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Letters

High risk of diabetes and metabolic syndrome in Indian women with gestational diabetes mellitus

Women with gestational diabetes mellitus (GDM) are at high risk of diabetes in later life [1]. There is no information on the risk of subsequent diabetes and metabolic syndrome in Indian women with GDM. At the Diabetes Unit, King Edward Memorial Hospital, Pune, India, 126 of 182 GDM women treated since 1994 were reviewed in the year 2002, 4.5 ± 2.0 years after delivery. These women were on average 30 (20–41) years old at the time of diagnosis of GDM, 74 (59%) had impaired glucose tolerance (IGT) and 52 (41%) had diabetes at the oral glucose tolerance test (OGTT) in pregnancy (WHO 1985). Seventy-seven (61%) had received insulin treatment during pregnancy.

Thirty-three of these women continued to be diabetic at discharge from hospital after delivery; a further 14 women were diagnosed diabetic later. At review, 11 were on insulin treatment, 20 on OHAs and 16 on lifestyle management. In the remaining 79, we performed a 75-g OGTT. Information during pregnancy was obtained from records. Those who attended the review did not differ significantly from those who did not with respect to standard risk factors for diabetes (age, family history of diabetes, obesity, gestation at diagnosis and level of glycaemia in pregnancy). At the time of review, these women were 34 (24–50) years old, 35 (28%) had a first-degree relative with Type 2 diabetes, 40 (32%) belonged to lower middle and 86 (68%) to higher middle class. Sixty-five were diabetic (52%, 18 newly diagnosed on OGTT), five (4%) had impaired fasting glucose (IFG), 19 (15%) had IGT and only 37 (29%) had normal glucose tolerance (NGT) (WHO 1997). Seventy-eight women (62%) were overweight (BMI ≥ 25 kg/m^2), 19 (15%) were obese (BMI > 30 kg/m^2) and 60 (48%) were centrally obese (WHR ≥ 0.85). Twenty-seven (21%) had hypertriglyceridemia (plasma triglycerides > 1.7 mmol/l), 74 (59%) had low plasma HDL concentration (HDL-cholesterol < 1.0 mmol/l) and 12 (10%) were hypertensive (blood pressure > 140/90 mmHg). Metabolic syndrome was defined as per WHO guidelines (hyperglycaemia with generalized or central obesity, dyslipidaemia and hypertension) [2]. Thirty-five diabetic women (55%), eight IGT (42%) and three NGT (7%) women could be classified as having metabolic syndrome.

At the time of review, diabetic women were older, were more obese and more centrally obese, had higher plasma cholesterol and triglyceride concentrations, higher blood pressure, but similar BMI and HDL-cholesterol concentration compared with those who showed IGT and NGT. During pregnancy, the diabetic women were more hyperglycaemic and had received insulin treatment more frequently than the other two groups (Table 1).

Logistic regression revealed that diabetic status at review was independently predicted by age at diagnosis of GDM (age ≥ 30 years OR 3.70, CI 1.47–9.29), history of diabetes in

Table 1 Comparison of GDM women who were diabetic, impaired glucose tolerant and normal glucose tolerant women at review

	NGT (42)	IGT (19)	DM (65)	*P*-value
At follow-up in 2002				
Age (years)	33.0 (29.0–35.3)	33.0 (28.0–38.0)	34.0 (31.5–38.5)	—
Height (cm)	153.5 (148.5–158.5)	156.0 (152.5–158.5)	155.5 (150.5–159.3)	0.032
Body mass index (kg/m^2)	25.8 (23.3–28.5)	25.4 (23.0–27.5)	26.2 (24.2–29.4)	0.584
Waist circumference (cm)	81.3 (77.1–88.5)	84.3 (79.4–92.6)	88.0 (81.4–95.7)	0.012
Waist-hip ratio	0.82 (0.77–0.86)	0.85 (0.78–0.89)	0.86 (0.82–0.91)	0.0001
Plasma cholesterol (mmol/l)	4.1 (3.5–4.7)	4.5 (3.9–5.2)	4.5 (3.9–5.2)	0.138
Plasma HDL cholesterol (mmol/l)	1.1 (0.9–1.3)	1.0 (0.9–1.2)	1.1 (0.9–1.2)	0.440
Plasma triglycerides (mmol/l)	0.9 (0.8–1.2)	1.3 (0.8–1.7)	1.3 (0.8–1.7)	0.047
Systolic BP (mmHg)	110 (100–120)	120 (110–120)	115 (110–128)	0.050
Diastolic BP (mmHg)	71 (68–76)	72 (70–80)	78 (70–82)	0.010
Metabolic syndrome (%)	7.0	42.0	55.0	0.010
Time since index pregnancy (years)	3.9 (2.6–5.3)	3.3 (1.9–4.9)	3.8 (2.4–6.4)	0.436
At diagnosis				
Fasting plasma glucose (mmol/l)	5.5 (4.7–6.3)	5.6 (4.6–5.9)	6.7 (5.6–7.7)	0.001
2 h plasma glucose (mmol/l)	9.3 (8.5–10.0)	9.4 (8.4–11.1)	11.1 (8.9–12.6)	0.003
Gestation (weeks)	33.5 (28.0–36.0)	30.0 (24.0–32.0)	28.0 (16.0–32.0)	0.001
Dose of insulin during pregnancy (units)	8 (4–15)	22 (14–34)	29 (10–40)	0.024

Values are median (IQR).

