Gestational Diabetes Mellitus: To Screen or Not to Screen?

Is this really still a question?

Discussion about gestational diabetes mellitus (GDM) is slowly creating traction on the best way forward. Recent evidence has confirmed that there is a continuum of risk for adverse maternal and fetal outcomes as the maternal glucose level rises (1,2). There is an increasing number of studies supporting the importance of fuel-mediated teratogenesis, including epigenetic influences, that are leading to intergenerational transmission of type 2 diabetes, features of the metabolic syndrome, and overall amplification of the current diabetes pandemic (3,4).

Treatment of women with GDM, variously defined, improves outcomes (5,6). New consensus guidelines for the diagnosis of GDM have been recommended by the International Association of the Diabetes and Pregnancy Study Groups (IADPSG) (7) based on the risk of adverse pregnancy outcomes, rather than the long-term maternal diabetes risk, alignment with diabetes complication risks outside of pregnancy, workload, or local consensus (8).

Although there has been a vigorous debate about the validity of the IADPSG diagnostic criteria, less attention has been paid to the other recommendations of universal testing and using a one-stage diagnostic glucose tolerance test (GTT) without preliminary risk factor screening and/or a glucose challenge test (GCT). The National Institutes of Health has recently highlighted the need for action toward standardization of GDM diagnostic criteria, but has not advocated adopting any of the IADPSG recommendations. Thus, there remains a recommendation to continue with risk factor screening and the use of a GCT (9).

In this issue of *Diabetes Care*, Avalos et al. (10) have used data from the ATLANTIC DIP study to retrospectively examine risk factor prediction of GDM, using different combinations of risk factors, in a mainly European population who were offered universal testing. The prevalence of GDM using the IADPSG criteria was 12.4%. Depending on the combination of risk factors used, 54–76% of women had at least one risk

factor present. However, the prevalence of GDM among women with no risk factors ranged from 2.7 to 5.4%, by itself not an inconsiderable figure. Women diagnosed with GDM, but without risk factors, had worse pregnancy outcomes than women with normal glucose tolerance (10), supporting the findings in a recent French study (11). In another recent European report, 20% of women diagnosed with GDM had no defined risk factors (12).

At one stage it was advised that women with low risk factors need not to be tested (13). However, reports from North America (14) and New Zealand (15) found that a large proportion (90 and 97.9%, respectively) of pregnant women would still require testing. A report from Australia found that 80% of women would still require testing and women with low risk factors still constituted 10% of the GDM population (16).

In the developed world with growing epidemics of obesity and diabetes, the majority of women in most populations will now have some risk factors depending on the criteria used (11,14-16). Clearly, women with no risk factors can develop GDM, and the outcomes are no different (17) in women identified by risk factors. Once clinicians have to make decisions in the screening process, it is more open to error, delays, and problems. We already know that where a variety of risk factors with cutoffs are used, busy clinicians will not necessarily recall who is to be screened (18), and this is associated with reduced penetration of screening among those at high risk (19). From a systems perspective, universal blood testing makes the detection of GDM in those at highest risk more likely to happen in day-to-day clinical practice.

Another method of screening involves a GCT. The origins of the GCT would require a forensic endocrinologist to resolve, and what clinical evidence was advanced at the time to support such a step would be interesting to contemplate. Given that only 44% of women in the study by Avalos et al. (10) accepted the offer of a one-stage test, what may have been the acceptance of a two-stage procedure? The GCT will inevitably delay the diagnosis of GDM and therefore treatment (20). However, the most serious concern about using a GCT is the no-show rate for the definitive GTT for women who are abnormal. In the Toronto Tri-Hospital Gestational Diabetes Project, 10% of women did not proceed with the GTT (21); in a New Zealand study, the rate was 23% (22); and, in hopefully a worst case scenario, a recent North American report found that only 36% attended the GTT (23).

Screening on the basis of risk factors will require most women to be tested and inevitably and knowingly miss women with GDM. GCT screening misses many of those with GDM with a modestly elevated fasting glucose and runs the risk of missing other women with GDM because of the inevitable no-show rate. It is open to speculation how the combination of risk factor screening and a GCT may compound the number of missed diagnoses.

It is difficult to find any health advantages in screening for GDM (rather than going straight to a diagnostic test), either on the basis of risk factors and/or a GCT. There are several health disadvantages. Although not explicitly stated, the only possible presumed advantage of screening is to reduce costs, and on this aspect there is a dearth of data (24,25). The direct and immediate costs of a GCT/GTT will vary with different health systems. In the overall costs of delivering obstetric services, this is likely to be minor, especially if the initial GTT fasting glucose can be used to decide whether a full GTT is required (26). There are some populations where women are unlikely to attend fasting (e.g., rural India), but in such cases, a two-step test is also likely to be associated with poor attendance at the second step and a one-step diagnostic step, of any kind, is preferred (27).

Although some uniformity would be desirable, screening based on risk factors would involve defining risk factors in the particular population and not just importing from a possibly irrelevant or unrepresentative population. Training and audits would have to be conducted to ensure that

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the people doing the screening are competent, and this would need to be reviewed periodically. The cost of the time taken for this would have to be a factor in the overall cost analysis.

For any method of screening, what is not factored and needs to be included are the costs associated with undiagnosed GDM. Screening will miss women with GDM, and undiagnosed women with GDM will have both maternal and fetal complications. In the Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) (6), the number of GDM cases that needed to be treated to prevent one serious perinatal complication was 34! Placing to one side, but not ignoring, any personal issues that a failure to diagnose may cause, what is the cost of unexpected obstetric interventions or a few days in a special care nursery compared with the costs of testing and treating GDM? Until these necessary questions are addressed and GDM is seen as one part of the cost of a totality of obstetric and perinatal services, screening based on risks and/or a GCT cannot be endorsed for either health or economic reasons.

