

Mild and severe diabetic ketoacidosis in children: a report of two cases

Vini Jamarin, Nanis Sacharina Marzuki

Diabetic ketoacidosis (DKA) is a severe complication of diabetes mellitus (DM) in children caused by insulin deficiency. This condition is often unidentified or diagnosed late, and treated with inadequate therapy. Diabetic ketoacidosis can lead to several complications, the most fatal being cerebral edema. We present two cases of DKA with different clinical presentation and severity. Early identification and proper management of DKA can help improve outcomes and avoid complications. [Paediatr Indones. 2022;62:291-4 DOI: 10.14238/pi62.4.2022.291-4].

Keywords: *diabetic ketoacidosis; diabetes mellitus*

Diabetic ketoacidosis is a severe complication of diabetes mellitus in children, and caused by insulin deficiency.¹ It is defined as hyperglycemia (blood glucose >200 mg/dL), venous pH < 7.3 or serum bicarbonate <15 mmol/L, and ketonemia (blood β -hydroxybutyrate \geq 3 mmol/L) or moderate to large ketonuria. The severity of DKA is categorized by the degree of acidosis: mild DKA (pH <7.3 and/or HCO_3^- <15 mmol/L), moderate DKA (pH <7.2 and/or HCO_3^- <10 mmol/L), and severe DKA (pH <7.1 with or without HCO_3^- <5 mmol/L).^{2,3}

In general, DKA may be unidentified, delayed, or misdiagnosed due to several factors, including lack of health care facilities in remote areas, subtle clinical presentations, unawareness of the symptoms, the patients avoiding medical assessment for fear of dreadful diagnosis, financial constraints, and regulations governing access to health care.

Inadequate treatment may lead to worse outcomes. The incidence of DKA is 10-70% in children with type 1 DM.⁴

Diabetic ketoacidosis can induce a vicious life-threatening cycle of hyperglycemia, hyperketonemia, osmotic diuresis, severe vomiting, dehydration, loss of electrolytes, greater stress hormone production, and, thus, more severe insulin resistance.³ The most fatal complication is cerebral edema.¹ Early identification and proper treatment of DKA are compulsory to prevent morbidity and mortality. Here we present two DKA cases with different clinical findings, severity, and management.

The cases

Case 1

A 2-year-old boy was referred with loss of consciousness due to DKA. The patient had been unconscious for eight hours before admission. In the three days prior, the patient gradually weakened and was less active

From the Bunda Women and Children Hospital, Jakarta, Indonesia.

Corresponding author: Vini Jamarin, Bunda Women and Children Hospital. Jl. Teuku Cik Ditiro No.28, Gondangdia, Menteng, Central Jakarta, Special Capital Region of Jakarta, 10350, Email: vinijamarin@gmail.com.

Submitted November 3, 2020. Accepted August 10, 2022.

than usual. According to his mother, the patient had been drinking and urinating more than usual in the 2-3 weeks before admission. No weight loss was observed. The patient's grandmother had type 2 DM. The initial assessment at the referring hospital reported Glasgow coma scale (GCS) of E2M2V2, blood pressure 89/59 mmHg, pulse rate 140/min, respiratory rate 30/min, and SaO₂ 98% with 2 lpm oxygen by nasal cannula. He had no positive meningeal signs. The boy's blood glucose was 563 mg/dL [N=52-98], and blood ketone was 4.3 mmol/L [N<0.6], and serum urea was 48 mg/dL [N=5-17]. His arterial blood gas showed severe metabolic acidosis with pH 6.72 [N=7.35-7.45], pCO₂ 15.8 mmHg [N=35-48], pO₂ 158 mmHg [N=83-108], HCO₃ 1.9 mmol/L [N=21-28], and base excess -34.3 [N=-2.4-2.3]. Fluid resuscitation and rehydration were commenced with normal saline and an insulin drip was administered with rapid acting insulin of 0.1 IU/kgBW/hour. The patient slowly regained consciousness and was referred to our hospital for advanced and intensive management.

