



# Euglycemic DKA in DM Type 2 with SGLT-2 Inhibitor Use

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## INTRODUCTION

Diabetic Ketoacidosis (DKA) is defined as a triad of hyperglycemia, anion-gap metabolic acidosis and ketonemia. However, euglycemic DKA can be seen in patients treated with insulin prior to arrival, decreased caloric intake, heavy alcohol use, pregnancy or Sodium Glucose Cotransporter2 (SGLT-2) inhibitor use. The mechanism behind SGLT-2 inhibitor use is centered on reduction of reabsorbed glucose and sodium in the proximal renal tubules. As patients with diabetes mellitus type 2 are often on multiple medications to help manage their blood sugar it is important that providers be aware of this medication side effect and keep DKA on the differential diagnosis for our type II patients on these medications.

134	100	14.4	150
5.0	8	1.03	

Tachypneic with 28 respirations/min  
UA with ketones and elevated SG  
CBC WBC 12.5 otherwise WNL  
Anion Gap 26  
Beta hydroxybutyrate 7.5

## CASE

A 50 y/o female with a past medical history of Diabetes Mellitus Type II, Hypertension, Migraine headache currently on linagliptin, metformin, and empagliflozin for her diabetes presented to the emergency room "feeling ill": body aches, nausea and vomiting, headache and some shortness of breath. The patient reported she had recently seen her PCP who renewed her medications two weeks ago and started a ketogenic diet around the same time.

When she arrived at the hospital, her initial lab work was suspicious for an elevated leukocytosis and large anion gap metabolic acidosis. Given her leukocytosis chest X-ray and infectious work-up were completed but largely unremarkable. A subsequent ABG was performed which showed a pH of 6.9, pCO2 18.4, PO2 107, and bicarb of 4.3. Her beta hydroxybutyrate was drawn and found to be 7.5 despite normal blood sugars. She was diagnosed with euglycemic DKA and admitted to the critical care service. She was maintained on an insulin drip with dextrose infusion and her anion gap closed without difficulty. She was eventually discharged on basal bolus insulin regimen with close endocrinology follow up.

## DISCUSSION

It is unclear whether DKA occurs at a higher frequency than it did before the introduction of SGLT-2 inhibitors were introduced in 2010.<sup>2</sup> Ketosis can also be seen in patients taking SGLT2 and as such in patients with symptoms concerning for DKA diagnosis should be made with beta hydroxybutyrate levels in the setting of anion gap acidosis, normal blood sugar levels should not exclude the diagnosis. Furthermore, normal blood sugars should clue the clinician into the use of dextrose containing fluids sooner.

Several mechanisms have been proposed centered on increased ketone body production and reabsorption. Because SGLT2 inhibitors decrease urinary excretion of ketone bodies and decrease blood

glucose in an insulin-independent manner, plasma glucose and urine ketone concentrations may be lower than what is typically expected in classic presentations of diabetic ketoacidosis. Risk factors include significant reduction in insulin, caloric restriction, stress of surgery, and infection.<sup>2</sup>

To minimize the risk of development of DKA in patients taking SGLT2 inhibitors patients should be counseled against excess alcohol intake, low carb or ketogenic diets. As such, this patient beginning a ketogenic diet in combination with her resumption of her diabetic medication regimen may have increased her likelihood of developing DKA

## CONCLUSION

In patients with diabetes mellitus type 2 on SGLT-2 inhibitors diabetic ketoacidosis should be kept on the differential diagnosis. Although uncommon, given its mechanism of action, it can cause DKA in individuals with hyper or euglycemia.

## REFERENCES

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Typical laboratory characteristics of diabetic ketoacidosis and hyperosmolar hyperglycemic state\*

	DKA			HHS
	Mild	Moderate	Severe	
Plasma glucose (mg/dL)	>250	>250	>250	>600
Plasma glucose (mmol/L)	>13.9	>13.9	>13.9	>33.3
Arterial pH	7.25 to 7.30	7.00 to 7.24	<7.00	>7.30
Serum bicarbonate (mEq/L)	15 to 18	10 to <15	<10	>18
Urine ketones <sup>†</sup>	Positive	Positive	Positive	Small
Serum ketones – Nitroprusside reaction	Positive	Positive	Positive	≤ Small
Serum ketones – Enzymatic assay of beta hydroxybutyrate (normal range <0.6 mmol/L) <sup>‡</sup>	3 to 4 mmol/L	4 to 8 mmol/L	>8 mmol/L	<0.6 mmol/L
Effective serum osmolality (mOsm/kg) <sup>§</sup>	Variable	Variable	Variable	>320
Anion gap <sup>§</sup>	>10	>12	>12	Variable
Alteration in sensoria or mental obtundation	Alert	Alert/drowsy	Stupor/coma	Stupor/coma

DKA: diabetic ketoacidosis; HHS: hyperosmolar hyperglycemic state.

\* There may be considerable diagnostic overlap between DKA and HHS.

<sup>†</sup> Nitroprusside reaction method.

<sup>‡</sup> Many assays for beta hydroxybutyrate can only report markedly elevated values as >6.0 mmol/L.

<sup>§</sup> Calculation: 2[measured Na (mEq/L)] + glucose (mg/dL)/18.

<sup>§</sup> Calculation: (Na+) – (Cl- + HCO3-) (mEq/L).

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