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A practical guide to pregnancy complicated by diabetes

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As the prevalence of diabetes is increasing, the number of pregnancies complicated by pre-exisiting diabetes or gestational diabetes is also rising. This presents a challenge to healthcare services in the UK to prevent adverse outcomes in babies born to mothers with diabetes, and clinicians in primary care have an important role to play, particularly in delivering pre-conception care for women with these conditions. This article discusses the pathophysiology and treatment of gestational and pre-exisiting diabetes during pregnancy and outlines the ideal pre-conception care pathway, as well as antenatal and obstetric care.

Learning objectives

After reading this article, the participant should be able to:

1. Identify the risk factors for the development of gestational diabetes.
2. Describe the ideal prepregnancy clinic and the optimum care that a pregnant woman with pre-existing diabetes should receive.
3. Outline the appropriate diabetes treatments for pregnant women with either gestational, type 1 or type 2 diabetes.
4. Define the obstetric management of a pregnancy complicated by diabetes.

Key words

- Gestational diabetes
- Prepregnancy care
- Pregestational diabetes

Diabetes prevalence is increasing in pregnancy, with pregestational diabetes (type 1 and 2 diabetes) affecting 1.3% of pregnancies (Lawrence et al, 2008), and a further 12% of pregnancies being complicated by gestational diabetes (O'Sullivan et al, 2011). As such, a comprehensive understanding of the challenges faced in such pregnancies is vital. Here, the main aspects of diabetes management relevant to primary care are reviewed.

Gestational diabetes

Gestational diabetes (GD) was for many years defined as the onset or first recognition of abnormal glucose tolerance during pregnancy, with diagnostic thresholds reflecting the mother's future risk of developing diabetes rather than pregnancy outcomes. However, more recently, the International Association of Diabetes and Pregnancy Study Group (IADPSG; IADPSG Consensus Panel et al, 2010) has taken a different approach, redefining classification into two groups: overt diabetes and GD (*Box 1*). NICE guidance (National Collaborating Centre for Women's and Children's Health [NCCWCH], 2008) recommends diagnosing GD using the World Health Organization diagnostic criteria (*Box 2*); however, it should be noted that these recommendations were issued prior

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to the availability of data from the HAPO (Hyperglycaemia and Adverse Pregnancy Outcomes) Study Cooperative Research Group et al (2008) trial, which has resulted in a significant change in clinical practice.

The new IADPSG criteria were based heavily, although not exclusively, on the results from the multicentre HAPO trial (HAPO Study Cooperative Research Group et al, 2008). This involved 25 505 people worldwide and showed a continuous relationship between maternal blood glucose levels and adverse pregnancy outcomes of "large for gestational age", pre-eclampsia, and caesarean section.

This landmark study showed that there was no cut-off value above which the risk of complications rose abruptly, but rather that risk rose steadily even with mean blood glucose values previously considered to be in the normal range. As a result, the above IADPSG values were adopted (diagnostic cut-offs reflect mean blood glucose levels at which the odds ratio for adverse outcome was 1.75) in order to intervene in groups previously unrecognised but significantly at risk of an adverse pregnancy outcome. This has, of course, resulted in an increase in the number of women diagnosed with GD.

Using the new IADPSG criteria, a prevalence of GD of 12.4% was found in the west of Ireland ATLANTIC DIP (Diabetes in Pregnancy) study (Dunne et al, 2009), which used universal screening at 24–28 weeks using a 75 g oral glucose tolerance test (OGTT). This prevalence rate was similar to that identified in the HAPO study in similar populations.

Risk factors for the development of GD have been well established:

- Family history of diabetes in a first degree relative.
- BMI ≥30 kg/m^2.
- Maternal age ≥30 years.
- Previous unexplained perinatal death.
- Previous GD.
- Current glycosuria.
- Long-term steroid use.
- Previous delivery of a baby weighing ≥4.5 kg.
- Polycystic ovarian syndrome.
- Polyhydramnios and/or macrosomia in existing pregnancy.
- Ethnicity associated with a high prevalence of diabetes (African, south or east Asian, Pacific islanders, Hispanic, Middle Eastern, Caribbean).

This list of risk factors has been identified by looking at populations with a high prevalence of type 2 diabetes according to WHO figures (Danaei et al, 2011). Individuals with the above risk factors should undergo blood glucose testing (random or fasting plasma glucose, with or without HbA_{1c} measurement) at their booking visit to exclude undiagnosed diabetes. A subsequent 2-hour 75 g OGTT between 24 and 28 weeks should be carried out if diabetes is not diagnosed. Universal screening at 24–28 weeks is desirable, as per

Box 1. Diagnostic criteria for overt diabetes and gestational diabetes (International Association of Diabetes and Pregnancy Study Group Consensus Panel et al, 2010).

