

Global Guideline

for Type 2 Diabetes

Chapter 17: Pregnancy

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Whenever pregnancy is complicated by diabetes, close liaison between health-care professionals involved in diabetes, obstetric and neonatal care will help to achieve the desired outcome of a healthy mother and baby.

This guideline only addresses areas of pregnancy care commonly affected by the co-existence of diabetes, and not routine obstetric care such as fetal scanning and monitoring.

Recommendations

■ Standard care

Pre-pregnancy counselling

- PR1 Identify possibility of pregnancy annually by direct questioning in all fertile women of child-bearing age with diabetes. Provide contraceptive advice where appropriate.
- PR2 Offer pre-pregnancy advice to all women so identified, including as appropriate:
- education on the management of pregnancy with diabetes
 - optimization of blood glucose control (pre-conception target DCCT-aligned HbA_{1c} <6.1 %)
 - stopping oral glucose-lowering drugs (metformin may still be indicated), and starting insulin where appropriate
 - optimization of blood pressure control (to <130/80 mmHg)
 - stopping ACE-inhibitors and A2RBs (use methyldopa, nifedipine MR, labetalol)
 - stopping statins and fibrates
 - assessment of eye and kidney damage (see *Eye screening, Kidney damage*); discuss and manage identified problems
 - assessment of thyroid function
 - advice on alcohol and smoking
 - folic acid therapy.

Screening for undiagnosed or new (gestational) diabetes in pregnancy

- PR3 In women at high risk of diabetes (previous gestational diabetes, obesity – especially abdominal obesity, population with high prevalence of diabetes) provide healthy lifestyle advice (nutrition and physical activity) from first pre-natal visit; check for hyperglycaemia at first pre-natal visit; perform 75-g OGTT [1] if indicated.
- PR4 In all women, measure plasma glucose at first visit after week 20 (24-28 weeks in low risk women); perform 75-g OGTT if abnormal.

- PR5 Manage as diabetes if fasting plasma glucose ≥ 7.0 mmol/l (>125 mg/dl) and/or 2-h plasma glucose ≥ 7.8 mmol/l (≥ 140 mg/dl).

Management during pregnancy

- PR6 Review understanding of management of diabetes in pregnancy, current drug therapy (see PR2), blood glucose control, diabetes complications, and presence of other medical conditions. Advise as appropriate.
- PR7 Examine eyes at first pre-natal visit and each trimester.
- PR8 Offer medical nutrition therapy and education. If overweight, advise a diet suitable for someone of optimal weight. Encourage moderate exercise such as walking.
- PR9 Review frequently, depending on achievement of blood glucose control targets, and management of other diabetes-associated and obstetric problems.
- PR10 Aim for DCCT-aligned HbA_{1c} < 6.0 %, or lower if safely achievable, using self-monitoring of blood glucose to 3.3-6.7 mmol/l (60-120 mg/dl), four times daily (pre-breakfast and 1-2 h after each meal), and insulin therapy if indicated.
- PR11 Manage insulin therapy through careful and intensive self-monitoring and dose adjustment, expecting a rise in insulin requirements as pregnancy proceeds. Insulin requirements may be further disturbed by hyperemesis or use of steroid therapy, and in-patient care may be needed.
- PR12 Monitor weight gain and blood pressure and advise/treat accordingly. Blood pressure should be $< 130/80$ mmHg, avoiding the use of renin-angiotensin system blocking drugs.

Labour and delivery

- PR13 Use intravenous insulin (if on insulin or if needed) during labour.
- PR14 Anticipate changed insulin requirements, and thus need for more frequent glucose monitoring, if continuing insulin postpartum and during lactation.
- PR15 Provide appropriate care and facilities for the newborn.
- PR16 At 45 to 60 days after pregnancy, check for diabetes in women who had developed new diabetes in pregnancy. If then non-diabetic, advise on the high risk of future diabetes, and preventative lifestyle measures. Advise check for diabetes annually.

■ Comprehensive care

- PR_C1 This would be as *Standard care* for screening, except that screening for new diabetes after week 20 might go direct to OGTT in situations with high prevalence and where health facilities are available.
- PR_C2 Specialist ophthalmological review can be offered throughout pregnancy.
- PR_C3 Personal dietetic support and fitness training can be offered throughout pregnancy.
- PR_C4 Self-monitoring of capillary blood glucose during pregnancy would be performed more frequently, at times of likely peak and trough plasma glucose concentrations. Continuous glucose monitoring would be a further possibility.
- PR_C5 HbA_{1c} will be performed at each clinical contact.
- PR_C6 Insulin delivery might be optimized by the use of continuous subcutaneous insulin infusion.

■ Minimal care

- PR_M1 Most of the procedures under *Standard care* can be offered by a specially trained health-care worker.
- PR_M2 If laboratory glucose testing is not easily available, capillary blood glucose measurement for fasting and 2-h OGTT estimation can be substituted, using a trained operator and a regularly validated meter system.
- PR_M3 Where resources allow only very limited access to self-monitoring of blood glucose, use in pregnant women should be a priority.
- PR_M4 If insulin availability is problematic, consider oral glucose-lowering drugs (not PPAR- γ agonists), with the proviso that safety in pregnancy is not fully established.

Rationale

With increasing numbers of women around the world developing Type 2 diabetes, and doing so at a younger age, and with women in many cultures tending to delay starting a family, the issue of diabetes complicating pregnancy has become increasingly important. These guidelines do not address prevention of Type 2 diabetes, so the increased risk of later development of diabetes in those who experience gestational diabetes (GDM) is not our principal concern here. We focus rather on the care of women with new diabetes in pregnancy, as well as the care of those who already have Type 2 diabetes. Although management of diabetes in pregnancy has been improving, women and their infants remain at higher risk for a number of complications

compared with non-diabetic pregnancy. The frequency of congenital anomalies is still high among infants of women with diabetes.

