ADIPS Consensus Guidelines for the Testing and Diagnosis of Gestational Diabetes Mellitus in Australia

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

The Hyperglycemia and Adverse Pregnancy Outcome study (HAPO) published in 2008[2] was a large, prospective, blinded, multinational, observational study that examined pregnancy outcomes in 23,316 women whose plasma glucose (PG) levels were ≤ 5.8mmol/L fasting and ≤ 11.1mmol/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.[3] These guidelines have been endorsed by several national organisations including the American Diabetes Association[4].

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.[5] 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 definition of GDM will remain as glucose intolerance of variable severity with onset or first recognition during pregnancy. The diagnosis of GDM will therefore include those women with previously undiagnosed abnormalities of glucose tolerance, as well as women with glucose abnormalities related to the pregnancy alone. A definitive diagnosis of non-gestational diabetes cannot be made until the post partum period. Because of this uncertainty, ADIPS does not currently recommend the use of the term “Overt Diabetes” (as proposed by IADPSG) to describe marked hyperglycaemia (consistent with diabetes if detected outside pregnancy) first detected in pregnancy. However, clinical judgement should be used to detect marked hyperglycaemia, especially in early pregnancy (first visit). These women 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 GDM for women with risk factor(s)

Women, not known to have pre-existing glucose abnormalities, but with risk factors for GDM (vide infra) should be tested early in pregnancy. We recommend a tiered approach to early glucose testing.

Moderate risk factors for GDM

- Ethnicity: Asian, Indian subcontinent, Aboriginal, Torres Strait Islander, Pacific Islander, Maori, Middle Eastern, non-white African
- BMI 25 – 35 kg/m^2

Women with either ethnicity or a body mass index (BMI) of 25 – 35 kg/m^2 as their only risk factor should be considered as "moderate risk" and should initially be screened with either a random or a fasting glucose test in early pregnancy, followed by a pregnancy OGTT (POGTT) if clinically indicated. The thresholds for further action are not clear at present and clinical judgement should be exercised.

High risk factors for GDM

- Previous GDM
- Previously elevated blood glucose level
- Maternal age ≥40 years
- Family history DM (1st degree relative with diabetes or a sister with GDM)
- BMI > 35 kg/m^2
- Previous macrosomia (baby with birth weight > 4500 g or > 90th centile)
- Polycystic ovarian syndrome
- Medications: corticosteroids, antipsychotics

Women at "high risk" of GDM (**one** high risk factor or **two** moderate risk factors) should undergo a 75 g POGTT, with venous plasma samples taken fasting, one hour and two hours at the first opportunity after conception.

Women considered as moderate or high risk but with normal early pregnancy glucose testing should have a repeat POGTT at the usual time of 24-28 weeks' gestation.[3] However a POGTT should be performed at any earlier time during pregnancy, if clinically indicated.

2. Recommendations for routine testing for GDM

All women not known to have GDM, should have a 75g 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.

3. Recommendations for diagnostic criteria for GDM

The HAPO study demonstrated no specific plasma glucose values above which the risk of adverse pregnancy outcomes was markedly increased. Therefore the IADPSG consensus panel recommended that cut points for the fasting, 1-hour and 2-hour plasma glucose levels associated with an odds ratio of 1.75 for adverse outcomes compared to the rates seen at mean glucose levels of the HAPO cohort should be designated the diagnostic levels for GDM. Primary outcomes of the HAPO study were birth weight >90thpercentile, caesarean section delivery, neonatal hypoglycaemia and cord C-peptide >90thcentile[2]. Outcomes used in determining cut points were excess fetal size and adiposity (>90th centile) and cord C-peptide.[3]

A diagnosis of GDM is made if one or more of the following glucose levels are elevated;

Fasting glucose	≥ 5.1mmol/L
1-hr glucose	≥ 10.0mmol/L
2-hr glucose	≥ 8.5mmol/L

Levels of evidence

The diagnostic criteria have been chosen from HAPO[2] - a large, observational study. 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)[6,7,8] which clearly demonstrate the benefits of treatment for both mother and fetus (Level 1 evidence) although the diagnostic criteria used in these studies were slightly different from the values selected 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_{1c} can be considered. A level of ≥ 48mmol/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_{1c} with lesser degrees of glucose intolerance.

4. Suggested treatment targets in GDM

It is recognized that glycaemic targets in the treatment of GDM 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.

5. Management in the post-partum period

Women diagnosed with GDM should have a 75g 2-hr OGTT, preferably at 6-12 weeks post-partum, with classification according to the WHO criteria.

Women diagnosed with GDM should have regular ongoing surveillance as they have an approximate 30% risk of a recurrence of their GDM in a subsequent pregnancy[9] and up to 50% risk of developing type 2 DM within 10-20 years.[10] 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 an HbA_{1c} when it is Medicare funded and approved for this purpose[11]. For women at lower risk, a fasting PG every 1-2 years should be sufficient.

6. Potential impact of the new diagnostic criteria for GDM

The new recommended diagnostic criteria will increase the prevalence of GDM.[12] Using IADPSG criteria, a prospective study in Wollongong demonstrated an increase from 9.6% to 13.0%.[13] A post hoc analysis of the HAPO sites in Australia demonstrated a prevalence in Brisbane of 12.1% and in Newcastle of 13.6%.[12]

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 have been moved to the section requiring further research. Also, with the advice of the RANZCOG, the early testing of women with risk factors for GDM has been stratified into moderate and high. The clinical accuracy of this stratification has been designated an area requiring further research and evaluation.

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 GDM, 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 gestational diabetes.

Early testing. Gestational diabetes 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 full OGTT 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 shown advantages of treatment for women with diagnostic glucose levels which differ from those being recommended in this guideline. The 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.[6,7,8] No randomised treatment trial has been conducted using the IADPSG 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,[14,15,16] 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):	≤ 5.0mmol/L
1-hour BG after commencing meal:	≤ 7.4mmol/L
2 hour BG after commencing meal:	≤ 6.7mmol/L

The 2 large RCTs [6,7] that demonstrated the benefits of treating gestational diabetes used 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_{1c}. This currently has limited use for the diagnosis, management and post partum assessment of women with GDM. More research regarding the use of glycoslylated products in GDM 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.

Overt diabetes. This term has been used for women who have a "diabetic" result on the pregnancy GTT and is suggestive of pre-existing diabetes. Although the demography of women who are becoming pregnant is changing, the proportion of women in this category in the Australian obstetric population is still likely to be small. We have avoided inclusion of this term as it adds an extra layer of complexity and possible confusion. Unless clinically indicated, these women will receive similar treatment to women with pregnancy hyperglycaemia and the matter will be resolved in the postpartum. Further research to define the prevalence of "diabetic level" hyperglycaemia in the Australian obstetric population is needed.

Risk stratification.
The ability of obstetric care providers to conduct early pregnancy testing for GDM based on the stratification of risk factors will require evaluation.

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VERSION 2:3/5/13