Pregnancy and Diabetes

Aim(s) and objective(s)
This guideline aims to highlight the importance of maintaining good glycaemic control in women of childbearing age contemplating pregnancy, during pregnancy and in the postnatal period to reduce the risk of obstetric and fetal complications.

Management prior to and during pregnancy should incorporate an intensive programme of metabolic, obstetric and neonatal supervision. In Lanarkshire, a multidisciplinary team, led by a named obstetrician and diabetologist, including a diabetes specialist nurse, diabetes specialist midwife and dietitian based at Wishaw General Hospital, provide comprehensive care from pre-pregnancy to postnatal review. Effective communication between all members of the team, including primary care is essential, recognising that the key member is the woman with diabetes.

This guideline offers information on how to achieve good glycaemic control and reduce the risk of complications.

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User group
Primary Care
Diabetes Specialist Staff
Midwives
Obstetric Staff
Paediatric Staff
Family Planning and Sexual Health Staff

This guideline is not intended to serve as a protocol or standard of care. That is best based on all clinical data available for an individual case and may be subject to change as scientific knowledge and technology advances and patterns of care evolve. Adherence to guideline recommendations will not ensure a successful outcome in every case, nor should it be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same result. Ultimately a judgement must be made by the appropriate healthcare professional(s) responsible for a particular clinical procedure or treatment plan following discussion with the patient, covering the diagnostic and treatment options available. It is advised that any significant departure from the guideline should be documented in the patient’s medical record at the time the decision is taken.

Guideline

INTRODUCTION
Type 1 and 2 diabetes are high risk states for both the woman and her unborn child.

- Severe hypoglycaemia and progression of microvascular complications can occur
- Ketoacidosis must be avoided (this can cause fetal death)
- There are increased risks of obstetric complications, such as miscarriage, maternal infection, pre-eclampsia, premature labour, polyhydramnios and failure to progress in first or second stage
- Fetal and neonatal complications include congenital malformation, macrosomia, late intrauterine death, fetal distress, hypoglycaemia, respiratory distress syndrome and jaundice
- Rates of fetal and neonatal loss and major congenital malformation are increased by at least two to threefold
CONTRACEPTION

Pregnancy should be planned and good contraceptive advice and pre-pregnancy counselling are essential.

- Contraception should be discussed on an individual basis with all women of childbearing age with diabetes as part of her annual review
- In general, the contraceptive advice for a woman with diabetes should follow that in the general population
- The combined oral contraceptive (COC) is contraindicated in women with diabetes depending on the presence and severity of diabetic complications and/or other risk factors for vascular disease
- Progestogen-only preparations, oral or intramuscular, may be suitable in these women
- Long-acting methods such as implants, intrauterine systems (IUS) and copper intrauterine devices (IUD) are safe methods of contraception which may be particularly suitable for use in women with diabetes. They are as effective as sterilisation and produce low circulating hormone levels
- Pregnancy should be planned and good contraceptive advice and pre-pregnancy counselling are essential

PRE-PREGNANCY CARE

Pre-pregnancy care provided by a multidisciplinary team is strongly recommended for women with diabetes. Attendance at a pre-pregnancy clinic is associated with a reduction in major congenital malformations, the rate of miscarriage and in complications of pregnancy. The essential components of a pre-pregnancy care programme include review and consideration of the medical (including pharmacological treatment), obstetric and gynaecological history; advice on glycaemic control to optimise HbA1c; screening for complications of diabetes and counselling for maternal and fetal complications.

All healthcare professionals in contact with women of childbearing age with diabetes should be aware of the importance of pre-pregnancy care. Initial advice should be sought from the diabetes specialist nursing team who can then refer onto the Joint Antenatal Clinic based at Wishaw General Hospital.

Pre-pregnancy glycaemic control should be maintained as close to the non-diabetic range as possible, taking into account risk of maternal hypoglycaemia.

