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Diabetic ketoacidosis in pregnancy: A case report

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Abstract---Pregnancy with diabetic ketoacidosis (DKA) increases maternal and perinatal morbidity and mortality. DKA is a rare complication of pregestational diabetes mellitus (DM) or gestational diabetes mellitus (GDM) during pregnancy. However, it could be life-threatening for the mother and fetus without correct diagnosis and treatment. This paper reports a case of DKA in 25 years old Female with 26/27 weeks gestational ages. This was the second pregnancy with bad obstetric history. The patient has a history of DM from a previous pregnancy. The diagnosis of DKA is based on the presence of hyperglycemia, ketone in urine, and metabolic acidosis. After aggressive fluid replacement, intravenous insulin therapy, correction of acidosis and electrolyte imbalance, the patient showed significant improvement. The baby was born spontaneously induced by oxytocin drip, with a birth weight of 900g, APGAR scores 0, and maceration grade 2. After being treated for six days in the intensive care unit and observed for three days in the ward, the patient was allowed to be outpatient in good condition. Rapid restoration of glycemic control is essential to prevent death in pregnant women with diabetes mellitus diabetic ketoacidosis.

Keywords---Diabetes Mellitus, Ketoacidosis, Pregnancy, Respiratory Distress, Intrauterine Fetal Death.

Introduction

Diabetic ketoacidosis (DKA) is characterised by hyperglycemia, metabolic acidosis, and ketosis is a severe complication of diabetes, often determining a medical emergency. Even if DKA occurs during pregnancy is rare, and if it is not promptly treated, it can compromise both the fetus and the mother. Furthermore, this condition, usually considered characteristic of type 1 diabetes, is now reported in type 2 and gestational diabetes mellitus (GDM) patients. So prevention, prompt recognition, and treatment of DKA are mandatory to reduce the burden of this condition (Grazia & Silvia, 2020).

The reported incidence of diabetes in pregnancy ranges from 6% to 7%, with 90% of these cases representing women with GDM. Diabetic ketoacidosis is exceedingly rare during pregnancy, with a reported incidence between 0.5% and 3% of all diabetic gestations. The incidence of diabetic ketoacidosis in pregnancy is expected to increase because of the increased frequency of type 2 DM and gestational diabetes during pregnancy due to the change in the demographics of pregnant women. Pregnancies in women 35 years or older are much more common than a decade ago. Advanced maternal age is associated with increased rates of obesity and both type 2 DM and GDM (Sibai, 2014).

Pregnancy is also associated with physiological changes that predispose a pregnant woman with diabetes to DKA. Some specific physiological reasons for DK in pregnancy are as follows (Mohan et al., 2017). First, pregnancy is a state of respiratory alkalosis associated with a compensatory drop in bicarbonate levels; this impairs the buffering capacity and makes the pregnant woman more prone to developing diabetic ketoacidosis. Second, relative insulin resistance in pregnancy along with enhanced lipolysis and elevated free fatty acids, form the base for DK in pregnancy. Third, hormonal changes, including increased levels of human placental lactogen, progesterone, and cortisol, impair maternal insulin sensitivity.

Case Report

Table 1
Blood examination result

Parameter	Result	Parameter	Result
Hb	13.5 gr/dL	RBG	390 mg/dL
Hct	37.2 %	BUN	32
WBC	19.440 10 ³ /uL	Creatinine	1.9 U/L
Platelete	491 10 ³ /uL	Albumin	2.8 g/dL
Neutrophil	80.7 %	SGOT	25 U/L
Lymphocytes	5.3 %	SGPT	15 U/L
NLR	15.2	Direct Bilirubin	0.43 mg/dL
Na	146 mmol/L	Total Bilirubin	0.83 mg/dL
K	3 mmol/L	HbsAg	Non reactive
Cl	112 mmol/L	PPT/APTT	15.1/30.1

Mrs. A, 25 y.o, was referred by the secondary hospital. She was diagnosed as pregnancy complicated by DKA and accompanied by profuse vomiting. She

complained of nausea and vomiting for three days, getting worse. After three days of hospitalization, complaints worsened, so she was referred to our hospital. The gestational age was 26/27 weeks, third pregnancy, and miscarried two previous pregnancies. The patient has diabetes mellitus and hypertension after the second pregnancy. The patient was getting oral anti-diabetic and anti-hypertension drugs, but she did not consume them regularly.