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References

- Metzger BE, Lowe LP, Dyer AR, et al.; HAPO Study Cooperative Research Group. Hyperglycemia and adverse pregnancy outcomes. N Engl J Med 2008;358:1991–2002
- 2. Moses RG, Calvert D. Pregnancy outcomes in women without gestational diabetes mellitus related to the maternal glucose level. Is there a continuum of risk? Diabetes Care 1995;18:1527–1533

- Franks PW, Looker HC, Kobes S, et al. Gestational glucose tolerance and risk of type 2 diabetes in young Pima Indian offspring. Diabetes 2006;55:460–465
- 4. Boney CM, Verma A, Tucker R, Vohr BR. Metabolic syndrome in childhood: association with birth weight, maternal obesity, and gestational diabetes mellitus. Pediatrics 2005;115:e290–e296
- Landon MB, Spong CY, Thom E, et al.; Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. A multicenter, randomized trial of treatment for mild gestational diabetes. N Engl J Med 2009;361:1339–1348
- Crowther CA, Hiller JE, Moss JR, McPhee AJ, Jeffries WS, Robinson JS; Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) Trial Group. Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. N Engl J Med 2005;352:2477–2486
- 7. Metzger BE, Gabbe SG, Persson B, et al.; International Association of Diabetes and Pregnancy Study Groups Consensus Panel. International Association of Diabetes and Pregnancy Study Groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. Diabetes Care 2010;33:676–682
- Cutchie WA, Cheung NW, Simmons D. Comparison of international and New Zealand guidelines for the care of pregnant women with diabetes. Diabet Med 2006; 23:460–468
- National Institutes of Health. National Institutes of Health Consensus Development Conference: Diagnosing Gestational Diabetes Mellitus, 2013. Available from http:// prevention.nih.gov/cdp/conferences/2013/ gdm/resources.aspx. Accessed 4 April 2013
- Avalos GE, Owens LA, Dunne F; ATLANTIC DIP Collaborators. Applying current screening tools for gestational diabetes mellitus to a European population: is it time for change? Diabetes Care 2013;36:3040–3044
- 11. Cosson E, Benbara A, Pharisien I, et al. Diagnostic and prognostic performances over 9 years of a selective screening strategy for gestational diabetes mellitus in a cohort of 18,775 subjects. Diabetes Care 2013;36:598–603
- 12. Chevalier N, Fenichel P, Giaume V, et al. Universal two-step screening strategy for gestational diabetes has weak relevance in French Mediterranean women: should we simplify the screening strategy for gestational diabetes in France? Diabetes Metab 2011;37:419–425
- American Diabetes Association. Gestational diabetes mellitus (Position Statement). Diabetes Care 1998;21(Suppl. 1):S60–S61
- 14. Williams CB, Iqbal S, Zawacki CM, Yu D, Brown MB, Herman WH. Effect of selective

screening for gestational diabetes. Diabetes Care 1999;22:418–421

- 15. Simmons D. Gestational diabetes mellitus: growing consensus on management but not diagnosis. N Z Med J 1999;112:45–46
- Moses RG, Moses J, Davis WS. Gestational diabetes: do lean young Caucasian women need to be tested? Diabetes Care 1998;21: 1803–1806
- Weeks JW, Major CA, de Veciana M, Morgan MA. Gestational diabetes: does the presence of risk factors influence perinatal outcome? Am J Obstet Gynecol 1994; 171:1003–1007
- Simmons D, Devers MC, Wolmarans L, Johnson E. Difficulties in the use of risk factors to screen for gestational diabetes mellitus. Diabetes Care 2009;32:e8
- 19. Simmons D, Rowan J, Reid R, Campbell N; National GDM Working Party. Screening, diagnosis and services for women with gestational diabetes mellitus (GDM) in New Zealand: a technical report from the National GDM Technical Working Party. N Z Med J 2008;121:74–86
- 20. Griffin ME, Coffey M, Johnson H, et al. Universal vs. risk factor-based screening for gestational diabetes mellitus: detection rates, gestation at diagnosis and outcome. Diabet Med 2000;17:26–32
- Sermer M, Naylor CD, Gare DJ, et al. Impact of increasing carbohydrate intolerance on maternal-fetal outcomes in 3637 women without gestational diabetes. The Toronto Tri-Hospital Gestational Diabetes Project. Am J Obstet Gynecol 1995;173: 146–156
- 22. Yapa M, Simmons D. Screening for gestational diabetes mellitus in a multiethnic population in New Zealand. Diabetes Res Clin Pract 2000;48:217–223
- 23. Sievenpiper JL, McDonald SD, Grey V, Don-Wauchope AC. Missed follow-up opportunities using a two-step screening approach for gestational diabetes. Diabetes Res Clin Pract 2012;96:e43–e46
- 24. Meltzer SJ, Snyder J, Penrod JR, Nudi M, Morin L. Gestational diabetes mellitus screening and diagnosis: a prospective randomised controlled trial comparing costs of one-step and two-step methods. BJOG 2010;117:407–415
- 25. Moses R, Fulwood S, Griffiths R. Gestational diabetes mellitus; resource utilization and costs of diagnosis and treatment. Aust N Z J Obstet Gynaecol 1997;37:184–186
- Agarwal MM, Dhatt GS, Shah SM. Gestational diabetes mellitus: simplifying the International Association of Diabetes and Pregnancy diagnostic algorithm using fasting plasma glucose. Diabetes Care 2010; 33:2018–2020
- Anjalakshi C, Balaji V, Balaji MS, et al. A single test procedure to diagnose gestational diabetes mellitus. Acta Diabetol 2009; 46:51–54