Continuous Glucose Monitoring in Pregnancy: New Insights Into Gestational Diabetes With More to Learn

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The prevalence of gestational diabetes mellitus (GDM) has increased substantially, with 30% more women diagnosed with this pregnancy complication over the past two decades (1). This increased prevalence is of concern given the association of GDM with adverse pregnancy outcomes as well as longer-term adverse outcomes for both women and their offspring (2,3).

Identification and treatment of GDM are clinically important, as treatment can lessen the frequency of some, but not all, short-term adverse outcomes (4,5). Treatment of GDM may be associated with better long-term metabolic outcomes in offspring, but this has been inconsistently demonstrated (6,7). One potential explanation for the inconsistent relationship between GDM treatment and the reduction of adverse maternal, perinatal, and childhood outcomes is that GDM diagnosis and treatment typically occur in the third trimester, which may be too late to ameliorate all the adverse effects associated with maternal hyperglycemia. However, reliable approaches for diagnosing or predicting GDM earlier in gestation have yet to be developed (8). In addition, the optimal glycemic targets for treatment of GDM once the diagnosis is made are incompletely understood (9).

Multiple investigators have tried to diagnose GDM earlier in pregnancy than the period of 24–28 weeks of gestation that typically is used, although these attempts have not resulted in an approach that reliably identifies women with GDM (10). One reason that this identification has been difficult is the significant change in glucose metabolism across the early part of pregnancy that occurs, as changes in maternal metabolism help meet the metabolic needs of the developing fetus (11–13). These changes include the development of significant insulin resistance and longitudinal alterations in glucose levels, particularly through the second and third trimesters (12). The variety and dynamism of these changes make the relationship between early and later dysglycemia complex. However, early dysglycemia typically has been evaluated with measures of glucose at a single (e.g., during fasting), or at most a few (e.g., after a glucose load), time points, thereby limiting the ability to discern associations that may exist between early and late dysglycemia (14). In addition, the glucose loads associated with oral glucose tolerance tests are commonly associated with symptoms such as headache, nausea and vomiting, and dizziness, which may be exacerbated in early pregnancy (15). A panel of experts has determined that insufficient data are available "to confidently recommend cutoff points for oral glucose tolerance testing early in pregnancy (e.g., prior to 20 weeks' gestation)" (16).

Given the clear relationship between levels of glycemia and adverse outcomes in both women and their offspring (2,17–19) as well as the known longitudinal changes (both moment to moment and over longer periods of time) of glycemic levels in pregnancy (11,12,20,21), CGM has the unique potential to provide insight into the relationship between early glycemic patterns and GDM diagnosis and, just as importantly, maternal and perinatal outcomes. Although the data regarding the associations between CGM values and GDM are so far limited, they have yielded results that suggest its utility in elucidating clinically relevant patterns in pregnancy that are not knowable if only cross-sectional glucose-related values are observed. For example, despite having similar fasting glucose and HbA_{1c} levels and no diagnosis of diabetes, pregnant individuals with obesity were shown to have higher daytime and nocturnal glucose levels than pregnant individuals with a normal BMI in both early and late pregnancy, which may have explained, in part, the excess fetal fat accretion observed in offspring of mothers with obesity (20). CGM also has revealed specific temporal glucose patterns among pregnant individuals with type 1 or 2 diabetes that were associated with large-for-gestational-age (LGA) birth to a greater extent than standard pre- and postprandial measures of glucose control (22). Finally, among individuals

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with treated GDM, those who gave birth to an LGA newborn had higher nocturnal glucose levels than individuals without an LGA birth (23). Accordingly, in a workshop focused on knowledge gaps concerning GDM, participants concluded that "capturing the richness of continuous data relating dysglycemia to adverse outcomes (is) of paramount importance" (8).

In this issue of *Diabetes Care,* Durnwald et al. (24) present a prospective cohort study evaluating glycemic patterns across gestation among individuals who did and did not develop GDM and who used continuous glucose monitoring (CGM). Participants were enrolled at <17 weeks' gestation and encouraged to wear a CGM as much as tolerated across gestation. Of the 768 individuals included in this analysis, 58 (8%) developed GDM after 24 weeks' gestation based on oral glucose tolerance test (OGTT) results. The authors found that individuals diagnosed with GDM after 24 weeks' gestation had higher mean glucose values prior to GDM diagnosis that were evident as early as 13 weeks' gestation, had greater variability in their glucose values, and spent less time within ranges of both 63–140 mg/dL (3.5–7.8 mmol/L) and 63–120 mg/dL (3.5–6.7 mmol/L). The GDM group also had consistently higher mean glucose levels during both the daytime and overnight periods compared with individuals without GDM. These patterns were consistent across all three trimesters of pregnancy before completion of the OGTT. Finally, the authors found that CGM metrics obtained prior to OGTT had the ability to predict GDM, with an area under the receiver operating characteristic curve of 0.81 when using second-trimester percent time >140 mg/dL to predict GDM. These data are the first to help us understand the pattern of glycemia that occurs prior to GDM diagnosis, which is critical to our attempts to understand whether earlier screening for dysglycemia in pregnancy can help to predict subsequent GDM and improve both perinatal and long-term metabolic outcomes for pregnant individuals and their offspring.

Strengths of this study include the robust sample size and amount of CGM-derived glucose data with detailed CGM profiles prior to administration of the OGTT, although data are limited prior to 13 weeks' gestation. These data also represent an important step forward in our understanding of both normoglycemia and dysglycemia across gestation. However, one limitation is that these glucose data are not correlated with perinatal outcomes, limiting our understanding of whether diagnosing and treating GDM in early pregnancy can improve perinatal outcomes. The authors include a predictive model indicating that early-pregnancy CGM data can identify those women who will have an abnormal OGTT after 24 weeks' gestation, offering optimism that CGM could be an alternative to OGTT-based screening in the future. However, the models in the current analysis did not incorporate other clinical characteristics linked to perinatal outcomes such as maternal BMI. In addition, the small number of individuals with GDM limits our understanding of optimal CGM-derived treatment targets once GDM is diagnosed.

These data offer good news, as they fill an important gap in our understanding of maternal glycemia across gestation. They also offer evidence that CGM is well tolerated, and even pregnant individuals without GDM are willing to wear this technology. Now our work begins to understand whether CGM-derived glucose metrics can provide an alternative to OGTT-based GDM testing, help us refine the timing of GDM screening to optimize short- and long-term maternal and child health outcomes, and identify the optimal treatment targets once GDM is diagnosed. Ongoing work, such as that of the Glycemic Observation and Metabolic Outcomes in Mothers and Offspring (GO MOMs) study (NCT04860336), will build on this foundation to help answer these important questions.

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