

Management of type 1 diabetes

Increased time-to-pregnancy in women with diabetes: An area for discussion in pre-conception counselling?



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It is well established that for women with diabetes the risks of pregnancy are greater than the general population. The most recent Confidential Enquiry into Maternal and Child Health (CEMACH, 2007) has shown

that despite considerable improvements in diabetes care during pregnancy, outcomes remain poor for mothers with diabetes and their babies.

Women with type 1 or type 2 diabetes have an increased risk of a number of adverse outcomes, including miscarriage, congenital abnormalities and perinatal death. For the mother there is an increased risk of progression of retinopathy or nephropathy. The pregnancy itself will potentially involve considerably more time spent with healthcare professionals and will have a major impact on lifestyle with a significantly increased risk of hypoglycaemia and severe hypoglycaemic events.

In light of this, CEMACH (2007), and subsequently NICE (National Collaborating Centre for Women's and Children's Health, 2008), have emphasised the importance of pre-pregnancy counselling for women with diabetes. This involves explaining to the person or couple the potential impact of pregnancy on the mother and baby and focusing on optimising diabetes and general health in the time before trying for a baby.

The article by Whitworth and colleagues (2011; summarised alongside) raises another

potential problem that should be considered when talking to potential mothers with diabetes. The data presented here suggest that women with type 1 or type 2 diabetes take substantially longer to become pregnant than those in the general population.

The study included 58 000 women, of whom 221 had type 1 diabetes and 88 had type 2 diabetes. For the general population, 89% (of those in the study) became pregnant in less than 1 year. For women with type 1 diabetes, only 80% were pregnant in less than 12 months. For women with type 2 diabetes the figure was even lower at 70%. Type 2 diabetes and insulin resistance may be associated with an increased risk of polycystic ovarian syndrome, but these differences remain significant when controlling for an irregular menstrual cycle.

The article is an epidemiological study and cannot tell us anything about the causes for the difference seen. We cannot assume that this all relates to glycaemic control, and need to be cautious as this is the first study to show these differences. However, women with diabetes may be unaware of the difficulties in achieving pregnancy, particularly if they have a normal menstrual cycle. This is perhaps another issue that needs to be discussed in pre-conception counselling.

Confidential Enquiry into Maternal and Child Health (2007) *Diabetes in Pregnancy: Are We Providing the Best Care? Findings of a National Enquiry: England, Wales and Northern Ireland*. CEMACH, London

National Collaborating Centre for Women's and Children's Health (2008) *Diabetes in Pregnancy: Management of Diabetes and its Complications from Preconception to the Postnatal Period*. NICE, London

“The data presented here suggest that women with type 1 or type 2 diabetes take substantially longer to get pregnant than those in the general population.”

DIABETOLOGIA



Decreased fecundability in women with T1D and T2D

Readability	✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 This study, based on the Norwegian Mother and Child Cohort Study, was undertaken to assess the effects of T1D and T2D on fecundability (as manifest by increased time-to-pregnancy [TTP]) in pregnant women.

2 Participants ($n=58\,004$; mean age, 29.8 years) were enrolled early in the course of their pregnancy and completed a questionnaire asking about TTP and a range of other factors, including demographics, lifestyle and maternal diseases.

3 A total of 221 cases of T2D and 88 cases of T1D were identified.

4 Fecundability odds ratios (FORs) and 95% confidence intervals (CIs) for T1D and T2D, adjusted for age and pre-pregnancy BMI, were calculated.

5 Some 11.2% of women without diabetes had a TTP of >12 months, compared with 19.5% of women with T1D and 29.6% of women with T2D.

6 Compared with women without diabetes, the adjusted FOR for those with T1D was 0.76 (95% CI, 0.64–0.89) and for those with T2D was 0.64 (95% CI, 0.48–0.84). These FORs did not change substantively and remained statistically significant after exclusions for irregular menstrual cycles and accounting for cycle length.

