Diagnosing Gestational Diabetes Mellitus: Rationed or Rationally Related to Risk?

The much-anticipated, weather-plagued National Institutes of Health (NIH) Consensus Development Conference on Diagnosing Gestational Diabetes Mellitus, held in Bethesda, Maryland, 4–6 March 2013, led to publication of a consensus panel report (1) that essentially maintains and promotes the status quo regarding gestational diabetes mellitus (GDM) diagnosis. The panel report contradicts current American Diabetes Association (ADA) recommendations (2). This commentary addresses several areas of disagreement.

The only constant is change, and this is most apparent with the demography of pregnancy. Perhaps the most disturbing omission from the NIH panel's report (1) is the lack of clear acknowledgment of the importance of the increasing prevalence of prediabetes and undiagnosed type 2 diabetes, outside pregnancy, in women of childbearing age (2). This omission effectively precludes any strategy for early detection of these potentially serious problems in pregnancy. Much of the NIH report expresses grave concerns about the possibility of a two- to threefold increase in GDM prevalence from the current estimate of 5–6%. However, the National Health and Nutrition Examination Survey (NHANES) 2005–2008 data (3) regarding U.S. women aged 18–44 years report frank diabetes in 4.5% of participants (1.7% undiagnosed) and prediabetes in 26.4%. While the current ADA (2) criteria for the diagnosis of GDM are based primarily on considerations of fetopathy, they still have an important role in identifying women with current or future abnormalities of glucose metabolism. Given the NHANES prevalence estimates for impaired glucose metabolism of ~30% in women of childbearing age and the general acknowledgment that glucose tolerance worsens and that glucose control is more important during pregnancy, it seems baffling that the NIH panel (1) wishes to "ration" GDM prevalence to 5–6% of pregnant women.

Currently, the most commonly used criteria for GDM in the U.S. and in other parts of the world are derived from the data collected by O'Sullivan and Mahan (4) from 1956 to 1957 and published in 1964, relating to the risk of developing diabetes following pregnancy. The history of their evolution since that time has been summarized by Naylor (5) and more recently updated by Coustan (6). To the dispassionate observer, it seems surprising that these criteria still predominate and are favored by the NIH panel. This may represent a form of clinical inertia (7). Simply stated, it is easier to continue an established (arbitrary) pattern of practice than to embrace change. Further, the outdated and methodologically incorrect National Diabetes Data Group (NDDG) criteria are still used in preference to the Carpenter-Coustan (CC) criteria (6) in many sites. One can speculate that this may be due to their higher diagnostic thresholds, which conveniently lower the frequency of GDM diagnoses. Astoundingly, despite their convoluted history, the CC criteria for GDM diagnosis are numerically extremely close to those derived from associations with diabetic fetopathy, recommended by the International Association of the Diabetes and Pregnancy Study Groups (IADPSG) (8) and endorsed by the ADA (2).

Should testing for GDM be a one-step or two-step procedure? The original studies of O'Sullivan involved uniform one-step administration of a 100-g oral glucose tolerance test (OGTT) (4,5), and diagnostic cutoffs were derived from such data. Protocols for simplified testing were developed later and generally involved a nonfasting glucose challenge test (GCT). At some uncertain point in the evolution of GDM diagnosis, the idea of the GCT as a screening test for low-risk women followed by a diagnostic OGTT appears to have metamorphosed into a two-step approach. The NIH panel argues that two-step testing is less burdensome for women but provides no data or evidence for this. By the panel's own summation, two-step testing involves an additional laboratory visit and collection of four additional blood draws for up to 23% of women. A recent systematic review (9) concluded that a two-step strategy misses ~25% of GDM cases diagnosed with the OGTT. These missed cases of GDM will result in adverse events, and the real burden and cost of these will need to be factored and compared with any hypothetical advantage of a two-stage procedure. Further, a recent Canadian audit (10) noted that only 36% of pregnant women with dysglycemia on initial testing proceeded to the recommended follow-up 75-g OGTT. Two-step testing, promoted by the NIH panel to limit false positives, clearly delays GDM diagnosis, misses 25% of GDM cases even with optimal follow-up, and gives the opportunity for multiple process errors.

Another highly contestable, but "comfortable," aspect of current practice has been the requirement for ≥2 OGTT values above threshold for the diagnosis of GDM. Anecdotal explanations of this practice (not used in other definitions of diabetes) refer to the poor reproducibility of 1950s' whole blood glucose assays (5) and concerns, echoed by the NIH panel, about labeling women as "having diabetes" on the basis of a single test. At least 10 studies (11–20) have compared women with one abnormal value (OAV) on the OGTT with those diagnosed as GDM and/or those considered normal. All have concluded that OAV women risk increased pregnancy complications, principally fetal overgrowth and hypertensive disorders of pregnancy. The one randomized controlled trial (RCT) in this group of women (21) reported improved outcomes with active treatment. Insisting on two abnormal OGTT values for the diagnosis of GDM limits GDM diagnoses, principally by excluding OAV women who are at similar risk of adverse outcomes. This appears irrational in the face of such consistent contrary evidence.

The NIH consensus panel identifies as a priority the conduct of a new RCT evaluating outcomes in women currently classified as "normal" according to prevalent U.S. criteria, but who would be considered abnormal by the IADPSG (8) and ADA (2). They wish such a trial to address "clinically important health and patient-centered outcomes," without providing any definitions of these terms. They implicitly

criticize previous high-quality RCTs by Crowther et al. (22) and Landon et al. (23), for including "highly motivated individuals" and being conducted in "academic medical centers." Presumably their ideal trial would involve unmotivated participants and untrained, inexperienced investigators. Given the known graded relationship between maternal glycemia and pregnancy outcomes and the fact that the two RCTs took 10 (22) and 6 (23) years to conduct, these proposals appear little more than procrastination dressed up as science.

No diagnostic process or set of OGTT criteria will ever be able to perfectly identify all women at risk for adverse pregnancy outcomes. However, synthesis of available epidemiologic and clinical trial data suggests that the IADPSG- and ADA-recommended criteria (refs. 8 and 2, respectively) represent a reasonable and responsible approach to identifying women with hyperglycemia in pregnancy who are likely to benefit from treatment.

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