



Alison Nankervis  
Jennifer Conn

# Gestational diabetes mellitus

## Negotiating the confusion

### Background

Recommendations to change the diagnostic criteria for gestational diabetes mellitus (GDM) are controversial. Two sets of criteria are currently in use in Australia, which has led to considerable confusion.

### Objective

This article discusses the rationale behind the proposed changes to the diagnostic criteria, and aims to clarify the current approach to the testing for and diagnosis of GDM in Australia.

### Discussion

Gestational diabetes mellitus has adverse effects on pregnancy outcomes and implications for the long term wellbeing of mother and infant. New information about the relationship between hyperglycaemia in pregnancy and fetal outcomes has led to the formulation of revised recommendations for testing and diagnosis of GDM. The changes to the diagnostic threshold will increase the numbers of women diagnosed with GDM by up to 50%. Evidence that management of GDM improves neonatal outcomes mandates a proactive approach to diagnosis and management. General practitioners will have an increasing role in managing GDM.

### Keywords

diabetes, gestational; diabetes, gestational/diagnosis; hyperglycaemia; pregnancy



Gestational diabetes mellitus (GDM) is associated with short and long term risks to mother and infant. Yet, there is considerable controversy as to how to diagnose GDM and provide optimal management during and after pregnancy. This article will try to make some sense of the current debate regarding 'old' versus 'new' diagnostic criteria, and provide practical guidance for the management and follow up of GDM in general practice.

### What is GDM?

GDM is defined as 'any degree of glucose intolerance with onset or first recognition during pregnancy'. GDM affects approximately 8–10% of pregnancies in Australia.<sup>1</sup> It includes previously unrecognised type 2 diabetes mellitus (DM) and, rarely, type 1 DM arising in pregnancy. In most women, GDM is asymptomatic and diagnosed on routine testing at 24–28 weeks gestation. Many, but not all, women have recognised risk factors for GDM (*Table 1*),

### Early testing for overt diabetes mellitus or GDM

The prevalence of abnormal glucose tolerance and obesity is increasing dramatically in women of childbearing age in Australia.<sup>2</sup> Universal testing for hyperglycaemia at the first pregnancy visit should be encouraged. Women with previous GDM, or those with multiple risk factors, ideally will have an oral glucose tolerance test (OGTT). The best means of testing lower risk women has not been defined, but a fasting or non-fasting plasma glucose (PG), or an HbA1c (although not currently Medicare reimbursed for this purpose) can be considered.<sup>3–5</sup> Many centres have added a non-fasting PG to their screening panel. Women with clearly elevated glucose levels early in pregnancy are managed as for pre-existing DM, including screening for complications.

### The Hyperglycemia and Pregnancy Outcome Study and revised diagnostic criteria for GDM

Until recently, GDM was diagnosed on the basis of maternal risk of future progression to type 2 DM.<sup>6</sup> The Hyperglycemia and Adverse Pregnancy Outcome Study (HAPO),<sup>7</sup> a large prospective multinational



study, investigated adverse fetal as well as maternal effects of gestational hyperglycaemia. A total of 23 316 women with fasting PG levels  $\leq 5.8$  mmol/L and levels at 2 hour post 75 g oral glucose load  $\leq 11.1$  mmol/L were investigated. Strong continuous correlations were found between maternal glucose levels at 24–32 weeks and a range of outcomes, the most significant of which were birth weight, cord C-peptide and percentage body fat; all  $>90$ th percentile. It is important to note that extensive adjustment was made for possible confounders, in particular, maternal obesity. While obesity increased the risk of adverse fetal outcomes, hyperglycaemia was an independent risk factor in every analysis. The blood glucose (BG) levels at 0, 1 and 2 hours, which equated to an odds ratio of 1.75 for the identified fetal parameters, were considered by the International Association of Diabetes and Pregnancy Study Groups (IADPSG) to be diagnostic of GDM. On this basis, new recommendations for testing and diagnosis of GDM were formulated.<sup>8</sup>

The Australasian Diabetes in Pregnancy Society (ADIPS) has endorsed these recommendations,<sup>9,10</sup> as have many countries and international organisations. The Royal Australian College of General Practitioners is yet to endorse the recommendations. The World Health Organization is expected to announce its position shortly.

