Gestational Diabetes

This article deals only with gestational diabetes. There is a separate Diabetes in Pregnancy article, which provides information about pregnancy in women with pre-existing diabetes.

Gestational diabetes mellitus (GDM) is any degree of glucose intolerance with its onset (or first diagnosis) during pregnancy and usually resolving shortly after delivery[1]. Pregnancy hormones decrease fasting glucose levels, increase fat deposition, delay gastric emptying and increase appetite. However, over the course of pregnancy, postprandial glucose concentrations increase as insulin resistance increases. This is normally countered by an increased production of insulin but in women with GDM there is an insufficient compensatory rise[2].

There is no clear agreement on diagnostic criteria[3]. Pregnancy hyperglycaemia without meeting GDM diagnostic criteria affects a significant proportion of pregnant women each year and is associated with a range of adverse pregnancy outcomes[4].

The National Institute for Health and Care Excellence (NICE) recommends that GDM should be diagnosed if the pregnant woman has either[5]:
- Fasting plasma glucose level of 5.6 mmol/L or above; or
- Two-hour plasma glucose level of 7.8 mmol/L or above.

Although the World Health Organization (WHO) now recommends that HbA1c can be used as a diagnostic test for diabetes, it is currently not recommended for diagnosis during pregnancy[6].

Many of the problems associated with GDM are common to established diabetes in pregnancy - hyperglycaemia promotes large-for-dates babies and is associated with adverse fetal and maternal outcomes. There is no agreement on the glycaemic threshold for these adverse outcomes - indeed, large studies have indicated a strong, continuous association of maternal glucose levels (below those diagnostic of diabetes) with increased birth weight, and significant associations with secondary outcomes such as preterm labour, shoulder dystocia, birth injury, intensive neonatal care requirement, hyperbilirubinaemia and pre-eclampsia. GDM increases the risk of developing diabetes later in life[7].

Epidemiology

GDM is a growing health concern in many parts of the world - it occurs in 2-5% of pregnancies but figures vary considerably depending upon the criteria used. GDM is increasing in prevalence worldwide in tandem with the dramatic increase in the prevalence of overweight and obesity in women of childbearing age[8].

Little is known about the burden of diabetes mellitus in pregnancy in low- and middle-income countries despite high prevalence and mortality rates in these countries[9].

Risk factors[2]

GDM is more likely with:
- Increasing age.
- Certain ethnic groups (Asian, African Americans, Hispanic/Latino Americans and Pima Indians).
- High BMI before pregnancy (three-fold risk for obese women compared to non-obese women).
- Smoking doubles the risk of GDM.
- Change in weight between pregnancies - an inter-pregnancy gain of more than three units (of BMI) doubles the risk of GDM.
- Short interval between pregnancies.
- Previous unexplained stillbirth.
- Previous macrosomia.
- Family history of type 2 diabetes or GDM - more relevant in nulliparous than parous women.

Protective factors
- Physical activity: there is only limited evidence available on the effect of exercise during pregnancy for preventing GDM[10].

Diagnosis

Screening

GDM is usually asymptomatic but has serious consequences that can be reduced by treatment.
NICE guidance suggests that screening should be offered at booking to women with the following risk factors for developing GDM:[5]:
- BMI >30 kg/m²
- Previous macrosomic baby ≥4.5 kg or above.
- Previous GDM.
- First-degree relative with diabetes.
- Family origin with a high prevalence of diabetes (South Asian, black Caribbean and Middle Eastern).

NICE recommends[5]:
- Fasting plasma glucose, random blood glucose, HbA1c, glucose challenge test and urinalysis for glucose should not be used to assess risk of developing GDM.
- Glycosuria of 2+ or above on one occasion or of 1+ or above on two or more occasions detected by reagent strip testing during routine antenatal care may indicate undiagnosed GDM. Consider further testing to exclude GDM.
- Use the two-hour 75 g oral glucose tolerance test (OGTT) to test for GDM in women with risk factors.
- Offer women who have had GDM in a previous pregnancy:
  - Early self-monitoring of blood glucose; or
  - A 75 g two-hour OGTT as soon as possible after booking (whether in the first or second trimester), and a further 75 g two-hour OGTT at 24-28 weeks if the results of the first OGTT are normal.

- Offer women with any of the other risk factors for GDM a 75 g two-hour OGTT at 24-28 weeks.

Glucose tolerance changes with the duration of the pregnancy so that the gestation at which the diagnosis was made should be recorded and, if made in the third trimester, there should be some caution about the clinical implications of impaired glucose tolerance[12].

Management[5, 12]

Treatment of GDM and good glycaemic control reduce serious perinatal morbidity and may also improve the woman's health-related quality of life[13, 14].

