

## First onset of diabetic ketoacidosis in teenagers with COVID-19: a case report from a limited health care setting



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### ABSTRACT

**Background:** Diabetic ketoacidosis (DKA) has been well-known as the main complication that is a potentially fatal emergency in some teenagers with type 1 diabetes mellitus (DM). Although children with diabetes are not at high risk for severe COVID-19 infection, it can hypothetically lead to type 1 DM and severe DKA. The aim of this article is to briefly discuss a case of a teenager with DKA and COVID-19.

**Case:** A 13 years old girl came in with abdominal pain, nausea, vomiting and dyspnea. She was alert but weak. Her blood pressure was 100/70 mmHg with 120 pulses and 35 breaths per minute. Oxygen saturation was at 99%. History of previous illness was denied. She was treated using a dyspepsia algorithm while waiting for the laboratory result. Later on, the test showed conditions of hyperglycemia, severe acidosis, ketonuria and a positive rapid COVID-19 antibody test. Hence, a diagnosis of DKA with probable COVID-19 was made and PCR for confirmation of COVID-19 diagnosis was scheduled. Oxygen support, rehydration, and insulin therapy were also given with a precautionary condition of possible COVID-19. In minutes, she developed respiratory distress that led her to be intubated and put on a ventilator. Due to a lack of facilities, a referral to a higher-level hospital was needed. However, since the referral process for probable COVID-19 patients required a long preparation, the patient died during the process.

**Conclusion:** Besides early diagnosis and prompt treatment, a well-coordinated referral system is crucial in managing DKA patients with possible COVID-19.

**Keywords:** awareness, COVID-19, diabetic ketoacidosis, referral.

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### INTRODUCTION

Almost five to ten percent of diabetes mellitus (DM) cases are type 1 DM. The same type is also found in  $\geq 85\%$  of children and teenagers diagnosed with DM.<sup>1</sup> Although there is no accurate epidemiology data regarding the incidence and prevalence of the disease, an overall increasing trend has been observed.<sup>2</sup> There is also no specific data about type 1 DM in Indonesia due to nationally complex data collection. However, a significant rise of cases around sevenfold from 2000 to 2010 has been suspected.<sup>3</sup>

In December 2019, many cases of unknown pneumonia emerged in Wuhan, China, and not so long after that, it spread to the whole world.<sup>4</sup> In February 2020, World Health Organization (WHO) officially identified the disease as coronavirus disease 2019 (COVID-19).<sup>5</sup>

Based on various sources, COVID-19 cases have increased exponentially.<sup>6</sup> However, although cases were commonly found in adults, cases in children were also showing an increasing trend.<sup>7</sup> Based on the severity, children usually had milder symptoms.<sup>8</sup>

If associated with COVID-19, DM in adults is usually linked to poor outcomes, suggesting the same thing will happen in kids and teenagers with the same disease.<sup>9</sup> The phenomenon was not true as prior studies showed better results in children.<sup>10</sup> However, there is a new concern regarding new cases of DM caused by COVID-19 infection.<sup>9</sup> Many pediatric patients with the first onset of DM after being infected by COVID-19 had diabetic ketoacidosis (DKA).<sup>9</sup> Therefore, this case study aimed to briefly describe the correlation between the first onset of DKA in teenagers and COVID-19 based on available literature.

### CASE PRESENTATION

A young 13 years old six months teenage girl came to the emergency room with sudden abdominal pain. The pain was described as sharp stabbing, similar to heartburn radiating to the back for 3 hours. Other than that, she felt stuffed around the chest, which made her hard to breathe. Before coming to the hospital, she drank antacid, but the symptoms worsened. Moreover, she felt nauseous and vomited three times. The vomit was yellowish with remnants of food. Other symptoms like fever, cough, flu, weight loss, increased appetite, and frequency of urination were denied. No abnormalities were found in her defecation and urination pattern. According to her father, the symptoms arose after being mad because her sister didn't come home. There was no history of gastric disease, asthma, allergy, seizures, or

diabetes mellitus. Contact with a positive COVID-19 patient was also denied.

On arrival, the patient was conscious but weak. Her blood pressure was 100/70 mmHg with 120 pulses per minute. The respiratory rate was 35 times per minute, with oxygen saturation of 99% and body temperature of 36.4 C. No abnormalities were found in physical examinations except for tenderness around the epigastrium area on the abdomen. All four extremities were warm with a capillary refill time of fewer than 2 seconds. The doctor then suggested the patient be admitted and performed various laboratory tests such as hematology, random blood sugar, electrolytes, urinalysis, kidney function, and blood gas analysis.