## Recommendations for routine testing and diagnosis of GDM

All women not known to have DM or GDM should have a standard 75 g OGTT at 24–28 weeks gestation. This renders the glucose challenge test redundant. The ADIPS and IADPSG criteria for the diagnosis of GDM are shown in *Table 2*.

Some pathology providers are using the revised criteria, while others are using the 'old' values. This situation has led to enormous confusion in Australia. How can general practitioners and others who provide care for pregnant women best approach this uncertainty? (See *Case study*.)

## Management of GDM

A critical question is whether treatment of GDM improves outcomes. Two large prospective, randomised controlled trials have used BG levels similar, but not identical, to the HAPO values, to investigate this. The Australian Carbohydrate Intolerance Study in Pregnant Women found a significant reduction in a composite of severe outcomes (death, shoulder dystocia, bone fracture and nerve palsy) in 510 women treated for GDM compared with 490 untreated women with similar OGTT results.<sup>11</sup> A similar study conducted by the United States Maternal-Fetal Medicine Units Network observed no significant difference in composite outcomes between the treatment and control groups, but did find a reduction in several secondary outcomes, including birth weight,

**Table 1. Risk factors for GDM**

- Previous GDM
- Previously elevated blood glucose level
- Ethnicity: south and southeast Asian, Aboriginal, Pacific Islander, Maori, Middle Eastern, non-Caucasian African
- Age  $\geq 40$  years
- Family history of diabetes mellitus (first degree relative with diabetes mellitus or a sister with GDM)
- Obesity, especially BMI  $>35$  kg/m<sup>2</sup>
- Previous macrosomia (baby with birth weight  $>4500$  g or  $>90$ th percentile)
- Polycystic ovarian syndrome
- Medications: corticosteroids, antipsychotics

**Table 2. ADIPS and IADPSG criteria for the diagnosis of GDM<sup>8,9</sup>**

Fasting PG: ( $\geq 5.1$  mmol/L)  
 1 hour PG: ( $\geq 10.0$  mmol/L)  
 2 hour PG: ( $\geq 8.5$  mmol/L)  
 A diagnosis of GDM is made on one or more of these values

fetal adiposity, shoulder dystocia, caesarean delivery and pre-eclampsia.<sup>12</sup>

## Glycaemic targets in GDM

No studies have defined optimal glycaemic targets in the treatment of GDM. ADIPS has recommended that self monitoring BG targets at 1 and 2 hours should be based on 2 standard deviations above the mean for normal pregnancy.<sup>13</sup>

- fasting capillary BG:  $\leq 5.0$  mmol/L
- 1 hour after commencing meal BG:  $\leq 7.4$  mmol/L
- 2 hours after commencing meal BG:  $\leq 6.7$  mmol/L.

A fasting BG target of  $<5.1$  mmol/L has been chosen from observational data, and to maintain consistency with the diagnostic fasting PG cut-off of 5.1 mmol/L. Further research, however, is required to define optimal targets.

## Management strategies

Lifestyle management is the preferred means of managing GDM. Diet is based around the principles of optimal nutrition and controlled weight gain. The carbohydrate content of the diet, with an emphasis on the quantity, distribution and type (low glycaemic index) of carbohydrate is critical. The effectiveness of diet can be monitored by measuring weight and self monitoring of BG levels.

Exercise can be helpful in lowering BG levels. The most acceptable form of exercise for most women is walking in their normal daily routine.<sup>14</sup>



## Pharmacological agents

### Metformin

The safety and efficacy of metformin was confirmed in the Metformin in Gestational Diabetes Study.<sup>15</sup> The long term effects on offspring are being carefully monitored, but outcomes to date are reassuring. Many centres are now using metformin as first line treatment, after lifestyle interventions, for GDM. There is a particular role for metformin in women who are obese, reluctant to take insulin, or already on large doses of insulin.

### Glibenclamide

Studies suggest that glibenclamide is safe to use during pregnancy, but the potential effect on already overburdened maternal pancreatic  $\beta$ -cells and vulnerable fetal  $\beta$ -cells prompts great caution in the use of this medication in treating GDM.