A diagnosis of overt diabetes can be made using the standard criteria for the diagnosis of diabetes:

- Fasting plasma glucose level of ≥7 mmol/L.
- Random plasma glucose level of ≥11.1 mmol/L.
- Or HbA_{1c} level ≥6.5% [48 mmol/mol]).

Women with gestational diabetes (GD) have a milder degree of glucose intolerance, with diagnosis requiring only one of the following:

- Fasting plasma glucose ≥5.1 mmol/L.
- 1-hour post 75 g glucose load ≥10.1 mmol/L.
- Or 2-hour post 75 g glucose load ≥8.5 mmol/L (while remaining below the threshold for overt diabetes outlined above).

The preferred method for diagnosing GD is a standard 75 g oral glucose tolerance test, with fasting, 1-hour and 2-hour plasma glucose values measured. This should be carried out between 24 and 28 weeks' gestation, when insulin resistance is increasing.

Box 2. Diagnostic criteria for gestational diabetes recommended by NICE (National Collaborating Centre for Women's and Children's Health, 2008).

The 2-hour 75 g oral glucose tolerance test (OGTT) should be used to test for gestational diabetes and diagnosis made using the criteria defined by the World Health Organization:

	Whole blood venous	Whole blood capillary	Plasma venous	Plasma capillary
Fasting	≥ 6.1 mmol/L	≥ 6.1 mmol/L	≥ 7.0 mmol/L	≥ 7.0 mmol/L
2 hours	≥ 6.7 mmol/L	≥ 7.8 mmol/L	≥ 7.8 mmol/L	≥ 8.9 mmol/L

Page points

1. Gestational diabetes (GD) treatment is based initially on lifestyle modification, and women should be managed in a combined obstetric/diabetes antenatal clinic. Women with GD should be educated on the benefits of good glycaemic control during pregnancy for their own health and that of their baby.
2. Despite improvements in glycaemic control over recent decades, rates of adverse pregnancy outcome in women with pre-existing type 1 and type 2 diabetes remain significantly elevated compared with the background population.

IADPSG guidelines, but varies according to local policies, and is not currently recommended by NICE (NCCWCH, 2008). In the absence of universal screening, high-risk criteria based on the above risk factors should be used to guide selective screening.

Pathophysiology of GD

During normal pregnancy, insulin requirements increase as gestation progresses. The normal pancreas responds via beta-cell hyperplasia occurring under the influence of prolactin and human chorionic somatotrophin resulting in increased insulin production. Insulin resistance also increases as a result of placental growth hormone, corticotrophin-releasing hormone and progesterone production. In spite of these changes in insulin regulation, blood glucose levels are lower than in the non-pregnant state due to increased glucose use (including fetal consumption), increased glycogen storage, and decreased hepatic glucose output. GD occurs when the mother's insulin secretion cannot compensate or the mother has increased insulin resistance usually due to associated obesity, or both, leading to hyperglycaemia.

Rationale for treatment

Persistent maternal hyperglycaemia leads to macrosomia, which increases the risk of serious obstetric complications – shoulder dystocia, brachial plexus injury and clavicular fracture. Infants of mothers with GD are at risk of hypoglycaemia, hypocalcaemia, jaundice and respiratory distress, resulting in more admissions to neonatal unit care (NNU). The risk of pre-eclamptic toxaemia (PET), pregnancy induced hypertension (PIH) and polyhydramniosis is increased in mothers affected by GD and delivery by caesarean section is more frequent (O'Sullivan et al, 2011).

The ACHOIS (Australian Carbohydrate Intolerance Study in Pregnancy; Crowther et al, 2005) demonstrated that children of mothers with "mild" GD (fasting blood glucose <5.3 mmol/L; *n*=1000) who were treated with diet, exercise, blood glucose monitoring, and insulin where indicated, were less likely (relative risk 0.33) to have a serious adverse perinatal outcome (composite outcome of stillbirth, shoulder dystocia, fracture or nerve injury) than those given routine care. These findings were confirmed by an American study of 958 women randomised to either usual antenatal care or treatment, which showed a significant reduction in shoulder dystocia, fetal overgrowth, caesarean section and hypertensive disorders (Landon et al, 2009).

GD treatment is based initially on lifestyle modification, and women should be managed in a combined obstetric/diabetes antenatal clinic. Women with GD should be educated on the benefits of good glycaemic control during pregnancy for their own health and that of their baby. Weight should be monitored throughout pregnancy to ensure appropriate weight gain.

