Gestational Diabetes Mellitus and Glucose Sample Handling

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Gestational diabetes mellitus (GDM) continues to provide challenges in terms of both diagnosis and management. Recent scientific discussions around the preanalytical processing of glucose samples from the glucose tolerance test (GTT) have generated considerable interest and debate (1,2).

For most women, the diagnosis of GDM is based on the measurement of plasma glucose after the GTT. The observational Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) study (3) and the consensus agreement about diagnostic criteria by the International Association of the Diabetes and Pregnancy Study Groups (IADPSG) (4) provided glucose thresholds for the diagnosis of GDM.

The HAPO study was meticulous in the preanalytical and analytical processing of glucose samples (3). Given that our current diagnostic criteria are based on the findings of the HAPO study, if results are to be comparable, the same meticulous processing must also be applied to glucose samples processed in routine clinical care.

A major source of preanalytical error in measuring glucose is loss of glucose from blood samples through glycolysis in red and white blood cells (5). Glucose is lost from the whole blood sample at a rate of 5–7% per hour at room temperature (5). Although sodium fluoride is intended to inhibit glycolysis, it is inadequate for the first 2 or more hours after collection (5,6).

In this issue of *Diabetes Care*, Potter et al. (7) have demonstrated the importance of strict preanalytical processing of glucose samples obtained during a GTT and the consequences of differences in preanalytical processing on the prevalence of GDM. Their study looked at two consecutive cohorts of pregnant women from the same region who underwent a 75-g oral GTT for the diagnosis of GDM. In the first cohort, recruited over a period of 28 months, samples were collected in sodium fluoride tubes and were kept at room temperature until completion of the test (delayed centrifugation). In the second cohort, recruited over a subsequent period of 16 months, samples were collected in sodium fluoride tubes and were centrifuged within 10 min (early centrifugation).

Potter et al. report that the mean fasting, 1-h, and 2-h glucose concentrations were all significantly lower when the samples were processed after delayed rather than early centrifugation. This finding is not new, but the study quantifies the impact of delayed centrifugation on the measured glucose concentration in blood samples from the GTT.

The fasting glucose samples were more impacted by the preanalytical sample handling than the 1-h and 2-h samples. This finding is biologically plausible given that, using a protocol of delayed centifugation, the fasting sample has a longer lag time between venipuncture and centrifugation than the remaining samples. Using the early centifugation protocol, the time between venipuncture and centifugation is short and consistent.

The crucial aspect of this study is the impact of preanalytical processing on the diagnosis of GDM. Potter et al. reported an increase in the prevalence of GDM from 11.6% to 20.6% upon changing to a protocol of early centrifugation, as was conducted in the HAPO study and from which the diagnostic criteria were derived.

The increase in the GDM diagnosis rate was predominately due to an increase in fasting glucose concentration and to a lesser degree 1-h glucose concentration. The greatest impact of the early centifugation protocol on the rate of GDM diagnosis was the increase in the number of women with a fasting glucose just above the threshold required for GDM diagnosis, in the range of 5.1–5.2 mmol/L. This observation reinforces the need for meticulous preanalytical sample handling.

There were some minor limitations in the study as outlined by the authors, but nothing that would explain the dramatic increase in the prevalence of GDM. This increase is large and therefore is relevant to clinical service provision, both at the diagnostic level and the clinical care level.

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The findings of this study (7) also have broad implications for the reporting of GDM data. Comparisons of prevalence data from different parts of the world, particularly from remote areas and places where the pathology services are not integrated, will need to take into account the methodology used, as this could have a major impact on the relevance of the findings and observations. Similarly, when large population-based databases of GDM prevalence are published, the preanalytical sample handling of GTT samples will be a crucial component of the methodology. Without attention to preanalytical processing and standardization, data quality will be compromised.

In their article, Potter et al. highlight an often overlooked aspect of the GTT. Without strict preanalytical oral GTT sample handling in routine clinical practice, our ability to accurately diagnose GDM and report GDM prevalence data will be flawed.

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