Case Report

Euglycemic Diabetic Ketoacidosis in Pregnancy: A Case Report and Review of Current Literature

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Diabetic ketoacidosis (DKA) in pregnancy is associated with high fetal mortality rates. A small percentage of DKA occurs in the absence of high glucose levels seen in traditional DKA. Prompt recognition and management is crucial. We report a case of a 30-year-old pregnant woman with type 1 diabetes mellitus admitted with euglycemic DKA (blood glucose <200 mg/dL). Initial laboratory testing revealed a severe anion gap acidosis with pH 7.11, anion gap 23, elevated β-hydroxybutyric acid of 9.60 mmol/L, and a blood glucose of 183 mg/dL—surprisingly low given her severe acidosis. The ketoacidosis persisted despite high doses of glucose and insulin infusions. Due to nonresolving acidosis, her hospital course was complicated by spontaneous intrauterine fetal demise. Euglycemia and severe acidosis continued to persist until delivery of fetus and placenta occurred. It was observed that the insulin sensitivity dramatically increased after delivery of fetus and placenta leading to rapid correction of ketoacidosis. This case highlights that severe ketonemia can occur despite the absence of severely elevated glucose levels. We discuss the mechanism that leads to this pathophysiologic state and summarize previously published case reports about euglycemic DKA in pregnancy.

1. Introduction

Euglycemic diabetic ketoacidosis (EDKA) is a biochemical triad consisting of blood glucose level less than 200 mg/dL, increased anion gap metabolic acidosis, and ketonemia [1]. The incidence of EDKA is reportedly between 0.8% and 1.1% of all pregnant DKA cases [2]. Euglycemia presents a diagnostic challenge often leading providers to believe ketoacidosis is less severe. As a result, EDKA can frequently go unrecognized. Prompt recognition of EDKA is critical in pregnancy, since fetal demise can be as high as 35% without appropriate treatment [3]. We report a case of EDKA in the third trimester of pregnancy and discuss the management challenges in a patient with euglycemia and a high ketone burden. We also summarize other reported cases of EDKA (Table 1).

2. Case Presentation

A 30-year-old gravida 2 para 0101 (0 full term, 1 preterm, 0 abortions, and 1 live child) woman at 32 weeks, 3 days gestation presented to our hospital with a two-day history of nausea and vomiting. Her prior medical history included type 1 diabetes mellitus on continuous glucose monitoring and insulin pump. She has had a history of prior episodes of diabetic ketoacidosis requiring hospitalization; however, as her home glucose readings were only marginally elevated at 100–200 mg/dL, she did not think to present to the hospital sooner than she did. Upon initial examination in the emergency department, she appeared uncomfortable with Kussmaul breathing. Fetal heart monitoring showed absent variability and recurrent late decelerations. Her initial admission laboratory results showed a blood glucose of 183 mg/dL, acidosis with an anion gap of 23, pH 7.11, β-hydroxybutyric acid (β-HA) 9.6 mmol/L (normal 0.02–0.27 mmol/L), and lactate 0.65 mmol/L (normal 0.3–1.5 mmol/L). The patient was admitted to the high risk obstetrics service for further management of her acidosis and resulting fetal distress. As the patient was initially euglycemic, insulin infusion was initiated at 2 units/h as per the institution’s DKA protocol. After four liters of bolus intravenous fluids, a maintenance fluid rate of 5% dextrose/0.45% NaCl solution at 250 mL/h was initiated.
Approximately four hours after admission, the patient's euglycemia continued to persist with serum glucose readings averaging 165 mg/dL (Figure 1). Given this euglycemia, the obstetrics team continued to cautiously titrate the patient's insulin drip. Over the next hour, her acidosis progressively worsened with a blood pH nadir of 6.97. Fetal heart tracings continually deteriorated. Unfortunately, the patient was not a surgical candidate for emergent fetal delivery due to her severe acidosis. Bicarbonate containing maintenance fluids were not utilized; however, a total of seven ampules of bicarbonate were administered to the patient throughout her hospitalization to attempt to stabilize the fetus, though bicarbonate containing drips were never initiated. The obstetrics team at this time consulted the medical intensive care unit (MICU) for assistance with further management. At this time, the MICU team consulted endocrinology for assistance with management. The patient's fluids were changed to a 10% dextrose containing fluids at 250 mL/h with the goal of intensifying the insulin infusion to correct the ketoacidosis. Despite this, however, the patient's respiratory status declined to the point of requiring intubation and mechanical ventilation. Approximately eight hours after admission, the fetal heart rate became difficult to detect, and intrauterine fetal demise was declared.

