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| RESEARCH ARTICLE

Diabetic Ketoacidosis Complications and Management in Pediatrics: A Narrative Review

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| ABSTRACT

Diabetic ketoacidosis (DKA) is an endocrine emergency that affects both newly diagnosed and long-term type I diabetic patients as a result of decreasing insulin levels in the blood, insulin resistance, and elevated levels of counter-regulatory hormones. A common and deadly acute consequence in kids with diabetes mellitus is diabetic ketoacidosis. When type I diabetes is newly diagnosed, it can be accompanied by diabetic ketoacidosis. It can also happen when type I diabetes is already present, such as when the demands of an acute illness are more than usual or when insulin administration is decreased as a result of missed doses or insulin pump failure. Furthermore, there are more reports of diabetic ketoacidosis events in kids with type II diabetes mellitus. Although the diagnosis is typically simple in a patient with established diabetes and the anticipated symptoms, a sizable portion of patients with new-onset diabetes initially present with diabetic ketoacidosis. Children with diabetic ketoacidosis are typically treated in an emergency room for the first time. The differential diagnosis of pediatric metabolic acidosis must take diabetic ketoacidosis into account as a significant factor. The pathogenesis, therapy, and probable consequences of this illness will be explained to emergency medicine doctors in this review (Heddy, 2021). The management of pediatric patients draws attention to the uncommon but fatal occurrence of cerebral edema and the excessive use of fluid boluses that may or may not be related to it. Guidelines for managing DKA in adults should not be applied to children and adolescents.

The diagnosis of DKA is based on clinical suspicion and subsequent laboratory confirmation:

- Hyperglycemia (sugar level greater than 11 mmol/L): diabetes warning sign.
- pH 7.3 and 15 mmol/L of bicarbonate indicate metabolic acidosis.
- Ketosis, which may include ketonuria or ketonaemia.

The severity of DKA depends on the acidity level:

- Mild: pH 7.3 and/or 15 mmol/L of bicarbonate; Moderate: pH 7.2 and/or 10 mmol/L of bicarbonate.
- Ketoacidosis associated with diabetes (DKA) Extremely severe: pH 7.1 and/or 5 mmol/L of bicarbonate.
- DKA can have various deadly consequences.
- Acute hypoglycemia (during treatment or as a result of utilizing an excessive amount of insulin pump) Cerebral edema, Acute hypokalemia, Acute hypoglycemia, Spontaneous pneumonia.

A, B, and C for initial CPR

If at all possible, weigh the patient and then use that weight in all calculations. Use an estimated weight from a centile chart or a weight from a recent medical visit as an alternative.

A. Make sure the airway is open. Insert an airway if a child is unconscious (Glasgow Coma Scale Score of 8). In the event that the patient is vomiting or has a reduced level of awareness, insert NGT, aspirate, and place on free drainage.

B. An oxygen-only face mask.

C. Draw blood when an IV cannula is in place.

Only if the patient is shocked (poor peripheral pulses, poor capillary filling with tachycardia, and/or hypotension) should you provide a bolus of 10 ml/kg 0.9% sodium chloride. Repeat the fluid bolus only after contacting a doctor or pediatric endocrinologist if shock symptoms continue.

| KEYWORDS

Cerebral edema, type I diabetes mellitus, type II diabetes mellitus, insulin-dependent diabetes mellitus, and pediatric diabetic ketoacidosis, often known as DKA

| ARTICLE INFORMATION

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1. Introduction

Diabetic ketoacidosis (DKA) is the acute complication of type I diabetes mellitus that requires hospitalization the most frequently in children. 70% of diabetes-related deaths in children under the age of 10 are brought on by DKA, which can be fatal. The main factor contributing to DKA mortality is cerebral edema. With the aim of ensuring tissue perfusion, reversing fluid and electrolyte depletion, stopping ketogenesis, and resuming normal cellular utilization and glucose metabolism, successful emergency department (ED) management of DKA necessitates prompt intervention, careful observation, and protocol-based hour-by-hour therapy adjustment. A full understanding of the pathogenesis of DKA, the proper treatments, and the monitoring requirements of this complex condition is essential for emergency clinicians. As the course of the treatment develops, they also need to be carefully aware of any potential problems. The dangerous complication of relative insulin insufficiency, diabetic ketoacidosis (DKA), primarily affects people with type I diabetes mellitus (DM). When insulin levels fall significantly behind the body's requirements, DKA can happen in type- II DM. High concentrations of water-soluble ketone bodies (KBs), which result in an acidotic physiological state, give DKA its name (Heddy, 2021).

The International Society for Pediatric and Adolescent Diabetes states that a diabetic patient has DKA if all of the following are present. Blood sugar >200 mg/dL (11 mmol/L) is considered to be hyperglycemia.

Venous pH 7.3 or serum bicarbonate 15 mEq/L (15 mmol/L) are indicators of metabolic acidosis in the treatment of children. The management of DKA in children and adolescents should not follow adult DKA management guidelines.

Ketosis is the presence of ketones in the urine (defined as "moderate or large" ketones) or blood (defined as >3 mmol/L beta-hydroxybutyrate).

When the body lacks or is unable to properly import glucose, KBs, which are produced by the liver during fatty acid metabolism, can be used as a fuel by the brain, heart, and skeletal muscle tissues.

The rare but dangerous occurrence of cerebral edema and the excessive use of fluid bolus that may or may not be related to it ar e highlighted.

Clinical suspicion and laboratory confirmation are used to make the diagnosis of DKA:

- ❖ Diabetes: hyperglycemia (blood sugar level > 11 mmol/L).
- ❖ Acidosis: Metabolic acidosis (pH 7.3, bicarbonate 15 mmol/L).
- ❖ Ketosis: ketonaemia or ketonuria.

The degree of acidity is a classification of DKA severity:

- Mild: pH 7.3 and/or bicarbonate 15 mmol/L; Moderate: pH 7.2 and/or bicarbonate 10 mmol/L.
- Extremely serious: pH 7.1 and/or bicarbonate 5 mmol/L
- Acute hypokalemia, acute hypoglycemia (during treatment or as a result of too much insulin), cerebral edema, acute hypoglycemia, and aspiration pneumonia are all life-threatening complications of DKA.

Confirm diagnosis:

History	Polydipsia, polyuria +/- weight loss
Clinical	Acidotic (Kussmaul) respiration Dehydration Drowsiness Abdominal pain/vomiting
Biochemical	High blood glucose (>11 mmol/L) Blood pH<7.3 and/or HCO3<15mmol/L Glucose and ketones in urine

Initial examinations include:

Venous blood gas, blood glucose and ketones, urea, and electrolytes (which serve as a guide until precise data are available).

