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Empagliflozin, Dulaglutide, and Atorvastatin during 1st weeks of pregnancy: a case report

Adel Alghamdi[1], Hashem Malki[2], Sultan Saleh AlNozha[3], Abeer Alsaeddi[4], Ameerah Alsaedi[5], Jehad Alqurashi[6]

1. *Diabetes Consultant, Diabetes Center of Hera General Hospital, Makkah, Saudi Arabia*
2. *Diabetes Consultant, Diabetes Center of Hera General Hospital, Makkah, Saudi Arabia*
3. *Consultant Diabetologist and Family Medicine, Diabetes and Endocrine Center, Hera General Hospital, Makkah*
4. *Family Medicine Consultant, Al-Hajj Street Primary Health Care, Makkah, Saudi Arabia*
5. *Endocrinology consultant, Diabetes Center of Al-Noor General Hospital, Makkah, Saudi Arabia*
6. *Public Health and Preventive Medicine Consultant, Makkah, Saudi Arabia*

Abstract:
Among women of reproductive age, type 2 diabetes mellitus (T2DM) is becoming increasingly common, raising the risk of miscarriage, birth defects, and infant mortality. Optimal glycemic control and maintaining a healthy weight can decrease the chances of experiencing these negative outcomes. Insufficient research has been conducted on dulaglutide, empagliflozin and atorvastatin to determine their impact on causing birth defects or miscarriages in pregnancy; hence, their use in pregnancy have not been approved by the Food and Drug Administration (FDA). The initial three months of pregnancy (1-13 weeks) are typically regarded as the most dangerous time. A case of 35-year-old woman who has had type 2 diabetes mellitus for two years. Prior to becoming pregnant, she was taking atorvastatin 10 mg daily, empagliflozin 10 mg daily, and dulaglutide 12.5 mg/week. At eight weeks gestation, she was seen for the first time in the diabetic clinic. Because dulaglutide, empagliflozin, and atorvastatin are not approved during pregnancy, they were stopped, and she was started on basal-bolus insulin therapy with dosing titration. The patient had an elective cesarean section at 38 weeks. The male newborn had normal weight for his age. There were no congenital defects or neonatal morbidities observed. There were no complications for the mother. Even though the outcome of this pregnancy is normal, the information presented here might be useful for exploring this issue further.

Introduction:
Obesity rates among adults in the US are on the rise, and are closely linked to the likelihood of developing diabetes (1). Among women of reproductive age, type 2 diabetes mellitus (T2DM) is becoming increasingly common, raising the risk of miscarriage, birth defects, and infant mortality(2). Optimal glycemic control and maintaining a healthy weight can decrease the chances of experiencing these negative outcomes (3). The impact of glucose-lowering drugs on weight needs to be taken into account when selecting them for overweight or obese T2DM patients (4,5). If a non-pregnant patient with type 2 diabetes does not achieve proper glycemic control with metformin, sulphonylurea or (basal) insulin, a Glucagon-like peptide-1 (GLP-1) agonist or Sodium-Glucose Transport Protein 2 (SGLT2) inhibitor can be recommended for weight reduction, hypoglycemia prevention, or reducing cardiovascular risk. This is a significant matter to address when managing non-pregnant with T2DM patients (4). During pregnancy, individuals with type 2 diabetes are primarily managed with insulin or metformin (3). The specific times when certain organs or anomalies are most vulnerable during pregnancy may differ. Nonetheless, the initial three months of pregnancy (1-13 weeks) are typically regarded as the most dangerous time (6). Dulaglutide and Empagliflozin approved by the Food and Drug Administration (FDA) for the treatment of T2DM in adults (7,8) . Dulaglutide a glucagon-like peptide-1 receptor agonist (GLP-1 RA) while Empagliflozin is Sodium-glucose Cotransporter-2 (SGLT2) Inhibitors (7,8). Insufficient research has been conducted on dulaglutide and empagliflozin to determine their impact on causing birth defects or

