Pregnancies of women with diabetes: 'Could do better! So let's get to it'

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The management of pregnancy in women with pregestational diabetes mellitus remains a challenging clinical problem. Recent data from the Confidential Enquiry into Maternal and Child Health (CEMACH; 2005) make sobering reading, with both the maternal and neonatal outcomes for women with type 1 diabetes (T1D) and type 2 diabetes (T2D) still significantly poorer than for women without diabetes. The ambition for us, with the widespread adoption and implementation of modern multidisciplinary care, to reach the St Vincent standards of pregnancy outcomes in women with diabetes approaching those for women without diabetes seems a distant dream with the gap no nearer closing.

The whole concept of vigilance and attention to detail in the management of carbohydrate intolerance in pregnancy was not helped by the suggestion from the National Institute for Health and Clinical Excellence (NICE; formerly the National Institute for Clinical Excellence) in its antenatal care guidelines that routine screening for gestational diabetes mellitus (GDM) did not improve outcomes (NICE, 2003). If nothing else, women at risk of GDM are the same women at risk of unrecognised, undiagnosed and untreated T2D, and the CEMACH data suggest that these women have particularly poor outcomes.

Indeed, Farrell et al (2002), in a large New Zealand study, showed that 13% of women with GDM had new-onset T2D on post-natal testing and that these women experienced the same increased congenital malformation rates as women with pre-existing T2D. Further, the recent paper on the Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS; Crowther et al, 2005), whose significance is expertly reviewed by Fraser (2006), seems to settle the issue that identification and treatment of GDM improves perinatal outcome. To prevent one serious perinatal outcome, 34 women need to be treated.

The paper from Roland and colleagues (see right) compares the outcome of pregnancies in women with T1D and T2D. They confirm that pregnancies in women with T2D are characterised by poor pregnancy planning, inadequate folic acid supplementation, and treatment with oral hypoglycaemic agents, all of which may contribute to the serious adverse outcomes affecting one in six such pregnancies. The relationship between use of oral hypoglycaemic agents and adverse outcomes is controversial and the authors suggest that the link is more probably that use of oral agents is a marker for poor pregnancy preparation rather than a direct effect of the drugs themselves.

The percentage of pregnancies having a serious adverse outcome was higher in women with T2D than those with T1D (16.4% versus 6.4%), with congenital abnormalities accounting for most of this difference (present in 12.3% and 4.4% of the respective pregnancies). The East-Anglian snap shot is almost entirely in line with the CEMACH data set in observing that women with T2D were significantly older, more obese and more often of non-Caucasian background than women with T1D, but the study shows that pregnancy in women with T2D is associated with a three-fold increase in risk of adverse outcome compared with women with T1D.

The authors challenge us to ensure that all women with T2D receive appropriate education and prenatal and antenatal care to reduce the adverse pregnancy outcomes to at least those of women with T1D. This is perhaps non-aspirational compared with the St Vincent declaration but none the less demanding and arguably more achievable – it is certainly a challenge we should take up!

Confidential Enquiry into Maternal and Child Health (CEMACH; 2005) *Pregnancy in women with type 1 and type 2 diabetes.* CEMACH, London

Crowther CA, Hillier JE, Moss JR et al (2005) Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. *New England Journal of Medicine* **352**(24): 2477–86

Farrell T, Neale L, Cundy T (2002) Congenital anomalies in the offspring of women with type 1, type 2 and gestational diabetes. *Diabetic Medicine* **19**(4): 322–6

Fraser R (2006) Gestational diabetes: after the ACHOIS trial. *Diabetic Medicine* **23**(Suppl 1): 8–11

National Institute for Clinical Excellence (NICE; 2003) *Antenatal care: Routine care for the healthy pregnant woman.* NICE, London

DIABETIC MEDICINE

Study highlights scope for improving pregnancy care

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

1 Previously collected data comparing outcomes of pregnancies between women with type 1 diabetes and those with type 2 diabetes have been conflicting.

2 This study aimed to compare these outcomes and to establish risk factors in women with type 2 diabetes for poor outcomes.

3 Prospective data collection was carried out for all pregestational diabetic pregnancies in ten UK hospitals.

4 In comparison with women with type 1 diabetes, those with type 2 diabetes were found to be less likely to have documented preconception counselling (28.7% versus 40.5%; $P<0.05$) and to be on folic acid at conception (21.9% versus 36.4%; $P<0.001$).

5 Pregnancies in women with type 2 diabetes were more likely to have serious adverse outcomes (16.4% versus 6.4%; $P=0.002$), which were mostly congenital abnormalities (12.3% versus 4.4%; $P=0.002$).

6 Three factors independently associated with congenital abnormalities were identified: folic acid supplementation (odds ratio [OR], 0.3; 95% confidence interval [CI], 0.09–1.0; $P=0.04$); body mass index (OR, 1.09; 95% CI, 1.01–1.18; $P=0.02$); and oral hypoglycaemic agents (OR, 1.8; 95% CI, 1.0–3.3; $P=0.04$).