| Authors            | Age (years) | Diabetic history | Gestational age | Admission blood glucose (mg/dL) | Outcome of mother | Outcome of fetus  |
|--------------------|-------------|------------------|----------------|---------------------------------|--------------------|-------------------|
| Bryant et al. [18] | 33          | Type 2 diabetes  | Third trimester | 134                             | Discharged home    | Emergent C-section at 35 weeks |
| Cardonell et al. [19] | 29          | Type 1 diabetes mellitus | Third trimester, 35 weeks | 87                             | Discharged home    | Nonemergent C-section at 34 weeks |
| Chico et al. [14]  | 29          | Gestational diabetes | Third trimester, 36 weeks | 140                            | Discharged home    | Nonemergent C-section at 36 weeks |
| Clark et al. [20]  | 34          | Gestational diabetes | Third trimester, 36 weeks | 140                            | Discharged home    | Nonemergent C-section at 36 weeks |
| Cullen et al. [21] | 30          | Type 1 diabetes mellitus | Third trimester, 36 weeks | 95                             | Discharged home    | Elective C-section at 39 weeks |
| Darbhamulla et al. [22] | 30          | Gestational diabetes | Third trimester, 33 weeks | 95                             | Discharged home    | Delivery at 38 weeks |
| Franke et al. [15] | 23          | Gestational diabetes | Third trimester, 32 weeks | 127                            | Discharged home    | Elective C-section at 35 weeks |
| Frise et al. [23]  | 40          | Gestational diabetes | Third trimester, 35 weeks | 52–85                           | Discharged home    | Delivery at 38 weeks |
| Guo et al. [4]     | 29          | Unknown           | Third trimester, 32 weeks | 124                            | Discharged home    | Intrauterine fetal demise |
| Kamalakannan et al. [24] | 28          | Type 1 diabetes mellitus | Third trimester, 36 weeks | 234                            | Discharged home    | Delivery at 37 weeks |
| Karpate et al. [25] | 25          | Unknown           | Third trimester, 37 weeks | 103                            | Discharged home    | Unknown |
| Lucero and Chapela [13] | 22          | Type 1 diabetes mellitus | First trimester, unknown weeks | 153                           | Discharged home    | Unknown |
| Madaan et al. [26] | 30          | Type 2 diabetes mellitus | Third trimester, 36 weeks | 75–155                          | Discharged home    | Elective C-section at 38 weeks |
| Madaan et al. [26] | 23          | Gestational diabetes | Third trimester, 34 weeks | 89–164                          | Discharged home    | Elective C-section at 37 weeks |
| Montoro et al. [27] | 26          | Type 1 diabetes mellitus | Third trimester, 34 weeks | 211                            | Discharged home    | Elective C-section at 34 weeks |
| Oliver et al. [28] | 29          | Type 1 diabetes mellitus | Third trimester, 28 weeks | 245                            | Discharged home    | Elective C-section at 34 weeks |
| Rivas et al. [29]  | 39          | Gestational diabetes | Third trimester, 32 weeks | 120                            | Discharged home    | Emergent C-section at 32 weeks |
| Tarif and Al Badr [30] | 37          | Type 2 diabetes mellitus | Third trimester, 35 weeks | 77                             | Discharged home    | Unknown |
| Yu et al. [31]     | 30          | Type 2 diabetes mellitus | Third trimester, 28 weeks | 121                            | Discharged home    | Elective C-section at 36 weeks |
Insulin dose (units/h)

production increases with advancing gestational age [5]. In

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Despite fetal demise, the patient's insulin requirements
were still larger than expected at 7 units/h. Endocrinology
believed that this was secondary to the placental hormones
still in the patient's circulation causing significant peripheral
insulin resistance. It was determined that until delivery
occurred, the patient would continue to have significant insu-
lin resistance. As soon as one hour after delivery, the patient's
insulin sensitivity rapidly improved, and glucose sequestration
by the placental circulation disappeared. Acidosis began to
rapidly improve. Her glucose now ranged between 200 mg/dL
and 400 mg/dL. Her insulin drip was rapidly weaned to
3 units/h, pH continued to rise to 7.33, and the anion gap
closed to 7 (Figure 1). The patient was extubated on hospital
day 2, and was discharged home three days later without any
further events.

3. Discussion

EDKA during pregnancy is an obstetric and medical emer-
gency. It is characterized by a state of marked insulin resis-
tance, severe electrolyte derangement, and only marginal
elevation of serum glucose. Early recognition and manage-
ment are crucial, since prolonged ketosis is associated with
neurologic complications, and even death in the fetus.

