DELL CHILDREN'S MEDICAL CENTER
EVIDENCE-BASED OUTCOMES CENTER

Diabetic Ketoacidosis and Diabetic Ketosis Non-Acidosis

Definition:

Diabetic Ketoacidosis (DKA) is the leading cause of morbidity and mortality in children with type 1 diabetes. The cause of DKA is a deficiency of insulin, with resultant unabated gluconeogenesis and lipolysis and impaired muscle glucose utilization. This generates hyperglycemia and ketosis with resultant osmotic diuresis causing water and electrolyte losses in addition to metabolic acidosis.

Incidence:

The frequency of DKA differs between established type 1 diabetes and new onset diabetes. The risk of DKA in established type 1 diabetes is 1-10% per patient per year.[1-6] In North America frequencies range from approximately 15- 70% for DKA at onset of diabetes.[7-13] DKA at diagnosis is more common in younger children (<2yr of age).

The incidence of clinically overt cerebral edema in national population studies is 0.5-0.9% and the mortality rate is 21-24%.[14-16] Up to 20% of cases of cerebral edema occur before initiating therapy, but generally it develops in the first 12 hours of treatment [17]. Mental status abnormalities occur in approximately 15% of children treated for DKA.[17-18]

Etiology:

DKA results from deficiency of circulating insulin and increased levels of the counter regulatory hormones: catecholamines, glucagon, cortisol and growth hormone.[19-20] Severe insulin deficiency occurs in previously undiagnosed type 1 diabetes mellitus and when patients on treatment deliberately or inadvertently do not take insulin, especially the long acting component of a basal-bolus regimen. As a result of low systemic insulin levels, ketones accumulate with the increase in lipolysis and ketogenesis which then cause decreased ketone body utilization, hence ketosis.[21]

Differential Diagnosis:

- Metabolic acidosis
- Respiratory acidosis
- Septic shock
- Asthma
- Pneumonia
- Respiratory distress syndrome
- Salicylate toxicity
- Acute abdomen
- Gastroenteritis
- Hyperosmolar hyperglycemic non-ketotic coma

Guideline Inclusion Criteria:

Pediatric patients age ≥ 12 months with:

- Hyperglycemia
- Glucosuria
- Ketonuria

OR

Historical features suspicious of diabetes.

Biochemical Criteria for the diagnosis of DKA:

- Venous pH < 7.3 **AND/OR** HCO_3 < 18 mmol/L
- **AND** Hyperglycemia with blood glucose > 200 mg/dL
- **AND** Ketones in Urine or ß-HB>1

Biochemical Criteria for diagnosis of Ketosis Non-acidosis:

- Venous pH ≥ 7.3 **OR** HCO_3 ≥ 18 mmol/L
- **AND** Urine Ketones >/= Small (15 mg/dL) **OR** ß-HB >/= 1 mmol/L

Guideline Exclusion Criteria:

Age < 12 months

Ketosis Non-Acidosis Inpatient Exclusion Criteria:
Age < 12 months
Diabetic Ketoacidosis
Cerebral Edema
Hyperglycemia hyperosmolar state
New onset diabetic

Ketosis Non-Acidosis ED Exclusion Criteria
Age < 12 months
Diabetic Ketoacidosis
Cerebral Edema
Hyperglycemia hyperosmolar state
Cystic Fibrosis
New onset diabetic

Critical Points of Evidence

Evidence Supports

- Emergency assessment should follow Pediatric Advanced Life Support (PALS) guidelines.
- Monitoring of the clinical and biochemical response to treatment is necessary.
- Fluid replacement should begin before starting insulin therapy.
- Patients should be assessed for warning signs of cerebral edema.
- Bicarbonate treatment is not recommended except for treatment of life-threatening hyperkalemia.

Evidence Against

- Exceeding greater than two times maintenance fluid rate in 24 hours unless objective evidence of shock and/or HHS, excessive fluids may increase risk for cerebral edema.
- Computed Tomography findings of increased intracranial pressure often occur too late for effective intervention.

Practice Recommendations and Clinical Management

Patient Assessment

Emergency assessment following PALS guidelines.[22-23]
(Strong recommendation, low-quality evidence)

Assess neurologic stability, consider using Glasgow Coma Scale (GCS).[24]
(Strong recommendation, low-quality evidence)

Assess for signs and symptoms of Cerebral Edema: [25]

