Issues With the Diagnosis and Classification of Hyperglycemia in Early Pregnancy

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In 2010, the International Association of the Diabetes and Pregnancy Study Groups (IADPSG) panel published consensus-based recommendations on the diagnosis and classification of hyperglycemia in pregnancy (1). Within that document, the recommendations regarding early pregnancy testing were designed to facilitate early detection and treatment of hyperglycemia (HbA_{1c} ≥6.5% [48 mmol/mol], fasting venous plasma glucose ≥7.0 mmol/L, random plasma glucose ≥11.1 mmol/L with confirmation) that, outside pregnancy, would be classified as diabetes. The term "overt diabetes" was suggested to describe these women. Subsequently, the World Health Organization (WHO) adopted the IADPSG criteria with some modifications and promoted the use of the term "diabetes in pregnancy" (2) for this group.

Cognizant that milder degrees of hyperglycemia would also be detected by early pregnancy testing, the IADPSG also recommended that fasting plasma glucose (FPG) in the range 5.1–6.9 mmol/L should be considered diagnostic of gestational diabetes mellitus (GDM) if noted at any time during pregnancy. More recent data from Italy (3) and China (4), where IADPSG diagnostic criteria were applied, have strongly challenged this recommendation, demonstrating a clear fall in FPG in early pregnancy and showing that early FPG ≥5.1 mmol/L is poorly predictive of later GDM at 24–28 weeks' gestation. Zhu et al. (4) suggested using FPG 6.1–6.9 mmol/L "at the time of booking and the first prenatal visit" as a pragmatic criterion for GDM diagnosis in China. To date, similar data have not been reported in other populations.

We note that no randomized controlled trial data exist regarding the balance between additional benefits and costs of detecting and treating degrees of hyperglycemia less severe than "overt" diabetes from early pregnancy.

The potential utility of HbA_{1c} in early pregnancy has also been addressed. In particular, a large cohort study from New Zealand (5) noted that HbA_{1c} ≥5.9% (41 mmol/mol) identified all cases of WHO diabetes in pregnancy and was associated with a twofold risk of congenital anomalies, preeclampsia, and shoulder dystocia and a threefold risk of perinatal deaths. The use of HbA_{1c} in this context is not currently endorsed by major national bodies and must carry some caveats because of the known limitations of the test. However, despite its poor sensitivity for impaired fasting glucose and impaired glucose tolerance, HbA_{1c} may offer a pragmatic means of identifying women at high risk of serious pregnancy complications and warrants further detailed evaluation.

In conclusion, we suggest that the use of the IADPSG fasting glucose threshold of ≥5.1 mmol/L for the identification of GDM in early pregnancy is not justified by current evidence and that an early HbA_{1c} ≥5.9% (41 mmol/mol) may identify women at higher risk for adverse pregnancy outcomes. In contrast to "standard" GDM testing at 24–32 weeks' gestation, insufficient data exist to confidently recommend cutoff points for oral glucose tolerance testing in early pregnancy (e.g., prior to 20 weeks' gestation). Current empirical approaches vary from application of "standard" (nonpregnant) thresholds to use of IADPSG/WHO thresholds throughout pregnancy. Normative data regarding early pregnancy

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glycemia and consequences of its detection and treatment are urgently required and should be a priority for future research.

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