Euglycemic Ketoacidosis And Development Of Gestational Diabetes Following COVID-19 Infection In Pregnancy: A Case Report

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Abstract

Background: Emerging evidence suggests that COVID-19 infection can significantly impact glucose metabolism. While diabetic ketoacidosis (DKA) is a well-known life-threatening complication, there are rare occurrences of euglycemic DKA (EDKA) in pregnant patients, including those with pre-existing type 1 or type 2 diabetes mellitus (DM) and gestational diabetes mellitus (GDM). However, our case report presents a unique scenario of a 29-year-old gravida 2+0 patient without any prior history or risk factors for GDM, who developed EDKA following COVID-19 infection during pregnancy.

Case Presentation: We present the case of a 29-year-old gravida 2+0 patient with no history of DM, who experienced EDKA at 28 weeks of pregnancy subsequent to COVID-19 infection. The diagnosis of EDKA requires a high index of suspicion, as it can lead to increased fetal morbidity and mortality if left unrecognized and untreated.

Conclusion: In this report, we have discussed the potential causes, differential diagnosis, and a multidisciplinary management approach for euglycemic diabetic ketoacidosis in pregnancy. Keywords—component; formatting; style; styling; insert (key words)

Introduction

Severe COVID-19 infection can lead to development of ketosis and ketoacidosis, even in individuals without diabetes mellitus. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), responsible for COVID-19, interacts with angiotensin-converting enzyme 2 (ACE2) receptors present in key metabolic organs and tissues, such as pancreatic beta cells, adipose tissue, the small intestine, and the kidneys. This suggests that the virus may induce various alterations in glucose metabolism, potentially complicating preexisting diabetes or introducing new disease mechanisms. Diabetic ketoacidosis (DKA) is a serious medical condition necessitating immediate intervention. While there are some documented cases of Euglycemic DKA (EDKA) in pregnant individuals with pre-existing type 1, type 2 Diabetes Mellitus (DM), or Gestational Diabetes Mellitus (GDM), occurrences in patients without a history of DM or risk factors for GDM during pregnancy appear to be rare. This underscores the need for further research and vigilance regarding the metabolic implications of COVID-19, particularly in diverse patient populations.

Case presentation

A 29-year-old woman, Gravida 2+0 with a BMI of 25.5, presented to the hospital at 28 weeks of gestation due to feelings of malaise, nausea, and vomiting. She was tested positive for SARS-CoV-2 infection six days prior to reporting these symptoms. She did not have any respiratory symptoms. Fetal movements were normal, and the patient had no significant medical or family history of Diabetes Mellitus. Upon admission, she exhibited symptoms of tachycardia and tachypnea, initially saturating at 98% on room air, but later requiring supplemental oxygen at 4L/min. Evidence of ketonuria and ketoacidosis was noted, supported by initial arterial blood gas analysis indicating metabolic acidosis. COVID-19 prognostic markers revealed elevated ferritin levels and lymphopenia, while chest computed tomography pulmonary angiography (CTPA) demonstrated extensive lung consolidation consistent with COVID pneumonia. Differential diagnoses considered included exacerbation of COVID pneumonia, metabolic ketoacidosis, and starvation-induced ketoacidosis. Throughout her hospitalization, treatment was guided by serial monitoring of clinical and biochemical parameters. Initial management was focused on correcting acidosis through fluid resuscitation, followed by insulin therapy to address rising blood glucose levels. Subsequent evaluation two weeks later led to a diagnosis of gestational diabetes mellitus (GDM), prompting a multidisciplinary approach to care in a high dependency unit. Treatment encompassed intravenous antibiotics, thromboprophylaxis, and steroid prophylaxis for fetal lung maturity, in case she needed delivery. Ketoacidosis was resolved after meticulous fluid and electrolyte management, culminating in improved

Table 1. Venous blood gas results and vital signs during admission.

	Day of Admission			
	0	2	3	5
pH	7.29	7.33	7.36	7.44
HCO3	10.9	11.1	14.3	20.6
BE	-13.9	-12.3	-9.8	-2.4
Na/K	138/2.94	136.6/3.65	139.9/3.6	140/3.5
pO2	10.9	11.5	12.5	7.3
pCO2	3.1	2.8	3.5	4.1
Ketones	4.7	2.9	2.8	0.5
Glucose	5	12.9	6.4	10.7
Respiratory Rate	34	26	19	17
Pulse	126	99	104	90
Sp02	96	97	96	97

clinical and biochemical parameters and eventually discharged home. Confirmatory investigations including serial imaging and oral glucose tolerance testing (OGTT) corroborated the diagnosis of GDM. The prompt identification of Euglycemic Diabetic Ketoacidosis (EDKA) facilitated appropriate intervention, underscoring the critical role of vigilant monitoring and interdisciplinary collaboration in managing complex obstetric conditions.

