DIABETES AND PREGNANCY

Pre-amble

At a time when the incidence of both pre- and gestational diabetes mellitus (GDM) is ever increasing, it is important to raise awareness to the screening, diagnosis and management of these important health issues that affect both mother and offspring.

The International Association of Diabetes and Pregnancy Study Group's (IADPSG) diagnostic criteria for the diagnosis of GDM have been accepted by the WHO and in ideal circumstances, following these guidelines (which include universal screening for GDM) would be advisable. *(Diabetes Care 2010; 33:676*)

Treating women with diabetes should ideally be done in a multi-disciplinary team (dietician, diabetes educator, obstetrician and physician). Obstetricians are encouraged to remain involved in the motivation, monitoring and management of the glycaemic control aspect of care and to ensure that where physician colleagues are involved, they are aware of the lower glycaemic targets in pregnancy.

No guideline can take all individual confounders into consideration and provide guidance to every eventuality. For this reason, it is imperative that the decisions (especially around the timing of delivery) take all aspects of the patient's risk profile into account to prevent adverse perinatal outcome.

Gestational Diabetes Mellitus (GDM)

Women first diagnosed with impaired glucose tolerance during the current pregnancy either have true GDM or previously undiagnosed pre-gestational (overt) diabetes mellitus. According to the IADPSG, true gestational diabetes mellitus is a mild hyperglycaemic state (fasting values 5.1 mmol/L - 6.9 mmol/L; 2-hour postprandial levels 8.5 mmol/L - 11.0 mmol/L) that typically occurs in the latter part of pregnancy and is thus not present at the time of conception and is expected to resolve following delivery. In an attempt to balance health economics with the benefits of increased detection of GDM, the UK still utilize the NICE guideline which employs selective screening and diagnostic criteria of fasting plasma glucose ≥5.6mmol/L or 2-hour postprandial level ≥7.8mmol/L. True GDM is associated with an increased prevalence and risk for maternal hypertensive disorders, fetal macrosomia and birth injuries as well as the potential to cause metabolic imprinting with long-term metabolic effects on the off-spring. Late fetal losses have also been documented in women with GDM especially if associated with hypertension and obesity.

Pre-gestational Diabetes Mellitus

This includes all women with known diabetes (Type 1, Type 2, or any other form of diabetes) and women presenting for the first time in pregnancy with undiagnosed pre-gestational diabetes. Women first diagnosed with hyperglycaemia at any time in pregnancy who meet the WHO criteria for overt diabetes have pre-gestational diabetes (fasting glucose value ≥ 7mmol/L, or 2-hour postprandial level ≥11.1 mmol/L, or HbA1C ≥ 6.5%). Type 2 diabetes is by far the most common form of diabetes encountered during pregnancy.

Poor glycaemic control has possible adverse effects on the mother and the growing fetus. Adversity is determined by the timing and the degree of hyperglycaemia. Pre-gestational diabetes, whether known or undiagnosed is present at conception.

Pre-gestational diabetes, if poorly managed, may result in numerous maternal, fetal and neonatal adversities. Maternal complications include an increased risk of first trimester miscarriages, pre-eclampsia, diabetic keto-acidosis, and operative deliveries. Fetal complications include an increased risk of congenital malformations, polyhydramnios, macrosomia with birth injuries and intra-uterine fetal death (IUD). The risk of neonatal respiratory distress syndrome, hypoglycaemia, hypocalcaemia and neonatal jaundice as well as perinatal mortality increases. Over-nutrition of the fetus, due to intra-uterine hyperglycaemia, has also been associated with metabolic imprinting and an increased risk of obesity and Type 2 diabetes in later life. Some evidence supports an associated increased risk for suboptimal neurocognitive outcomes.

Pre-conception care of women with known diabetes

Pre-conception care in women with known diabetes mellitus is essential (see below). Women with diabetes who are planning to fall pregnant should be informed of the importance of good glycaemic control and folic acid supplementation before conception. A planned pregnancy is ideal to establish a healthy lifestyle, optimize weight, attend to glycaemic control, exclude contra-indications to pregnancy and to review current use of medication (hypoglycaemic therapy and other).

Lifestyle

A healthy lifestyle should be promoted with the view of optimizing weight before conception and include looking at food intake (content and amount) and exercise. A dietitian may be very helpful to establish this goal, especially if weight loss is required.

Glycaemic control should be evaluated and optimized

- The type of hypoglycaemic agent currently in use must be safe in pregnancy (Metformin (Glucophage®), glibenclamide (Daonil®) and Insulin only), and if not must be changed. More recent evidence shows that glibenclamide, although used in GDM, crosses the placenta and should therefore only be used in selected cases and as supported by an endocrinologist.
- The degree of control must be evaluated and optimized to reach target before conception, without causing hypoglycaemia (home glucose monitoring and HbA1c).
- Inform patient regarding target glucose values in the fasting state (4.0 – 5.5 mmol/L) and 2-hours postprandially (< 6.7 mmol/L). Target HbA1c is 6.0 - 6.5%.
- If control on oral therapy in women with Type 2 DM is suboptimal, insulin therapy should be considered.