While waiting for the lab results, the patient was treated using the dyspepsia algorithm with an injection of ranitidine 1 mg/kg and ondansetron 0,1 mg/kg per administration. Because the patient experienced dyspnea, a nasal cannula with 4 liters of oxygen per minute was given. After 1,5 hours, the abdominal pain and overall patient condition got better. However, an hour later, the patient suddenly experienced a loss of consciousness with a blood pressure of 70 per palpation. The pulse was weak, the respiratory rate increased to 40 times per minute with an oxygen saturation of 80%, and the extremities were cold. The doctor administered fluid loading with 500 ml of ringer lactate solution. Afterward, her blood pressure improved to 90/50 mmHg. Pulse was still weak but palpable at 112 times per minute. The respiratory rate was slightly improved to 31 times per minute. However, the saturation decreased significantly to 56%, and the extremities remained cold. The laboratory results were out when the patient's condition deteriorated and are shown in Table 1.

Based on physical and laboratory examinations, the patient was diagnosed with severe diabetic ketoacidosis with suspicion of cerebral edema and COVID-19. The patient's condition continued to deteriorate until intubation and ventilation were needed. Due to the lack of facilities in the hospital, the patient had to be referred. However, due to the positive rapid antibody test, the procedure had to be done meticulously, taking longer

**Table 1. Lab Examination.**

Examination	Results
<b>Hematology</b>	
Leukocytes	28.650/mm <sup>3</sup>
Neutrophils	78.8%
Lymphocytes	11.8%
Monocytes	9.0%
Eosinophils	0.2%
Basophils	0.2%
Hemoglobin	14.9 g/dL
Hematocrit	44.6%
Thrombocytes	458.000/mm <sup>3</sup>
<b>Random Blood Sugar</b>	782 mg/dL
<b>Electrolytes</b>	
Sodium	118.2 mg/dL
Potassium	6.43 mg/dL
Chloride	91.1 mg/dL
<b>Urinalysis</b>	
pH	6
Density	1250
Protein	+2
Erythrocyte	4-6
Leukocytes	6-8
Bacteria	-
Fungi	-
Nitrite	-
Ketone	+4
<b>Kidney Function</b>	
Urea	41 mg/dL
Creatinine	0.78 mg/dL
<b>Arterial Blood Gas (ABG)</b>	
pH	6.861
pCO <sub>2</sub>	16.9 mmHg
pO <sub>2</sub>	251 mmHg
BEEcf	<-39 mmol/L
HCO <sub>3</sub>	3.0 mmol/L
SaO <sub>2</sub>	99%
<b>COVID-19 Rapid Antibody Test</b>	Reactive

than usual. Unfortunately, before the referral process was successful, the patient deteriorated and passed away.

## DISCUSSION

Age, when the first onset of type 1 DM occurs, varies. However, data from multiple hospitals showed two incidence primes, between 5-6 and 11 years old.<sup>11</sup> In 2002-2003, the incidence of type 1 DM in America reached its peak among children aged 5 - 9 and 10 - 14 years old.<sup>12</sup> Furthermore, data from 2003-2009 in the age group of 10 - 14 showed more female children with type 1 DM (60%).<sup>3</sup> The rise in incidence during puberty might

be caused by insulin resistance due to increased growth and sexual hormones. These changes were suspected as the cause of DKA.<sup>13</sup> A study in Saudi Arabia revealed that 55.3% of DM type 1 patients experienced DKA when they were first diagnosed. This phenomenon was found more in women than men, with a ratio of 1.4:1.<sup>14</sup> Similarly, in the presented case, the patient in this study was a female with DKA on her first time being diagnosed with type 1 DM during puberty.

Most type 1 DM patients had a classic clinical course involving polydipsia, polyuria, polyphagia, and tremendous weight loss.<sup>11</sup> However, unspecific

