

# **ADIPS Consensus Guidelines for the Testing and Diagnosis of Hyperglycaemia in Pregnancy in Australia and New Zealand (modified November 2014)**

**Nankervis A, McIntyre HD, Moses R, Ross GP, Callaway L, Porter C, Jeffries W,  
Boorman C, De Vries B, McElduff A for the Australasian Diabetes in Pregnancy Society**

The Australasian Diabetes in Pregnancy Society (ADIPS) originally formulated recommendations for the testing and diagnosis of gestational diabetes mellitus (GDM) in 1991.<sup>1</sup> These guidelines were primarily based on expert opinion. With some local variations, the ADIPS guidelines have been used since that time. In the light of recent evidence, ADIPS has elected to revise these guidelines in the current document. Recommendations for future research are summarised at the end of this document.

The Hyperglycemia and Adverse Pregnancy Outcome study (HAPO) published in 2008<sup>2</sup> was a large, prospective, blinded, multinational, observational study that examined pregnancy outcomes in 23,316 women whose plasma glucose (PG) levels were  $\leq 5.8$ mmol/L fasting and  $\leq 11.1$ mmol/L 2-hrs post 75g oral glucose load. This study reported a strong correlation between increasing maternal glucose levels at 24-32 weeks gestation and a range of adverse maternal and fetal outcomes. Subsequent consideration by the International Association of Diabetes and Pregnancy Study Groups (IADPSG), with Australasian representation, resulted in the formulation of new consensus guidelines for the testing and diagnosis of GDM.<sup>3</sup> These guidelines have been endorsed by several national organisations and the World Health Organisation (WHO)<sup>4</sup>.

There has been a change in the demographics of women becoming pregnant and an increase in the rate of type 2 diabetes mellitus (DM) in the Australian community.<sup>5</sup> This has resulted in more women of childbearing age having abnormalities of glucose tolerance, including undiagnosed DM, detected for the first time during pregnancy.

The WHO refers to hyperglycaemia in pregnancy with sub-division into DM and GDM. Women with DM are at higher risk of major pregnancy complications and require urgent attention, including evaluation for other complications of undiagnosed diabetes.

## **1. Recommendations for early testing for hyperglycaemia in pregnancy for women with risk factor(s)**

Women, not known to have pre-existing glucose abnormalities, but with risk factors for hyperglycaemia in pregnancy (vide infra) should be tested early in pregnancy. The method of testing must be based on clinical judgement, local health care policy and possible risk stratification (see section requiring further research). Women deemed at higher risk should ideally have a pregnancy OGTT (POGTT) or a HbA1C

## **Risk factors for hyperglycaemia in pregnancy**

- Previous hyperglycaemia in pregnancy
- Previously elevated blood glucose level
- Maternal age  $\geq 40$  years
- Ethnicity: Asian, Indian subcontinent, Aboriginal, Torres Strait Islander, Pacific Islander, Maori, Middle Eastern, non-white African
- Family history DM (1<sup>st</sup> degree relative with diabetes or a sister with hyperglycaemia in pregnancy)
- Pre-pregnancy BMI  $> 30$  kg/m<sup>2</sup>
- Previous macrosomia (baby with birth weight  $> 4500$  g or  $> 90^{\text{th}}$  centile)
- Polycystic ovarian syndrome
- Medications: corticosteroids, antipsychotics

### **Routine testing for hyperglycaemia in pregnancy**

All women not previously known to have pre pregnancy diabetes or hyperglycemia in pregnancy should undergo a 75 g POGTT at 24 – 28 weeks gestation.

All women should be tested, as stratification by risk factors is unreliable. The glucose challenge test (GCT) lacks both sensitivity and specificity and is no longer part of the diagnostic algorithm. There is also no need for a 3 day high carbohydrate diet before the POGTT.

### **Recommendations for diagnostic criteria for hyperglycaemia in pregnancy**

ADIPS has accepted the WHO<sup>4</sup> recommendations for the diagnostic classification of hyperglycaemia first detected at any time during pregnancy. These recommendations are:

Hyperglycaemia first detected at any time during pregnancy should be classified as either:

- (1) diabetes mellitus in pregnancy or;
- (2) gestational diabetes mellitus.

