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Clinical presentation and outcome of COVID-19 infection in Type 2 Diabetes Mellitus: a preliminary data from a tertiary hospital in Jakarta during the early days of the pandemic



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ABSTRACT

Introduction: This study aimed to review the clinical characteristics and outcomes of COVID-19 patients presented with in-hospital hyperglycemia or pre-existing type 2 diabetes (T2DM).

Methods: This is a retrospective study conducted in Fatmawati General Hospital, Indonesia, from March 18th-Apr 30th, 2020. We reviewed medical records of 27 COVID-19 patients presented with either in-hospital hyperglycemia (11, 12.2%) or pre-existing T2DM (16, 17.8%) from a total of 90 confirmed COVID-19 cases admitted in our hospital.

Results: Critical conditions occurred in 50% of T2DM and 54.55% of the in-hospital hyperglycemia group. Mortality was documented in 68.75% of T2DM and 81.82% of in-hospital hyperglycemia group. Hypoglycemia, diabetic ketoacidosis, lactic acidosis and ketosis

were found in 12.5%, 25%, 18.75%, and 25% of individuals with T2DM, respectively, resulting in a high mortality rate. Meanwhile, diabetes-related complications were rare among the in-hospital hyperglycemia group. However, respiratory failure (45.45% vs. 6.25%) and septic shock (27.27% vs. 6.25%) were more frequent than in the T2DM group.

Conclusion: In this preliminary study, a high mortality rate was documented among COVID-19 patients with preexisting T2DM and in-hospital hyperglycemia. In T2DM subjects, diabetes related-complications contributed to a higher mortality rate, while in-hospital hyperglycemia group, respiratory failure and septic shock were more frequent.

Keywords: COVID-19, diabetes, hyperglycemia, outcome, Indonesia

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INTRODUCTION

The global pandemic of Coronavirus disease 2019 (COVID-19) caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS CoV-2) may result in severe clinical conditions that are potentially lethal.¹⁻³ As of June 3rd, 2020, more than 6.2 million cases of COVID-19 and about 380.000 deaths were reported worldwide.⁴ One of the risk factors of mortality is pre-existing diabetes condition.⁵⁻⁷ In an initial report from Wuhan, China, diabetes is present in 9.8% of COVID-19 cases.⁸ Indonesia had around 10.7 million diabetes population, but no report available regarding how COVID-19 affected Type 2 Diabetes Mellitus (T2DM) population.⁹ In this study, we reported clinical characteristics, treatments and outcomes of COVID-19 patients presented with hospital hyperglycemia or pre-existing type 2 diabetes (T2DM) in our hospital.

METHODS

This is a retrospective study conducted in Fatmawati General Hospital, Jakarta, Indonesia. Subjects were recruited from March 15th to April 30th. All subjects were retrospectively followed until the final follow-up on May 12th, 2020. Our hospital is a tertiary hospital appointed by the government as a referral hospital for COVID-19 cases. We reviewed medical records of all confirmed COVID-19 cases with pre-existing T2DM or had manifested in-hospital hyperglycemia. A confirmed COVID-19 case was defined as a patient with positive results of real-time reverse-transcriptase-polymerase-chain reaction (RT-PCR) assay of nasal/oral-pharyngeal swab specimen. Pre-existing T2DM was defined as subjects previously diagnosed with T2DM by a physician or on anti-diabetic medications upon admission. In-hospital hyperglycemia was defined as subjects had random blood glucose levels above

140 g/dL during hospitalization.¹⁰ Pregnant women with gestational diabetes were excluded from this study.