ORAL MEDICATION BEFORE AND DURING PREGNANCY

Folic acid

Neural tube defects in high-risk pregnancies are associated with lower levels of folate. All women with diabetes should be prescribed high dose pre-pregnancy folate supplementation (Folic Acid 5mg once daily), continuing up to 12 weeks gestation.

Metformin and sulphonylureas

Metformin and sulphonylureas are not associated with an increase in congenital malformation or early pregnancy loss. While metformin and glibenclamide may be used to treat GDM (gestational diabetes mellitus), sulphonylureas other than glibenclamide should not be used during pregnancy due to placental passage.

Statins

Statins should be avoided during pregnancy as congenital malformations have been reported and decreased synthesis of cholesterol may affect fetal development.
ACE inhibitors
Angiotensin converting enzyme (ACE) inhibitors have been associated with an increase in risk of congenital malformation and both ACE inhibitors and angiotensin receptor blocking medication should be avoided throughout pregnancy.

Nutritional Management
It is good clinical practice to provide dietary advice to women before, during and after pregnancy. Advice on diet and exercise should be offered in line with recommendations for adults with diabetes.

Smoking and Alcohol Consumption
Women with diabetes contemplating pregnancy, during and after pregnancy should receive advice and support in relation to smoking cessation and alcohol consumption in line with the general population.

Glucose monitoring
Postprandial glucose monitoring should be carried out in pregnant women with gestational diabetes and considered in pregnant women with type 1 or type 2 diabetes. In people with type 1 or type 2 diabetes, as long as hypoglycaemia can be minimised, aim to achieve blood glucose:

- between 4 and 6 mmol/l pre-prandial
- <8 mmol/l one hour postprandial, or
- <7 mmol/l two hours postprandial
- >6 mmol/l before bed.

Diabetes specialist nurses and midwives have an important role in educating women on the need for self blood glucose monitoring and intensive insulin regimens during pregnancy.

Insulin Therapy
Rapid-acting insulin analogues (lispro and aspart) appear safe in pregnancy and may be considered in individual patients where hypoglycaemia is problematic. NPH insulin should remain the basal insulin of choice in pregnancy unless the clinical benefit of a basal insulin analogue has been demonstrated on an individual basis. Women should be advised that while most commonly used regular human insulins are licensed for use during pregnancy, other insulins and oral glucose-lowering agents (e.g. metformin, glibenclamide, other sulphonylureas, detemir) are not.

COMPLICATIONS DURING PREGNANCY

Obstetric Complications
These risks should be managed as for pregnant women without diabetes.

Metabolic Complications
During pregnancy, hypoglycaemic unawareness and severe hypoglycaemia are common. Diabetic ketoacidosis can develop more rapidly, at lower levels of blood glucose and in response to therapeutic glucocorticoids (administered if premature delivery is anticipated). Women and their partners need education on the management of hypoglycaemia, including the use of glucagen, avoiding hypoglycaemia during driving and on the recognition and prevention of ketoacidosis, which may result in fetal death. Local emergency contact arrangements must be explicit.

MICROVASCULAR COMPLICATIONS
Diabetic retinal and renal disease can deteriorate during pregnancy.

Retinopathy
Poor glycaemic control in the first trimester and pregnancy-induced or chronic hypertension are independently associated with the progression of retinopathy. Examination of the retina prior to conception and during each trimester is advised in women with type 1 and type 2 diabetes. More frequent assessment may be required in those with poor glycaemic control, hypertension or pre-
existing retinopathy. Early referral of pregnant women with referable retinopathy to an ophthalmologist is recommended due to the potential for rapid development of neovascularisation. Women should be reassured that tight glycaemic control during and immediately after pregnancy can effectively reduce the long term risk of retinopathy.

