

# Gestational Diabetes Is a Key Population Health Opportunity

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**D**iagnosing and treating gestational diabetes (GD) can have long-term positive effects on the health of the mother and baby, warranting a distinct focus on the condition, according to speakers at an Institute for Value-Based Medicine (IVBM) event held in Cleveland, Ohio, on October 26, 2023. Moreover, according to IVBM faculty, pregnant women are much more receptive to diet, obesity, exercise, and cardiovascular advice, potentially improving long-term health and reducing comorbidities.

“Whether it’s macrosomia, birth injury, or jaundice, we know there’s an increased risk of stillbirth [as well as] diabetes, obesity, and heart disease later in life for these babies, so treatment for these mothers is really important,” said IVBM faculty member Stacey Ehrenberg, MD, a maternal-fetal medicine specialist in the Department of Obstetrics and Gynecology at Cleveland Clinic. “We know the incidence of these complications is directly related to [a pregnant woman’s] glucose control. The higher the blood sugars are, the more often their blood sugars are high, the more often we see complications. Controlling blood sugars is the most important thing, [because] glucose crosses the placenta and goes to the baby.”

There are 2 main scenarios for diabetes in pregnancy, Ehrenberg noted: those with preexisting diabetes and those who develop diabetes in the second or third trimester of pregnancy, or GD. However, it is not uncommon for preexisting diabetes to be undiagnosed, warranting earlier screening in women who are overweight or obese, Ehrenberg explained. This category of diabetes is labeled diabetes diagnosed in the first trimester and does not fall under the GD header, with screening ideally taking place at 15 weeks’ gestation. These patients will likely require additional treatment following pregnancy.

In addition to weight, there are several factors to consider when screening for patients with preexisting diabetes, including

physical inactivity, family history of diabetes, ethnicity, hypertension, triglycerides greater than 250 mg/dL, previous hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>) of 5.7% or greater, impaired glucose tolerance, impaired fasting glucose, polycystic ovary syndrome, and a history of cardiovascular disease. If there has been a prior pregnancy, other factors include having a child with a birth weight of more than 4000 g.

Given the ongoing obesity epidemic, there is only a small group of patients who do not need to be screened for diabetes, according to Ehrenberg. Characteristics of these patients include age 25 years or younger, low-risk ethnic origin, body mass index (BMI) less than 25, no previous history of impaired glucose tolerance, as well as no previous history of obstetrical outcomes associated with GD for those with a second pregnancy.

“Who is included, then, in the population who needs to be tested? Well, pretty much everybody,” Ehrenberg said. “It takes longer to figure out who not to test than to just test everybody. I think I have 5 patients a week who actually meet the criteria to not be tested, and this is not an exaggeration.”

There are 2 diagnostic approaches for screening patients, with the most common in the United States being the 2-step process. The 1-step approach results in a GD diagnosis for approximately 16% to 18% of patients, whereas the 2-step method has a lower rate of approximately 8% to 10%, Ehrenberg estimated during her talk.

Although studies have compared the 2 methods, it is unclear whether there is an advantage to treating the additional patients detected with the 1-step method. One study<sup>1</sup> published in the *New England Journal of Medicine (NEJM)* in 2021 concluded that 1-step testing doubled the rate of detection of GD vs the 2-step method (16.5% vs 8.5%, respectively) but did not affect the risks of infants being large for gestational age (8.9% vs 9.2%), adverse perinatal outcomes (3.1% vs 3%), primary

cesarean section (24% vs 24.6%), or gestational hypertension or preeclampsia (13.6% vs 13.5%). These findings, teamed with others, have led to the 2-step approach being the preferred method of detection.

### Treatment Following Diagnosis

For many patients with GD, management of the disease will be a new concept and diagnosis should include counseling on glucose monitoring, diet, exercise, oral hypoglycemics, and insulin. In a panel discussion at the IVBM event, the group described the benefits of a multidisciplinary treatment approach to GD care. The panel, moderated by event chair Diana Isaacs, PharmD, BCPS, BCACP, BC-ADM, CDCES, director of education and training in diabetes technology at Cleveland Clinic, included specialists in cardiology, diet and nutrition, pharmacy, as well as advanced practice providers. Cleveland Clinic employs a multidisciplinary technique that hits each of these areas, the panelists noted, which also provides ease of care through housing these services in 1 location.

For diet and exercise, the panel recommended a low carbohydrate diet and 30 minutes of nonweight-bearing moderate exercise 5 times a week. A larger proportion of patients tend to stick to diet and exercise recommendations during pregnancy, as these patients tend to be more motivated, the panelists agreed. Diet and exercise together have been shown to improve glycemic control and cardiovascular fitness.<sup>2</sup> Moreover, the combination of diet and exercise led to improvements in rates of macrosomia and infants large for gestational age.<sup>3</sup>

One key is to advise patients to eat “twice as healthy” instead of “eating for 2,” said Cara D. Dolin, MD, MPH, assistant professor of obstetrics/gynecology and reproductive biology at Cleveland Clinic Lerner College of Medicine of Case Western Reserve University. “It’s important to focus on the foods they eat,” she said. “Patients should be filling half their plates with fruits and vegetables, which are high in fiber and vitamin content and make them feel fuller, leaving less room for unhealthy things. They should avoid drinking sugary beverages and eating processed and fast food.”