HbA1C, TFTS, Coeliac antibodies, lipid profile after admission, anti-GAD and anti-IA2 antibodies, and further studies only if necessary with new onset diabetes:

• If an infection is suspected, perform a thorough blood count, CXR, CSF, throat swab, blood culture, urine culture, and sensitivity tests, among other tests (leukocytosis is frequent in DKA and does not always imply sepsis) (Heddy, 2021).

2. Comprehensive clinical evaluation and observation

So that later comparisons can be made by others, evaluate and note your findings in the notes. Dehydration levels are frequently overestimated, which is harmful. Calculations should not include more than 8% dehydration without first consulting an on-call pediatric endocrinologist or pediatrician.

1. Degree of Dehydration

Mild (<5%)	**is only just clinically detectable**
Moderate (=5%)	**dry mucous membranes, reduced skin turgor**
Severe, shock	**above with sunken eyes, poor capillary return, thready rapid pulse (reduced blood pressure is not likely and is a very late sign)**

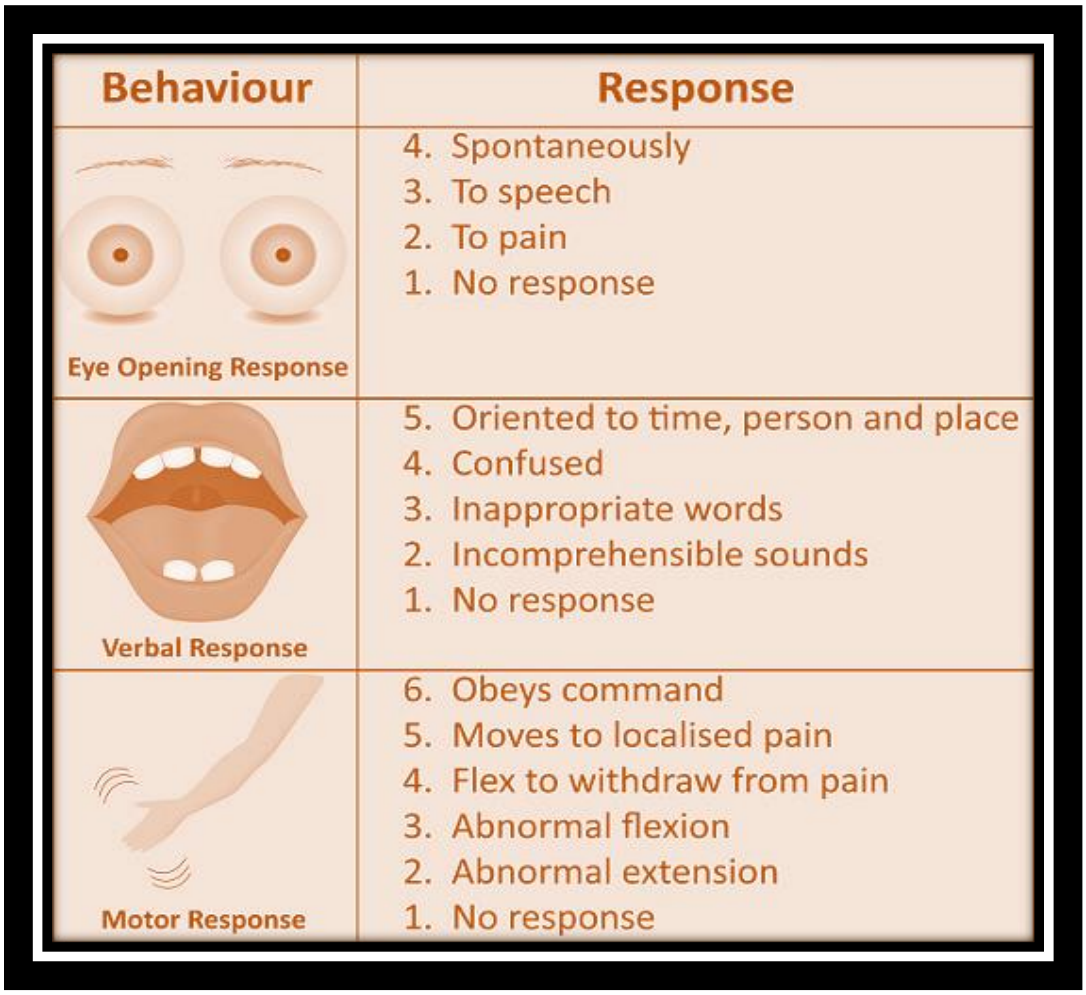
2. Conscious Level

Whether or not the child is sleepy at admission, perform hourly neurological observations (including Glasgow Coma Score).

If in a coma upon admission or if their condition worsens later:

- ❖ If a transfer to PICU is possible, do so.

- Coma is correlated with the degree of acidosis, whereas cerebral edema is suggested by indications of increased intracranial pressure.
- Take into account implementing cerebral edema management (if there is a high level of suspicion, begin therapy before transfer).



Glasgow Coma Score

3. A thorough examination should be performed with a focus on looking for signs of: Cerebral edema, which can cause headaches, irritability, a slowed heartbeat, rising blood pressure, and a loss of consciousness (papilledema is a late sign).

- Illness
- Ileus

4. If any of the following conditions occur: severe acidosis (pH 7.1) with apparent hyperventilation;
Severe dehydration and shock; poor level of consciousness with a high risk of aspiration from vomiting; or very young (under 2 years old), consult a PICU physician.

The wards lack sufficient staff to conduct efficient monitoring. Both patients in the PICU and those who are not in an HDU should have their ECGs monitored. Consider an NG tube.

Transfer to another hospital may not be essential in cases where there are no PICU/HDU facilities available until ventilatory support becomes necessary. However, even in standard pediatric wards, ALL children with DKA are high-dependency patients who require a high amount of nursing care, typically 1:1.

Senior nursing staff must conduct the following observations:

Strict fluid balance, including hourly measurements of fluid input and output (urinary catheterization may be necessary for young or sick children), hourly capillary blood glucose measurements, as well as 2-4 hourly bedside blood ketone testing, hourly (or more

frequent) blood pressure, heart rate, and respiratory rate, and hourly (or more frequent) neurological observations looking for warning signs of cerebral edema.

Reporting any change in neurological status, the onset of a headache, inappropriate slowing of the pulse rate, recurrence of vomiting, rising blood pressure, decreased oxygen saturation, rapidly rising serum sodium concentration, or any change in the level of consciousness or behavior right away, even if it happens at night.

Noting any alterations in the ECG trace, particularly T wave alterations, could indicate hyper- or hypokalemia (Wolfsdorf et al., 2018).

3. Fluid therapy

All fluids, including those administered in the ER and while traveling to the ward, should be meticulously documented.

1. The amount of fluids

Use the fluid calculator or the fluid table below to calculate the maintenance fluid rate + shortfall and correct it over 48 hours. Consider correcting the shortfall over a 72-hour period if there is hypernatremia (corrected Na > 150 mmol/L) or hyper osmolality (osmolality > 310 mmol/L).