**Nephropathy**

There is an association between pre-existing nephropathy (microalbuminuria or albuminuria) and a poorer pregnancy outcome. Proteinuria increases transiently during pregnancy, returning to a pre-pregnancy level within three months of delivery. The incidence of worsening chronic hypertension or pregnancy-induced hypertension/pre-eclampsia is high in women with nephropathy. Worsening nephropathy and superimposed pre-eclampsia are the most common causes of pre-term delivery in women with diabetes. Women with diabetic nephropathy require careful monitoring and management of blood pressure. ACE inhibitors and angiotensin receptor blocking medications should be avoided as they may adversely affect the fetus. Appropriate antihypertensive agents which may be used during pregnancy include methyl dopa, labetalol and nifedipine.

**FETAL ASSESSMENT**

An early pregnancy scan is considered good practice to confirm viability in women with pre-existing diabetes, particularly when changes in medication are required or diabetes control is suboptimal. A detailed anomaly scan, at around 20 weeks gestation enables detection of many major structural abnormalities. In pregnancies complicated by maternal diabetes, the fetus is at risk of both macrosomia and intrauterine growth restriction (IUGR). The risk of macrosomia is greater when there has been poor glycaemic control. The risk of IUGR is greater in women with vascular complications of diabetes (retinopathy, nephropathy) or when pre-eclampsia develops. Fetal monitoring includes cardiotocography (CTG), doppler ultrasound and ultrasound measurement of fetal growth and liquor volume. The clinical judgement of an obstetrician experienced in diabetic pregnancy is essential.

**GESTATIONAL DIABETES (GDM)**

Gestational diabetes can be defined as carbohydrate intolerance of variable severity with onset or first recognition during pregnancy. This definition will include women with abnormal glucose tolerance that reverts to normal after delivery, those with undiagnosed type 1 or type 2 diabetes, and rarely women with monogenic diabetes. If type 1 or type 2 diabetes is presumed (e.g. due to early presentation or grossly elevated blood glucose), urgent action is required to normalise metabolism.

There is a continuous relationship between maternal glucose level (fasting, 1 hour and 2 hours after 75 g OGTT) at 24-28 weeks and pregnancy outcomes (macrosomia, fetal insulin, clinical neonatal hypoglycaemia and Caesarean section).

**Screening for GDM**

Risk factors for gestational diabetes

- BMI >30
- Previous macrosomic baby weighing 4.5 kg or more
- Previous gestational diabetes
- Family history of diabetes (first degree relative with diabetes)
- Family origin with a high prevalence of diabetes: South Asian (specifically women whose country of family origin is India, Pakistan or Bangladesh), Black Caribbean, Middle Eastern (specifically women whose country of family origin is Saudi Arabia, United Arab Emirates, Iraq, Jordan, Syria, Oman, Qatar, Kuwait, Lebanon or Egypt).
Early pregnancy
At booking all women should be assessed for the presence of risk factors for Gestational Diabetes. All women with risk factors should have HbA1c or fasting glucose measured. Women in early pregnancy with levels of HbA1c ≥48 mmol/mol, fasting ≥7.0 mmol/l or random glucose ≥11.1 mmol/l, diagnostic of diabetes should be treated as having pre-existing diabetes. Women with intermediate levels of glucose (HbA1c 42 to 46 mmol/mol), fasting glucose 5.1 to 6.9 mmol/l or random glucose 8.6 to 11.0 mmol/l should be assessed to determine the need for immediate home glucose monitoring and, if the diagnosis remains unclear, assessed for gestational diabetes by 75 g OGTT at 24-28 weeks.

While the characteristics of HbA1c in early pregnancy should be close to those out with pregnancy, it should be noted that normal HbA1c falls in later pregnancy, potentially resulting in false negative results.

Later pregnancy
Women with risk factors for GDM should be screened using 75 g oral glucose tolerance test (OGTT) at 24-28 weeks of gestation. A fasting plasma glucose at 24-28 weeks is recommended in low-risk women.