Women with GD are advised to check capillary blood glucose measurements regularly – fasting, pre-meals, 1-hour post meals and at bedtime. Targets are a blood glucose level of <5 mmol/L pre-meals and fasting, and <7 mmol/L 1-hour post-prandially. If they fail to meet these targets (i.e. above target on three or more occasions, despite medical nutritional therapy for 2 weeks), insulin therapy is generally prescribed. These targets are from the authors' clinical practice (Heath Service Executive, 2010) and are more stringent than the NICE guidelines (NCCWCH, 2008). As mentioned previously, however, the HAPO (HAPO Study Cooperative Research Group et al, 2008) trial results were not published at the time of the NICE recommendations.

Pregestational diabetes

Despite improvements in glycaemic control over recent decades, rates of adverse pregnancy outcome in women with pre-existing type 1 and type 2 diabetes remain significantly elevated compared with the background population. Local, national and international studies show that stillbirth (SB) is five times and neonatal death (NND) three times more common in women with diabetes than in the

general population. PIH and PET are three times more common. One key principle of management of women with type 1 or type 2 diabetes is prepregnancy care (PPC).

Structured PPC takes the form of a dedicated hospital clinic, delivered by a combination of diabetes nurse specialists, midwife specialists, dietitians, diabetologists or obstetricians. A standardised approach to providing PPC, and discussing relevant medical issues (as outlined further below), may be aided by the use of a proforma document, and a "checklist" style approach. Clinic sizes tend to be smaller than general diabetes clinics, allowing more frequent recall, and less waiting time for new referrals. Primary care providers are well placed also to increase the proportion of women availing of PPC, and to help with this, every diabetes consultation in women of child-bearing age, both in hospital and the community, should include a brief but thorough evaluation of plans for pregnancy, potential risks, need for strict glycaemic control and current method of contraception. In particular, return visits for updated contraceptive prescriptions could prompt such a discussion.

In a recent UK study of 680 women with either type 1 or type 2 diabetes, PPC was associated with a decrease in adverse outcomes (stillbirth, neonatal death and congenital malformations) to 1.3% in attendees compared with 7.8% in non-attendees (Murphy et al, 2010). A dedicated prepregnancy clinic is the gold standard of care but despite this, the UK CEMACH (Confidential Enquiry into Maternal and Child Health, 2005) report showed that only 17% of UK maternity centres offer such a service. PPC offers the opportunity to optimise diabetes care as early as possible – ideally at least 3–6 months prior to attempting to conceive – aiming to achieve an HbA_{1c} level of a person without diabetes (<6% [<42 mmol/mol]) while avoiding hypoglycaemia. Fasting and pre-meal blood glucose levels of <5 mmol/L, and 1-hour postprandial levels of <7 mmol/L are the target.

Other aspects of prepregnancy care

Optimal glycaemic control as described above is only one aspect of PPC. PPC also offers the opportunity to optimise overall diabetes care. Medications that have known or potential teratogenic effects – particularly angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, or statins – need to be discontinued. If blood pressure control is required, methyldopa or labetalol may be used. Advice should also be given with regard to smoking cessation and to avoid alcohol intake.

In PPC there is time to discontinue oral agents and initiate insulin or change regimens. There is also time to re-educate women on the recognition and risks of hypoglycaemia especially in relation to driving. The woman and her partner can be educated on the appropriate use of glucagon. Education with regard to the potential effects of pregnancy on diabetes management also needs to be discussed, for example the management of hyperemesis gravidarum and signs of diabetic ketoacidosis (DKA). In particular, it should be noted that ketoacidosis may occur at lower blood glucose levels than in a non-pregnant woman. All people with type 1 diabetes should know how to self-monitor serum ketones. *Table 1* summarises medication and advice for women with type 1 or type 2 diabetes.

Neural tube defects are more common (odds ratio 4.2) in infants of mothers with

Page points

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2. Medications that have known or potential teratogenic effects – particularly angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, or statins – need to be discontinued.
3. Education with regard to the potential effects of pregnancy on diabetes management also needs to be discussed, for example the management of hyperemesis gravidarum and signs of diabetic ketoacidosis.

Table 1. Medication and advice for pregnant women with pre-existing type 1 or type 2 diabetes.

	Type 1	Type 2	Common to type 1 and type 2
Glycaemic control	Change to MDI regimen if appropriate.	Stop oral agents. Change to MDI regimen if appropriate.	Change to MDI regimen if appropriate.
Hypoglycaemia	Education. Glucagon.	Education.	Education.
DKA	Educate regarding ketone monitoring.		
Hyperemesis	Insulin management. Ketone monitoring.	Insulin management.	Insulin management.

DKA=diabetic ketoacidosis; MDI=multiple daily injections.

