DKA is defined by the clinical triad of :

- Hyperglycemia (the hallmark)
- Metabolic acidosis
- Raised levels of ketone bodies in blood and urine.

Euglycemic diabetic ketoacidosis (EDKA) is defined by the triad of:

- Increased anion gap metabolic acidosis
- ketonemia
- Normoglycemia (blood glucose level of < 250 mg/dl)

EDKA was first coined by Munro *et al.*, (1973). when they noticed 37 out of 211 patients presented with blood sugar levels < 300 mg/dl, serum HCO3- of 10 mmol/l and ketonemia. Normoglycemia was later redefined as < 250 mg/dl.

EDKA can occur in both T1DM and T2DM patients. The entire mechanism is predicated on a condition of general starvation, which results in ketosis while preserving normoglycemia .

EDKA is predominantly caused by an imbalance of insulin and counter-regulatory hormones, as well as a high glucagon/insulin ratio. If EDKA is not detected early and treated effectively with fluids, insulin and dextrose, it can lead to major consequences, including considerable dehydration.

Etiology of EDKA:

Some conditions leading to EDKA due to lack of carbohydrate consumption and resulting in ketosis: gastroparesis, anorexia, fasting, excessive alcohol intake, ketogenic diet

Triggers for EDKA: pancreatitis, pregnancy, surgery, glycogen storage disorders, infectious diseases, cocaine intoxication, liver cirrhosis, use of insulin pump, and post bariatric surgery in patients with T1DM.

SGLT2 inhibitors, such as canagliflozin, dapagliflozin, empagliflozin, and ertugliflozin, are a novel class of oral anti-diabetic medications that can cause EDKA. EDKA may be more likely in diabetic patients taking SGLT2 inhibitors who have a lower BMI and less glycogen in their bodies. Infection, Surgery, trauma, a serious sickness, limited food intake, recurrent vomiting, gastroparesis, dehydration, and low insulin dosages are all potential triggers for episodes.

Mechanisms of EDKA caused by SGLT-2 inhibitors are shown in Fig.1 below

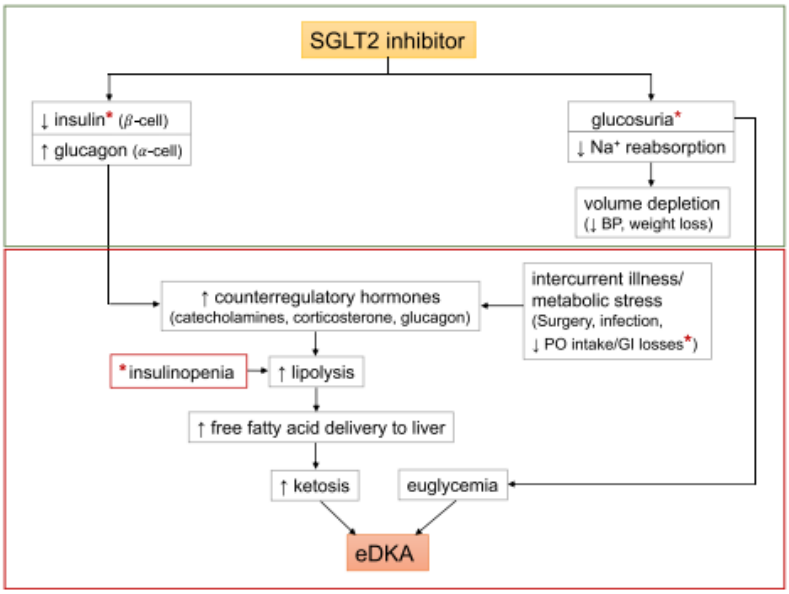

Figure 1. Proposed role of sodium-glucose cotransporter 2 (SGLT2) inhibition in euglycemic diabetic ketoacidosis (eDKA). Classic DKA results from insulin deficiency (absolute or relative) and concurrent increase in counter-regulatory hormones leading to ketosis, hyperglycemia, and osmotic diuresis. In contrast, SGLT2 inhibitor therapy in a well-compensated individual at baseline causes glucosuria, mild volume depletion, and lower serum glucose levels, associated with decreased insulin secretion (green box). During times of intercurrent illness and/or metabolic stress (eg, surgery or gastrointestinal illness), decreased carbohydrate intake coupled with lower serum glucose levels can further depress insulin secretion. This can ultimately lead to eDKA (red box). *Possible pathways of carbohydrate deficiency and causes of insulinopenia. Abbreviations: BP, blood pressure; PO, oral.

The clinical presentation may vary for different patients but will be comparable to those seen in hyperglycemic DKA, however without the polydipsia, polyuria due to normoglycemia, or significant mental status abnormalities.

After diagnosing EDKA, the management is nearly identical to DKA. The basis of treatment is IV fluids to rapidly rectify dehydration. The administration of insulin drip in combination with a dextrose-containing fluid is the second most critical step in the therapy until normalization of the anion gap and HCO3- levels. Regular checks for urine ketones and ABG analysis to determine anion gap are recommended .

Because the serum glucose level in EDKA is < 250 mg/dL, D5% should be administered to the fluids first to minimize hypoglycemia and expedite ketosis clearance. If ketoacidosis persists on D5%, consider increasing the dose of dextrose to 10%

K+ levels should also be closely watched, as total body K+ levels will most certainly be low, necessitating IV K+ and other electrolyte supplements. As is customary for the management of DKA, blood sugar levels should be monitored every hour and electrolytes every 4 hours at the very least. Patients who are on SGLT2 inhibitors should stop taking them as soon as the diagnosis is confirmed.

Lactic acidosis is a type of metabolic acidosis caused by insufficient lactic acid clearance in the bloodstream. Lactate is a result of anaerobic respiration that is generally removed from the bloodstream by the liver, kidneys, and skeletal muscles. When the body's buffering systems are overworked, lactic acidosis develops, resulting in a pH of 7.25 and plasma lactate

levels of 5 mmol/L. Tissue hypoperfusion and/or hypoxia are the most common causes. As a result, during anaerobic respiration, pyruvic acid is preferentially converted to lactate.

Hyperlactatemia is when serum lactate level is > 2 mmol/l.

There are 2 types of lactic acidosis:

- Type A (associated with tissue hypoxia): Hypoperfusion (cardiac failure, suppression of myocardium resulting from toxicity and vascular abnormalities).
  Hypoxemia due to respiratory failure, asphyxia, acute anemia, CO poisoning, acute haemorrhage.
- Type B (without tissue hypoxia) due to underlying illnesses: sepsis, Diabetes, CKD, liver failure, acute viral infections, malaria, cholera, malignancy, drug induced toxicity (e.g., metformin, paracetamol, alcohol, antiepileptics, sorbitol)

Any patient with metabolic acidosis (pH < 7.3) should be investigated for hyperlactatemia. Increased Anion gap (> 12 mEq/l) may raise suspicion of lactic acidosis.

Lactic acidosis is commonly found in patients with DKA. Various factors lead to increased lactate levels in patients with DKA such as anaerobic glycolysis due to insufficient tissue oxygenation and perfusion, as well as metabolic disturbances

The 'alternative fuel theory' suggests that the outcome of lactic acidosis in DKA may be better than expected based on lactate levels.