2. Fluid types

- 40 mmol/L of potassium chloride and 0.9% sodium chloride. Before starting to administer insulin, run for one hour at the calculated rate.

Use a 1000 ml bag of potassium chloride (20 mmol/L) and sodium chloride (0.9%). 20 mmol more of potassium chloride should be added.

- Add glucose to the solution once the blood glucose level has dropped to 17 mmol/L2.

Use a 1000 ml bag of glucose at 5%, sodium chloride at 0.9%, and potassium chloride at 20 mmol/L. 20 mmol more of potassium chloride should be added.

- If the plasma sodium level is dropping, keep administering 0.9% sodium chloride and 40 mmol/L potassium chloride (with or without glucose, depending on blood glucose levels), and you might want to consider cutting back on the fluid intake.
- Checking electrolytes and urea two hours after the start of resuscitation and subsequently, at least every four hours can assist in identifying trends.

3. Oral fluids

- Nil orally unless mild DKA is being treated with oral fluids and subcutaneous insulin. If you have gastric paresis, you could need a N/G tube.
- Oral intake may continue, and the IV infusion rate may be lowered proportionately if there is good clinical improvement before the 48-hour rehydration period is up. At this stage, subcutaneous insulin injections can be switched on for the majority of patients.

4. Potassium

- Unless anuria is suspected, potassium should be administered right away to the rehydration solution once the kid has been revived. If you have acute renal failure or if your K+ level is greater than 6 mmol/L, talk to a consultant.
- Although initial plasma levels of potassium may be low, normal, or even high, potassium is primarily an intracellular ion, and there is always a significant loss of total body potassium. Once insulin is started, the levels in the blood will decrease.
- Ensure that the potassium chloride content of each 1000 ml bag of liquid is 40 mmol/L. Sometimes more is needed.
- A hypokalemic state. Utilize a cardiac monitor and keep a close eye out for T wave variations. The first warning sign that serum K+ has fallen below 3.0 mmol/L may be a flattening of the T waves on the ECG monitor. Potassium chloride at a rate of 0.5 mmol/kg/hr for 4 hours, then reevaluate (Wolfsdorf et al., 2018).

5. Insulin management

After at least an hour of intravenous fluid delivery, try to start insulin administration.

Following the administration of potassium and rehydration fluids, blood glucose levels will begin to decrease. Some data points to an increased risk of cerebral edema with early initiation of insulin.

Keep in mind to start the insulin!!!

> 50 units of regular (Act rapid or Humulin R) or analog (Novo rapid, Humalog) insulin should be added to 49.5 ml of 0.9% sodium chloride. This gives a solution of 1 unit/ml. Watch what you label. It might go on for the entire day.

- Unless otherwise instructed, start the infusion at 0.1 units/kg/hr. (small children may be started on insulin at 0.05 units/kg/hr).
- Change the solution to contain 5% glucose after the blood sugar level drops to 17 mmol/L (0.9% sodium chloride + 5% glucose + 40 mmol/L potassium chloride). DO NOT lower the rate of insulin infusion. To stop ketogenesis, the insulin dose must be kept constant at 0.1 units/kg/hour.
- To help prevent cerebral oedema, consider introducing glucose sooner if the first rate of blood glucose decline is greater than 5-8 mmol/L per hour or if the patient is highly hyperosmolar. Talk about it with the pediatrician or pediatric endocrinologist on call.
- Target Blood Glucose: When treating DKA, aiming for a blood glucose range of 8–10 mmol/L is safer than attempting to normalize.
- (4 mmol BGL) hypoglycemia. DO NOT stop the insulin infusion during the infusion of glucose, as insulin is required to stop ketone formation. After administering a 10% glucose bolus comprising 2 mL/kg, increase the infusion's glucose concentration (to a maximum of 10%). For an hour, there may be a temporary drop in insulin.
- If the blood glucose level rises out of control or the pH level does not improve within 4-6 hours, speak with senior medical specialists, re-evaluate (possible sepsis, insulin errors, or other conditions), and think about starting the complete therapy again.
- Turn off the pump before starting DKA treatment in children receiving CSII pump therapy (continuous subcutaneous insulin infusion) (Wolfsdorf et al., 2018).

Insulin management in mild DKA

- Subcutaneous insulin delivery may begin if there is less DKA and good oral intake. Before starting insulin, check the regulations in your neighborhood.
- Because they are insulin resistant, these folks may need greater insulin dosages.
- Even if they are allowed to eat and drink, prescribe a sliding scale for extra-rapid acting drugs if the patient has severe hyperglycemia (>30mmol/L). Analog insulin (0.1-0.15 u/kg/dose) should be given every four hours on a PRN basis overnight for BGLs more than 15 mmol/L. If there is any clinical worsening or the acidosis is not improving, the algorithm should be followed, including checking the TPR and neurological observations hourly, checking the BGL and blood gas after two hours, then every four hours, and checking the blood gas and blood gas every eight hours.

6. Sodium bicarbonate is rarely or never needed. Continuous acidosis frequently signifies insufficient insulin or resuscitation. Bicarbonate should only be administered to kids who have circulatory failure and are alarmingly acidotic (pH 6.9). In cases of acute shock, it just serves to make the heart contract more. It should only be discussed with a PICU specialist or pediatric endocrinologist.

7. Phosphorus

Phosphorus, another ion that is primarily present inside of cells, is continually being depleted. Potentially extremely low plasma levels. There is no proof that replacing phosphate has any therapeutic advantages in either adults or children, and phosphate therapy may cause hypocalcemia.

8. Preventative use of anticoagulants

There is a significant risk of femoral vein thrombosis when femoral lines are inserted in young, severely unwell children with DKA; consult a pediatrician about this.

4. Cerebral oedema

has a mortality rate of about 25%, is unpredictable and is more common in young children and diabetics who have just been diagnosed. Although the exact causes are unknown, this therapy seeks to reduce the risk by slowly correcting the metabolic imbalances (Ugale et al., 2012).

- ❖ A headache and a slowing of the heartbeat (>20 bpm not related to sleep or first resuscitation) are two signs and symptoms of cerebral oedema.
- ❖ Alteration in neurological state (incontinence, restlessness, irritability, and increased sleepiness).
- ❖ Particular neurological symptoms, such as cranial nerve palsies
- ❖ • Increased O2 saturation and rising blood pressure (diastolic BP >90mmHg); abnormal posture.

Convulsions, papilledema, and respiratory arrest are more severe alterations that come later and are linked to a very bad prognosis.

4.1 Management

Inform your child's pediatrician or pediatric endocrinologist as away if cerebral edema is detected. As you arrange for transfer to PICU, do the following actions right away: Rule out hypoglycemia as a potential reason for any changes in behavior.