Treatment Stages:

In Stage 1, emphasis was placed on correcting ketoacidosis, with COVID-specific investigations and treatment initiated according to established protocols and multidisciplinary team consensus.

Stage 2 witnessed incremental clinical improvement, characterized by normalization of bicarbonate, potassium, and base excess levels, alongside a decrease in oxygen requirements.

In Stage 3, Persistent hyperglycemia prompted the introduction of sliding scale insulin therapy. Despite the absence of prior diabetic history, the patient's clinical course mirrored that of EDKA.

Finally, in Stage 4, normalization of both clinical and biochemical parameters facilitated the patient's discharge, affirming the efficacy of a staged treatment approach in managing EDKA and its associated sequelae.

Discussion

Euglycemic diabetic ketoacidosis (EDKA) was first described by Munro et al. in 1973 among individuals with type 1 diabetes mellitus (DM). Common causes of EDKA mentioned in the literature currently include low caloric intake, fasting or starvation, pregnancy, pancreatitis, cocaine intoxication, prolonged vomiting

Table 2. Key biochemical parameters and vital signs during the different stages of management.

Stage	Glucose levels	Ketones	Acidosis	Lactate	Oxygen saturation (%)	Pulse Rate	Respiratory rate
1	Normal	Increased	Increased	Normal	93	Increased	Increased
2	Normal	Stable	Increased	Increased	96	Increased	Increased
3	Increased	Stable	Stable	Increased	98	Decreased	Decreased
4	On Insulin	Stable	Stable	Stable	98	Decreased	Decreased

or diarrhea, insulin pump use, and the recent use of SGLT2 inhibitors like empagliflozin and canagliflozin. Recently, there have been two case reports of patients developing euglycemic DKA during pregnancy, potentially associated with fetal morbidity and mortality if left untreated and undiagnosed. Both of these pregnant women tested positive for SARS-CoV-2, and only one had a previous history of DM. Pregnancy represents a diabetogenic state due to hormonal changes promoting insulin resistance, predisposing individuals to gestational diabetes mellitus (GDM). Development of GDM is influenced by pre-pregnancy risk factors such as raised BMI, ethnicity, previous history of GDM, and macrosomia. COVID-19 infection during pregnancy can lead to transient beta cell dysfunction and the development of GDM. Additionally, normal blood glucose levels can be associated with ketoacidosis, as in our case , likely due to increased glycogenolysis, lipolysis, and ketogenesis during fasting, which may be exacerbated by conditions such as viral infections. Ketones are produced in the liver from free fatty acids, and excess production can result in ketosis and subsequent ketoacidosis. COVID-19 may accelerate fat beta-oxidation, leading to ketosis and ketoacidosis. A direct link between COVID-19 and type 2 diabetes mellitus (T2DM) exists, with the virus binding to ACE2 receptors in the pancreas, causing acute beta-cell dysfunction and transient T2DM. Concerns regarding ACE-inhibitor treatment facilitating virus entry may increase morbidity and mortality in SARS-CoV-2 infected patients. Strategic management of EDKA may necessitate escalation to intensive care units for hemodynamic monitoring and acid-base correction, with initial focus on rehydration using Hartmann's solution and 5% dextrose infusion combined with insulin to reduce ketosis. Potassium supplementation may be necessary to maintain serum levels, and specific biochemical parameters guide correction of EDKA. Schneider et al. reported that 2-9% of diabetic pregnancies are complicated by diabetic ketoacidosis, with a fetal mortality rate of 90%. Early diagnosis is challenging due to normal initial serum glucose levels, but fetal abnormalities can normalize with acidosis correction. Emergent cesarean delivery may be required if maternal condition deteriorates, but individualized management is necessary due to

potential COVID-19-related complications involving respiratory and cardiovascular systems.

Conclusion

Euglycemic diabetic ketoacidosis (EDKA) should be considered even in non-diabetic pregnant women, particularly when compounded by additional stressors such as infectious diseases. Routine ketone testing is imperative in pregnant individuals experiencing vomiting to promptly establish a correct diagnosis and initiate appropriate treatment. COVID-19 infection has been shown to exacerbate glucose metabolism, increasing the risk of developing euglycemic ketoacidosis during pregnancy. Therefore, heightened vigilance is warranted for COVID-19 patients presenting with ketoacidosis, especially those with pre-existing diabetes, in order to mitigate associated mortality from COVID-19 complications. Further research is needed to elucidate the mechanisms underlying COVID-19-induced DKA and inform targeted management strategies.

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