

Diabetic Ketoacidosis Upon Diagnosis: A Biochemistry Case Study

by

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Background

Diabetes mellitus is a metabolic disorder characterised by hyperglycemia. The two main types of diabetes mellitus are type 1 diabetes mellitus (T1DM) and type 2 (T2DM), which exhibit similar symptoms while having two very different pathophysiologies (Alam et al., 2014).

The symptoms of both T1DM and T2DM include unexplained weight loss, polyuria, blurred vision, poor wound healing, polydipsia, and most importantly, hyperglycemia. Severe hyperglycemia can lead to diabetic ketoacidosis if not treated with insulin. Insulin is a hormone that is made by the beta cells of the pancreas; it allows glucose to enter cells and leave the blood, lowering blood glucose levels.

T2DM most often occurs in people over the age of 40, but even those younger than 40, including children, can develop T2DM (Thakur et al., 2022). Diagnoses of T2DM represent 90% of all diabetes diagnoses. T2DM is characterised by producing too little insulin or insulin resistance. Usually, healthy lifestyle choices can delay the onset of T2DM or prevent it entirely.

T1DM is an autoimmune disorder that occurs when beta cells of the pancreas are destroyed and thus no longer produce insulin, resulting in elevated blood sugar. Although T1DM can occur at any age, onset is usually around childhood or adolescence. Moreover, onset is relatively sudden; symptoms can develop over a few weeks or months, but it can take months or years until the symptoms are noticed (CDC, 2022). As it is not lifestyle related, T1DM cannot be prevented or delayed. The exact cause of the autoimmune condition is as yet unknown, but viral exposure, genetic factors, and environmental triggers are hypothesised to be involved (Jayasinghe et al., 2022).

Ketoacidosis (an elevated amount of ketone bodies in the blood) is almost always seen in T1DM patients upon diagnosis due to a lack of insulin, but rarely in those with T2DM. Ketoacidosis occurs because insulin deficiency means that glucose cannot enter cells to be used as fuel. Insulin is the hormone that allows for glucose entry into cells. Instead, fat is broken down into free fatty acids that undergo beta oxidation into acetyl coA, which fuels the Krebs cycle (i.e., the TCA cycle). One symptom of ketoacidosis is breath that smells like acetone, a ketone compound commonly found in nail polish remover.

Medical Terminology

Hyperglycemia: High blood glucose; blood glucose greater than 6.9 mmol/L while fasting or greater than 10.0 mmol/L two hours after a meal (Mouri & Badireddy, 2023).

Ketone: A chemical compound that contains a carbonyl group (C=O) that is attached to two adjacent carbons on either side of the carbonyl group.

Pathophysiology: The physical processes or mechanisms underlying a disease.

Polyuria: Excessive urination.

Polydipsia: Excessive thirst.

Case

A 10-year-old girl, AJ, presents to the ER due to uncontrollable vomiting and flu like symptoms. Nurses report that her vitals are stable, and she appears to be behaving normally.

Her father complains of AJ's recent fatigue, sleeping around 14 hours a day. He suspects that AJ has the flu because her siblings have been sick for a couple of days already. The girl's father mentions that she drinks around 7 litres of water a day, and wakes up three to four times a night to use the bathroom; he reports that these symptoms have been going on for four or five months.

Upon physical examination by the ER physician, a scent of nail polish is observed. The physician notes that AJ appears to be incredibly drowsy, but conscious. Her breathing is shallow and rapid. At 9 PM, she is given an insulin infusion. At 11 PM, laboratory tests are run again. Blood ketone levels have decreased slightly, however, urine ketone levels have increased by 40%. AJ has been vomiting since admission.

Table 1. AJ's emergency room laboratory values.

<i>Blood Analysis</i>	<i>9 PM</i>	<i>11 PM</i>	<i>3 AM</i>	<i>6AM</i>	<i>Reference Values</i>
Insulin ($\mu\text{IU/mL}$)	0.0	-	-	-	<8.4
Random Blood Sugar Test (mmol/L)	55.3	54.2	55.0	43.2	3.3–5.5
Blood Ketone (mmol/L)	2.0	1.6	1.0	0.6	<0.6
Bicarbonate (mmol/L)	5.0	9.0	18.2	-	21–28
Arterial pH	7.25	7.10	7.28	7.38	7.35–7.45.
<i>Urine Analysis</i>					
Ketone (mg/dL)	50	62	50	28	<20

Around 12 AM, nurses report a new symptom to AJ's assigned physician: her breathing has become increasingly fast and deep. Note that at the beginning of AJ's admission, her breathing was rapid, but shallow. This new pattern of breathing, known as Kussmaul respiration, is often seen in diabetic patients in diabetic ketoacidosis. This is an attempt by the respiratory system to increase blood pH by expelling carbon dioxide. AJ has not stopped vomiting. An IV antiemetic as well as a bicarbonate drip were administered at 11:30 PM.