- Optimal glycaemic control must, however, always be assessed against the individual patient's risk of hypoglycaemia. It is sometimes necessary, especially in women with brittle Type 1 diabetes, to accept higher than ideal glucose and HbA1c targets.
- The importance of continued monitoring during pregnancy must be discussed and a home monitoring device provided if not already in use.
- An HbA1c of more than 10%, in view of its significant association with teratogenicity, should be regarded as a relative contra-indication to pregnancy.

Diabetes related complications

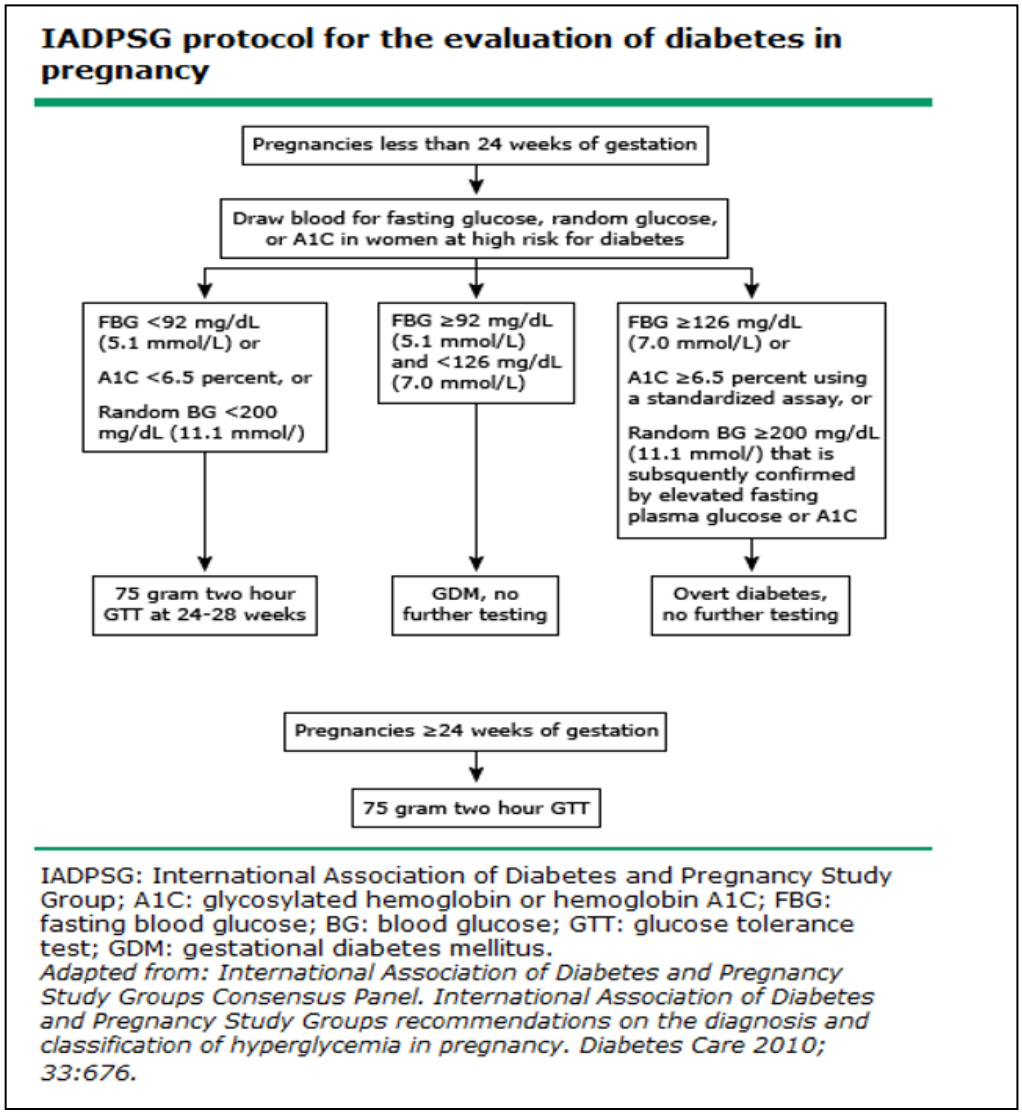
- Screen for potential diabetes-related eye and kidney involvement if not done recently (within 6 months). This will entail quantification of urinary protein excretion and ophthalmological review.
- Women with established diabetes-related complications should be carefully counselled regarding the safety of a planned pregnancy.

Medication and supplements

- The list of medication (other than hypoglycaemic agents) that the patient is taking must be carefully reviewed and medication discontinued or changed if safety in pregnancy is not established (ACE-inhibitors, statins etc.)
- Women using ACE-inhibitors or ARBs should be changed to a safer alternative such as a sustained-release calcium channel blocker.
- The use of supplements and other medications known to optimize pregnancy outcome in women with diabetes could be considered:
    - Start folate 5mg/day supplementation three months prior to conception and continue for up to at least 12 weeks' gestation.
    - Start aspirin 150 mg nocte in the first trimester and continue until 36 weeks to decrease the known increased risk of pre-eclampsia.
    - Calcium supplementation (1g per day) is also indicated for the prevention of hypertension especially in women with a calcium deficient diet.