- ➢ Give either mannitol 0.5 to 1.0 g/kg (2.5 to 5 ml/kg Mannitol 20% over 20 minutes) OR 3% sodium chloride (hypertonic saline) at a rate of 5 ml/kg over 5 to 10 minutes. If any warning signals (such as a headache or slowing of the heartbeat) appear, this must be administered as quickly as possible.
- ➢ Limit IV fluids to half maintenance and recalculate deficiency replacement over 72 instead of 48 hours.
- ➢ The child must be transferred to the pediatric intensive care unit (or the intensive care unit if the child lives outside of Auckland) and discussed with the pediatric endocrinologist and/or the Starship PICU specialist. Intubate and ventilate only after a qualified physician is on hand.
- ➢ After the kid is stable, rule out other diagnoses with a CT scan because other intracerebral events (such as thrombosis, hemorrhage, or infarction) can occur and present similarly.
- ➢ If there is no improvement after two hours, repeating the Mannitol dose or using 3% sodium chloride (hypertonic saline) may be necessary.
- ➢ Ensure that every incidence is meticulously recorded in medical records, including dates and timings.

4.2 Other DKA-related associations call for particular management:

- ➢ Constant stomach pain is typical and can be brought on by ileus, gastritis, bladder retention, and liver enlargement. Once DKA is stable, ask for a surgical opinion and be on the lookout for appendicitis. In DKA, an increased amylase level is typical.
- ➢ Other issues include type II diabetes ketosis, interstitial pulmonary oedema, hyperosmolar hyperglycaemia, TB, atypical infections (such as fungal infections), and pneumothorax/pneumo-mediastinum; with the on-call specialist, discuss these (Ugale et al., 2012).

5. Etiology

Despite the fact that ketone bodies are always present in the blood, they only reach pathogenic concentrations when the body is unable to utilize glucose (for instance, during fasting, hunger, hard exercise, or due to an issue with insulin production). Although insulin production in type-2 diabetes may be normal, it might not be enough to carry glucose into cells (Al Zahrani & Al Shaikh, 2019).

Triglycerides (TG) make up the majority of body fat. When the body's glucose storage spaces are full, the liver breaks down the TG into three fatty acids (FAs) and a glycerol molecule. The FAs are capable of being oxidized, whereas glycerol changes into glucose. If there is enough insulin available, this glucose will be utilized as fuel (Jawaid et al., 2019).

Without insulin, the body cannot utilize the glucose created by the glycerol metabolism, and dangerous amounts of unused glucose build up pollution that has entered the urine.

When blood glucose is low or cannot be used due to a lack of insulin, ketones are the brain's principal source of energy. The brain cannot store fuel; thus, it can only use glucose and ketones as fuel.

However, glycogen can be stored and used by skeletal muscle. About 70% of the body's total glycogen is kept in the muscles, where it can be converted to glucose as needed through a process known as glycogenolysis (Jawaid et al., 2019).

6. Epidemiology

The most prevalent cause of hospitalization, death, and morbidity in children with type I diabetes mellitus is DKA, which is frequently present at the time of diagnosis (in about 3% of children in the United States and Canada) (Kao et al. 2020) (Edge et al., 2001). The death rate ranges from 0.15 to 0.31 percent of patients. DKA is also seen in kids with type II diabetes, though less frequently (Sapru et al., 2005).

DKA at the time of type 1 diabetes mellitus' initial presentation: About 30% of children in the United States and Canada have DKA at the time of receiving a type I diabetes diagnosis (Kao et al., 2020). The following are some factors that make DKA more likely in kids with type I diabetes when it first manifests:

- Young age (less than five years old, especially under two years) (Wolfsdorf et al., 2006)
- Children who live in nations with a low frequency of type I diabetes, low socioeconomic level, and ethnic minorities. Delayed diabetes diagnosis (Edge et al., 2001).

An examination of 139 individuals with newly diagnosed type I diabetes mellitus who visited a single center in the United States revealed the significance of socioeconomic level. Additionally, it has been demonstrated that the prevalence of type I diabetes in the population is negatively associated with the frequency of DKA at the time of presentation of type I diabetes, showing a higher frequency of missed diagnoses of type I diabetes (Rewers et al., 2008).

DKA in children with a confirmed diagnosis of type I diabetes mellitus: DKA occurs annually at an incidence of 6–8% in children with a confirmed diagnosis of type I diabetes (Cengiz et al., 2013).

The following factors affect the likelihood of DKA:

Peripubertal and pubertal teenage females, gastroenteritis with vomiting and dehydration, a history of mental problems (including eating disorders), family conflict, poor access to healthcare (underinsured), failure of an insulin pump, and insulin omission; and A significant prospective study carried out in the United States found that only 5% of children with established diabetes developed DKA episodes. Similar findings were also made in the UK. DKA in people with type 2 diabetes: Children with type II diabetes may experience ketosis and DKA less commonly than obese African American teenagers. When 69 patients (9 to 18 years old) who had DKA were retrospectively analyzed, almost 13% had type 2 diabetes (Rewers et al., 2008).

6.1 Pathophysiology

The physiologic disturbance in DKA is caused by a number of interrelated pathways:

1. Osmotic diuresis and serum hyperosmolarity are brought on by hyperglycemia.

2. Glycosuria precedes osmotic diuresis, hyperosmolarity, and dehydration. Decompensation and impaired renal function are both possible, along with significant levels of free water loss.

3. Metabolic acidosis develops as ketones accumulate. Through compensatory hyperventilation, carbon dioxide is evacuated.

