Type 2 diabetes, reproductive health and pregnancy

Recommendations

Recommendations	Reference	Grade*	
Pre-pregnancy and pregnancy with existing type 2 diabetes			
Before attempting to become pregnant, women with type 1 or type 2 diabetes should receive pre-conception counselling that includes optimal diabetes management, including nutrition, preferably in consultation with a multidisciplinary pregnancy team to optimise maternal and neonatal outcomes	1 Diabetes Canada, 2018	C, level 3	
Before attempting to become pregnant, women with type 2 diabetes should strive to attain a pre-conception glycated haemoglobin (HbA1c) as close to normal as is safely possible (ideally \leq 6.5%) to decrease the risk of congenital anomalies, pre-eclampsia, macrosomia and other complications	2 American Diabetes Association, 2019	В	
Before attempting to become pregnant, women with diabetes should discontinue medications that are potentially embryopathic, including any from the following classes:	1 Diabetes Canada, 2018		
 angiotensin-converting enzyme inhibitors (ACEIs) inhibitors and angiotensin receptor blockers (ARBs) prior to conception in women with hypertension alone upon detection of pregnancy in women with chronic kidney disease statins 		C, level 3 D, consensus D, level 4	
Women on metformin and/or sulfonylureas pre-conception may continue on these agents, if glycaemic control is adequate, until pregnancy is achieved	1 Diabetes Canada, 2018	C, level 3	
Women on other glucose-lowering medications should switch to insulin prior to conception, as there are no safety data for the use of other glucose-lowering medications agents in pregnancy	1 Diabetes Canada, 2018	D, consensus	
Women with pre-pregnancy diabetes should take a 5 mg (but not exceeding) daily dose of folate, starting at least one month prior to conception, for the first trimester, to protect against neural tube defects	3 Scottish Intercollegiate Guidelines Network, 2017 4 RACGP, 2016	В	
Pre-pregnancy care provided by a multidisciplinary team is strongly recommended for women with diabetes	3 Scottish Intercollegiate Guidelines Network, 2017	С	
*Refer to 'Explanation and source of recommendations' for explanations of the levels and grades of evidence.			

Contraception

Contraception advice should follow guidelines that apply to women without diabetes. However, as the risks associated with pregnancy in women with diabetes are high, it is particularly important to consider long-acting reversible contraception (LARC) as a first-line option to avoid unplanned pregnancy.⁵ Use of the non-hormonal copper intrauterine contraceptive device (IUCD) might be preferred over the combined oral contraceptive pill, depending on any risks or contraindications caused by the presence of diabetes complications. In all cases, contraception choice should be based on the woman's preferences, considering the risks and benefits and the presence of diabetes-related complications.

Smoking combined with diabetes and the use of the combined oral contraceptive pill significantly elevates vascular risks.

For more information, refer to the World Health Organization *Medical eligibility criteria for contraceptive use*.

Information about contraceptive choice is available from the National Diabetes Services Scheme (NDSS) website.

Sexual problems

Men

Men with diabetes are three times more likely to develop erectile dysfunction than men without diabetes.⁶ The prevalence in men aged >40 years with diabetes may be as high as 50%, and incidence increases by approximately 10% per annum.

Men with diabetes are also affected by erectile dysfunction at an earlier age, with occurrence approximately a decade earlier.^{6,7} In addition, diabetes is associated with lower testosterone levels in men.⁸ This might contribute to reduced libido and aggravate or exacerbate erectile dysfunction.

Healthy Male: Andrology Australia provides a clinical summary guide for the management of male erectile dysfunction.

Women

Sexual dysfunction in women is often under-reported and could co-exist with underlying depression.

Women with diabetes might experience higher rates of sexual dysfunction than women without diabetes: rates of depression, anxiety and psychological distress are higher in people with diabetes and may contribute to sexual dysfunction in women and men.^{9,10} It is also fair to say that sexual dysfunction in women could be linked to complications of diabetes, namely vascular and neuropathic complications; however, more research is needed to assess this.^{11,12}

Symptoms of sexual dysfunction in women include:

- · decreased or total lack of interest in intimacy or sexual relations
- · decreased or no sensation in the genital area
- a degree of anorgasmia
- dryness in the vaginal area, leading to dyspareunia.

Genital infections such as monilial vaginitis occur more frequently in women with diabetes and may contribute to sexual dysfunction. People taking sodium glucose co-transporter 2 (SGLT2) inhibitors are at higher risk of genital infections.¹³

More information about evaluating and managing female sexual dysfunction can be found in a paper by Krakowsky and Grober.¹⁴

It is important to enquire about sexual problems in the annual review and manage physical and emotional aspects. A sexual desire questionnaire or screening tool (eg the Decreased Sexual Desire Screener¹⁵) will help with diagnosis and treatment.

