International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

Management and Challenges of Diabetic Ketoacidosis in Pregnancy: A Multidisciplinary Approach

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Abstract: ***This article examines the management and challenges associated with diabetic ketoacidosis (DKA) during pregnancy, a serious complication of diabetes that poses risks to both the mother and fetus. DKA in pregnancy is characterized by uncontrolled hyperglycaemia, metabolic acidosis, and ketosis, and can be triggered by factors such as non-compliance with treatment, infections, and excessive vomiting. The article presents case studies highlighting different clinical scenarios, diagnostic criteria, and treatment strategies. Improved antenatal care and screening have led to a decline in DKA incidence, but it remains a significant concern due to its rapid onset and potential delays in diagnosis. The article emphasizes the importance of a multidisciplinary approach involving obstetricians, endocrinologists, and other specialists in managing DKA during pregnancy. Early recognition, aggressive management, and addressing underlying factors are crucial for improving maternal and fetal outcomes.***

Keywords: Diabetic ketoacidosis, pregnancy, management, multidisciplinary approach, hyperglycaemia

1. Background

Diabetic ketoacidosis (DKA) is a dreadful acute complication of diabetes and is a life-threatening condition for the mother as well as the fetus. It is characterized by uncontrolled hyperglycemia, metabolic acidosis and ketosis[1]. Although it is more commonly seen in case of type 1 diabetes, it has been recognized in type 2 diabetes and rarely in gestational diabetes, affecting 0.5-3% of diabetic pregnancies[1]. Ketoacidosis can precipitate in conditions of excessive stress, excessive vomiting, diarrhea, infection, preterm labour and others. DKA during pregnancy affects the fetus both at the time of the event and following. The risk of fetal demise has decreased overtime but remains substantially higher than the baseline risk (2-3%) in women with type 1 diabetes[2].

With improved antenatal diabetes screening and the availability of early and frequent prenatal care, the incidence of diabetic ketoacidosis in pregnancy has declined. However, it is still a major concern in pregnancy since it tends to occur more rapidly than in non-pregnant patients often causing delay in diagnosis. The purpose of this article is to exemplify series of cases of DKA in pregnancies and review the literature on this rare alarming condition.

Case 1
A 33 years old female G2P1L1 with known type 2 diabetes for 4 years presented at 29 weeks POG with acute onset of breathlessness and altered sensorium since morning. Patient's husband gave history of patient being non complaint with insulin and oral hypoglycemic agents and had poor antenatal visits. On examination, patient was drowsy and not responding to command (GCS E3V2M4), had tachypnea, tachycardia and oxygen saturation was 88% on room air and 100% on NRBM. On local examination, patient had perianal abscess. Fetal bradycardia was noted on doppler and later there was intrauterine fetal demise which was confirmed by obstetric scan.

Investigations
Total leukocyte count: 19800/cumm; plasma random glucose: 451 mg/dl; Serum sodium: 130 mEq/L; Serum potassium: 6.68 mEq/L; Serum bicarbonate: 3.9 mEq/L; Hba1c: 8.9%; Serum CRP: 254.86 mg/dl; Serum creatinine: 1.17 mg/dl; Serum urea: 36 mg/dl; Arterial blood pH: 6.85; Arterial pCO2: 12 mm Hg; Arterial pO2: 142 mm Hg; Arterial bicarbonate: 0 mmol/L; Arterial lactate: 1.6 mmol/L; Arterial blood glucose: 464 mg/dl; urine ketone bodies: 3+; urine sugar: 3+; Pus culture showed growth: Staphylococcus aureus and candida species (non candida albicans); chest radiograph: normal; Echo showed grade 1 TR with mild PAH

Management
Patient was admitted in intensive care unit and resuscitated with oxygen supplementation, iv fluids, iv antibiotics, insulin infusion as per the protocol for diabetic ketoacidosis and bicarbonate correction. Surgery reference sought and perianal abscess drained. Once patient was stabilized and acidosis was reversed, delivery was induced. Patient was then continued on iv antibiotics, insulin and started on OHAs. Patient improved gradually. She was shifted to ward and started on physiotherapy. Patient improved symptomatically and was then discharged on oral antibiotics and OHAs.