Table 2
Blood examination result

Urine test			
Parameter	Result	Parameter	Result
Protein	+ 1	Albumin-creatinine urine ratio (ACR)	≥ 300
Erythrocyte	+ 3	PCR	≥ 0.5
Leucocyte	-	Ketone	+3
Glukose	+ 3		

On physical examination, that was a decrease in consciousness with Glasgow Coma Scale (GCS) 2-3-4. Blood pressure was 148/92 mmHg, and pulse was 138x/ minutes. Respiratory rate was 30-34x/minutes, Kusmaull type, Oxygen saturation was 97% (with O₂ supplementation via NRM, ten liters per minute). On Obstetric status, that was no heartbeat of the fetus and no sign of parturition.

Table 3
Blood examination result

Blood Gas Analysis	
Parameter	Result
pH	7.11
pCO ₂	12 mm/Hg
pO ₂	143 mm/Hg
BE	-25.2 mmol/L
HCO ₃	3.8 mmol/L
SO ₂	98%

The patient has been treated in the Intensive Care Unit (ICU), resuscitated, and put on a ventilator. After maternal stabilization, intravenous fluid administration, insulin therapy, electrolyte imbalance has been corrected, Bicarbonate administration, termination of pregnancy by oxytocin drip. The baby was born, 900 gram, APGAR score was 0, grade 2 maceration.

Discussion

Pathophysiology

Hyperglycemia and rapid ketogenesis are hallmarks of DKA. Both a shortage of insulin and an overabundance of glucagon and other counter-regulatory hormones play a role in these issues and their clinical manifestations. Glucose

enters the cell normally as a result of the presence of insulin. The cell can then utilize glucose as a source of nutrients and energy. Glucose cannot enter the cell when insulin is absent. When a cell is starved, it releases counter-regulatory hormones, including glucagon, catecholamines, and cortisol, to help it survive. These anti-regulatory hormones are in charge of giving the cell an alternate source of nutrients and energy. Hepatocytes break down fatty acids from adipose tissue to ketones in the gluconeogenesis process, subsequently used by the body's cells for nutrition and energy production. The lack of insulin also contributed to increased lipolysis and decreased reutilization of free fatty acids, thereby providing more substrate for hepatic ketogenesis (Foley et al., 2011).

Ketone bodies are generally thought to be fairly powerful acids. The body reacts physiologically to repair metabolic acidosis caused by a drop in pH in most bodily fluids caused by a buildup of these acids. The respiratory rate and depth increase in an attempt to evacuate carbon dioxide (Kussmaul respirations), initiating a compensatory tendency toward respiratory alkalosis. Serum bicarbonate levels fall, and as a result, the anion gap rises abnormally. Poor glucose utilization causes severe hyperglycemia in addition to increased fatty acid synthesis. Untreated hyperglycemia causes substantial glycosuria, resulting in severe osmotic diuresis. As a result, dehydration and electrolyte depletion may occur, and heart failure and death may occur if untreated (Foley et al., 2011).

Metabolic Acidosis in Pregnancy

Pregnancy-related metabolic alterations predispose to ketosis. The variables that lead to an elevated risk of diabetic ketoacidosis and their differential influence during pregnancy's three trimesters. Pregnancy is a condition of insulin resistance. Insulin sensitivity has been shown to drop by 56% during the first 36 weeks of pregnancy. The synthesis of insulin-antagonistic hormones such as human placental lactogen, prolactin, and cortisol contributes to this. As a result, the insulin need gradually increases during pregnancy, explaining why diabetic ketoacidosis is more common in the second and third trimesters. In addition to the natural elevation in progesterone during pregnancy, decreased gastrointestinal motility increases carbohydrate absorption, causing hyperglycemia (Kamalakaran et al., 2003).