Discharge and Follow-Up

After ketoacidosis and hyperglycemia was treated, AJ displayed enhanced mental clarity and less lethargy. Kussmaul respirations ceased around 3 AM. AJ was referred to the endocrinology department and was given a diagnosis of T1DM. It is not uncommon for diabetics to be diagnosed when having a life-threatening emergency such as diabetic ketoacidosis (DKA). T1DM is insulin dependent, and thus, AJ was started on both long-acting (insulin glargine) and short-acting insulin therapy via injections and switched over to an insulin pump and continuous glucose monitor (CGM) after three to four months.

Questions

1. Diabetes is characterised by elevated blood glucose. Does the patient have T1DM or T2DM? Support your answer with data from the physical examination, history, and laboratory values.

2. What is the primary treatment for high blood glucose? What can be injected into AJ to treat her ketone bodies? Explain how each treatment works to improve these conditions.
3. Suggest an explanation for the increased concentration of ketone bodies in the urine and a decrease of ketone bodies in blood from 9–11 PM.
4. Explain why the concentration of ketone bodies is elevated concurrently with cases of high blood sugar. Use Figure 1 to aid in answering.

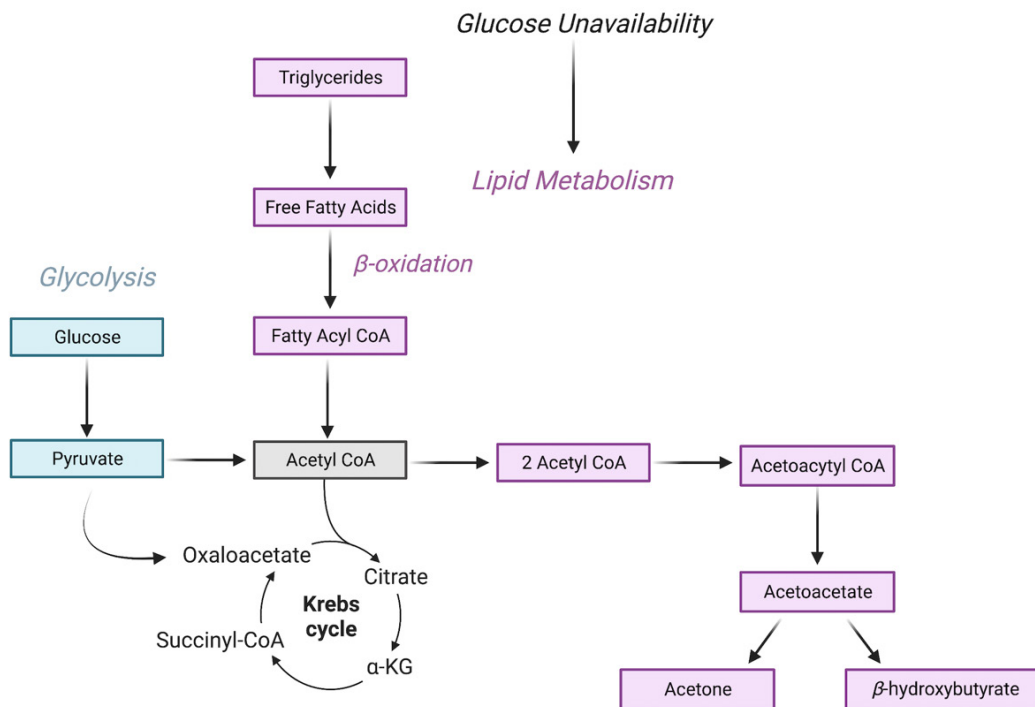


Figure 1. Metabolic pathways. Observe that both triglycerides and glucose can feed into the Krebs cycle to produce ATP.

5. What caused the scent of nail polish in the patient?
6. What is the net charge of beta-hydroxybutyric acid at physiological pH? Describe how and why the molecule affects blood pH.

7. Suggest a possible reason for the increase in bicarbonate concentration from 9–11 PM even though the bicarbonate drip had only been administered at 11:30 PM.
8. The body reacts to blood pH imbalances via compensatory responses. Is it possible for acidosis to directly cause an alkaline arterial pH? Justify your answer.
9. Why would AJ’s expulsion of CO₂ lead to an increase in blood pH?

10. If the pCO₂ measured in the patient is higher than the predicted value, what acid-base imbalance does that suggest is occurring concurrently? (See Table 2.)

Table 2. Acid-base imbalances.

<i>Imbalance</i>	<i>Presentation</i>
Respiratory Acidosis	↓ pH ↑ pCO ₂
Respiratory Alkalosis	↑ pH ↓ pCO ₂
Metabolic Acidosis	↓ pH ↓ HCO ₃ ⁻
Metabolic Alkalosis	↑ pH ↑ HCO ₃ ⁻

11. Winter’s formula is a mathematical formula used to calculate whether there is adequate respiratory compensation by the body in a state of metabolic acidosis by predicting the levels of dissolved carbon dioxide in the blood:

$$pCO_2 \text{ (mmHg)} = 1.5 ([HCO_3^-]) + 8 \pm 2$$

Use Winter’s formula to estimate AJ’s pCO₂ at admission.

12. AJ’s measured pCO₂ was found to be 16 mmHg. What does this say about AJ’s respiratory compensation?

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