Page points

1. People with type 1 diabetes are best managed on a multiple daily injection (basal–bolus) regimen, with three pre-meal injections of rapid-acting insulin analogue and a long-acting human insulin or insulin analogue.
2. Metformin is not approved for use in pregnancy, but is commonly prescribed in the pre-conception period, especially in women with associated polycystic ovary syndrome or fertility issues, and is approved in this capacity by the NICE guidelines.

diabetes, and all women with pre-existing diabetes should take high-dose (prescription-only) folic acid 5 mg once-daily for at least 3 months prior to pregnancy, and up until 12 weeks gestational age (Medical Research Council Vitamin Study Research Group, 1991; Macintosh et al, 2006). Increasingly, vitamin D is being shown to be deficient in Irish women (O'Riordan et al, 2008). Deficiency is greater in overweight and obese women (Kayaniyil et al, 2010). Vitamin D deficiency is associated with increasing insulin resistance (Holick, (2007), which may make blood glucose management more difficult. Consequently, vitamin D should be measured and supplemented if required.

Many women with pregestational diabetes will be overweight or obese. Obesity is independently associated with adverse pregnancy outcomes both for the mother and the infant and is an independent risk factor for congenital malformations (Owens et al, 2009). In the ATLANTIC DIP cohort of women with type 1 and type 2 diabetes, only 37% had a normal BMI while 18% were obese (defined as a BMI >30 kg/m^2) (Dunne et al, 2009). PPC with attention to diet and exercise should focus on reducing, and where possible normalising, BMI prior to conception. This will also help with fertility, which may be a problem in these women. Exercise will have an additional beneficial effect on diabetes control, improving insulin resistance.

Medical nutritional therapy is a key component of achieving glycaemic control, with a focus on regulating carbohydrate intake and opting for low glycaemic index carbohydrates. Contraception should be continued until the HbA_{1c} level is <6% (<42 mmol/mol). In the absence of overt vascular disease (if present, the combined oral contraceptive pill should not be prescribed), contraception choices remain the same as in the general population, subject to the usual cautions and contraindications.

Insulin therapy in pregestational diabetes

People with type 1 diabetes are best managed on a multiple daily injection (basal–bolus) regimen, with three pre-meal injections of rapid-acting insulin analogue and one or more injections of long-acting human insulin or insulin analogue.

In a randomised controlled trial (RCT) the short-acting insulin analogues aspart and lispro were shown to be effective and well-tolerated and associated with a significant reduction in hypoglycaemia compared with human short-acting insulin (Mathiesen et al, 2007). The choice of basal insulin varies from person to person. The long-acting insulin analogues (insulin detemir and insulin glargine) have not yet completed RCTs in pregnancy, although anecdotal evidence from a large number of pregnancies does not raise any cause for concern, and they are frequently continued. Intermediate-acting insulin (for example, neutral protamine Hagedorn [NPH]) remains the basal insulin of choice for pregnant women with either type 1 or type 2 diabetes, due to its proven efficacy and reassuring safety data. Women on continuous subcutaneous insulin infusion (insulin pump therapy) may continue. Women trained in structured carbohydrate counting (such as Dose Adjustment for Normal Eating) may also continue. As pregnancy is associated with changes in insulin resistance, insulin doses will undergo significant changes. Patients should be advised of this.

Non-insulin therapies

Women with type 2 diabetes will need to change to insulin in the prepregnancy period if receiving PPC, or as soon as pregnancy is reported if not. Metformin is not approved for use in pregnancy, but is commonly prescribed in the pre-conception period, especially in women with associated polycystic ovary syndrome or fertility issues, and is approved in this capacity by NICE guidance if the benefit outweighs the risk (NCCWCH, 2008).

Metformin has been used in a randomised controlled trial in women with GD (Rowan et al, 2008) and no safety issues have emerged from that study, or from a follow-up study of infants up to 2 years after index pregnancy. However, given limited data so far, it may be prudent to limit its use to high-

risk pregnancies only, in situations where metformin is believed to be of benefit. Risks and benefits should be discussed fully with the individual.

Glibenclamide showed no evidence of excess risk in small trials (Langer et al, 2000), but is not approved for use in pregnancy due to lack of adequate safety data. Other sulphonylureas, and other classes of antidiabetes medication – e.g. acarbose, dipeptidyl peptidase-4 inhibitors, glucagon-like peptide-1 receptor agonists, thiazolidinediones and meglitinides – are not approved for use during pregnancy and should not be prescribed to women in whom pregnancy is a possibility.

Uptake of pre-conception care

Despite the proven benefits of PPC, uptake remains poor. A recent UK study found that only 27% of people availed of prepregnancy care (Murphy et al, 2010). The authors' local data shows that women with pre-existing diabetes remain unprepared for pregnancy, with 49% conceiving with an HbA_{1c} level of >7% (>53 mmol/mol) while only 43% were on folic acid pre-conception (Dunne et al, 2009). All healthcare providers, both in primary and secondary care, need to be aware of the adverse outcomes observed in pregnancies complicated by diabetes and the vast potential for reducing these adverse events through structured PPC.

