

## Guidelines for the Management of Gestational Diabetes Mellitus

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### 1 INTRODUCTION

The Hyperglycemia and Adverse Pregnancy Outcome study that published in 2008 had 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.(1) The study confirmed a strong continuous association between maternal glucose levels at 24-32 weeks gestation and a range of adverse maternal and fetal outcomes. This has led to the new diagnostic definition proposed by the International Association of the Diabetes and Pregnancy Study Groups,(2) which were subsequently adopted by the American Diabetes Association (3), the Australasian Diabetes in Pregnancy Society (4), the World Health Organization (WHO)(5), and other global official bodies.(6)

At the same time, both the Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) and Maternal-Fetal Medicine Units trials have shown that antenatal treatment of a mild degree of maternal hyperglycemia reduced these adverse outcomes.(7-8) The ACHOIS study was further supported by cost-effectiveness analysis.(9)

This guideline was updated taking reference to the recent evidence, WHO, NICE guideline and recommendations of other international bodies.(3-5,10)

### 2 DIAGNOSTIC CRITERIA AND CLASSIFICATION

The HKCOG adopts the revised WHO definition and classification published in 2013:

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

- Diabetes mellitus (DM) in pregnancy, or
- Gestational diabetes mellitus (GDM)

DM in pregnancy should be diagnosed if one or more of the following criteria are met:

- fasting PG  $\geq 7.0$  mmol/L
- 2-h PG  $\geq 11.1$  mmol/L following a 75 gram oral glucose load
- Random PG  $\geq 11.1$  mmol/L in the presence of diabetes symptoms

GDM should be diagnosed at any time in pregnancy if one or more of the following criteria are met following a 75 gram glucose load:

- fasting PG 5.1-6.9 mmol/l
- 1-hour PG  $\geq 10.0$  mmol/l
- 2-hour PG 8.5-11.0 mmol/l

Women who have been diagnosed DM or pre-diabetes (impaired fasting glucose or impaired glucose tolerance) prior to pregnancy should not be included into this classification.

### 3 SCREENING FOR HYPERGLYCAEMIA IN PREGNANCY

Universal screening was recommended by WHO (5) and was approved by the United States Preventive Services Task Force. (11) HKCOG supports universal screening by 75 gram oral glucose tolerance test (OGTT) at 24-28 weeks of gestation as long as resource is available.

If universal screening cannot be done, HKCOG recommends that all pregnant women, with any risk factor identified at the

booking visit, should be offered a 75 gram OGTT at 24-28 weeks of gestation (Table 1). Test should also be offered to women who present with clinical features that might be caused by maternal hyperglycaemia (Table 2), or women with risk factor but booked after 28 weeks of gestation.

There have been a few studies suggesting that HbA1c may be a useful screening test to detect hyperglycaemia in pregnancy and has been adopted by some units. (12-15) However, there is still insufficient evidence to support its routine use for screening and it is not yet endorsed by any international bodies.

|                             |                                                                                                                                                                                                                                                                                      |
|-----------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Personal and family history | <ul style="list-style-type: none"> <li>Advanced maternal age <math>\geq 35</math> years</li> <li>Obesity: BMI <math>\geq 25</math> kg/m<sup>2</sup> before pregnancy or at booking in the first trimester</li> <li>Family history of DM in 1<sup>st</sup> degree relative</li> </ul> |
| Medical history             | <ul style="list-style-type: none"> <li>Polycystic ovarian syndrome</li> <li>Autoimmune disease</li> <li>Chronic hypertension</li> <li>Long-term use of medication that is diabetogenic (e.g. systemic corticosteroids, tacrolimus etc.)</li> </ul>                                   |
| Past pregnancy              | <ul style="list-style-type: none"> <li>Previous macrosomic baby weighing <math>\geq 4</math> kg</li> <li>Previous GDM or DM in pregnancy</li> </ul>                                                                                                                                  |
| Current pregnancy           | <ul style="list-style-type: none"> <li>Multiple pregnancy</li> </ul>                                                                                                                                                                                                                 |

Table 1. Risk factors of hyperglycaemia in pregnancy.

|                                                                                                                                                                                                                                                                                                                                               |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"> <li>Large-for-date fetus (AC <math>\geq 90^{\text{th}}</math> centile or estimated fetal weight <math>\geq 90^{\text{th}}</math> centile)</li> <li>Polyhydramnios</li> <li>Glycosuria (of 2+ or above on 1 occasion or of 1+ or above on 2 or more occasions detected by reagent strip testing)</li> </ul> |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

Table 2. Clinical features suggesting hyperglycaemia in pregnancy

### 4 EARLY DETECTION OF GDM AND SCREENING FOR PRE-GESTATIONAL DM IN THE FIRST TRIMESTER

It remains controversial whether early recognition of GDM in the first trimester and early treatment help to reduce its complications. This definition of GDM applies at any time during pregnancy. As the fasting PG declines by about 0.5 mmol/L during pregnancy by the end of the first or early in the second trimester, testing early might over-diagnose GDM in non-obese women who have fasting PG values close to

the cut-off point. (5) Nevertheless, it is still recommended that a fasting PG value in early pregnancy 5.1 mmol/L or above should be classified as GDM.

