Childhood ketoacidosis (DKA)

What is diabetic ketoacidosis?

Diagnosis of diabetic ketoacidosis (DKA) is based on the biochemical triad of ketonaemia, hyperglycaemia, and acidaemia.[1]

Diabetic ketoacidosis is the leading cause of mortality in childhood diabetes.[2] The primary cause of DKA is absolute or relative insulin deficiency:

- Absolute - eg, previously undiagnosed type 1 diabetes mellitus or a patient with known type 1 diabetes who does not take their insulin.
- Relative - stress causes a rise in counter-regulatory hormones with relative insulin deficiency.

DKA can be fatal

Important information

DKA is a life-threatening complication of type 1 diabetes mellitus. Careful and timely intervention is required to optimise glycaemic control and reduce the risk of mortality and devastating complications. Of these, cerebral oedema is the leading cause of death, with a mortality rate of approximately 25%.[3]
The other common causes of death are:[4]
- Hypokalaemia - which is preventable with good monitoring.
- Aspiration pneumonia - thus, use of a nasogastric tube in the semi-conscious or unconscious is advised.
- Inadequate resuscitation.

Pathophysiology[5]

- Deficiency of insulin.

- Rise in counter-regulatory hormones, including glucagon, cortisol, growth hormone, and catecholamines.
- Thus, inappropriate gluconeogenesis and liver glycogenolysis occur compounding the hyperglycaemia, which causes hyperosmolarity and ensuing polyuria, dehydration and loss of electrolytes.
- Accelerated catabolism from lipolysis of adipose tissue leads to increased free fatty acid circulation, which on hepatic oxidation produces the ketone bodies (acetoacetic acid and beta-hydroxybutyric acid) that cause the metabolic acidosis.
- Potassium moves from the intracellular to the extracellular space in a switch with hydrogen ions that accumulate. Much of this extracellular potassium is then eliminated in urine, creating total body hypokalemia.

A vicious circle is usually set up as vomiting usually occurs compounding the stress and dehydration; the cycle can only be broken by providing insulin and fluids; otherwise, severe acidosis occurs and can be fatal.

Biochemical criteria [4]

Important information
The biochemical criteria required for a diagnosis of DKA to be made are: - Hyperglycaemia (>11 mmol/L). - Acidaemia (pH<7.3). - Ketosis (blood ketones >3 mmol/L or urine ketones ++). Severity: - pH <7.1 = Severe DKA (10% dehydration). - pH <7.2 = Moderate DKA (5% dehydration). - pH <7.3 = Mild DKA (5% dehydration).

How common is DKA in children? (Epidemiology) [6] [7]

- There is wide geographic variation in the frequency of DKA at onset of type 1 diabetes; rates inversely correlate with the regional incidence of type 1 diabetes.
- Frequencies range from 15% to 70% in Europe and North America.

- DKA at diagnosis is more common in children aged under 5 years, and in children whose families do not have ready access to medical care for social or economic reasons.
- The risk of DKA in established type 1 diabetes is 1-10% per per year. The risk is increased in:

    - Children with poor metabolic control or previous episodes of DKA.
    - Peripubertal and adolescent girls.
    - Children with psychiatric disorders, including those with eating disorders.
    - Children with difficult or unstable family circumstances.
    - Children who omit insulin.
    - Children with limited access to medical services.
    - Insulin pump therapy (as only rapid- or short-acting insulin is used in pumps, interruption of insulin delivery for any reason rapidly leads to insulin deficiency).

Childhood ketoacidosis symptoms[4]

Young children are more likely to have DKA as the first presentation of type 1 diabetes than older children.[8] DKA is the first presentation of diabetes in 30-40% of paediatric cases.[9]

Children with DKA may present with any or all of the following common symptoms of the condition:

- Polyuria/polydipsia.
- Weight loss.
- Abdominal pain.
- Weakness.
- Vomiting.
- Confusion.

