

Managing pre-existing diabetes prior to and during pregnancy

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Keywords

breastfeeding, diabetes,
postpartum care,
preconception care,
pregnancy

Aust Prescr 2024;47:2–6

<https://doi.org/10.18773/austprescr.2024.002>

SUMMARY

Women with pre-existing diabetes who are planning a pregnancy ideally should receive high-quality, multidisciplinary preconception care in a specialist centre; this has been shown to improve pregnancy outcomes.

Optimising glycaemic management is essential prior to conception and throughout pregnancy and breastfeeding to minimise adverse events.

Low-dose aspirin is recommended from 12 weeks gestation for prevention of pre-eclampsia.

Breastfeeding is highly advantageous in women with pre-existing diabetes; women often need additional support with establishment and maintenance of breastfeeding.

High-quality postpartum care and effective contraception are essential.

Introduction

The prevalence of pre-existing diabetes is about 0.6% of pregnancies in Australia.¹ In this article, we focus on the most common forms of pre-existing diabetes (type 1 and type 2 diabetes) and their potential adverse effects on pregnancy. This article will not discuss the management of gestational diabetes.

Women with pre-existing diabetes have a higher risk of adverse events and outcomes in pregnancy than women without diabetes and women who develop gestational diabetes.^{2,3} Adverse events and outcomes in pregnancy directly correlate with suboptimal glycaemic management, both before and throughout pregnancy¹. Women with pre-existing diabetes are more likely to have babies at increased risk of:⁴

- neonatal hypoglycaemia
- fetal macrosomia (i.e. large for gestational age)
- congenital anomalies
- major morbidity, often requiring neonatal intensive care
- perinatal mortality.

There is also an increased risk of early pregnancy loss (before 12 weeks gestation), maternal admission to intensive care, and caesarean section before labour.

For these reasons, all women with pre-existing diabetes should be referred to specialist services experienced in caring for women with diabetes in pregnancy, as this has been shown to improve pregnancy outcomes.

This article summarises the most important messages from the comprehensive consensus document,

The Australasian Diabetes in Pregnancy Society (ADIPS) 2020 guideline for pre-existing diabetes and pregnancy.¹

Preconception care

All women (not only those with diabetes) should receive preconception advice about optimising their health before pregnancy; however, many women present to their primary care physician having become pregnant without preconception advice. Ideally, a preconception (or early pregnancy) discussion should include advice on:

- smoking and alcohol cessation
- vaccinations
- sexually transmitted disease screening
- cervical cancer screening
- healthy lifestyle.

Women with pre-existing diabetes benefit from high-quality preconception care, preferably from a multidisciplinary team. This can reduce their risk of adverse outcomes in pregnancy. Important factors to address before conception (or as early as possible in pregnancy) include:

- folic acid supplementation
- optimisation of glycaemic management
- review of all medications (both antihyperglycaemic and other)
- screening for, and management of, diabetes-related complications
- baseline investigations.

Folic acid supplementation

Women with pre-existing diabetes are at increased risk of their baby having a neural tube defect. Folic acid is recommended from 3 months before conception until 12 weeks gestation¹. Whether a higher dose of folic acid is required in these patients is unclear and contentious, and the decision should be individualised in consultation with the patient’s specialist. Further studies are ongoing to determine the optimal dose.

Optimising preconception glycaemic management

Women with diabetes planning a pregnancy should be advised about preparation for pregnancy, achieving and maintaining optimal glycaemic targets, and improving their outcomes.^{2,5} It is very important to allow time to optimise glycaemic management (minimising both hyper- and hypoglycaemia) prior to conception.³ Clinicians should discuss with women potential adverse outcomes for a pregnancy conceived before optimal glycaemic management has been achieved. Ideally, reliable contraception should be used until the woman’s glycated haemoglobin (HbA1c) is 6.5% or less.