It is often controversial as to when GDM requires treatment. A study showed that the treatment (dietary intervention, self-monitoring of blood glucose, and insulin therapy, if deemed necessary) of mild GDM (defined as positive OGTT but fasting glucose <5.3 mmol/L) did reduce the risks of fetal overgrowth, shoulder dystocia, caesarean delivery and hypertensive disorders but not a composite primary outcome (based upon stillbirth or perinatal death and neonatal complications, including hyperbilirubinaemia, hypoglycaemia, hyperinsulinaemia and birth trauma)[15].
Antenatal care[5]

Women should receive routine antenatal care but in addition:

**Monitoring blood glucose**
Advise pregnant women with GDM who are on a multiple daily insulin injection regimen to test their fasting pre-meal, one hour post-meal and bedtime blood glucose levels daily during pregnancy.

Advise pregnant women with GDM to test their fasting and one hour post-meal blood glucose levels daily during pregnancy if they are on diet and exercise therapy, or taking oral therapy (with or without diet and exercise therapy) or single-dose intermediate-acting or long-acting insulin.

**Target blood glucose levels**
Agree individualised targets for self-monitoring of blood glucose, taking into account the risk of hypoglycaemia.

Advise maintaining capillary plasma glucose below the following target levels, if these are achievable without causing problematic hypoglycaemia: fasting glucose 5.3 mmol/L and glucose levels 7.8 mmol/L one hour after meals, or 6.4 mmol/L two hours after meals.

Advise women with GDM, who are on insulin or glibenclamide, to maintain their capillary plasma glucose level above 4 mmol/L.

**Monitoring HbA1c**
- Measure HbA1c levels in all women with GDM at the time of diagnosis to identify those who may have pre-existing type 2 diabetes.
- Do not use HbA1c levels routinely to assess a woman's blood glucose control in the second and third trimesters of pregnancy.

**Detecting congenital malformations**
Offer women with pre-existing diabetes or GDM an ultrasound scan for detecting fetal structural abnormalities, including examination of the fetal heart, at 20 weeks.

**Monitoring fetal growth and well-being**
Offer pregnant women with pre-existing diabetes or GDM ultrasound monitoring of fetal growth and amniotic fluid volume every four weeks from 28 to 36 weeks.

**Non-drug treatment**
Most women with GDM can be treated with lifestyle modifications[16].

- Body weight - weight loss should be aimed for with women with a BMI >27.
- Diet - all women with GDM should receive dietary advice from a specialist dietician - food choices should reflect the nutritional demands of pregnancy and concentrate on the need for micronutrient-rich food.
- Physical activity:
  - There is limited randomised controlled trial evidence available on the effect of exercise during pregnancy for preventing pregnancy glucose intolerance or GDM[10].

**Medication**
Insulin is the gold standard for treatment of hyperglycaemia during pregnancy, when lifestyle measures do not maintain glycaemic control. However, certain oral hypoglycaemic agents may be safe and acceptable alternatives[17].
NICE recommends:

- Offer a trial of changes in diet and exercise to women with GDM who have a fasting plasma glucose level below 7 mmol/L at diagnosis.
- Offer metformin to women with GDM if blood glucose targets are not met using changes in diet and exercise within 1-2 weeks.
- Offer insulin instead of metformin to women with GDM if metformin is contra-indicated or unacceptable to the woman.
- Offer addition of insulin to the treatments of changes in diet, exercise and metformin for women with GDM if blood glucose targets are not met.
- Offer immediate treatment with insulin, with or without metformin, as well as changes in diet and exercise, to women with GDM who have a fasting plasma glucose level of 7.0 mmol/L or above at diagnosis.
- Consider immediate treatment with insulin, with or without metformin, as well as changes in diet and exercise, for women with GDM who have a fasting plasma glucose level of between 6.0 and 6.9 mmol/L, if there are complications such as macrosomia or hydramnios.
- Consider glibenclamide for women with GDM in whom blood glucose targets are not achieved with metformin but who decline insulin therapy, or who cannot tolerate metformin.

**Insulin treatment**

Rapid-acting insulin analogues (aspart and lispro) have advantages over soluble human insulin during pregnancy.

Advise women with insulin-treated diabetes of the risks of hypoglycaemia and impaired awareness of hypoglycaemia in pregnancy, particularly in the first trimester. Advise pregnant women with insulin-treated diabetes always to have available a fast-acting form of glucose (eg, dextrose tablets or glucose-containing drinks).

Offer women with insulin-treated diabetes continuous subcutaneous insulin infusion (CSII) during pregnancy if adequate blood glucose control is not obtained by multiple daily injections of insulin without significant disabling hypoglycaemia.

**Ketone testing and diabetic ketoacidosis**

Advise pregnant women with GDM to seek urgent medical advice if they become hyperglycaemic or unwell. Test urgently for ketonaemia if a pregnant woman with any form of diabetes presents with hyperglycaemia or is unwell, to exclude diabetic ketoacidosis.

**Intrapartum care**

- **Preterm labour**
  Diabetes should not be considered a contra-indication to antenatal steroids for fetal lung maturation or to tocolysis. Do not use betamimetic medicines for tocolysis in women with diabetes.

