بنام خداوند بخشنده مهربان

DIABETIC KETOACIDOSIS

Pathophysiology

- Syndrome in which insulin deficiency and glucagon excess combine to produce a hyperglycemic , dehydrated , acidotic patient with profound electrolyte imbalances
- All derangements producing DKA are interrelated and based on insulin deficiency
- DKA may be caused by cessation of insulin intake or by physical or emotional stress , despite continued insulin therapy

- When hyperglycemia becomes sufficiently marked , glucose is excreted in urine
- Hyperosmolarity and dehydration are the most important determinants of patient's mental status
- Glucose in renal tubules draws water, Na, K , Mg , Ca , P , and other ions from the circulation into urine
- Osmotic diuresis + Poor intake and vomiting = Dehydration and Electrolyte imbalance

- Total sodium level is normal or low (95%)
- K , Mg , and P deficits are also usually marked
- Reported serum values for these electrolytes are often higher than actual body stores (Dehydration and Acidosis)

- Adipose tissue in patient with DKA fails to clear the circulation of lipids
- Insulin deficiency results in increase circulating FFAs
- FFAs partially oxidized and converted in liver to acetoacetate and β-hydroxybutyrate
- Combination of increased ketone production with decreased ketone use leads to ketoacidosis

- Acidosis plays a prominent role in clinical presentation of DKA
- Acidotic patient attempts to increase lung ventilation (Kussmaul breathing)
- Bicarbonate is consumed
- Acidosis compounds the effects of ketosis and hyperosmolality to depress mental status
- Acidemia is not invariably present, even with significant ketoacidosis
- Ketoalkalosis has been reported in diabetic patients vomiting for several days and in some with severe dehydration and hyperventilation

- DKA most commonly occurs in patients with type 1 diabetes and is associated with inadequate administration of insulin, infection, or MI
- DKA can also occur in type 2 diabetics and may be associated with any type of stress, such as sepsis or GI bleeding
- Approximately 25% of all episodes of DKA occur in patients whose diabetes was previously undiagnosed

Clinical Features

- Most patients complain of recent history of polydipsia, polyuria , polyphagia, visual blurring, weakness, weight loss, nausea, vomiting, and abdominal pain
- Approximately 50% of patients, especially children, report abdominal pain.
- In adults , abdominal pain more often signifies actual abdominal disease that may be triggering the DKA.

Physical examination

- May or may not demonstrate a depressed sensorium
- Tachypnea with Kussmaul breathing , Tachycardia , Frank hypotension or orthostatic blood pressure changes, Odor of acetone on the breath, and signs of Dehydration
- Elevated temperature is rarely caused by DKA itself and suggests an inciting infection

Differential Diagnosis

- Alcoholics with Kussmaul's breathing , fruity odor to the breath , and acidemic blood gas values may have *alcoholic ketoacidosis*
- These patients may be euglycemic or hypoglycemic
- Alcoholic ketoacidosis accounts for approximately 20% of all cases of ketoacidosis
- Ketoacidosis can also develop with *fasting*, commonly in the third trimester of pregnancy and in nursing mothers who do not eat

- The differential diagnosis for DKA is broad and includes any entity that may cause elevated anion gap acidosis, ketosis, or both

- Presence of DKA should not exclude investigation for other causes of anion gap metabolic acidosis , such as sepsis, poisoning , or lactic acidosis, because physiologic stress from one of these other causes can precipitate DKA

Diagnostic Testing

- Initial tests allow preliminary confirmation of the diagnosis and initiation of therapy
- Subsequent tests are carried out to determine degree of dehydration, acidosis, and electrolyte imbalance and reveal the precipitant of DKA
- Laboratory studies should include serum glucose, electrolyte, and venous blood pH
- Serum ketoacid levels are not necessary to diagnose DKA
- If determination of pH is the sole concern, VBG samples correlate well with ABG

- Blood gas usually reveals a low Ph , with the aforementioned rare exception of a concomitant alkalemia, resulting in a pseudo-normalization of the pH
- Metabolic acidosis with an anion gap
- Although rare, there have been case reports of a normal anion gap

- Glucose level is usually elevated above 350 mg/dL; however, euglycemic DKA (BS ≤ 300 mg/dL) has been reported in up to 18% of patients

- If an potassium level is not available an ECG can reveal signs of hyperkalemia or hypokalemia

- Initial serum potassium levels are typically normal or high However total body potassium usually declines by several hundred milliequivalents .In combination with the insulin doses administered in DKA, can result in life-threatening hypokalemia.