We reviewed all clinical symptoms, signs, and laboratory findings of patients based on the patient's medical chart. Gastrointestinal problems were defined as patients presented with nausea or vomiting, or diarrhea upon admission. Laboratory assessment consisted of complete blood count, glucose profile, and electrolytes obtained at the time of admission. Meanwhile, data on blood gas analysis, random blood glucose, c-reactive protein, procalcitonin, lactate, creatinine, urea, creatinine kinase, uric acid, ferritin, aspartate transaminase, alanine aminotransferase, bilirubin, and d-dimers were taken from the result during admission. All other necessary laboratory assessments were performed as clinically indicated. The abnormality of the radiologic assessment was determined based on the description of the patient's medical chart. Respiratory failure was determined based on arterial blood gases results, in which PaO₂ level less than 60 mmHg. Acute Kidney Injury was diagnosed according to the Kidney Disease Improving Global Outcomes (KDIGO) definition.¹¹ Shock was defined according to the 2016 third International Consensus Definition for Sepsis and Septic Shock.¹² Diabetes Ketoacidosis criterion was adapted from

Kitabchi et al.¹³ Lactic acidosis was defined as a record of plasma lactate concentration of >5 mmol/L. Hypoglycemia was defined according to American Diabetes Association (ADA) criteria.¹⁴ Ketosis was defined as a record positive on blood beta-hydroxybutyrate analysis. Critical conditions are defined as patients present with respiratory failure, septic shock or admitted to the intensive care unit.

Continuous variables were expressed as mean with standard deviation (SD) or median with interquartile range (IQR). Categorical variables were expressed as frequency (percent) and counts. No imputation was made for missing data. All data were analyzed using STATA 15.0 version. The study has been approved by Fatmawati General Hospital ethics committee No. 12/KPP/VI/2020.

RESULTS

There are 90 confirmed COVID-19 cases admitted to our hospital during the study period, 11 (12.2%) cases presented with in-hospital hyperglycemia and 16 (17.8%) cases presented with T2DM. All cases' median age was 59.31 (9.19) years old, with males and females represented approximately equal (Table 1). Fever (74.07%), cough (51.85%) and dyspnea (92.59%) were among the most common

Table 1. clinical characteristics of the subjects according to disease severity and mortality

Characteristics	Total	Severity		Mortality	
		Non-critical	Critical	Survive	Death
Age (yr)– median (IQR)	59.31 (9.19)	60.33 (22.69)	59.27 (13.88)	66.03 (32.16)	59.21 (14.50)
< 60 yr – n (%)	14/27 (51.85)	6/13 (46.15)	8/14 (57.14)	2/7 (28.57)	12/20 (60)
≥ 60 yr – n (%)	13/27 (48.15)	7/13 (53.85)	6/14 (42.86)	5/7 (71.43)	8/20 (40)
Sex – n (%)					
Female	12/27 (44.44)	7/13 (53.85)	5/14 (35.71)	3/7 (42.86)	9/20 (45)
Male	15/27 (55.56)	6/13 (46.15)	9/14 (64.29)	4/7 (57.14)	11/20 (55)
Fever on admission – n (%)	20/27 (74.07)	9/13 (69.23)	11/14 (78.57)	5/7 (71.43)	15/20 (75)
Fever on hospitalization – n (%)	15/27 (55.56)	5/13 (38.46)	10/14 (71.43)	3/7 (42.86)	12/20 (60)
Symptoms – n (%)					
Cough	14/27 (51.85)	7/13 (53.85)	7/14 (50)	3/7 (42.86)	11/20 (55)
Dyspnoea	25/27 (92.59)	12/13 (92.31)	13/14 (92.86)	6/7 (85.71)	19/20 (95)
Sore throat	3/27 (11.11)	1/13 (7.69)	2/14 (14.29)	0/7 (0)	3/20 (15)
Nasal congestion	2/27 (7.41)	1/13 (7.69)	1/14 (7.14)	1/7 (14.29)	1/20 (5)
Fatigue	5/27 (18.52)	3/13 (23.08)	2/14 (14.29)	2/7 (28.57)	3/20 (15)
GI problems	7/27 (25.93)	1/13 (7.69)	6/14 (42.86)	1/7 (14.29)	6/20 (30)
Comorbidity – n (%)	15/27 (55.56)	8/13 (61.54)	7/14 (50)	5/7 (71.43)	10/20 (50)
Hypertension	10/27 (37.04)	5/13 (38.46)	5/14 (35.71)	4/7 (57.14)	6/20 (30)
Coronary artery disease	7/27 (25.93)	4/13 (30.77)	3/14 (21.43)	2/7 (28.57)	5/20 (25)
Cerebrovascular disease	2/27 (7.41)	1/13 (7.69)	1/14 (7.14)	0/7 (0)	2/20 (10)
Chronic obstructive pulmonary disease	2/27 (7.41)	2/13 (15.38)	0/14 (0)	1/7 (14.29)	1/20 (5)
Chronic kidney disease	2/27 (7.41)	0/13 (0)	2/14 (14.29)	0/7 (0)	2/20 (10)

