

CASE STUDY: PRE-CONCEPTION PLANNING IN T2DM:

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The prevalence of type 2 diabetes (T2D) in Australia is rising, including in young women of reproductive age. T2D confers a higher risk of maternal and fetal risks, which are mainly attributable to hyperglycaemia, associated metabolic syndrome components and, when present, chronic complications of diabetes. T2D may be undiagnosed prior to pregnancy. GPs play a key role in identifying and counselling women with T2D before and during pregnancy. Early detection and management are vital to allow for risk factor modification and encouraging a healthy lifestyle to reduce the adverse effects of T2D on women and their children.

*Alice is a 33-year-old female who presents to her general practitioner seeking advice on pre-conception planning. She has already been known to have T2DM for 7 years and her HbA1c is 8.7%. Her current management includes Metformin 1g PO daily and Semaglutide (Ozempic) SC 0.5mg weekly. **What are the risks for pregnancies in women with T2D?***

Risks of T2DM in pregnancy

There is an increased risk of diabetic embryopathy for the offspring of women with pre-existing diabetes mellitus. The rate of congenital anomalies is 8-10%, compared to 2.1% in the general population (1). These anomalies may affect any organ system but include:

- Congenital heart disease
- Anencephaly
- Microcephaly
- Renal anomalies

T2D also increases the risk of maternal and neonatal outcomes, such as:

- Increased rates of miscarriage
- Gestational hypertension and pre-eclampsia
- Large for gestational age/Macrosomia
- Intrauterine growth restriction
- Caesarean delivery
- Neonatal hypoglycaemia
- Neonatal intensive care unit admission
- Stillbirth or neonatal death
- Deterioration of existing diabetes-related complications

The risk of these adverse outcomes substantially increases once HbA1c \geq 8.5%.

Given her current HbA1c is elevated at 8.7% and the fact that she is treated with semaglutide, she is strongly encouraged to use reliable contraception. It is discussed with Alice that conception should ideally occur once HbA1c \leq 6.5% to minimise the risk of pregnancy complications and at least 2 months after semaglutide is ceased, given the evidence of teratogenicity in animal models. In the meantime, she is advised to commence taking pre-natal supplements including high dose folic acid and to have a complete medications review and diabetes complications assessment.

Prenatal medications

Women with T2DM should commence taking folic acid 5mg daily 2-3 months prior to starting to try for pregnancy

Medication reviews

- Medication lists should be reviewed regarding safety for pregnancy.
- **Diabetes Management:** Safe medications before and in early pregnancy include insulin and metformin.
- Sulphonylurea agents should ideally be ceased pre-pregnancy.
- GLP-1 period receptor analogues, SGLT2 inhibitors, thiazolidinediones and DPP4 inhibitors should not be prescribed in women of reproductive age, unless they are using reliable contraception. They should be ceased during the pregnancy planning period.

It is strongly advised that Alice ceases semaglutide (Ozempic) at least two months before trying to conceive, due to its long half-life and the concern about teratogenicity in animal models.

Close attention should also be placed on other medications which may be prescribed as part of T2D management as they can be potentially harmful. These including statins (2), ACE inhibitors (ACEi) (3) and angiotensin receptor blockers (ARB) (3).

Statins should be ceased pre-pregnancy.

If ACEi and ARB are being used for **hypertension** management, they should be changed to alternative antihypertensive agents considered safe in pregnancy. These include labetalol, methyldopa, nifedipine and hydralazine.

However, if an ACEi or ARB is being used for **nephroprotection**, it should be continued until a positive pregnancy test is obtained, as the benefits are deemed to outweigh the risk.

On review of her complication status, Alice has significant albuminuria of 32 mg/mmol/day. Otherwise, her renal function is normal with creatinine 56 and eGFR > 90. She is normotensive with a blood pressure of 110/70 mmHg. Her last eye check was done five years ago and did not reveal any retinopathy. She has been urged to have an eye check as soon as possible as it is well overdue, and before pregnancy, especially as semaglutide has been affiliated with new-onset or worsening diabetic retinopathy. Once again, it was emphasised to Alice that until all measures have been addressed, contraception should be continued to mitigate the risk of unplanned pregnancy and the risk of increased adverse pregnancy outcomes.

Pre-conception assessment for T2DM-related complications

Prior to pregnancy, an HbA1c target of $\leq 6.5\%$ (48 mmol/mol) is advised to minimise the risk of congenital abnormalities (4).

Diabetes complication assessment should be part of diabetes-specific pre-pregnancy planning.

This includes:

- Eye check for retinopathy (increased risk of progression in pregnancy)
- Nephropathy (any degree increases risk of hypertension/pre-eclampsia, small babies, early delivery; increased risk of progression in pregnancy if the patient has stage 4-5 CKD)
- Neuropathy (rare to progress in pregnancy)
- Gastroparesis (symptoms may worsen in pregnancy)
- Cardiovascular, cerebrovascular, and peripheral vascular disease
- Periodontal disease (particularly increased risk of gingivitis in pregnancy)

In particular, semaglutide (Ozempic) has been associated with new onset or worsening of pre-existing retinopathy, which is an additional reason that Alice requires an eye check prior to coming off contraception and trying to conceive.

Fortunately, Alice did not have retinopathy on a repeat dilated eye examination, and no other complications were present. Varicella zoster and rubella serology were checked, and she was immune on both. She was referred to an obstetrician for a detailed obstetric check prior to her proceeding to pregnancy.

The following resource for pre-conception planning in T2DM are useful for both healthcare professionals and patients:

- *For patients*
 - [NDSS Pregnancy Planning Checklist](#)
 - [NDSS Having a Healthy Baby Guide for Women with Type 2 Diabetes](#)
- *For healthcare professionals*
 - [Pre-pregnancy Planning and Care for Women with Diabetes \(online learning\)](#)
 - [ADIPS 2020 Guideline for Pre-existing Diabetes and Pregnancy](#)
Rudland, V.L., Price, S.A., Hughes, R., Barrett, H.L., Lagstrom, J., Porter, C., Britten, F.L., Glastras, S., Fulcher, I., Wein, P., Simmons, D., McIntyre, H.D. and Callaway, L. (2020), ADIPS 2020 guideline for pre-existing diabetes and pregnancy. Aust N Z J Obstet Gynaecol, 60: E18-E52.

References

1. McElduff A, Ross GP, Lagstrom JA, et al. Pregestational diabetes and pregnancy: an Australian experience. Diabetes Care 2005; 28: 1260-1261
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