Diabetes-related complications

Retinopathy

Women should be screened for retinopathy, treated as required, and counselled regarding the risk of progression of retinopathy in pregnancy. A high HbA_{1c} level at the start of pregnancy or abrupt tightening of glycaemic control can potentially worsen pre-existing retinopathy (Diabetes Control and Complications Trial Research Group, 2000). This should not stop efforts to achieve targets quickly in pregnant women with suboptimal glycaemic control.

Retinal screening should be carried out each trimester in women without pre-existing retinopathy, while those with retinopathy should be screened every 6 weeks and have active follow-up with an ophthalmologist.

Nephropathy

Microalbuminuria and overt nephropathy are associated with adverse pregnancy outcomes in relation to the development of PET and PIH, which may result in a premature delivery (Ekbom et al, 2001). Stillbirth is also more common. There is also the potential for permanent worsening of renal function, especially in those with a prepregnancy creatinine level of >124 µmol/L. In this group, about 45% will have an irreversible decline in renal function during pregnancy (Purdy et al, 1996). This position should be discussed in detail with such individuals prior to attempts to conceive, and specialist opinion sought.

Neuropathy

Neuropathy may result in hypoglycaemic unawareness in pregnancy and may contribute to hyperemesis gravidarum if gastroparesis is present. Uterine contractions may also be affected, leading to increased risk of caesarean section, and post-partum haemorrhage due to uterine atony. Carpal tunnel syndrome may worsen if oedema is present (Padua et al, 2001).

Cardiovascular disease

Although rare, the standardised mortality ratio for ischaemic heart disease is 44.8 for women aged 20–29, and 41.6 for women aged 30–39 years (Laing et al, 2003). Therefore, although uncommon, the possibility of cardiovascular disease in younger women needs to be borne in mind, and the woman referred for appropriate assessment if this is suspected.

Thyroid disease

All women should have thyroid function tests checked pre-conception as untreated thyroid disease – both hyperthyroidism (low birth weight, pre-term labour, stillbirth) and hypothyroidism (pre-term delivery, pre-eclampsia, neuropsychological impairment) – can have adverse consequences in pregnancy.

Page points

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2. Retinal screening should be carried out each trimester in women without pre-existing retinopathy, while those with retinopathy should be screened every 6 weeks and have active follow-up with an ophthalmologist.
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Page points

1. Insulin is the pharmacological treatment of choice in all women with diabetes during pregnancy.
2. Insufficient evidence exists to recommend the routine use of metformin in gestational diabetes, but an ongoing trial is examining the use of metformin in pregnant women with type 2 diabetes. None of the sulphonylureas or the newer oral antidiabetes drugs nor injectable therapies are suitable for use in pregnancy at this time.

Thyroid peroxidase antibodies should be checked in women with diabetes experiencing fertility issues. If antibodies are positive, a small dose of thyroxine (50 µg) may improve conception rates even in the presence of normal thyroid function (Negro et al, 2006).

Antenatal care

Glycaemic control

As stated above, insulin is the pharmacological treatment of choice in all women with diabetes during pregnancy.

Insulin is uptitrated weekly to reach the desired glycaemic targets mentioned earlier, and it should be emphasised that insulin doses need to rise progressively as a consequence of increasing insulin resistance. In addition to self-monitoring of blood glucose, HbA_{1c} levels are tested on a 2- to 4-weekly basis, aiming for <6% (<42 mmol/mol). In interpreting these, however, it should be noted that trimester specific ranges are more appropriate, as HbA_{1c} levels are lower in the general population during pregnancy than in a non-pregnant woman with diabetes.

Trimester-specific HbA_{1c} reference ranges for women without diabetes are: first trimester, 4.8–5.5% (28–36 mmol/mol); second trimester 4.4–5.4% (24–36 mmol/mol); third trimester 4.7–5.7% (27–39 mmol/mol) (O'Connor et al, 2010). Peripartum insulin infusion will be required for people on insulin during pregnancy.

When resuming oral therapy, women on insulin pre-conception can return to their normal doses. Breastfeeding women, however, require either more carbohydrate, or a 25% reduction in the prepregnancy regimen. GD women can stop insulin on delivery of the placenta, with blood glucose monitoring for 24 hours afterwards. All plans for delivery should be clearly documented prior to delivery in the patient record.

Non-insulin therapy

In the largest trial of its kind to date, 363 women treated with metformin showed no increased risk of perinatal complications versus those treated with insulin (Rowan et al, 2008). Insufficient evidence exists to recommend the routine use of metformin in gestational diabetes, but an ongoing trial is examining the use of metformin in pregnant women with type 2 diabetes. None of the sulphonylureas or the newer oral antidiabetes drugs nor injectable therapies are suitable for use in pregnancy at this time.