- Severe headache
- Mental status changes (e.g., irritability, decreased cooperation, disorientation, decreased level of consciousness)
  - Many patients in DKA are lethargic, but this usually improves quickly on therapy.
- Bradycardia/hypertension/respiratory insufficiency (Cushing's triad)
  - Be aware of the normal heart rate for the age.
  - The heart rate in a patient with DKA should decrease with IV fluid therapy, but not to below the normal range.
- Recrudescence of vomiting
  - Most patients in DKA are vomiting on presentation, but this should improve on therapy.
- One or both pupils fixed and dilated
- Papilledema
- Focal neurologic signs
- Polyuria secondary to diabetes insipidus or, conversely, oliguria secondary to syndrome of inappropriate antidiuretic hormone (SIADH)
- Coma

(Strong recommendation, low-quality evidence)

Consider assessment for patients at high risk for cerebral edema complications:

- Age < 24 months
- GCS < 13 after volume resuscitation
- Presenting pH < 7.15
- Presenting HCO_3 < 5 mEq/L
- Presenting PCO_2 < 10 mmHg

- Presenting BUN > 30 mg/dL
- Calculated serum osmolality > 350 [2 x Na + (glucose/18) + (BUN/2.8)]

- Corrected Na < 140 mEq/L or decreasing at 2 hour labs
- Patient received IV bicarbonate or insulin bolus
- Patient received > 40 mL/kg total initial volume replacement (include fluids received prior to arrival to DCMC)
- Developmental delay or any condition that compromises communication
- Abnormal neurological exam after volume resuscitation
- Other organ system dysfunction
- History of Cerebral Edema
- Intractable vomiting
- Glucose > 800 ml/dL

Assess for clinical signs of DKA: [26]

- Dehydration
- Tachycardia
- Tachypnea
- Deep, sighing (Kussmaul) respiration; breath has the smell of acetone
- Nausea, vomiting
- Abdominal pain that may mimic an acute abdominal condition
- Confusion, drowsiness, progressive reduction in level of consciousness and, eventually, loss of consciousness. • Polyuria/polydipsia

Laboratory Testing

Beta-hydroxybuterate (ß-HB)should be measured immediately for all patients. ß-HB should be monitored every four hours until (ß-HB) levels are ≤ 1 mmol/L for patients being treated for DKA and monitored every two hours for patients being treated for ketosis non-acidosis to monitor response to treatment.[27-34]
(Strong recommendation, high-quality evidence)

Blood glucose should be measured immediately for all patients. Routine monitoring for ketosis non-acidosis patients is recommended. Blood glucose should be rechecked after initial fluid resuscitation. Hemoglobin A1C should be measured to assist in diagnosis. [25, 35]
(Strong recommendation, low-quality evidence)

Basic Metabolic Panel (BMP)should be measured to assist in diagnosis. Routine monitoring for DKA and ketosis non-acidosis patients is recommended.[25]

Magnesium, Phosphorous, and Calcium should be measured to assist in diagnosis. Magnesium and phosphorus should be measured every eight to twelve hours. [25]
(Strong recommendation, low-quality evidence)

Urinalysis with micro should be ordered as a diagnostic test. Consider urinalysis with culture in febrile patients or if patient history is suggestive of infection.
(Strong recommendation, low-quality evidence)

Routine monitoring of urine ketones is recommended for ketosis non-acidosis patients. [25]
(Strong recommendation, high-quality evidence)

Imaging

Cranial computed tomography scan should be obtained to rule out other possible intracerebral causes of neurologic deterioration after treatment for cerebral edema especially in patients with herniation or signs of herniation.[36-39]
(Strong recommendation, low-quality evidence)

Management

Fluid resuscitation should begin immediately and may need to be repeated until tissue perfusion is adequate. [25]
(Strong recommendation, moderate-quality evidence)

Patient intake and outtake should be closely monitored and recorded. [25]

Diabetic Ketoacidosis Management in the Emergency Department:

Suspend insulin pump, if applicable to patient.

Initial fluid resuscitation with normal saline. [25]
(Strong recommendation, moderate-quality evidence)

Prompt admission to PICU for any patient at high risk for cerebral edema, showing signs of herniation, or meeting insulin drip requirements.
(Strong recommendation, low-quality evidence)

Routine monitoring of neurologic status, vital signs, and blood glucose is recommended. [25, 35]
(Strong recommendation, low-quality evidence)

Patient should be placed on Cardio-respiratory Monitor and Pulse Oximeter. [40-41]
(Strong recommendation, low-quality evidence)

Bicarbonate administration is not recommended except for treatment of life-threatening hyperkalemia. [14, 25-26]
(Strong recommendation, high-quality evidence)

Diabetes Ketoacidosis Management in the Pediatric Intensive Care Unit:

Routine monitoring of neurologic status, vital signs, and blood glucose is recommended. [25]
(Strong recommendation, low-quality evidence)

Patient should be placed on Cardio-respiratory Monitor and Pulse Oximeter. [40-41]
(Strong recommendation, low-quality evidence)

Bicarbonate administration is not recommended except for treatment of life-threatening hyperkalemia. [14, 25-26]
(Strong recommendation, high-quality evidence)

