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Coronavirus disease 2019 (COVID-19): A case report in a patient with diabetic ketoacidosis and hypertension



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ABSTRACT

Background: Until May 2020, Indonesia is still on COVID-19 emergency status. South Jakarta is part of the Special Capital Region of Jakarta that has applied large-scale social restrictions. The Indonesian government has extended Jakarta's large-scale social restrictions to Friday, May 22nd, 2020 to curb the spread of the corona-virus that causes COVID-19.

Case report: Patients with diabetic ketoacidosis and hypertension were infected with SARS-CoV-2. He had traveled from Saudi Arabia a week before and already has a fever. Arriving in Indonesia, the patient showed symptoms of worsening disease, experienced coughing, shortness of breath, and sore throat. The patient does not inject insulin due to loss of appetite. On March 30th, 2020, a laboratory examination showed high blood sugar levels (369 mg/dL) followed by positive ketones bodies. On April 2nd, 2020, the patient was designated as a confirmed case of COVID-19 after a

positive polymerase chain reaction test. The rapid diagnostic test also showed a positive IgM. Management of patient includes giving O₂ through the non-rebreathing oxygen mask, infusion of sodium chloride, 20 IU Apidra[®], 12 IU Lantus[®] injection, Oseltamivir orally, Levofloxacin, Paracetamol, Vitamin C, Candesartan, Concor. This therapy was continued until April 5th, 2020. On April 5th, the patient complained about a cold sensation all over his body. The patient died on the afternoon of April 6th, 2020 (8 days of hospitalization) due to sudden cardiac arrest and acute respiratory distress syndrome. Cardiopulmonary resuscitation was done with standardized protocol with no avail.

Conclusion: Diabetic ketoacidosis and hypertension worsen the condition of COVID-19 patients. There are many unknown disease progression outcomes in these patients.

Keywords: COVID-19, SARS-CoV-2, diabetes mellitus, hypertension

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INTRODUCTION

Several journals wrote an editorial about Coronavirus Disease 2019 (COVID-19).^{1,2} On February 11th 2020, the World Health Organization (WHO) announced that COVID-19 is caused by Novel Coronavirus (2019-nCoV). The International Committee on Taxonomy of Viruses has renamed the previously provisionally named 2019-nCoV as Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2).³

Like other countries in the world, Indonesia is one of the countries that is still experiencing the COVID-19 outbreak. Until now, Indonesia is still in a COVID-19 pandemic emergency. It was further stated that COVID-19 disaster emergency status in Indonesia-determined by the *Badan Nasional Penanggulangan Bencana* (BNPB) would end on May 29th, 2020.⁴ Data on May 28th, 2020, the Government of Indonesia through the "Satuan Tugas Percepatan Penanganan COVID-19" recorded population of Indonesians tested positive for COVID-19 reached 23.851, with 6.057 patients have recovered, and 1.473 died.⁵

Patients referred to special hospitals that handle COVID-19 have a variety of background diseases that accompany them, including patients with diabetes mellitus (DM). It has stated that hyperglycemia worsens the prognosis and increases the risk of death in diabetics, as well as in COVID-19 patients. Also, it appears that hyperglycemia status is associated with poor outcomes in COVID-19 patients on hospital admission.⁶⁻⁸ The increased mortality in COVID-19 patients is due to coagulation changes induced by hyperglycemia. Apart from hyperglycemia, the worsening of endothelial function and overproduction of cytokines also cause coagulation changes. It was demonstrated that COVID 19 patients associated with severe pneumonia disease and septic shock with characteristic strong increases in plasma IL-6 and D-dimer levels. Thus, elevated blood glucose could worsen the prognosis of Covid-19 patients. Therefore, pasien covid-19 who has complications with diabetes increases the risk of shock and multiple organ failure and thus requires ICU care.⁸ Treatments for the rapid normalization of hyperglycemia can help improve the prognosis in

COVID-19 patients.^{2,8} This study reported a case of diabetic ketoacidosis and hypertension in patients infected with SARS-CoV-2.