Screening for hyperglycaemia in pregnancy

Screening based on the IADPSG guidelines (Diabetes Care; 2010) is strongly advocated. Although the guidelines propose universal screening of all women at 24-28 weeks of gestation, this recommendation is dependent on local resources and could, if resources are limited, be modified to only include individuals identified as high- risk based on the presence of risk factors as outlined later. It is also advised that high- risk patients should undergo a fasting blood glucose and HbA1c at first antenatal visit, resources allowing, to exclude overt diabetes and be re-tested at 24 weeks if the initial evaluation is normal.



Selective screening with a two-hour 75 g oral glucose tolerance test (OGTT) is indicated as follows:

- Women with a prior history of GDM must be screened for hyperglycaemia at first visit.
- Repeated glycosuria of more than 1+, irrespective of gestation, warrants testing.
- Women with risk factors as listed below are regarded as high risk and should be screened at 24-28 weeks of gestation:
    - Obesity (BMI at booking above 30 kg/m^2)
    - Previous macrosomic baby above 4.5 kg
    - Unexplained IUD with previous pregnancy
    - First degree relative with diabetes
    - Ethnic family origin with high prevalence of diabetes (South-Asian descent)
        - Prior infant with a congenital abnormality
        - Maternal age >40 years
        - Chronic use of corticosteroids
        - Patient with acanthosis nigricans
        - Patients with polycystic ovarian syndrome

The diagnostic criteria for Overt DM and GDM following an OGTT at screening in pregnancy are shown in Table 1.

Table 1 Diagnostic criteria following screening with 75 g OGTT in pregnancy

Blood glucose	Gestational diabetes	Overt diabetes in pregnancy
Fasting	5.1 – 6.9 mmol/L	≥ 7 mmol/L
One-hour post glucose load	≥ 10 mmol/L	not applicable
Two-hour post glucose load	8.5 – 11 mmol/L	≥ 11.1 mmol/L

One of more of these laboratory blood glucose criteria must be met for the diagnosis of GDM or overt DM; For diagnostic purposes, glucometer measurements should be used with caution. HbA1C is not used to diagnose GDM.

Management of diabetes mellitus in pregnancy

The management of any woman with hyperglycaemia in pregnancy will be influenced by the type of diabetes, the presence of diabetes-related complications and other associated metabolic abnormalities especially obesity and hypertension. Optimal treatment of women with diabetes in pregnancy can only be achieved with the combined contribution of a multidisciplinary team that should include, apart from the obstetrician, a diabetes educator and dietitian. Women with pre-existing Type1 diabetes mellitus represent a specialized high-risk subgroup that is ideally managed in pregnancy by a multidisciplinary team that should also include an experienced diabetologist.

The management of hyperglycaemia in pregnancy can be divided into the following major categories:

- *Education with regard to the disease process, monitoring of blood glucose, benefits and risks of pharmacological interventions and a discussion of treatment targets*
- *Attention to lifestyle specifically related to food-intake, weight control and exercise*
- *Pharmacological therapy (if required)*
- *Proposed follow-up plan*
- *Fetal monitoring*
- *Mode and timing of delivery*

a. Gestational diabetes mellitus (GDM)

*The patient with GDM has new onset hyperglycaemia, typically in the latter part of pregnancy. Optimizing lifestyle is successful to reach target glucose values in the majority of these women. Patients are not expected to have existing diabetes-related complications and required investigations in this regard should be minimal.*Education (assisted by diabetes educator)

Disease process:

- Explain how the physiological insulin resistance of pregnancy unmasks the limited ability of the pancreas and thus indicates a marked increased risk to develop overt diabetes in later life, underscoring the importance of a healthy lifestyle and ideal body weight.

- Explain that although the hyperglycaemia is expected to resolve after delivery that the risk of overt diabetes remains and emphasize the major importance of early and continued postpartum surveillance.

Monitoring of blood glucose:

All women should be supplied with a home-monitoring device and educated to use it optimally with regard to finger-prick technique and timing of testing throughout the pregnancy.

Benefits and risks of pharmacological interventions

- Hypoglycaemic drugs with confirmed safety in pregnancy that include metformin, metformin SR, glibenclamide (the only safe sulphonylurea), insulin and insulin analogues
- Educate regarding risk of hypoglycaemia, especially with use of insulin, how to recognize and how to manage.

Discussion of treatment targets

- Explain importance of optimal glycaemic control for the growing baby both in terms of short-term and long-term health.
- Explain the association of poor glycaemic control with maternal hypertensive disorders.
- Set clear glucose targets to ensure safe optimal control, aim for fasting values of 4.0–5.5mmol/L and postprandial values < 6.7mmol/L.
- Explain the purpose of doing an HbA1c and aim for a value of less than 6.0 - 6.5%.
- Avoid hypoglycaemia defined in pregnancy as a blood glucose ≤ 3.5 mmol/L.

i. Lifestyle

Medical nutrition therapy and weight control

Refer to a dietician for an individualised diet plan (medical nutrition therapy) with aim to modify content to ease glycaemic control and to ensure weight control if required.