There is a relative increase in famine throughout pregnancy, particularly in the second and third trimesters. The fetus and placenta require a substantial quantity of maternal glucose as a primary energy source, resulting in lower maternal fasting glucose. This, in conjunction with relative insulin insufficiency, increases free fatty acids, which are subsequently metabolized to ketones in the liver. Nausea and vomiting are prevalent in early pregnancy due to increased human chorionic gonadotropin and more significant esophageal reflux in later stages. The stress and fasting condition that results raises insulin-antagonistic hormones. This, combined with the resulting dehydration, leads to the development of ketoacidosis. Increased minute alveolar ventilation during pregnancy causes respiratory alkalosis, which is compensated for by increased renal bicarbonate excretion. As a result, the buffering capacity is reduced when exposed to an acid load such as ketones (Kamalakaran et al., 2003).

Diagnosis

The case that we report has some significant similarities with the cases of DKA reported in the literature. In this case, the diagnosis of DKA was made based on clinical and laboratory. The patient complains of excessive nausea and vomiting, and body weakness. Physical examination revealed decreased consciousness, tachycardia, and Kussmaul breathing, which are typical for DKA.

The signs and symptoms of diabetic ketoacidosis during pregnancy are not pathognomonic and tend to develop faster during pregnancy than in the nonpregnant state. An episode of diabetic ketoacidosis may be the initial presentation that leads to a diagnosis of type 1 diabetes. Intractable nausea and vomiting in a known diabetic patient warrant laboratory evaluation for diabetic ketoacidosis. Hyperglycemia leads to glucosuria, intravascular volume depletion, increased diuresis, and dehydration. In advanced disease, there might be Kussmaul respirations and a fruity odor in the patient's breath. Lethargy and central nervous system manifestations are also an effect of the buildup of ketoacidosis that could lead to a state of disorientation, obtundation, and even coma resulting from cerebral edema (Sibai, 2014).

When DKA in pregnancy is suspected, laboratory investigation is required to confirm the diagnosis and to assess the severity of the disease and its possible cause. The following diagnostic criteria for DKA in pregnancy are stated in the Joint British Diabetes Societies Inpatient Care Group guidelines (Mohan et al., 2017):

- a. Blood ketone level more than or equal 3.0 mmol/l (or) urine ketone level more than 2+.
- b. Blood glucose level more than 11.0 mmol/l or known diabetes mellitus.
- c. Bicarbonate level less than 15.0 mmol/l and/or venous pH less than 7.3.

Laboratory results are hyperglycemia (random blood sugar 390 mg/dL), hypokalemia (3 mmol/L), hypoalbuminemia (2.8 g/dL), elevated serum creatinine (1.9 U/L), metabolic acidosis, ketonuria, glucosuria with anion gap (33.2 mmol/L).

Risk Factor

Various Triggers of DKA in pregnancy have been reported. A history of cessation of insulin therapy in person with diabetes was the precipitating factor for DKA in 40% of cases. Obstetrical intervention such as beta-2-agonists for tocolysis or corticosteroids for fetal lung maturation can be precipitating factors for DKA (Risa et al., 2013). Factor that predispose the DKA in pregnancy include accelerated starvation (especially in the 2nd and 3rd trimesters), dehydration, decreased caloric intake (nausea or hyperemesis gravidarum), decreased buffering capacity (compensated respiratory alkalosis of pregnancy), stress, and increased production of insulin antagonist (human placental lactogen, prolactin and cortisol) (Veciana, 2013).

