Do the New Threshold Levels for the Diagnosis of Gestational Diabetes Mellitus Correctly Identify Women at Risk?

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Pregnant women with gestational diabetes mellitus (GDM) are at risk for certain neonatal complications. The International Association of the Diabetes and Pregnancy Study Groups (IADPSG) blood glucose level (BGL) diagnostic thresholds correspond to an odds ratio of at least 1.75 for selected complications (1). In the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study (2), 16.1% of subjects had GDM, with the majority (11.1%) having one elevated BGL only (1). As the thresholds are statistically validated, subjects with GDM must have a risk of ≥1.75. But is this the case? All three BGL thresholds were defined independently. For example, when the 2-h BGL threshold was defined, the impact of fasting and 1-h BGLs were not considered. Their elevation should increase the risk of complications associated with raised 2-h BGLs. Alternatively, could normal fasting and 1-h BGLs reduce that risk? Are two normal BGLs protective?

The data for subgroups with only one elevated BGL are unpublished. To estimate these, HAPO data for macrosomia (birth weight >90th centile) were evaluated [see Table 2 in Metzger et al. (2)] using the IADPSG stepwise approach (1). There were 23,217 subjects and 2,221 cases of macrosomia (prevalence 9.6%). The number having GDM (fasting blood glucose [FBG] ≥5.1 mmol/L) was 1,927 (8.3%). This should comprise all cases in FBG categories 7 (217) and 6 (672) and a proportion from category 5 (1,038 of 1,883). In those with GDM, the calculated number of pregnancies with macrosomia was 352, with a risk ratio (RR) of 0.223.

Thus, 21,290 subjects with a normal FBG and 1,869 cases of macrosomia (prevalence 8.8%) remain. Similar methods revealed 1,352 (5.7%) subjects with GDM (normal FBG, 1-h BGL >10 mmol/L), and the corresponding number of pregnancies with macrosomia was 199–204 (RR 0.177–0.183 [proportional to cases previously identified in BGL categories 5–7]).

Finally, 19,967 subjects had two normal (fasting and 1-h) BGLs with 1,665–1,670 cases of macrosomia (prevalence ~8.4%). There were only 488 (2.1%) subjects with GDM (2-h BGL >8.5 mmol/L only) with 60–67 cases of macrosomia (RR 0.139–0.158 [proportional to cases previously identified in BGL categories 5–7]). This contrasts the expected 89 cases of macrosomia based on an RR for FBG of 0.223 ($P < 0.05$ by χ^2 test).

This stepwise exploratory analysis of the effect of known normal BGLs on risk demonstrates progressive decreases in the prevalence of macrosomia and RRs of GDM pregnancies having macrosomia compared with expected rates (FBG rates derived from the whole cohort).

The statistical power underpinning IADPSG thresholds may be significantly reduced in subgroups having one elevated BGL only. If confirmed, it suggests the IADPSG thresholds may not apply to these subgroups and that higher thresholds should apply. These subgroups represent the majority (~70%) identified by the IADPSG criteria. Potentially <50% of them may have a risk exceeding the specified odds ratio of 1.75. In other words, two normal BGL parameters may be protective. However, the IADPSG criteria correctly identify at-risk subjects with three elevated BGL parameters, suggesting that no single BGL adequately defines risk and that all three BGL parameters should be assessed together.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

Author Contributions. M.d'E. is the guarantor of this work and, as such had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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