In our emergency room, six hours after initial management, the patient had gradually regained consciousness (GCS of E2M4V3). His blood pressure was 108/68 mmHg, pulse rate 145/min, respiratory rate 36/min with Kussmaul breathing, and temperature 37.2°C. His body weight was 12 kg (normal weight/age curve). Random blood glucose was 200 mg/dL (on insulin drip 0.1 IU/kgBW/hour). Arterial blood gas showed improved metabolic acidosis of pH 7.1 [N=7.35-7.45], PCO₂ 9.3 mmHg [N=35.0-45.0], PO₂ 139.3 mmHg [N=95-100], HCO₃ 2.9 mmol/L [N=22-26], base excess -24.2 mmol/L [N=-2.5-2.5], sodium 142 mmol/L [N=132-145], potassium 3.5 mmol/L [N=3.1-5.1], and chloride 124 mmol/L [N=96-111]. Urinary ketone and glucose were +4. The patient was admitted to the intensive care unit and treated as follows: oxygen 10 lpm with rebreathing mask, intravenous fluid containing dextrose 10%, potassium, and normal saline, insulin drip of 0.7 IU/kgBW/hour, and 500 mg ceftriaxone twice/day.

The next day, even though his blood glucose was getting under control (random blood glucose ranged from 93-303 mg/dL), and urinary as well as serum ketone were negative, he remained not fully conscious (E3M5V3). Patient had developed cerebral edema, which was confirmed by CT scan, and subsequently treated with 6 g mannitol intravenously three times/day.

After two doses of intravenous mannitol, the patient slowly regained consciousness over the next five hours. Mannitol was stopped thereafter. The patient was fed 1,200 kcal/day orally, divided into three meals and three snacks. Insulin was then switched to a subcutaneous basal-bolus regimen, including 2 IU rapid insulin three times a day (before meals) as boluses, and 6 IU long-acting insulin at night before bedtime as basal. Random blood glucose ranged from 103-394 mg/dL. The biochemical tests showed low C-peptide of 0.18 ng/mL [N=1.1-4.4] and high HbA1c of 11.2% [N<5.7], therefore, the diagnosis of type 1 DM was established. Parental education on self-management of type 1 DM was initiated before discharge.

Case 2

A 7-year-old boy complained about frequent and urgent urination for the two weeks before admission. This complaint occurred day and night up to 3-4 times per hour, and he often wet the bed. He also drank more frequently than usual, consuming up to two litres per day. There was no complaint of weight loss. Initially, the patient's mother thought the child had bedwetting because of anxiety related to a current family issue. Previously, the patient had been healthy without any history of serious illness. The patient's grandfather had a history of type 2 DM.

On physical examination, the child was fully conscious and had pulse rate 90x/minute, respiratory rate 22x/minute, and temperature 36.5°C. His body weight was 27.6 kg (normal weight/age) and his height was 130 cm (normal height/age). No data on previous weight was available. Other physical examinations were within normal values. Random blood glucose revealed an extremely high level of 581 mg/dL (N=80-140). The urinalysis results showed glucosuria (+3) and ketonuria (+3).

Based on the history, physical examination, and initial laboratory workup, the patient was diagnosed with mild DKA. He was admitted to the hospital and was treated with subcutaneous rapid insulin of 3 x 5 IU before meals and long-acting insulin 1 x 10 IU before bedtime (total insulin daily dose of 0.9 IU/kgBW/day). Blood glucose was checked seven times/day: three times before meals, three times two hours after meals, and once at midnight, with a target of 100-180 mg/dL. At first, his blood sugar dropped drastically

to 99 mg/dL and returned to normal with a value of 125 mg/dL within 18 hours of treatment. The patient was given a diet of 1800 kcal/day, which was divided into three big meals and three snacks. In addition, the patient also received oral rehydration to overcome mild dehydration.

Laboratory results confirmed the diagnosis of type 1 DM with mild DKA: HbA1c 11.2% [N<5.7] and C-peptide 0.3 ng/mL [N=1.1-4.4]. Other blood test results were as follows: Hb 15.4 g/dL [N=11.5-14.5], Ht 41.6% [N=37-45], platelets 373,000/uL [N=140-400x10³], leukocytes 9,400/uL [N=5000-11000], urea 30.8 mg/dL [N=7-17], creatinine 0.4 mg/dL [N<0.9], sodium 133 mmol/L [N=132-145], potassium 3.9 mmol/L [N=3.1-5.1], and chloride 84 mmol/L [N=96-111]. Blood gas analysis showed compensated metabolic acidosis with pH 7.48 [N=7.35-7.45], PCO₂ 24.4 mmHg [N=35.0-45.0], PO₂ 152.3 mmHg [N=95-100], HCO₃ 17.7 mmol/L [N=22-26], base excess -3.8 mmol/L [N=-2.5-2.5].