Obstetric management

Antenatal

Obstetric management for the diabetic pregnancy, while similar to that for other higher risk pregnancies (i.e. increased fetal ultrasound monitoring including second trimester anomaly scan, third trimester scans for fetal wellbeing and growth, and frequent antenatal clinic visits), differs in some respects. Particular attention is paid to blood pressure and urinalysis, given the increased incidence of pre-eclampsia in people with diabetes, and near-normal blood glucose in the presence of diabetic ketoacidosis. If antenatal steroids are indicated for fetal lung maturation (usually prior to 34 weeks), they may be given, but hospital admission for strict glycaemic control with intravenous insulin is necessary.

Delivery

Planning of the timing and mode of delivery is important in women with diabetes. The standard practice of early induction of labour for all pregnancies complicated by diabetes at 38–39 weeks is no longer the case. This was done to minimise the risks of spontaneous labour with a macrosomic fetus – shoulder dystocia, birth trauma, and emergency caesarian section – and to avoid the increasing risk of stillbirth, which is greater at 39–40 weeks. The approach is now individualised, and the obstetrician and medical team work together, considering factors such as estimated fetal weight, glycaemic control, and medical and obstetric history to determine the optimal mode and timing of delivery.

Advice from an anaesthetist is advisable if significant medical complications are apparent. Tocolytic agents may cause

hyperglycaemia, and should only be given after consultant-level discussion between the obstetric and diabetes team involved in the woman's care. caesarean section rates remain high, however, occurring in 43% of women with diabetes compared with 27% of controls in the ATLANTIC DIP cohort, the difference being explained by higher rates of emergency section in those with diabetes (Dunne et al, 2009).

Postpartum care

Women with GD have a significantly increased lifetime risk of diabetes. A recent meta-analysis shows a relative risk of 7.43 for development of diabetes in women with a history of GD (Bellamy et al, 2009). Significant risk factors for the development of type 2 diabetes include family history of diabetes, increasing BMI and insulin use in pregnancy. The authors' practice is to assess for persistent glucose intolerance 6–12 weeks postpartum with a standard 75 g OGTT, using the standard criteria for diagnosis of diabetes in the non-pregnant population, in line with American Diabetes Association (2011) recommendations. In addition to postpartum screening, women should be screened every 1–3 years with an OGTT thereafter.

NICE guidance (NCCWCH, 2008) differs somewhat, however, in recommending fasting blood glucose alone for postpartum follow-up and annual screening thereafter. Although the initial postpartum screen is carried out in hospital, subsequent routine testing is usually carried out in primary care, which has the advantage of frequently caring for the child also, allowing an extra opportunity to target the mother for screening that may otherwise be missed.

Assessment for persistent postpartum glucose intolerance should be carried out 6–12 weeks postpartum with a standard 75 g OGTT, using the standard criteria for diagnosis of diabetes in the non-pregnant population. In addition to postpartum screening, women should be screened every 1–3 years with an OGTT thereafter. If further pregnancy is planned, women should be counselled that the risk of GD recurring is up to 41% (Getahun et al, 2010), and that pre-conception care is desirable. A random blood glucose test should be carried out when women with a history of GD are booked in. Breastfeeding appears to confer some protection against progression to type 2 diabetes (O'Reilly et al, under final review), and should be encouraged.

Complications in the child

Morbidity is greater in infants of mothers with diabetes. This may occur as a result of neonatal hypoglycaemia (secondary to persistent hyperinsulinaemia in the absence of maternal glucose supply). Hypoglycaemia is defined as a glucose level of <2.6 mmol/L in the neonate (Lucas et al, 1988).

To avoid unnecessary intervention, blood glucose levels should not be checked until 2–3 hours after birth if the baby remains well (Heck and Erenberg, 1987). If hypoglycaemia is present, neonatal intensive care admission may be indicated. Breastfeeding soon after birth (within 1 hour) helps to stabilise neonatal blood glucose concentrations and should be encouraged (expressing breast milk is an alternative if feeding is not possible). Respiratory distress syndrome is more common in infants born to mothers with diabetes (Robert et al, 1976), again likely to be due to the effect of hyperinsulinaemia on lung maturation. Hypocalcaemia (defined as a calcium level of <1.8 mmol/L) occurs in 10–20% of infants (Mimouni et al, 1986), but usually resolves without treatment.

The offspring of women with diabetes during pregnancy have also been shown to be twice as likely to be overweight as adults, and up to four times as likely to develop metabolic

Box 3. Desirable steps to be taken at referral for pre-conception care (but should not delay referral).

- Measure blood pressure.
- Measure weight/BMI.
- Measure urinary albumin/creatinine ratio.
- Give smoking cessation advice.
- Give advice regarding alcohol intake.
- Advise that a 3–6 month wait may be necessary before attempting to conceive.
- Commence folic acid 5 mg once-daily.

