Starvation Ketosis Versus Euglycemic Diabetic Ketoacidosis in Pregnancy: A Case Report Highlighting the Diagnostic Overlap

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ABSTRACT

Introduction: Starvation ketosis in pregnancy, though rare, is increasingly recognized, underscoring the need for a better understanding of its pathophysiology. Prolonged fasting or inadequate carbohydrate intake leads to elevated ketone levels, which can adversely affect maternal and fetal health. Early diagnosis via ketone monitoring and clinical assessments, is essential. The clinical presentation and laboratory profile of starvation ketosis overlap with euglycemic diabetic ketoacidosis (DKA), often creating a diagnostic dilemma.

Case Presentation: A 28-year-old female with gestational diabetes presented at 37 weeks of gestation with a 3-day history of nausea, vomiting, and abdominal pain. She had been unable to eat for 60 hours, consuming only small sips of water. Laboratory workup revealed high-anion gap metabolic acidosis with elevated β-hydroxybutyrate. Other causes of high-anion gap metabolic acidosis were ruled out, leading to a diagnosis of starvation ketosis versus euglycemic DKA. The patient was treated with dextrose supplementation to meet caloric needs, along with an insulin infusion. As her nausea improved, she tolerated an oral diet and was gradually weaned off intravenous dextrose. She recovered well and delivered a healthy infant at 38 weeks of gestation via spontaneous vaginal delivery.

Discussion: During starvation, the body transitions from glucose to lipid metabolism, producing ketone bodies as an alternative energy source. While ketoacidosis typically develops after 10 to 14 days in nonpregnant individuals, pregnancy-induced insulin resistance increases susceptibility, allowing ketoacidosis to develop within 24 hours, particularly in the third trimester.

Conclusions: Treatment of starvation ketosis in pregnancy involves aggressive caloric replacement through dextrose infusions and insulin supplementation. Early intervention and maintaining a high index of clinical suspicion are crucial to prevent adverse complications for both mother and fetus.

INTRODUCTION

Ketoacidosis during pregnancy can be manifested as both diabetic ketoacidosis (DKA) and starvation ketosis. Starvation ketosis in pregnancy is a metabolic state that occurs when the body shifts from using glucose to ketone bodies as a primary energy source due to prolonged fasting or inadequate caloric intake.[1] During pregnancy, maternal metabolism undergoes significant adaptations to support fetal growth, including increased insulin resistance and enhanced fat metabolism. These changes predispose pregnant individuals to ketosis and metabolic acidosis during periods of caloric deprivation, which can adversely affect maternal and fetal health. Euglycemic DKA is a close differential diagnosis for starvation ketosis.[1]

We report a case of ketoacidosis in late pregnancy that presents such a conundrum. The patient was successfully managed with dextrose and insulin infusions. The intricate underlying biochemical interactions and hormonal changes that predispose pregnant females to this condition are discussed.

CASE PRESENTATION

A 28-year-old female with a history of gestational diabetes presented at 37 weeks of gestation with nausea, vomiting, and abdominal pain of 3 days' duration. During this time, she was unable to eat for 60 hours and only consumed only small sips of water. She was diagnosed with gestational diabetes at 34 weeks and was started on 4 units of insulin aspart before supper. Her

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home blood glucose levels usually ranged from 90 to 150 mg/dL. Upon admission, she was in acidosis, with a pH of 7.22 (reference range, 7.32–7.42), bicarbonate level of 9 mmol/L (reference range, 21–33mmol/L), anion gap of 17 mmol/L (reference range, 2–16 mmol/L), and β-hydroxybutyrate level of 5.11 mmol/L (reference range, 0.00–0.39 mmol/L).

In the context of gestational diabetes with high-anion gap metabolic acidosis, the differential diagnoses included DKA, starvation ketoacidosis, and alcoholic ketoacidosis. The patient's glycated hemoglobin (HbA1C) was 5.3%. DKA was considered less likely due to normal blood glucose levels and the absence of sodium-glucose cotransporter 2 (SGLT2) inhibitor use. Nevertheless, given the history of gestational diabetes, euglycemic DKA of pregnancy was also considered. She reported no alcohol consumption in the prior 3 days, and serum ethanol levels were undetectable; thus, alcoholic ketoacidosis was unlikely.

A septic workup, including white blood cell count, lactic acid level, and inflammatory markers, yielded normal results. The patient denied exposure to chemicals such as antifreeze or excessive use of acetaminophen. Serum methanol, acetaminophen, and isopropyl alcohol levels were undetectable.