Exercise

Encourage patient to exercise, ideally to do 30 minutes of moderate intensity exercise daily.

ii. Evaluation of existing diabetes complications

- Investigations in the patient with GDM can be limited to the determination of a serum creatinine level and quantification of urinary protein excretion at baseline to aid in cases where hypertension may develop later.
- Existing complications not expected and retinal screen thus not necessary.

iii. Pharmacological therapy (if required)

- Only indicated if target glucose values are not obtained with modification of lifestyle factors after time period of 2 weeks.
- Patient must perform home glucose monitoring by doing morning fasting, preprandial (30 minutes before meals) and postprandial (2 hours after meals) glucose measurements before and after every meal.
- Initiate metformin therapy as proposed first choice. Start with metformin 500mg bd and increase to metformin 850mg tds if required to reach target and in absence of gastro-

intestinal side-effects. Consider metformin SR if patient develops gastro-intestinal side-effects. Start with 500mg nocte only and increase to maximum dose of 2000mg as single nocte dose. Follow-up in 2 weeks.

- If glucose targets are not reached, consider addition of insulin.

  Suggested initiation in insulin naïve patient (can be done as in-patient, as out-patient and with help of physician if so preferred):
  - Start with intermediate human NPH insulin or long acting insulin analogue therapy at night.
  - Calculate starting dose of 0.1u/kg.
  - Administer insulin 30 minutes before bedtime and patient should have a snack just before going to sleep.
  - Monitor fasting value to determine required dose and monitor 02h00 value for safety
  - If fasting glucose remains high, increase nocte insulin in a stepwise manner (increments to not exceed 2-4u at a time) until fasting glucose is within normal range provided that the 02h00 value is not lower than 5 mmol/L.
  - Once fasting level is normal or in cases where 02h00 value reaches 5mmol/L, check for post-prandial excursions and if necessary, add short acting insulin.
  - Identify the meal with the largest excursion and administer 2-4u short acting human insulin 30 minutes prior to that meal or use short-acting insulin analogues with that meal. Increase by 2u until the postprandial value is in target. Apply same principle to the other meals.
  - Use glucose profile and HbA1c (not more often than on a monthly basis) to confirm that control is optimal.

iv. Follow-up plan
- Monitor and maintain home glucose profiling throughout pregnancy. Patients must bring along glucose profiles at each visit.
- Patient may be followed-up 2-weekly until 36 weeks, or patient can send a glucose profile 2 weekly to the practice. Thereafter, weekly until delivery.
- Adjust therapy continuously to maintain target values and to minimize the risk of over-treatment and hypoglycaemia.

v. Fetal monitoring

- Offer/refer for detail anomaly scan at 18-22 weeks including four-chamber view of fetal heart and outflow tracts.
- Perform baseline umbilical artery Doppler studies at 24-26 weeks. Perform fetal evaluation for growth and weight, monthly until 36 weeks

vi. Mode and timing of delivery

- Timing of delivery needs to consider all obstetric, medical and psychosocial factors and an individualised approach is advised. Offer delivery from 38 weeks. However, if the baby shows no signs of macrosomia or growth restriction, there is no concomitant hypertension and the glycaemic control is good, delivery can be carefully postponed up to 40 weeks (provided fetal and maternal well-being is confirmed weekly).
- Advise elective Caesarean section if EFW is > 4kg at term and baby has typical diabetic morphometry (AC > 90th centile, HC +/- 50th centile)
- Offer patients with diabetes and co-morbidities such as morbid obesity and systemic disease an anaesthetic assessment in the third trimester

b. Pre-gestational Type 2 diabetes mellitus

The patient with Type 2 DM may be known with pre-existing diabetes mellitus or may be diagnosed with previously unknown diabetes, during pregnancy. Patients with known Type 2 diabetes ideally should have a planned pregnancy. Management principles for patients with Type 2 diabetes are similar to patients with GDM in many aspects. Documentation of pre-existing diabetes complications, however, should be more comprehensive and pre-pregnancy therapy in women known with diabetes adjusted to ensure that only medications known to be safe in pregnancy are used, and that optimal targets are reached if not already addressed before conception.

i. Education (assisted by diabetes educator)

Disease process:

- Explain how the physiological changes of pregnancy modify glucose homeostasis and that changes in pharmacological therapy to maintain good glycaemic control in pregnancy are expected.
- Emphasize the need for careful glucose monitoring throughout pregnancy to maintain ideal glucose control and to ensure safety and limit the risk of hypoglycaemia.

Monitoring of blood glucose:

All women should be supplied with a home monitoring device and educated / reminded how to use it optimally with regard to finger-prick technique and timing of testing.

Benefits and risks of pharmacological interventions

- Only use hypoglycaemic drugs with confirmed safety in pregnancy (this includes metformin, metformin SR, glibenclamide (only safe sulphonylurea) and insulin. See comments relating to use of glibenclamide in section on pre-conception care.
- Educate regarding risk of hypoglycaemia, especially with insulin, how to recognize and how to manage.

