
Obstetrics Guidelines

SUBJECT: DIABETIC KETOACIDOSIS IN PREGNANCY

I. Overview

- A. Diabetic ketoacidosis (DKA) is an acute medical emergency associated with fetal loss rates in excess of 50%.
- B. Maternal mortality rates are generally less than 1%.
- C. DKA in pregnancy most commonly occurs in women with pregestational, insulin dependent diabetes who are poorly controlled or in women newly diagnosed with insulin dependent diabetes.
- D. DKA may be provoked by an exposure to a stress such as infection, surgery, or labor

II. Pathophysiology [See Appendix 1]

III. Signs and Symptoms of DKA:

Malaise	Nausea/Vomiting
Headache	Polyuria/polydypsia
Dry mouth	Shortness of breath
Weight loss	Abdominal pain
Dehydration	Mental status changes

IV. Diagnosis of DKA:

- A. Initial STAT labs include: CBC, serum electrolytes, BUN, creatinine, glucose, arterial blood gases, bicarbonate, urinalysis, lactate, serum ketones
- B. Blood sugar: DKA can occur with blood sugars less than 200 mg/dl in pregnancy
- C. Serum ketonemia: Positive, given in dilutional titer
- D. Acidosis: arterial pH less than 7.35**
- E. Electrolytes + Anion Gap: Defined as $Na - (Cl + HCO_3)$ greater than 12. The reduction in HCO_3 is proportional to the increase in concentration of keto acids and therefore, the anion gap = decrease in HCO_3

V. Treatment of Diabetic Ketoacidosis

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A. Goals of therapy

1. Re-hydration
2. Correction of acidemia
3. Normalization of serum glucose
4. Restoration of electrolyte homeostasis
5. Elimination of the underlying cause

B. Management Guideline

1. Make a clear diagnosis (Blood gas; blood sugar; anion gap; serum ketones)
2. Admit to L&D, APSD or medical intensive care unit per MFM discretion (typically a 12-24 hour period of intensive monitoring/treatment is anticipated). To contact UIMC Rapid Response team: Dial 778 [RRT]; give location to operator [see UIMC Clinical Care Guideline G 18-5 for details].
3. Frequent monitoring of maternal blood pressure, heart rate, pulse oximetry and continuous electronic fetal monitoring (as appropriate based on gestational age).
4. Hourly intake and output. Foley catheter should be placed in all severely obtunded or comatose patients.
5. Other labs as indicated include liver function test, chest x-ray, sepsis work-up and cultures.
6. Fluid replacement
 - a. Initial fluid (0.9 NS only)
Over first hour: 1 liter
Over next 2 hours: 500 ml/hr
Over next 4-6 hours: 250 ml/hr to replace Na deficit, to correct hypotension, increase urine output (if low)
 - b. After BP and urine output stabilize may change fluids to 0.45 NS at 250-500 cc/hr and then may decrease infusion rate

and

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- c. **Goal is correction of total fluid deficit over 12-24 hours. Typical needs range between 6-8 liters.**
 - d. When blood sugar falls below 250 mg/dl, add 5% Dextrose to IV fluids (D5 .45 NS) at 150-250 ml/hr to help prevent cerebral edema caused by rapid decrease in glucose. Insulin infusion should be continued to keep serum glucose between 150 and 200 mg/dL until metabolic control is achieved.
 - e. Avoid lactate-containing solution as this will aggravate acidosis.
9. Insulin therapy
- a. Blood sugar is monitored every 1 hour while on an insulin drip.
 - b. Initial dose of regular insulin is 0.4 units/kg as IV bolus
 - c. Begin insulin drip with regular insulin at 5-10 units/hour
 - d. Double insulin infusion rate if blood sugar is not decreased by 25% in 2 hours.
 - e. As blood sugar falls below 250 mg/dl add 5% dextrose to fluids as above (D5 .45 NS).
 - f. Decrease infusion to 1-2 units/hr as blood sugar falls below 150 mg/dl.
 - g. When the patient is eating, may switch to long-acting insulin.
10. Potassium replacement
- a. Loss usually 5-10 meq/kg. As acidosis is corrected, potassium will re-enter cell and serum potassium level will fall.
 - b. If the initial potassium level is normal or low begin replacement immediately with 10 meq/hr. Alternatively, KCl (40 meq/L) can be added to each liter of replacement fluid (rate of 150-250 ml/hr). This will give approximately 5-10 meq/hr replacement. The potassium dose should be reduced by 50% if the patient remains oliguric.
 - c. If the initial potassium is high, begin replacement at 10 meq/hr after adequate urinary output is established.

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- d. Replacement potassium concentration should never be greater than 40 meq/hr.
- e. Monitor potassium levels every 2-4 hours during treatment. Oral potassium should be given for 1 week after acute DKA to correct the total body deficit.