7 Such factors are amenable to treatment.

Roland JM, Murphy HR, Ball V et al (2005) The pregnancies of women with Type 2 diabetes: poor outcomes but opportunities for improvement. *Diabetic Medicine* **22**(12): 1774–7

'After a mean follow-up of 4.3 years, 12 recipients were still alive and 11 remained euglycaemic.'

'Cardiac dysfunction was detected in 94% of people with anaemia and 66% of people without anaemia (P<0.001).'

DIABETES CARE

Increased cancer risk associated with diabetes treatments

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

1 It has been shown epidemiologically that type 2 diabetes raises the risk of cancer.

2 Based on the hypothesis that treatments which augment insulin levels might promote cancer, this population-based cohort study was carried out to assess the relationship between diabetes treatments and cancer-related mortality.

3 Saskatchewan Health databases were used to identify 10 309 new sulphonylurea or metformin users.

4 Over a mean follow-up of 5.4 years, cancer-related mortality was recorded in 4.9% of sulphonylurea users, 3.5% of metformin users and 5.8% of insulin users.

5 A multivariate Cox regression model was used to calculate adjusted hazard ratios (HRs) for cancer-related mortality.

6 A greater risk of cancer-related mortality was found in sulphonylurea users compared with metformin users (HR, 1.3; 95% confidence interval [CI], 1.1–1.6; *P*=0.012).

7 Insulin use, irrespective of other diabetes treatments, was also found to be associated with increased cancer-related mortality (HR, 1.9; 95% CI, 1.5–2.4; *P*<0.0001).

8 It is not clear from the data whether the associations found are due to negative effects of sulphonylureas and insulin, a protective effect of metformin, or some other factor.

Bowker SL, Majumdar SR, Veugelers P, Johnson JA (2006) Increased cancer-related mortality for patients with type 2 diabetes who use sulfonylureas or insulin. *Diabetes Care* **29**(2): 254–8

CLINICAL TRANSPLANTATION

Pancreas transplants shown to give good glycaemic control

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

1 While it is has been shown that pancreas transplants can be effective in people with type 1 diabetes, the situation is less clear in type 2 diabetes.

2 Seventeen transplants in people with type 2 diabetes were carried out at the authors' centre between 1994 and 2002 (six were pancreas alone, four were pancreas after kidney and seven were a simultaneous pancreas–kidney transplant).

3 One recipient died perioperatively, but the other 16 recipients became euglycaemic.

4 After a mean follow-up of 4.3 years, 12 recipients were still alive and 11 remained euglycaemic.

Nath DS, Gruessner AC, Kandaswamy R (2005) Outcomes of pancreas transplants for patients with type 2 diabetes mellitus. *Clinical Transplantation* **19**(6): 792–7

CLINICAL SCIENCE

Haemoglobin could be a marker for cardiac dysfunction

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

1 In people with diabetes, anaemia is both common and associated with complications.

2 Anaemia's role in heart failure has been established; the authors postulated that, in addition, anaemia may increase the risk of cardiac dysfunction in people with type 2 diabetes.

3 Transthoracic echocardiography was used in 228 consecutive adults with type 2 diabetes to assess haemoglobin level.

4 Cardiac dysfunction was detected in 94% of people with anaemia and 66% of people without anaemia (*P*<0.001).

5 The predictive utility of known cardiac risk markers (brain natriuretic peptide, C-reactive protein and arginine vasopressin) was removed after adjusting for haemoglobin, suggesting that this inexpensive measurement may be a useful risk marker.

Srivastava PM, Thomas MC, Calafiore P et al (2006) Diastolic dysfunction is associated with anaemia in patients with Type II diabetes. *Clinical Science* **110**(1): 109–16

CURRENT MEDICAL RESEARCH AND OPINIONS

Addition of RSG to submaximal MET may be alternative to maximal MET

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

1 The aim of this randomised, double-blind study was to compare the efficacy, safety and tolerability of rosiglitazone (RSG) added to submaximal doses of metformin (MET) with that of dose escalation of the maximal tolerated MET dose, in people with type 2 diabetes.

2 RSG added to submaximal-dose MET was found to be at least as effective as maximal-dose MET after 24 weeks.

3 In addition, a higher proportion of the group receiving combination therapy reached HbA_{1c} <7% (58.1% versus 48.4%) and ≤6.5% (40.9% versus 28.2%).

Weissman P, Goldstein BJ, Rosenstock J et al (2005) Effects of rosiglitazone added to submaximal doses of metformin compared with dose escalation of metformin in type 2 diabetes: the EMPIRE Study. *Current Medical Research and Opinions* **21**(12): 2029–35