Case 2
A 36 years old female, G4P1L1A2 at 31 weeks POG with a known case of hypothyroidism and with gestational hypertension on antihypertensives came with complaints of breathlessness and vomiting since 1 day and sudden altered sensorium. Patient was a known case of type 2 diabetes since 7 years and was non complaint with insulin since 2 years. Patient had renal abscess 2 years ago which was drained and stent was placed for 2 years. On examination, patient had tachypneic with a saturation of 70% on room air, tachycardia and elevated BP readings. GRBS was 326 mg/dL. Bilateral crepitations with rhonchi were present on auscultation. USG showed intrauterine fetal demise.

Investigations
Total leukocyte count: 16900/cumm; plasma random glucose: 402 mg/dl; Serum sodium: 126 mEq/L; Serum potassium: 5.82 mEq/L; Serum chloride: 97 mEq/L; Hba1c: 7.8%; Serum creatinine: 2.39 mg/dl; Serum urea: 52 mg/dl; Serum CRP: 150.67 mg/L; Serum albumin: 2.59g/dL; Arterial blood pH: 7.04; Arterial pCO2: 46 mm Hg; Arterial pO2: 32 mm Hg; Arterial bicarbonate: 14.3 mmol/L; Arterial lactate: 4.3 mmol/L; Arterial blood glucose: 382 mg/dl; Troponin I: 0.10 ng/ml; Blood culture showed growth: Coagulase negative staphylococci and enerococcus faecalis; Urine culture: Acinetobacter baumanni and Candida glabrata; ET culture: Acinetobacter baumannii; Echo showed global LV hypokinesia and severe LV dysfunction with ejection fraction 30%

Management
Patient was intubated in the casualty and then shifted to the ICU and put on mechanical ventilation. A nephrology opinion was sought in view of elevated urea and creatinine, oliguria and the patient was advised dialysis. A dialysis catheter was inserted into the right femoral vein and patient underwent dialysis. Later a right IJV access was secured. Cardiology opinion was taken in view of echo changes. Patient was diagnosed with postpartum cardiomyopathy and she was started on dobutamine and nor adrenaline infusion for hypotension. Patient then had multiple episodes of GTCS. A neurology opinion was sought and she was started on antiepileptic drugs. EEG done showed severe attenuation of background activity. An endocrinology opinion was sought for management of diabetes mellitus. An ophthalmology opinion was sought to look for retinopathy and fundoscopy was normal. Blood, urine and ET cultures showed growth and antibiotics were administered as per sensitivity reports. Once patient was stabilized, delivery was induced with oxytocin. Patient improved symptomatically. She was weaned off the ventilator and extubated. She was then shifted to ward. Patient developed hematoma in right thigh which gradually subsided. Repeat blood cultures were sterile. Patient and her husband were counseled regarding contraception. Patient received her first dose of hepatitis B vaccination and was counseled regarding schedule of remaining doses. With multidisciplinary approach, patient symptomatically improved over the course of hospital stay with no further episodes of seizures or fever spikes. She was then discharged with stable vitals.

Case 3
A 30 years old female presented at 26 weeks + 5 days POG in her first pregnancy with a two-day history of persistent vomiting, weakness and headache. She was initially managed at peripheral hospital and then referred to higher centre in view of diabetic ketoacidosis. Patient was a known case of type 2 diabetes since 6 years and was on insulin. Patient had skipped insulin for 2 days due to vomiting. On admission, patient was drowsy, tachypneic, tachycardic and dehydrated. Systemic examination was normal. Fetal heart sounds were present at the time of admission.

Investigations
Total leukocyte count: 33000/cumm; Serum sodium: 127 mEq/L; Serum potassium: 5.23 mEq/L; Serum chloride: 95.7 mEq/L; Serum bicarbonate: 2.2 mEq/L; Hba1c: 7.6%; Serum creatinine: 1.12 mg/dl; Serum urea: 40 mg/dl; Arterial blood pH: 6.90; Arterial pCO2: 12 mm Hg; Arterial pO2: 50 mm Hg; Arterial bicarbonate: 0 mmol/L; Arterial lactate: 1.8 mmol/L; Arterial blood glucose: 409 mg/dl; urine ketone bodies: 3+; urine sugar: 3+

Management
Patient was admitted in intensive care unit and resuscitated with oxygen supplementation, iv fluids. Endocrinology reference was sought, insulin infusion and bicarbonate correction given. Fetal heart sounds were later absent and ultrasound confirmed intrauterine fetal demise. After stabilizing the patient, correcting electrolytes and acidosis, she was shifted to labour room and delivery was induced. Patient was shifted back to ICU post-delivery and monitored. Patient improved symptomatically and shifted to ward. She was then discharged with OHAs and antibiotics. During follow up, patient had LMN type of facial palsy and was treated.