11. Correction of acidosis

- a. Most cases will correct with the above treatments. (If acidosis worsens, contact Rapid Response Team...DT to give contact info)
- b. Bicarbonates are rarely needed and should only be used if the pH is less than 7.10; this patient is gravely ill and is typically in an intensive care unit.
- c. Rapid correction of acidosis with bicarbonate will cause an iatrogenic metabolic alkalosis and a paradoxical fall in CSF pH. **This causes a worsening of cerebral acidosis and an increase in obtunded mental status.**

12. Broad spectrum antibiotics should be initiated pending results of sepsis work-up and cultures, if indicated.

13. Fetal considerations

- a. All pregnant patients with a >24 weeks, live fetus should be monitored continuously for fetal heart rate.
- b. Fetuses exposed to maternal acidosis may have decreased variability and late decelerations. The ominous patterns will typically correct themselves with correction of maternal metabolic disturbance. Maternal oxygen therapy is always useful in nonreassuring fetal heart rate.
- c. **Delivery of a compromised fetus should be undertaken ONLY after the mother is metabolically stable.**
- d. **Avoid use of betamimetics and corticosteroids while DKA is being controlled.**

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APPENDIX

PATHOPHYSIOLOGY

- A. DKA results from a relative or absolute lack of circulating insulin and/or an excess of counter regulatory hormones. In pregnancy, DKA is usually precipitated by a stressful event.
- B. Action of regulatory hormones are listed below:
1. Insulin: Promotes glucose uptake in fat, liver, and skeletal muscle. Stimulates adipocytes to store free fatty acids and inhibits lipolysis, gluconeogenesis, and glycogenolysis.
 2. Glucagon: Augments hepatic ketone production and increases glucose output by inducing glycogenolysis and gluconeogenesis. Reduces concentration of malonyl-coA by inhibiting synthesis (blocks acetyl-coA carboxylase) and by reducing 3 carbon precursors (suppress glycolysis and pyruvate kinase activity) with glucagon excess see a 300% enhancement in ketone production independent of free fatty acid availability.
 3. Catecholamines: Excreted during conditions of stress, dehydration, or acidosis and stimulates free fatty acid release and glycogenolysis. Also stimulates cellular alpha receptors which blunt liver and tissue response to insulin.
 4. Cortisol: Also released under conditions of stress and enhances ketone production.
 5. HPL, Prolactin: Decrease glucose tolerance, increase insulin resistance, decrease storage of hepatic glycogen and increase glucose production.

Basic Mechanism of DKA

- A. Decreasing insulin/glucagon ratio interrupts normal production and disposal of glucose and causes hyperglycemia and ketosis.
- B. Because of the inability to use glucose, oxidative metabolism of ketones occurs. This process yields b-hydroxybutyrate and acetoacetate which decrease pH, increase respiratory rate and cause a compensatory respiratory alkalosis.
- C. The metabolic buffering system is depressed.

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- D. Gluconeogenesis in the liver adds to hyperglycemia and decreased liver amino acid stores.
- E. Increased osmotic pressure leads to fluid and electrolyte imbalance with increased water and electrolyte loss.
- F. Acidosis causes potassium to leave the intracellular space in exchange for hydrogen ions. The serum potassium concentration may be normal but total body stores are low.
- G. As dehydration continues there is a progression to decreased cardiac output, hypotension, shock, and death.

Laboratory Changes in DKA

- A. Blood sugar: DKA can occur with blood sugars less than 200 mg/dl in pregnancy.
- B. Serum Ketonemia: Positive, given in dilutional titer.
- C. Urinalysis: Evidence of ketonuria and glucosuria (both need to be present).
- D. Acidosis: arterial pH less than 7.35.
- E. + Anion Gap: Defined as $\text{Na} - (\text{Cl} + \text{HCO}_3)$ greater than 12. The reduction in HCO_3 is proportional to the increase in concentration of keto acids and therefore, the anion gap = decrease in HCO_3 .
- F. Electrolytes: Decrease in sodium (<135 mg/dL) and potassium (initially values are in the normal range and will trend down as DKA resolves).
- G. Pre renal azotemia.
- H. Liver enzymes: may see slight increase.
- I. Water Deficit: secondary to osmotic diuresis; on the order of 100-150 ml/kg or 4-12 liters.
- J. Lactate: should be normal or just minimally elevated

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REFERENCES

1. ACOG Technical Bulletin #200, December, 2001
2. Brunfield CG, Huddleston JF: The management of diabetic ketoacidosis in pregnancy. Clin Obstet Gynecol 1984; 27:50.
3. Drury MI, Greene AT, Stronge JM: Pregnancy complicated by clinical diabetes mellitus: A study of 600 pregnancies. Obstet Gynecol 1984; 27:50.
4. Gabbe, SG, Graves, CR. Management of Diabetes Mellitus Complicating Pregnancy [High-Risk Pregnancy Series: An Expert's View]. Obstetrics & Gynecology. ACOG, 102 (40, October, 2003, p857-868.
5. Genuth SM: Constant intravenous insulin infusion in diabetic ketoacidosis. JAMA 1973; 223:1348.
6. Golde SH: Diabetic ketoacidosis in pregnancy. In Clark SL, Phelan JP, Cotton DB (Eds): Critical care obstetrics. Medical Economics Co, MJ 1987.
7. Hollingsworth DR, Cousings L: Endocrine and Metabolic disorders: Disorders of carbohydrate metabolism. In Creasy RK, Resnik R (Eds) Maternal Fetal Medicine. CV Mosby Co., 2004 ;
8. Lobue C, Goodlin RC: Treatment of fetal distress during diabetic ketoacidosis. J Reprod Med 1978; 20:101.
9. Nelson DM: Diabetes and pregnancy. In Arias F (Eds) High Risk Pregnancy and Delivery. CV Mosby Co., 1984.
10. Ramin, Kirk. Diabetic Ketoacidosis in Pregnancy. Obstetrics and Gynecology Clinics. 1999; 26:481-488.

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