Glycaemic targets preconception and during pregnancy, for women with pre-existing diabetes who use continuous glucose monitoring

For women who use continuous glucose monitoring devices to enhance glycaemic management, achieving optimal glycaemic targets can reduce adverse outcomes for both mother (e.g. pregnancy loss) and baby (e.g. neonatal hypoglycaemia, fetal macrosomia). Suggested glycaemic targets for continuous blood glucose monitoring in women with pre-existing diabetes preconception and during pregnancy are listed in Table 1.¹

Glycaemic targets preconception and during pregnancy, for women with pre-existing diabetes who do not use continuous glucose monitoring

Women with pre-existing diabetes who do not use continuous blood glucose monitoring should self-monitor their blood glucose concentrations 6 to 10 times per day preconception and during pregnancy, aiming for the glycaemic targets listed in Table 2.¹

Preconception screening for comorbidities and complications

All women with pre-existing diabetes considering pregnancy should be screened for comorbidities and complications associated with diabetes before they conceive. This includes assessment of their mental health, dental health, and for comorbidities including hypertension, coronary artery disease, retinal disease

Table 1 Glycaemic targets preconception and during pregnancy, for continuous blood glucose monitoring in women with pre-existing diabetes [NB1]¹

Parameter	Glycaemic targets preconception and during pregnancy
optimal range of euglycaemia	blood glucose concentration 3.5 to 7.8 mmol/L
total duration of euglycaemia (% of 24-hour period)	euglycaemia for more than 70% (i.e. more than 16.8 hours) per 24-hour period
total duration of hypoglycaemia (% of 24-hour period)	blood glucose concentration below 3.5 mmol/L for less than 4% (i.e. less than 1 hour) per 24-hour period AND blood glucose concentration below 3.0 mmol/L for less than 1% (i.e. less than 24 minutes) per 24-hour period
glycaemic variability (%CV)	less than 36%

CV = coefficient of variation

NB1: There is insufficient evidence to specify optimal glycaemic targets preconception and during pregnancy, for continuous blood glucose monitoring in women with type 2 diabetes;¹ however, these targets are reasonable for women with pre-existing type 2 diabetes.

Table 2 Glycaemic targets preconception and during pregnancy, for self-monitoring blood glucose concentrations in women with pre-existing diabetes [NB1]¹

	Blood glucose concentration preconception	Blood glucose concentration during pregnancy
fasting and pre-meal	less than 6.0 mmol/L	4.0 to 5.3 mmol/L
1 hour post-meal	less than 8.5 mmol/L	5.5 to 7.8 mmol/L
2 hours post-meal	less than 7.5 mmol/L	5.0 to 6.7 mmol/L

NB1: Self-monitoring blood glucose concentrations preconception and during pregnancy should be performed 6 to 10 times per day at various times and during various activities.

(diabetic retinopathy), kidney disease, autonomic neuropathy, diabetic foot disease and vitamin B₁₂ deficiency. In addition to routine pregnancy investigations, the recommended investigations for all women with diabetes include:

- kidney function tests—serum electrolyte and creatinine concentrations, estimated glomerular filtration rate
- liver biochemistry
- spot urine albumin–creatinine ratio
- fasting lipid concentrations
- HbA1c
- vitamin B₁₂ concentration
- folate concentration.

Women with type 1 diabetes should be screened for associated autoimmune diseases, such as thyroid disease and coeliac disease. Suggested investigations include thyroid stimulating hormone, thyroid peroxidase auto-antibodies and coeliac auto-antibodies.

Preconception review of medicines

A careful review of all medicines is required for women with pre-existing diabetes planning pregnancy. The harms and benefits of each medicine should be assessed with respect to safety during pregnancy and breastfeeding.

Antihyperglycaemic drugs

Decisions about continuation of insulin analogues and metformin should be individualised. These should not be stopped abruptly, as maintaining euglycaemia is the primary consideration. For women with type 2 diabetes, metformin can be continued and insulin added as required to achieve glycaemic targets. All patients require specialist management of their insulin requirements.

Other noninsulin antihyperglycaemic drugs should be stopped preconception, or as soon as pregnancy is detected (mainly because of potential fetal risks and other unknown risks of new drugs), and replaced with insulin. This includes:

- glucagon-like peptide-1 (GLP-1) receptor agonists
- sodium-glucose cotransporter 2 (SGLT2) inhibitors
- dipeptidyl peptidase-4 (DPP-4) inhibitors
- sulfonylureas.

Cardiovascular drugs

Drugs that block the renin angiotensin system, including angiotensin converting enzyme inhibitors (ACEIs) and angiotensin II receptor blockers (ARBs), should be stopped preconception or as soon as pregnancy is detected (if unplanned), because of the potential risk of fetal kidney damage. In women with diabetic kidney disease and proteinuria, the harms and benefits of stopping these drugs preconception need careful consideration – these drugs may be stopped when pregnancy is diagnosed or early in the first trimester with specialist consultation.