Clinical signs:

- Dehydration.
- Kussmaul breathing.
- Ketotic smell.
- Lethargy, drowsiness.

Differential diagnosis

Other causes of metabolic acidosis:

- Overdose - eg, salicylates, iron, ethylene glycol, ethanol.
- Lactic acidosis.
- Inborn errors of metabolism such as ethylmalonic acidaemia.
- Acute kidney injury.
- Gram-negative septicaemia.

Investigations[4] [10]

On arrival in hospital, a child or young person with suspected DKA should have immediate:

- Capillary blood glucose.
- Capillary blood ketones (beta-hydroxybutyrate) if near-patient testing is available, urinary ketones if not.
- Capillary or venous pH and bicarbonate.

Further investigations should include:

- Plasma blood glucose.
- Renal function - may reveal a pattern consistent with dehydration; potassium may also be abnormal (If laboratory measurement of serum potassium is delayed, perform an ECG for baseline evaluation of potassium status).
- Venous pH, bicarbonate and blood gases.

- Repeated monitoring of near-patient testing for blood ketones - this is superior to testing for urinary ketones, which are unhelpful for ongoing monitoring.
- Urine dipstick - looking for ketones and infection.
- FBC - leukocytes increased with left shift (not necessarily caused by infection) - but fever is not normal in DKA.
- Consider blood and urine cultures, CXR, CSF, throat swab and other appropriate samples if there is any indication of possible infection. Always look for precipitating causes - eg, urinary tract infection, chest infection, etc.
- Assessment and monitoring of conscious level.
- Weight.
- ECG.

Childhood ketoacidosis treatment and management [4] [10]

The cornerstones of management are fluid and potassium replacement, weight-based fixed-rate intravenous insulin infusion (FRIII), and close biochemical monitoring of capillary ketones, serum electrolytes, venous pH and capillary glucose. It is not necessary to use arterial blood to assess acid-base status; venous sampling is sufficient as the difference between arterial and venous pH/HCO_3 is not significant enough to influence diagnosis or management of DKA. The child's long acting analogue insulin should be continued alongside the FRIII to prevent rebound hyperglycaemia when intravenous treatment is stopped. [1]

The following is a brief summary of the main care pathway and should not be considered as a complete guide to the management of paediatric DKA. The BSPED has full information, including a calculator for individual patient care.

Where should the patient be managed? [4]

All children with DKA require a high level of nursing care and should be considered high-dependency patients. Those aged under 2 years or with severe DKA, require one-to-one nursing, ideally on a high-dependency unit.

Initial treatment

If shocked (tachycardia, prolonged central capillary refill, poor peripheral pulses, hypotension [late sign]), resuscitation:

- Airway +/- NG tube.
- Breathing 100% O_2.
- Circulation: 10mL/kg 0.9% sodium chloride or Plasmalyte 148. Repeat until circulation restored. By 40 mL/kg discuss with senior doctor and consider inotropes.

If not shocked:

- Slow bolus of 10 mL/kg 0.9% sodium chloride or Plasmalyte 148 over 30 min.

Further management

- Calculate fluid requirements: a calculator is available at the BSPED guideline reference link for this article.
- Use fluid (10 mL/kg 0.9% sodium chloride or Plasmalyte 148) with 40 mmol/L potassium (check serum K+ in normal range and urine output first).
- Start insulin at 0.05 or 0.1 units/kg/hour 1-2 hours after starting fluids.

Observations

- Hourly blood glucose and 1-2 hourly blood ketones.
- Hourly neurological observations and fluid balance.
- Check electrolytes at two hours, then four-hourly.

Management of persisting acidosis

- Re-evalutate fluid balance. May require further resuscitation fluid .
- Check insulin rate and running properly.
- Consider sepsis and other differentials.
- Consider restarting the management protocol.

When blood glucose falls below 14 mmol/L

- Change fluids to contain 5% glucose.
- Continue monitoring as above.