Starvation ketoacidosis was considered the more likely diagnosis due to the patient's prolonged fasting and the high caloric requirements of the third trimester. In the first 24 hours, she received 4 L of 5% dextrose, equivalent to 200 g of dextrose (800 kcal). With glucose infusion, her blood glucose levels increased to 140 to 160 mg/dL. She was started on a regular insulin infusion at 50 units over 24 hours. However, she continued to experience nausea, which limited her ability to eat solid food. During the first 24 hours of hospitalization, her acidosis resolved (Table).

Because the patient received only 800 kcal despite 4 L of 5% dextrose, we changed the intravenous (IV) fluid to 10% dextrose on day 2. She received 5 L of 10% dextrose, equivalent to 500 g of dextrose (2000 kcal), and 97 units of regular insulin via infusion. Due to a substantial potassium deficit, she required approximately 200 mEq of potassium replacement, resulting in potassium levels ranging from 3.6 to 3.8 mEq/L. With adequate caloric supplementation after 24 hours, her β-hydroxybutyrate level normalized to 0.06 mmol/L and her anion gap decreased to 9 mmol/L.

The patient had a prepregnancy body mass index classified as obese. On admission, her weight was 160 lb (72.5 kg). Accounting for the additional calorie needs of the third trimester, her estimated caloric needs were 2268 to 2631 kcal per day.[2] During the first 24 hours, she consumed minimal liquids and no solid food. Her oral intake was less than 100 kcal in the initial 24 hours after admission. To meet the caloric requirements, she received continuous glucose and insulin infusions to avoid hyperglycemia.

By day 3, her condition improved with symptomatic relief and resolution of ketoacidosis. She was able to tolerate solid food but struggled to meet the caloric requirement of at least 2500 kcal/day. Consequently, she remained on 10% dextrose infusions targeting blood glucose levels around 100 mg/dl and was transitioned to a basal-bolus insulin regimen with 20 units of insulin glargine twice daily and supplemental insulin lispro every 4 hours. By day 4, she tolerated 3 meals a day and was discharged home with follow-up scheduled in 2 to 3 days. She later delivered a healthy female infant at 38 weeks of gestation through spontaneous vaginal delivery.

Table. Laboratory Values in the First 24 Hours of Admission

	At Admission	12 Hours	24 Hours
pH	7.22	7.31	
pCO_2 (mmHg)	27	23	
Serum bicarbonate (mg/dL)	9	12	15
Anion gap (mmol/L)	17	18	7
Glucose (mg/dL)	158	111	116
Beta hydroxy butyrate (mmol/L)	5.11	2.20	0.06
Lactate (mmol/L)	0.7		
Urine analysis	3+ ketones		
Potassium (mEq/L)	4.5	3.5	3.6

Abbreviations: pCO2, partial pressure of carbon dioxide

DISCUSSION

Understanding normal metabolism is crucial for grasping abnormalities associated with disease. When carbohydrate stores are adequate, glucose serves as the primary fuel for most tissues and is metabolized through glycolysis. Aerobic tissues metabolize pyruvate to acetyl-CoA, which enters the citric acid cycle for complete oxidation to carbon dioxide and water molecules. This is linked to the formation of adenosine triphosphate (ATP) in the process of oxidative phosphorylation. Glycolysis can also occur anaerobically (in the absence of oxygen), resulting in lactate as the end product.[3]

During starvation, the body transitions from carbohydrate to lipid metabolism for energy, conserving glucose for the central nervous system and red blood cells. This shift is regulated by low insulin and high epinephrine and norepinephrine levels, which stimulate the release of long-chain fatty acids and glycerol from peripheral fat stores by increasing intracellular cyclic adenosine monophosphate (cAMP) levels, leading to the phosphorylation and activation of hormone-sensitive lipase.[4]

These fatty acids are then transported into hepatocytes, where they undergo β-oxidation in the mitochondria to generate acetyl-CoA. When acetyl-CoA levels are elevated, they enter the ketogenic pathway, leading to the production of ketone bodies—acetoacetate and 3-hydroxybutyrate. These ketone bodies are released into the bloodstream and serve as an alternative energy source for various tissues, including the brain, thus maintaining energy homeostasis during prolonged fasting.[1]