In this case, the precipitating factor of the DKA was noncompliance to treatment of diabetes. The patient had been diagnosed with diabetes mellitus 2 years earlier

and received oral antidiabetic drugs, but he doesn't take the medicine regularly. In the 1st trimester of pregnancy, an oral glucose tolerance test (OGTT) 50 gram was examined with a result of 282 g/dL. So that the diabetes therapy was changed to insulin 3x4iu intramuscular. In addition, 3 days before being admitted to the hospital, she also complained of profuse nausea and vomiting which indicated dehydration which reduced caloric intake.

Fetal Complication

On obstetrical examination, that was no fetal heartbeat. That was no data about the decrease of fetal movement because the patient was unconscious. After the fetus was born, grade 2 maceration was found, with a sign of peeling skin. It could be assumed that fetal death occurred more than 48 hours.

DKA in pregnancy did not lead to any maternal deaths but was associated with an exceptionally high perinatal mortality. The stillbirth rate in the population of women with DKA was 160 per 1000 births, compared to the stillbirth rate in the general population in 2018 in the UK of 3.51 per 1000 births and the overall stillbirth rate from 2014 to 2018 in pregnant women with type 1 or type 2 diabetes of 13.7 per 1000 births (Diguisto et al., 2022). The exact mechanisms by which maternal DKA jeopardizes fetal well-being are not fully understood, and published material is scarce in this field. It is known that the keto-acids, as well as glucose, readily cross the placental barrier. Several pathophysiologic aspects of DKA probably contribute to fetal loss. It is unclear whether it is maternal acidosis, hyperglycemia, severe dehydration (resulting in decreased uteroplacental perfusion), or electrolyte balances that have the most harmful effect on the fetus (Veciana, 2013).

The significant mortality rate linked with diabetic ketoacidosis reflects an unfavorable intrauterine environment. Possible mechanisms include (Kamalakkanan, 2003):

- a. Decrease in uteroplacental blood flow due to osmotic diuresis leading to volume depletion, and maternal acidosis can result in fetal hypoxia.
- b. Maternal acidosis may result in fetal acidosis and electrolyte imbalance.
- c. If severe, maternal hypokalaemia and fetal hyperinsulinemia could cause fetal hypokalaemia leading to fetal myocardial suppression and fatal arrhythmias.
- d. Maternal hypophosphatemia associated with diabetic ketoacidosis can cause a decrease in 2,3-diphosphoglycerate, leading to impaired delivery of oxygen to the fetus.
- e. Fetal hyperinsulinemia resulting from maternal hyperglycemia increases fetal oxygen requirement by stimulating oxidative metabolic pathways.

Treatment

Diabetic ketoacidosis in pregnancy is an obstetric and medical emergency and therefore requires prompt and aggressive treatment in a specialized care unit. Physicians should provide management with special expertise in the area, ideally including maternal-fetal medicine and medical endocrinology specialists, an

obstetric anesthesiologist, and skilled nursing support. The principles of management of diabetic ketoacidosis during pregnancy are the same as those in the nonpregnant state. They consist of aggressive volume replacement, intravenous (IV) insulin therapy, correction of acidosis and abnormal electrolytes, correction of the underlying pathology, and intensive monitoring of maternal and fetal response to the treatment (Sibai, 2014).

Initial fluid replacement is first accomplished with normal saline. In patients with diabetic ketoacidosis, the fluid deficit is typically 100 mL/kg of body weight, which is equivalent to 6–10 L based on maternal weight. Immediate effects of this aggressive hydration are hemodilution and increased tissue perfusion, resulting in a decrease in glucose and potassium levels. It is essential to replace 75% of the fluid deficit during the first 24 hours of treatment, and the total volume should be completed within 48 hours. Isotonic normal saline is administered at a rate of 1–2 L/h for 1–2 hours. Once this is completed, normal saline is then administered at a rate of 250–500 mL/h and continued until glucose values are less than 250 mg/dL. Once this is achieved, administration of an IV solution with 5% dextrose is started. The subsequent choice for fluid replacement depends on the hydration state, serum electrolyte levels, and hemodynamic stability, and it should be continued until the calculated fluid deficit is corrected. Close hemodynamic monitoring should be performed during the first 4 hours; this includes hourly urine output through an indwelling catheter and vital signs surveillance every 15 minutes (Sibai, 2014).