Managing hyperglycaemia in pregnancy

For information about gestational diabetes mellitus, please refer to the section 'Gestational diabetes mellitus'.

Pregnancy with pre-existing diabetes

Clinical context

Sub-optimal glycaemic management at conception and early in pregnancy is associated with increased risk of congenital malformations and first trimester miscarriages.

Women with pre-existing diabetes (types 1 and 2) are more prone to the complications of pregnancy such as higher rates of pre-eclampsia prematurity and caesarean section.¹⁶ In addition, pregnancy may accelerate maternal complications of diabetes, such as diabetic retinopathy (see the section 'Microvascular complications: Diabetes-related eye disease').¹⁷ Both maternal and fetal complications are increased by diabetes. Risk is progressive with increasing glycaemia.¹⁸

Optimising glycaemic management can mitigate these risks, the likelihood of birth trauma, and the risk of early induction of labour and need for caesarean section.

Women of reproductive age with existing diagnoses of diabetes should be advised of the benefits of contraception to prevent inadvertent pregnancy before glycaemia can be optimised. Women should be advised of the need for advice, education and support to achieve optimal glycaemic control before pregnancy.

Women with type 2 diabetes and polycystic ovary syndrome or irregular periods must be advised that improved fertility may accompany use of therapies, including metformin.

In practice

Pre-pregnancy

Where possible and practicable, formal, diabetes-specific pregnancy planning should occur prior to pregnancy.

This should be patient-focused, support self-management and involve a multidisciplinary team. Planning should include assessment of diabetes-related complications, review of all medications and commencement of folic acid (no more than 5 mg/day).⁴

Deferring pregnancy should be recommended until glycaemic control is optimal. Women should be reassured that any reduction in glycated haemoglobin (HbA1c) towards the individualised target is likely to reduce the risk of congenital malformations.

Refer to the NDSS for advice on pre-pregnancy blood glucose targets.

Medications should be reviewed and ceased or replaced as appropriate, ideally before pregnancy during the planning period, or urgently once pregnancy is confirmed. Consultation with local specialist services is advised. Agents such as sulfonylureas, glitazones, SGLT2 inhibitors and incretin-based therapies will need to be reviewed or ceased, and insulin therapy instituted.

Table 1 presents safety profiles and advice for diabetes medications in pregnancy.

Practice Points: Before and during pregnancy

- Counsel the patient that the risks associated with diabetes in pregnancy can be reduced, but not eliminated.
- Recommend a reliable form of contraception until blood glucose control is optimised.
- Advise that optimising HbA1c with a balanced diet, physical activity, healthy weight management and appropriate diabetes medication may positively affect pregnancy outcomes.
- Review sick day management plans, and discuss the need for insulin therapy possibly prior to conception and throughout the pregnancy.
- Revise hypoglycaemia prevention and management.
- Advise that nausea and vomiting in pregnancy may affect blood glucose control.
- Aim for blood glucose to be as close to the normal (non-diabetic) range as possible, ensuring risks of maternal hypoglycaemia are minimised. This reduces risk of spontaneous abortion, congenital abnormalities, pre-eclampsia, retinopathy progression and stillbirth.¹
- Review self-monitoring of blood glucose (SMBG) and/or continuous glucose monitoring (CGM) to determine if medication adjustment and/or commencement of insulin is required, and assess risk of hypoglycaemia. Some patients may be eligible for NDSS-subsidised access.
- Recommend higher folate supplementation (up to 5 mg per day), starting one month before pregnancy⁴ and continuing until 12 weeks of gestation, to reduce the risk of neural tube defects.
- Be aware that women treated for hypothyroidism may require higher doses of thyroid hormone replacement therapy. Based on reassessment, a suggested dose change is an increase of 30% once there is a positive pregnancy test (eg if on one tablet per day, increase by two tablets per week).¹⁹
- Advise examination of the retina prior to conception and during each trimester for women with types 1 and 2 diabetes. More frequent assessment may be required if retinopathy is present. Patients with active, moderate-severe non-proliferative retinopathy or with proliferative retinopathy who have not had an ophthalmological assessment within the preceding six months should undergo testing prior to pregnancy to see if the retinopathy is stable enough for pregnancy.
- Test renal function if this has not been done within the preceding three months. Elevated creatinine
 or estimated glomerular filtration rate (eGFR) <45 mL/min/1.73 m² or an albumin-to-creatinine
 ratio >30 mg/mmol is an indication for pre-pregnancy nephrology assessment.²⁰