Evidence-base

The evidence-base for much diabetes pregnancy management is poor, and relies on some cohort studies, an occasional RCT, some retrospective analysis, and considerable clinical experience. Much of the data pertaining to Type 2 diabetes derives from people with Type 1 diabetes or studies of mixed populations. The only guideline formally addressing the area (Type 2 diabetes) is the Canadian guideline (in which most of the recommendations are consensus) [2], though consensus guidelines based on non-formal evidence review were also

prepared by IDF (Europe) [3]. The SIGN guideline [4] includes pregnancy, focusing on Type 1 diabetes, while ADA standards of care include pre-conception care and screening for diabetes in pregnancy [5].

Screening for GDM (defined as glucose intolerance of variable severity with onset or first recognition during pregnancy – which will include undiagnosed Type 2 diabetes) is a controversial issue (and the ongoing HAPO study may help here) [2]. Whether or not, and whom, to screen is likely to depend on prevalence of Type 2 diabetes in women of child-bearing age in the population under consideration; it is difficult therefore to develop universally appropriate recommendations. GDM is an asymptomatic condition most of the time, and there has been no RCT to test the effectiveness of its detection. Diagnostic and management levels remain uncertain. Cohort studies have shown increased risk of adverse outcomes according to levels of plasma glucose, independently of age, obesity and other risk factors. RCTs have shown that treatment of hyperglycaemia in pregnancy reduces macrosomia. The Canadian guideline recommends all pregnant women be screened for GDM between weeks 24 and 28 [2], while different strategies are outlined in other guidelines which address this [4,5,6]. A recent paper has supported the utility of detecting and managing GDM [7].

The guidelines present a confusing picture as regards screening tests for GDM. The use of a 4.7 mmol/l (85 mg/dl) cut-off for fasting plasma glucose is suggested from two analyses [8,9], but other studies have suggested higher cut-offs. Fasting glucose may not be the most appropriate measure, however, and the 75-g OGTT (fasting and 2-h values) advocated by WHO [1] is increasingly used internationally, as noted in a Brazilian study [10].

The Canadian and IDF (Europe) guidelines note the importance of blood glucose control in the first trimester for avoidance of fetal malformation, and the adverse effects of hyperglycaemia throughout pregnancy. Insulin is regarded as the natural means of improving blood glucose control in pregnancy where lifestyle measures fail, although metformin is increasingly regarded as safe. Frequent self-monitoring of blood glucose is a normal part of insulin therapy, in particular where insulin requirements are changing as in pregnancy, and where stricter targets may lead to increased risk of serious hypoglycaemia [2]. Special considerations surrounding labour and delivery have been reviewed recently [11].

Experience with rapid-acting insulin analogues has been reassuring for insulin lispro although no formal trials are available [12]. Experience with long-acting insulin analogues

is still very thin [2], and unless other clear advantage is apparent (previous major gain in blood glucose control over NPH insulin-based regimens) they are not generally used in pregnancy. Use of oral glucose-lowering drugs is still controversial, and mostly derives from experience of widespread use in some developing countries and in polycystic ovarian syndrome (see Canadian guideline [2]), but this mostly applies to glyburide and to metformin. Newer drugs are therefore assumed to be contra-indicated.

Consideration

Despite the poor evidence-base, it is clear that the consequences of poor management of diabetes in pregnancy (high risk of maternal and neonatal complications, dead and deformed babies) are such that this is a prime area where investment of health-care resources is appropriate. Furthermore, considerable consensus exists over the need for continued monitoring of complications for acceleration of diabetes-induced damage, and the early use of insulin therapy to tight targets backed by self-monitoring. While the issue of methods and schedules for screening for new-onset diabetes in pregnancy is diverse and confused, the need for detection is not in dispute, and again there is clear consensus that the OGTT in some form has an important role, and that tight blood glucose management in those testing positive is indicated. Some other areas of care, such as the need for folic acid supplementation, and the high risk of future diabetes in those remitting from diabetes after delivery, also seem secure. A particularly difficult issue relates to the use of oral glucose-lowering drugs during pregnancy in places where insulin supply is tenuous, and Type 2 diabetes in pregnancy common. However, while it is nearly impossible to exclude a low incidence of adverse effects (<1 in 100), the potential gain – if this (glyburide/metformin) is the only means of improving glucose control – would seem to be higher.

Implementation

Liaison with obstetric colleagues is a first step in implementation of these recommendations, such that joint protocols can be devised for screening for diabetes, and for pregnancy and post-pregnancy management. Health-care professionals need to be trained on pregnancy-specific lifestyle adaptation, insulin use, and complications screening. Availability of such staff needs to be assured. Where resources are scarce, the availability of insulin and self-monitoring equipment may need to be prioritized to this area, and supplies assured. Laboratory resources for clinical monitoring of glucose control and assessment of renal damage should be provided. Pre-pregnancy services may need to be organized separately.

Evaluation

Monitoring of outcome of diabetic pregnancy (healthy and unhealthy neonates) may seem logical, but because of small number problems is not a powerful tool of quality assurance. Investigation of each neonatal death may be more useful. Delivery weight of the infant and achieved maternal HbA_{1c} in each trimester are useful surrogate outcomes. Structural review should be of the existence of joint management protocols addressing the above recommendations, and appropriate availability of staff.

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