CASE REPORT

The patient was a 51-years-old male who was referred to Pasar Minggu Regional General Hospital (RSUD Pasar Minggu), South Jakarta, Indonesia, on the afternoon, March 30th, 2020. He was initially treated at Medistra Hospital in Jakarta, Indonesia, with complaints that in the morning he had a fever, cough, and shortness of breath the day before being admitted to the hospital. The patient previously had a history of type 2 diabetes mellitus (T2DM), while hypertension was refused, and there was no record of heart disease. Before being admitted to the hospital, this patient regularly went to the hospital for check-ups, including control of blood sugar and blood pressure. He had traveled from Saudi Arabia a week before, already having a fever. Arriving in Indonesia, the patient showed symptoms of worsening disease, experienced coughing, shortness of breath, and sore throat. The patient didn't take any insulin injections due to the loss of appetite. During the hospital admission in Pasar Minggu Regional General Hospital (RSUD Pasar Minggu), South Jakarta, Indonesia, general condition was well with the Glasgow Coma Scale (GCS) of 15, with a slight increase in vital signs; recorded blood pressure was 140/80 mmHg, heart rate (HR) 80 beats per minute (bpm), temperature 38.1°C, respiratory rate (RR) 24 times per minute, O₂ saturation (SpO₂) 90% to 95% using the non-rebreather mask (NRM) 10 liters per minute (lpm). On physical examination, hyperemic pharynx, vesicular pulmonary auscultation in both lung fields were found, and the heart sounds were within normal limit. On March 30th, 2020, a laboratory examination was carried out, which

showed that the blood sugar level of 369 mg/dL and positive ketones bodies.

On April 2nd, 2020, the patient was designated as a confirmed case of COVID-19 after a positive polymerase chain reaction (PCR) test. In addition, the results of the rapid diagnostic test (RDT) showed positive Ig M. Management of patient includes giving O₂ 8 lpm through NRM, infusion of sodium chloride (Na Cl) 0.9% 500 cc in amount of 28 drops per minute, subcutan injection of 20 IU Apidra®, 12 IU subcutan Lantus® injection each night, 2x75 mg Oseltamivir orally, 1x750 mg Levofloxacin orally, 3x1 gram Paracetamol injection, 2x400 mg vitamin C injection, 1x8 mg Candesartan, and 1x2.5 mg Concor. This therapy was continued until April 5, 2020. On April 5th, the patient complained about a cold sensation all over his body. On the following morning of April 6th 2020, GCS was 15, the pain score was 0, SpO₂ was 97%, eating and drinking being done via oral, spontaneous bowel, and bladder movements were also recorded. Treatment management at that time consisted of O₂ 8 lpm, infusion of sodium chloride (Na Cl) 0.9% 500 cc with 28 drops per minute, Oseltamivir, Levofloxacin, Paracetamol and vitamin C injection were given according instruction. Such treatment does not improve the patient's condition. The patient died in the afternoon of April 6th 2020, eight days after hospitalization. This patient had a sudden cardiac arrest and acute respiratory distress syndrome. Cardiopulmonary resuscitation was performed according to standard protocols but was unsuccessful.

Vital signs and examinations of COVID-19 patients with diabetic ketoacidosis and hypertension are presented in Table 1. Laboratory results of COVID-19 patients with diabetic ketoacidosis and hypertension are presented in Table 2, while random blood glucose monitoring of COVID-19

Table 1. Vital signs and examinations of COVID-19 patients with diabetic ketoacidosis and hypertension

Date of Hospitalization	March 2020				April 2020			
	30	31	1	2	3	4	5	6
Temperature (°C)	38.0	38.1	36.3	36.9	37.0	36.1	36.5	36.6
Blood Pressures								
- Systolic (mmHg)	110	140	140	140	140	150	120	100
- Diastolic (mmHg)	80	80	80	90	90	80	70	60
HR	90	80	86	100	82	90	110	92
RR	29	24	24	24	20	26	23	24
SpO ₂ (%)	90	94	95	95	97	95	95	97
PCR SARS-CoV-2				+				
RDT (Ig M)						+		

Abbreviations: °C=degrees Celsius, %=percent, mmHg=millimeters of mercury, HR=heart rate, RR= respiratory rate, SpO₂=oxygen saturation, PCR= Polymerase Chain Reaction, RDT=rapid diagnostic test, Ig M= Immunoglobulin M.

Table 2. Laboratory results of COVID-19 patients with diabetic ketoacidosis and hypertension