After three days of hospitalization, the patient was discharged with type 1 DM education, independent blood sugar monitoring, as well as rapid and basal insulin treatment. On follow-up at the outpatient clinic, the patient's blood sugar levels were well controlled with the suggested basal-bolus regimen.

Discussion

We present two cases with contrasting DKA clinical severity and degree of acidosis. Detecting classic symptoms and signs of DM in children such as increased polyuria, polydipsia, and weight loss in 2 to 6 weeks is rather difficult in some cases. Besides, these symptoms only appear after about 80% of the pancreatic islets have been destroyed,^{4,5} and may be interpreted as other conditions. Failure to consider the possibility of DM may result in delayed diagnosis and increased risk of DKA.⁵ The clinical signs of DKA are dehydration, tachycardia, tachypnea, deep sighing respiration, acetone-scented breath, nausea and/or vomiting, abdominal pain, blurry vision, confusion, drowsiness, progressive decrease in level of consciousness, as well as loss of consciousness.² The first case came with loss of consciousness and an emergency state of severe DKA. On the other hand, the second case presented fully conscious, with mild dehydration and mild DKA. Symptoms common to

both patients were increased frequency of drinking and urinating. Early detection of cases with polydipsia and polyuria is important and should be followed with suspecting and screening for DM.

The first case had severe metabolic acidosis with pH 6.72 [N=7.35-7.45], HCO₃ 1.9 mmol/L [N=21-28], and base excess -34.3 [N=-2.4-2.3]. However, the clinician at the referring hospital did not treat him with bicarbonate, nor did we, even though the patient arrived at our hospital with severe acidosis. The use of bicarbonate is controversial, because no beneficial effects have been recorded in patients with pH 6.9 to 7.14. According to the *International Society for Pediatric and Adolescent Diabetes (ISPAD) Clinical Practice Consensus Guidelines 2018*, bicarbonate administration is not recommended except for treatment of life-threatening hyperkalemia or unusually severe acidosis (pH < 6.9), with evidence of compromised cardiac contractility.² A controlled trial in DKA-induced juvenile mice showed that brain water content was significantly increased in DKA mice receiving combined insulin and bicarbonate therapy, indicating the development of cerebral edema.⁶ The effect of using bicarbonate may, paradoxically, cause acidosis of the central nervous system, contributing to cerebral edema.^{4,7} Moreover, rapid correction of acidosis with bicarbonate results in hypokalemia, which in turn will lead to sodium load and contribute to serum hypertonicity.⁷

Even though we did not use bicarbonate to treat the first case, he still experienced cerebral edema. Diabetic ketoacidosis-cerebral edema (DKA-CE) has been observed with imaging in children upon DKA presentation.⁶ The pathomechanism of DKA-CE in the early stage of treatment is not fully understood, but might be related to abrupt changes in serum osmolality after rapid fluid administration.^{2,6} However, more recent studies have shown that dehydration and cerebral hypoperfusion itself may be associated with DKA-CE. Hence, an alternative hypothesis is that intrinsic factors of DKA may cause cerebral edema, which could worsen during fluid administration. The hypothesis also emphasizes that the severity of cerebral edema is correlated with the degree of dehydration and hyperventilation at presentation, but not with initial osmolality or osmotic changes during treatment.²

Risk factors of cerebral edema in children with DKA include younger age (<5 years), presentation

with new onset type 1 DM, and longer duration of symptoms.^{2,7} Our first case was a 2-year-old boy with new onset of type 1 DM, which fit the criteria for cerebral edema risk factors. Increased serum urea at DKA presentation is associated with an increased risk of cerebral edema. This association may reflect the severity of dehydration in these patients. In DKA cases who develop signs and symptoms suggestive of cerebral edema, prompt management should be carried out without waiting for CT scan evaluation.^{7,8,9} Decision-to-treat DKA cases with suspected cerebral edema are not affected by the head CT results and, in fact, obtaining the CT may lead to a significant delay in hyperosmolar therapy.^{8,9}