symptoms. Furthermore, gastrointestinal problems were found in more than a quarter of the cases. More than half of the cases had comorbidity (55.56%), with hypertension being the most common finding.

Normal chest imaging on X-ray was uncommon findings. Chest CT was not routinely performed (14.8%), in which ground-glass opacity was found in 75% of subjects. Among laboratory findings, more than half of all cases presented with normal leukocyte counts, most of them presented with Lymphopenia and had neutrophil to lymphocyte ratio (NLR) above than three. Compared to non-critical cases, subjects with critical conditions tend to have higher lactate (90% vs. 50%) and higher C-reactive protein (CRP) levels (83.33% vs. 18.18%) (Table 2).

According to our findings, antibiotics were administered intravenously to 88.89% of cases and all of the critical cases. Chloroquine was given to 74.07% of all cases, and death occurred in 65% of cases. Furthermore, none of the patients in whom chloroquine was withhold survived during hospitalization (n=7). We also noted that among patients treated with chloroquine, 15% of patients developed hypoglycemia. Meanwhile, no hypoglycemia episodes were found in those untreated. In all patients who got mechanical ventilation, continues renal replacement therapy, hemodialysis, and transferred to the intensive care unit reached a 100% mortality rate (Table 3).

In patients who had pre-existing T2DM, non-critical condition and mortality tend to be lower in patients who already got insulin during admission (non-critical condition 50% vs. 66.67%; mortality 40% vs. 60%) (Table 4). Complications related to diabetes occurred in 12.5%-25% of all cases. Thus, patients who developed diabetes-related complications had high mortality (hypoglycemia 50%; diabetic ketoacidosis 100%; lactic acidosis 100%; ketosis 75%). During hospitalization (180 mg/dL), optimal blood glucose level was only found in 7.14% of cases. When we put a lower cut-off on blood glucose level during hospitalization (140 mg/dL), there were no differences in the patient's outcome. High blood glucose level during hospitalization (above 180 mg/dL) was found in 100% of non-survive cases.

Moreover, in patients who presented with in-hospital hyperglycemia, diabetes-related complications were rare (0-9.0%) (Table 5). However, compared to pre-existing T2DM, a complication related to COVID-19, including respiratory failure, septic shock, and AKI, tend to be higher (respiratory failure 45.45% vs. 6.25%; septic shock 27.27% vs. 6.25%; acute kidney injury 9.09% vs. 25.0%). During hospitalization, blood

glucose level below 180 mg/dL was found in 57.14% cases and 33.33% of non-survive cases. When we put a lower cut-off on blood glucose level during hospitalization (140 mg/dL), the mortality ratio was dropped to half (16.67%).

DISCUSSION

In this study, we report the clinical characteristics and the outcome of our first 27 COVID-19 patients presented with diabetes or in-hospital hyperglycemia. To our knowledge, this is the first study to analyze the clinical characteristic and the outcome of COVID-19 cases with pre-existing T2DM or hospital hyperglycemia in Indonesia. Among patients with pre-existing T2DM, the critical conditions developed in 50% of cases, and the mortality rate was 68.75%. Moreover, patients presented with in-hospital hyperglycemia, critical conditions developed in 54.55%, and the mortality rate was 81.82%. A previous study with a larger sample size in Wuhan, China, fatal cases of COVID-19 with pre-existing T2DM occurred in 20.3% of cases.⁸ In a meta-analysis from Chinese, including 1527 patients, 9.7% of all COVID-19 cases had diabetes, and it increased the risk of developing severe disease or requiring ICU by two-fold.⁶ Data from the United States, including 184 patients with diabetes and/or uncontrolled hyperglycemia, the mortality rate of COVID-19 was 14.8% (pre-existing diabetes) and 41.7% (uncontrolled hyperglycemia).⁷