miscarriages in pregnancy; hence, their use in pregnancy have not been approved by the FDA (7,8). In animal study, Dulaglutide dose-dependently resulted in decreased fetal weight and/or growth, delayed ossification, irregular ossification, and/or skeletal variants like wavy ribs in rat, mouse, and rabbit models without systemic inflammation (9). Maternal weight loss and decreased food intake were the main outcomes of these effects (9). Weight loss in mothers was linked to lower embryonic survival(9). Animal Study of empagliflozin did not exhibit developmental toxicity when a dose that did not cause maternal toxicity was given during the organogenesis period of the first trimester (9). In the literature, nine cases of unintended pregnancies among women with type 2 diabetes have been exposed to dulaglutide during first trimester (10,11). Seven pregnancies ended in live births with no neonatal complications except for the presence of mild bilateral renal pyelectasis in one birth while two women electively terminated their pregnancies (10,11). Eight of the 21 pregnancies involving empagliflozin in humans included the following pregnancy outcomes: two spontaneous abortions, one elective termination, one ectopic pregnancy, three healthy infants without congenital abnormalities, and one premature infant (9).

Statins, also known as Hydroxymethylglutaryl-coenzyme A (HMG-CoA) reductase inhibitors, are commonly utilized to treat high cholesterol and have been proven to lower the risk of cardiovascular disease-related deaths and illnesses (12–14). With a rise in obesity and heart disease among younger people, and more women choosing to have children at a later age, the usage of statins has gone up in patients at childbearing age (15). Due to theoretical concerns regarding possible teratogenesis and the role of cholesterol in the developing embryo, statins have been contraindicated during pregnancy (16). The US Food and Drug Administration (FDA) requested on July 20, 2021, that the "Pregnancy Category X" label for statins be removed (17). Recent evaluations indicate that statin therapy may have a safe and beneficial impact on individuals with homozygous familial hypercholesterolaemia and on pregnant women with pre-eclampsia(18). A multicenter observational prospective controlled study that compared 249 pregnancies exposed to statins with 249 control pregnancies with no teratogenic effect of statins was conducted(19). The results of a cohort study that looked at the teratogenic potential of statins in 1152 women who took them during the first trimester showed no evidence of a significant teratogenic effect (20). Nevertheless, it is still necessary to consider worries about the safety of statin treatment on fetuses during pregnancy.

Case presentation:

We describe a 35-year-old woman who has had type 2 diabetes mellitus for two years. Prior to becoming pregnant, she was taking atorvastatin 10 mg daily, empagliflozin 10 mg daily, and dulaglutide 1.5 mg/week. The patient had no micro or macrovascular complication and was overweight (body mass index = 28.8 kg/m2). At eight weeks gestation, she was seen for the first time in the diabetic clinic. With a HbA1c of 7.5 percent, diabetes was uncontrol. Because dulaglutide, empagliflozin, and atorvastatin are not approved during pregnancy, they were stopped, and she was started on basal-bolus insulin therapy with dosing titration education. She also received diet counseling to help manage her diabetes during pregnancy. With frequent follow up in the clinic the insulin dosage was raised to reach the desired blood glucose level. All fetal biometry measurements were normal and showed no signs of fetal growth abnormalities during routine fetal biometry ultrasounds performed during pregnancy. An anatomy survey was done at 31 weeks of gestational age and it appeared normal. Due to a history of two prior cesarean deliveries, the patient had an elective cesarean section at 38 weeks. The male newborn had normal weight for his age. There were no congenital defects or neonatal morbidities observed. There were no complications for the mother during the cesarean delivery.

Discussion:

Atorvastatin, dulaglutide, and empagliflozin had no effect on fetal growth. In both the mother and the fetus, no abnormalities or complications were observed. the safety of using these medications while pregnant cannot be taken into consideration. Nonetheless, these findings may advance our understanding the effect of them on fetal development. Poor pregnancy outcomes in these women are largely caused by suboptimal diabetic control, which is linked to unplanned pregnancies like the one we report (21). Additionally, these women can be treated with medications that effectively control their weight and diabetes, but they may have negative effects during pregnancy (7,22). Before becoming pregnant, diabetic women should be educated on the significance of blood glucose control (23,24). Additionally, they ought to be informed about the diabetes medications that are contraindicated during pregnancy. Additionally, if a diabetic woman plans to become pregnant, she should be informed that she should only take safe, well-studied diabetic medications for both the fetus and pregnant (23,24).

Conclusion:

More research is needed to confirm or establish the safety of dulaglutide, empagliflozin, and atorvastatin, even though our case had a normal outcome with no complications. To consider its safety, more information is required.

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