- **Timing and mode of birth**
  Advise women with GDM to give birth no later than 40+6 weeks, and offer elective birth (by induction of labour or by caesarean section if indicated) to women who have not given birth by this time. Consider elective birth before 40+6 weeks for women with GDM if there are maternal or fetal complications.

  Diabetes should not in itself be considered a contra-indication to attempting vaginal birth after a previous caesarean section.

  Explain to pregnant women with diabetes who have an ultrasound-diagnosed macrosomic fetus about the risks and benefits of vaginal birth, induction of labour and caesarean section.

**Postpartum care**

Women who have been diagnosed with GDM should discontinue blood glucose-lowering therapy immediately after birth.

For women who were diagnosed with GDM and whose blood glucose levels returned to normal after the birth: offer lifestyle advice (including weight control, diet and exercise).

Offer a fasting plasma glucose test 6-13 weeks after the birth to exclude diabetes. If a fasting plasma glucose test has not been performed by 13 weeks, offer a fasting plasma glucose test, or an HbA1c test if a fasting plasma glucose test is not possible, after 13 weeks. Do not routinely offer a 75 g two-hour OGTT.

- Advise women with a fasting plasma glucose level below 6.0 mmol/L or HbA1c level below 39 mmol/mol (5.7%) that:
  - They have a low probability of having diabetes at present.
  - They should continue to follow the lifestyle advice (including weight control, diet and exercise) given after the birth.
  - They will need an annual test to check that their blood glucose levels are normal.
  - They have a moderate risk of developing type 2 diabetes. Offer them advice on preventing type 2 diabetes. See separate Prevention of Type 2 Diabetes article.

- Advise women with a fasting plasma glucose level between 6.0 and 6.9 mmol/L, or HbA1c level between 39 and 47 mmol/mol (5.7% and 6.4%), that they are at high risk of developing type 2 diabetes, and offer them advice, guidance and interventions to help prevent type 2 diabetes.
• Advise women with a fasting plasma glucose level of 7.0 mmol/L or above that they are likely to have type 2 diabetes. Offer them a diagnostic test to confirm diabetes.
• Advise women with an HbA1c level of 48 mmol/mol (6.5%) or above that they have type 2 diabetes and refer them for further care.

Offer an annual HbA1c test to women who were diagnosed with GDM who have a negative postnatal test for diabetes.

Offer women who were diagnosed with GDM, early self-monitoring of blood glucose or an OGTT in future pregnancies. Offer a subsequent OGTT if the first OGTT results in early pregnancy are normal.

Complications[7]

• When using the WHO diagnostic criteria, GDM is associated with macrosomia, large for gestational age, perinatal mortality, pre-eclampsia and delivery by caesarean section[19]. Other complications for the baby include shoulder dystocia, birth injuries (eg. bone fractures and nerve palsies) and hypoglycaemia.
• Long-term adverse health outcomes in infants born to mothers with GDM may include:
  • Sustained impairment of glucose tolerance.
  • Subsequent obesity (although not when adjusted for size).
  • Impaired intellectual achievement.

Prognosis

• The perinatal risks to mother and baby are similar to those with known diabetes, mainly relating to the problems of a large baby.
• Treatment of GDM is effective in reducing macrosomia, pre-eclampsia and shoulder dystocia[19].
• Current evidence does not show that treatment of GDM has an effect on neonatal hypoglycaemia or future poor metabolic outcomes[20].
• Most women will apparently recover after the pregnancy but with about a 1 in 2 chance of recurrence in a future pregnancy[21].
• For the women themselves, GDM is a strong risk factor for diabetes and metabolic syndrome[22].
• Children whose mothers had GDM are more likely to be obese.

Editor’s Note

January 2018 - Dr Hayley Willacy has read the recent paper in PLoS med looking at risks for mothers who have had gestational diabetes[23]. In the first large population-based study in the United Kingdom, there are reports on the increased risk for cardiovascular disease in women diagnosed with GDM, and quantification of the high incidence of type 2 diabetes and hypertension for these women in the postpartum period. The main finding is that women diagnosed with gestational diabetes are almost 3 times as likely to develop ischaemic heart disease as women without GDM. Among the women who developed IHD, only a third also developed type 2 diabetes in the postpartum period, suggesting the risk for cardiovascular disease is not always mediated by type 2 diabetes. Less than 60% had some form of glycaemic measurement in the first postpartum year and this fell over time. Cardiovascular risk factors were generally poorly monitored in this group.

Further reading & references

5. Diabetes in pregnancy: management of diabetes and its complications from preconception to the postnatal period; NICE Clinical Guideline (February 2015)
6. Use of Glycated Haemoglobin (HbA1c) in the Diagnosis of Diabetes Mellitus; World Health Organization, 2011
12. Pregnancy and diabetes; Diabetes UK


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