Estimation fluid deficit of this patient was 6.8 L. before being referred to dr. Soetomo hospital, the patient had been resuscitated with NaCl 0,9% 30 drops per minute. Fluid resuscitation history from the previous hospital was 1145 mL/ 24 hours on the first day and 800 mL for the next 8 hours. Inadequate fluid resuscitation made worsening of Diabetic Ketoacidosis in this case.

For the absolute or relative insulin deficiency that precipitates DKA, insulin treatment must be initiated to correct the metabolic disturbances (Risa et al., 2013). Correction of hyperglycemia is best achieved with IV short-acting insulin. Regular insulin is administered as an 8- to 10-unit bolus followed by 0.1 units/kg/h until the serum bicarbonate and anion gap normalize and serum ketones become absent. Because correction of acidemia takes much longer than correction of hyperglycemia, insulin should be continued at a basal infusion rate of 1–2 units/h after normoglycemia is established and to be discontinued only after the first subcutaneous dose of regular insulin is administered (Sibai, 2014).

This patient had a known history of DM in a previous pregnancy. The patient has received therapy by an Internist but did not take medicine regularly. At the beginning of her current pregnancy, the results of the OGTT 50 grams was 282 g/dl, and the patient received Novorapid 3x4 iu insulin therapy. The insulin dose should be adjusted according to the response of therapy. When the initial complaint of nausea and vomiting occurred, high blood sugar results (527 mg/dL). This poor control of her blood sugar could lead to Diabetic Ketoacidosis complications. Rapid regulation with four units of insulin has been given to this patient, and from the evaluation, the patient's blood sugar dropped to 286 mg/dL.

The use of bicarbonate is not recommended, as there is no evidence of a beneficial effect, and it may be harmful to the patient and the fetus. Bicarbonate inhibits the compensatory hyperventilation that washes out carbon dioxide (CO₂), leading to an increment in CO₂ partial pressure (PCO₂), which may, in turn, decrease fetal oxygen delivery. In addition, the patient may develop paradoxical cerebral acidosis because the CO₂ diffuses through the blood-brain barrier faster than the infused bicarbonate. Further, bicarbonate administration delays the washout of ketosis and can worsen hypokalemia (Mohan et al., 2017).

Some authors recommend bicarbonate administration during severe acidemia (pH less than 7) or in patients complicated by cardiac dysfunction, sepsis, or shock (Sibai, 2014). The patient was given Bicarbonate 50 mEq/30 minutes considering heavy acidosis could worsen, and death could be occurring. The side effect of bicarbonate could be ruled out because of Intrauterine fetal death

Correction of electrolyte imbalances, particularly hypokalemia, should start as soon as adequate renal function is documented. Serum levels of potassium may appear deceptively normal or slightly elevated, but the total body potassium is usually low. In diabetic ketoacidosis, the total potassium deficit is typically 5–10 mEq/L. During the administration of insulin, volume replacement, and correction of acidosis, potassium shifts from the extracellular to the intracellular space. To prevent fatal arrhythmias, it is essential to keep serum potassium levels between 4 and 5 mEq/L (Sibai, 2014). This patient had an increased pulse, and laboratory results show hypokalemia (3 mmol/L), so it is necessary to be given potassium immediately. This patient received a KCL 100mEq/L.