Variables	Days of measurement								Reference range
	March 2020			April 2020					
	30	31	1	2	3	4	5	6	
Hb (g/dL)	13		13.1			12.4			13.2-17.3
Ht (%)	47		40			39			40-52
Leukocyte (.10 ³ /μL)	9.8 H		13.1 H			9.4			3.8-10.6
Thrombocyte (.10 ³ / μL)	292		257			385			150-440
Erithrocyte (.10 ⁶ / μL)			4.59			4.26			4.40-5.90
RDW (%)			12.5			12.9			11.5-14.5
MCV (fL)			87			90			80-100
MCH (pg)			29			29			26-34
MCHC (g/dL)	33 L		33 L			32			34-36
Basophil (%)	0.0		0.0			0.0			0.0-1.0
Eosinophil (%L)	0 L		0 L			2.0			2.0-4.0
Band (%L)	79 L		2.0 L			3.0			3.0-5.0
Segmented (%)	17 H		91.0			75			50.0-70.0
Limphocyte (%L)	4.0 L		6.0 L			15			25.0-40.0
Monocyte (%L)	1.0		1.0			5			2.0-8.0
NLR	4.64		15.2			5.0			
ESR (mm/hour)	91			85	85	85		-	< 20
Keton bodies	+								negative
Total Bilirubin (mg/dL)	0.36							0.36	0.3-1.0
Direct Bilirubin (mg/dL)	0.14							0.14	0-0.3
Indirect Bilirubin (mg/dL)	0.22							0.22	0.3-1.9
AST (U/L)	40							40	< 50
ALT (U/L)	25							25	< 50
Ureum (mg/dL)	34					46		34	<48
Creatinine (mg/dL)	1.25					1.18		1.25	0.7-1.3
CRP (mg/dL)	212					82.3			< 5
Troponin T (ng/L)				35					<50
Blood gas analysis									
pH	7.22		7.34	7.4	7.41			7.4	7.37-7.45
pCO ₂ (mmHg)	22.7		41.8	40.9	41.5			33.7	33.0-44.0
pO ₂ (mmHg)	161.2		195.2	161.9	147.3			147	71.0-104.0
HCO ₃ (mmol/L)	9.3		23.0	28.4	26.5			21.2	22.0-29.0
SO ₂ (%)	99.1		99.6	99.2	99.3				94-100 %
BE (mmol/L)	-15.9		-2.1	4.6	2.2			-1	(-2) – (+3)
TCO ₂ (mmol/L)	10.0		25.1	29.7	27.7				23.0-27.0
t (°C)	39.5		39.5	38.2	40.1			38.6	36.5-37.5
Natrium (mmol/L)	139				146	146			135-145
Kalium (mmol/L)	4.5				5.10	5.10			3.5-5
Chlorida (mmol/L)	102				101	101			98-108

Abbreviations: Hb=hemoglobin, Ht=hematocrit, RDW= red cell distribution width, MCV=mean corpuscular volume, MCH=mean corpuscular hemoglobin, MCHC=mean corpuscular hemoglobin concentration, NLR=neutrophil (NEU)-to-lymphocyte (LYM) ratio, ESR=erythrocyte sedimentation rate, AST=aspartate aminotransferase RBS=random blood sugar, ALT= Alanine aminotransferase, CRP=C-reactive protein, pH=potential for hydrogen, pCO₂=partial pressure of carbon dioxide, pO₂= partial pressure of oxygen HCO₃=bicarbonate, SO₂=sulfur dioxide, BE= base excess, TCO₂=total carbon dioxide t=body temperature, °C=degrees Celsius, g/dL=grams per deciliter, %=percent, μL=microns per liter, fL=femtoliters, pg=picograms, %L=percent liter), mm/hour=millimeters per hour, mg/dL=milligrams per deciliter; mmHg= mm Hg=millimeters of mercury, mmol/L=milli mol per liter.

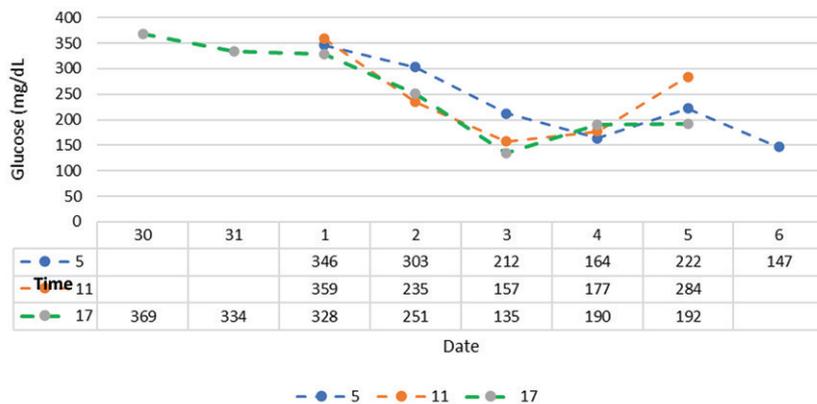


Figure 1. Random blood glucose monitoring of COVID-19 patients with diabetic ketoacidosis and hypertension.