Discussion of treatment targets:

- Explain importance of optimal glycaemic control for the growing baby both in terms of short-term and long-term health.
- Explain the association of poor glycaemic control with maternal hypertensive disorders.

- Set clear glucose targets to ensure safe optimal control, aim for fasting values of 4.0 – 5.5mmol/L and postprandial values < 6.7mmol/L.
- Explain the purpose of doing an HbA1c and aim for a value of less than 6.0 - 6.5%.
- Avoid hypoglycaemia (defined in pregnancy as a blood glucose ≤ 3.5mmol/L).

ii. Lifestyle

Diet and weight control

Refer to dietician for an individualised diet plan with aim to modify content to ease glycaemic control and to ensure weight control if required.

Exercise

Encourage patient to exercise, ideally to do 30 minutes of moderate intensity exercise daily

iii. Evaluation of existing diabetes complications

Investigations in the patient with Type 2 diabetes should include the following:

- Full medical exam to look for long-term complications of diabetes
- Retinal screen if not done within the last 6 months, repeat in pregnancy as deemed necessary or indicated by attending ophthalmologist
- Perform a serum creatinine level and quantify urinary protein excretion at booking visit.
- Refer to a nephrologist / physician if creatinine above 120µmol/L or eGFR of < 45ml/min/1.73m^2, or 24-hour urine protein quantification >2g/24 hours

iv. Pharmacological therapy

- Review current pharmacological therapy and discontinue oral hypoglycaemic medication not proven to be safe in pregnancy. Continue metformin and insulin (if in use) at current dose. Glibenclamide may be considered in individual cases if sulphonylurea therapy is deemed beneficial (refer to prior comments).
- If glucose control in target based on home profile and hypoglycaemic program at booking, confirm optimal control with HbA1c measurement (ideally < 6.5%) and continue with glucose profiling at home and two-weekly assessments.
- Patient must perform home glucose monitoring by doing morning fasting, preprandial (30 minutes before meals) and postprandial glucose values (2-hours after meals) before and after every meal. Follow-up in two weeks.
- If glucose targets not reached and patient
    - only on metformin, then optimise metformin dose if not yet maximum allowed dose and follow-up with glucose profile in two weeks *or*
    - on maximum metformin dose, consider addition of insulin with principles exactly as described for patient with GDM in section on insulin management of GDM with initial addition of nocte intermediate acting insulin or long-acting insulin analogue therapy *or*
    - on maximum metformin dose and current insulin program, modify insulin therapy as necessary and after discussion with patient and ideally in consultation with a

physician / diabetologist. The recommended insulin regimes can include the following:

- nocte intermediate acting insulin / long-acting insulin analogue in combination with prandial short-acting insulin or insulin analogue with all or with selected meals depending on glucose profile (basal bolus / step-up program)
- fixed combinations of intermediate acting insulin and short acting insulin or insulin analogues given twice a day prior to breakfast and supper with timing dependent on type of insulin used (30 minutes before meals on human short acting combination and with meals or 15 minutes prior to meals if short-acting insulin analogue combinations)

- Use glucose profile and monthly HbA1c to confirm that control is optimal and glucose values in target.

v. Follow-up plan

- Monitor and maintain home glucose profiling throughout pregnancy. Patients must bring along glucose profiles at each visit.
- Patient may be followed-up 2-weekly until 36 weeks, or patient can send a glucose profile 2 weekly to the practice. Thereafter, weekly until delivery.
- Adjust therapy continuously to maintain target values and to minimize the risk of over-treatment and hypoglycaemia.

vi. Fetal monitoring

- Offer early fetal anatomy (+/-nuchal) scan at 13 weeks.
- Offer detail anomaly scan at 20 weeks.
- Perform umbilical artery Doppler studies at 24-26 weeks.
- Fetal growth needs to be monitored both for macrosomia and (unexpected) poor growth. Growths scans are ideal at 30-32 weeks and again at 36 weeks' gestation.

vii. Mode and timing of delivery

- Offer delivery at 38 weeks. If patient declines, document that she has been well-informed. Continue weekly feto-maternal surveillance (including CTG twice per week) until delivery.
- Opt for elective Caesarean section if EFW is > 4kg at term and baby has typical diabetic morphometry (AC > 90th centile, HC +/- 50th centile)
- Offer patients with diabetes related complications and co-morbidities such as morbid obesity and systemic disease an anaesthetic assessment in the third trimester.

c. Pre-gestational Type 1 diabetes mellitus

The patient with Type 1 DM may be known with pre-existing diabetes mellitus or may be diagnosed with previously unknown diabetes for the first-time during pregnancy (unusual, but encountered). Patients with known Type1 diabetes should ideally have a planned pregnancy and undergo extensive pre-conception counselling. The patient with known Type 1 diabetes has unique challenges in pregnancy and this category of patients must be managed by a multidisciplinary team with a special interest in diabetes. This team must include a diabetologist. Patients are often treated

on intensive insulin programs with a significant risk of treatment-induced hypoglycaemia. This risk is exacerbated in pregnancy where normal physiology modifies insulin requirement, and also in the presence of existing diabetes related complications. All patients are thus advised to carry sweets with them and to be provided with a glucagon home-kit if the risk is deemed significant. Individualised treatment programs should be advocated and supervised by an obstetrician- diabetologist team and falls beyond the scope of a general guideline. Documentation of pre-existing diabetes complications must be comprehensive.