ANOVA, *P*-value adjusted for mother's age at the time of measurements.

DM, diabetes mellitus; IGT, impaired glucose tolerance; NGT, normal glucose tolerance.

first degree relative (OR 2.40, CI 1.09–5.29), 2-h plasma glucose at the diagnostic OGTT during pregnancy (> 10 mmol/l OR 3.60, CI 1.54–8.45) and higher waist-hip ratio (WHR) at review (> 0.85 OR 2.48, CI 1.15–5.39). Time since index delivery and socio-economic status were not significant predictors in this analysis.

We compared prevalence of diabetes in these GDM women with that in 456 normal mothers of similar age who were followed up and studied 8 years after delivery of their child. Crude prevalence rate of diabetes in GDM women (52%) was 13 times higher than that in normal mothers (4%) [3]. For those between 20 and 29 years, it was 27 times higher in GDM mothers (29.2 vs. 1.1%) and in 30–39 years it was 15 times higher (54.8 vs. 3.6%). Prevalence rate of diabetes in National Urban Diabetes Survey (NUDS) in 20–29 year-old women was 2.4% and in 30–39 year-olds it was 6.8%, again considerably lower than that in GDM mothers [4]. Follow-up studies of GDM women revealed much lower cumulative incidence rates for Type 2 diabetes in white Caucasians (< 10%), but high rates in East Indians in Trinidad (62%) and Zuni Indian women in New Mexico (30%) at similar duration of follow-up (~5 years) [5].

In summary, we found very high rates of diabetes and impaired glucose tolerance at the young age of 34 years in women who were diagnosed GDM. One in six of our GDM women continued to be diabetic after pregnancy and three more developed hyperglycaemia within 4 years of delivery. The former group probably consists of women with pre-gestational diabetes. Two in five GDM women had metabolic syndrome at this young age and this suggests a high risk of cardiovascular disease in future. Risk of diabetes was increased by positive family history of diabetes, older age, higher glycaemia in pregnancy and higher WHR at review. Our results suggest that young Indian women should be screened for diabetes in pregnancy and also highlight the need to introduce a programme to prevent diabetes and metabolic syndrome in those diagnosed with GDM.

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A case of primary antiphospholipid syndrome and Type 2 diabetes mellitus with large artery thromboses successfully treated by abdominal stent implantation

Antiphospholipid syndrome (APS), originally reported by Hughes in 1983, is defined as an arterial or venous thrombosis, repeated spontaneous abortion, thrombocytopenia, neurological signs and a positive reaction for antiphospholipid antibody [1]. Thromboses in large arteries, such as in the aorta, are rare, and no association between APS and Type 2 diabetes mellitus (T2DM) has been reported. We present a patient with T2DM and foot ulcers from multiple large artery thromboses due to APS, which were successfully treated by abdominal stent implantation and recombinant human epidermal growth factor (rhEGF) administration.

A 37-year-old man, a smoker with a history of diabetes and hypertension for 2 years, was admitted due to multiple painful ulcers with gangrene of the right foot of a month's duration. He had suffered from intermittent claudication in both lower extremities some 6 years previously, but had treated himself with herb medication with unknown ingredients. His body mass index (BMI) was 23.8 kg/m^2, and he had no family history of diabetes. Fasting plasma glucose and HbA_{1c} levels were 8.6 mmol/l and 6.3%, respectively, and fasting serum insulin and C-peptide levels 216.4 pmol/l and 4.9 μg/l. Serum total cholesterol and triglyceride levels were 2.61 mmol/l and 1.05 mmol/l, respectively. His platelet count was low at 103 000/mm^3, and his prothrombin time (PT) and activated partial thromboplastin time (APTT) were prolonged to 14.2 s and 56.8 s, respectively. He had no evidence of neuropathy on physical examination or by nerve conduction velocity testing. Macroalbuminuria of 1393.6 mg/day was detected by 24-h urine collection, but this slowly returned to the normal range (18.0 mg/day) after 3 months.

Examination showed that in the right foot, necrotic tissues covered the distal parts of the third and fourth toes and the entire fifth toe, and second-degree skin ulcers were associated with infection in the dorsal region of the fifth metatarsal bone. Peripheral pulses were only weakly detected in both inguinal regions, and were absent distally.