Conclusion

Diabetic ketoacidosis is rare, but more severe complications in pregnancy also have a terrible outcome for the mother and fetus. The physiological changes during pregnancy make Diabetic ketoacidosis is easier to occur. Management of Diabetic Ketoacidosis cases with a multidisciplinary approach provided by special expertise in hospital, ideally including maternal-fetal medicine specialists and medical endocrinologists, obstetric anesthesiologists, and nursing skills support. Rapid recovery of glycemic control is very important to prevent death in pregnant women with Diabetic Ketoacidosis.

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Conflict of interest

The authors have no conflict of interest to declare

Ethical approval

Consent for publication was obtained from the patient's parents. We have made an effort to remove any possible clues of identifying the patient. There is no ethical issue in this case report as to our knowledge.

Authors contributions

AD drafted the manuscript and collected data, AS and HTJ critically revised the manuscript for important intellectual content. All authors have read and approved the manuscript and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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References

- Al-Hamid, R. (2021). Bureaucracy culture change of administrative services on COVID-19 pandemic era. *International Journal of Social Sciences and Humanities*, 5(3), 192–202. <https://doi.org/10.53730/ijssh.v5n3.1720>
- Diguisto, C., Strachan, M. W. J., Churchill, D., Ayman, G., Knight, M. (2022). A study of diabetic ketoacidosis in the pregnant population in the United Kingdom: Investigating the incidence, aetiology, management and outcomes. *Diabetic Medicine*, 39(4): 1–11. <http://doi.org/10.1111/dme.14743>.
- Grazia, M. & Silvia B. (2020). Gestational Diabetes A Decade after the HAPO Study *Front Diabetes. Karger*, 2020. p. 123–31. <http://doi.org/10.1159/000487096>.
- Gunatilake, R. P. & Foley, M. R. (2011). Diabetic Ketoacidosis in Pregnancy. In: Foley, M. R., Strong Thomas, H. J., Garite, T. J. (2011). *Obstetric Intensive Care Manual*, 3ed. New York, NY: McGraw-Hill Education. p. 135–43.
- Kamalakannan, D., Baskar, V., Barton, D. M., Abdu, T. A. M. (2003). Diabetic ketoacidosis in pregnancy. *Postgr Med J*, 79(934): 454–7. <http://doi.org/10.1136/pmj.79.934.454>
- Mohan, M., Mrcog, M., Ahmed, K., Baagar, M., Bch, M. B., Mrcp, C. (2017). Management of diabetic ketoacidosis in pregnancy. *The Obstetrician & Gynaecologist*, 19(1): 55–62. <https://doi.org/10.1111/tog.12344>.
- Narotama, I. B. I., & Sintaasih, D. K. (2022). The role of job satisfaction in mediation the effect of self-efficacy and job insecurity on turnover intention. *International Research Journal of Management, IT and Social Sciences*, 9(4), 494–513. <https://doi.org/10.21744/irjmis.v9n4.2108>
- Risa, M., Masami, H., Daisuke, F., Masami, S., Yoko, N., Sayaka, T., Keisuke, A., Sosuke, K., Hiroko, Y., Hekiko, S., Yoshiki, Y., Hideki, O. M. (2013). Diabetic Ketoacidosis in a Patient with the First Episode of Type 1 Diabetes During Pregnancy: a Case Report. *Bulletion Osaka Med Coll*, 59(1): 17–20.
- Sibai, B. M. & Viteri, O. A. (2014). Diabetic Ketoacidosis in Pregnancy. *Obstet Gynecol*, 123(1): 167–78. <https://doi.org/10.1097/AOG.000000000000060>.
- Suryasa, I. W., Rodríguez-Gámez, M., & Koldoris, T. (2021). Health and treatment of diabetes mellitus. *International Journal of Health Sciences*, 5(1), i-v. <https://doi.org/10.53730/ijhs.v5n1.2864>
- Veciana, M. De. (2013). Diabetes ketoacidosis in pregnancy. *Semin Perinatol* 37(4): 267–73. <http://dx.doi.org/10.1053/j.semperi.2013.04.005>.