i. Education (assisted by diabetes educator)

Disease process

- Explain how the physiological changes of pregnancy modify glucose homeostasis and that changes in pharmacological therapy to maintain good glycaemic control in pregnancy are expected and that the risk of hypoglycaemia is increased.
- Emphasize the need for careful glucose monitoring throughout pregnancy to maintain ideal glucose control and to ensure safety and limit the risk of hypoglycaemia.

Monitoring of blood glucose

All women should have a home monitoring device and finger-prick technique and timing of measurements should be re-discussed and evaluated.

Benefits and risks of pharmacological interventions

- Educate regarding risk of hypoglycaemia

Discussion of treatment targets

- Explain importance of optimal glycaemic control for the growing baby both in terms of short-term and long-term health.
- Explain the association of poor glycaemic control with maternal hypertensive disorders and potential acute maternal metabolic complications similar to non-pregnancy.
- Set clear glucose targets to ensure safe optimal control, aim for fasting values of 4.0 – 5.5mmol/L and postprandial values < 6.7mmol/L
- Explain the purpose of doing an HbA1c and aim for a value of less than 6.0 - 6.5% (even lower in select cases)
- Avoid hypoglycaemia defined in pregnancy as a blood glucose ≤ 3.5 mmol/L

ii. Lifestyle

Medical Nutritional

Refer to dietician for an individualised diet plan after the insulin program has been finalized. The aim of the diet plan is to ensure that the carbohydrate content, distribution and timing, is synchronized with the individual's insulin to ensure safe and optimal glycaemic control. The dietician is an integral part of the MDT and it is strongly advised that patient should be monitored by the dietitian throughout pregnancy on a regular basis. The dietitian should immediately be informed of any change in the insulin treatment program so as to adjust meal timing if necessary.

Exercise

Exercise advice should be individualised based on glucose control and presence of diabetes related complications

iii. Evaluation of existing diabetes complications

Investigations in the patient with Type 1 diabetes must be comprehensive and should include the following:

- Full medical exam to look for long-term complications of diabetes
- Retinal screen if not done within the last 6 months, repeat in pregnancy as deemed necessary or indicated by attending ophthalmologist
- Do a serum creatinine level and quantify urinary protein excretion at booking visit.
- Refer to a nephrologist / physician if creatinine above 120µmol/L, eGFR of < 45ml/min/1.73m^2, or 24-hour urine protein quantification >2g/24 hours.

iv. Pharmacological therapy

Insulin therapy is indicated in all patients with a diagnosis of Type 1 diabetes mellitus. The ideal treatment program is a basal-bolus insulin regime provided by multiple insulin injections daily or via insulin infusion provided by insulin pumps. In a basal bolus program intermediate human NPH insulin or long-acting insulin analogue therapy is given subcutaneously once or twice a day to provide basal requirements of insulin and is combined with short acting human insulin or insulin analogue therapy at meal-times to provide cover at the time of carbohydrate intake. Infusion pumps provide a constant infusion of short acting insulin analogues and the infusion rate is modified as needed. Fixed combinations of intermediate acting insulin and short acting insulin or insulin analogues given twice a day prior to breakfast and supper with the timing dependent on type of insulin used (30 minutes before meals on human short acting combination and with meals or 15 minutes prior to meals if short-acting insulin analogue combinations) provide alternate insulin delivery.

- Familiarize yourself with the patient's insulin program
- If the patient's glucose control is good, continue on the regime that the patient is familiar with.
- If glucose control is in target based on home profile and hypoglycaemic program at booking, confirm optimal control with HbA1c measurement (ideally < 6.5%) and continue with glucose profiling at home and two-weekly assessments.
- Patient must perform home glucose monitoring by doing morning fasting, preprandial (30 minutes before meals) and postprandial glucose values (2-hours after meals) before and after every meal. Follow-up in two weeks.
- If glucose targets not reached on current insulin program, consider switching to basal bolus regime or optimize existing basal insulin program ideally in consultation with a physician / diabetologist
    - Consider admission to hospital for this process.
    - Calculate total daily insulin requirement (based on weight (0.2 to 0.5u/kg), current total insulin requirements and degree of hyperglycaemia).
    - Administer ~ 50% as intermediate acting insulin, given 30 min before bedtime (maximum starting dose of 30u).