Diagnosis of GDM
There is a continuous relationship between maternal glucose level (fasting, one hour, two hours after 75 g OGTT) and fetal growth. The internationally agreed criteria for gestational diabetes using 75 g OGTT is:

- fasting venous plasma glucose ≥5.1 mmol/l, or
- one hour value ≥10 mmol/l, or
- two hours after OGTT ≥8.5 mmol/l

Note: Women with frank diabetes by non-pregnant criteria (fasting venous glucose ≥7 mmol/l, random glucose ≥11.1 mmol/l) should be managed within a multidisciplinary clinic as they may have type 1 or type 2 diabetes and be at risk of pregnancy outcomes similar to those of women with pre-gestational diabetes.

Management of GDM
Pregnant women with GDM should be offered dietary advice, blood glucose monitoring and be treated with glucose-lowering therapy depending on fasting and postprandial targets. Metformin or glibenclamide may be considered as the initial pharmacological management option where blood glucose levels remain above target despite dietary intervention.

- ≥5.5 mmol/l pre-prandial or ≥7 mmol/l two hours postprandial on monitoring at ≤35 weeks
- ≥5.5 mmol/l pre-prandial or ≥8 mmol/l two hours postprandial on monitoring at >35 weeks
- any postprandial values are >9 mmol/l.

DELIVERY
Women with diabetes should be delivered in consultant-led maternity units under the combined care of a physician with an interest in diabetes, obstetrician, and neonatologist. The timing of delivery should be determined on an individual basis. However, women with diabetes requiring insulin or oral glucose-lowering medication who have pregnancies which are otherwise progressing normally should be assessed at 38 weeks gestation with delivery shortly thereafter, certainly by 40 weeks. Women who are at risk of pre-term delivery should receive antenatal corticosteroids as an inpatient with close monitoring and regulation of diabetes control. Women with diabetes have a higher rate of Caesarean section. The progress of labour should be monitored as for other high-risk women, including continuous electronic fetal monitoring. Intravenous insulin and dextrose should be administered as necessary to maintain blood glucose levels between 4 and 7 mmol/l.
INFANTS OF MOTHERS WITH DIABETES
Cot side blood glucose measurement, indicative of hypoglycaemia, in neonates, whichever method is used, should be confirmed by laboratory measurement. Neonatal hypoglycaemia is defined at blood glucose <2.6 mmol/l and is associated with adverse short and long term neurodevelopmental outcomes.

Early feeding is advised to avoid neonatal hypoglycaemia and to stimulate lactation. Breast feeding is recommended for infants of mothers with diabetes, but mothers should be supported in the feeding method of their choice.

Insulin, metformin and glibenclamide are considered compatible with breast feeding, although the infant should be observed for signs of hypoglycaemia. The antihypertensives commonly used in pregnancy: labetalol, nifedipine and methyldopa are found in breast milk in low concentration and are considered appropriate for use in breastfeeding mothers; although with labetalol the infant should be monitored for bradycardia and hypotension. Of the ACE inhibitors, angiotensin-II receptor antagonists and Statins are not recommended in breast feeding.

POSTNATAL CARE
Women with type 1 or type 2 diabetes may require adjustment of their treatment regimen postnataally. Women with gestational diabetes should be investigated 6 weeks postnatally to clarify the diagnosis and exclude type 1 or type 2 diabetes. The opportunity should also be taken to provide lifestyle advice to reduce the risk of development of subsequent type 2 diabetes. Screening for progression to Type 2 Diabetes should be carried out annually using HbA1c for 5 years. Postnatal follow up should be seen as an opportunity to initiate pre-pregnancy care for any subsequent pregnancy. Appropriate contraception should be provided and the importance of good glycaemic control emphasised. Breast feeding should be encouraged to benefit mother and baby but it may necessitate insulin dose adjustment and a dietetic review.

JOINANT ANTE NATAL CLINIC CONTACT DETAILS
Wishaw General Hospital 01698 366640 or 01698 366427
Refer any patient with diabetes who becomes pregnant to the joint antenatal clinic urgently through SCI Gateway
Seek interim advice from the diabetes specialist nursing service.

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