

Gestational Diabetes Mellitus: Time to Change our Approach to Screening, Diagnosis and Postpartum Care?

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There is much confusion internationally regarding the optimal method of diagnosing gestational diabetes mellitus (GDM). In an effort to resolve this conundrum, the large, multicentre Hyperglycemia and Adverse Pregnancy Outcome (HAPO) trial was undertaken (1).

The HAPO study demonstrated a strong, continuous and positive association between maternal glucose and increased birth weight and fetal hyperinsulinemia at levels below the current Canadian Diabetes Association (CDA) guidelines, diagnostic thresholds for GDM. However, no obvious glucose thresholds were found for fetal overgrowth and a variety of other maternal and neonatal outcomes. Thus, controversy continues to surround appropriate diagnostic thresholds for GDM. The daunting task of finding international consensus for GDM diagnosis has been spearheaded by the International Association of Diabetes and Pregnancy Study Groups (IADPSG). This group was initially formed through the efforts of various study groups around the world, to facilitate the HAPO study. The Canadian Diabetes in Pregnancy Study group (CanDIPS) also joined the IADPSG and contributed to deliberations regarding diagnostic criteria for GDM at conferences, and in working and writing groups. The IADPSG guidelines were published recently in the journal *Diabetes Care* (2).

The objectives of this article are to: introduce the IADPSG guidelines; highlight the key differences between them and the current CDA guidelines; discuss the impact of implementing the IADPSG recommendations in Canada; and emphasize the importance of postpartum follow-up of women with GDM.

SCREENING AND DIAGNOSTIC TESTING FOR GDM **Key differences and impact of the IADPSG guidelines for Canada**

Identification of overt diabetes first diagnosed during pregnancy

There has been an alarming increase in the prevalence of type 2 diabetes in women of reproductive age. Diabetes screening in high-risk individuals should occur prior to conception, so that women with diabetes are referred to appropriate resources for optimal blood glucose (BG) control prior to conception. Sadly, the extent to which type 2 diabetes is identified prior to pregnancy varies greatly worldwide, in part because it depends on the patient's ability to pay for this service in many countries. Thus, the proportion of patients with previously undiagnosed type 2 diabetes who are currently classified as having GDM varies widely worldwide, and this limits our ability to compare different studies. If pre-conception diabetes screening has not occurred, the IADPSG recommendations for diagnosing overt diabetes listed in Table 1 should be performed immediately after the pregnancy is confirmed. By screening for overt diabetes and excluding these patients from a diagnosis of GDM, it will be easier to compare studies. Further research is required to determine the most appropriate test and thresholds for diagnosing overt diabetes during pregnancy.

If we fail to exclude overt diabetes in pregnancy from GDM, we risk inadequate care of patients with overt diabetes, who carry a

Table 1: Current CDA and IADPSG recommendations

Diagnostic criteria	CDA recommendations	IADPSG recommendations
Screening	<ul style="list-style-type: none"> In women at high risk in their first trimester, and in all women at 24-28 weeks pregnant, do a 50-g glucose screen followed by 1-h PG If 1-h PG: <ul style="list-style-type: none"> <7.8 mmol/L: normal; retest only if risk factors increase 7.8-10.2 mmol/L: perform an OGTT ≥10.3 mmol/L: diagnosis is GDM 	<ul style="list-style-type: none"> 50g glucose screen eliminated
Diagnostic test	75-g OGTT	75-g OGTT
Thresholds		
Fasting PG	5.3 mmol/L	5.1 mmol/L
1-h PG	10.6 mmol/L	10.0 mmol/L
2-h PG	8.9 mmol/L	8.5 mmol/L
GDM diagnosed if ...	2 values ≥ thresholds	1 value ≥ thresholds
IGT	1 value ≥ thresholds	diagnosis eliminated
Identification of overt diabetes	<ul style="list-style-type: none"> Not diagnosed until postpartum test done 	In all or only high-risk women* measured FPG or random PG or A1C with first prenatal bloods. Overt diabetes diagnosed if: <ul style="list-style-type: none"> A1C ≥6.5% at any time in pregnancy. FPG ≥7.0 mmol/L. Random PG ≥11.1 mmol/L if reconfirmed by FPG or A1C

* Recommendation for population to be screened should be determined based on local or national risk for diabetes

A1C = glycated hemoglobin

CDA = Canadian Diabetes Association

FPG = fasting plasma glucose

GDM = gestational diabetes mellitus

IADPSG = International Association of the Diabetes and Pregnancy Study Groups

IGT = impaired glucose tolerance

OGTT = oral glucose tolerance test

PG = plasma glucose

much greater risk of maternal hypertension, neonatal congenital malformations and stillbirth; we also risk unnecessarily aggressive care of GDM patients who have much lower risks of these complications.

Elimination of gestational impaired glucose tolerance

One or more elevated plasma glucose (PG) results on an oral glucose tolerance test (OGTT) in pregnancy is a predictor for future increased risk of diabetes in the affected woman as well as for neonatal macrosomia, especially if isolated fasting glucose is observed (3). This IADPSG recommendation will increase the number of women officially diagnosed with GDM. The impact of this recommendation will likely be small, since many Canadian

centres provide similar management to women with GDM and gestational impaired glucose tolerance (IGT).