Page points

1. Women with gestational diabetes (GD) have a significantly increased lifetime risk of diabetes. A recent meta-analysis shows a relative risk of 7.43 for development of diabetes in women with a history of GD.
2. A random blood glucose test should be carried out when women with a history of GD are booked in. Breastfeeding appears to confer some protection against progression to type 2 diabetes, and should be encouraged.

Box 4. Case report.

Narrative

Ms M is a 31-year-old patient of your practice for the past 3 years, with a 17-year history of type 1 diabetes, and is a current smoker. She has had reasonable glycaemic control during her time with the practice, with an HbA_{1c} level of 7.5% (58 mmol/mol) on a multiple daily injection regimen. However, she has a history of suboptimal control and non-proliferative retinopathy on her last screening 18 months ago, and has had no recent albumin/creatinine ratio recorded. She attends now as she is getting married in 2 months time and wishes to start a family as soon as possible after this, although she is currently taking the combined oral contraceptive pill.

Discussion

Several aspects of diabetes management should be discussed here. Pre-conception care is advisable whenever possible, and this woman's early presentation allows time to optimise glycaemic control. She should be advised that it may take 3–6 months for this, and, in the meantime, contraception should be continued. Folic acid 5 mg should be prescribed, and advice regarding smoking cessation given. Also, a discussion regarding the need for vigilance with regard to complications (including further eye screening now and screening for proteinuria), and the small possibility of progression during pregnancy should be discussed. Referral at this stage to the local preconception clinic is indicated.

Box 5. Case report.

Narrative

Ms R is a 36-year-old woman originally from Bangladesh, but resident in the UK for 2 years. She has three previous children, all born in Bangladesh, the last of whom weighed 4.6 kg at birth. She is now 12 weeks pregnant with her fourth child, and presents to the practice prior to booking at the antenatal clinic. Urine analysis confirms pregnancy, but also demonstrates glycosuria (++ on dipstick).

Discussion

The birthweight of her last child suggests the possibility of underlying undiagnosed type 2 diabetes in that pregnancy. This, coupled with her ethnic origin, and finding of glycosuria on dipstick, means that Ms R is significantly at risk of gestational diabetes (GD) and should be evaluated as soon as possible with a 75 g oral glucose tolerance test (OGTT), and referred for combined medical/obstetric antenatal care immediately if positive. If negative, the OGTT should be repeated at 24–28 weeks – a time when insulin resistance is increasing, and the risk of GD increases.

syndrome (Clausen et al, 2009). Impaired glucose tolerance has been demonstrated in up to one third of adolescents born to mothers whose pregnancy was complicated by diabetes (Silverman et al, 1995; Sobngwi et al, 2003).

Conclusions

The management of a pregnancy complicated by diabetes is an intensive process, involving very frequent direct patient contact with multiple disciplines, a strict regimen of dietary and exercise measures, and frequent blood glucose monitoring.

Women with diabetes during pregnancy also require more hospital visits for review by members of the multidisciplinary team. This has wider implications – time taken from work, childcare arrangements and transport arrangements all place a significant emotional and financial burden on the individual and her family, complicating what can be a stressful time even in the uncomplicated pregnancy. This should be borne in mind from a practical perspective, and scheduling appointments together where possible, and maintaining regular telephone contact outside of hospital visits may go some way towards alleviating stress.

Given the ongoing rise in the number of pregnancies complicated by diabetes (mainly GD or type 2 diabetes), it is inevitable that primary care practitioners will see an increasing number of these women, and play a significant role in coordinating their overall care. Primary care practitioners are also ideally placed to help increase the proportion of women with diabetes availing of pre-conception care. Knowledge of the specific problems faced in the diabetic pregnancy is therefore essential, and will become an ever more important skill to master over the coming years. ■

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"The management of a pregnancy complicated by diabetes is an intensive process, involving very frequent direct patient contact with multiple disciplines, a strict regimen of dietary and exercise measures, and frequent blood glucose monitoring."

CPD module

Online CPD activity

Visit www.diabetesandprimarycare.co.uk/cpd to record your answers and gain a certificate of participation

Participants should read the preceding article before answering the multiple choice questions below. There is ONE correct answer to each question. After submitting your answers online, you will be immediately notified of your score. A pass mark of 70% is required to obtain a certificate of successful participation; however, it is possible to take the test a maximum of three times. Before accessing your certificate, you will be given the opportunity to evaluate the activity and reflect on the module, stating how you will use what you have learned in practice.

1. Which one of the following is not a risk factor for the development of gestational diabetes? Select ONE option only.
A. Previous gestational diabetes.
B. BMI ≥30 kg/m^2.
C. Previous baby <4 kg birthweight.
D. First degree relative with diabetes.
E. Age ≥40 years.