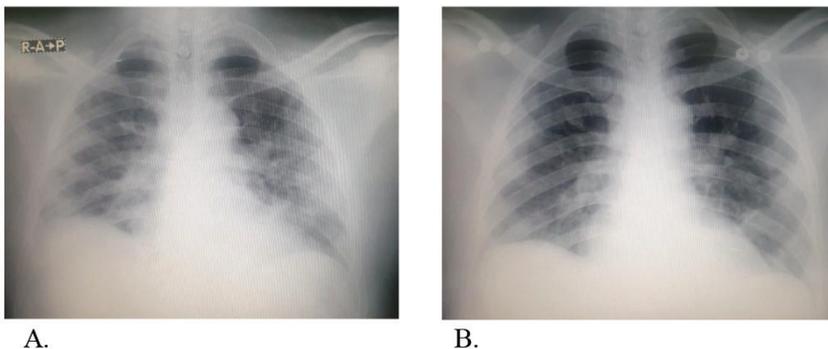


Figure 2. Chest radiographs of COVID-19 patients with diabetic ketoacidosis and hypertension. A. Chest radiographs of the patient obtained on April 31st 2020 at the hospital. The chest xray shows that the patient had pneumonia with infiltrates in right perihilar and left paracardial (bilateral infiltrates). B. Chest radiographs of the patient obtained on May 3rd 2020 at the hospital. The infiltrates in both lungs have improved markedly.

patients with diabetic ketoacidosis and hypertension are presented in [Figure 1](#). Chest radiographs of COVID-19 patients with diabetic ketoacidosis and hypertension are presented in [Figure 2](#).

DISCUSSION

COVID-19 patients are predominantly male and elderly. Complementary diseases in these patients include lung disease, arterial hypertension and DM.⁹ Additionally, 20,276 people with COVID-19 were recorded, 59.6% were male, and 19.3% were found to have DM. In more detail, it was also reported that COVID-19 patients experienced pneumonia, fever as the most common symptom followed by cough.¹⁰ The recent study reported that the mortality rate of COVID-19 patients increased from 2.3% to 15% due to complications of DM. In this regard, it has been reported that the mortality rate for COVID-19 patients with DM complications in China reaches

7.3%, which was significantly higher compared with patients without a comorbidity record.¹¹ Microbiological analysis is very important for the diagnosis of COVID-19 patients. Until now, polymerase chain reaction (PCR) is a tool used to detect nucleic acids in SARS-CoV-2 as the cause of COVID-19. SARS-CoV-2 nucleic acid detection can be done using a sputum sample, throat swab, and lower respiratory tract secretions.¹² Nasopharyngeal swab for this patient showed the presence of nucleic acid for SARS-CoV-2. Likewise, the results of the serological test showed the presence of Ig M for SARS-CoV-2. This result indicated an acute infection of SARS-CoV-2 that strongly correlates with the 13th day of the disease course since the first day of fever a week before the hospitalization.

Recent studies have reported that SARS-CoV-2 coinfection with diabetes can lead to stressful conditions resulting in increased secretion of glucocorticoids and catecholamines. This condition causes COVID-19 patients with diabetes complications to experience increased blood sugar levels.¹¹ Also, the human pancreas expressed angiotensin-converting enzyme 2 (ACE2); thus, the SARS-CoV-2 might enter and cause acute β -cell dysfunction. These conditions were leading to acute hyperglycemia and transient of T2DM. It has been reported that in the pancreas, binding of the SARS coronavirus to its receptors (ACE2) causes islet cell damage and reduces insulin release. It has been reported that >50% of the patients developed diabetes during hospitalization. A previous study showed that the pancreas of diabetic mice exhibited increased ACE2 activity. This fact indicates that COVID-19 patients with T2DM are very susceptible to coronavirus infection.¹³ There is another possibility that dipeptidyl peptidase 4 (DPP-4) plays a role in SARS-CoV-2 infection in people with diabetes.¹⁴ A previous study reported that a transgenic mouse model of type 2 diabetes showed the expression of DPP-4 receptors in pulmonary alveolar cells. Moreover it has been reported that transgenic diabetic mice with MERS-coronavirus infection have severe conditions. Besides that, also noted that DM is also correlated with weight loss and pneumonia.¹⁵

A previous studies have reported that optimal control of blood sugar levels during hospitalization reduces the risk of death in Covid-19 patients. It can be explained that COVID-19 patients who experience hyperglycemia cause changes in the coagulation system, immune system and cytokine regulation. On the other hand, Covid-19 patients are associated with pneumonia, which exhibits a number of abnormal coagulation parameters. The coagulation abnormalities that occur in COVID-19 patients have been associated with higher mortality

rates. Therefore, it is necessary to recommend the use of insulin infusion for COVID-19 patients, so that blood sugar levels in accordance with the desired target.⁸