On the other hand, women who might be at risk of pre-pregnancy DM (Table 3) should be screened in as soon as possible. At risk women should be offered fasting PG, HbA1c, or 75 gram OGTT (Table 4). Those who screened negative should be offered a 75 gram OGTT at 24-28 weeks of gestation. IADPSG suggested a diagnosis of pre-pregnancy DM in women with HbA1c 6.5% or more in the first trimester.

|                             |                                                                                                                                                                                                                                                                                                                                                                                                  |
|-----------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Personal and family history | <ul style="list-style-type: none"> <li>• Advanced maternal age <math>\geq 40</math> years</li> <li>• BMI <math>\geq 30</math> kg/m<sup>2</sup></li> <li>• Strong family history of DM (especially GDM and/or DM among siblings)</li> </ul>                                                                                                                                                       |
| Medical history             | <ul style="list-style-type: none"> <li>• History suggesting of previous hyperglycaemia</li> <li>• Metabolic syndrome</li> <li>• Polycystic ovarian syndrome with known insulin resistance, obese phenotype</li> <li>• Autoimmune disease</li> <li>• Chronic hypertension</li> <li>• Long-term use of medication that is diabetogenic (e.g. systemic corticosteroids, tacrolimus etc.)</li> </ul> |
| Past pregnancy              | <ul style="list-style-type: none"> <li>• Previous GDM or DM in pregnancy</li> <li>• Previous unexplained stillbirth</li> <li>• Previous congenital malformations that could be compatible with diabetic embryopathy</li> </ul>                                                                                                                                                                   |

Table 3. Women at risk of pre-pregnancy DM that could have been undiagnosed

|              |                                       |
|--------------|---------------------------------------|
| Fasting PG   | $\geq 7.0$ mmol/l                     |
| HbA1c        | $\geq 6.5\%$                          |
| 75 gram OGTT | As defined for GDM or DM in pregnancy |

Table 4. Tests for pre-pregnancy DM in early pregnancy

## 5 MANAGEMENT FOR HYPERGLYCAEMIA FIRST DETECTED IN PREGNANCY

Women diagnosed with hyperglycaemia in pregnancy should be informed about the implications of the diagnosis and offered appropriate intervention. (10) Each unit should have a team including dietitian, diabetic nurse, obstetrician and endocrinologist to provide a multidisciplinary care.

- Refer all women to a dietitian.
- Advise them to eat a healthy diet and recommend foods with a low glycaemic index.
- Advise regular exercise (such as walking for 30 minutes after a meal) to improve glycaemic control.
- Educate on capillary blood glucose monitoring to maintain glucose levels below the following targets:
  - Fasting: 5.3 mmol/l
  - &
  - 2 hours postprandial: 6.8 mmol/l
- Offer metformin if blood glucose targets are not met after diet and exercise therapy within 1–2 weeks.

- Offer addition of insulin to diet therapy, exercise and metformin if blood glucose targets are not met.
- Consider immediate treatment with insulin, with or without metformin, together with diet and exercise therapy for women who have
  - Fasting PG  $\geq 7.0$  mmol/l at diagnosis.
  - Fasting PG 6.0 - 6.9 mmol/l with complications such as macrosomia or polyhydramnios.
- Consider glibenclamide for women in whom blood glucose targets are not achieved with metformin but who decline insulin therapy or who cannot tolerate metformin.

Women diagnosed with hyperglycaemia in pregnancy should be offered regular surveillance on fetal growth. Elective induction of labour before 41 weeks of gestation is not necessary for women with GDM having good glycaemic control and without macrosomia or other obstetric indication.

## 6 POSTNATAL MANAGEMENT

Women should be encouraged on breastfeeding. They can resume or continue to take metformin and glibenclamide immediate after birth as required, but should avoid other forms of oral hypoglycaemic agents while breastfeeding.

Women diagnosed with hyperglycaemia in pregnancy should be informed about the increased risk of future DM and hyperglycaemia in future pregnancy and should be offered lifestyle advice including weight control, diet and exercise. They

should be offered a postnatal test at 6-12 weeks to exclude DM. There is no consensus on the best postnatal testing.(16,17) HKCOG suggests either OGTT or HbA1c (with or without fasting glucose). It has to be emphasized that this should not be a one off testing, but should be at regular interval. Women with higher risk for progression on the basis of the testing result (Table 5) or background risk (obesity, strong family history of DM, insulin required during pregnancy, metabolic syndrome, etc.) should require more frequent testing (yearly) then those at lower risk (3-yearly).

|            | High probability of progression                          | Low probability of progression |
|------------|----------------------------------------------------------|--------------------------------|
| 75 g OGTT  | Impaired fasting glycaemia or Impaired glucose tolerance | normal                         |
| HbA1c*     | 5.7% - 6.4%                                              | <5.7%                          |
| Fasting PG | 5.6 – 6.9 mmol/l                                         | <5.6 mmol/l                    |

Table 5. Probability of progression to DM based on the postnatal testing result

[\*HbA1c levels could be affected in the presence of certain haemoglobinopathies that are common in our locality; assay method without interference with haemoglobinopathies are recommended.(18)]

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This guideline was produced by the Hong Kong College of Obstetricians and Gynaecologists as an educational aid and reference for obstetricians and gynaecologists practicing in Hong Kong. The guideline does not define a standard of care, nor is it intended to dictate an exclusive course of management. It presents recognized clinical methods and techniques for consideration by practitioners for incorporation into their practice. It is acknowledged that clinical management may vary and must always be responsive to the need of individual patients, resources, and limitations unique to the institution or type of practice. Particular attention is drawn to areas of clinical uncertainty where further research may be indicated.

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