A peripheral angiogram of the aorta and its major branches revealed total occlusion at the left proximal common iliac artery, severe partial stenosis at the ostium of the right common iliac artery, and large amounts of thrombus at the lower abdominal aorta. The right popliteal artery was totally occluded, and multifocal occlusions were observed distally in the popliteal artery. A whole-body bone scan revealed associated osteomyelitis in the ulcerated right foot. Percutaneous transluminal angioplasty (PTA) was performed using a Medi-tech®

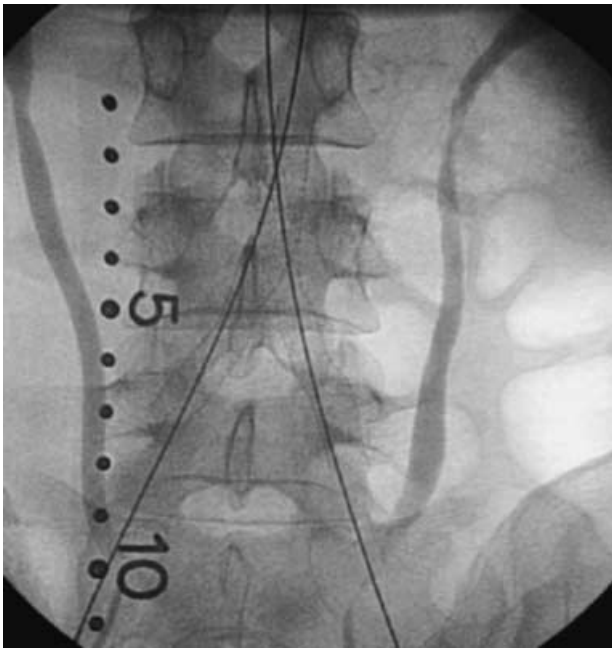

Figure 1 The percutaneous transluminal angioplasty (PTA) balloon (Medi-tech® Ultra-thin™ Diamond™ Balloon Dilatation Catheter) was inserted along the wire and inflated from the abdominal aorta to both right and left common iliac arteries, then two stents (Cordis S.M.A.R.T.™ Nitinol Stent Transhepatic Biliary System 10 × 80 mm; Johnson & Johnson) were inserted along the wire and deployed from the abdominal aorta to both right and left common iliac arteries.

(Watertown, MA, USA) Ultra-thin™ Diamond™ Balloon Dilatation Catheter in the abdominal aorta and in both common iliac arteries. Two stents (Cordis S.M.A.R.T.™ Nitinol Stent Transhepatic Biliary System 10 × 80 mm; Johnson & Johnson, Cordis Corporation, Miami, FL, USA) were inserted into each abdominal aorta and both common iliac arteries as shown in Fig. 1. After stent implantation, 400 mg of cilostazol were given and continuous anticoagulation was immediately started to prevent thrombosis recurrence [2]. Necrectomies were repeatedly performed for the right 3rd, 4th, and 5th phalanges. The right foot lesion gradually improved and rhEGF (Daewoong Pharm, Seoul, Korea) was administered to the exposed right foot lesion to promote ulcer wound healing. With self-application of rhEGF and a daily dose of 5 mg of warfarin, with an international normalization ratio (INR) targeted to ≥ 2.0, the patient is now well without foot pain or ulcer recurrence.

Because the duration of hyperglycaemia was short, and glycaemic control excellent, we performed immunological tests to exclude other causes of large artery thromboses. Antiphospholipid profiles revealed that both anticardiolipin IgG (41.5 U/ml; ELISA, Zeus, NJ, USA) and lupus anticoagulant [manual dilute Russell viper venom time (DRVVT) ratio of 1.8 by ACL-3000, Instrumental Laboratory, Milan, Italy] were positive, suggesting APS, which was confirmed by repeating these tests after 6 weeks. As stated above, APS presents a variety of clinical spectrums, and is easily overlooked if not suspected. Antiphospholipid testing should be considered even in a diabetic patient if he or she presents atypically, such as at a young age, diabetes of short duration, good glycaemic control, or the absence of diabetic neuropathy.

Large artery thrombosis caused by APS is rare, but subclavian arterial thrombosis in a patient with systemic lupus erythematosus and descending aortic thrombosis has been reported [3,4]. The presence of antiphospholipid antibody increases the risk of thrombosis, and those who have lupus anticoagulant (LA) or increased anticardiolipin antibody titres have five times more risk of thrombosis than those who are negative [5]. The large artery thromboses observed in our case might be explained by a possible synergism between the unusual combination of diabetic vascular dysfunction and the thrombogenic tendency of APS.

APS is rarely associated with Type 2 diabetes, and treatment of thromboses by stent insertion in APS has not been reported. Moreover, it is unclear whether the coexistence of Type 2 diabetes and APS is a coincidence or a consequence of an unidentified association. Thus, further studies are needed to clarify the relationship between diabetes and APS.

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