In the first trimester, calorie intake does not need to increase but should increase by 340 calories in the second trimester and by 452 in the third, assuming the patient started at a normal weight.<sup>4</sup> For those with obesity, it should be even less, Dolin explained. The focus should be on fruits and vegetables, with an avoidance of sugar, processed foods, and fast foods. Exercise should be moderate-intensity aerobic activity, with an overall sentiment of sitting less and moving more. “Exercise is safe and recommended in pregnancy,” she said.

Overall, 30% to 40% will not achieve glucose control with diet alone and will require medical intervention, Ehrenberg noted. Although there are oral medications available, such as glyburide

and metformin, these medications cross the placenta and their long-term impact when taken during pregnancy is unknown. As a result, insulin is widely considered the frontline treatment of choice for managing GD.

The type of insulin and the delivery timing can be individualized to each patient, with neutral protamine Hagedorn (NPH) and lispro being the most frequently selected insulins. Ehrenberg noted that lispro is associated with a lower incidence of maternal hypoglycemia compared with other insulin choices. Each insulin has a unique onset of action, peak time of action, and duration of action that can be tailored to fit the patient’s needs.

Typically, the insulin starting dose is based on weight, beginning at 0.7 units/kg/day in the first trimester. This should be increased by 0.1 units/kg/day each trimester of pregnancy, as the need for insulin typically rises throughout pregnancy. The dose of insulin can be divided in several ways, with one method being two-thirds in the morning and one-third at night. Ehrenberg also noted that lispro and NPH could be combined in various formats, such as lispro at meals and NPH at bedtime.

### Pregnancy Is a Population Health Opportunity

In many cases, pregnant women are highly engaged in their health care during pregnancy, opening a “golden opportunity” for education and intervention for other health-related issues beyond GD, Dolin explained. These include the management of existing obesity or chronic hypertension and education around how to maintain a healthy lifestyle following pregnancy.

“I view pregnancy as a public health opportunity. This is really a golden opportunity to engage patients with underlying chronic disease, when they have increased contact with health care providers and increased awareness of healthy behaviors,” Dolin said. “They are often more receptive to advice, especially if framed to benefit the baby. This is an opportunity for lifestyle changes and improved habits that will last beyond the pregnancy.”

More than one-third (40%) of women between the ages of 20 and 39 years in the United States have obesity, Dolin noted. Of these, 9% have class 3 obesity, or a BMI over 40.<sup>5</sup> Obesity is strongly associated with several comorbidities, including type 2 diabetes and chronic hypertension. In pregnancy, obesity is also associated with several maternal, fetal, and neonatal risks, Dolin noted. Hypertension during pregnancy is also tied to preeclampsia, maternal mortality, and other adverse outcomes.

According to an American College of Obstetricians and Gynecologists bulletin,<sup>6</sup> there is a 20% risk of preeclampsia with diabetes and a 25% risk with chronic hypertension. With obesity, however, the risk of preeclampsia increases by 2 to 3 times. Outside of preemptive management of these

conditions, the best treatment for prevention of preeclampsia remains low-dose aspirin, Dolin noted.

“Cardiovascular disease is the leading cause of maternal mortality in the United States,” she said. “It is responsible for more than a quarter or more of pregnancy-related deaths. It is very important when taking care of patients with diabetes and pregnancy to understand their underlying cardiovascular risk so we can make sure they remain healthy.”

If chronic hypertension is diagnosed following pregnancy, it can still be effectively treated, according to findings published in *NEJM*. In the 2408-patient study,<sup>7</sup> treatment with antihypertensive therapy reduced the risk of a composite end point for adverse pregnancy outcomes compared with a control group. Those in the active treatment arm experienced an adverse outcome 30.2% of the time compared with 37% in the control arm (risk ratio, 0.82; 95% CI, 0.73-0.92;  $P < .001$ ). The rates of infants small for gestational age were similar between arms.

Capitalizing on the increased health vigilance surrounding pregnancy, there is a window of opportunity that Dolin labeled preconception for discussing obesity and hypertension. Determining when pregnancy is on the horizon comes down to conversations with the patient, for which Dolin recommended using the One Key Question format.<sup>8</sup>

Individuals with obesity who are not yet pregnant have a much larger list of potential treatment options, including glucagon-like peptide 1 (GLP-1) agonists. Significant data do not yet exist for the impact of the GLP-1 agonists on weight loss, such as semaglutide (Wegovy) and tirzepatide (Zepbound), during pregnancy; however, they can be effectively used during the preconception phase to help with obesity management. If this approach is taken, faculty at the event recommended stopping the GLP-1 agonist 1 to 4 weeks prior to conception to prevent any unknown effects. To further plan the pregnancy, Dolin recommended counseling on methods of contraception.