In the nonpregnant population, this process typically occurs at moderate levels, preventing ketoacidosis. High ketone body concentrations stimulate insulin release (despite low glucose levels), increasing adipose tissue sensitivity to insulin's inhibitory effect on fatty acid release; furthermore, ketone bodies directly inhibit lipol-

ysis. Thus, it typically takes 10 to 14 days of starvation for ketoacidosis to develop in nonpregnant individuals. In contrast, during pregnancy, hormonal changes—including placental hormones such as glucagon-like peptides and human placental lactogen—cause relative insulin resistance. This makes pregnant individuals more prone to ketosis, especially in the third trimester, with ketoacidosis developing as early as 24 hours into starvation.[1] This vulnerability is underscored by the significantly increased energy demands of late-stage pregnancy. According to the Academy of Nutrition and Dietetics, women with a healthy prepregnancy weight require an average of 2200 to 2900 kcal/d.[2] While the first trimester typically does not require additional calories, the second and third trimesters necessitate an extra 340 and 450 kcal, respectively.[2] When these heightened metabolic requirements are unmet, even brief periods of fasting can rapidly precipitate ketosis.

Distinguishing between starvation ketoacidosis and euglycemic DKA in pregnancy is diagnostically challenging. Both conditions can present with elevated serum β-hydroxybutyrate, acetonemia, and ketonuria.[5-11] In the case described, prolonged fasting for 60 hours likely precipitated ketosis, which was exacerbated by the underlying insulin resistance of gestation, making euglycemic DKA the most plausible diagnosis. The rapid correction of acidosis with caloric replacement supports starvation ketoacidosis of pregnancy as the likely etiology.

Given the overlapping laboratory profiles and clinical features, differentiating starvation ketoacidosis from euglycemic DKA in pregnancy requires careful consideration of the illness trajectory and response to treatment. Acknowledging this diagnostic dilemma is crucial, as it underscores the need for heightened clinical suspicion and prompt treatment in pregnant patients presenting with ketoacidosis, regardless of their glycemic status. It is often difficult to clearly distinguish between the two conditions. Nevertheless, treatment with adequate calories, insulin supplementation to avoid hyperglycemia, and correction of electrolyte imbalance is the mainstay of management in both conditions.

CASE STUDIES

A review of the literature reveals previous case reports by JM Land,[6] Cecere et al,[7] Mahoney et al,[12] and Sinha et al,[13] which describe pregnant patients in their third trimester presenting with acidosis (pH 7.0-7.2). These patients were managed with IV fluids with or without 5% or 10% dextrose and, in some cases, sodium bicarbonate. Subsequently, they underwent emergent cesarean deliveries, resulting in either healthy deliveries or stillbirths. Additional case studies by Patel et al[8] and Frise et al[9] also report fluid resuscitation alone, following which their patients underwent emergent cesarean deliveries to prevent maternal and fetal complications.

In contrast, our patient was managed with caloric replacement using 10% dextrose, supplemented with insulin infusion to avoid hyperglycemia and electrolyte replacement. This approach effectively reversed ketoacidosis, leading to a healthy vaginal delivery at 38 weeks gestation without emergent surgical intervention. Chausse et al[10] also reported treating a 24-year-old patient with 10% dextrose and insulin, resulting in an uncomplicated vaginal delivery at 38 weeks. Karpate et al[11] described managing a patient with fixed-dose insulin as well, which led to the delivery of a healthy infant.

To our knowledge, there is no reported literature detailing the diagnostic overlap between starvation ketosis and euglycemic DKA. However, euglycemic DKA in pregnancy is well documented in multiple case reports by Yasin et al,[5] Karpate et al,[11] Jaber et al,[14] Chico et al,[15] and Wazir et al,[16] where patients were managed per DKA protocols. These patients usually had a history of type 1 or type 2 diabetes prior to pregnancy, and DKA was usually triggered by infections such as COVID- 19, urinary tract infection, or other intercurrent illness.

CONCLUSIONS

Starvation ketosis in pregnant women, particularly during the third trimester, is increasingly recognized due to hormonal changes that cause relative insulin resistance and heightened caloric needs. As demonstrated in this case, even brief periods of fasting can precipitate ketosis.

This case study highlights the importance of maintaining a high index of suspicion for starvation ketosis and the need for timely caloric replacement during pregnancy, typically through dextrose and insulin supplementation. If IV dextrose does not quickly reverse acidosis, clinicians should investigate other potential causes of high-anion gap metabolic acidosis. Ultimately, early recognition and appropriate nutritional management are vital to prevent life-threatening complications for both mother and fetus.

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