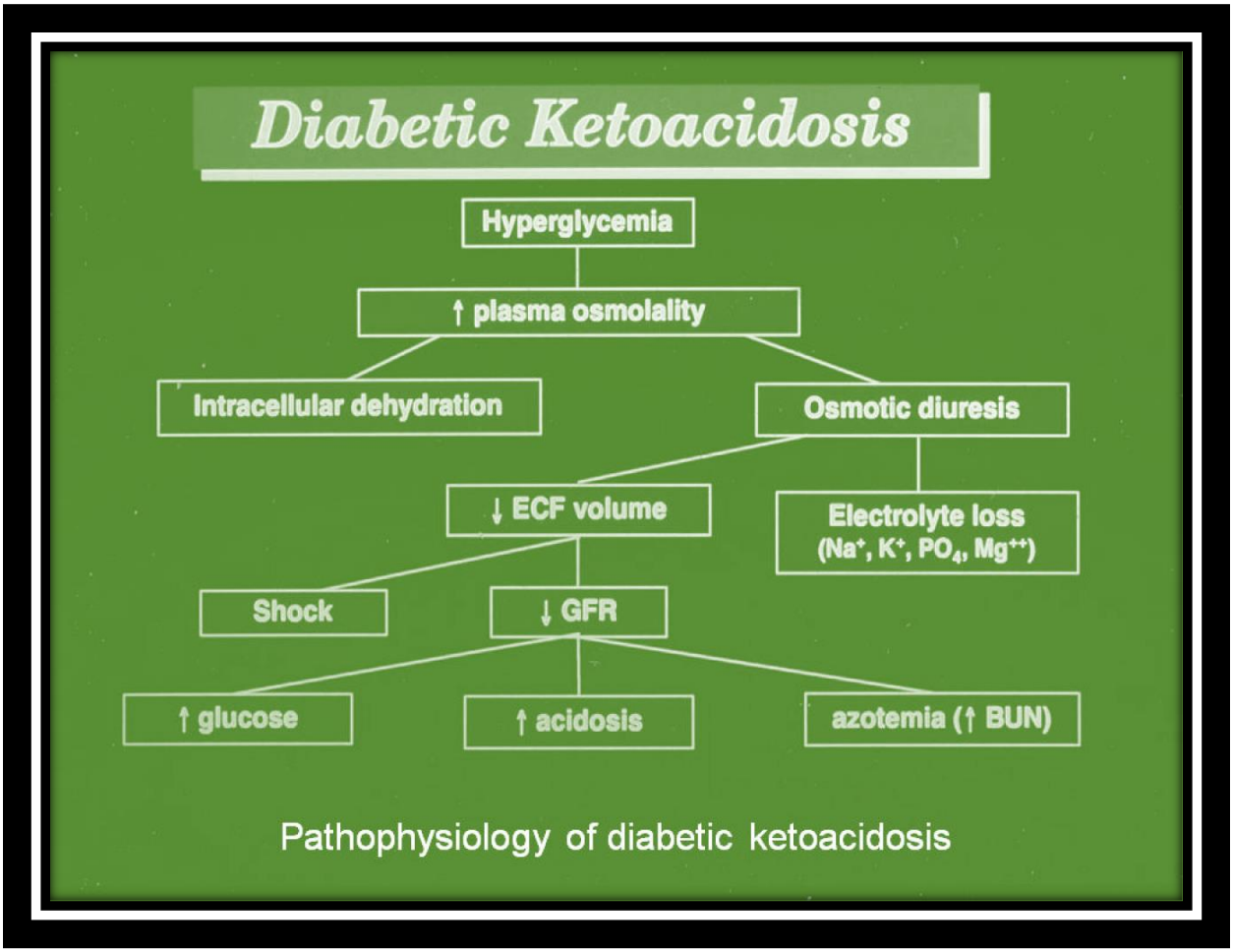
4. Children with DKA frequently have a 3 to 6 mEq/kg potassium deficiency. However, serum potassium levels are frequently normal or slightly elevated upon presentation because of the transfer of potassium ions from the intracellular to the extracellular region. Osmotic diuresis, elevated aldosterone levels in response to intravascular volume loss, and ketoacid excretion can also result in urinary potassium loss.

5. For every 100 mg/dL (5.5 mEq/L) increase in blood glucose above 100 mg/dL, pseudohyponatermia results in a 1.6 mEq/L decrease in the observed serum salt ("Hyperglycemia-Induced Hyponatremia," 1974).

6. Osmotic diuresis brought on by glycosuria causes phosphate deficit in children. However, the serum phosphate level is frequently normal or even slightly elevated initially due to extracellular phosphate shift caused by both metabolic acidosis and insulin deficiency. When this transcellular shift is reversed during DKA treatment, phosphorus levels frequently decrease (Kebler et al., 1985).

7. Elevated blood urea nitrogen (BUN) concentrations in DKA patients have been linked to the severity of hypovolemia. Additionally, abrupt increases in serum creatinine may signify acute kidney damage (AKI).

6.2 Pathophysiology



7. Ketoacidosis

After glucose is broken down during glycolysis, Kreb's cycle, and the electron transport chain, adenosine triphosphate (ATP), the cell's energy currency, is produced. Glucose is the main carbon-based substrate required for this process in blood. When there is a shortage of glucose, tissues use fuel obtained from fat called ketone bodies. Low insulin levels and high levels of counter-regulatory hormones, such as glucagon, typically enhance the liver's production of ketone bodies (Miles et al., 1983).

Deficiency and resistance cause an unfavorable ratio of insulin to glucagon, which activates hormone-sensitive lipase and breaks down triglycerides in peripheral storage, releasing long-chain fatty acids and glycerol. This happens, for example, when catecholamine levels are high under physiological stress.

Hepatocytes in the splanchnic bed absorb the fatty acids, which are largely attached to albumin. By joining the fatty acids to coenzyme A (CoA) during beta-oxidation, the fatty acids in the hepatic mitochondria produce Acetyl-CoA. A pair of carnitine palmityl transferase processes are involved in the combination of low insulin and high glucagon activity in the liver cells, which speeds up the entry of the Acyl-CoA into the mitochondria (Edgerton et al., 2009).

There are three potential outcomes for acetyl coenzyme A:

1. Enter the Krebs cycle, where it will be oxidized to produce adenosine triphosphate (ATP) and carbon dioxide (CO2)

2. Used in the cytoplasm to produce fatty acids

3. Follow the metabolic route that leads to ketosis to produce acetoacetic acid.

The oxidative capacity of the Krebs cycle becomes saturated due to the production of large amounts of Acetyl-CoA in the more severe forms of each of these conditions, which leads to a spillover entry of Acetyl-CoA into the ketogenic pathway and the subsequent production of acetoacetic acid, the first "ketone body." The acetoacetic acid may subsequently be nonenzymatically

decarboxylated to acetone, which is not an acid, or reduced to beta-hydroxybutyric acid, which is likewise an organic acid. Acetone is eliminated through urination or exhalation rather than converting back to Acetyl-CoA. When glucose availability is decreased, ketones function as a substitute water-soluble energy source (Edgerton et al., 2009).

8. Histopathology

Diabetes is a chronic condition, and people with poorly managed diabetes frequently experience DKA episodes. Chronically increased HbA1c levels predict micro- and macro-vascular problems of diabetes, albeit it is difficult to describe the effects of repeated episodes.

Rapid osmolar changes can cause cerebral edema in up to 1% of DKA patients. Watch for bradycardia, headache, papilledema, irritability, rising blood pressure, and a dropping Glasgow coma scale (GCS) as indicators of an unexpected rise in intracranial pressure. Mortality from cerebral edema is close to 25%. Significant neurological morbidity affects survivors.

9. Toxicokinetics

In the human body, beta-hydroxybutyrate (BHB), acetoacetate, and acetone are the three main ketone molecules.

Since beta-hydroxybutyrate makes up around 75% of the ketones in DKA, it is the most accurate way to gauge the severity of the condition. BHB is measured using serum lab tests and whole blood ketone test strips. The majority of urine test strips check for acetoacetate and acetone.

Since BHB is transformed into acetone and acetoacetate, it is possible to detect BHB in the blood for up to 24 hours before these molecules show up in the urine. Therefore, even after adequate DKA treatment stops the synthesis of BHB, urine ketone tests can rise. Acetone is slowly released into the bloodstream and eliminated through the urine after being deposited in adipose tissue.