“The most important thing they can do before they get pregnant is to try to lose weight. [This is] easier said than done, but even just 5% to 10% of body weight loss drastically improved perinatal outcomes,” Dolin said. “The GLP-1 receptor agonists are not currently compatible with pregnancy or approved for that, but we know a lot of patients with diabetes and obesity are using that to treat their diabetes or obesity.”

The amount of weight gained during pregnancy will vary depending on the starting BMI for each patient, she added. For those with class 3 obesity, it may even be appropriate to lose weight during pregnancy. Across all classes of obesity,<sup>9</sup> the average recommended range of total weight gain is 11 to 20 lb. For those with a BMI between 18.5 to 24.9, weight gain should range between 25 and 35 lb. In general, she noted, more than half of women exceed these guidelines for

gestational weight gain, increasing the likelihood of high-risk births or infants large for gestational age.<sup>10</sup>

Adding to this, Dolin noted that excessive gestational weight gain could lead to higher rates of postpartum weight retention. She noted that patients retain approximately 12 lb after pregnancy, with a quarter of women retaining 20 lb or more at 12 months postpartum. To help manage postpartum weight, Dolin recommended that patients should be advised on the benefits of breastfeeding. In addition to a host of other benefits, breastfeeding has also been found to improve cardiovascular risk, she added. For those on medications beyond pregnancy, she recommended use of the LactRx app to measure what could pass through the breast milk.

### Technology Use During Pregnancy

Several types of technology are available for the management of diabetes, including continuous glucose monitors (CGMs) and automated insulin pumps. Results on their efficacy throughout pregnancy have primarily come from studies of those with type 1 diabetes, as insurance coverage for these devices is nonexistent in the context of pregnancy.

CGMs shed light on glycemic trends, which may change throughout pregnancy. Even for patients with type 1 diabetes or a long history of managing the disease, pregnancy may still significantly alter their established patterns, said IVBM faculty member M. Cecilia Lansang, MD, MPH. In these scenarios, the trends in blood glucose and the ability to adjust management strategies can be invaluable, added Lansang, professor of medicine at Cleveland Clinic Lerner College of Medicine of Case Western Reserve University and director of endocrinology and diabetes technology in the Department of Endocrinology, Diabetes, and Metabolism at Cleveland Clinic.

In general, the glycemic variability detailed with a CGM cannot be gathered using finger stick self-monitoring of blood glucose, Lansang explained. Furthermore, she argued that CGM use results in less hyperglycemia and hypoglycemia compared with finger sticks. Additionally, studies have shown lower birth weight, less preeclampsia, and fewer cesarean sections in patients who used a CGM vs those who self-monitored. In a Chinese study of pregnant women with GD,<sup>11</sup> CGM was compared with routine care and resulted in a lower rate of preeclampsia and primary cesarean section ( $P < .05$ ).

There are several FDA-cleared CGM systems for pregnancy, with Lansang drawing attention to the FreeStyle Libre and Dexcom G7 devices. Additionally, other devices can be used off-label. One of the major concerns with CGM is not necessarily the efficacy but rather the costs associated with the device. Lansang argued that many of the benefits are worth the added expenses. She estimated the cost for the first month of finger sticks to be \$338,

whereas the cost could reach \$500 for the device, sensor, and reader combined.

In a panel discussion that followed, the faculty seemed convinced that CGM should be used during pregnancy and noted a lack of insurance coverage as a leading reason for the lack of uptake. In the end, even in the setting of GD, the group felt CGM was the optimal approach vs routine finger sticks.

“Of course, insurance is the issue, but finger pricks have so many variables that are attached to it. There are many things that have to be considered, which is not to say CGM is without interferences, but not to the same extent that finger prick does,” Lansang said. “If you want less pain and hassle, with some data to back it up, I’d say it is priceless.”

Additionally, the faculty discussed other technology for insulin delivery, specifically insulin pumps. For those with type 1 diabetes who become pregnant, studies have demonstrated that the use of an insulin pump is associated with lower HbA<sub>1c</sub> during pregnancy without the risk of severe hypoglycemia and diabetic ketoacidosis, said Kevin Borst, DO, director of the Endocrine Disorders in Pregnancy Center at Cleveland Clinic.

Recent findings published in *NEJM* also showed the benefits associated with automated insulin delivery during pregnancy in those with type 1 diabetes. In this study,<sup>12</sup> the maternal glucose level was in the target range 68.2% of the time for those using a closed-loop system vs 55.6% of the time for standard care. Secondary end points showed similar findings for hyperglycemia, overnight glucose levels, and HbA<sub>1c</sub> levels. Moreover, there was very little time spent in hypoglycemia.

“Should a closed-loop system have a pregnancy-specific glucose target or an algorithm? Yes, I believe it should, but right now they do not,” Borst said. “I would love if they had this, and my hope is that, over time, the companies will come up with this. But as of right now, all this is off-label, and we do the best we can with what we have.”

**Author Information:** Mr Inman is an employee of MJH Life Sciences, parent company of the publisher of *The American Journal of Accountable Care*.

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