Statins and other lipid-lowering therapies should be stopped preconception or as soon as pregnancy is detected, because of the potential risks to fetal brain development and long-term developmental effects.

Pregnancy care

Women with pre-existing diabetes who are pregnant ideally should be referred to a specialist multidisciplinary service for pregnancy

management. Key elements of high-quality pregnancy care for diabetes include:^{1,6}

- optimal glycaemic management
- nutritional advice
- aspirin for pre-eclampsia prevention
- regular physical activity
- attention to mental health.

Regular assessment of fetal growth and wellbeing is essential, with serial fetal growth scans every 2 to 4 weeks from 28 weeks, and weekly cardiotocography from 34 weeks gestation.^{1,6}

Optimising glycaemic management in pregnancy

Specialist management of women with pre-existing diabetes in pregnancy is proven to be most beneficial for maternal and fetal health outcomes. Sometimes collaborative care is undertaken between a specialist and:

- a general practitioner with a high level of experience with diabetes in pregnancy
- credentialled diabetes educators in high-volume diabetes-in-pregnancy clinics.

In rural and remote healthcare settings, telemedicine is a very useful way of accessing specialist care.

Self-monitoring blood glucose concentrations (6 to 10 times per day)¹ or continuous blood glucose monitoring is recommended for all women with pre-existing diabetes who are pregnant. Continuous blood glucose monitoring is valuable for determining the impact of various factors on glucose management, including sleep, stress, illness, insulin dosing, insulin timing, and rebound after hypoglycaemic episodes. Fine-tuning glycaemic management during pregnancy helps to provide holistic care to the woman. Glycaemic targets recommended during pregnancy are listed in Table 1 and Table 2.

Assessment of HbA1c in each trimester is useful. The preconception and first-trimester target for HbA1c is 6.5% or less. Throughout pregnancy, increased turnover of red blood cells reduces HbA1c. It is ideal to aim for an HbA1c of 6% or less as pregnancy progresses into the second and third trimesters; however, this should never occur at the expense of more frequent episodes of hypoglycaemia.

Insulin requirements in pregnancy

Insulin requirements usually decrease in the early first trimester, then rise progressively from around 16 weeks gestation until 36 weeks gestation, before declining towards term. Insulin doses should be reviewed (under the guidance of a specialist)

every 1 to 2 weeks in pregnancy to ensure optimal glycaemia. If a woman's insulin requirements have significantly reduced, or she has episodes of hypoglycaemia, a careful specialist evaluation is required; this does not warrant immediate delivery. Some women with type 2 diabetes will continue to use metformin throughout pregnancy, and in most cases will require insulin therapy as well.

If labour starts spontaneously or is induced prior to 35 weeks gestation, betamethasone is often given to enhance fetal lung maturation. Blood glucose concentration typically rises 4 to 5 hours after betamethasone injection, with maximal effect at around 24 hours after the first injection. Post-betamethasone hyperglycaemia requires specialist management, with additional insulin delivered via insulin pump, subcutaneous injection or an insulin infusion.

Pre-eclampsia prevention

Pre-eclampsia is more common in women with pre-existing diabetes, and contributes to significant maternal and fetal morbidity and mortality.^{1,7} Type 1 diabetes poses a higher risk of pre-eclampsia (15 to 20%) than type 2 diabetes (10 to 15%).¹ For prevention of pre-eclampsia, all women with pre-existing diabetes should be offered aspirin 100 to 150 mg orally, daily with the evening meal, from 12 weeks gestation.¹

Calcium supplementation for women with poor dietary intake is also recommended for prevention of pre-eclampsia⁸ from 12 weeks gestation. The suggested dosage is calcium carbonate 600 mg orally, twice daily.¹

Blood pressure and urinalysis should be checked at every antenatal visit.

Hypoglycaemia in pregnancy

In women with pre-existing diabetes, severe hypoglycaemia is more common during pregnancy, especially from 7 to 12 weeks gestation. Discussion about the prevention, detection and treatment of hypoglycaemia is essential for all women with diabetes. Relatives and carers should also be informed about identification and emergency management of severe hypoglycaemia.