    - The other 50% is to be given as short acting insulin 30 minutes prior to each meal (divide evenly over the three meals)
    - Determine glucose values 30 minutes before and again 2 hours after each main meal. Monitor for 24 to 48 hours before making any changes.
    - Pay attention to the morning fasting HGT first and make changes to evening dose of intermediate acting insulin by increments of 2-4u until normal value is reached provided that a safe 02h00 value is maintained (≥ 5 mmol/L)
    - Next compare pre- and post- prandial values. If there is an increase of > 2mmol/L over meals and the post-prandial value is not within the target range, then increase short acting insulin by 2u, until target is reached.
    - Consider a second dose of intermediate acting insulin when pre-prandial values at lunch and supper remain high.
- Use glucose profile and monthly HbA1c to confirm that control is optimal and glucose values in target.

v. Follow-up plan
- Monitor and maintain home glucose profiling throughout pregnancy. Patients must bring along glucose profiles for each visit.
- Patient may be followed-up 2-weekly until 36 weeks, or patient can send a glucose profile 2 weekly to the practice. Thereafter, weekly until delivery.
- Adjust therapy continuously to maintain target values and to minimize the risk of over-treatment and hypoglycaemia.

vi. Fetal monitoring

- Offer early fetal anatomical surveillance (+/- NT) scan at 11-13 weeks.
- Offer/refer for detail anomaly scan at 20 weeks including four-chamber view of fetal heart and outflow tracts.
- Perform umbilical artery Doppler studies at 24-26 weeks.
- Fetal growth needs to be monitored both for macrosomia and (unexpected) poor growth. Growths scans are ideal at 30-32 weeks and again at 36 weeks' gestation.

vii. Mode and timing of delivery

- Timing of delivery needs to be considered carefully on an individual basis if there is poor fetal growth, brittle glycaemic control or hypertension. If earlier delivery is not indicated, planned delivery should be offered from 38 weeks. If patient declines, document that she has been well-informed. Continue weekly feto-maternal surveillance (including CTG 1-2 times per week) until delivery.
- Opt for elective Caesarean section if EFW is > 4kg at term and baby has typical diabetic morphometry (AC > 90th centile, HC +/- 50th centile)
- Offer patients with diabetes-related complications and co-morbidities such as morbid obesity and systemic disease an anaesthetic assessment in the third trimester.

Management of women with diabetes in labour

a. Gestational diabetes mellitus

- Stop oral agents once in active labour, or the night before an elective caesarean section.
- Check HGT hourly – aim for a value between 4 and 7mmol/L during labour.
- If patient is NPO, start a maintenance infusion of 10u short-acting insulin or insulin analogues in 1 litre of 5% Dextrose. Start at an infusion rate of 100ml/hour.
- Aim to maintain hourly HGT between 4 and 7mmol/L
- If HGT is > 8mmol/L, change the solution and remix a new solution with 12 to 14u short-acting insulin or insulin analogues in 1 litre 5% Dextrose. Administer at 100mls/hour. Discard old solution.
- If HGT is < 4mmol/L, change the solution and remix a new solution with 6 to 8u short-acting insulin or insulin analogues in 1 litre 5% Dextrose. Administer at 100mls/hour. Discard old solution.
- Perform continuous CTG monitoring during labour.
- Consider lithotomy position with delivery.
- Be aware of risk of shoulder dystocia.
- Notify paediatrician regarding imminent delivery

b. Type 2 diabetes mellitus

- If patient only on oral agents then manage the same as for Gestational Diabetes
- If patient is using insulin, start a maintenance infusion of 10u short-acting insulin or insulin analogues in 1 litre of 5% dextrose. Start at an infusion rate of 100ml/hour.
- Aim to maintain hourly HGT between 4 and 7 mmol/L.
- If HGT is > 8mmol/L, change the solution and remix a new solution with 12 to 14u short-acting insulin or insulin analogues in 1 litre 5% Dextrose. Administer at 100mls/hour. Discard old solution.
- If HGT is < 4mmol/L, change the solution and remix a new solution with 6 to 8u short-acting insulin or insulin analogues in 1 litre 5% Dextrose. Administer at 100mls/hour. Discard old solution.
- Perform continuous CTG monitoring during labour.
- Consider lithotomy position with delivery. Be aware of risk of shoulder dystocia.
- Notify paediatrician regarding imminent delivery

c. Type 1 diabetes mellitus

- Start a maintenance infusion of 10u short-acting insulin or insulin analogues in 1 litre of 5% dextrose. Start at an infusion rate of 100ml/hour.
- Aim to maintain hourly HGTs between 4 and 7mmol/L.
- If HGT is > 8mmol/L, change the solution and remix a new solution with 12 to 14u short-acting insulin or insulin analogues in 1 litre 5% Dextrose. Administer at 100mls/hour. Discard old solution.

- If HGT is < 4mmol/L, change the solution and remix a new solution with 6 to 8u short-acting insulin or insulin analogues in 1 litre 5% Dextrose. Administer at 100mls/hour. Discard old solution.
- Perform continuous CTG monitoring during labour.
- Consider lithotomy position with delivery. Be aware of risk of shoulder dystocia
- Notify paediatrician regarding imminent delivery.