The incidence of DKA is higher in pregnant patients
compared to nonpregnant patients, 8.9% vs. 3.1%, respectively
[4]. A number of physiologic changes occur in pregnancy
predisposing one to severe ketoacidosis [4]. This occurs via
multiple mechanisms, the first being marked insulin resistance
during pregnancy from several hormones including human
placental lactogen, placental insulinase, and progesterone.
These hormones peak in the second and third trimesters and
can inhibit the effects of maternal insulin resulting in relative
insulin deficiency [4]. This could explain why DKA is most
common during the second and third trimesters (Table 1).
To compensate for the increased insulin resistance, insulin
production increases with advancing gestational age [5]. In

our case, it is likely that the mother had relative insulin
deficiency in the setting of an acute illness and underlying
insulin resistance leading to ketosis. Other contributory fac-
tors for increased incidence of DKA in pregnancy include
lower serum bicarbonate levels (19–20 mEq/L), which occur
as a compensatory mechanism for pregnancy-induced
respiratory alkalosis.

The mechanism underlying ketosis in pregnancy is similar
to that of nonpregnant patients. Ketosis occurs much more
rapidly in diabetic patients that are pregnant. In the third
trimester alone, the maternal metabolic rate increases by an
average of 30% compared to prepregnancy [6]. As a result,
even short periods of starvation in pregnant patients
predispose them to developing ketosis. Metzger et al. showed
that pregnant patients had higher levels of free fatty acids and
β-HA after a 12 h fast compared to nonpregnant patients [7].
This might serve as a mechanism to provide nutrition to the
fetus during periods of decreased caloric intake. In our case,
the patient had decreased oral intake for 36 h prior to pres-
entation. The relative insulin deficiency, prolonged starvation,
and upregulation of counterregulatory hormones were the
likely driving factors for the severe ketonemia observed in our
patient.

Not only does ketosis occur much more rapidly in pregnant
diabetic patients, it also occurs at much lower serum glucose
levels compared to nonpregnant patients [4]. The proposed
mechanisms are as follows. First, placental glucose transporters
(GLUT-1, GLUT-4, and GLUT-9) are increased during preg-
nancy. Among those on insulin therapy, placental expression
of these receptors is increased even further [8]. As a result of
increased placental glucose transporters, maternal levels may
be only marginally elevated despite a high ketone burden.
Second, euglycemia may also occur due to the physiologic
hemodilution that occurs due to increased plasma volume in
pregnancy [9]. Third, glomerular filtration rate can increase by
60% from the first trimester to around 4 weeks postpartum,
contributing to an osmotic diuresis and thus, absence of
marked hyperglycemia despite a high ketone burden [10].

DKA during pregnancy is associated with multiple imme-
 diate and late fetal complications. Immediate complications
include high fetal mortality rates at 27%–35%, decreased uter-
ine perfusion, fetal hypoxia, and recurrent late decelerations
[3, 11, 12]. Our patient had multiple late decelerations on
presentation likely reflecting the severity and duration of
acidosis. Generally, it is recommended to continue the preg-
nancy while attempts are made to identify and correct the
physiologic derangement. Typically, once the acidosis is
corrected, fetal abnormalities improve [4, 12 – 16]. Emergent
cesarean delivery should only be attempted if the maternal
condition worsens, but this is associated with high maternal
morbidity and mortality. Long term effects of ketoacidosis
include impaired brain development. One study found an
inverse relationship with maternal ketonemia and mental
development index scores (lower scores indicating inadequate
development) at two years of age [17]. Prevention remains a
key aspect of managing diabetic pregnant patients. Women
should be counseled on checking serum ketones in cases of
acute illness or if blood glucose levels begin to rise above their
baseline.

![Blood glucose levels and insulin drip rates throughout the patient's hospitalization by day and time of significant events.](image1)

**Figure 1:** Blood glucose levels and insulin drip rates throughout the patient's hospitalization by day and time of significant events.
4. Conclusions
Despite a normal presenting blood glucose level, it is imperative to have a high suspicion for ketoacidosis in an acidic pregnant patient with diabetes mellitus or gestational diabetes. Placental sequestration of blood glucose can make DKA a diagnostic and therapeutic challenge. Serum ketones must be checked in any diabetic patient during periods of illness. High doses of insulin may be required despite euglycemia to correct acidosis and ketonemia.

Our case highlights the diagnostic and treatment challenges associated with EDKA, and its accompanying complications including fetal demise. The mainstay of treatment remains early recognition and timely administration of fluids, carbohydrates, and insulin.

Conflicts of Interest
The authors declare that they have no conflicts of interest.

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