IV fluid resuscitation should be maintained to expand volume, as required to restore peripheral circulation. "Two-bag" system is recommended to enable faster response time in making IV fluid therapy changes. [25, 42]
(Strong recommendation, low-quality evidence)

If the Potassium is < 5.5 mEq/dL and patient is voiding well include potassium replacement therapy as part of fluid resuscitation. [25]
(Strong recommendation, low-quality evidence)

The rate of fluid administration should not exceed 2 times the usual daily maintenance requirement. [25]
(Strong recommendation, moderate-quality evidence)

Insulin therapy should be started after starting fluid resuscitation. [25]
(Strong recommendation, high-quality evidence)

Regular insulin at 0.05 – 0.1 units/kg/hour in normal saline IV until ß-HB < 1 mmol/L is recommended.[25, 43]
(Strong recommendation, high-quality evidence)

Ketosis Non-acidosis Management:

Routine (every hour) monitoring of vital signs is recommended.[40-41]Cardio-respiratory Monitor recommended for patients treated in the Emergency Department.
(Strong recommendation, low-quality evidence)

IV Fluid should be administered with components and rates based on consultation with endocrinologist.
(Strong recommendation, low-quality evidence)

If corrected Na is less than to 140 mEq/L maintenance fluids should contain normal saline. [44-46]
(Strong recommendation, low-quality evidence)

If corrected Na is greater than or equal to 140 mEq/L maintenance fluids should contain ½ normal saline. [44-46]
(Strong recommendation, low-quality evidence)

Alternating carbohydrate-free and carb-containing fluids may be necessary depending on the patient's tolerance for PO and glucose levels.
(Strong recommendation, low-quality evidence)

Insulin should be administered to patients based on the patient's home correction for hyperglycemia, every two hours.
(Strong recommendation, low-quality evidence)

Patients with moderate to large ketones defined as urine ketones ≥ 40 **or** ß-HB ≥ 2 mmol/L, should receive additional insulin.
(Strong recommendation, low-quality evidence)

Insulin should not be given more frequently than every 2 hours.
(Strong recommendation, high-quality evidence)

Cerebral Edema Management:

Protect airway; intubation may be necessary for the patient with impending respiratory failure.[25]
(Strong recommendation, moderate-quality evidence)

Fluid rate should be reduced by one-third.[25]
(Strong recommendation, moderate-quality evidence)

Patients head should be elevated to 30°.[25]
(Strong recommendation, moderate-quality evidence)

Hypertonic saline (3%) should be administered 5 mL/kg over 30 minutes. [47-53]
(Strong recommendation, moderate-quality evidence)

Mannitol should be administered over 20 minutes and repeated if there is no initial response after 30 minutes to 2 hours. [25,54]
(Strong recommendation, moderate-quality evidence)

Hyperosmolar agents should be readily available at the patient's bedside. [25]
(Strong recommendation, high-quality evidence)

Consults/Referrals:

Endocrinology should be notified when a patient is suspected of having DKA.

Endocrinology should be consulted for diagnosis of DKA or Ketosis Non-acidosis and during treatment.

PICU Attending should be consulted STAT if the patient is high risk for cerebral edema or exhibiting signs of herniation.

PICU Attending should be consulted/notified as soon as the patient is determined to meet DKA criteria and if any of the following occur:

- Glucose < 80 mg/dL
- Glucose falling > 100 mg/dL/Hour
- Urine output < 1mL/kg/hour over 2 hours **OR** negative fluid balance
- Intractable vomiting
- Change in mental status (including severe or increasing headache)

Patient Disposition

Admission Criteria

Pediatric Intensive Care Unit:

- Patients that meet biochemical criteria for DKA.
- Patients with suspected **or** definite Cerebral Edema.
- Patients with hemodynamic instability.

Inpatient:

Patients that meet biochemical criteria for Ketosis Non acidosis and any of the following:

- Ketones ≥ moderate OR ß-HB > 1 mmol/L 2 hours after initiation of treatment in the emergency department
- Not tolerating PO 2 hours after initiation of treatment in the emergency department
- Psychosocial issues that necessitate inpatient treatment

Follow-Up Care

Inpatient Discharge Instructions

Diabetic Ketosis Sick Day Plan

Consult Endocrinology

Emergency Department Discharge instructions

Diabetic Ketosis Sick Day Plan

Consult Endocrinology

Discharge Criteria

Inpatient

Patient should have all of the following:

- ß-HB decreasing or < 0.6 mmol/L

Discuss w/endocrinology for ß-HB 0.6 - 1.9 mmol/L

- Patient is tolerating PO

Emergency Department

Patient should have all of the following:

- Urinary ketones are negative to trace **OR** ß-HB decreasing or < 0.6 mmol/L

Discuss w/endocrinology for ß-HB 0.6 - 1.9 mmol/L

- Blood glucose < 200 ml/dL **OR** decreasing

AND

- Patient is tolerating PO

Outcome Measures

Emergency department & hospital length of stay
Emergency department & hospital readmission rate
Rate of hospital admissions

Addendums

Diabetic Ketosis – Sick Day Plan

ADDENDUM 1

Assessment for patients at high risk for cerebral edema complications

- Age < 24 months
- GCS < 13 after volume resuscitation
- Presenting pH < 7.15
- Presenting HCO_3 < 5 mEq/L
- Presenting PCO_2 < 10 mmHg
- Presenting BUN > 30 mg/dL
- Calculated Serum osmolality> 350 [2 x Na + (glucose/18) + (BUN/2.8)]
- Corrected Na < 140 mEq/L or decreasing at 2 hour labs
- Patient received IV bicarbonate or insulin bolus
- Patient received > 40 mL/kg total initial volume replacement (include fluids received prior to arrival to DCMC) • Developmental delay or any condition that compromises communication
- Abnormal neurological exam after volume resuscitation
- Other organ system dysfunction
- History of Cerebral Edema
- Intractable vomiting
- Glucose > 800 mg/dL

Hyperglycemic Hyperosmolar State (HHS) criteria

Hyperglycemic hyperosmolar state (HHS), also referred to as hyperosmolar nonketotic coma, may occur in young patients withT2DM, but rarely in T1DM subjects.

Criteria for HHS include:

- plasma glucose concentration >33.3 mmol/L (600 mg/dL)
- arterial pH >7.30
- serum bicarbonate >15 mmol/L
- small ketonuria, absent to mild ketonemia
- effective serum osmolality >320 mOsm/kg
- stupor or coma

Possible sources of snacks

Snack	Volume	CHO	Snack	Volume	CHO
Saltine Crackers	1 Pkg (2 crackers)	4 grams	Graham Crackers	1 Pkg (3 crackers)	15 grams
Jello Snacks	1 Pkg (8oz)	17 grams	Pudding Snacks	1 Pkg (8oz)	23 grams
Peanut Butter Crackers	1 Pkg (6 crackers)	23 grams	Gatorade	8oz	14 grams

ADDENDUM 2

Diabetic Ketosis – Sick Day Plan

SICK DAY PLAN WITH SMALL, MODERATE, OR LARGE KETONES

- **Please rest for the remainder of your illness**. If you have moderate or large ketones in your urine, you should not exercise, even if you feel well.
- Return to the emergency room for chest pain, confusion, vomiting that does not stop with medication or if you are concerned about your child and do not feel able to care for them.
- **Drink lots of fluids**: 8 ounces of caffeine free, sugar free liquids every 30 minutes.
- **Check for ketones** with all urine, or check for blood ketones every two hours until ketones are negative.
- **Check blood sugar every two hours** until you are no longer having ketones in your blood or urine.
- If you normally give insulin injections at home, **do not stop giving insulin**. Give your **normal home correction** of rapid insulin (Novolog [insulin aspart], Humalog [insulin lispro], or Apidra or Fiasp [insulin aspart]) every 2 hours with rapid insulin (Novolog, Humalog, or Apidra). Give your **normal carbohydrate coverage** for meals. Do not forget to give your normal **dose of long acting insulin** (i.e. Lantus, Basaglar, Toujeo, Semlgee, glargine, Levemir or Tresiba) in addition to other management.
- If you are on an insulin pump at home, please **be sure to change your pump site, reservoir/cartridge, fill with new insulin, and reconnect the pump to the new site**. Continue with your normal home insulin pump settings as well as correction and coverage. It is **OK to resume basal rate** through the pump, but if ketones remain small to large, correction dose should be given by pen or syringe (not your pump).
- For blood glucose less than 70, give 15 grams of juice by mouth and recheck your blood glucose in 15 minutes. **Please repeat this until blood sugar is over 70**. Always have Glucagon available for severe low blood glucose levels.
- **Call the diabetes care line (512–628–1830) tomorrow morning** (_____/_____) to discuss your child's management, or if you have any questions or concerns.
- Call the diabetes care line (512–628–1830) for a high or low blood sugar that is sustained, if sugars do not respond to your normal management, or if your ketones are getting more severe on two consecutive checks. If it is after clinic hours please call MedLink (512-323-5465) and tell them that you have a very sick diabetic child to have the on-call doctor paged.

Today in the emergency department, it was found that your child has ketones in his or her blood or urine.