2. Which one of the following treatments is approved for use in pregnancy? Select ONE option only.
A. Insulin aspart.
B. Insulin glargine.
C. Insulin detemir.
D. Liraglutide.
E. Gliclazide.

3. Which of the following contraceptive methods are contraindicated in women with diabetes? Select ONE option only.
A. Combined oral contraceptive pill.
B. Progesterone-only pill.
C. Depot progesterone.
D. All of the above.
E. None of the above.

4. Which of the following is not an essential component of the pre-conception consultation? Select ONE option only.
A. Current HbA_{1c} level.
B. Screening for complications.
C. Prescription for folic acid 5 mg once daily.
D. Counselling regarding risk of conception with suboptimal control.
E. Prescription of angiotensin-converting enzyme inhibitor if blood pressure ≥130/80 mmHg.

5. Which of the following plasma glucose values is not consistent with a diagnosis of gestational diabetes? Select ONE option only.
A. Fasting glucose level of 5.8 mmol/L.
B. 75 g oral glucose tolerance test (OGTT) gives a 1-hour value of 9.9 mmol/L.
C. Random plasma glucose value of 14 mmol/L.
D. 75 g OGTT – 2 hour value of 8.8 mmol/L.
E. None – all the above are consistent with a diagnosis of gestational diabetes.

6. Infants of mothers with diabetes in pregnancy are NOT at risk for which one of the following complications? Select ONE option only.
A. Brachial plexus injury.
B. Neonatal hypoglycaemia.
C. Neonatal hypercalcaemia.
D. Respiratory distress.
E. Obesity later in life.

7. In the neonate, how is hypoglycaemia defined? Select ONE option only.
A. Blood glucose level of <4.6 mmol/L.
B. Blood glucose level of <3.6 mmol/L.
C. Blood glucose level of <5.6 mmol/L.
D. Blood glucose level of <2.6 mmol/L.
E. Blood glucose level of <1.6 mmol/L.

8. Ms A is a 32-year-old woman with a new diagnosis of type 2 diabetes. Her BMI is 39 kg/m^2. She is asymptomatic, on no regular medication, and does not smoke. The OGTT shows a fasting blood glucose level of 5.8 mmol/L and a 2-hour value of 11.3 mmol/L. Her HbA_{1c} level is 7.2% (55 mmol/mol), and her blood pressure is 128/83 mmHg. Ms A has never been pregnant, but is now in a stable relationship and is anxious to conceive. What is the best course of action? Select ONE option only.
A. Diet control alone, as her HbA_{1c} level is only mildly abnormal.
B. Commence metformin 850 mg twice daily. Advise against trying to conceive until further notice.
C. Advise against conceiving for now, refer her to the prepregnancy service at her next visit if her HbA_{1c} level remains over target.
D. Dietary advice, discuss suitable reliable methods of contraception, explaining that conception not currently ideal. Prescribe folic acid 5 mg once-daily. Refer now to prepregnancy diabetes service.
E. Given her BMI, refer her now to a local hospital-based diabetes service for consideration for liraglutide treatment before trying to conceive.

9. Ms P has type 1 diabetes and is currently at 29 weeks gestation. She attends the surgery today with a 2-day history of diarrhoea and vomiting. She has not been able to take her regular insulin regimen as she has not been eating, and has reduced her long-acting insulin dose (by two-thirds, to 6 units) to avoid hypoglycaemia. In your surgery, she looks mildly dehydrated, her blood glucose level is 13 mmol/L and urinary ketones are 3+ on dipstick. What is the best course of action? Select ONE option only.
A. Encourage fluids and prescribe antiemetics.
B. Advise her to increase her basal insulin dose, continue correction doses of rapid-acting insulin and see tomorrow to ensure ketones are cleared.
C. Refer to emergency department for immediate management of blood glucose control and volume status.
D. Put back on usual dose of long-acting insulin and small amounts of rapid-acting insulin for correction.
E. Advise to stop long-acting insulin for now as not eating normally, and increase correction doses of short-acting insulin.

10. Ms B is a 40-year-old woman whose last pregnancy was complicated by gestational diabetes, requiring insulin. She has no significant medical history, and has a brother with type 2 diabetes and her BMI is 31 kg/m^2. She gave birth to a healthy 3.8 kg baby, exclusively bottle fed, and now attends the practice for follow-up of her 4-month old son, who is recovering well from a recent hospital admission for croup. What is the best course of action? Select ONE option only.
A. Supply a glucose meter for regular checking of blood glucose levels. See in 1 month to assess glycaemic control.
B. Take no further action unless she becomes pregnant again.
C. Check her HbA_{1c} level to assess overall glycaemic control.
D. Start metformin 850 mg twice-daily for glycaemic control.
E. Rescreen now for persistent diabetes with fasting plasma glucose.