The second patient came with mild DKA and mild dehydration. The high level of hemoglobin [15.4 g/dL; (N=11.5-14.5)] indicated dehydration. Even though he did not present with pure acidosis [pH 7.48 (N=7.35-7.45)], he was in a compensated metabolic acidosis state, in which his respiratory function compensated for the metabolic acidosis, as shown in the blood gas analysis: PCO₂ 24.4 mmHg (N=35.0-45.0), PO₂ 152.3 mmHg (N=95-100), HCO₃ 17.7 mmol/L (N=22-26), base excess -3.8 mmol/L (N=-2.5-2.5). Accordingly, despite the low HCO₃ level, bicarbonate was not necessarily administered. As the dehydration and hyperglycemic states are overcome, the acidosis level gradually decreases. The second case showed milder presentation and underwent less aggressive treatment, due to parental awareness of frequent and urgent urination, as well as the pediatrician's suspicion of the symptoms, namely, polydipsia and polyuria. In this case, earlier recognition led to less aggressive treatment and, consequently, a better outcome.

In conclusion, we report two children who were diagnosed with different degrees of DKA. Early recognition of DM in children is important in order to prevent DKA and reduce its fatal complications, including cerebral edema. Cautious, yet appropriate fluid therapy to resolve volume depletion and acidosis is also essential in reducing complications.

Conflicts of interest

None declared.

References

1. Hursh BE, Ronsley R, Islam N, Mammen C, Panahiotopoulos C. Acute kidney injury in children with type 1 diabetes hospitalized for diabetic ketoacidosis. *JAMA Pediatr.* 2017;171:e170020. DOI:10.1001/jamapediatrics.2017.0020.
2. Wolfsdorf JJ, Glaser N, Agus M, Fritsch M, Hanas R, Rewers A, et al. ISPAD Clinical Practice Consensus Guidelines 2018: Diabetic ketoacidosis and the hyperglycemic hyperosmolar state. *Pediatr Diabetes.* 2018;27:155-77. DOI: 10.1111/pedi.12701.
3. Andriyani D, Wahyudhi A, Anggriawan SL. Diabetic ketoacidosis with acute kidney injury in prepubertal children: a report on two cases. *Paediatrica Indonesiana.* 2017;56:360-8. DOI: 10.14238/pi56.5.2016.360-8.
4. Raghupathy P. Diabetic ketoacidosis in children and adolescents. *Indian J Endocrinol Metab.* 2015;19:S55-7. DOI: 10.4103/2230-8210.155403.
5. Couper JJ, Haller MJ, Greenbaum CJ, Ziegler AG, Wherrett DK, Knip M, et al. ISPAD clinical practice consensus guidelines 2018: stages of type 1 diabetes in children and adolescents. *Pediatr Diabetes.* 2018;27:20-7. DOI: 10.1111/pedi.12734.
6. Rose KL, Pin CL, Wang R, Fraser DD. Combined insulin and bicarbonate therapy elicits cerebral edema in a juvenile mouse model of diabetic ketoacidosis. *Pediatr Res.* 2007;61:301-6. DOI: 10.1203/pdr.0b013e318030d193.
7. Kotori VM, Gashi N, Toro H. Severe ketoacidosis at onset of type 1 diabetes in children due to late diagnosis. *Diabetologia Croatica.* 2007;36:59-65.
8. Soto-Rivera CL, Asaro LA, Agus MS, DeCoursey DD. Suspected cerebral edema in diabetic ketoacidosis: is there still a role for head CT in treatment decisions? *Pediatr Crit Care Med.* 2017;18:207-12. DOI: 10.1097/PCC.0000000000001027.
9. Vavilala MS. Imaging for cerebral edema in diabetic ketoacidosis, time to zap the CT? *Pediatr Crit Care Med.* 2017;18:281-2. DOI: 10.1097/PCC.0000000000001037.