Ketones are made when the body is unable to use glucose for energy and has to burn fat. Missing insulin does, infections, the flu, or even a cold can cause the body to not use insulin or glucose correctly and instead burn fat for energy. When this occurs, ketones can build up dangerously in the blood and urine. Always test for ketones when your child has:

• Any Illness
• Unexplained blood sugar above 300
• Diarrhea, nausea, or vomiting
• Fever of 100.4ºF (38ºC) oral or 101.4°F (38.5°C) rectal or higher

Based on the tests done in the emergency department today, it does not appear that your child has or diabetic ketoacidosis or DKA. DKA is a dangerous condition that is often caused by the body having a lack of insulin. This can happen if your child misses taking his or her insulin injections, or if your child gets an infection. Symptoms of ketoacidosis include:

• Nausea and vomiting
• Stomach cramps
• Rapid, deep breathing
• Fruity-smelling breath
• Blurred vision

Even though your child does not currently have ketoacidosis, he or she may develop this problem if his or her illness worsens. Ketoacidosis is very serious. If you are concerned that your child is getting sicker, please discuss with the endocrinologist on call, or bring your child back to the emergency department immediately.

Our healthcare team has discussed your child's case with the endocrinologist on call today, and we have decided as a team that it is safe for you to care for your child's ketosis at home today. Please see the sick-day plan below for further details.

Other notes:

- **Stick to your usual diet and meal plan if your child can eat.** This will help regulate your child's blood sugar and keep him or her from becoming dehydrated.
- **If your child can't eat,** have him or her sip fruit juices, soft drinks with sugar, or ice cubes made from juice or sugar water. Or try gelatin, frozen juice bars, or low-fat ice cream. If you were given medicine for nausea to use at home (i.e. Zofran/ondansetron) please use this as needed to help with nausea and vomiting.
- **Make sure your child drinks plenty of water.** Your child has to stay hydrated.
- **Test blood sugar often.** Test as often as indicated in the sick-day plan. And continue checking your child's blood sugar even if he or she isn't eating. A rise in hormones can cause the blood sugar level to rise. That means insulin must still be injected to keep your child safe and his or her blood sugar in the target range.
- **Do not skip insulin.** ALWAYS continue giving insulin. Adjust the amount of insulin you give your child according to the sick-day plan. But do NOT skip insulin, even if your child is vomiting. Skipping insulin could lead to DKA Call your child's doctor if you aren't sure how much insulin you should give your child.

Sick Day Supplies to have in your house:
▯ Sugar free fluids - diet soda, sugar-free Jell-O and popsicles, broth
▯ Fluids with sugar- regular soda, Gatorade, popsicles, Jell-O
▯ Hard candy- peppermints, Lifesavers
▯ Glucose gel or tablets
▯ Medicines- for fever, cough, diarrhea
▯ Medicine for nausea - Zofran/ondansetron
▯ Glucagon Emergency Kit or Basqimi nasal spray, G-voke or Zegalogue Auto-injectors
▯ Ketones strips

Always keep emergency phone numbers on hand when away from home or traveling.

Diabetes Office Line: 512-628-1830

Emergency Medlink line: 512-323-5465- ask for the pediatric endocrinologist on call

- *Dr. Susan Nunez*
- *Dr. Rajani Prabhakaran*
- *Dr. Shona Rabon*
- *Dr. Stephanie Tacquard*
- *Dr. Bonnie Leyva*
- *Dr. Amy Rydin*