The coagulation abnormalities in COVID-19 patients, it also has been reported that complications of diabetes also lead to the formation of ketone bodies in the blood. We know that the formation of ketone bodies occurs due to high blood acid levels as a result of complications of diabetes, so it is called diabetic ketoacidosis (DKA). This patient did not have insulin a week before hospital admission, with random blood glucose of 369 mg/dL, arterial pH 7.22, and positive ketones bodies when admitted into the hospital, confirming the diagnosis of DKA. DKA in this patient could be induced by insulin deficiency, history of not taking any insulin injection for one week, and SARS-CoV-2 infection. We suggest that SAR-CoV-2 infecting the patient in this case may have damaged the islets and caused acute insulin-dependent DM.¹² The patient's condition in this case was similar to the other cases where the COVID-19 patient showed the presence of DKA.¹⁶

Apart from experiencing T2DM, the patient, in this case, was noted to have a mean blood pressure of 140/90 mmHg. This fact is in accordance with the results of previous studies, which state that the COVID-19 patient experiences cardiovascular complications. It should be noted that the COVID-19 patient experienced a significant increase in troponin T levels.¹⁷

The COVID-19 patient, in this case, showed lymphocytopenia. This fact is in accordance with the results of previous studies, which state that COVID-19 patients usually show lymphocytopenia on hospital admission compared with thrombocytopenia and leukopenia.¹² Lymphocytopenia has occurred from the first day to 8th day of treatment, with neutrophil (NEU)-to-lymphocyte (LYM) ratio (NLR) 4.64, 15.2 and 5.0. Besides that, it has been reported that NLR was positively correlated with the risk of COVID-19. A previous studies showed that 46.1% of COVID-19 patients aged ≥ 49.5 years and NLR ≥ 3.3 exacerbated the disease.¹⁸ An NLR 4.64 when this patient was admitted has demonstrated the possibility of worsening within six days. Besides that, high CRP in these patients (212 mg/dL) also gives signs of severe inflammation. High CRP levels in this study, according to with statement that CRP levels were positively correlated with the severity of lung lesion and disease severity.¹⁹ High CRP level on the 1st day, in this case, reflected with chest radiograph result on April 31st, with marked bilateral infiltrates. The chest lesion was improved on the 5th day, which was

also correlated with lower CRP levels (82.3 mg/dL) on the next day.

The case-patient showed good vital signs for seven days of treatment, except for the heart rate between 100-110 bpm. Most of the blood glucose tests performed on this patient were done in the last days of hospitalization and showed a level of 147 mg/dL. Acidosis also improved on the last day of treatment in this patient, who was shown a change in blood pH from 7.2 to 7.4. The reality, patient has died on the 15th day of the disease's course or on the 8th day of hospitalization, due to sudden cardiac arrest. There were no signs of multiple organ failure in this patient. The case-patient also had normal kidney and liver function, creatinine 1.25 mg/dL, aspartate aminotransferase (AST) 40 U/L, and alanine aminotransferase (ALT) 25 U/L. We note the results of previous studies showing that there are several causes of death in DKA patients, including cerebral edema, and other rare causes such as hypokalemia, hypocalcemia, hypoglycemia, sepsis, and pulmonary edema. Besides, there were also reports of sudden cardiac arrest in COVID-19 patients.²⁰⁻²³ We are do not know whether this patient had an enlarged aorta during his hospitalization. There has been a case report that incidental finding of aortic enlargement should not be disregarded as it might contribute to pathological processes.²⁴ From this case, we need attention because COVID-19 can cause myocardial injury.^{17,20}

It should be noted that three patients of COVID-19 with DKA complications, one of whom died.¹⁵ In this case, it shows that the management has not given good results because the patient is suffering from DKA and hypertension. Therefore, there is a need for increased attention to COVID-19 patients with DKA and hypertension. That needs to be done to reduce the risk of death in COVID-19 patients who experience complications of DKA and hypertension.

CONCLUSION

DKA and hypertension worsen the condition of COVID-19 patients. There were many unknown disease progression outcomes in COVID-19 patients.

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CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

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AUTHORS CONTRIBUTIONS

Conceptualization: MLEP, RAD. Data acquisition: RAD, DUN, and TR. Data analysis or interpretation: all authors. Drafting of the manuscript: MLEP, RAD. Critical revision of the manuscript: RAD, and DUN. Approval of the final version of the manuscript: all authors.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

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