- Basic metabolic panel should be obtained to evaluate for an anion gap, potassium and glucose levels, and renal function
- Magnesium deficits are common in DKA, we recommend determining these levels as well
- UA : In addition to the presence of ketones, may also help confirm a urinary tract infection as a precipitant of DKA
- Whether to obtain blood or urine cultures should be determined by the clinical picture

- Sodium level is often misleading in DKA . It is often low in presence of significant dehydration
- When hyperglycemia is marked dilutional hyponatremia occure
- Elevated lipid levels cause pseudohyponatremia
- True value of sodium level may be approximated by adding 1.6 mEq/L to the sodium value on on the laboratory report for every 100-mg/dL glucose above the normal

- Acidosis and hyperosmolarity shift K , Mg , and P from the intracellular to extracellular space
- Dehydration results in hemoconcentration, which contributes to normal or high initial serum K , Mg , and P , even with profound total body deficits
- Effect of acidosis on serum potassium level determination can be corrected by subtracting 0.6 mEq/L from laboratory potassium level for every 0.1-decrease in pH
- As insulin is administered , patient needs considerable potassium replacement

- All laboratory determinations must be interpreted with caution
- Serum creatinine level may be falsely elevated
- Leukocytosis more closely reflects degree of ketosis than presence of infection.

  Only elevation of band neutrophils has been demonstrated to indicate the presence of infection
- Diagnosis of pancreatitis : Lipase should be the blood test of choice

TABLE 115.4 Typical Laboratory Values in Diabetic Ketoacidosis and Hyperglycemic Hyperosmolar State

	DKA	HHS
Glucose (mg/dL)	>350	>700
Sodium (mEq/L)	Low 130s	140s
Potassium (mEq/L)	≈4.5–6.0	≈5
Bicarbonate (mEq/L)	<10	>15
Blood urea nitrogen (mg/dL)	25–50	>50
Serum ketones	Present	Absent

TABLE 115.3 Average Fluid and Electrolyte Deficits in Severe Diabetic Ketoacidosis[a]

Weight	Water (mL/kg)	Sodium (mEq/L)	Potassium (mEq/L)	Chloride (mEq/L)	Phosphorus (mEq/L)
≤10 kg	100–120	8–10	5–7	6–8	3
10–20 kg	80–100	8–10	5–7	6–8	3
≥20 kg	70–80	8–10	5–7	6–8	3

Management

- When possible , intubation should be avoided
- Comatose DKA patient, especially if vomiting, requires intubation however. Once patient is intubated , maintenance of hyperventilation prevents worsening acidosis
- Hypovolemic shock requires aggressive fluid resuscitation , and clinicians should consider other possible causes of shock

- When hyperglycemia, ketosis, and acidosis have been established, fluid, electrolyte, and insulin therapy should be initiated

Intravenous Fluids

- Severely dehydrated adult patient is likely to have a fluid deficit of 3 to 5 L.
- No uniformly accepted formula exists for the administration of fluid in this disorder
- In hypovolemic shock, isotonic crystalloid solution should be given as rapidly as possible in adult or in boluses of 20 mL/kg in the child until a systolic pressure of 80 mm Hg is obtained.

- Marked dehydration in the absence of clinical shock or heart failure : 1 L in the first hour
- In general, 2 L of fluid resuscitation during the first 1 to 3 hours is followed by a slower infusion of a hypotonic solution, such as 0.45% normal saline solution
- Patients without extreme volume depletion may be successfully treated with a lower volume of IV fluid replacement
- Initial bolus of 20 mL/kg during the first hour is usual fluid resuscitation therapy for a child
- Fluid rate should be adjusted according to age, cardiac status, and degree of dehydration to achieve a urine output of 1 to 2 mL/kg/h.

