

Diabetic ketoacidosis and Covid-19 management in a term pregnant patient; A case report

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April 29, 2022

Abstract

Background: Covid-19 can have remarkable effects on pregnancy, and pregnant women with this infection are at higher risk for developing ketoacidosis. In this case report, we report a 35-year-old pregnant woman infected with Covid-19 with early manifestations of ketoacidosis during term pregnancy.

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Consent for publication: Written informed consent was obtained from the patient to publish this report accordance with the journal's patient consent policy.

Abstract

Background: Covid-19 can have remarkable effects on pregnancy, and pregnant women with this infection are at higher risk for developing ketoacidosis. In this case report, we report a 35-year-old pregnant woman infected with Covid-19 with early manifestations of ketoacidosis during term pregnancy.

Keywords: Pregnancy, Ketoacidosis, Covid-19, Euglycemic.

Background

In December 2019, a novel coronavirus later named Covid-19 appeared in Wuhan, China and quickly developed into a worldwide pandemic (1).

Covid-19 can have significant effects on pregnancy and a pregnant woman with this infection may have symptoms such as shortness of breath, fatigue, and lethargy. Pregnant women are at higher risk for developing ketosis, and concomitant infections may lower the metabolic threshold at which ketoacidosis happen (2).

Certain hormones production during pregnancy such as progesterone, cortisol and prolactin can increase the risk of ketoacidosis by boosting insulin resistance (3). Blood glucose level less than 200 mg/dL, increased anion gap metabolic acidosis, and ketonemia are the biochemical triad for euglycemic diabetic ketoacidosis (Dka) (4).

In this case report, we report a Covid-19 infected pregnant woman with primary manifestation of ketoacidosis at term pregnancy and discuss the management challenges with euglycemia and a high ketone burden.

Case presentation

On 5 November 2021, a 35-year-old G3P02L02 with a gestational age of 34⁺⁵ weeks was admitted to our hospital with a shortness of breath function class 2, myalgia, complaining of headache, tachycardia, fatigue and productive coughs that caused chest pain while started 1 week ago and intensified 2 days ago. The patient had several visits to the general practitioner and received serum therapy before admission, but did not recover. Her past medical history reported tachycardia in her past pregnancy and left lobe thyroid nodule that are compatible with papillary thyroid carcinoma through fine needle aspiration which was diagnosed at eighth week of pregnancy and according to the absence of lymphadenopathy and extrathyroidal invasion, postpartum surgery was recommended.

She had a history of tachycardia in previous pregnancy and had also been treated with Inderal for the last 5 years before discontinuing it for pregnancy. During this pregnancy, she did not have any referrals for heart problems. The patient was also being treated with levothyroxine due to hypothyroidism. Continuing the history of previous diseases, she also had a mild gestational diabetic mellitus (GDM) since 5th month of pregnancy and had been under treatment with 6-unit bedtime detemir. The patient had a platelet count of 70,000 at the admission, but no schistocytes were seen in the peripheral blood smear.

Investigation and treatment

At primary presentation, the patient's shortness of breath qualified her for routine SARS-CoV-2 PCR testing. Her blood pressure was 110/70 mm Hg, and she had a heart rate of 120 beats per minute. Her peripheral oxygen saturation was 97 percent and she had a respiratory rate of 35; She also had a history of contacting her husband, who was positive for Covid-19. The SARS-CoV-2 PCR test came back positive in the next day. Due to positive High-Resolution CT-Scan and pulmonary involvement of forty percent and severe tachypnea, she was hospitalized at intensive care unit for four days. Figure.1. According to PH level of 7.33, PCO₂ level of 16.7, bicarbonate level of 8.2 and a high anion gap of 21, the patient was diagnosed with ketoacidosis. Table.1.

A number of differential diagnoses were considered for this patient. Serum osmolality of 296.2 mOsm/KG and an osmolality gap of 7 mOsm/kg, ruled out the alcohol intoxication in this patient. High anion gap of 21 mmol/L and stage 2 chronic kidney disease epidemiology collaboration also excluded renal tubular acidosis and uremic acidosis from our differential diagnoses, respectively. D-dimer level of 2130 ng/ml was also checked in this patient for pulmonary embolism ruling out. The patient underwent cardiac echo and had a BNP level checked for cardiomyopathy, which was reported negative. Fetal sonography was also reported to be normal during pregnancy.

Patient's blood glucose was 70 at the first presentation; therefore, serum dextrose 5% and regular insulin infusion for maintaining blood glucose level in the normal range, were established for patients' ketoacido-

sis. Figure.2. Extensive treatment was performed with Oxygen therapy, remdesivir, dexamethasone and tocilizumab for patient's infection with Covid-19.