1. Diabetes mellitus in pregnancy should be diagnosed by the 2006 WHO criteria for diabetes if one or more of the following criteria are met:

- (a) Fasting plasma glucose  $\geq 7.0$  mmol/l ;
- (b) 2-h plasma glucose  $\geq 11.1$  mmol/l following a 75 g oral glucose load;

- (c) a random plasma glucose  $\geq 11.1$  mmol/l in the presence of diabetes symptoms.
2. The diagnosis of gestational diabetes mellitus at any time during pregnancy should be based on any one of the following values:
- (a) Fasting plasma glucose 5.1–6.9 mmol/l ;
  - (b) 1-h post 75 g oral glucose load  $\geq 10.0$  mmol/l\*;
  - (c) 2-h post 75 g oral glucose load 8.5–11.0 mmol/l .

\*there are no established criteria for the diagnosis of diabetes mellitus in pregnancy based on the 1-h post-load value

Diabetes in pregnancy may not necessarily be confirmed as diabetes in the postpartum period. Diabetes is more likely to be confirmed in the postpartum period when the hyperglycaemia in pregnancy is diagnosed early and/or the degree of hyperglycaemia is marked.

## Levels of evidence

The diagnostic criteria are in accord with those chosen by the WHO. The 0, 1 and 2 hour values were chosen to identify the same risk of an adverse fetal outcome at each time point.

There are 2 large, RCTs (and other intervention studies)<sup>6,7,8</sup> which clearly demonstrate the benefits of treatment for both mother and fetus (Level 1 evidence) although the diagnostic criteria used in these studies were not consistent, and are slightly different from the values selected by the WHO and used in these guidelines.

In areas where the rate of undiagnosed type 2 diabetes is thought to be high, or in remote areas where the performance of a POGTT may be logistically difficult, a measurement of HbA<sub>1c</sub> can be considered. A level of  $\geq 48$ mmol/mol (6.5%) is diagnostic of diabetes outside pregnancy and very likely represents previous undiagnosed type 2 diabetes. There is insufficient evidence to correlate lower levels of HbA<sub>1c</sub> with lesser degrees of glucose intolerance.

## 2. Suggested treatment targets in GDM

It is recognised that glycaemic targets in the treatment of hyperglycaemia in pregnancy vary between centres and clinicians around Australia. This issue is discussed further in the section of this document entitled “Areas for further research”. Clinician judgement should guide practice in this area, both in the setting of overall glucose targets and the glucose thresholds which would lead to pharmacological treatment of individual women.

### **3. Management in the postpartum period**

Unless clinically contraindicated, women diagnosed with GDM, and some women with DM, should have a 75g 2-hr OGTT, preferably at 6-12 weeks post-partum, with classification according to the WHO criteria.

Women diagnosed with hyperglycaemia in pregnancy should have regular ongoing surveillance as they have an approximate 30% risk of a recurrence of their hyperglycaemia in a subsequent pregnancy<sup>9</sup> and a risk of developing type 2 DM ranging from 1.5-10% per year<sup>10,11</sup>. The frequency and nature of this surveillance will depend on future pregnancy plans and the perceived risk of converting to type 2 DM. Women contemplating another pregnancy should have an OGTT annually. Women being tested for the possible development of type 2 DM should have a GTT or a HbA<sub>1c</sub> every three years with more frequent testing depending on clinical circumstances<sup>12</sup>. For women deemed at low risk, a fasting plasma glucose or HbA<sub>1c</sub> every 1-2 years should be sufficient.

### **4. Potential impact of the new diagnostic criteria for hyperglycaemia in pregnancy**

The new recommended diagnostic criteria will increase the prevalence of hyperglycaemia in pregnancy.<sup>13</sup> Using IADPSG / WHO criteria, a prospective study in Wollongong demonstrated an increase from 9.6% to 13.0%.<sup>14</sup> A post hoc analysis of the HAPO sites in Australia demonstrated a prevalence in Brisbane of 12.1% and in Newcastle of 13.6%.<sup>13</sup>

## Acknowledgements

This second version of the guidelines has been produced with the assistance of the Royal Australasian College of Obstetrics and Gynaecology (RANZCOG) and the Royal College of Pathologists of Australia (RCPA). With the advice of the RCPA, the OGTT in pregnancy has been designated the pregnancy OGTT (POGTT). With the advice of the RANZCOG, the treatment targets and risk stratification have been moved to the section requiring further research.