2. Discussion

Diabetic ketoacidosis is a serious metabolic disorder. With the improved antenatal care and better screening of diabetes in pregnancy, the incidence of maternal and fetal mortality related with DKA is supposedly decreasing in recent years. Maternal mortality secondary to DKA is around 5-15% and fetal death rate of 9-36% were reported[1,3,4,5].

Pregnancy is a diabetogenic state with relative insulin resistance, enhanced lipolysis and elevated free fatty acids, respiratory alkalosis associated with a compensatory drop in bicarbonate levels which impair buffering capacity making pregnant women more prone to develop DKA[1,6]. Hormonal changes like increased levels of human placental lactogen, progesterone and cortisol also impair maternal insulin sensitivity[1,6].

In case 1 and case 2, the precipitating factor of the DKA was noncompliance to the treatment and possible underlying infection. In case 3, the precipitating factor along with noncompliance to treatment was excessive vomiting. Other precipitating factors are listed in table 1[8,9,10]. The signs and symptoms, laboratory manifestations of DKA in pregnancy are similar to that of non-pregnant patients but tend to develop faster in pregnancy and can occur at lower blood glucose levels often causing delay in diagnosis[4,5]. In this study, all cases had hyperglycemia and levels of bicarbonate were extremely low.

Table 1. Precipitating Factors for Diabetic Ketoacidosis in Pregnancy

• Protracted vomiting, starvation
• Infections (pyelonephritis, respiratory, chorioamnionitis, ear infection, cellulitis, tooth abscess)
• Undiagnosed diabetes
• Poor control of blood sugars or poor compliance with treatment
• Insulin pump failure

- Use of β-sympathomimetic agents for tocolysis
- Steroid use for fetal lung maturation or for chronic medical disorders
- Diabetic gastroparesis

Table 2. Diagnosis of Diabetic Ketoacidosis

Signs and Symptoms

- Hyperventilation - tachypnea
- Sinus tachycardia
- Hypotension or dehydration
- Change in sensorium, disorientation, or coma
- Kussmaul respirations or fruity breath
- Nonreassuring fetal tracing
- Polyuria or polydipsia
- Nausea or vomiting
- Abdominal pain or contractions
- Blurred vision
- Muscle weakness

Laboratory Findings

- Plasma glucose level (usually greater than 250 mg/dL)
- Arterial pH less than 7.30
- Anion gap greater than 12 mEq/L
- Elevated base deficit
- Positive serum/urine ketones, especially 3β - hydroxybutyrate (most abundant)
- Falsely normal potassium level might be present
- Low serum bicarbonate (often less than 15mEq/L)
- Elevated serum blood urea nitrogen and creatinine resulting from dehydration and possible renal failure

Diabetic ketoacidosis is a medical and obstetric emergency demanding prompt and aggressive management in ICU by a multidisciplinary team. If not corrected, DKA can progress to a state of inadequate tissue perfusion, diminished cardiac and renal function, multiorgan failure and even death[10]. The principles of management of diabetic ketoacidosis during pregnancy are the same as that in the non-pregnant state. They consist of aggressive volume replacement, intravenous insulin therapy, correction of acidosis and abnormal electrolytes, search and correction of precipitating factor and rigorous monitoring of maternal and fetal response to the treatment[1,3,6]. Bicarbonate correction during DKA is still debatable[5,6,11]. Administration of bicarbonate may be associated with profound alkalosis or worsening acidemia secondary to increased partial pressure of CO_2, leading in turn to impaired fetal oxygen transfer[5]. Some authors recommend bicarbonate administration during severe acidosis or in patients complicated by cardiac dysfunction, sepsis or shock[12]. In above cases, considering severity of acidemia (pH less than 7.3) and low bicarbonate level, correction of bicarbonate was performed.