7 The authors concluded that their results provide evidence of substantially decreased fecundability for women with T1D or T2D, even among those with a normal menstrual cycle.

Whitworth KW, Baird DD, Stene LC et al (2011) Fecundability among women with type 1 and type 2 diabetes in the Norwegian Mother and Child Cohort Study. *Diabetologia* **54**: 516–22

“Continuous glucose monitoring was concluded to provide similar benefits in glycaemic control in people with T1D using either multiple daily injection or continuous subcutaneous insulin infusion therapy.”

DIABETES CARE

CGM yields similar glycaemic benefits for people using MDI or CSII therapy

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓

1 The authors of this 6-month prospective study compared the use of continuous glucose monitoring (CGM) in adults with T1D on multiple daily injection (MDI) therapy versus continuous subcutaneous insulin infusion (CSII) therapy.

2 Sixty participants (30 using MDI and 30 using CSII) were enrolled. Baseline characteristics were similar for all participants (mean age and T1D duration in MDI group, 39.0 years and 22.2 years, respectively; mean age and T1D duration in CSII group, 36.8 years and 21.9 years, respectively).

3 Participants were blinded from the CGM data for the first 4 weeks, after which the data were made available to them, with clinic visits every 4 weeks.

4 Mean baseline HbA_{1c} levels for the CSII and MDI groups were 7.61% (59.7 mmol/mol) and 7.63% (59.9 mmol/mol), respectively ($P>0.05$). HbA_{1c} change at 12 weeks was similar in both groups ($P=0.03$).

5 Compared with blinded use of CGM, unblinded use was associated with similar but significant reductions in HbA_{1c} and glycaemic variability parameters.

6 Similar changes in mean glucose and glucose variability indices were observed in both groups at 3 and 6 months (intensive insulin therapy analysis, $P>0.05$).

7 CGM was concluded to provide similar benefits in glycaemic control in people with T1D using either MDI or CSII therapy.

Garg SK, Voelkle MK, Beatson CR et al (2011) Use of continuous glucose monitoring in subjects with type 1 diabetes on multiple daily injections versus continuous subcutaneous insulin infusion therapy: A prospective 6-month study. *Diabetes Care* **34**: 574–9

DIABETES CARE

Utility of CGM for warning of hypos

Readability	✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓

1 This randomised trial aimed to identify factors predictive of severe hypoglycaemia (SH), and to evaluate the use of continuous glucose monitoring (CGM) to warn of SH.

2 Participants ($n=436$) with T1D were randomised to CGM ($n=224$) or home blood glucose monitoring (control group; $n=212$), and followed-up for

12 months. After 6 months, the control group initiated CGM until study end.

3 A higher SH rate was associated with the occurrence of SH in the previous 6 months, and female sex. An eight-fold increase in SH frequency was observed when 30% of CGM values were ≤ 70 mg/dL (≤ 3.9 mmol/L) on the previous day ($P<0.001$).

4 SH in the previous 6 months was found to be the strongest predictor of SH, and CGM-measured hypoglycaemia was associated with SH the next day ($P<0.001$).

Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group, Fiallo-Scharer R, Cheng J et al (2011) Factors predictive of severe hypoglycemia in type 1 diabetes: analysis from the Juvenile Diabetes Research Foundation continuous glucose monitoring randomized control trial dataset. *Diabetes Care* **34**: 586–90

DIABETIC MEDICINE

Impaired hypo awareness increases hypo frequency

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! factor	✓✓✓

1 This study explored the frequency and nature of hypoglycaemia in people with T1D and impaired hypoglycaemia awareness (HA).

2 Blood glucose levels were measured four times daily for 4 weeks in 19 people with T1D

with normal HA and 19 people with impaired HA.

3 Hypoglycaemia frequency in people with impaired HA was double that in those with normal HA ($P=0.003$). A seven-fold higher incidence of asymptomatic hypoglycaemia was observed in those with impaired HA than those with normal HA ($P=0.001$).