9.1 Levels of Serum Ketones

1. Normal is less than 0.6 mmol/L

2. Low to moderate: 0.6 mmol/L to 1.5 mmol/L

3. Between 1.6 and 3.0 mmol/L is high and increases the risk of getting DKA.

4. Over 3.0 mmol/L: Likely DKA, needs urgent medical attention (Kangin et al., 2020)

9.2 Levels on a urine ketone strip

It's usual to have no ketones in the pee.

- Low/moderate blood ketones are equal to one plus (+) ketones in urine ketones strips.
- A high blood level of ketones is equal to two plus (++) ketones in urine.
- Severe blood ketones are equal to three plus (+++) ketones in the urine.
- Some drugs, including captopril and valproate, can cause false-positive ketones in urine tests. With expired urine strips or delayed urine testing, false-negative ketones in the urine can happen. Blood ketone levels should be the first indicator of treatment success, as was described before. Urine ketone levels, in the absence of blood tests, can aid in diagnosis but are of low yield in assessing therapy effectiveness (Ramachandran & Rajendran, 2018).

10. Historical and physical

Patients with Type I DM who are sick should be checked for DKA, which can coexist with or be brought on by other acute conditions (infection, trauma, etc.). There could be a history of polydipsia, polyuria, polyphagia (early), anorexia (late), weight loss, exhaustion, or recurrent infection. Poor academic performance, a lack of focus, altered mental status, and bewilderment are among the symptoms that patients and parents could mention.

Children with type I diabetes of new onset frequently have a gaunt, dehydrated appearance. Children with newly diagnosed type 1 diabetes may have a gaunt, dehydrated appearance. Due to glycosuria and osmotic diuresis, dehydration, thirst, and polyuria are frequently present at the time of presentation.

Additionally, typical symptoms are stomach discomfort, pain, nausea, and vomiting. In the first episode of DKA, some children may be misdiagnosed with viral gastroenteritis.

Traditional signs of metabolic acidosis in patients include quick, deep breaths (Kussmaul respirations). As acetone is exhaled through the respiratory system, the breath may smell fruity.

Correlated to the degree of acidity, neurologic symptoms range from alert to lethargic and drowsy to comatose (Edge et al., 2006).

11. Evaluation

Serology results demonstrating metabolic acidosis and hyperglycemia provide a conclusive diagnosis of DKA. Ketone testing is not required but can be useful.

A number of laboratory and point-of-care diagnostics are used to diagnose DKA. These consist of:

- Anion gap: (Na+K) -(Cl+HCO3) is the formula used to compute the anion gap. The "gap" in anions is caused by unmeasured ketone acids, especially BHB. The AG generally ranges from 6 to 12 mEq/L, with levels above 15 being common in DKA.
- Blood sugar: It typically exceeds 200 mg/dL (11 mmol/l) and occasionally exceeds 1000 mg/dL. DKA in children is associated with only modest blood glucose increases.
- Serum BHB concentration: In these patients, BHB levels are often higher than 31 mg/dL.
- Creatinine and blood urea nitrogen (BUN)
- Electrolytes in serum
- Venous pH and partial pressure of CO2 (pCO2): A pH below 7.2 portends a worse prognosis and frequently suggests the necessity for admission to an intensive care unit.
- Acetoacetate and acetone, but not BHB, cause the Nitroprusside test strip to respond with urinary ketone. Many medical facilities employ urine test strips for diagnosis despite their lack of precision and accuracy.
- Blood lactate concentration: Lactate can help rule out lactic acidosis if it is present in the blood. In the case of sepsis, which may be a triggering factor in many DKA patients, it is also a crucial prognostic marker.
- Hemoglobin A1c (HbA1c): This is useful in assessing the degree of glucose control in patients with known diabetes.
- Antibodies related to diabetes: Zinc transporter 8 antibodies, insulin autoantibodies, glutamic acid decarboxylase antibodies, and islet cell antibodies are not helpful for treating DKA. In 80 to 85% of new patients, however, their existence confirms the diagnosis of type 1 diabetes mellitus.
- C-peptide concentrations: They help distinguish between diabetics who are insulin-sufficient and those who are insulin-deficient by serving as a measure of beta-cell function. The diagnosis of type I diabetes mellitus (T1DM) is linked to a result of less than 0.2 nmol/l.

Based on the following factors, DKA can be classified as mild, moderate, or severe:

Table 1

Features	Mild DKA	Moderate DKA	Severe DKA
Venous pH	7.2 to <7.3	7.1 to <7.2	<7.1
Serum bicarbonate (mEq/L)	10 to <15*	5 to 9	<5*

From: Pediatric Diabetic Ketoacidosis

Table 1 shows how severe diabetic ketoacidosis is in youngsters.

For more susceptible individuals, such as those in low-resource environments or young children, higher bicarbonate thresholds may be employed, such as bicarbonate 7 mEq/L for severe DKA and 18 mEq/L for mild DKA.

12. Case presentation

After a brief illness, our patient, M. D., a 5-year-old boy, arrived at the Eldora Hospital's emergency room severely dehydrated. He had been housed by her father, who said that the patient had a three-week or longer history of exhaustion and weight loss with polyuria, progressive thirst and a two-day history of vomiting with stomach pain. The middle kid in a family of three, this patient had previously been healthy. Social services were aware of the family because of some child care concerns, but there was no relevant personal or family history of a similar problem.

Dr. Hameedo handled the case in the emergency room and made a prompt diagnosis of DKA. At the time of examination, the patient weighed 16 kg, had a Glasgow Coma Score (GCS) of 10/15 (E 2, V 3, M3), and was extremely dehydrated. He was breathing rapidly—32 breaths per minute—and keeping her airway open. With the aid of a rebreathing mask and 3 L of oxygen, his oxygen saturation was kept between 95 and 100%. His temperature was 37°C, his heart rate was tachycardia at 130 beats per minute, and his blood pressure was 85/45 mm Hg. Sunken eyes, diminished capillary refill time, decreased skin turgidity, and dry mucus membranes were further examination results. His initial blood sugar reading was 610 mg/dl. He had an unfathomable base excess, a pH of 6.8 that indicated he was acidotic, and a bicarbonate level of 4 mmol/L. Due to the patient's estimated level of dehydration, the pediatric intensivist from the pediatric intensive care unit (PICU) recommended vigorous fluid resuscitation for the patient. He received a push-like initial management bolus of 10 mL/kg of normal saline (NS) after the saline treatment. Two more quick boluses of 10 mL/kg of NS were administered at intervals of 30 minutes as He continued to be dehydrated, had tachycardia, and had impaired capillary refill. He was also started on a short acting insulin infusion at 0.1 units/kg/hr. HbA1C 10.5%, CBC HG 9.6, WBC5.3, PLT520, ABG, Urine analysis glucose+4, ketones+3, a normal chest X-ray, and sinus tachycardia on a 12-lead electrocardiogram were among the investigations carried out. Her initial blood analysis revealed mildly abnormal levels of 123 sodium, 4.9 potassium, Ca 10.0, CL 95, urea, 45 creatinine, and 6.9 109/L of white blood cells. Following blood cultures had been obtained., he was started on intravenous ceftriaxone. The patient didn't require intubation at any point during her hospital stay and was airlifted to the Provincial PICU to continue receiving treatment after around three hours. He was deemed to be disoriented and lethargic upon arrival to the PICU, although her GCS had increased to 12/15. Her blood sugar had increased to 369, and his arterial blood gas pH remained acidotic at 7. Her blood pressure was 100/60 mm Hg, and his tachycardia had decreased to 100 beats per minute. The patient recovered without incident after being admitted to the PICU, and 48 hours later, when his blood sugar level had decreased to 125, he was released from the PICU and transferred to the general pediatric unit.

