchange in the lungs results in a decrease in oxygen saturation in the blood (Shenoy *et al.,* 2020). The results of this study described that generally, patients do not experience shortness of breath which is characterized by oxygen saturation in the normal range, which is 95-100. Although the average oxygen saturation of patients after treatment was 96.19, some patients had low oxygen saturation when they first received treatment, namely: 84, and after treatment decreased to 71, this saturation value occurred in patients who failed to receive treatment therapy (die).

CONCLUSION

The results of laboratory tests in this study showed that COVID-19 treatment therapy in patients with comorbid diabetes was effective in reducing the amount of virus in the blood ($p< 0.001$), reducing gds values ($p< 0.001$), Hba1c ($p< 0.05$) and lowering D-Dimer values. ($p<0.005$). However, it did not affect creatinine values ($p>0.452$) and oxygen saturation ($p>0.05$).

CONFLICT OF INTEREST

All authors declare no conflict of interest.

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