Management of falling blood glucose (below 6 mmol/L)

- Change fluids to contain 10% glucose.
- Do not reduce insulin below 0.05 units/kg/hour if ketones >1 mmol/L.
- If glucose falls below 4 mmol/L, commence management of hypoglycaemia.

Cerebral oedema

Cerebral oedema is associated with 25% mortality and usually manifests within the first 12 hours.

Risk factors include:

- Younger age.
- New-onset diabetes mellitus.
- Longer duration of symptoms.

Signs of cerebral oedema include:

- Headache, irritability.
- Slowing heart rate.
- Reduced Glasgow Coma Scale (GCS) or coma.
- Signs of raised intracranial pressure.

Management of cerebral oedema

- Give 5 mL/kg 2.7% sodium chloride or 20% mannitol 2.5-5 mL/kg.
- Restrict IV fluids by 50%.

- Transfer to ICU may be appropriate - may need intubation and ventilation, which should only be performed by an experienced clinician.
- Alternative diagnoses may need to be considered (eg, thrombosis, haemorrhage, infection) and a CT brain scan will help delineate the cause.

Resolution of DKA

- Clinically well, tolerating oral fluids, blood ketones <1 mmol/L or pH normal.
- Start SC insulin THEN stop IV insulin one hour later.

Complications of diabetic ketoacidosis

- Cerebral oedema.
- Hypoglycaemia.
- Hypokalaemia.
- Sepsis/systemic infections.
- Aspiration pneumonia.
- Venous thromboembolism.
- Appendicitis - consider if there is ongoing abdominal pain.
- Others - eg, pneumothorax, interstitial pulmonary oedema, hyperosmolar hyperglycaemic non-ketotic coma.

Prevention of recurrence[1]

DKA is preventable; patient education and support must be integral to type 1 diabetes mellitus care.

After recovery, discuss the factors which might have led to the episode. Educate the patient and/or care-givers on the management of diabetes, and prevention of DKA, including:

- Adherence to therapy.

- Early symptoms of DKA.
- Managing intercurrent illnesses (sick day rules).
- Sources of support and advice.

Prognosis

When DKA is recognised and treated immediately, the prognosis is excellent. However, when a patient has prolonged or multiple courses of DKA or if DKA is complicated by cerebral oedema then the prognosis can be very poor.[11]

Cerebral oedema associated with DKA is more common in children than in adults. In the UK around 70-80% of diabetes-related deaths in children under 12 years of age are caused as a result of cerebral oedema.[10] [12]

DKA at the time of diagnosis of type 1 diabetes may be associated with poor long-term metabolic regulation and residual beta cell function.[13] However, one study found that DKA severity at diagnosis was associated with higher initial HbA1c, but not glycaemic control from six months post-diagnosis.[14]

Further reading

- Type 1 diabetes in adults: diagnosis and management; NICE Guidelines (August 2015 - last updated August 2022)
- Management of Type 1 Diabetes Mellitus during illness in children and young people under 18 years (Sick Day Rules); Association of Children's Diabetes Physicians, BSPED, Children and Young People's National Diabetes Network
- Fayfman M, Pasquel FJ, Umpierrez GE; Management of Hyperglycemic Crises: Diabetic Ketoacidosis and Hyperglycemic Hyperosmolar State. Med Clin North Am. 2017 May;101(3):587-606. doi: 10.1016/j.mcna.2016.12.011.
- Diabetes - type 1; NICE CKS; August 2022 (UK access only)
- Dhatariya KK, Vellanki P; Treatment of Diabetic Ketoacidosis (DKA)/Hyperglycemic Hyperosmolar State (HHS): Novel Advances in the Management of Hyperglycemic Crises (UK Versus USA). Curr Diab Rep. 2017 May;17(5):33. doi: 10.1007/s11892-017-0857-4.

Authored by:	Peer Reviewed by: Dr Krishna Vakharia, MRCGP	
Originally Published: 20/11/2023	Next review date: 19/11/2022	Document ID: doc_1942