symptoms were found in several cases, which made the diagnosis process tricky and confusing at times. For example, hyperventilation could be diagnosed as pneumonia or asthma. Abdominal pain was usually accused as the cause of acute abdomen and polyuria that was wrongly taken as a sign of urinary tract infection. Multiple vomit episodes usually lead to a diagnosis of gastroenteritis.<sup>15</sup> These unspecific symptoms potentially delayed the diagnosis of DKA.<sup>15</sup> Timespan from first symptoms to DKA varied among patients, between hours to months.<sup>16</sup> These delays might lead to some fatal casualties. Furthermore, the delay in women patients usually happened without any apparent reason.<sup>14</sup> In America, a study by Munoz et al. with 2526 patients found that 16% of patients diagnosed with DM type 1 before 18 had been misdiagnosed due to the high cases of infection happening during the period.<sup>17</sup> A similar result was achieved in Malaysia's cohort study by Mavinkurve et al. Among 119 respondents below 18 years old, 46 had been misdiagnosed during their first visit. Most of those children had respiratory (36.9%) and gastrointestinal diseases (34.8%).<sup>18</sup> Delay in diagnosis was proven correlated to DKA.<sup>17</sup> In this study case, the timespan between symptoms of DKA happened quickly in a matter of hours without any classic signs such as polydipsia, polyuria, polyphagia and rapid weight loss that led to DM. Symptoms on the gastrointestinal tract made the patient suspected to suffer from dyspepsia and be treated accordingly. The patient's condition deteriorated fast, only in a matter of hours after the patient was admitted to the ER.

Screening regarding COVID-19 infection was performed to determine which ward the patient would be admitted to. The chosen test was COVID-19 Rapid Antibody Test. The test came out positive in this patient, suggesting the patient had an antibody to COVID-19 and DKA happened alongside COVID-19.<sup>19</sup> Another case study explained COVID-19 pathophysiology and its correlation to DKA. As generally known, SARS-CoV2 bonded with angiotensin-converting enzyme 2 (ACE2) to enter the cells.<sup>19</sup> Those receptors converted angiotensin-2 to angiotensin, that reduced inflammation and increased insulin production.<sup>19</sup> Other

than the respiratory tract, ACE2 receptors were also found in the gastrointestinal tract and pancreas, suggesting that SARS CoV-2 bind to the receptor, causing downregulation of ACE2 receptors in the pancreas and disrupting  $\beta$  cells.<sup>19</sup> The downregulation of these receptors also caused the accumulation of angiotensin-2, which contributed to insulin resistance. This mechanism is suspected of having DM type 1 in COVID-19 patients.<sup>19</sup> One of the inflammatory cytokines, interleukin-6 (IL-6), increased in COVID-19 patients due to hyperinflammatory conditions.<sup>19</sup> The same cytokine also increased in DKA patients and was involved in ketone body formation.<sup>19</sup> The bad clinical manifestation might happen due to those conditions interacting simultaneously. However, this was hypothetical since the IL-6 level was not measured. COVID-19 infection was also possibly linked to lipolysis and ketogenesis activation.<sup>20</sup> Li et al. did a study with 600 COVID-19 inpatients.<sup>20</sup> More than 6% were in ketosis based on blood and urine examination, but only 35% had DM.<sup>20</sup> This result hinted that COVID-19 could also lead to ketosis that worsened DKA in patients. According to the dad's testimony in this study, the patient felt abdominal pain after being mad. To note, alteration of mental status can be the first sign of acidosis.<sup>20</sup>

The primary cause of death in DM type 1 is DKA. In developing countries, this mostly happens due to delays in diagnosis and treatment.<sup>21</sup> As reported, the patient was first treated based on dyspepsia symptoms that did not include fluid therapy. Fluid therapy, the major treatment in DKA cases other than insulin, was not given as the laboratory results were still unavailable.<sup>11</sup> As mentioned before in this research, DKA progression could happen fast, and it occurred in this patient. The patient's condition got worse to the point where she needed ventilation only a matter of hours after arriving at the ER. Due to a lack of facility, the doctor suggested the patient be referred. However, it was difficult to do, especially to refer patients with probable COVID-19 during the pandemic. The study by Bellan et al. in Italy showed fewer referrals between ER in one of the hospitals there, from 5.691 cases in 2019 to 3.059 cases in 2020 in the same

time frame.<sup>22</sup> This happened because of the fear of being infected by COVID-19 and lack of access to the hospital.<sup>22</sup> Therefore, it is crucial to have a structured referral procedure for COVID-19 patients that need life-saving treatment.

## CONCLUSION

COVID-19 is suspected of causing and exacerbating DKA through several mechanisms. Therefore, early diagnosis and prompt treatment are crucial to achieving expected outcomes.

## CONFLICT OF INTEREST

No conflict of interest was reported.

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## ETHICAL CLEARANCE

Parents had given their consent regarding their children's data published in this study.

## AUTHOR CONTRIBUTION

All authors contributed to this paper's data collection, compilation, and publication.

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