The most common symptoms in our study were dyspnea, fever and cough. These findings support prior reports describing symptoms of COVID-19 in individuals with diabetes.^{8,15} In our study, the majority of cases presented with dyspnea. This finding might be related to the criteria for hospitalization developed in Indonesia, in which only severe cases were treated in the referral hospitals. Our study also found that GI symptoms were common findings (26%). About half of critical cases and one-third of non-survive cases in this study developed GI symptoms. Compared to the general population, the proportion of GI problems in this study was relatively high. In a recent meta-analysis including 6686 patients with COVID-19, the pooled prevalence of digestive symptoms was 15%, including nausea or vomiting, diarrhea, and anorexia.¹⁶ The study also revealed that those with digestive involvement tend to progress to severe or critical disease and a poor outcome.¹⁶

The most common comorbidity found in this study was hypertension. According to a study conducted in China, hypertension was the most prevalent comorbidity in the general population. It was also a significant risk factor of reaching

Table 2. Laboratory and radiographic findings

Characteristics	Total	Severity		Mortality	
		Non-critical	Critical	Survive	Death
Chest x-ray – n (%)					
Normal	1/26 (3.85)	0/12 (0)	1/14 (7.14)	0/7 (0)	1/19 (5.26)
Unilateral infiltrate	4/26 (15.38)	1/12 (8.33)	3/14 (21.43)	0/7 (0)	4/19 (21.05)
Bilateral infiltrate	21/26 (80.77)	11/12 (91.67)	10/14 (71.43)	7/7 (100)	14/19 (73.68)
Chest CT – n (%)					
Ground glass appearance	3/4 (75)	0/0 (0)	3/4 (75)	0/7 (0)	3/4 (75)
Laboratory findings – n (%)					
PO2 <60%	6/27 (22.22)	0/0 (0)	6/14 (42.86)	0/0 (0)	6/20 (30)
White cell count					
< 4.000 /mm ³	3/27 (11.11)	2/13 (15.38)	1/14 (7.14)	2/7 (28.57)	1/20 (5)
4.000-10.000/mm ³	16/27 (59.26)	8/13 (61.54)	8/14 (57.14)	4/7 (57.14)	12/20 (60)
> 10.000/ mm ³	8/27 (29.63)	3/13 (23.08)	5/14 (35.71)	1/7 (14.29)	7/20 (35)
Lymphopenia	22/26 (84.62)	9/12 (75)	13/14 (92.86)	5/7 (71.43)	17/19 (89.47)
Neutrophil lymphocyte ratio > 3	23/26 (88.46)	10/12 (83.33)	13/14 (92.86)	5/7 (71.43)	18/19 (94.74)
Thrombocytopenia	6/27 (22.22)	4/13 (30.77)	2/14 (14.29)	2/7 (28.57)	4/20 (20)
Distribution of other findings					
C-reactive protein ≥ 10 mg/L	12/23 (52.17)	2/11 (18.18)	10/12 (83.33)	0/7 (0)	12/16 (75)
Procalcitonin > 0.5 ng/mL	10/19 (52.63)	0/7 (0)	10/12 (83.33)	0/6 (0)	10/19 (76.92)
Lactate dehydrogenase ≥ 2.5 U/L	13/18 (72.22)	4/8 (50)	9/10 (90)	3/6 (50)	10/12 (83.33)
AST > 68 U/L	8/27 (29.63)	2/13 (15.38)	6/14 (42.86)	2/7 (28.57)	6/20 (30)
ALT > 80 U/L	4/27 (14.81)	2/13 (15.38)	2/14 (14.29)	2/7 (28.57)	2/20 (10)
Creatinine > 1.33 mmol/dL	5/27 (18.52)	1/13 (7.69)	4/14 (28.57)	1/7 (14.29)	4/20 (20)
d-Dimer > 500 mg/dL	17/17 (100)	8/8 (100)	9/9 (100)	7/7 (100)	10/10 (100)
Minerals – median (IQR)					
Sodium (n=27)	131 (11)	131 (9)	131.5 (11)	133 (11)	131 (10.5)
Potassium (n=27)	3.36 (0.88)	3.63 (0.94)	3.2 (0.7)	3.39 (0.7)	3.34 (1.31)
Chloride (n=27)	100 (5)	100 (3)	99 (5)	100 (6)	99.5 (5)