## Areas requiring further research

These guidelines are based on available evidence and expert opinion. In many cases, the available data are not definitive. In the opinion of the ADIPS writing group, the following questions will need to be addressed.

**Resource allocation.** It is acknowledged that the increased prevalence of hyperglycaemia in pregnancy, even with potential revised models of care, will have resource implications. ADIPS would welcome participation in any comprehensive review of obstetric and neonatal resource allocation relating to hyperglycaemia in pregnancy.

**Early testing.** Hyperglycaemia of pregnancy is generally diagnosed in the late second or early third trimester. Early detection and treatment may potentially improve outcomes. However, there is a dearth of evidence in this area. We see a critical need for well-designed studies to determine the most appropriate means of testing for gestational diabetes in early pregnancy and to explore the outcomes of early treatment interventions.

**Alternatives to the GTT.** In some geographic areas, it is difficult for a fasting test or POGTT to be conducted. More research is required to assess the clinical utility of using diagnostic fasting levels in early pregnancy and random glucose levels (with confirmatory testing) at any time during the pregnancy. Much will depend on how local antenatal services are organised and on the preferences of the obstetric care providers and their patients.

**Diagnostic criteria.** Two large studies have already shown advantages of treatment for women with diagnostic glucose levels which differ (and are slightly higher) from those being recommended in this guideline. The current 0, 1 and 2 hour values were chosen to identify the same risk of an adverse fetal outcome at each time point. ADIPS acknowledges the need for future studies comparing the new criteria with previous criteria.

**Treatment targets.** Intervention studies for “mild” hyperglycaemia in pregnancy have demonstrated benefits from treatment.<sup>6,7,8</sup> No randomised treatment trial has been conducted using the WHO diagnostic criteria for inclusion and no trial has defined the optimal treatment targets. However, extrapolating from HAPO data, and considering recent information about glycaemia in normal pregnancy,<sup>15,16,17</sup> the following self-monitoring blood glucose treatment targets are suggested based on 2SDs above the mean values for pregnant women without known risk factors.

Fasting capillary blood glucose (BG):  $\leq 5.0$ mmol/L

1-hour BG after commencing meal:  $\leq 7.4$ mmol/L  
2 hour BG after commencing meal:  $\leq 6.7$ mmol/L

The 2 large RCTs <sup>6,7</sup> have demonstrated the benefits of treating hyperglycaemia in pregnancy using treatment targets of fasting  $< 5.3$  and  $5.5$  mmol/L and 2 hour values of  $< 6.7$  or  $7$  mmol/L respectively. There is level 1 evidence for a two-hour value of  $6.7$  mmol/L. The fasting target of  $< 5.1$  has been chosen from observational data. There is level 1 evidence for a value of  $< 5.3$  mmol/L. The one-hour target of  $< 7.4$  mmol/L is based on the normal glucose levels in a small number of normal pregnant women. There is no evidence to indicate the risk-benefit ratio of treating to this target.

These suggestions are for self-measured capillary blood glucose (BG) levels. The reliability of these measurements is dependent on multiple factors, including the intrinsic accuracy of meters. When considering BG levels in individual women, the patterns of glycaemia are more important than individual results. Outlying BG levels are likely to be due to dietary or other lifestyle-related factors. In general, at least 2 elevated levels, at a given testing time, in 1 week, after consideration of dietary factors, should be a prompt to consider additional therapy.

These recommendations regarding treatment targets have been based on consensus discussions within ADIPS relating to limited but “best available” data. The validity of these treatment targets will need to be evaluated.

**HbA<sub>1c</sub>.** This currently has limited use for the diagnosis, management and postpartum assessment of women with hyperglycaemia in pregnancy. More research regarding the use of glycated products in hyperglycaemia in pregnancy is required.

**Cost effectiveness studies.** Existing published cost / benefit analyses suggest that the new criteria will be cost effective in improving pregnancy outcomes and longer term maternal health. However, longer term follow up and evaluation of the impact of the new criteria on possible disease prevention in later life will be very difficult.