4 Adults with T1D and impaired HA were found to be at an increased risk of asymptomatic hypoglycaemia, and severe hypoglycaemia, than those with normal HA.

Schopman JE, Geddes J, Frier BM (2011) Frequency of symptomatic and asymptomatic hypoglycaemia in type 1 diabetes: effect of impaired awareness of hypoglycaemia. *Diabet Med* **28**: 352–5

DIABETES CARE

Insulin restriction in women with T1D

Readability	✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓

1 Non-adherence to insulin regimens to avoid weight gain in women with T1D is a well-known problem.

2 The authors of this study aimed to determine the distinguishing characteristics of women who report stopping insulin restriction at 11 years of follow-up from those who continue to support insulin restriction.

3 Using self-reported surveys, insulin restriction, diabetes self-care behaviours, diabetes-specific distress, and psychiatric and eating disorder symptoms were assessed in 207 women with T1D (mean age, 44 years).

4 At follow-up, 20 of 60 baseline insulin restrictors had stopped restriction, reporting improvements in all criteria listed above. Thirty-four women reported new restriction.

5 The authors concluded that fear of weight gain and problems with self-care are integral to the emergence and resolution of insulin restriction.

Goebel-Fabbri AE, Anderson BJ, Fikkan J et al (2011) Improvement and emergence of insulin restriction in women with type 1 diabetes. *Diabetes Care* **34**: 545–50

DIABETIC MEDICINE

Dead-in-bed and sudden death in T1D

Readability	✓✓✓✓
Applicability to practice	✓✓
WOW! factor	✓✓✓

- The authors identified all unwitnessed deaths in two childhood-onset (age, <18 years) T1D registries ($n=329$).
- Cause of death had been reviewed and assigned to 255 people; 19 were sudden unexplained deaths and seven met dead-in-bed (DIB) criteria.
- It was concluded that sudden death in people with T1D seems to be increased 10-fold and associated with male sex, while DIB individuals had a high HbA_{1c} level and insulin dose, and low BMI.

Secret AM, Becker DJ, Kelsey SF et al (2011) Characterizing sudden death and dead-in-bed syndrome in type 1 diabetes: analysis from two childhood-onset Type 1 diabetes registries. *Diabet Med* **28**: 293–300

DIABETIC MEDICINE

Microaneurysm count predicts retinopathy

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓

- This multicentre, randomised clinical trial aimed to assess the association between baseline retinal microaneurysm score and progression/regression of retinopathy, and response to candesartan treatment in people with either T1D or T2D.
- The progression analysis comprised 893 people with T1D and 526 with T2D with retinal microaneurysms only at baseline; the regression analysis comprised 483 people with T1D and 216 with T2D.
- Progression and regression of was defined as two or more step

changes on the Early Treatment Diabetic Retinopathy Study scale.

- Participants were randomised to candesartan 32 mg daily or placebo, and followed-up for 4.6 years.
- A higher microaneurysm score at baseline predicted and increased risk of retinopathy progression (hazard ratio [HR] per microaneurysm score, 1.08 for T1D [$P<0.0001$]; HR, 1.07 for T2D [$P=0.0174$]), and a reduced likelihood of regression (HR, 0.79 in T1D [$P<0.0001$]; HR, 0.85 in T2D [$P=0.0009$]).
- Treatment with candesartan was associated with a reduced risk of microaneurysm score progression.
- The authors concluded that microaneurysm counts are important prognostic indicators of worsening retinopathy.

Sjolie AK, Klein R, Porta M et al (2011) Retinal microaneurysm count predicts progression and regression of diabetic retinopathy. Post-hoc results from the DIRECT Programme. *Diabet Med* **28**: 345–51

“Sudden death in people with T1D seems to be increased 10-fold and associated with male sex, while ‘dead-in-bed’ individuals had a high HbA_{1c} level and insulin dose, and low BMI.”