



## Euglycemic diabetic ketoacidosis and COVID-19: A combination to foresee in pregnancy

Diabetic ketoacidosis (DKA) is a serious complication of diabetes, becoming a life-threatening event to both the mother and the fetus.<sup>1</sup> Euglycemic diabetic ketoacidosis (eu-DKA) is defined by a biochemical triad: blood glucose levels below 200 mg/dL, increased anion gap metabolic acidosis, and ketonemia.<sup>2,3</sup> Eu-DKA is extremely rare in obstetric practice<sup>4-6</sup> and requires a high degree of suspicion for diagnosis.<sup>7</sup>

COVID-19 infection may cause ketosis or ketoacidosis in the general population and can also induce DKA for those with diabetes.<sup>8</sup> Diabetes does not seem to increase the risk of COVID-19 occurring but is more frequent in patients with severe COVID-19.<sup>9</sup> Very few cases of eu-DKA have been reported in pregnant women with COVID-19.<sup>10</sup>

We present the case of a 29-year-old woman who is obese (BMI 31.5 kg/m<sup>2</sup>), with gestational diabetes diagnosed at 27 weeks of gestation (initial glycosylated hemoglobin [HbA1c] 5.9%) and suboptimal metabolic control. Weight gain of 20 kg occurred during pregnancy. She was admitted at 34 weeks of gestation due to bilateral COVID-19 pneumonia and metabolic ketoacidosis, a plasma glycemia of 9.4 mmol/L. The analysis highlights a mild normochromic normocytic anemia, leukopenia, plateletopenia with D-dimer elevation; and elevation of inflammatory parameters (polymerase chain reaction 69.7 mg, interleukin-6 65.6 pg/mL, lactate dehydrogenase 780 UI/L) and worsening metabolic rate with HbA1c 7.2%. The patient reported a decrease in intake the previous days.

She was treated with oxygen therapy, remdesivir, and enoxaparin for COVID-19 pneumonia. Serum therapy, bicarbonate, and endovenous insulin perfusion were administered for DKA. Eu-DKA was resolved, but glyce-mic control was difficult with a daily requirement of 300 IU of insulin, maintaining hyperglycemia (capillary glycemic controls 6.6-11 mmol/L).

Once the patient seroconverted (immunoglobulin G [IgG] for SARS-CoV-2 became positive), the insulin

requirements dropped abruptly, resulting in severe hypoglycemia. Eventually, the cesarean section was advanced to the 36th week of pregnancy due to persistent hypoglycemia. The newborn was female, weighing 3900 g without neonatal hypoglycemia. In the immediate postpartum period, the patient presented correct glycemic controls without insulin. Two months after delivery, the patient showed normal glycemic levels, without insulin and an HbA1c of 5.2%.

Eu-DKA should be considered as potential complication of diabetes during pregnancy, particularly in acute COVID-19 infection.<sup>10,11</sup> It remains unclear if COVID-19 infection per se increases the risk of diabetic ketosis, but an unusually high number of COVID-19 patients develop DKA.<sup>12-15</sup> The requirements of insulin in our case were clearly associated to the evolution of viremia: with extremely high demands during the peak fever and proinflammatory storm followed by a sudden drop when recovering from the infection.

Another challenging aspect is to determine the most favorable time for delivery. In most cases, cesarean section was performed emergently at early gestational ages,<sup>11</sup> with the subsequent neonatal hypoxia and/or acidosis.<sup>4</sup> In our case, we stuck to the stabilization of maternal metabolic abnormalities first, with close fetal monitorization.<sup>4</sup> The cesarean section was performed due to persistent maternal hypoglycemia to protect the fetal brain.<sup>16</sup>

We aim to highlight the possibility of eu-DKA in the context of COVID-19 to quickly diagnose and provide the appropriate treatment, reducing morbimortality. Additionally, the timing of delivery can be challenging and requires weighing out benefits and risks according to maternal and fetal status.

The patient signed an informed consent form, and the ethics committee authorized the dissemination of her clinical case.

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**REFERENCES**

- Barski L, Eshkoli T, Brandstaetter E, Jotkowitz A. Euglycemic diabetic ketoacidosis. *Eur J Intern Med.* 2019;63:9-14. doi:10.1016/j.ejim.2019.03.014
- Jaber JF, Standley M, Reddy R. Euglycemic diabetic ketoacidosis in pregnancy: a case report and review of current literature. *Case Rep Crit Care.* 2019;20:8769714. doi:10.1155/2019/8769714
- Modi A, Agrawal A, Morgan F. Euglycemic diabetic ketoacidosis: a review. *Curr Diabetes Rev.* 2017;13(3):315-321. doi:10.2174/1573399812666160421121307
- Sibai BM, Viteri OA. Diabetic ketoacidosis in pregnancy. *Obstet Gynecol.* 2014;123(1):167-178. doi:10.1097/AOG.0000000000000060
- Darbhamulla S, Shah N, Bosio P. Euglycaemic ketoacidosis in a patient with gestational diabetes. *Eur J Obstet Gynecol Reprod Biol.* 2012;163(1):118-119. doi:10.1016/j.ejogrb.2012.03.011
- Muppidi V, Meegada S, Challa T, Siddamreddy S, Samal S. Euglycemic diabetic ketoacidosis in a young pregnant woman precipitated by urinary tract infection. *Cureus.* 2020;12(3):e7331. doi:10.7759/cureus.7331
- Karpate SJ, Morsi H, Shehmar M, Dale J, Patel C. Euglycemic ketoacidosis in pregnancy and its management: case report and review of literature. *Eur J Obstet Gynecol Reprod Biol.* 2013;171(2):386-387. doi:10.1016/j.ejogrb.2013.09.034
- 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):1935-1941. doi:10.1111/dom.14057
- Apicella M, Campopiano MC, Mantuano M, Mazoni L, Coppelli A, Del Prato S. COVID-19 in people with diabetes: understanding the reasons for worse outcomes. *Lancet Diabetes Endocrinol.* 2020;8(9):782-792. doi:10.1016/S2213-8587(20)30238-2
- Pikovskiy M, Tan MY, Ahmed A, Sykes L, Agha-Jaffar R, Yu CKH. Euglycaemic ketoacidosis in pregnant women with COVID-19: two case reports. *BMC Pregnancy Childbirth.* 2021;21:427. doi:10.1186/s12884-021-03928-w
- 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. doi:10.1016/j.diabet.2020.07.008
- Armeni E, Aziz U, Qamar S, et al. Protracted ketonaemia in hyperglycaemic emergencies in COVID-19: a retrospective case series. *Lancet Diabetes Endocrinol.* 2020 Aug;8(8):660-663. doi:10.1016/S2213-8587(20)30221-7
- Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *JAMA.* 2020;323(13):1239-1242. doi:10.1001/jama.2020.2648
- 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):e241745. doi:10.1136/bcr-2021-241745
- Espinosa M, López M, Rivas M, Durruty P, Valdés P. Cetoacidosis normoglicémica en paciente embarazada con neumonía por COVID-19. Reporte de un caso clínico. *Rev Chil Obstet Ginecol.* 2020;85(Suppl 1):S90-S96.
- Amendoeira S, McNair C, Saini J, Habib S. Glucose homeostasis and the neonatal brain: a sweet relationship. *Neonatal Netw.* 2020;39(3):137-146. doi:10.1891/0730-0832.39.3.137