- Fluid resuscitation alone may help lower hyperglycemia
- Large volume of glucose may be cleared by kidneys in response to renal perfusion
- Mean plasma glucose has been noted to drop by 18% after administration of saline solution without insulin
- Acidosis decreases after fluid infusion
- Although fluid administration decreases serum glucose concentration and improves acidosis, administration of insulin for correction of ketoacidosis is necessary .

Potassium

- Potassium replacement is invariably needed
- Initial potassium level is often normal or high, despite a large deficit because of severe acidosis
- Potassium levels often plummet with correction of acidosis and administration of insulin
- Once potassium levels reach 5.0 to 5.5 mEq/L and the patient is making urine, potassium should be administered while monitoring renal function
- In patients with relatively lower serum potassium concentration at presentation hypokalemia may become life-threatening when insulin therapy is administered

- Insulin should only be initiated once K has been replaced to achieve levels of 3.3 mEq/L or higher

- It was once believed that there was always a P deficit in DKA. If the measured serum P level is low, it should be replaced with potassium phosphate

TABLE 115.5 American Diabetes Association Recommendations for Potassium and Phosphorus Repletion

Potassium <3.3 mEQ/L	Replete to >3.3 mEQ/L before starting insulin
Potassium 3.3–5.5 mEQ/L	Supplement potassium to maintain these levels while starting insulin
Potassium >5.5 mEQ/L	Do not start potassium supplementation until <5.5 mEQ/L
Phosphorous <1.0 mEQ/L	Initiate supplementation with potassium phosphate

Insulin

- DKA cannot be reversed without insulin, and insulin therapy should be initiated as soon as the K level is determined
- IV bolus before the infusion is no longer recommended
- IV infusion the route of choice in sicker DKA patients
- Current initial therapy of choice, is regular insulin infused at 0.1 units/kg/h up to 5 to 10 units/h, mixed with IV fluids

- Because half-life of IV regular insulin is 3 to 10 minutes, insulin should be administered IV by infusion rather than repeated bolus
- When the blood glucose has dropped to 250 to 300 mg/dL, adding dextrose to the IV fluids reduces the risk of iatrogenic hypoglycemia and rapid shifts in osmolarity
- In patients with euglycemic DKA, dextrose should be added to the IV fluids at the start of insulin therapy

Magnesium

- Magnesium deficiency is a common problem
- Magnesium deficiency may exacerbate vomiting and mental changes, promote recalcitrant hypokalemia and hypocalcemia, or induce fatal cardiac dysrhythmia
- If there is a concern for hypomagnesemia, we recommend adding magnesium to the IV fluids, with the typical adult patient requiring 1 to 3 g for repletion

Sodium Bicarbonate

- In the past, sodium bicarbonate was recommended for severely acidemic patients
- Research has demonstrated worse outcomes for patients receiving bicarbonate
- Unless needed to stave off impending cardiac arrest in a severely acidemic patient, we do not recommend routine bicarbonate administration

Complications

- Precipitating causes of DKA may have associated morbidity and mortality rates equal to or worse than those of DKA itself
- Morbidity is largely iatrogenic (Hypokalemia , Hypoglycemia , alkalosis , pulmonary)
- Mortality in treated DKA is approximately 5% to 7%
- Primary causes of death remain infection, especially pneumonia, arterial thromboses, shock
- Cerebral edema a rare but important cause of morbidity and mortality in children

- Cerebral edema should be considered when patient in DKA becomes altered or lapses into a coma after the reversal of acidosis

- Cerebral edema generally occurs 6 to 10 hours after the initiation of therapy, often without warning signs, and the associated mortality rate is 90%.

- Cerebral edema is less common in adults or children older than 5 years and appears to be most strongly associated with severity of illness (acidemia and azotemia),

Disposition

- Most patients with DKA require hospital admission, often to ICU
- All pregnant diabetic patients in DKA require admission and consultation with an endocrinologist and obstetrician specializing in the care of high-risk pregnancies
- Some children (initial pH ≥ 7.35; bicarbonate ≥ 20 mEq/L) who can tolerate oral fluids after 3 or 4 hours of treatment may be discharged home with a reliable caregiver
- Patients who have mild DKA may be treated as an outpatient if the patient or parent can understand discharge instructions and are able to return, underlying causes do not require inpatient therapy, and close follow-up is confirmed


pix2pix.org