References

1. Hanas R, et al. 2-year national population study of pediatric ketoacidosis in Sweden: predisposing conditions and insulin pump use. Pediatr Diabetes 2009: 10: 33–37.
2. Rosilio M, et al. Factors associated with glycemic control. A cross-sectional nationwide study in 2,579 French children with type 1 diabetes. The French Pediatric Diabetes Group. Diabetes Care 1998: 21: 1146–1153.
3. Smith CP, et al. Ketoacidosis occurring in newly diagnosed and established diabetic children. Acta Paediatr 1998: 87:537–541.
4. Morris AD, et al. Adherence to insulin treatment, glycaemic control, and ketoacidosis in insulin-dependent diabetes mellitus. The DARTS/MEMO Collaboration. Diabetes Audit and Research in Tayside Scotland. Medicines Monitoring Unit. Lancet 1997: 350: 1505–1510.
5. Rewers A, et al. Predictors of acute complications in children with type 1 diabetes. JAMA 2002: 287: 2511–2518.
6. Cengiz E, et al. Severe hypoglycemia and diabetic ketoacidosis among youth with type 1 diabetes in the T1D Exchange clinic registry. Pediatr Diabetes 2013: 14: 447–454.
7. Rewers A, et al. Presence of diabetic ketoacidosis at diagnosis of diabetes mellitus in youth: the Search for Diabetes in Youth Study. Pediatrics 2008: 121: e1258–e1266.
8. Levy-Marchal C, et al. Clinical and laboratory features of type 1 diabetic children at the time of diagnosis. Diabet Med 1992: 9:279–284.
9. Komulainen J, et al. Ketoacidosis at the diagnosis of type 1 (insulin dependent) diabetes mellitus is related to poor residual beta cell function. Childhood Diabetes in Finland Study Group. Arch Dis Child 1996: 75:410–415.
10. Levy-Marchal C, et al. Geographical variation of presentation at diagnosis of type I diabetes in children: the EURODIAB study. European and Dibetes. Diabetologia 2001: 44 (Suppl3): B75–B80.
11. Hanas R, et al. Diabetic ketoacidosis and cerebral oedema in Sweden--a 2-year paediatric population study. Diabet Med 2007: 24:1080–1085.
12. Rodacki M, et al. Ethnicity and young age influence the frequency of diabetic ketoacidosis at the onset of type 1 diabetes. Diabetes Res Clin Pract 2007: 78: 259–262.
13. Usher-Smith JA, et al. Variation between countries in the frequency of diabetic ketoacidosis at first presentation of type 1 diabetes in children: a systematic review. Diabetologia 2012: 55: 2878–2894.
14. Glaser N, et al. Risk factors for cerebral edema in children with diabetic ketoacidosis. The Pediatric Emergency Medicine Collaborative Research Committee of the American Academy of Pediatrics. N Engl J Med 2001: 344:264–269.
15. Edge JA, et al. The risk and outcome of cerebral oedema developing during diabetic ketoacidosis. Arch Dis Child 2001: 85:16–22. 16. AU Glaser N, et al. Risk factors for cerebral edema in children with diabetic ketoacidosis. The Pediatric Emergency Medicine Collaborative Research Committee of the American Academy of Pediatrics. Pediatric Emergency Medicine Collaborative Research Committee of the American Academy of Pediatrics SO N Engl J Med. 2001;344(4):264.
16. Lawrence SE, et al. Population-based study of incidence and risk factors for cerebral edema in pediatric diabetic ketoacidosis. J Pediatr 2005: 146: 688–692.
17. Glaser NS, et al. Frequency of sub-clinical cerebral edema in children with diabetic ketoacidosis. Pediatr Diabetes 2006: 7: 75–80.
18. Glaser NS, et al. Correlation of clinical and biochemical findings with diabetic ketoacidosis-related cerebral edema in children using magnetic resonance diffusion weighted imaging. J Pediatr 2008: 153: 541–546.
19. Foster DW, et al. The metabolic derangements and treatment of diabetic ketoacidosis. N Engl J Med 1983: 309: 159–169.
20. Kitabchi AE, et al. Hyperglycemic crises in adult patients with diabetes: a consensus statement from the American Diabetes Association. Diabetes Care 2006:29: 2739–2748.
21. Brink S, et al. Sick day management in children and adolescents with diabetes. Pediatric Diabetes 2014: 15 (Suppl. 20): 193-202.
22. Kleinman ME, et al. Pediatric advanced life support: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Pediatrics 2010: 126: e1361–e1399.
23. Kleinman ME, et al. Pediatric basic and advanced life support: 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations. Pediatrics 2010: 126: e1261–e1318.
24. Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale Lancet 1974: 2: 81–84.
25. Wolfsdorf J, et al. Diabetic ketoacidosis and hyperglycemic hyperosmolar state. Pediatr Diabetes 2014; 15(suppl. 20):154-179
26. Glaser N, et al. Risk factors for cerebral edema in children with diabetic ketoacidosis. The Pediatric Emergency Medicine Collaborative Research Committee of the American Academy of Pediatrics. N Engl J Med. 2001 Jan 25;344(4):2649.
27. Wiggam MI, et al. Treatment of diabetic ketoacidosis using normalization of blood 3- hydroxybutyrate concentration as the endpoint of emergency management. A randomized controlled study. Diabetes Care 1997: 20: 1347–1352.
28. Vanelli M, et al. The direct measurement of 3-beta-hydroxy butyrate enhances the management of diabetic ketoacidosis in children and reduces time and costs of treatment. Diabetes Nutr Metab 2003: 16(5–6): 312–316.
29. Ham MR, et al. Bedside ketone determination in diabetic children with hyperglycemia and ketosis in the acute care setting. Pediatr Diabetes 2004: 5: 39–43.
30. Rewers A, et al. Bedside monitoring of blood beta-hydroxybutyrate levels in the management of diabetic ketoacidosis in children. Diabetes Technol Ther 2006: 8: 671–676.
31. Prisco F, et al. Blood ketone bodies in patients with recent-onset type 1 diabetes (a multicenter study). Pediatr Diabetes 2006: 7: 223–228.
32. Noyes KJ, et al. Hydroxybutyrate near-patient testing to evaluate a new end-point for intravenous insulin therapy in the treatment of diabetic ketoacidosis in children. Pediatr Diabetes 2007:8: 150–156.
33. Klocker AA, et al. Blood beta-hydroxybutyrate vs. urine acetoacetate testing for the prevention and management of ketoacidosis in Type 1 diabetes: a systematic review. Diabet Med 2013: 30: 818–824.
34. Sheikh-Ali M, et al. Can serum beta-hydroxybutyrate be used to diagnose diabetic ketoacidosis? Diabetes Care 2008: 31: 643–647.
35. Corl DE, et al. Evaluation of point-of-care blood glucose measurements in patients with diabetic ketoacidosis or hyperglycemic hyperosmolar syndrome admitted to a critical care unit. J Diabetes Sci Technol. 2013 Sep 1;7(5):126574.
36. Kanter RK, et al. Arterial thrombosis causing cerebral edema in association with diabetic ketoacidosis. Crit Care Med 1987: 15: 175–176.
37. Roe TF, et al. Brain infarction in children with diabetic ketoacidosis. J Diabetes Complications 1996: 10: 100–108.
38. Rosenbloom AL. Fatal cerebral infarctions in diabetic ketoacidosis in a child with previously unknown heterozygosity for factor V Leiden deficiency. J Pediatr 2004: 145: 561–562.
39. Keane S, et al. Cerebral venous thrombosis during diabetic ketoacidosis. Arch Dis Child 2002: 86: 204–205.
40. Malone JI, et al. The value of electrocardiogram monitoring in diabetic ketoacidosis. Diabetes Care 1980: 3: 543–547.
41. Soler NG, et al. Electrocardiogram as a guide to potassium replacement in diabetic ketoacidosis. Diabetes 1974:23: 610–615.
42. Poirier MP, et al. A prospective study of the "two-bag system" in diabetic ketoacidosis management. Clin Pediatr (phila). 2004 Nov-Dec;43(9):80913.