Postnatal management of women with diabetes

a. Gestational diabetes

i. Breastfeeding

- All babies born to mothers with GDM or diabetes, should be assessed by a paediatrician.
- Women with GDM should be strongly encouraged to breastfeed. Ideally, counselling should start in the antenatal period, and early breastfeeding initiation facilitated. Ongoing breastfeeding support is advised as studies show a higher incidence of early breastfeeding cessation in mothers with both GDM and diabetes.
- Benefits of breastfeeding specific to diabetes include decreased risk of diabetes for the mom and the offspring, quicker return to pre-pregnancy weight for the mom and lower rates of obesity for the offspring.

ii. Medication adjustment directly postpartum

- In true GDM all hypoglycaemic treatment (oral and insulin) should be stopped as glycaemia should return to normal. In-hospital glycaemic surveillance to confirm this, is advised.

iii. Counselling, Advice and Follow-up

- Counselling of women with GDM presents a precious opportunity to advise about the significant risk of future disease (including Type II DM, chronic hypertension and cardiac disease), and the importance of long-term lifestyle intervention.
- At 6-12 weeks postpartum an oral glucose tolerance test (OGTT) should be performed, ideally in all women, to exclude persistent diabetes (using appropriate non-pregnancy diagnostic criteria). If resources are limited, fasting plasma glucose (FPG) may be used as an alternative screening method.
- If the OGTT / FPG is *normal*, women should be encouraged to formally re-evaluate their glucose homeostasis annually (OGTT ideal, FPG alternative). They should be advised that GDM may occur in future pregnancies.
- If criteria for *prediabetes* is met (with the OGTT at 6-12w postpartum), intensive lifestyle intervention should be encouraged and metformin may be considered.

b. Type 2 diabetes mellitus

i. Breastfeeding

- See section under GDM.

- Although metformin and sulfonylurea agents are excreted into breastmilk, current evidence shows that the concentration is far below that which may cause concern for neonatal effect. If higher dosages of sulfonylurea are used, the neonate may be observed for symptoms of hypoglycaemia. The benefits of breastfeeding still far outweigh any potential risk and should not be discouraged if women are on oral medication.

ii. Medication adjustment directly postpartum

- In most cases, it is advisable to stop any insulin started in pregnancy and revert to oral medication used prior to pregnancy (including sulfonylurea), although the dose may need to be lowered.

iii. Counselling, Advice and Follow-up

- Reliable contraception should be offered.
- Planned pregnancy with assessment preconception (to optimise glucose control, hypertension, any target organ involvement and plan early pregnancy intervention e.g. aspirin and nuchal scan) should be promoted as noted in this guideline.
- Long term surveillance by a physician is advised.

c. Type 1 diabetes

i. Breastfeeding

- Insulin is required for the initiation of lactation. Women with Type 1 diabetes thus may have a delay in establishing breastfeeding. Insulin (including analogues) is excreted in breastmilk. This is not a contra-indication to breastfeeding and may even improve neonatal gut health.

ii. Medication adjustment directly postpartum

- It is critical to avoid hypoglycaemia postpartum. There is a significant decrease in insulin requirements postpartum. Most often, the postpartum requirements are even less than pre-pregnancy. This is especially true in the first 7 days postpartum regardless whether the patient breastfeeds.
- It is advisable to reduce total insulin dose by 25-30% directly after delivery and to continue adjusting according to the glucose profile.

iii. Counselling, Advice and Follow-up

- Ongoing glycaemic surveillance and adjustment of insulin therapy is advised throughout the puerperium (preferably with the input of the patient's regular physician).
- Reliable contraception should be promoted to allow for an adequate inter-pregnancy interval and preconceptual optimization.

Management of diabetic keto-acidosis (DKA) in pregnancy

- Manage in conjunction with Physician or Intensive Care Specialist

Management of pre-term labour in patients with diabetes

- Diabetes in not a contra-indication to antenatal steroids or to tocolysis. Enhanced surveillance of glucose levels is necessary for 72 hours after initiation of betamethasone.
- Offer admission to patients requiring antenatal steroids, and give additional insulin according to an agreed protocol.
- Avoid beta-mimetic medicines for tocolysis in women with diabetes.

Definitions

Term, acronym or abbreviation	Definition
CTG	Cardiotocograph
DKA	Diabetic Keto-Acidosis
EFW	Estimated Fetal Weight
FPG	Fasting Plasma Glucose
GDM	Gestational Diabetes Mellitus
HGT	Haemoglucotest
NT scan	Nuchal Translucency Scan
OGTT	Oral Glucose Tolerance Test

Addendum A

This document (credit to Mrs Lourentia van Wyk, RD) may be used to standardise frequency and documentation of glucose monitoring.

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Authorship

These guidelines were drafted by a clinical team from Mediclinic and were reviewed by a panel of experts from SASOG and the BetterObs clinical team. All attempts were made to ensure that the guidance provided is clinically safe, locally relevant and in line with current global and South African best practise. Succinctness was considered more important than comprehensiveness.

All guidelines must be used in conjunction with clinical evaluation and judgement; care must be individualised when appropriate. The writing team, reviewers and SASOG do not accept accountability for any untoward clinical, financial or other outcome related to the use of these documents. Comments are welcome and will be used at the time of next review.

Released on date: 2019 12 01