After infectious aggravation was ruled out, the medications were stopped. He received intense teaching throughout his four days in a general unit and was discharged with no residual impairment while taking twice-daily intermediate acting insulin and ultrafast acting insulin to cover meals.

13. Discussion

This situation encourages discussion of current guidelines for fluid resuscitation in pediatric diabetic ketoacidosis (DKA), which are used in many hospitals. Most Canadian and worldwide specialists currently advise starting early fluid resuscitation with 10 to 20 mL/kg IV NS within the first 1 to 2 hours and up to 30 mL/kg only if the shock is suspected.

13.1 Management / Treatment

The primary objectives of treating DKA may vary depending on the institution, but they always remain the same. The best course of action entails treating dehydration, addressing hyperglycemia, treating ketosis, and treating acidosis, all while keeping a careful eye on the patient's clinical signs and symptoms and lab results. Another important component of DKA care is efforts to pinpoint the contributing factors and provide treatment. Individual responses to treatments need to be taken into account, therefore, Particular populations (Abulebda et al., 2019).

Pediatric, obstetric, chronic kidney disease, euglycemic DKA, and, more recently, COVID-19 individuals are just a few of the high-risk patient populations that have been recognized as needing a specialized strategy for management tracking treatment response (Weinberger et al., 2018).

The resolution requirements, according to the ADA recommendations, are blood sugar levels less than 11.2 mmol/L (200 mg/dL) and any two of the following: venous pH greater than 7.3, an anion gap less than or equal to 12 mmol/L (mEq/L), and serum bicarbonate levels greater than or equal to 15 mmol/L (mEq/L). According to JBDS recommendations, DKA must be resolved if the pH is greater than 7.3 and the blood ketone content is less than 0.6 mmol/L or 6.2 mg/dl (Gunn et al., 2016).

The ABCs and fluid resuscitation are the first steps in treating DKA. Once the patient has reached a state of stability, insulin therapy can start, typically via continuous infusion.

1. General resuscitation: If necessary, consider intubation and give 100% oxygen to the patient. For individuals who are unconscious, insert a nasogastric tube and a urinary catheter. It is important to get dependable intravenous (IV) access, ideally two large-bore accesses, one for blood draws and the other for administering drugs and insulin.

2. Perform a clinical assessment to look for any indications of infection or other provoking factors and treat accordingly.

3. Calculating insulin and other medication dosages requires accurate patient weight.

4. Regular insulin should be supplied continuously at a rate of 0.1 units/kg/hour during insulin therapy. In cases of milder diabetic ketoacidosis or when IV infusion pumps are not available, subcutaneous insulin may be utilized. When the serum glucose concentration falls to 250 mg/dL, dextrose should be given to the IV fluid infusion. When the blood glucose level drops below 150

mg/dL, higher dextrose concentrations, such as 10 to 12.5%, may be utilized. This enables full recovery from ketoacidosis while maintaining insulin infusion. The insulin infusion rate should never be decreased before the ketoacidosis has been fully or nearly fully cured. However, insulin infusion rates may be reduced in malnourished patients with enhanced insulin sensitivity to prevent hypoglycemia. Children with DKA should not receive insulin boluses since they may develop cerebral edema as a result. Consider delaying the start of an insulin infusion until the serum potassium has been determined to avoid a serious worsening of hypokalemia.

5. When the aforementioned objectives are met, the insulin infusion is discontinued.

- The patient is able to consume drugs.
- A blood sugar level under 200 mg/dL
- Closed serum anion gap or a BHB concentration of 10.4 mg/dL or less
- Serum bicarbonate above 15 mEq/L or venous pH above 7.3

6. IV fluids: Used to treat both hyperglycemia and dehydration.

- A 10-mL/kg bolus of lactated ringers or normal saline as the first IV fluid.
- A second 10 mL/kg IV fluid bolus may be administered if the patient exhibits shock.

7. As was already established, hyperglycemia causes pseudohyponatremia. Therefore, if salt levels do not rise or continue to fall with treatment, sodium levels should be regularly checked, and higher sodium concentrations should be utilized in IV fluids.

8. Careful observation and a thorough understanding of lab results should guide potassium replacement. If the first potassium level indicates hyperkalemia, potassium supplementation should be postponed until the potassium level returns to normal, intact urine voiding is confirmed, and normal renal function is observed. An acidotic patient with normal initial potassium levels may really have extremely low total body potassium levels. After ruling out renal impairment, patients with normal or low serum potassium need to receive a replacement. Initial insulin infusion should be postponed in DKA patients who have hypokalemia, and potassium supplementation should come first, as described above. Electrocardiograms and the serum potassium levels can both be utilized for monitoring.

9. When the anion gap is normal, the serum BHB level is below 10.4 mg/dL, and the venous pH is below 7, ketoacidosis is cured.3. It is accomplished by lowering the amount of ketones produced by the liver, increasing metabolism with insulin, and increasing elimination with better hydration.