Table 3. COVID-19 Treatment

Characteristics – n (%)	Total	Severity		Mortality	
		Non-critical	Critical	Survive	Death
Antibiotics					
Oral	14/27 (51.85)	8/13 (61.54)	6/14 (42.86)	4/7 (57.14)	10/20 (50)
Intravenous	24/27 (88.89)	10/13 (76.92)	14/14 (100)	6/7 (85.71)	18/20 (90)
Antivirus					
Oral	20/27 (74.07)	10/13 (76.92)	10/14 (71.43)	7/7 (100)	13/20 (65)
Intravenous	2/27 (7.41)	0/13 (0)	2/14 (14.29)	0/7 (0)	2/20 (15.38)
Antifungal	8/27 (29.63)	0/13 (0)	8/14 (57.14)	0/7 (0)	8/20 (40)
Systemic glucocorticoid	8/27 (29.63)	1/13 (7.69)	7/14 (50)	1/7 (14.29)	7/20 (35)
Chloroquine	20/27 (74.07)	10/13 (76.92)	10/14 (71.43)	7/7 (100)	13/20 (65)
Mechanical ventilation	10/27 (37.04)	0/13 (0)	10/14 (71.43)	0/7 (0)	10/20 (50)
Use of continues renal-replacement therapy	3/27 (11.11)	0/13 (0)	3/14 (21.43)	0/7 (0)	3/20 (15)
Use of hemodialysis (new)	2/27 (7.41)	0/13 (0)	2/14 (14.29)	0/7 (0)	2/20 (10)
Admission to intensive care unit	10/27 (37.04)	0/13 (0)	10/14 (71.43)	0/7 (0)	10/20 (50)

Table 4. Diabetes profile in COVID-19 cases with pre-existing type-2 diabetes

Pre-existing diabetes – n (%)	Total N=16	Severity		Mortality	
		Non-critical n=8 (50)	Critical n=8 (50)	Survive n=5 (31.25)	Death n=11 (68.75)
Diabetes treatment on admission					
Insulin – n (%)	4/8 (50)	3/6 (50)	1/2 (50)	2/3 (66.67)	2/5 (40)
Oral anti diabetic – n (%)	5/8 (62.5)	4/6 (66.67)	1/2 (50)	2/3 (66.67)	3/5 (60)
Diabetes related complication					
Hypoglycemia – n (%)	2/16 (12.50)	1/8 (12.5)	1/8 (12.5)	1/5 (20)	1/11 (9.09)
Diabetic ketoacidosis – n (%)	4/16 (25.0)	0/8 (0)	4/8 (50)	0/5 (0)	4/11 (36.36)
Lactic acidosis – n (%)	3/16 (18.75)	0/8 (0)	3/8 (37.5)	0/5 (0)	3/11 (27.27)
Ketosis – n (%)	4/16 (25.0)	3/8 (37.5)	1/8 (12.5)	1/5 (0)	3/11 (27.27)
COVID-19 related complication					
Respiratory failure – n (%)	1/16 (6.25)	0/8 (0)	1/8 (12.5)	0/5 (0)	1/11 (9.09)
Septic shock – n (%)	1/16 (6.25)	0/8 (0)	1/8 (12.5)	0/5 (0)	1/11 (9.09)
Acute kidney injury – n (%)	4/16 (25.0)	1/8 (12.5)	3/8 (37.5)	1/5 (20)	3/11 (27.27)
Random blood glucose level (g/dL)					
On admission – median (IQR) (n=16)	237 (138)	214 (69)	253 (370.5)	219 (52)	243 (223)
During hospitalization – median (IQR) (n=14)	362.5 (171)	317.5 (112)	475.5 (216.5)	346.5 (187)	414.5 (257)
- < 180 g/dL – n (%)	1/14 (7.14)	1/6 (16.67)	0/8 (0)	1/4 (25)	0/10 (0)
- < 140 g/dL – n (%)	1/14 (7.14)	1/6 (16.67)	0/8 (0)	1/4 (25)	0/10 (0)
Fasting blood glucose level (g/dL) – median (IQR) (n=12)	257 (149)	199.5 (111)	299.5 (145)	199.5 (111)	299.5 (145)

