

Obesity



Gestational diabetes: Metabolic damage occurs early in pregnancy

Shahrad Taheri
Professor of Medicine, Weill Cornell Medicine-Qatar, Doha

The prevalence of gestational diabetes (GDM) is increasing worldwide. The International Diabetes Federation (2015) estimates that, globally, one in seven births is affected by GDM. Maternal obesity is a key risk factor for GDM, and other risk factors include maternal age, ethnicity, family history of diabetes, maternal smoking, previous GDM, multiparity, previous adverse pregnancy outcomes and a previous large baby.

GDM is associated with multiple risks for the mother and fetus. These include maternal hypertensive disorders, greater rates of operative and interventional deliveries and attendant complications, polyhydramnios, stillbirth, fetal and perinatal death, fetal macrosomia, shoulder dystocia, congenital anomalies, and neonatal hypoglycaemia and other neonatal metabolic complications. Women with previous GDM also have a seven-fold increased risk of developing type 2 diabetes.

In addition to these complications, there is a potential increased risk of obesity in children born to mothers with GDM (Dabelea and Pettitt, 2001; Fadl et al, 2014). GDM results in preferential development of adipose tissue over lean tissue in the fetus, resulting in a “thin-fat” phenotype, in which the baby is the same size as a non-GDM baby but has more fat.

Supporting the thin-fat hypothesis is a new study from Venkataraman and colleagues (summarised alongside). The authors conducted a retrospective analysis of the pregnancies of 153 women with GDM and 178 controls in India.

At 12 weeks’ gestation, fetal measurements were similar in both groups. At 20 weeks’ gestation, however, fetuses in the GDM group had higher anterior abdominal wall thickness (a measure of excess adiposity) but smaller head circumference, abdominal circumference, femur length and biparietal diameter, indicating the thin-fat phenotype. Higher anterior abdominal wall thickness persisted at 32 weeks’ gestation. There was an independent relationship between the mothers’ blood glucose levels and abdominal adiposity in the fetus. At birth, baby size did not differ between the groups, but the babies born to mothers with GDM had greater adiposity. There was a higher prevalence of caesarean deliveries in the GDM group.

These findings support the view that key deleterious fetal metabolic changes can occur in early pregnancy, prior to screening tests for GDM that are conducted in the second trimester. Preventing GDM is a key priority for reducing obesity and type 2 diabetes, but more research is needed to identify the best approaches. It is also important to diagnose GDM as early as possible, preferably in the first trimester. The challenge is to develop effective screening tools to achieve this. ■

Dabelea D, Pettitt DJ (2001) Intrauterine diabetic environment confers risks for type 2 diabetes mellitus and obesity in the offspring, in addition to genetic susceptibility. *J Pediatr Endocrinol Metab* **14**: 1085–91

Fadl H, Magnuson A, Östlund I et al (2014) Gestational diabetes mellitus and later cardiovascular disease: a Swedish population based case-control study. *BJOG* **121**: 1530–6

International Diabetes Federation (2015) *IDF Diabetes Atlas* (7th edition). IDF, Geneva, Switzerland. Available at: <http://www.diabetesatlas.org> (accessed 01.08.17)

Diabetologia

Increased fetal adiposity prior to diagnosis of GDM

Readability ////

Applicability to practice ///

WOW! Factor ////

1 In this case-control study, the authors compared fetal size and adiposity in 153 South Asian women with gestational diabetes (GDM) and 178 control subjects matched for age and parity.

2 In addition to standard fetal biometric variables, anterior abdominal wall thickness – a marker of fetal adiposity – was measured at 20 and 30 weeks’ gestation using archived scans.

3 At 20 weeks’ gestation, fetuses of women who were later diagnosed with GDM had a higher abdominal wall circumference (2.63 mm vs 2.39 mm; $P < 0.0001$) but smaller measurements of other biometric variables, indicating a disproportionate increase in adipose tissue over lean body mass.

4 These differences persisted at 32 weeks’ gestation and after adjustment for maternal age, BMI, parity, gestational weight gain, fetal sex and gestational age at scan.

5 Maternal fasting plasma glucose levels at 24–28 weeks were significantly associated with abdominal adiposity at 20 and 32 weeks after adjustment for other risk factors; however, 1-hour and 2-hour glucose levels were not.

6 These results indicate that GDM is associated with higher fetal adiposity from as early as 20 weeks’ gestation, prior to diagnosis of GDM.

7 The study was limited by its retrospective design and South Asian, primarily middle-class cohort. The authors call for larger, prospective studies in other ethnic populations.