10. Better rehydration also helps to treat lactic acidosis.

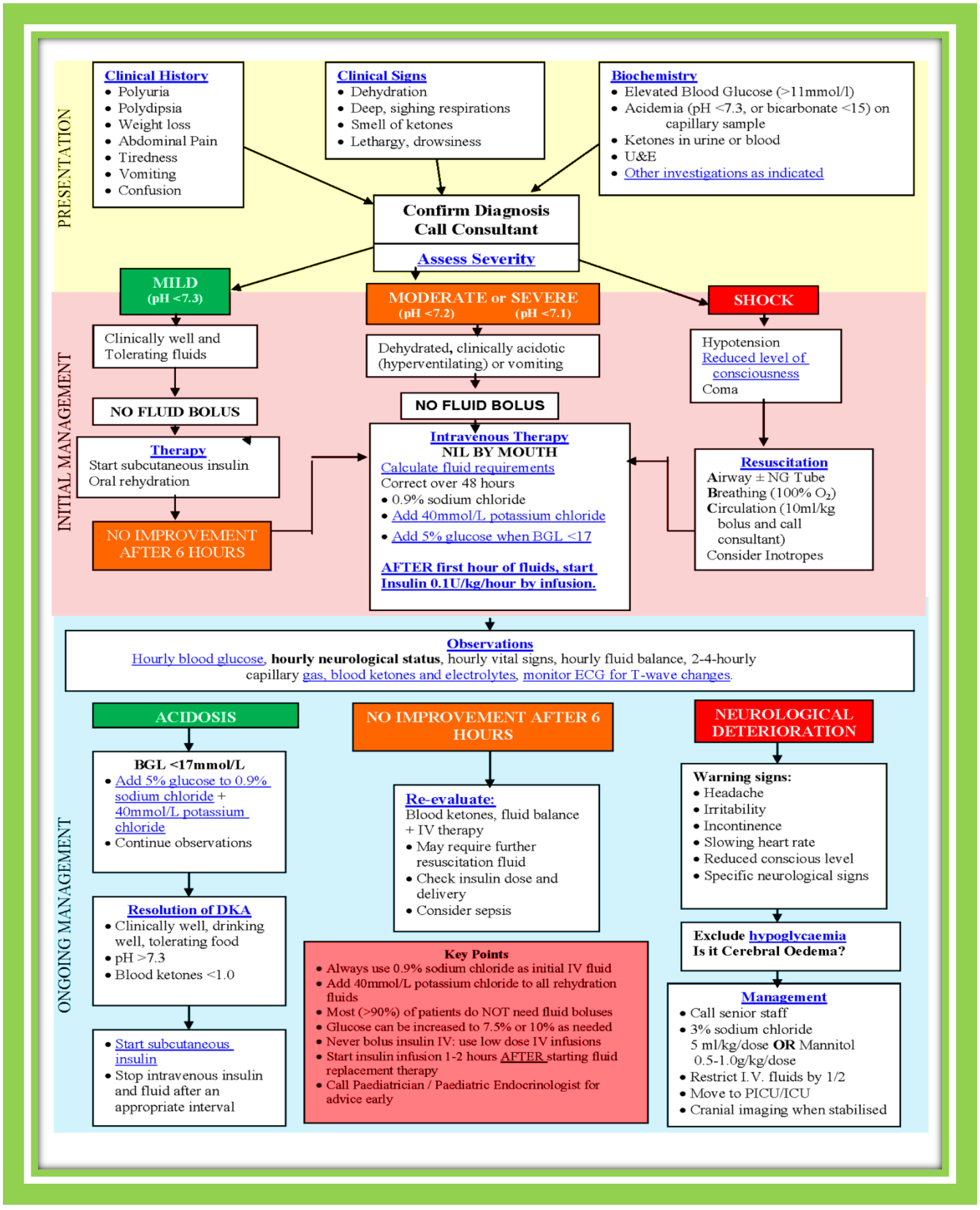
11. Bicarbonate therapy is often avoided in children with DKA, with the exception of those who are in cardiac or pericardial arrest, have hyperkalemia that is life-threatening or have severe acidosis (pH 6.9 with symptoms).

12. High-level nursing is required, along with frequent clinical evaluations and every two hours of biochemical blood indicators.

13. Once the patient's clinical condition has improved, the anion gap has closed, and the acidosis has been corrected, diet can be resumed, and insulin can be transferred to subcutaneous injection. Before ending the infusion, long-acting or baseline insulin should be given.

14. Prevention: Identify the root cause of the acute DKA episode and develop a plan of action with the kid and any other caregivers (Weinberger et al., 2018).

13.2 Management of DKA algorithm



Differential diagnoses include:

Gastroenteritis, lactic acidosis, sepsis, hyperosmolar hyperglycemic nonketotic syndrome, myocardial infarction, and starvation ketosis.

Diabetes medication overdose; toxicologic exposure (to ethylene glycol, methanol, paraldehyde, and salicylate); uremia; respiratory acidosis; and respiratory distress syndrome.

13.2 Prognosis

Prognosis with improvements in medicine and intensive care, the prognosis gets better (Stockman, 2007). In the United States and other resource-developed nations like Canada and the United Kingdom, mortality rates range from 0.15 to 0.31%(Noyes et al., 2007). The majority of fatalities are caused by cerebral damage environments with high mortality rates and little resources.

13.3 Complications

Cerebral damage and edema are the juvenile DKA complications that are most feared:

- In 0.3% to 0.9% of pediatric DKA cases, develops.
- Mortality is between 21-24%.
- Danger signs include severe acidosis, severe dehydration, high blood pressure, and noticeably elevated BUN.
- 4. Etiology: Uncertain; nonetheless, it was first believed to be caused by a quick IV fluid replacement. Nonetheless, this theory is now debatable because a recent PECARN study from 2018 found no difference in neurological outcomes.
- Can appear at any time, whether it's before, during, or after therapy, but it usually does so within 12 hours (Scibilia et al., 1986).
- Signs and symptoms include altered mental status, a recent headache, frequent vomiting, urine incontinence, and the Cushing Triad (hypertension, erratic breathing, and bradycardia).
- Even though the CT scan of the head is normal, cerebral edema may not initially be seen, necessitating the start of treatment.
- Treat with strong suspicion:

1. Mannitol (0.5–1 g/kg IV over 15 minutes): An osmotic diuretic that causes the brain parenchyma to lose water. If the first dose doesn't work, you might try a second one (Krane et al., 1985).

2. Hypertonic saline (3%) 30 minutes at 2.5 mL/kg

- Consultation with a neurosurgeon
- Other complications include cognitive impairment, venous thrombosis, and increases in pancreatic enzymes (Quintana, 2004).
- Hypokalemia, Hypoglycemia, Rhabdomyolysis, Pulmonary Edema, Multiple Organ Dysfunction Syndrome, Cardiac Arrhythmias, and Acute Kidney Injury (Krane et al., 1985)

13.4 Prevention

It is crucial to address the typical precipitating reasons that we have outlined in the preceding section in order to prevent DKA occurrences. The management of sick days for diabetes patients must take into account infection, one of the most obvious reasons. The management of sick days should include instructing patients and, if possible, family members or caregivers to closely monitor their blood sugar levels, modifying the insulin dose for patients taking insulin or oral hypoglycemic, and measuring or monitoring patients' blood pressure.

14. Conclusion

This was a thorough analysis of DKA in which we addressed crucial issues for comprehending its pathophysiology and how to treat it in both the adult and juvenile populations. It attempted to incorporate accepted clinical guidelines and expert recommendations.

We must accept that each patient will require a unique approach to treating their DKA. The purpose of consensus recommendations is to provide broad therapeutic objectives. Recognizing that the best course of treatment.

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