Table 5. Diabetes profile in COVID-19 cases with hospital hyperglycemia

Hospital Hyperglycaemia – n (%)	Total N=11	Severity		Mortality	
		Non-critical n=5 (45.45)	Critical n=6 (54.55)	Survive n=2 (18.18)	Death n=9 (81.82)
Diabetes related complication					
Hypoglycemia – n (%)	1/11 (9.09)	1/5 (20.0)	0/6 (0)	0/2 (0)	1/9 (11.11)
Diabetic ketoacidosis – n (%)	0/11 (0)	0/5 (0)	0/6 (0)	0/2 (0)	0/9 (0)
Lactic acidosis – n (%)	1/11 (9.09)	0/5 (0)	1/6 (16.67)	0/2 (0)	1/9 (11.11)
Ketosis – n (%)	0/11 (0)	0/5 (0)	0/6 (0)	0/2 (0)	0/9 (0)
COVID-19 related complication					
Respiratory failure – n (%)	5/11 (45.45)	0/5 (0)	5/6 (83.33)	0/2 (0)	5/9 (55.56)
Septic shock – n (%)	3/11 (27.27)	0/5 (0)	3/6 (50)	0/2 (0)	3/9 (33.33)
Acute kidney injury – n (%)	1/11 (9.09)	1/5 (20)	0/6 (0)	0/2 (0)	1/9 (11.11)
Random blood glucose level (g/dL)					
On admission – median (IQR) (n=11)	158 (50)	144 (44)	168 (128)	188 (16)	144 (38)
During hospitalization – median (IQR) (n=7)	191 (132)	142 (74)	227.5 (130)	117 (0)	198.5 (107)
- < 180 g/dL – n (%)	4/7 (57.14)	2/3 (66.67)	1/4 (25)	1/1 (100)	2/6 (33.33)
- < 140 g/dL – n (%)	2/7 (28.57)	1/3 (33.33)	1/4 (25)	1/1 (100)	1/6 (16.67)
Fasting blood glucose level (g/dL) – median (IQR) (n=3)	156 (91)	141 (30)	217 (0)	156 (0)	171.5 (91)

composite end-point, including admission to intensive care unit, invasive ventilation, and death.¹⁷ Another study reported a similar finding, hypertension was one of the risk factors for developing severe cases in COVID-19 patients.¹⁸ However, our study showed inconsistent results, in which 50% and 60% of hypertensive patients developed critical conditions and death. Meanwhile, 52.94% and 82.35% of normotensive patients also developed critical cases and death. This may partly be due to the COVID-19 patients referred to our center, a tertiary referral hospital, were more likely

in severe conditions. Also, the difference between the study population and small sample size might explain these results, hence further study is needed.

Although Chest CT was more sensitive than a chest x-ray,¹⁹ it was not routinely performed in this study. The predominant pattern of abnormality observed in chest X-ray was bilateral involvement or bilateral lesion. This finding supports other previous studies.^{8,20,21} Among laboratory findings, most of all cases presented with Lymphopenia, elevated NLR, and elevated level of CRP. The prevalence was even higher in severe cases. We also noted that 22% of all

cases in our study developed hypoxemic respiratory failure, 37% of all cases were admitted to ICU, and all of them were not survive. In the general population, acute respiratory distress syndrome developed in COVID-19 patients were likely to be admitted to the ICU and might succumb to the disease. The risk factor of mortality in this population was elderly and those with comorbidities, including diabetes.²² Immune response impairment and chronic inflammation were the basis of increased coronavirus severity in the T2DM population and associated with a higher propensity to SARS CoV-2 infection.^{23,24} Hyperglycemia alters innate immunity, induce endothelial dysfunction also promotes pro-coagulant state.²⁴