Hypoglycaemic episodes can be managed with short-acting carbohydrates (e.g. oral glucose paste or tablets, jelly, juice, sugar), followed by complex carbohydrates (e.g. sandwich). Severe hypoglycaemia with altered consciousness must be urgently managed with subcutaneous or intramuscular glucagon injection and calling an ambulance. Glucagon is safe to use in pregnancy.

Hypoglycaemia and driving

All women with diabetes treated with insulin are at risk of developing unexpected hypoglycaemia, more so when they are pregnant. They should be advised about legislation relating to driving with the possibility of hypoglycaemia. Ideally, advise women that:

- they will usually need to eat breakfast before driving in the morning because their fasting blood glucose concentrations will often be 5 mmol/L or lower
- they should always test their blood glucose concentration before driving and should not drive if they feel unwell, or their blood glucose concentration is 5 mmol/L or lower.⁹

Sick-day management and risk of diabetic ketoacidosis in pregnancy

Women with pre-existing diabetes who are pregnant should be reminded about sick-day management, which is more relevant during pregnancy. The risk of developing diabetic ketoacidosis (DKA) is higher in pregnancy. The risk is higher with intercurrent illness (e.g. infection), while fasting or on low carbohydrate diets, if insulin is omitted, or with certain medications (e.g. corticosteroids).^{1,10}

A high index of suspicion for DKA is required in pregnancy because it can occur at lower blood glucose concentrations than is typical in nonpregnant women. It can even occur when women are euglycaemic. If a woman feels unwell, or her blood glucose concentrations are persistently high (e.g. above 10 mmol/L), she should check her blood ketone concentration.

Blood ketone concentration can be assessed using a finger-prick blood test. If DKA in pregnancy is suspected, specialist management and urgent transfer to hospital is required.

Retinal and kidney screening in pregnancy

Diabetic retinopathy can paradoxically worsen in response to improving glycaemic management during pregnancy and requires specialist monitoring to prevent deterioration.^{1,11} Women should have retinal screening preconception, or early in the first trimester.¹ Consider repeating retinal screening in the third trimester, or earlier if diabetic retinopathy has been detected.

Kidney screening should be repeated in each trimester of pregnancy, especially if the person has any degree of diabetic kidney disease or hypertension. Screening usually entails measurement of serum creatinine concentration, and a spot urine albumin-creatinine ratio or protein-creatinine ratio. Diabetic kidney disease requires specialist management during pregnancy to prevent deterioration.^{1,11}

Care at the time of birth

Women with pre-existing diabetes who are pregnant require a multidisciplinary approach when planning the timing and mode of birth. This allows for a diabetes management plan to be implemented for the birth. Most institutions have strict protocols for management through labour and delivery.

Neonatal assessment and management will be required.

Postpartum care

Breastfeeding

Breastfeeding has maternal and neonatal benefits for all women, including women with pre-existing diabetes.¹² These women benefit from high-quality educational counselling about breastfeeding and hypoglycaemia prevention. Breastfeeding improves long-term metabolic outcomes for babies, and has been associated with improved glycaemic management and better long-term cardiovascular outcomes for mothers.¹² Lactation support may be required, particularly for women with type 2 diabetes, who tend to have delayed postpartum breastmilk production (delayed secretory activation).¹³

Other postpartum care

Women need close management of diabetes postpartum, including additional nutritional advice and support. For women with type 1 diabetes, insulin requirements following delivery are usually about half the prepregnancy dose, and should be adjusted as required.

Women with type 2 diabetes who required insulin during pregnancy may not require it postpartum. Decisions about their prepregnancy antihyperglycaemic drugs should be made by a specialist on an individual basis. All other prepregnancy medicines need to be reviewed. Aspirin and ACEIs are safe during breastfeeding. Statins should not be restarted until breastfeeding has stopped.

A postpartum contraception plan should have been discussed before birth. Contraception and ongoing diabetes follow-up must be assured.

Women with type 1 diabetes need careful follow-up to assess for postpartum thyroiditis. Thyroid function tests should be performed at 6 weeks, 3 months and 6 months postpartum.

Conclusion

The management of women with pre-existing diabetes prior to and during pregnancy is a highly complex area of medicine that requires specialist management from preconception to postpartum. ◀

Conflicts of interest: Leonie Callaway and Fiona Britten are authors of the Australian Diabetes in Pregnancy Society (ADIPS) 2020 Guideline for Pre-existing Diabetes and Pregnancy.

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