Table 1. Safety and risks of common diabetes medications before and during pregnancy			
Medication	Category in pregnancy	Advice	
Sulfonylureas	С	Review or cease and institute insulin therapy	
SGLT2 inhibitors	D		
Incretin-based therapies (eg DPP4i, GLP-1 RA)	B3/C (exenatide)		
Glitazones	B3		
Metformin	С	Not associated with an increase in congenital malformation or early pregnancy loss, but remains category C ²¹	
		Could be used as an adjunct to other therapies, including insulin, in type 2 diabetes, both pre-conception and during pregnancy. ²² Consult with specialist endocrine and obstetric services	
Insulin			
Aspart, lispro	A	Safe to use	
Detemir	A	Safe to use (PBS-listed for type 1 diabetes only)	
Glargine	B3	Insufficient evidence about use. Patients already stabilised on glargine may continue, but the B3 category rating should be discussed with patient	
Isophane, or NPH insulin		NPH is the most common long-acting insulin choice during pregnancy for women with type 2 diabetes	
Antihypertensives ²³		ACE inhibitors and ARBs should be discontinued during the pregnancy planning period, or as soon as pregnancy is confirmed	
Methyldopa	A	Safe	
Clonidine	B3	May cause temporary rise in glucose	
Spironolactone	B3	Seek advice	
Moxonidine	B3	Seek advice	
Calcium channel blocker	С	Avoid (except nifedipine)	
β-blockers	С	Avoid (except labetalol and oxprenolol)	
Thiazide and loop diuretics	С	Seek advice	
ACE inhibitors	D	Contraindicated	
ARBs	D	Contraindicated	
Statins		Discontinue during the pregnancy planning period, or as soon as pregnancy is confirmed	

*For definitions of the Australian categories for prescribing medicines in pregnancy, visit the Therapeutic Goods Administration, Australian categorisation system for prescribing medicines in pregnancy.

ACE, angiotensin-converting enzyme; ARBs, angiotensin receptor blockers; DPP4i, dipeptidyl peptidase-4 inhibitors; GLP-RA, glucagon-like peptide-1 receptor agonists; NPH, neutral protamine Hagedorn; PBS, Pharmaceutical Benefits Scheme; SGLT2, sodium glucose co-transporter 2

Antenatal care

Insulin therapy will need regular review and titration to achieve glycaemic goals.

Intensive glycaemic control guided by SMBG or CGM, versus SMBG alone, has been shown to improve neonatal outcomes in type 1 diabetes in pregnancy.²⁴ However, studies that included people with type 2 diabetes in pregnancy have failed to demonstrate this benefit.²⁵

Close surveillance for new diabetes complications and monitoring of existing complications should occur routinely.

GPs should provide timely and appropriate support and referral for women who are experiencing an unplanned pregnancy where risks of abnormal pregnancy outcomes are elevated.

Ultrasound screening is advised at 10–13 weeks' gestation (with biochemistry) for trisomies, and at 18–20 weeks for congenital cardiac and other malformations. Pregnant women with diabetes should be offered ultrasound monitoring of fetal growth and amniotic fluid volume every four weeks from 28–36 weeks.²⁰ Fetal growth and wellbeing monitoring should occur under specialist supervision. It is recommended to refer to your local specialist endocrine and obstetric services.

During pregnancy

Patients should be referred to specialised diabetes antenatal care as soon as possible, as multidisciplinary shared care is considered best practice.²⁰ A multidisciplinary team ideally involves:

- GP
- · endocrinologist
- midwife
- obstetrician
- credentialled diabetes educator
- accredited practising dietitian
- psychologist.

Postpartum

The GP should maintain or re-establish contact with mother and child as early as practicable to address any issues arising from the pregnancy, labour, surgery or breastfeeding and to review medications.

Metformin may be continued while breastfeeding with minimal effect on the baby.²⁶ Breastfeeding may alter glucose levels, so glycaemic monitoring, oral medications and insulin need careful review during breastfeeding to minimise the risk of hypoglycaemia.

Re-establishing glycaemic management goals, reassessment of complications and timely contraceptive advice are also appropriate in the postpartum period.

Resources

The **Australian Government Department of Health** has produced a practice summary for managing diabetes in pregnancy in its *Clinical practice guidelines: Pregnancy care*. The relevant extract has been reproduced in Appendix 4.

Diabetes Australia has produced a pregnancy planning list.

Diabetes UK has developed a guide to pregnancy for women with diabetes.

The NDSS and Diabetes Australia have produced a guide to planning and managing pregnancy for women with type 2 diabetes.

The Royal Australian College of General Practitioners has information on antenatal care for Aboriginal and Torres Strait Islander people with diabetes in Chapter 2 of the *National guide to a preventive health assessment in Aboriginal and Torres Strait Islander people.*

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