Failure to correct severe acidosis of the patient in the first four days of hospitalization despite treatment, high respiratory rate, disorder in nonstress test (NST), closed cervix and patients poor condition led to fetal distress and made us unable to accomplish natural vaginal delivery for this patient; Therefore, termination of pregnancy by cesarean section was performed using induction on the fourth day of hospitalization. Thyroid tests were also suitable for termination of pregnancy. By performing the mentioned workups, patient attained a better condition.

Vital parameters at the next day were a blood pressure of 115/75mmHg, heart rate of 78 beats per minute, temperature of 37.5°C, oxygen saturation of 98% and a respiratory rate of 22 breaths per minute. The newborn's Apgar score in the first and fifth minutes was 8 and 9, respectively. The patient's platelets count also improved and increased by 180,000 on the day of discharge.

Due to the lack of sufficient evidence for the management of these patients, based on the Dka treatment protocol in non-pregnant patients, we performed the treatment with serum dextrose infusion 100cc per hour, regular insulin infusion between 6 to 12 units per hour and potassium chloride administration. We also monitored the patient's blood sugar within a safe range for pregnancy.

Discussion

Ketones are organized in the liver from free fatty acids. ketosis is a results of reduction in ketone consumption which can be clinically evident by elevated blood concentrations of ketone bodies (β - and hydroxybutyrate, acetone acetoacetate). Covid-19 might accelerate fat breakdown and induce ketosis, with further extension of ketoacidosis (1).

Euglycemic Dka is a rare and acute life-threatening metabolic emergency that the normal blood glucose may delay diagnosis and treatment. This problem is likely due to poor oral intake, treatment with insulin prior to arrival in the hospital, in pregnant women and with SGLT2 inhibitors consumption (5).

Dka must be distinguished from other causes of high anion gap metabolic acidosis including lactic acidosis (which can be associated with metformin consumption), aspirin or acetaminophen toxicity, methanol or ethylene glycol poisoning and chronic kidney disease. Although none of these disorders cause ketoacidosis, several types of acidosis may coexist, such as lactic acidosis and ketoacidosis (6, 7).

In this report, we introduced a patient who has been infected with Covid-19 virus in the context of a mild GDM and normal blood sugar with moderate pulmonary involvement and unexpectedly severe ketoacidosis. Euglycemic Dka is a rare extrapulmonary manifestation of Covid-19 that has been reported in both diabetic and non-diabetic patients, as well as in pregnant and non-pregnant women.

Our patient presented with shortness of breath, fatigue and productive coughs with intensification from two days ago. At the onset, the complaints were particularly ascribed to respiratory effects of Covid-19. Differential diagnosis was expanded when the blood gas analysis showed a high anion gap metabolic acidosis that was not due lactate or toxic agents. Urinalysis showed ketone bodies and lower limit normal blood glucose concentrations at admission. The remaining diagnosis was euglycemic Dka based on the high metabolic demand in pregnancy.

Due to the lack of proteinuria, high blood pressure, hemolysis and increased liver enzymes, preeclampsia also ruled out in this patient.

There are several facts about the physiopathology of ketoacidosis during infection with Covid-19. Like any other disease, these patients may not receive a proper intake due to gastrointestinal complaints which can lead to starvation or fasting Dka (8).

On the other hand, ketogenesis increases in pregnancy and the prevalence of ketoacidosis is higher in pregnant women than in non-pregnant women: 8.9% vs. 3.1%, respectively, due to the increase in the level of hormones

secreted by the placenta such as placental lactogen and prolactin, which cause insulin resistance by the antagonistic effects of insulin, and by stimulating lipolysis, increase the production of free fatty acids as a substrate for the production of body ketones (9).

Ketoacidosis also occurs in pregnant women with diabetes in the presence of lower blood sugar, because pregnancy is associated with increased utilization by creating a hypermetabolic condition and reducing glucose production in the body (10).

Covid-19 virus has the ability to bind to the ACE2 receptor in the lungs and pancreas, and by inactivating it, it disrupts insulin secretion and hyperglycemia. Also, by increasing excessive fluid absorption through the RAAS system it can cause causes an irreversible state which can lead to underlying diseases occurrence (11).

Our patient, as in other cases reported from the third trimester of pregnancy has this complication, and is mild to moderate in terms of the severity of lung involvement, the rate of arterial blood oxygenation and biochemical factors associated with the severity of Covid-19 infection, as other cases reported from mild to medium. It seems that the metabolic acidosis of these patients is not consistent with the severity of Covid-19 (2, 12), and the association between Covid-19 infection and pregnancy is sufficient to cause severe metabolic acidosis.