Neither metformin nor glibenclamide have been approved for use in pregnancy in Australia. Other oral agents are contraindicated in pregnancy.<sup>16</sup>

### Insulin

Insulin is safe and effective in the management of GDM. A common regimen is modified multidose, with a short acting insulin analogue administered before meals as required, and a medium acting insulin at bedtime if fasting BG levels are elevated. Both insulin aspart and lispro have established safety profiles in pregnancy. Insulin glargine has been used widely in pre-gestational DM and detemir is the subject of a reassuring prospective clinical trial in pregnancy. However, insulin isophane (NPH) is still widely used as the basal insulin in GDM. Hypoglycaemic events in insulin-treated GDM are neither common nor severe.

## Management post-partum

There are particular benefits in encouraging breastfeeding in women who have had GDM. Evidence suggests there are weight advantages to mother and infant, both of whom are at increased risk of overweight.

All women diagnosed with GDM should have a 75 g OGTT at 6–12 weeks post-partum. As women with GDM have a 50% risk of developing type 2 DM within 20 years, they need to be tested regularly for DM. While an OGTT is currently considered the gold standard, HbA1c is easier to perform and is likely to be used for post-GDM testing in the future.<sup>17,18</sup>

## Potential impact of the new diagnostic criteria

The prevalence of GDM is likely to increase to around 12–14% with the new diagnostic criteria.<sup>19</sup> Resources will need to be used creatively and strategically to cope with the increased demand. Effective management of the epidemic of GDM has the potential to impact powerfully on the wellbeing of women and their

children.<sup>20</sup> GDM therefore warrants appropriate diagnosis and watchful management of affected women in the long term. General practitioners will play an increasing role in the management of GDM.

## Key points

- GDM has adverse implications for pregnancy outcomes and the long term health of women and their children.
- Because of the high prevalence of risk factors for GDM, universal testing for overt diabetes is recommended early in pregnancy.
- All women not known to have DM should have an OGTT at 24–28 weeks gestation. The glucose challenge test is no longer recommended.
- Management of GDM improves neonatal outcomes.
- Women with GDM should be tested for DM 6–12 weeks post-partum, and thereafter 1–2 yearly.
- The increased numbers of women diagnosed with GDM will have major implications for resource allocation.
- Research is urgently needed in many areas: early diagnosis, impact of new criteria, treatment targets, costs and long term follow up.

## Case study

A 32 year old primigravida woman has been seeing you for management of her pregnancy in a shared care capacity with a large metropolitan hospital. She has a remote family history of type 2 DM and no relevant past history. You organise an OGTT at 26 weeks gestation. Her pathology report is shown in *Table 3*.

**Table 3. Pathology results**

Patient results	Normal values
Fasting PG: (5.4 mmol/L)	Fasting PG: (<5.1 mmol/L)
1 hour PG: (9.2 mmol/L)	1 hour PG: (<10 mmol/L)
2 hour PG: (7.8 mmol/L)	2 hour PG: (<8.5 mmol/L)
Result: gestational diabetes mellitus	

You are used to working with the old diagnostic values, as is the hospital. Clearly, she would not have GDM using these criteria. Yet according to the report she has GDM.

### What do you do?

At the moment it is reasonable to take an absolutely pragmatic approach. If the laboratory has used the new criteria, accept this diagnosis. Viewed from a medicolegal framework, this woman has been reported as having GDM and should be treated as such. If you are working within the framework of the 'old' criteria, regard all women who fulfil those criteria as having GDM.

## Authors

Alison Nankervis MBBS MD FRACP, is Clinical Head, Diabetes, Department of Diabetes and Endocrinology, Royal Melbourne Hospital, VIC. [alison.nankervis@mh.org.au](mailto:alison.nankervis@mh.org.au)



Jennifer Conn MBBS FRACP MClinEd, is an endocrinologist, Department of Diabetes and Endocrinology, Royal Melbourne Hospital, VIC.

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correspondence [afp@racgp.org.au](mailto:afp@racgp.org.au)