Treatment of DKA in pregnancy

Fluid therapy

Estimate fluid deficit of ~100ml/kg body weight

- Monitor fluid balance
- 0.9% NaCl at 1000ml/hr for 2 hours
- Switch to 0.45% NaCl at 250ml/hr
- When glucose <250ml/hr, switch to 0.45% NaCl with 5% dextrose

Correct 75% of fluid deficit over 24 hours and the remaining in next 24-48 hours

Insulin therapy

IV bolus of 0.1 U/kg of insulin

IV infusion of 0.1 U/kg/hr of insulin to decrease serum glucose by 50-75 mg/dl/hr

(if serum glucose not decrease by 50 mg/dl/hr in first hour, double the dose of insulin; when serum glucose <200 mg/dl, decrease rate of infusion to 0.05 U/kg/hr)

Target serum glucose post DKA: 100-150 mg/dl

Resume subcutaneous insulin once patient is stable and tolerating oral intake (maintain IV insulin after the first dose of subcutaneous insulin)

Search and treatment of precipitating event

Electrolyte replacement

Potassium(K+): Anticipate a K+ deficit of 5-10 mEq/kg body weight

Maintain adequate urine output (0.5 ml/kg/hr) and serum K+ between 4-5 mEq/l

- If serum K+ <3.3 mEq/l, hold insulin infusion
- If serum K+ >5.3 mEq/l, no treatment
- If serum K+ is between 3.3-5.3 mEq/l, add 20-30 mEq to each liter of replacement fluids

Bicarbonate: Usually not necessary

The decision to continue pregnancy or to terminate in the setting of diabetic ketoacidosis can be challenging and it must be individualized based on maternal status, fetal status and gestational age, maternal and fetal response to treatment. DKA per se is not an indication for emergent delivery. It is important to first stabilize the maternal condition before planning delivery. If fetal status deteriorates or if the maternal condition worsens despite aggressive management, delivery is warranted. In above cases, all patients had intrauterine fetal demise and delivery was induced after stabilizing the patient.

Ketoacids can readily cross the placenta. Whether it is the maternal acidosis, hyperglycemia, severe volume depletion or electrolyte imbalance that is contributing to increased fetal loss is unclear[13]. The possible mechanisms include decrease in uteroplacental blood flow due to osmotic diuresis leading to volume depletion and maternal acidosis that can cause fetal hypoxic insult and maternal acidosis could lead to fetal acidosis and electrolyte imbalance[14]. Data on neurological consequences of diabetes ketoacidosis is lacking. The most severe central nervous system complication associated with DKA is cerebral edema[15]. Neurological complications like seizures in case 2 and LMN type of facial palsy in case 3 were seen.

Diabetic ketoacidosis is a rare, severe complication of diabetes in pregnancy with adverse effect on both the mother and the fetus. Prevention, early recognition and hospitalization, aggressive management with multidisciplinary approach are paramount in the management of diabetic ketoacidosis. Women with pre-gestational and gestational diabetes should be educated about the importance of compliance with the treatment, prenatal visits, measurement and recording of glucose values. Also,obstetricians should be aware of the precipitating factors that can trigger DKA in pregnancy, complications, management and follow up of DKA patients. With adequate surveillance and timely management, the maternal and fetal outcome can be improved.

3. Conclusion

Diabetic ketoacidosis during pregnancy presents a complex challenge requiring prompt intervention and comprehensive care. While the incidence of DKA in pregnancy has decreased, its potential impact on both maternal and fetal health demands continued vigilance. The cases discussed underscore the importance of adherence to treatment, regular monitoring, and the need for a multidisciplinary team approach. Improved patient education, close collaboration among healthcare professionals, and timely interventions are essential for mitigating risks and ensuring positive outcomes for both mothers and their unborn children.

4. Patient Perspective

During follow up, all patients were debriefed. All cases were surprised at the extent of metabolic derangement caused because of noncompliance to the therapy. Patients were not aware that their insulin intake was suboptimal. It was an emotionally challenging situation for families and for patients as well. Case 1 were grateful for early recovery. Case 2 found it was difficult to cope with newer cardiovascular and neurological complications. Case 3 had challenging time to overcome the loss of their first child (patient had conceived with fertility treatment) and were surprised with newer complication (facial palsy) during follow up. All patients and their families were thankful to doctors for their remarkable efforts.

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