Venkataraman H, Ram U, Craik S et al (2017) Increased fetal adiposity prior to diagnosis of gestational diabetes in South Asians: more evidence for the “thin-fat” baby. *Diabetologia* **60**: 399–405

N Engl J Med

Bariatric surgery vs medical therapy for T2D: 5-year outcomes

Readability ////
 Applicability to practice ////
 WOW! Factor //

- 1 This article presents the 5-year outcomes of the STAMPEDE (Surgical Treatment and Medications Potentially Eradicate Diabetes Efficiently) study, in which 150 obese people with T2D were randomised 1:1:1 to medical therapy, Roux-en-Y gastric bypass (RYGB) or sleeve gastrectomy (SG).
- 2 At 5 years, the primary outcome, an HbA_{1c} of ≤42 mmol/mol (≤6.0%), was achieved by 5%, 29% and 23% of people in the medicine, RYGB and SG groups, respectively, while 21%, 51% and 49% achieved an HbA_{1c} of ≤53 mmol/mol (≤7.0%).
- 3 Both surgery groups had reductions in mean HbA_{1c} of 23 mmol/mol (2.1%), compared with 3 mmol/mol (0.3%) in the medicine group.
- 4 In addition, the RYGB and SG groups both had greater reductions in mean body weight (23% and 19% vs 5%) and triglyceride levels (40% and 29% vs 8%) compared with medical therapy, and greater increases in mean HDL-cholesterol levels (32% and 30% vs 7%) and quality of life scores (17 and 16 vs 0.3 points on the RAND 36-item Health Survey).
- 5 No major late surgical complications occurred except for a reoperation due to a gastric fistula in year 4. Four participants had required further surgery in the first year of follow-up. Mild anaemia was more common in the two surgical groups than in the medicine group.
- 6 The benefits of surgery were observed both in people with a BMI <35 kg/m² and in those with more severe obesity, which suggests that surgery may be indicated in people with T2D and only mild obesity.

Schauer PR, Bhatt DL, Kirwan JP et al (2017) Bariatric surgery versus intensive medical therapy for diabetes – 5-year outcomes. *N Engl J Med* **376**: 641–51

Diabetologia

Effects of intensive lifestyle modification on neuropathy

Readability ////
 Applicability to practice ////
 WOW! Factor //

- 1 The Look AHEAD (Action for Health in Diabetes) study began in 2001 and randomised 5145 overweight or obese people with T2D to an intensive lifestyle intervention or to standard support and education.
- 2 Failure to meet the primary endpoint of a reduction in cardiovascular morbidity and mortality meant that the active interventions were stopped in 2012, but observational follow-up has continued.
- 3 These authors assessed the effect of the Look AHEAD interventions on diabetic peripheral neuropathy. All participants completed the Michigan Neuropathy Screening Instrument (MNSI) questionnaire, which assesses neuropathy symptoms, annually.
- 4 MNSI scores were similar between the groups at baseline; however, after 1 year, the intervention group had significantly lower scores than controls (mean, 1.7 vs 2.0; *P*<0.001), indicating fewer symptoms.
- 5 Scores increased over time but remained significantly lower in the intervention group for the first 3 years and in the final years of follow-up.
- 6 In both groups, better MNSI scores were associated with greater reductions in weight, HbA_{1c} and serum lipid levels.
- 7 Examinations 1–2 years after study closure revealed no differences in physical measurements of peripheral neuropathy, except for light touch sensation, which was significantly better in the intervention group when measurements were combined for both toes.

Look AHEAD Research Group (2017) Effects of a long-term lifestyle modification programme on peripheral neuropathy in overweight or obese adults with type 2 diabetes: the Look AHEAD study. *Diabetologia* **60**: 980–8

Diabetes Obes Metab

Dual dapagliflozin and exenatide in obese people without T2D

Readability ///
 Applicability to practice ////
 WOW! Factor ///

- 1 Results of this phase II, single-centre, randomised controlled trial have been published previously. A combination of once-daily dapagliflozin and once-weekly exenatide was shown to be effective versus placebo in reducing weight and glycaemia in 50 obese people without T2D.
- 2 Participants who completed the original 6-month study were invited to continue in an open-label extension for a further 6 months. In total, 21 people continued on dapagliflozin/exenatide and 17 placebo recipients switched to the therapy.
- 3 At 6 months, the therapy group had lost significant weight while the placebo group had not (4.5 kg vs 0.4 kg). This effect continued at 1 year, with a further (non-significant) reduction of 1.2 kg in people who continued on therapy. People who switched to the active therapy had comparable weight loss (4.2 kg) to those who received it in the original trial.
- 4 Reductions in HbA_{1c} of around 3 mmol/mol (0.3%) were observed in both groups at 1 year.
- 5 Body composition also improved, with reductions in waist circumference of 6.7–7.3 cm and reductions in total adipose tissue of 5.31 L (outcome not measured in the original placebo group).
- 6 No unexpected safety or tolerability issues were observed, and discontinuation rates were comparable to those of approved pharmacotherapies for obesity.

Lundkvist P, Pereira MJ, Katsogiannis P et al (2017) Dapagliflozin once daily plus exenatide once weekly in obese adults without diabetes: sustained reductions in body weight, glycaemia and blood pressure over 1 year. *Diabetes Obes Metab* 27 Mar [Epub ahead of print]

“These results indicate that gestational diabetes (GDM) is associated with higher fetal adiposity from as early as 20 weeks’ gestation, prior to diagnosis of GDM.”