**Ultrasonography.** Intensity of therapy has been adjusted depending on the results of ultrasonographic assessment of fetal growth (in particular measurements of fetal abdominal circumference). Research will be required to see if this is a viable option in our population and with the ultrasound services available.

**Risk stratification.** The cited risk factors for hyperglycaemia in pregnancy are unlikely to be all of equivalent predictive value and further research is required to determine whether some risk factors could be designated “high”. The ability and accuracy of obstetric care providers to conduct early pregnancy testing for hyperglycaemia in pregnancy based on the potential stratification of risk factors will require evaluation, and will be influenced by the frequency of abnormal glucose tolerance in the local population.

## References

1. Martin FIR for the Ad Hoc Working Party. The diagnosis of gestational diabetes. *MJA* 1991; 155: 112
2. HAPO Collaborative Research Group. Hyperglycemia and adverse pregnancy outcomes. *New Eng J Med* 2008; 358:1991-2002
3. IADPSG 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
4. Report of a World Health Organization Consultation Diagnostic criteria and classification of hyperglycaemia first detected in pregnancy: A World Health Organization Guideline. *Diabetes Research and Clinical Practice* 2014;103: 341-63.
5. Dunstan D, Zimmet P, Welborn T, Sicree R, Armstrong T, Atkins R, Cameron A, Shaw J & Chadban S on behalf of the AusDiab Steering Committee 2001, *Diabetes & Associated Disorders in Australia - 2000: the Accelerating Epidemic - Australian Diabetes, Obesity & Lifestyle Report*, International Diabetes Institute, Melbourne
6. Crowther CA, Hiller JE, Moss JR, McPhee AJ, Jeffries WS, Robinson J. Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. *New Eng J Med* 2005; 352:2477-2486
7. Landon M, Spong C, Thom E, Carpenter M, Ramin S, Casey B, Wapner R, Varner M, Rouse D, Thorp J, Jr., Sciscione A, Catalano P, Harper M, Saade G, Lain K, Sorokin Y, Peaceman A, Tolosa J, Anderson G. A multicenter, randomized trial of treatment for mild gestational diabetes. *The New Eng J Med* 2009; 361:1339-1348
8. Han S, Crowther CA, Middleton P. Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria (Review). *The Cochrane Library* 2012, issue 1
9. Moses RG. The recurrence rate of gestational diabetes mellitus in subsequent pregnancies. *Diabetes Care* 1996; 19: 1348-1350.
10. Lee AJ Hiscock RJ Wein P Walker SP Permezel M Gestational Diabetes Mellitus: Clinical Predictors and Long-Term Risk of Developing Type 2 Diabetes A retrospective cohort study using survival analysis *Diabetes Care* 30:878–883, 2007
11. Bellamy L, Casas J, Hingorani A, Williams D. Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis. *The Lancet* 2009; 373: 1773 – 1779.
12. Simmons DS, Walters BNJ, Wein P, Cheung NW. Guidelines for the management of gestational diabetes mellitus revisited. *Med J Aust* 2002; 176: 352.
13. Metzger B, Sacks D, Hadden D, Maresh M, Deerochanawong C, Dyer A, Lowe L, Coustan D, Hod M, Oats J, Persson B. Frequency of Gestational Diabetes Mellitus at Collaborating Centers Based on IADPSG Consensus Panel–Recommended Criteria: The Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study. *Diabetes Care* March 2012; 35:526-528

14. Moses RG, SanGil F, Morris G, Petocz P, Garg D. Impact of the potential new diagnostic criteria on the prevalence of gestational diabetes mellitus in Australia. *Med J Aust* 2011; 194: 338-340
15. Riskin-Mashiah S, Damti A, Younes G, Auslander R. Normal fasting plasma glucose levels during pregnancy: a hospital-based study. *Journal of Perinatal Medicine* 2011;39:2: 209-211
16. Hernandez T, Friedman J, Van Pelt R, Barbour L. Patterns of Glycemia in Normal Pregnancy. *Diabetes Care* 2011; 34: 1660-68.
17. Moses R, Moses M, Russell K, Schier G. The 75 g GTT in pregnancy. A reference range determined on a low risk population and related to selected pregnancy outcomes. *Diabetes Care* 1998; 21: 1807-1811.