43. Kitabchi AE. Low-dose insulin therapy in diabetic ketoacidosis: fact or fiction? Diabetes Metab Rev 1989;5:337-63.
44. Katz MA. Hyperglycemia-induced hyponatremia--calculation of expected serum sodium depression. N Engl J Med 1973;289:843-4.

45. Metzger D. Diabetic ketoacidosis in children and adolescents: An updated and revised treatment protocol. BC Medical Journal 2010;52:24-31.

46. Hillier TA, Abbott RD, Barrett 43. EJ. Hyponatremia: evaluating the correction factor for hyperglycemia. Am J Med 1999;106:399-403.

47. Curtis JR, et al. Use of hypertonic saline in the treatment of cerebral edema in diabetic ketoacidosis (DKA). Pediatr Diabetes 2001: 2:191–194.

48. Kamat P, et al. Use of hypertonic saline for the treatment of altered mental status associated with diabetic ketoacidosis. Pediatr Crit Care Med 2003: 4: 239–242.

50. Shabbir N, et al. Recovery from symptomatic brain swelling in diabetic ketoacidosis. Clin Pediatr (Phila) 1992: 31:570–573.

51. Roberts MD, et al. Diabetic ketoacidosis with intracerebral complications. Pediatr Diabetes 2001: 2: 109–114.

52. Brenkert TE, et al. Intravenous hypertonic saline use in the pediatric emergency department. Pediatr Emerg Care. 2013 Jan;29(1):71-3. doi: 10.1097/PEC.0b013e31827b54c3.

53. Banks CJ, et al. Review article: hypertonic saline use in the emergency department. Emerg Med Australas. 2008 Aug;20(4):294-305. doi:10.1111/j.1742- 6723.2008.01086.x. Epub 2008 May 6.

54. Franklin B, et al. Cerebral edema and ophthalmoplegia reversed by mannitol in a new case of insulin-dependent diabetes mellitus. Pediatrics 1982: 69: 87–90.

2023 Updates:

55. Canbulat Sahiner, N., Turkmen, A. S., Acikgoz, A., Simsek, E., & Kirel, B. (2018). Effectiveness of two different methods for pain reduction during insulin injection in children with Type 1 diabetes: Buzzy and ShotBlocker. Worldviews on Evidence-Based Nursing, 15(6), 464-470.