With regard to the severity of pulmonary involvement with Covid-19 in this patient, it may be possible to suggest the patient's blood type, which was O positive, as a protective factor (13). The patient was diagnosed with papillary thyroid carcinoma in the first trimester of pregnancy. Regarding the association between the patient with Covid-19 and ptc, although factors such as inflammation, immunity, obesity, and oxidative stress are involved, it is not yet clear whether Covid-19 infection could increase or decrease the risk of ptc (14).

Regarding the prognosis of Covid-19 infection in ptc patients, studies so far have shown that in addition to age and underlying disease effecting on the hospitalization process of ptc patients with Covid-19, the treatments and severity of Covid 19 disease in PTC patients were not correlated. Overall, the rate of hospitalization and mortality in ptc patients are lower compared to other cancers at the time of Covid-19 infection (15).

Conclusion:

Despite normal blood glucose levels, it is important to suspect ketoacidosis in a pregnant patient with acidosis. Urinary ketones should be monitored in any diabetic patient during periods of illness. Our case highlights the diagnostic and therapeutic challenges associated with euglycemic DKA and its associated complications. Fetal death is one of the mainstays of treatment, early detection and timely administration of fluids, carbohydrates and insulin.

Declaration section

Ethical approval and consent to participate: The study and all experimental protocols were approved by the Professional Ethics Committee of the Golestan University of Medical Sciences. The informed consent was also obtained from the patient for the implementation of this project.

All methods were carried out in accordance with relevant guidelines and regulations.

Consent for publication: Consent has been obtained from the patient to participate in the study and dissemination of the information in accordance with the principles of confidentiality.

Availability of data and materials: Not applicable.

Competing interests: The authors declare no competing interest.

Funding: The Golestan University of Medical Sciences financially supported this work.

Role of the Funder/Sponsor: The funder had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Authors contribution:

A.F and F.M performed data entry and writing article. E.A and F.A performed visiting patient and data collection. F.M and A. F and B.KH performed data collection and article review.

Acknowledgment: Special thanks to all the fellow authors who contributed to this article.

Abbreviations

Diabetic ketoacidosis (Dka)

Gestational diabetic mellitus (GDM)

Nonstress test (NST)

Figure 2. Blood glucose level from admission to discharge of the patient

Table 1. Relevant laboratory results at admission

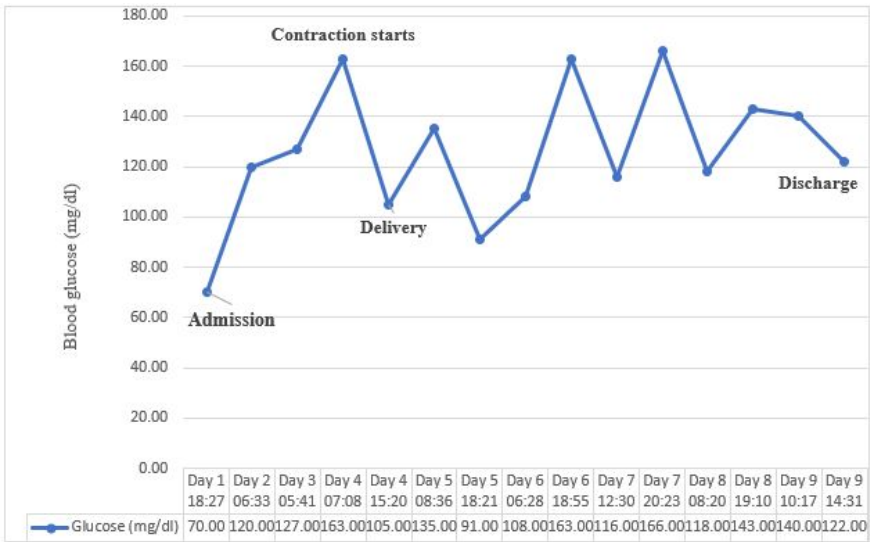
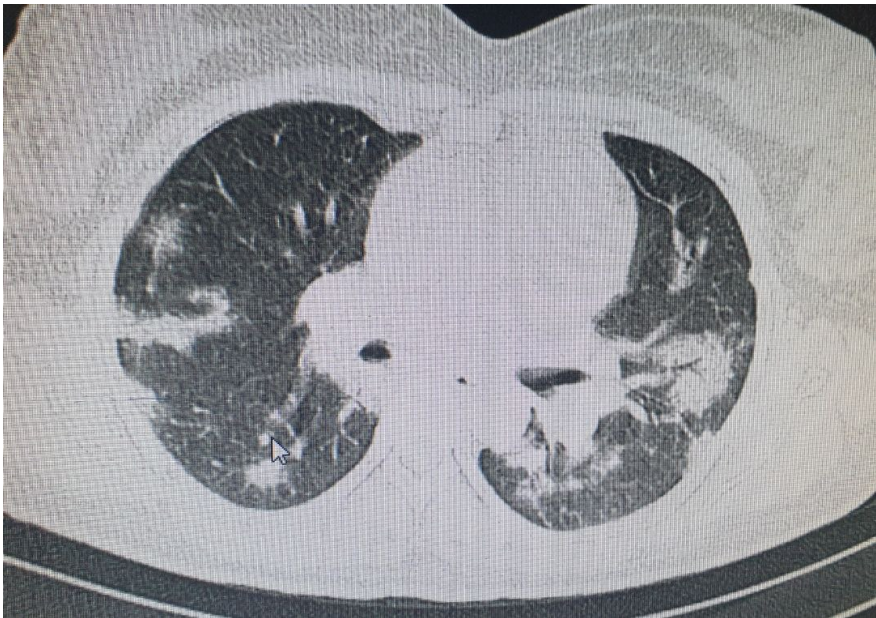
References:

1. Li J, Wang X, Chen J, Zuo X, Zhang H, Deng A. COVID-19 infection may cause ketosis and ketoacidosis. *Diabetes Obes Metab.* 2020;22(10):1935-41.
2. Thorne I, Steele S, Martineau M, Girling J. Case series of COVID-19 infection in pregnancy complicated by ketoacidosis and symptomatic breathlessness. *Obstetric Medicine.* 2021.
3. Smati S, Mahot P, Bourdiol A, Ploteau S, Hadjadj S, Cariou B. Euglycaemic ketoacidosis during gestational diabetes with concomitant COVID-19 infection. *Diabetes Metab.* 2021;47(2):101181.
4. Jaber JF, Standley M, Reddy R. Euglycemic Diabetic Ketoacidosis in Pregnancy: A Case Report and Review of Current Literature. *Case Rep Crit Care.* 2019;2019:8769714.
5. Gabow PA. Disorders associated with an altered anion gap. *Kidney Int.* 1985;27(2):472-83.
6. Kraut JA, Madias NE. Serum Anion Gap: Its Uses and Limitations in Clinical Medicine. *Clinical Journal of the American Society of Nephrology.* 2007;2(1):162-74.
7. Prentice AM, Prentice A, Lamb WH, Lunn PG, Austin S. Metabolic consequences of fasting during Ramadan in pregnant and lactating women. *Hum Nutr Clin Nutr.* 1983;37(4):283-94.
8. Kamalakannan D, Baskar V, Barton DM, Abdu TAM. Diabetic ketoacidosis in pregnancy. *Postgraduate Medical Journal.* 2003;79(934):454-7.
9. Nasa P, Chaudhary S, Shrivastava PK, Singh A. Euglycemic diabetic ketoacidosis: A missed diagnosis. *World J Diabetes.* 2021;12(5):514-23.
10. Guo RX, Yang LZ, Li LX, Zhao XP. Diabetic ketoacidosis in pregnancy tends to occur at lower blood glucose levels: case-control study and a case report of euglycemic diabetic ketoacidosis in pregnancy. *J Obstet Gynaecol Res.* 2008;34(3):324-30.
11. Lim S, Bae JH, Kwon HS, Nauck MA. COVID-19 and diabetes mellitus: from pathophysiology to clinical management. *Nat Rev Endocrinol.* 2021;17(1):11-30.
12. van Amesfoort JE, Werter DE, Painter RC, Hermans FJR. Severe metabolic ketoacidosis as a primary manifestation of SARS-CoV-2 infection in non-diabetic pregnancy. *BMJ Case Rep.* 2021;14(4).

13. Shokri P, Golmohammadi S, Noori M, Nejadghaderi SA, Carson-Chahhoud K, Safiri S. The relationship between blood groups and risk of infection with SARS-CoV-2 or development of severe outcomes: A review. *Reviews in Medical Virology*. 2022;32(1):e2247.

14. Deligiorgi MV, Siasos G, Vakkas L, Trafalis DT. Charting the Unknown Association of COVID-19 with Thyroid Cancer, Focusing on Differentiated Thyroid Cancer: A Call for Caution. *Cancers*. 2021;13(22):5785.

15. Kathuria-Prakash N, Mosafari T, Xie M, Antrim L, Angell TE, In GK, et al. COVID-19 Outcomes of Patients With Differentiated Thyroid Cancer: A Multicenter Los Angeles Cohort Study. *Endocr Pract*. 2021;27(2):90-4.



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