One single glucose load test

There is no evidence that a single glucose test for GDM will be any more or less effective for influencing maternal or neonatal outcomes of GDM. Elimination of the simpler 1-h 50-g glucose screening could result in the delay of pregnant women being tested for GDM. A single-step test may result in earlier diagnosis and treatment of women with GDM. In an urban Canadian centre, Meltzer and colleagues demonstrated that cost analysis favoured the 2-step approach when direct patient expense was included in their analysis, except where very high-risk ethnic groups were involved (4).

Lower glycemic thresholds for a diagnosis of GDM

Implementation of IADPSG thresholds would mean that a significantly greater proportion of women would be diagnosed with GDM. HAPO data suggest this could approach 17.8% of pregnant women, compared with approximately 8% if GDM and gestational IGT presently diagnosed are considered. IADPSG thresholds are the maternal glucose values from HAPO associated with a 1.75-fold increase of large-for-gestational age, elevated C-peptide, high neonatal body fat or a combination of these factors, compared with the mean maternal BG values of women studied. Randomized controlled trials in GDM suggest that rates of macrosomia, maternal weight gain, shoulder dystocia and hypertension in pregnancy should be reduced by glycemic management of women diagnosed at IADPSG thresholds (5,6).

The most compelling reason to reject IADPSG thresholds stems from the recognition that the outcomes upon which they are based are not necessarily serious negative outcomes. Rather, they are surrogate markers for other key clinical outcomes, i.e. future poor metabolic outcomes in offspring, and neurologic complications resulting from birth trauma. Randomized controlled trials in GDM have not had sufficient power to assess serious outcomes independently, nor has there been long-term follow-up of the offspring of the women involved in these studies, apart from a small Canadian study. Malcolm and colleagues showed that tight maternal glycemic control of GDM compared with minimal intervention did not reduce rates of glucose intolerance in offspring at ages 7 to 11 years, and there was an insignificant trend for more abnormal glucose tolerance in the treated group (9% [5/47]) vs. the control group (0% [0/25]) (7). Given the small sample size and incomplete follow-up in this study, it is difficult to draw definitive conclusions.

Offspring exposed to maternal dysglycemia in utero have increased risk of poor metabolic outcomes later in life (7). However, the relative causal contributions of genetic/epigenetic factors, in utero glycemic/nutritional environment, early infant feeding choices and lifestyle factors in the home remain speculative. Experimental human data showing that alterations in maternal glycemia can modify the offspring's future risk of poor metabolic outcomes are lacking, despite epidemiologic data in humans and experimental animal data that support this hypothesis (8,9).

No one would dispute that the incidence of type 2 diabetes is increasing rapidly and that the development of a novel intervention to reverse this trend is urgently desired. The hypothesis that diabetes begets diabetes by in utero exposure to maternal

hyperglycemia, and that diabetes can be reversed by treating at-risk mother-fetus pairs, is an attractive one. Many fear the consequences of not embracing this hypothesis now, especially given the decades of follow-up study required to support it. To that end, we must ask ourselves if there is any potential harm in accepting this hypothesis as true now and applying the implications that arise.

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Other well-intentioned dietary manipulations in pregnancy have had negative long-term consequences for offspring (10). Greater maternal consumption of meat and fish in the second half of pregnancy has been linked with higher systolic blood pressure in adult offspring at 27 to 30 years of age (10). An excess of small-for-gestational-age (SGA) neonates has occurred when excessively strict mean BG levels have been achieved in GDM (11). SGA is also associated with poor metabolic outcomes, particularly when offspring are subsequently exposed to overnutrition postnatally (12). Additionally, the diagnosis and treatment of GDM may be stressful for some women; indeed, maternal stress has been associated with poor metabolic consequences in offspring (13).

If we accept the IADPSG thresholds, then we must ensure that medical practices which may increase long-term risks—i.e. maternal stress, rates of SGA neonates, and breastfeeding failure, resulting from higher rates of early infant separation and unnecessary caesarean-section deliveries—are avoided when women are labelled with GDM, as has occurred in the past (6,14). We must also assess how population health strategies to achieve a desirable pre-conception weight, appropriate pregnancy weight gain and use of low-dose Aspirin in women at risk of pregnancy-induced

hypertension compare with the cost of GDM management. These unanswered questions should cause us, in Canada, to pause before rushing to endorse or implement the IADPSG guidelines without careful deliberation, in conjunction with our obstetrical colleagues, of the evidence and the potential consequences.

POSTPARTUM MANAGEMENT OF WOMEN WITH A HISTORY OF GDM

Breastfeeding should be strongly encouraged in women with GDM. Research supports the beneficial effects of breastfeeding in reducing the long-term risk of obesity in offspring and maternal risk of metabolic syndrome (15).

Postpartum testing of women with GDM is required to clarify glucose tolerance outside of pregnancy, so that appropriate recommendations about prevention or treatment of diabetes are provided. This is particularly important in women who go on to have future pregnancies and have persistent diabetes or develop diabetes pre-conception, so as not to miss the opportunity to intervene and prevent congenital malformations in their offspring. The cumulative risk for dysglycemia after a diagnosis of GDM approaches 90% in some populations. Unfortunately, many women do not receive adequate postpartum care, perhaps because it is not clear who “owns” the problem: the patient, the primary care physician, the obstetrician or the diabetes-in-pregnancy team. Postnatal FPG alone may miss up to half of the woman with diabetes and virtually all those with IGT (16). The CDA sub-committee for the dissemination and implementation of clinical practice guidelines has developed tools for patients and doctors to assist in prompting postpartum testing, which were released in Spring 2010. Let’s all use these tools and seize the opportunity to prevent diabetes, diabetes-related complications and congenital malformations.

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