56. Philadelphia, T. C. H. of. (2023, January). Diabetic Ketoacidosis (DKA) Clinical Pathway—Emergency Department [Text]. The Children's Hospital of Philadelphia. https://www.chop.edu/clinical-pathway/diabetes-type1-with-dka-clinical-pathway

57. Children's Hospital of Orange County, CHOC Children's, Bg, R. Diabetic Ketoacidosis (DKA) Emergency Department 2 Bag System Care Guideline. (2020) https://www.choc.org/wp/wp-content/uploads/2020/11/DKACareGuideline-CriticalCare.pdf

58. Texas Children's Hospital. Nichols, J. (2019). TEXAS CHILDREN'S HOSPITAL. Diabetic Ketoacidosis (DKA) Clinical Guideline (May 2019). https://www.texaschildrens.org/sites/default/files/uploads/documents/outcomes/standards/DKA.pdf

59. Clinical Pathways | Children's Hospital Colorado. (n.d.). Retrieved June 26, 2023, Diabetic Ketoacidosis (DKA). (July 2021) https://www.childrenscolorado.org/health-professionals/clinical-resources/clinical-pathways/

60. UNMH Pediatric Diabetic Ketoacidosis Pathway, (January 2022) University of New Mexico. Guidelines and Pathways https://hsc.unm.edu/medicine/departments/emergency-medicine/_docs/clinical_resources/pediatric-ed/pedru-pathways/pediatric-diabetic-ketoacidosis-pathway.pdf

61.DKA Protocol. BC Children's Hospital. (2019), from http://www.bcchildrens.ca/health-professionals/clinical-resources/endocrinology-diabetes/dka-protocol

62.McKeon, A. (2023, January 26). A new way to measure DKA. Boston Children's Answers. https://answers.childrenshospital.org/dka-shortening-icu-stays/

63. Diabetic Hyperglycemia/DKA, .Johns Hopkins All Children's Hospital. (May 2022) https://www.hopkinsallchildrens.org/Health-Professionals/Clinical-Pathways/Diabetic-Hyperglycemia-DKA

64. MD, J. W., MD, Josh Bukowski. (2017, July 3). PEM Pearls: Treatment of Pediatric Diabetic Ketoacidosis and the Two-Bag Method. ALiEM. https://www.aliem.com/pediatric-diabetic-ketoacidosis-two-bag-method/

65. AHRQ Quality Indicators. (n.d.). Pediatric Quality Indicator 15 (PDI 15) Diabetes Short-term Complications Admission Rate June 2018. https://qualityindicators.ahrq.gov/

66. Fluid Infusion Rates for Pediatric Diabetic Ketoacidosis. (2018). New England Journal of Medicine, 379(12), 1181–1184. https://doi.org/10.1056/NEJMc1810064

67. Wolfsdorf, J. I., Glaser, N., Agus, M., Fritsch, M., Hanas, R., Rewers, A., Sperling, M. A., & Codner, E. (2018). ISPAD Clinical Practice Consensus Guidelines 2018: Diabetic ketoacidosis and the hyperglycemic hyperosmolar state. Pediatric Diabetes, 19(S27), 155–177. https://doi.org/10.1111/pedi.12701

68. Nallasamy K, Jayashree M, Singhi S, Bansal A. Low-Dose vs Standard-Dose Insulin in Pediatric Diabetic Ketoacidosis: A Randomized Clinical Trial. JAMA Pediatr. 2014;168(11):999–1005. doi:10.1001/jamapediatrics.2014.1211

69. Kuppermann, N., Ghetti, S., Schunk, J. E., Stoner, M. J., Rewers, A., McManemy, J. K., Myers, S. R., Nigrovic, L. E., Garro, A., Brown, K. M., Quayle, K. S., Trainor, J. L., Tzimenatos, L., Bennett, J. E., DePiero, A. D., Kwok, M. Y., Perry, C. S., Olsen, C. S., Casper, T. C., … Glaser, N. S. (2018). Clinical Trial of Fluid Infusion Rates for Pediatric Diabetic Ketoacidosis. New England Journal of Medicine, 378(24), 2275–2287. https://doi.org/10.1056/NEJMoa1716816

70. Glaser, N. S., Ghetti, S., Casper, T. C., Dean, J. M., Kuppermann, N., & Pediatric Emergency Care Applied Research Network (PECARN) DKA FLUID Study Group (2013). Pediatric diabetic ketoacidosis, fluid therapy, and cerebral injury: the design of a factorial randomized controlled trial. Pediatric diabetes, 14(6), 435–446. https://doi.org/10.1111/pedi.12027

DELL CHILDREN'S MEDICAL CENTER
EVIDENCE-BASED OUTCOMES CENTER

EBOC Project Owner: Dr. Nunez, MD

Approved by the Diabetes Management Evidence-Based Outcomes Center Team

Revision History

Original Draft Date Approved: March 7, 2016
Revisions June 2023: Updated Algorithms to align to Guideline updates and new order sets (Diabetes Admit, Ketosis-Serum, Ketosis-Urine, DKA). Implemented insulin drips in ED.
Next Review Date: June 2027

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