Our study showed better outcomes in patients treated with chloroquine compared to those untreated. The effect of chloroquine against SARS Co-V-2 infection by inhibiting the in vitro replication of several coronaviruses is still debatable regarding its side effect.²⁵ However, a preliminary report from Chinese authorities suggesting a more rapid declined in fever, improvement of lung CT, and a shorter time of recovery in chloroquine treated group and suggested chloroquine inclusion in COVID-19 treatment guidelines.²⁶ On the other hand, hypoglycemia episode was found in 15% of patients treated with chloroquine and none in those untreated. We noted that the mortality of hypoglycemia in this study reached 67%. Even though the chloroquine hypoglycemic effect's underlying mechanism remains unclear, it has been postulated that chloroquine improved pancreatic beta-cell function.²³ Caution should be taken when the drug is administered to the T2DM population, and a dose adjustment of oral anti-diabetic drugs and insulin might be necessary to prevent the hypoglycemic event.²³

Our study showed that acute complications of diabetes were commonly observed in the T2DM group compared to the in-hospital hyperglycemia group. The presence of any acute complication was associated with a high mortality rate. In a study involving 658 hospitalized COVID-19 patients, ketosis occurred in 6.58% of all groups, and in 35.7% T2DM group, it was also related to increased hospital stay and mortality.²⁷ It was suggested that COVID-19 accelerate the fat breakdown and induce ketosis with further development of ketoacidosis.²⁷ Moreover, we found that COVID-19 related complications, including respiratory failure, septic shock, and also acute kidney injury incidence were found higher in the hyperglycemic group compared to the T2DM group.

Evidence shows that hyperglycemia increased mortality risk in COVID-19 patients, including

those without previous T2DM diagnosis. In this study, optimal blood glucose control was achieved in only 7.41% of all T2DM patients. The reason behind this finding was high levels of stress, inflammation, lack of adequate protocol for glucose management and change in diet in COVID-19 patients.²⁸ Special attention was also needed for patients who were given corticosteroids as a management plan, as it can cause corticosteroid-induced-hyperglycemia.

We found that poor blood glucose control was found in 100% of death cases in the pre-existed T2DM group and 66.667% hyperglycemic group. A recent study showed that hyperglycemia increased the cytokine release and favored nonenzymatic glycosylation of the ACE2 receptors.²⁹ It is also suggested that hyperglycemia is a very bad prognostic factor for COVID-19, thus it needs an early blood glucose normalization.³⁰ In a study conducted in China, including 952 COVID-19 patients with pre-existing T2DM, well-controlled blood glucose is correlated with reduced risk of adverse outcomes and all-cause mortality in COVID-19 and pre-existing T2DM. Glucose control is essential in controlling COVID-19 infection and its complications.

We also found that a lower blood glucose target (140 mg/dL) during hospitalization might give benefit in the hyperglycemic group. Formerly, a glucose target of 140-180 mg/dL is reasonable in most critically ill patients. An attempt to maintain tight blood glucose control (80-100 mg/dL) may harm the patient by causing hypoglycemia and increasing the mortality rate.²⁸ However, hypoglycemia incidence was rare in hyperglycemic groups. Our current findings prompt further investigations considering the accumulating evidence regarding this new emerging disease, notably with improved study methods and larger sample size.

CONCLUSION

In conclusion, COVID-19 cases presented with T2DM or hospital hyperglycemia in Indonesia had poor outcomes and high mortality rates. Optimal blood glucose control is challenging yet important in reducing adverse outcomes and mortality.

AUTHOR CONTRIBUTION

All authors contribute equally in this study.

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CONFLICT OF INTEREST

The authors declare no conflict of interest

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